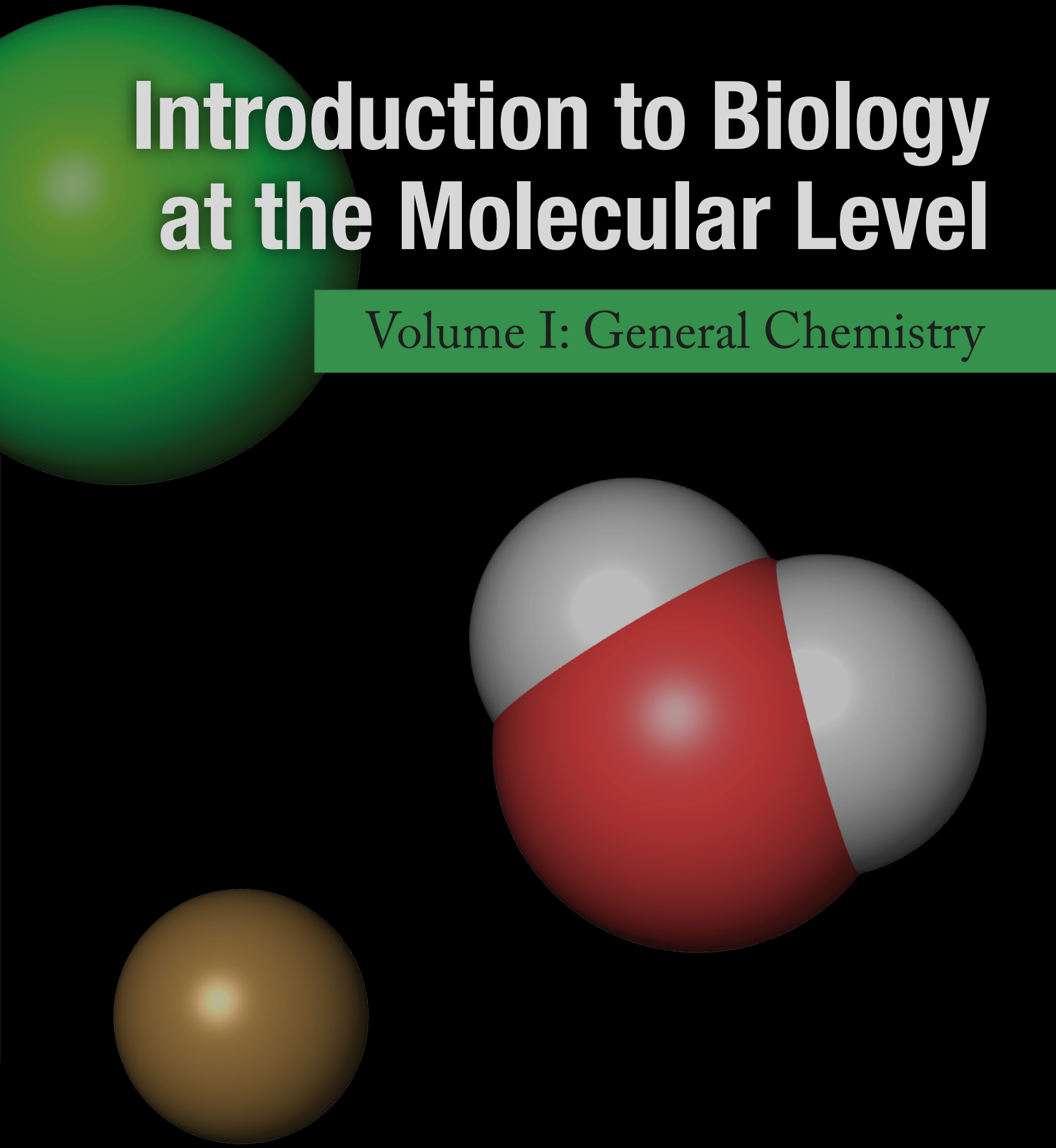
Introduction to Biology at the Molecular Level

Volume I: General Chemistry



Michael Shogren-Knaak

Introduction to Biology at the Molecular Level

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Introduction to Biology at the Molecular Level
Volume I: General Chemistry

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Preface

Almost a decade ago, I was asked by my department whether I would be willing to take over the teaching of "Structure and Reactions of Biochemical Processes." This one-semester course is aimed at introducing non-biochemistry majors to biochemical processes through an exposure to general chemistry, organic chemistry, and biochemistry. Intrigued by the challenge of distilling a wide range of topics into forty-five classes, and excited by the opportunity to share this material with a broader audience, I said yes. To prepare for the course, I considered a number of textbooks. However, I was unsatisfied with what I found. Many were unfocused, covering topics that were irrelevant to living systems, with some feeling like they had simply been stapled together from sections of textbooks intended for a different audience. Others seemed inaccessible to beginning students, being overly technical and formal, as well as unconnected to students' own lives and experiences. On top of that, most of the textbooks I reviewed were too expensive. As a course that was not a focus of most of the students' majors, it was hard to justify having them spend up to several hundred dollars for textbooks that weren't a great fit. Thus, for many years I taught the course without a textbook. Over time, though, I've realized that students would benefit from a focused, accessible, and inexpensive resource, and what you are holding is my first attempt at providing just that.

Introduction to Biology at the Molecular Level is a series of books that takes the reader on a journey from individual atoms to biomolecule interactions in cells. The series consists of multiple volumes, with Volume I (this one) being devoted to general chemistry, Volume II to organic chemistry, Volume III to biomolecules, and Volume IV to biomolecules working together to accomplish cellular functions. The core of these volumes focuses on the topics that are required to understand biomolecules and their roles, eliminating extraneous details that would distract from this goal. That said, for those who want or need a deeper look at various topics, that material can be found in the Further Exploration sections of each chapter. Unlike most textbooks, the chapters are written in a bit more of an informal and personal style, to make what is often intimidating material into something that is, hopefully, more approachable. In terms of cost, each volume in the series is available in two forms, though only Volume I exists at the time of this writing: as free PDF files of the textbook, available on the publisher's website, ribosomepress.com; and as low-cost paperback textbooks that are sold at as close to cost as possible. Further, by splitting the material into multiple volumes, readers can choose which volumes they want to purchase based on the content of the course they are taking or their interests.

This series is intended for anyone who is interested in learning about biological systems at the molecular level. The material only expects the reader to have a math background of high-school algebra and a familiarity with basic science topics that are typically covered in a general science course. Thus, a reader from any background can potentially come in with no chemistry knowledge and complete the series with a good working understanding of general chemistry, organic chemistry, and biochemistry. That said, this series can also serve as a refresher for folks already in the biological sciences at any level. Indeed, I view the content of the core and Further Exploration sections as being everything I think a first-year graduate student in biochemistry should know.

As mentioned earlier, this first volume is devoted to general chemistry and focuses on concepts that are most important to understanding biological systems. This means the book is not meant to be a full replacement for a general chemistry textbook. Additionally, this book leans heavily on conceptual models to make general chemistry easier to understand and apply. It's important to stress, and for the reader to remember, that these models and intuitions are often only useful simplifications. As they say, the map is not the territory. Many systems that you will encounter in real life will be more complicated

than the examples used here (chosen mainly for their simplicity and illustrative value). This is especially true of biological systems, where billions of years of evolution have often favored the baroque over the easily scrutable. With all those limitations in mind, I feel that this volume will give readers a solid foundation for a genuinely deep understanding of general chemistry, and hopefully do so in a way that is enjoyable.

A book like this wouldn't be possible without the help and support of many people, and I can't thank them enough. That includes: Amy Andreotti, Mark Hargrove, John Kuriyan, Brian McPhail, Nathan Thole, and Traci, Jasper, and Calder Shogren-Knaak. If you have any comments or suggestions, I'd love to hear them. You can reach me through the publisher's website, ribosomepress.com. Good luck on your journey.

—MSK, Aug 2026.

How to Use This Book

The following is a quick guide to using this book as effectively as possible.

If you want to focus on learning the fundamentals of general chemistry, I recommend starting with the volume's table of contents (pages viii–ix) to get a lay of the land. Then read the core sections of Chapters 1–6 (which span pages 1–198), skipping the Further Exploration sections of each chapter.

If you are interested in a deeper dive into the topics covered in the core sections, check out the Further Exploration sections of each chapter. These sections build on the chapter's earlier material, and the specific topics covered are listed in the volume's table of contents.

If you are only looking to review or explore a specific topic, you can either search for the topic in the index (pages 207–234) or peruse the volume's table of contents. The book's sections and sub-sections are designed to be as self-contained as possible, though earlier topics may be referenced in later sections.

General chemistry is a rich and complex subject, and mastering the material takes work. I know personally that the first time I try to learn any new material, only a fraction of it sticks. Repeated exposure is key, and I recommend reading the material multiple times, spaced out over time. The figures in the chapters reinforce and extend concepts covered and should be studied closely. It is also useful to see if you can describe the material in the chapters in your own words. For the terminology in the chapters, there is a glossary of essential terms in the back of the book (pages 201–206). Not only is this list a useful resource for learning the meaning of various terms, but it is also a good study tool for testing whether you know the core terms and concepts in general chemistry. Yet another important way to reinforce your understanding of the material is to work practice problems. At the time of this volume's initial publication, there are no published study guide questions available, and you may need to look for other resources. That said, a separate companion study guide for this volume is planned, and you can check the publisher's website (ribosomepress.com) for availability.

To explore topics beyond general chemistry, volumes devoted to organic chemistry (Volume II), biomolecules (Volume III), and biomolecules at work (Volume IV) are planned. See the Series Content (page vii) for the full chapter list across all four volumes. Again, check the publisher's website for their availability, and more generally for the latest series developments.

—MSK, Aug 2026.

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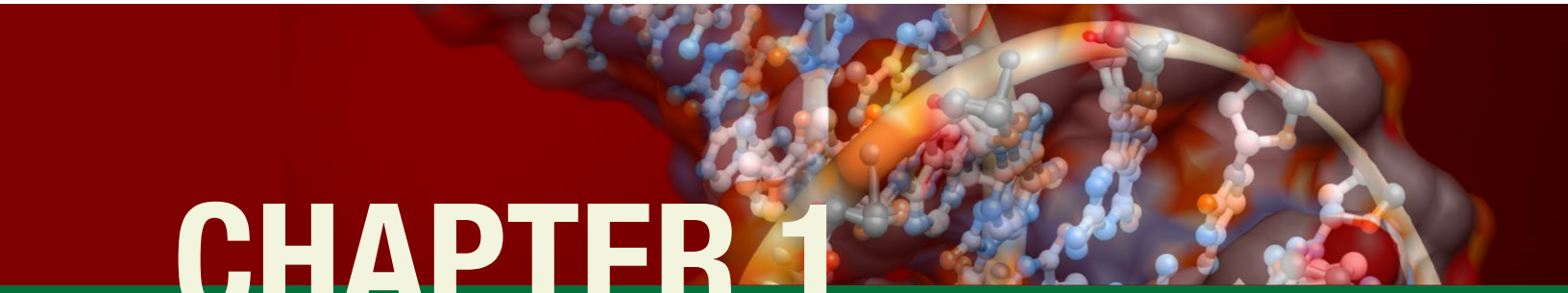
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CHAPTER 1
Molecules and Atoms

Motivation and Overview: In this book series, our goal is to gain an understanding of biological systems at the molecular level, as many biological phenomena have a molecular basis. In this chapter we start this process with a brief survey of molecules that are biologically relevant and see that, while some biological molecules are relatively simple, most are quite complex. Nonetheless, all molecules are built from atoms, providing a unified way to approach molecules big and small. To understand atoms, we discuss the different types that occur, what atoms are made of, and why atoms react to create more complex molecules. We conclude with a brief exploration of the simplest of particles, those composed of a single atom.

A. Introduction to Biological Molecules

What are biological molecules? Before we can answer that, it is useful to try to place them in their context within biological systems.

1.1 The Molecular Scale

There are many ways to understand biological systems (**Figure 1.1**). At one extreme of the size scale, it is possible to study how organisms interact with one another and their environment. Zooming in, the features and workings of the whole organism, as well as its organs and tissue, can be examined. Going smaller yet, we get to the cells that make up the tissues. It is here that we begin to discern our first molecules, which are inside and outside the cell, as well as on the surface of the cell membrane. What these molecules are and how they behave and interact will be the focus of this book series.

Examining biological systems at every scale reveals unique and important information. One of the benefits of studying biological systems at the molecular level is that molecules are the foundation upon which every other level of organization is built, and in many cases phenomena observed at higher levels of organization can be directly connected to molecule-level features.

For example, in your body the things that make one cell different from another, say a liver cell from a muscle cell, depend on the molecules that comprise those cells (**Figure 1.2A**). A liver cell will have protein molecules that aren't present in a muscle cell, or are present to a lesser extent, and vice versa. These molecular differences impart properties that are unique to each cell. Indeed, this idea can be extended beyond cells to entire organisms, where differences in molecular composition and organization ultimately dictate whether an organism is a human, a fly, a bacterium **(Figure 1.2B)**, or something else. In fact, examining the molecular instructions stored in cells, their DNA, can reveal how and why these differences arise.



Figure 1.1 Biology at Different Scales. From organisms (bears) interacting with each other and their environment, we go smaller and smaller, showing individuals, organs, tissue (muscle fiber), cells, organelles (mitochondria), biomolecules (a hemoglobin protein), and atoms. We will focus on molecules, moving to larger and smaller scales when appropriate.



Figure 1.2 Variety in Life. A) Cells in our body differ in their appearance and function. Shown on the left are hepatocyte cells, cells that comprise roughly 80% of the liver. On the right are heart muscle cells. B) Living organisms also differ tremendously. Left is a human baby. In the middle a fruit fly. On the right is a cluster of bacteria on a slide. While there are many molecules shared between disparate cell types and organisms, differences in the number and kinds of molecules that are present ultimately create differences at the cellular and organism level.

As another example, our understanding of human health and the treatment of diseases is often grounded in features at the molecular level. When your body experiences aches and pains, one cause is that your body makes molecules that interact with other cellular molecules to signal pain (**Figure 1.3,** top branch). Pharmaceutical molecules, like aspirin, can be ingested to treat pain and work by preventing some of these pain-signaling molecules from being made (Figure 1.3, bottom branch).

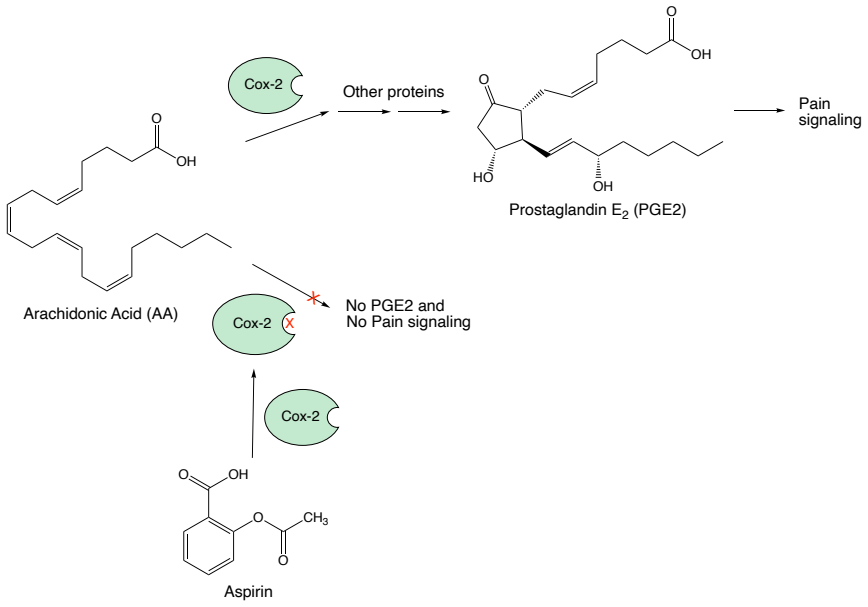


Figure 1.3 Pain Signaling and its Inhibition by Aspirin. Prostaglandin E2 (PGE2) is a molecule involved in inducing inflammatory pain in the body. PGE2 is synthesized in several steps from arachidonic acid (AA), where in the first step AA is bound by the protein cyclooxygenase-2 (COX-2) and converted to an intermediate compound in the PGE2 synthesis pathway. Aspirin can bind to COX-2 at the same site that AA binds and irreversibly inactivate the protein, preventing AA from being converted to PGE2. Without PGE2 the body experiences reduced inflammatory pain. Note, the effects of aspirin are more complicated than depicted, as aspirin can inhibit other cyclooxygenases, and the products of the cyclooxygenases are used to synthesize more than just PGE2.

1.2 Biologically Relevant Molecules, Big and Small

Biological molecules are important, but what are they? In the simplest terms, a molecule is a collection of atoms held together. While this definition helps, it just raises the question as to what atoms are. The nature of atoms will be addressed in depth shortly, but for now we can think of them as little balls that can potentially be stuck together with each other to make molecules. Even with this simplistic picture, we see that biological molecules can be highly diverse both in terms of their size and complexity.

Some biologically-relevant particles are relatively small and simple. For example, sodium and chloride ions are single atoms with a charge that are essential for the proper functioning of cells. You might be familiar with these ions, as they compose table salt, a compound that packs many copies of each of these ions into a single grain of salt, a salt crystal (**Figure 1.4A**). In cells and tissues, sodium and chloride ions are not in the form of crystals, but instead are dissolved in water, much as table salt can be dissolved

in a glass of water (**Figure 1.4B**). In the dissolved state, sodium and chloride ions are like individual balls that are charged sodium and chloride atoms.

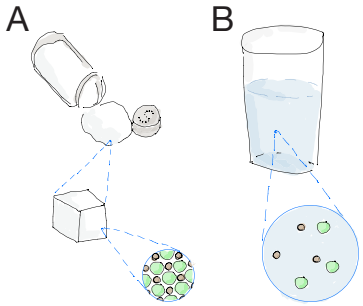


Figure 1.4 Table Salt in Salt Crystals and Dissolved in Water. A) Table salt is made up of cubic crystals of sodium ions (smaller brown spheres) and chloride ions (larger green spheres) packed together in a regular arrangement (shown in two-dimensions, but packing extends in three-dimensions). B) When salt dissolves in water the ions are dislodged from their crystal packing and the sodium and chloride ions move freely throughout the solution.

Larger and more complicated biological molecules are represented by simple organic compounds. These molecules include compounds that we can acquire from our diet, such as amino acids, sugars, lipids, and nucleotides, as well as molecules like ATP and NADH that are generated from breaking down the compounds in our food (**Figure 1.5**). As depicted in the figure, these molecules are composed of more than one atom, and generally such molecules contain tens to hundreds of different atoms stuck together in various arrangements.

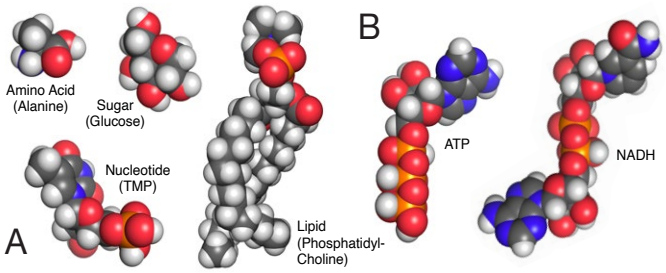


Figure 1.5 Simple Organic Molecules. Shown are some biologically relevant compounds assembled from carbon (black spheres), hydrogens (white spheres), oxygens (red spheres), nitrogens (blue spheres), and phosphorus atoms (orange spheres). The molecules in A are used on their own and are also building blocks of more complex biological molecules, while those in B are used for energy storage and production.

Biological molecules like proteins are even larger and more complex (**Figure 1.6**).

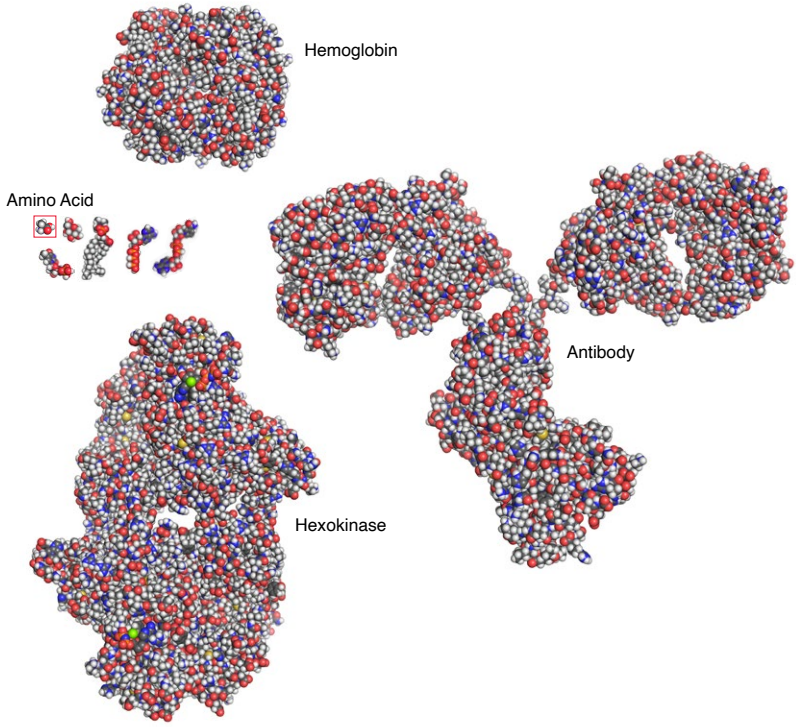


Figure 1.6 An Example of a More Complex Biomolecule, Proteins. Shown are various proteins found in the body. For scale, the simpler organic molecules from the last figure are shown on the left for comparison. Proteins are assembled from amino acids, and a single amino acid from the last figure is highlighted with a red box.

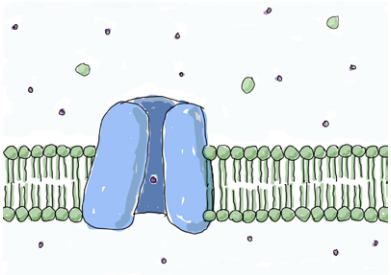


Figure 1.7 Different Types of Molecules Interacting in a Biological Context. Shown is a schematic image of molecules that might be found in and around a cell membrane. The blue shape is a protein, green shapes are organic molecules, and purple circles are single atom ions. Here, the protein floats in a layer of interacting organic molecules that form the cell membrane. The protein functions to transport certain single atom ions across the membrane. Outside the membrane, various single atom ions and organic molecules swim amongst many water molecules that are not shown.

Proteins are molecules that perform a wide range of functions in organisms, and examples include antibodies, which help your body fight foreign invaders; hemoglobin, which transports oxygen through your body; and hexokinase, a protein involved in the breaking down of sugars to harvest their energy. Proteins are much larger than the simple organic molecules discussed earlier (shown as an inset in Figure 1.6). In fact, as we will discuss in depth in a later chapter, proteins are generally composed of hundreds of amino acids, one of the simple organic compounds shown in Figure 1.5. Consequently, proteins contain thousands to tens of thousands of atoms and these atoms can be seen in Figure 1.6 as numerous little balls that form the proteins.

In cells, the full range of sizes is present, with particles at each level of complexity playing important roles. For example, **Figure 1.7** schematically depicts a portion of a cell membrane, where a big biomolecule, a protein, interacts with a small particle, a single atom ion, to transport it across the membrane. The membrane itself is composed of many organic molecules.

B. The Building Blocks of Molecules

The diversity and complexity of biological molecules can seem overwhelming, but the fact that all molecules are composed of atoms provides a unified way to approach these molecules. By starting with simpler particles, such as those composed of a single atom, we can then proceed to connect individual atoms to build our way up to more and more complex molecules. Let's dive into the details of atoms.

1.3 Atoms as Building Blocks

Different atoms have different properties: They can vary in their sizes, how many atoms they can connect to, and the geometry and nature of those connections. For example, in comparing chloride ion, a constituent of table salt (Figure 1.4), and carbon, a component of small organic molecules like sugars (Figure 1.5), the two differ in many ways (**Figure 1.8**). The chloride atoms in salts are larger than carbon atoms in organic molecules.

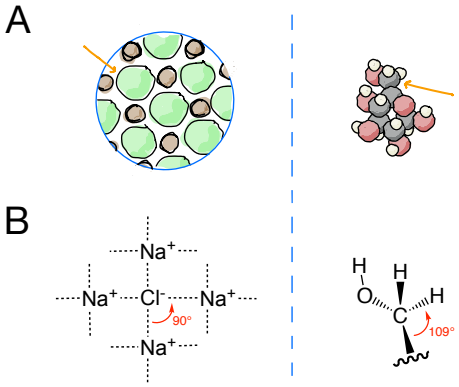


Figure 1.8 Differences in Atoms Within Molecules. Highlighted are some differences between a chloride atom in a crystal of table salt and a carbon atom in the sugar glucose. A) Images of atoms in a molecule, where the atoms are represented as spheres. On the left is one layer in a crystal of table salt, where green circles are atoms of chloride and brown ones are of sodium. On the right is a single molecule of glucose sugar, where black circles are carbon atoms, red ones are oxygen atoms, and white ones are hydrogen atoms. The orange arrows indicate the atoms focused on in part B. B) Atoms in the structures from part A that highlight the angle and type of interaction with neighboring atoms. On the left, the chlorine atom is negatively charged. This allows the atom to interact with positively charged sodium atoms. Within the plane shown, there are four such interactions, known as ionic bonds. Not shown is that chloride also has an ionic bond with a sodium atom directly above and below the plane shown. The angle made between all sodium atoms (with the chlorine as the vertex) is 90°. On the right, the carbon atom is uncharged. It forms interactions with four different atoms through what are known as covalent bonds. When four bonds are made, the orientation of the bonds is tetrahedral, where the angle of the bonds (with the carbon at the vertex) are all about 109°.

Additionally, chloride atoms in salts are charged and interact with oppositely charged atoms and molecules in a way that is relatively flexible in terms of how many atoms are present and how they are oriented in different chlorine-containing salts. Carbon tends to connect to at most four atoms, and those connections tend to have very specific geometries, with the four atoms attached to carbon in the sugar glucose being rigidly held at about 109° away from each other.

The distinct properties of different atoms make them suited for making particular kinds of molecules. If we want to consider all of the kinds of molecules we could build, we need to examine all of the types of atoms that are available. That set of atoms is shown in what is known as the periodic table of elements.

1.4 The Periodic Table of Elements

The periodic table of elements is an organized list of every possible type of atom (**Figure 1.9**), where each type of atom is known as an element. There are over one-hundred different elements that are known (118 currently), each with its own box in the table.

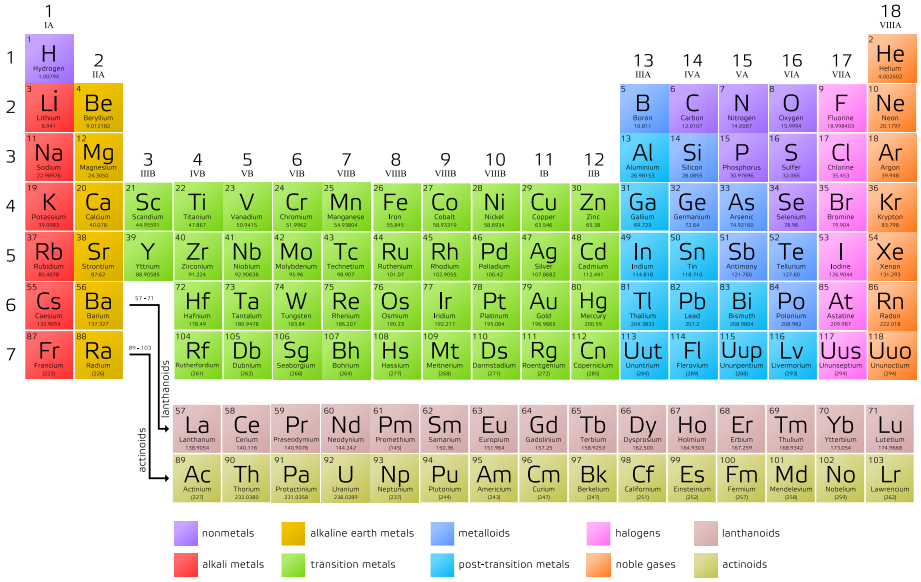


Figure 1.9 The Periodic Table of Elements.

The identity of an element can be specified in a number of different ways. Each element has a unique name, such as carbon (**Figure 1.10**), sodium, calcium, iron, etc. A shorthand for these names is often used and consists of one to two letters, the first of which is capitalized. If there is a second one, that letter is in lower case. These abbreviations may or may not directly correspond to the full name of the element. As examples, carbon is C (Figure 1.10), sodium is Na, calcium is Ca, and iron is Fe. Each element also has a unique atomic number, which is shown in the upper left corner of the element's box. For example, hydrogen has an atomic number of 1. The element with an atomic number of 6 is carbon (Figure 1.10). The elements of the periodic table are organized into rows and columns (Figure 1.9), where the number of columns can vary from row to row (the first row has two columns, while the second row has eight columns). Rows and columns can also be used to specify an element. Hydrogen is found in the first row and first column of the table, while carbon is found in the second row and fourth column of its row.

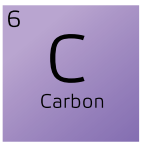


Figure 1.10 Atomic Names, Abbreviations, and Numbers. Shown is the entry for the element carbon. The element name (carbon) is written out, with the abbreviation for the element above (C). The atomic number for the element is shown in the upper left corner, which is 6 for carbon.

Knowing and understanding the properties of over one hundred elements is a lot. Luckily for us, in biological systems only a subset of these elements are frequently encountered (**Figure 1.11**). Organic compounds are primarily built from six elements, sometimes

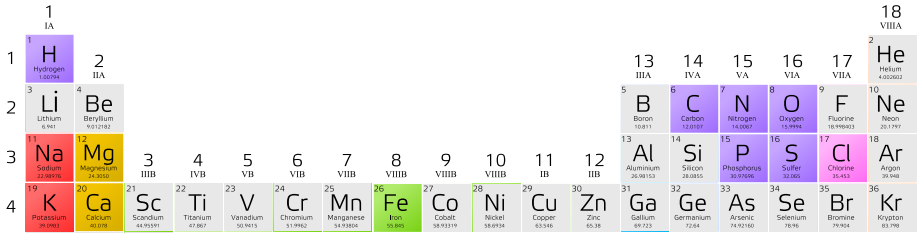


Figure 1.11 Elements Focused on in the Book. The organic elements are shown in purple. Non-organic (inorganic) elements of interest are highlighted in the other colored boxes. Only the first four rows of the table are shown.

abbreviated as CHNOPS, i.e., carbon (C), hydrogen (H), nitrogen (N), oxygen (O), phosphorus (P), and sulfur (S). Additionally, through the book we will continually return to the elements chlorine (Cl), sodium (Na), potassium (K), magnesium (Mg), calcium (Ca), and iron (Fe). Going forward, it is crucial to master the names of these elements, their abbreviations, and their positions in the periodic table.

C. Atomic Structure

For the elements that are prominent in biological systems, what are their properties that allow them to form biologically-relevant molecules? To address this we need to delve into the structure of atoms.

1.5 Components of Atoms

Atoms are composed of three types of sub-atomic particles: protons, neutrons, and electrons, and atoms of different elements possess different numbers of each of these particles (**Figure 1.12**).

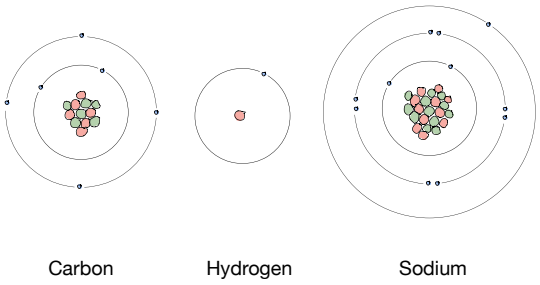


Figure 1.12 Example Atoms. Shown are schematic representations of a typical carbon, hydrogen, and sodium atom. Protons are red circles, neutrons are green circles, and electrons are blue circles.

Protons, neutrons, and electrons differ from each other in several ways. Each particle has a different electric charge (**Figure 1.13A**). Protons are positively charged, electrons are negatively charged, and neutrons are electrically neutral, having no charge. The subatomic particles also vary in their mass (Figure 1.13A). Protons and neutrons have close to identical masses, while electrons are much lighter, weighing roughly 1/1,800th the mass of either a proton or neutron. Finally, these particles differ in their location in atoms (**Figure 1.13B**). All of the protons and neutrons in an atom are at its center, in what is known as the atomic nucleus. In the nucleus, the protons and neutrons are close to one another relative to the electrons, which on average are quite distant from the protons and neutrons.

A

	Charge	Relative Mass
Proton	+	1
Neutron	0	1
Electron	–	1/1,800

B

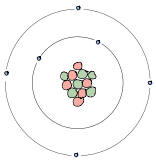


Figure 1.13 Features of Protons, Neutrons, and Electrons. A) Protons, neutrons, and electrons differ in their charge and their relative masses. Size is used as a proxy of mass in the picture, but this depiction is not accurate, as the "size" of an electron in an atom is actually quite complicated. B) Schematic of the location of protons, neutrons, and electrons for an example atom, carbon. The protons and neutrons constitute the nucleus. Electrons surround the nucleus and their positions can be described in terms of shells, though an accurate description of where they actually "are" is quite complicated (see Section F for more details).

1.6 Protons and the Identity of Atoms

So how are the subatomic particles in an atom related to which element it is? The number of protons in an atom dictates its identity. For example, hydrogen atoms always have one and only one proton (**Figure 1.14**, top). A hydrogen atom could not have two protons, because then that atom would be a different element, a helium atom (Figure 1.14, middle). The number of protons an element has is equivalent to its atomic number. Thus, on the periodic table (shown previously in Figure 1.9), the element with an atomic number of six is carbon, because carbon atoms have six protons (Figure 1.14, bottom). An atom of Lawrencium, with an atomic number of 103, would have a whopping 103 protons in its nucleus.

1.7 Neutrons and Atomic Mass

Along with protons, the nucleus of atoms contains neutrons. How many neutrons? For a given element that number can vary, but generally there is one value that predominates. For the organic elements the number of neutrons tends to be close to its number of protons: For example, the most common form of carbon has 6 neutrons for its 6 protons (**Figure 1.15A**, left). Similarly, the most common forms of nitrogen, oxygen, and sulfur atoms also contain the same number of neutrons as their number of protons. That said, the number of protons and neutrons doesn't have to be the same. The most common form of hydrogen atoms has 1 proton and 0 neutrons (**Figure 1.15B**, left), and the most common form of phosphorus has 15 protons and 16 neutrons. In general for non-organic elements, as the atomic number of an element gets higher, the discrepancy

between proton and neutron number tends to increase, where the largest atoms tend to have significantly more neutrons than protons.

While for each element, one particular neutron count predominates, other numbers are possible. In addition to the most common form of carbon with 6 protons and 6 neutrons, there are some carbon atoms that contain 7 neutrons (about 1 in 100) (Figure 1.15A, middle), 8 neutrons (around 1 in 1,000,000,000,000) (Figure 1.15A, right), or rarer yet, some other number of neutrons. Similarly, hydrogen most commonly has no neutrons, but can have 1 proton and 1 neutron (one in about 6,500), or one proton and two neutrons (trace amounts) (Figure 1.15B). The different forms of an element (i.e. ones that differ in their number of neutrons) are called isotopes.

For the element hydrogen, the isotopes have their own name: protium with zero neutrons, deuterium with one neutron, and tritium with two neutrons (Figure 1.15B). However, in general, isotopes of an element are indicated with the sum of their protons and neutrons. For example, carbon (6 protons) with 6 neutrons is carbon-12, with 7 neutrons is carbon-13, and with 8 neutrons is carbon-14 (Figure 1.15A). Other ways to describe isotopes are discussed in Further Exploration Section E.

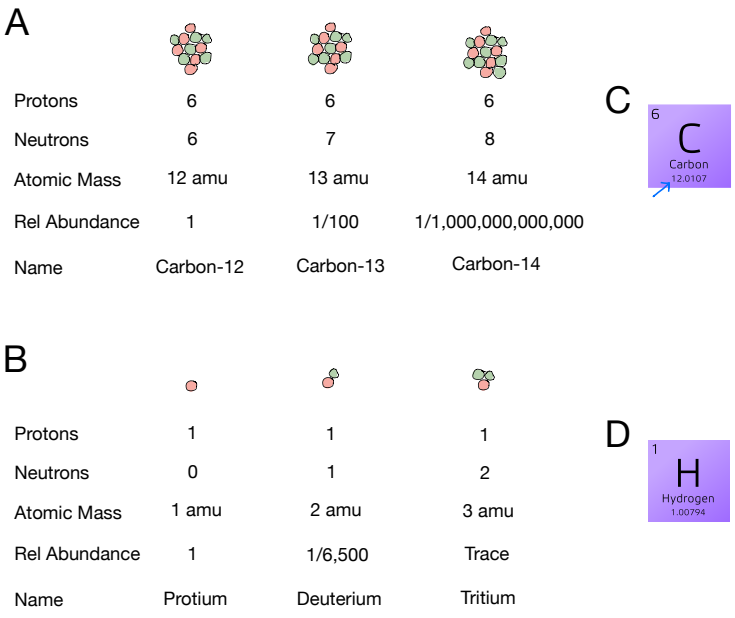


Figure 1.15 Neutrons, Atomic Mass, and Isotopes. On the left are features of the nuclei for different isotopes of A) carbon, and B) hydrogen. On the right are the average atomic masses (indicated by the blue arrows) for C) carbon and D) hydrogen, as reported from their entry in the periodic table.

In a chemical and biological context, the number of neutrons in an atom mostly does not have much of an effect on its chemical properties (an exception to this is the instability of certain atoms covered in Further Exploration Section E - Radioactivity), but neutrons do affect how heavy an atom is, i.e. its mass. The weight of an atom, known as its atomic mass, is largely dictated by how many protons and neutrons it contains (we will ignore the much smaller mass of the electrons, as well as some other factors). We can define a unit of mass called an atomic mass unit (amu) that is effectively equivalent to the mass of one proton. Because the mass of protons and neutrons is nearly the same, we can calculate the approximate mass of an atom in atomic mass units as simply the sum of the number of protons and neutrons:

$$\text{approximate atomic mass (in amu)} = \#\text{ protons} + \#\text{ neutrons} \qquad (1.1)$$

For example, the most common isotope of carbon with 6 protons and 6 neutrons has an atomic mass of 12 amu:

$$\text{atomic mass most common isotope carbon} = 6\text{ amu} + 6\text{ amu} = 12\text{ amu} \qquad (1.2)$$

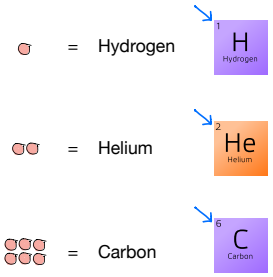


Figure 1.14 Protons, Elements, and Atomic Numbers. The number of protons in an atom (red circles) dictates which element it is. The number of protons an element has is also its atomic number, as indicated with the blue arrow on the top left corner of its entry in the periodic table.

The average atomic mass for an element is typically listed on the periodic table below the element's name (Figure 1.15C and D). For carbon, this is 12.011 amu and not 12 amu. The primary reason for this discrepancy is that 12.011 amu represents the average mass of all of the naturally occurring isotopes of carbon, not just for its most common isotope, carbon-12. Carbon-13 and carbon-14 have bigger atomic masses of 13 amu and 14 amu, respectively. However, because of their low abundances, they only skew the average mass of carbon up slightly from 12 amu.

On the periodic table, the number of neutrons found in an atom is not given. However, using the element's atomic number and atomic mass, it is possible to determine the number of neutrons found in the most common isotope of the element. To do so, we can take the atomic mass of the element (rounded to the nearest whole number to reflect the atomic mass of the most common isotope) and subtract the atomic number:

$$\text{neutrons in an element} = \text{atomic mass} - \text{atomic number} \quad (1.3)$$

Note, this equation is just a rearrangement of Equation 1.1 and simply says that the atomic mass (# protons + # neutrons) minus the atomic number (# of protons) is equal to the number of neutrons. As an example, for a phosphorus atom, how many neutrons are present in the element's most common isotope? Using Equation 1.3, we can see phosphorus typically has 16 neutrons:

$$\text{neutrons for the most common isotope of P} = 31 - 15 = 16 \text{ neutrons} \quad (1.4)$$

This equation also works for any isotope of an element. For example, if we wanted to calculate how many protons and neutrons are present in the radioactive isotope Uranium-235, using the atomic number of uranium, we can see that this isotope has 92 protons (true for any uranium isotope) and 235 - 92 = 143 neutrons (which is different from its most common isotope).

While atomic masses in and of themselves can be useful, they are most often used to calculate the weight of a molecule, its molecular mass. The molecular mass of a compound is simply the sum of all of the atomic masses of the elements that comprise it. Suppose you wanted to calculate the molecular mass of methane, the main component of natural gas. The molecular formula for methane is CH_4. That is to say, one molecule of methane contains 1 carbon atom and 4 hydrogen atoms. To calculate the molecular mass of methane, we simply add up the masses of all of the atoms in the molecule:

$$\text{molec mass methane} = \text{mass C's} + \text{H's} = (1 \times 12 \text{ amu}) + (4 \times 1 \text{ amu}) = 16 \text{ amu} \quad (1.5)$$

In the next chapter we will see that the molecular mass of a compound can be useful in a number of contexts.

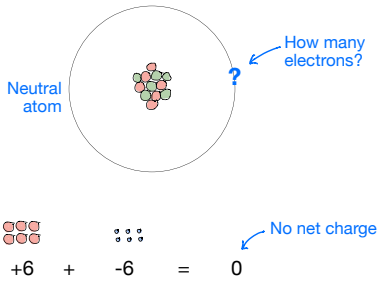


Figure 1.16 Relationship Between Protons and Electrons in Elements. Elemental atoms are neutral, meaning they have no net charge. As protons and electrons are opposite in charge, the number of positive protons in an element therefore must be matched by negative electrons. In the example shown, the six protons (red circles) of carbon are matched by six electrons (blue circles). Note, the number of neutrons (green circles), which are uncharged, don't affect the number of electrons.

1.8 Number of Electrons and Their Arrangement

How many electrons do atoms have? The atoms of elements are uncharged, meaning the charge of the protons and electrons must offset each other. Thus, the number of electrons is equal to the number of protons:

$$\text{electrons in a neutral atom} = \#\text{ protons} \quad (1.6)$$

For example, a carbon atom has six protons (atomic number of six), meaning that elemental carbon also has six electrons (**Figure 1.16**).

As mentioned earlier, the electrons of an atom surround the nucleus. However, their precise arrangement is quite complicated. That said, for most of the chemistry we encounter in this book, we will find that a simple model for organizing the electrons is sufficient (for those curious, a more accurate description of electron distributions can be found in Section F, Further Exploration - Atomic Orbitals). In this model, we can think of the nucleus occupying the center of the atom, like the sun is positioned at the center of our solar system. Electrons then are found in certain shells, a bit like planets found in specific orbits. However, unlike planets in orbits, multiple electrons can occupy a given shell. As seen in **Figure 1.17**, hydrogen's 1 electron occupies one shell, while for an atom of elemental sodium, its 11 electrons are distributed across 3 shells: 2 in the innermost shell, 8 in its middle shell, and 1 in its outermost shell.

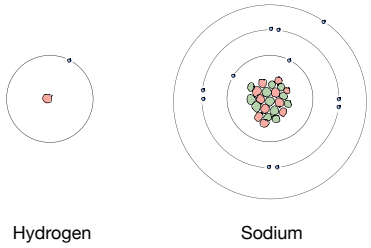


Figure 1.17 Electron Shells. A simple model of distributing electron around an atom is to envision electrons occupying shells around the nucleus, where different shells are filled to varying extents in different atoms.

How can we predict how many shells an atom will have, and how many electrons will be in each shell? Answering both questions is possible using the periodic table. The number of occupied electron shells for a neutral atom is equal to which row the element is in (**Figure 1.18A**).

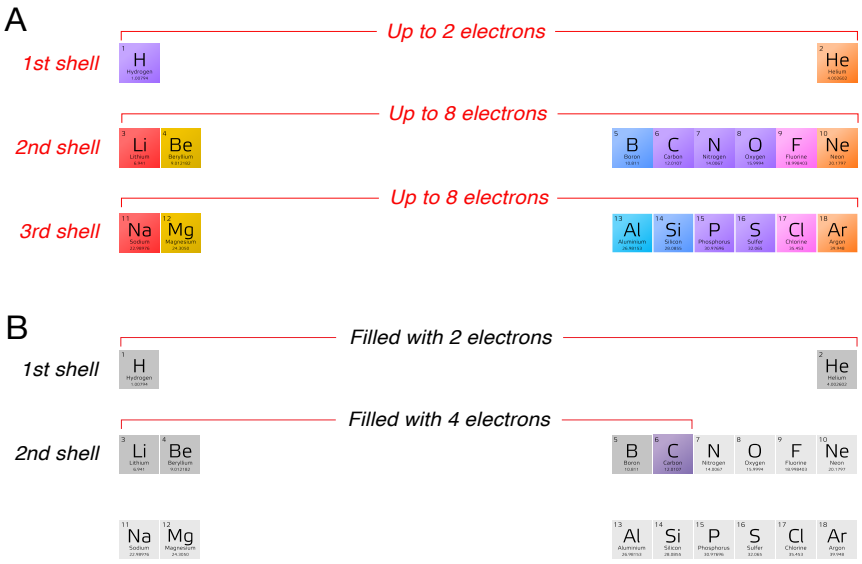


Figure 1.18 Filling of Electron Shells. A) Different shells and their capacities. The first shell can accommodate up to two electrons (two columns for the first row). The second and third shells can accommodate up to eight electrons (eight columns in either the second or third rows). B) Shells fill sequentially up to the position of the element. For example, carbon, in the second row, has two shells. The first shell fills completely with two electrons. Carbon is in the 4th column, so of the eight possible electrons it could accommodate, the second shell is filled with four electrons. As the valence electrons are those in the outermost shell, carbon being in the fourth column has four valence electrons.

For example, hydrogen is in the first row, meaning it has 1 electron shell. Sodium, in the third row, has 3 occupied electron shells. Carbon, in the second row, has 2.

How many electrons can be fit into each shell? For a given row, the number of columns in that row dictates how many electrons can occupy that shell (Figure 1.18A). The first row of the periodic table has two columns, meaning up to 2 electrons can occupy that shell; the second row has eight columns, meaning that shell can hold up to 8 electrons; and the third row has eight columns, suggesting that 8 electrons occupy this shell. In fact, our simple model starts to break down by the time we get to the third row. However, for the atoms that we will be dealing with, our model is good enough.

How do we fill these shells with electrons? For shells prior to the last one, we fill them completely. Then for the last shell, we add electrons equivalent to the column number that element is in. As an example, for carbon (**Figure 1.18B**) we fill the first shell with 2 electrons. Then, since carbon is in the fourth column of its row, we put 4 electrons in the second shell. Together this is 6 electrons, the amount we expect for carbon with an atomic number of 6. For a sodium atom with 11 electrons, the first shell is completely filled with 2 electrons, the second shell is filled with 8 electrons, and the third shell has 1 electron.

As we will see, the shell furthest from the nucleus is especially important and is given a special name, the valence shell. Electrons found in the valence shell are valence electrons.

A simple way to tell how many valence electrons an atom has is to determine which column it's in:

$$\text{number of valence electrons} = \text{column \# of the element} \tag{1.7}$$

Hydrogen in the first column has 1 valence electron. Carbon in the fourth column has 4 valence electrons (Figure 1.18B). Sodium in the first column has 1 valence electron.

Elements with the same number of valence electrons (i.e., those in the same column) tend to have similar properties. Just as it is important to know the names and abbreviations of the 6 organic and 6 non-organic elements used throughout the book (Figure 1.11), knowing how many valence electrons each has is also useful.

D. Atomic Stability and Reactivity

How much atoms react with other atoms and the ways they do so varies. Here we explore some of the factors that lead to reactivity differences and how we can group atoms with similar reactivities and properties. We end by considering the most stable and simple group of elements: single atom elements.

1.9 Atom Reactivity

There are many ways to understand the reactivity of atoms. One simple but powerful idea is that atoms are often most stable with a full valence of electrons - that is, they are "happiest" when they have a full outermost shell of electrons. As we'll see later in the section, some atoms start with a full valence. However, most don't. These atoms tend to react with other atoms to achieve a full valence.

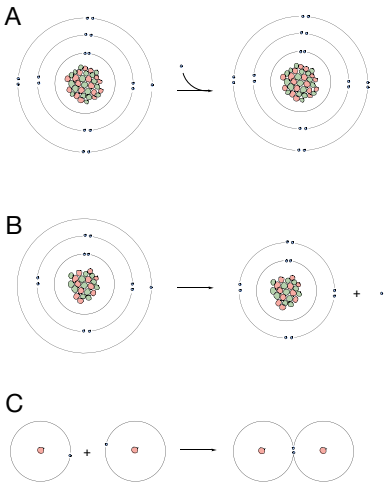


Figure 1.19 Three Ways Atoms Can Obtain a Filled Valence. A) An atom (like the chlorine atom shown) can grab one or more electron from somewhere to complete its outermost (valence) shell. B) An atom (like a sodium atom) can give away one or more electrons to empty out its outermost shell, leaving it with a filled shell below. C) Two atoms (like two hydrogen atoms) can share valence electrons to complete their outermost shell.

Atoms without a full valence can obtain one by: taking on one or more electrons; giving an electron or electrons away; or sharing one or more electrons (**Figure 1.19**). Which strategy an atom uses depends on what element it is, as well as the atoms it can interact with. So, an atom might take an electron in one context, but share electrons in another.

One quantitative measure that can help predict whether an atom will tend to take, give, or share electrons is its electronegativity. The electronegativity of an element is how much an atom "wants" electrons, where the larger the value, the more electronegative the atom. **Figure 1.20** shows the electronegativity of the elements in the periodic table.

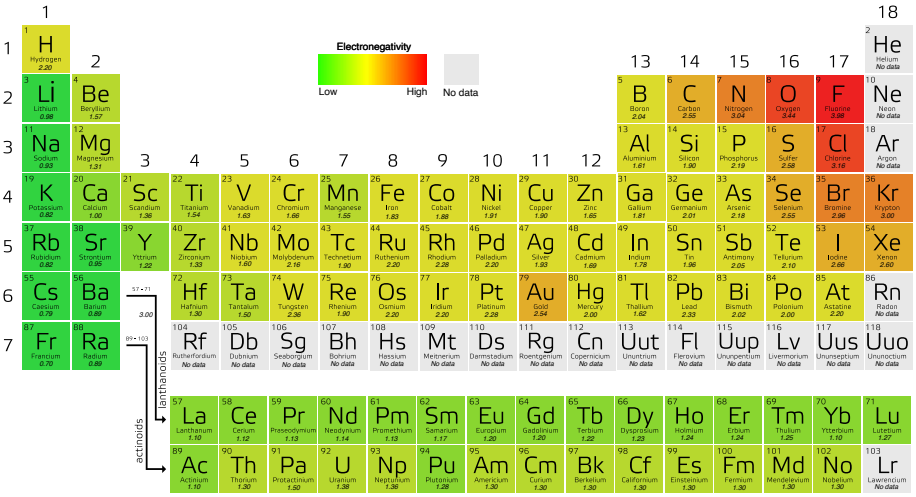


Figure 1.20 Electronegativity of the Elements. The electronegativity of each element (its affinity for electrons) is indicated qualitatively by the color of its background, and quantitatively by the value listed under the element's name.

We can see that chlorine atoms are quite electronegative, having an electronegativity value of 3.16 (**Figure 1.21A**). This means that compared to a sodium atom with an

electronegativity value of 0.93 (Figure 1.21A), a chlorine atom would have a much greater affinity for an electron than the sodium atom, and potentially could take it from sodium (**Figure 1.21B**). Equivalently, because sodium is much less electronegative than chlorine, it is willing to lose an electron to chlorine. In contrast, if the electronegativities of two atoms are quite close to one another, they would be more likely to share electrons. For example, even though chlorine is quite electronegative, if it encounters another chlorine atom, because the two have close electronegativities (in fact identical), they would share electrons (**Figure 1.21C**).

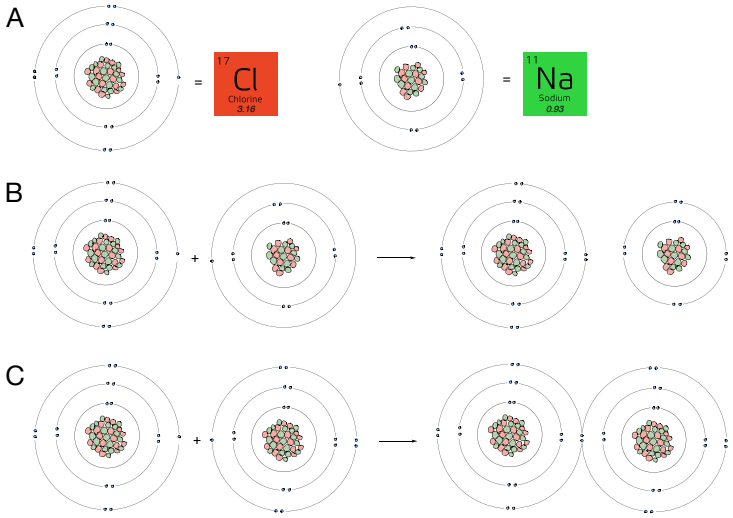


Figure 1.21 Electronegativity and Achieving a Filled Valence. A) A chlorine atom is one electron short of a filled valence and is strongly electronegative (the red box indicates strong electronegativity according to Figure 1.20). A sodium atom has one electron in excess of a filled valence and is weakly electronegative (the green box indicates weak electronegativity according to Figure 1.20). B) When a chlorine and sodium atom encounter each other, the electronegativity difference is large enough that the chlorine atom can take an electron from the sodium atom, providing each with a filled valence. C) Two chlorine atoms that encounter one another each have strong electronegativities. Since their electronegativities are matched, they are "willing" to share an electron to achieve a full valence.

In looking at the electronegativity values of the elements in Figure 1.20, several trends are apparent. As we move across a row to the right, the elements tend to get more electronegative. In contrast, as we move down a column, the electronegativity decreases. Fluorine, being in the rightmost column before the final column and in the second row, is the most electronegative element - that is, it wants electrons more than any other element, and potentially will take electrons to achieve a full valence. At the other extreme, francium, found in the bottom left corner of the table, has a very low electronegativity and wants an electron the least. In fact, this low affinity for electrons generally translates into a greater willingness to part with an electron to achieve a full valence, and we could describe francium not only as having a low electronegativity, but also having a high electropositivity (a measure of an atom's tendency to donate electrons). Elements in between these extremes, such as the organic elements, have intermediate electronegativities that tend to be relatively similar in value, meaning that these atoms often end up sharing electrons.

How can we understand these trends in electronegativity? Although not entirely accurate, a useful idea is that the closer an atom is to achieving a full valence, the more electronegative or electropositive it will be. Consider several elements in the third row of the periodic table (Figure 1.20). Chlorine is on the right side of this row. It is very close to having a full valence and could do so if it could just pick up one more electron. Thus, it is very electronegative. Similarly, a sodium atom, left-most in the row, is very close to having a full valence — it just needs to give away its one valence electron — making it highly electropositive. Contrast those atoms with carbon, which is in the middle of the row. It has an intermediate electronegativity, as it is relatively far from being able to achieve a full valence by either gaining or losing an electron.

While this model is a useful shorthand for understanding an atom's affinity for electrons, a more accurate model is based on the overall attraction between the positive charge of an atom's nucleus and the negative charge of a valence electron. Here, stronger electronegativity results when a valence electron experiences greater attractions to the

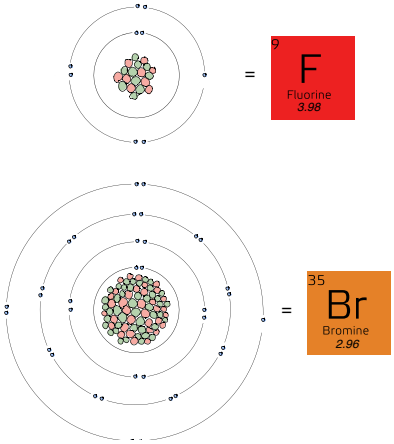


Figure 1.22 Electronegativity Decreases with Increasing Numbers of Electron Shells. Shown for comparison are the schematic structures and electronegativities of two elements in the same column, fluorine and bromine (a redder box represents a greater electronegativity value). Valence electrons in fluorine are in the second electron shell, while those in bromine are in the fourth (note, for bromine, the rules for filling shells are more complicated than described so far – more details can be found in Section F).

nucleus. When going across a row, the number of protons in the nucleus increases, increasing the pull on a valence electron (it should be noted that the number of electrons also increases going across a row, but that increase in total negative charge has less of an effect than increasing the total charge in the nucleus). In moving down a column, extra electron shells are added (**Figure 1.22**). This both increases the average distance between a valence electron and the nucleus (reducing the attraction) and adds more electrons — a whole filled shell — between the valence electrons and the nucleus (these effects end up predominating over the increase in nuclear charge in going down a column).

Groupings of Elements

Just as the electronegativity of an atom can be understood in part by its position in the periodic table, so can other properties. Elements in the same column tend to behave similarly and are often grouped together.

The elements in the last column of the periodic table (farthest to the right) have full valences and are relatively unreactive (**Figure 1.23A**). They are known as the noble gases and are discussed further in the next subsection.

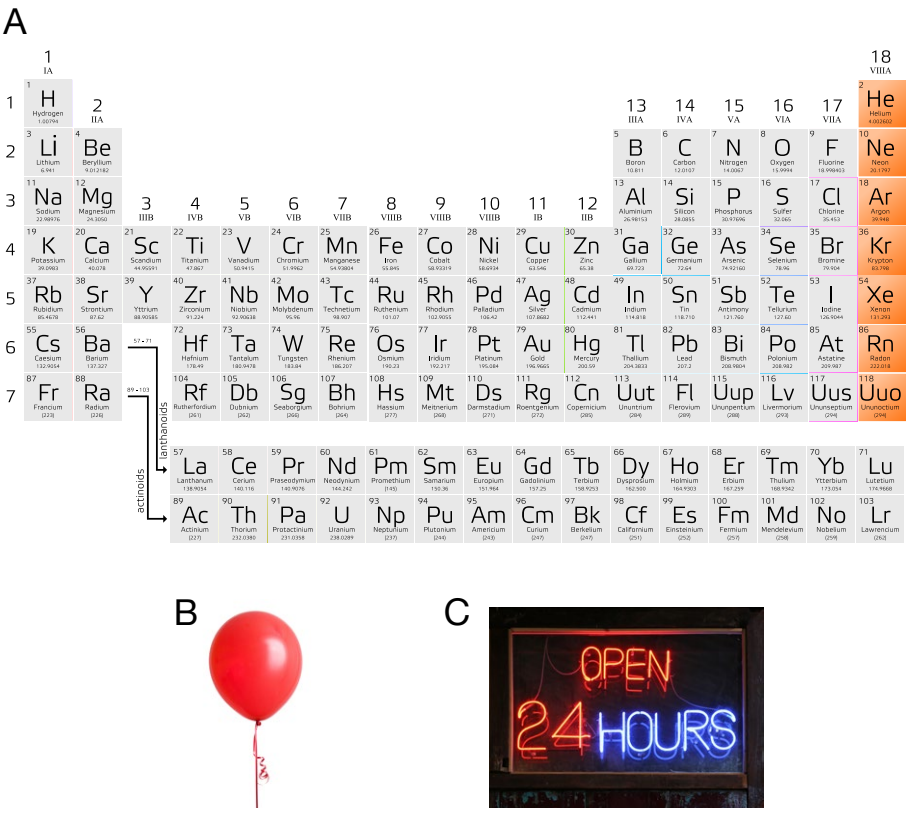


Figure 1.23 The Noble Gases. A) The elements that constitute the noble gases are shown in orange. Examples of noble gas molecules include B) helium gas in a balloon, and C) various noble gases in glass tubes in a neon sign. For the helium balloon, the relatively light atomic mass of helium relative to the other gases makes it less dense than other air molecules, causing the balloon to be buoyant and float (Subsection 2.18 and section 4F explore density and properties of gases). For neon signs, different noble gases impart a different color. For the sign shown, the red is likely due to neon gas and the blue to xenon gas. In neon signs energy is supplied to remove an electron from the gas. When this atom regains an electron, energy is released in the form of light.

Elements in the second to last column are known as the halogens and include the elements chlorine, fluorine, bromine, and iodine (**Figure 1.24A**). These atoms are all one electron away from achieving a full valence and are generally strongly electronegative. Thus, they tend to be quite reactive, taking electrons from other atoms if they can. This can make halogen compounds useful as disinfectants. For example, chlorine gas can be used to sterilize drinking water (**Figure 1.24B**). Although chlorine gas is not a single atom of chlorine, the chlorine atoms in the molecule and those formed from it still have a strong affinity for electrons. If electrons are ultimately lost from the atoms of biomolecules found in microbes that live in the water, the biomolecules can become heavily damaged, killing the microbe.

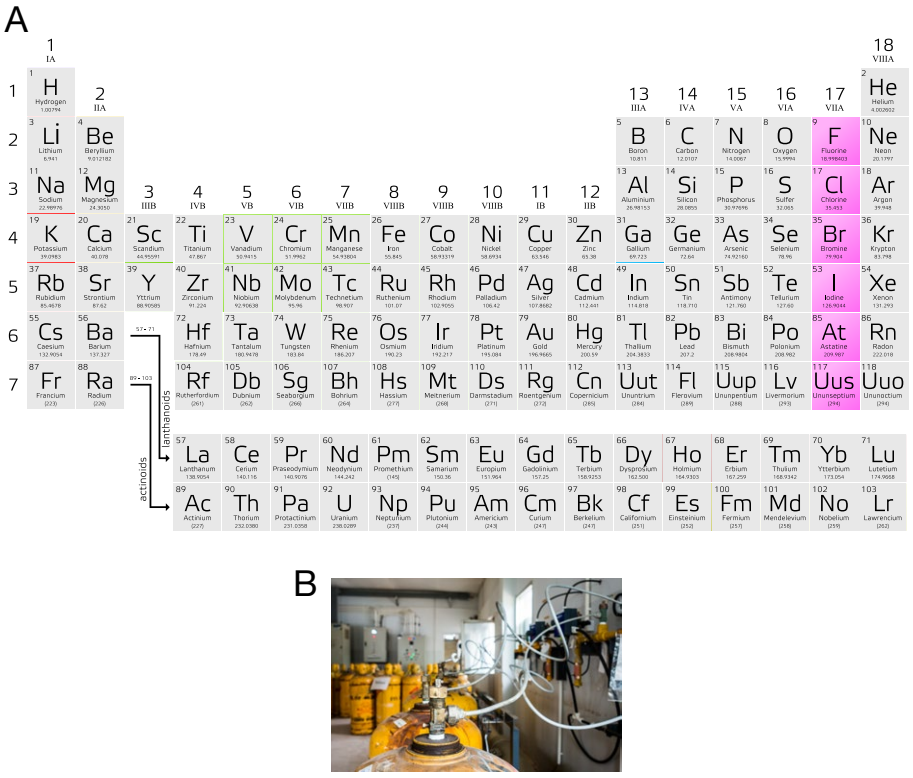


Figure 1.24 The Halogens. A) The elements that constitute the halogens are shown in pink. B) Chlorine gas (Cl_2) cylinders used for disinfection in water treatment. The chlorine in chlorine gas can effectively take electrons from microbes in water, killing them. The gas is unlikely to take the electrons from the molecules of the microbe directly, but instead forms reactive chlorine-containing intermediates with water. Such molecules and related compounds can be directly added as a disinfectant instead and are commonly used in swimming pools and commercial formulations of bleach.

While the halogens are elements that tend to gain electrons to achieve a full valence, metals are elements that tend to lose electrons for a full valence. Elements that have metal or metal-like properties dominate the periodic table, and a couple of the groups of metals are shown in **Figure 1.25A**. The elements of the first column (the alkali metals) have especially low electronegativities and high electropositivities, donating electrons to other atoms when possible. These metals include sodium, potassium, and lithium.

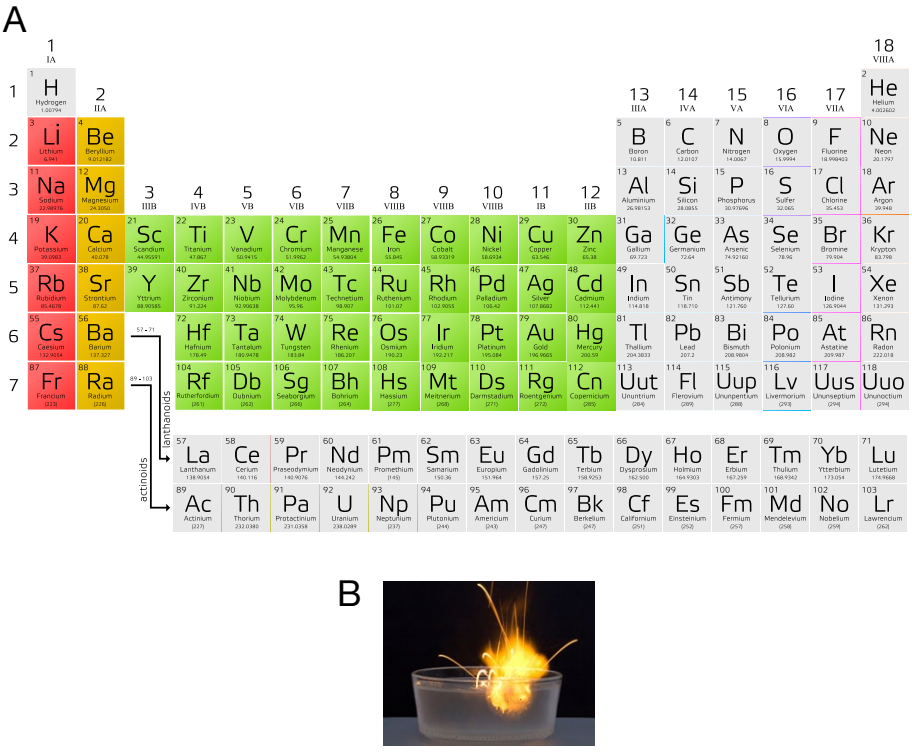


Figure 1.25 Selected Metal Elements. A) Shown are the alkali metals in red, the alkaline earth metals in yellow, and the transition metals in green. B) Sodium metal in water can react violently. The sodium metal donates its electron to water molecules. The reaction generates hydrogen gas and enough energy for the hydrogen gas to potentially ignite and burn (combining with oxygen in the air to make water and release more energy).

You may be familiar with the reactivity of sodium. When sodium metal is added to water, it can cause an explosion via the process of donating its valence electron (**Figure 1.25B**).

Metals in the second column of the periodic table (Figure 1.25A) need to lose two electrons to achieve a full valence. Although not as reactive as the metals in the first column, they tend to still react to lose both of their valence electrons. These metals (the alkaline earth metals) include elements such as magnesium and calcium.

Starting from the fourth row of the periodic table, the elements from the third to twelfth column form a block of metals known as the transition metals (Figure 1.25A). The transition metals include elements such as iron, nickel, copper, and zinc, and many others. When transition metals react, they tend to lose two or more electrons and have complicated properties and reactivities beyond the scope of this book (although some discussion of how their electrons are uniquely arranged is covered in Further Exploration Section 1.F).

The majority of the organic elements (C, N, O, P, and S) are between the halogens and metals (**Figure 1.26**). While still reactive, the elements tend not to be as electronegative or electropositive as the halogens or metals, respectively. They generally have too many electrons to gain or give up to achieve a full valence of electrons, so tend to share their electrons. Oxygen is a bit different from the other elements in this group, being quite electronegative. Nonetheless, in biological molecules, oxygen tends to take one electron at most, and generally shares electrons like the other elements in this group.

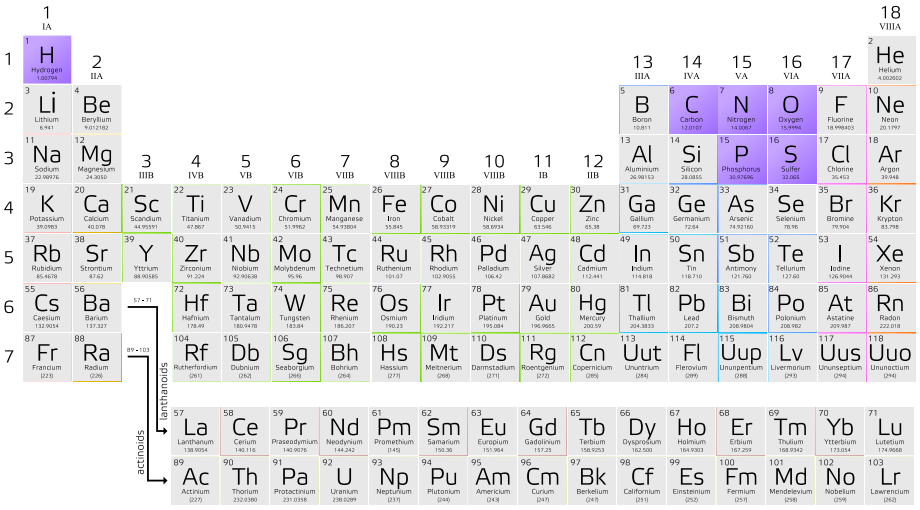


Figure 1.26 The Organic Elements. The elements that constitute the organic elements are shown in purple.

The last group to consider is a group of one: hydrogen, the last of the organic elements (Figure 1.26). Like the halogens, hydrogen is one electron away from a full valence. Similar to the first column metals, it can potentially give away an electron. Finally, like the other organic elements, it has an intermediate electronegativity, meaning that sharing of electrons with other atoms is also feasible.

1.10 Single Atom Elements

Through most of the book, we will be discussing molecules composed of many atoms. However, single atoms can be stable and encountered. The simplest of those are the noble gases (Figure 1.23A). Because the noble gases have a full valence, they do not tend to react with other elements, and are happy to be single atoms. Further, their chemically inert nature generally doesn't favor interactions between noble gas atoms

or with other molecules. The lack of such interactions makes these elements gases at room temperature and standard pressure (gases are discussed in Chapters 2 and 4). You may have some experience with helium in balloons and various noble gases in neon signs (Figure 1.23B and C). However, because noble gases are both largely unreactive and non-interacting, they do not have much of a role in biological systems and will not be discussed in subsequent chapters.

Where to from here: In this chapter we began our journey to understanding biologically-relevant molecules by discussing the properties of atoms that make up these molecules. In the further exploration sections, we look at some more features of atoms, including how instability of atomic nuclei leads to radioactivity (Section E) and a more complete description of how electrons exist in atoms (Section F). In subsequent chapters we will begin building atoms into more complex molecules. However, before we do that, in the next chapter we take a slight detour to introduce quantitative ways to describe the amounts of atoms and molecules.

E. Further Exploration - Radioactivity

As mentioned earlier (and developed further in the rest of the book), in biological systems the main reactivity of atoms comes from their valence electrons. However, occasionally an atom's nucleus itself is unstable, resulting in what is known as radioactive decay. Such atoms can occur naturally or be made, and they are used in a variety of applications including medical imaging and treatments, research, energy production, and military weaponry. Although the theoretical basis of radioactivity is beyond the scope of what we can cover, in this section we will examine what types of atoms are radioactive, what is produced from radioactive decay, and how energetically and rapidly decay occurs. We will end the section with a brief overview of some of the applications and potential dangers of radioactivity.

1.11 Radioactivity and Nuclear Stability

When the nucleus of an atom is unstable, the atom is considered radioactive, as it can undergo radioactive decay to achieve greater stability. What factors dictate the stability of an atom's nucleus? Its total number of protons and its ratio of neutrons to protons.

For elements with relatively few protons, such as the organic elements, stable atoms occur when the ratio of neutrons to protons is close to one, and the commonly encountered forms of these atoms are not radioactive. Recall, carbon has several isotopes. Carbon-12, the most common form of carbon (98.93%), has 6 protons and 6 neutrons. However, carbon can also have an additional neutron (seven total) in the form of carbon-13 (about 1 in 100 carbon atoms), or even two extra neutrons (eight total) in the form of carbon-14 (around 1 in 1,000,000,000,000 carbon atoms). Of these isotopes, only the one with the greatest ratio of neutrons to protons, carbon-14, is radioactive. Similarly, hydrogen-1 and hydrogen-2, with 0 and 1 neutrons, respectively, are not radioactive, while hydrogen-3 (2 neutrons and 1 proton) is.

In general, for elements early in the periodic table (roughly the first three rows), significant deviations from an equal number of protons and neutrons lead to unstable atoms (**Figure 1.27**). As the number of protons in an element increases (roughly the next three rows), nuclear stability requires a greater number of neutrons, so stable isotopes have a greater ratio of neutrons to protons. Deviations from this ratio result in unstable isotopes. When elements become large enough, even increased numbers of neutrons are not sufficient to stabilize an atom. Specifically, for elements with more than 82 protons, there are no stable isotopes - that is, all elements above lead are unstable in any form and undergo radioactive decay. **Table 1.1** lists some example radioactive isotopes that are discussed in this section.

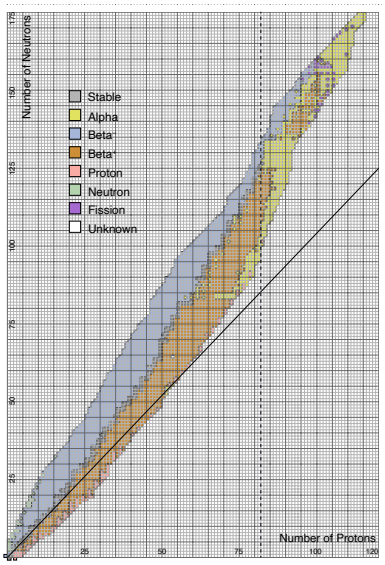


Figure 1.27 Stable and Unstable Isotopes of the Elements. Stable isotopes are shown in gray. Unstable (radioactive) isotopes are shown in non-gray colors, where the specific color indicates the most common natural pathway of decay for that particular isotope. The black diagonal line indicates isotopes with an equal number of protons and neutrons. Note, the stable isotopes of elements with a low number of protons largely fall on this line, but elements with more protons tend to have substantially more neutrons than protons. Elements with more than 82 protons, lead (dotted line), have no stable isotopes.

Isotope	P	N	Frac	Decay	Energy (MeV)	k_{decay} (s^{-1})	Half-Life
Carbon-14	6	8	$\sim10^{-12}$	β^-	0.16	3.9×10^{-12}	5,730 yrs
Fluorine-18	9	9	-	β^+, γ	0.63, 0.51	1.1×10^{-4}	1.8 hrs
Hydrogen-3	1	2	$\sim10^{-18}$	β^-	0.019	1.8×10^{-9}	12 yrs
Iodine-131	53	78	-	β^-, γ	0.61, 0.34	1.0×10^{-6}	8.0 dys
Phosphorus-32	15	17	-	β^-	1.7	5.7×10^{-7}	14 dys
Radon-222	86	136	-	α, γ	5.6	2.1×10^{-6}	3.8 dys
Uranium-235	92	143	0.007	α	4.6	3.1×10^{-17}	7.0×10^{8} yrs
Uranium-236*	92	144	-	Fission, γ	200	-	-
Uranium-238	92	146	0.993	α	4.3	4.9×10^{-18}	4.5×10^{9} yrs

Table 1.1 Information About Various Radioactive Isotopes. The specific radioisotopes shown are ones discussed in this section and ordered alphabetically by element name. P and N indicate number of protons and neutrons, respectively. Frac is the percent of atoms of this element that are present as this isotope. A dashed line indicates a fraction that is very low/not determined. Decay refers to the most common decay pathways. Energies of emitted particles are shown in mega electron-Volts. For atoms with an atomic number less than radon, this energy is for the most abundant emitted particles. For radon and above, the energy is the total energy released per atom. The decay rate constant is denoted as k_{decay} and is in units of reciprocal seconds. Half-lives for each isotope are reported either in days, hours, or years. The asterisk on uranium-236 indicates it is the isotope generated via neutron bombardment of uranium-235.

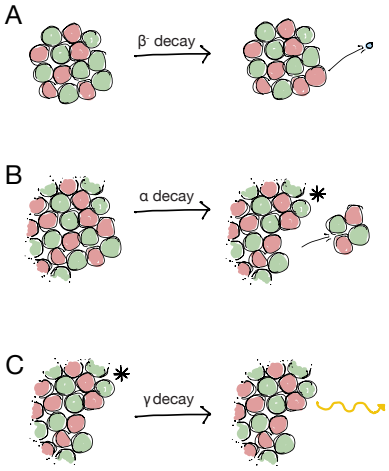


Figure 1.28 Common Radioactive Decay Processes. Protons are depicted as red circles, neutrons as green circles, electrons as small blue circles, and gamma rays as wavy yellow lines. An asterisk indicates a nucleus with excess energy. In all three examples, the structure of the nuclei and emission products have been simplified to focus attention on these particles. A) An example of beta (β) decay. In β^- decay, a neutron is converted to a proton with ejection of an electron, a beta particle. The original atom becomes a new element with one additional proton but no significant change in atomic mass. Other types of beta decay exist but are not shown here. B) An example of alpha (α) decay. In alpha decay, an atom's nucleus (only a small portion shown) ejects a particle containing two protons and two neutrons, an alpha particle. The original atom becomes a new element with two fewer protons and four atomic mass units lighter. C) An example of gamma (γ) decay. In gamma decay, gamma rays are emitted from the atom, while the components of the nucleus are unchanged. Gamma decay occurs when the nucleus has excess energy to dissipate, which often occurs after alpha and beta decay.

1.12 Types of Radioactive Decay

When an atom is radioactive, its nucleus will change to increase its stability. This can happen a number of different ways, but we will focus on the most common ones: processes that lead to alpha, beta, and gamma emission. But before we do that, let's take a quick digression on another way to depict isotopes, which will help us follow what happens in the decay process. Instead of denoting isotopes with their element name and atomic weight (for example carbon-14, with 6 protons and 8 neutrons), an isotope can be written with the element's abbreviation preceded by both a superscript and subscript. The superscript indicates the sum of the protons and neutrons (i.e. the atom's atomic mass and which isotope it is), while the subscript indicates the number of protons (i.e. what element it is and implicitly the total positive charge of the atom):

$$^{atomic\ mass}_{proton\ number}\mathrm{X} \tag{1.8}$$

For example, carbon-14 can also be represented as $^{14}_{6}\mathrm{C}$. Since the name of the element specifies the number of protons, sometimes the proton subscript is dropped (i.e. carbon-14 can also be represented as $^{14}\mathrm{C}$). Because we want to track what happens to the protons and neutrons during radioactive decay, we will use the more verbose notation.

Returning to the different types of radioactive decay, a common way for an atom to deal with an excess of neutrons to protons is to undergo what is known as beta minus decay, β^- decay (often just called beta decay, although beta decay includes more than just beta minus decay). In this process, an electron ends up being emitted (**Figure 1.28A**). This electron is not produced from the electron shells of the atom, but comes from the nucleus, where decay of a neutral neutron creates an electron and a proton. Because the atom gains a proton, it is converted into a new element. As an example, radioactive carbon-14 commonly undergoes the following β^- decay:

$$^{14}_{6}\mathrm{C} \longrightarrow {}^{14}_{7}\mathrm{N} + {}^{0}_{-1}\mathrm{e} + \mathit{energy} \tag{1.9}$$

Here, the radioactive decay of the excess neutron in carbon-14 results in a new proton and an ejected electron. This electron (often called a beta particle in this context) is denoted with the same notation as the atoms. Its superscript stresses that the mass of the electron is very small relative to the protons or neutrons in the atom (effectively zero), while the subscript indicates that the particle carries a negative charge. The proton generated from the neutron remains in the nucleus. Since protons and neutrons have roughly the same mass, the atomic mass of the atom does not change (the superscript 14 remains a 14). On the other hand, the number of protons does (the subscript 6 goes to a 7), causing the carbon to become the next element on the periodic table, a nitrogen. For completeness' sake, during β^- decay a non-interacting and nearly massless antineutrino is also generated but is not shown in Equation 1.9 or Figure 1.28A. The energy released in the decay is shared between the electron and the antineutrino.

When an atom goes from an unstable form to a more stable one, energy is released. The amounts of energy that result from nuclear decay on a per atom basis are quite large and can be released in several different ways. In β^- decay, some of the energy is transferred to the electron, causing the electron to be ejected with a high amount of kinetic energy and traveling at a high speed.

An alternative mechanism of radioactive decay is alpha decay (**Figure 1.28B**). Alpha decay is seen most commonly for later elements of the periodic table that have too many protons to be stable. In alpha decay, an alpha particle consisting of two protons and two neutrons is ejected. The alpha particle is equivalent to the nucleus of a helium atom, and so is often depicted as such. As an example, the most common isotope of uranium, uranium-238, can decay into an isotope of thorium:

$$^{238}_{92}\mathrm{U} \longrightarrow {}^{234}_{90}\mathrm{Th} + {}^{4}_{2}\mathrm{He} + \textit{energy} \qquad (1.10)$$

Like beta decay, the ejected particle has substantial kinetic energy (though the helium nucleus is much more massive than the electron of β^- emission, and therefore tends to travel more slowly). Also like beta decay, the decay process changes the nature of the element, because the number of protons changes (uranium to thorium in our example). However, instead of gaining a proton, alpha decay results in the loss of two protons (hence, uranium with 92 protons is converted to an element two earlier in the periodic table, thorium, with 90 protons). Unlike beta decay, the atomic mass of the radioisotope also changes, since 2 protons and 2 neutrons are lost (in our example uranium-238 with an atomic mass of 238 becomes a thorium isotope with an atomic mass that is four less, 234 amu).

Another commonly encountered decay process is gamma decay (**Figure 1.28C**). Frequently, when an atom undergoes alpha, beta, or other decay processes, there is still an excess of energy. This energy can be released in the form of gamma rays (also sometimes described as a gamma radiation or gamma particles). Gamma rays and x-rays (produced outside of the nucleus) can overlap in the electromagnetic spectrum and are functionally the same in this region. However, historically gamma rays have been defined to have shorter wavelengths and higher energies than x-rays (**Figure 1.29**).

While alpha, beta, and gamma decay are the most common mechanisms for stabilizing radioactive atoms, they are not the only ones. Although β^- decay converts an excess neutron to a proton and an ejected electron, beta decay also denotes a process for nuclei with not enough neutrons. In β^+ decay, a proton is converted to a neutron and a positively charged electron anti-particle, a positron. In a different process, electron capture, electrons in the inner shells of atoms combine with a proton to generate a neutron. Recall, in alpha decay an unstable nucleus ejects both protons and neutrons in the form of a helium atom. However, some heavy atoms can spontaneously split their nucleus into fragments closer in size, as well as emitting neutrons. This process is known as nuclear

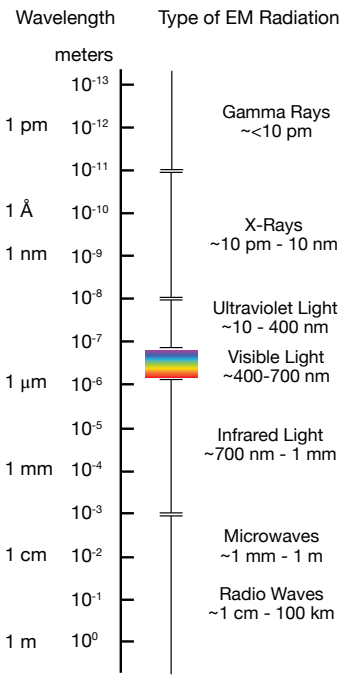


Figure 1.29 Gamma Rays in the Electromagnetic Spectrum. Gamma rays are a form of electromagnetic radiation with the shortest wavelengths and highest energies. Visible light is part of the electromagnetic spectrum, as well as x-rays, which overlap with longer wavelength gamma rays. Cutoffs between different forms of electromagnetic radiation are approximate and somewhat arbitrary.

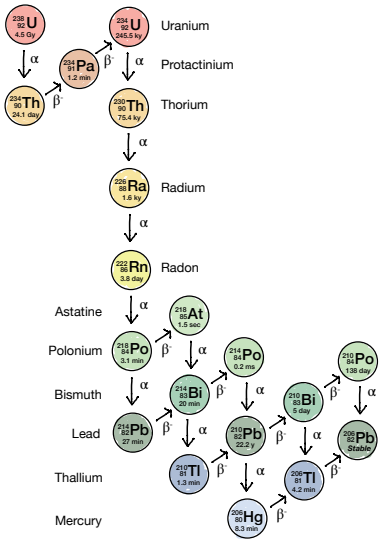


Figure 1.30 Example of a Complicated Multi-Decay Pathway. Shown are different pathways for the decay of radioactive uranium-238 to stable lead-206 through a series of alpha and beta decays. Not shown are gamma decays. The uranium is converted to many different element in the process, including radon gas, discussed later. Some radioisotopes are only present for very short time, while others persist for long periods. These differences are reflected in the half-lives shown for each isotope.

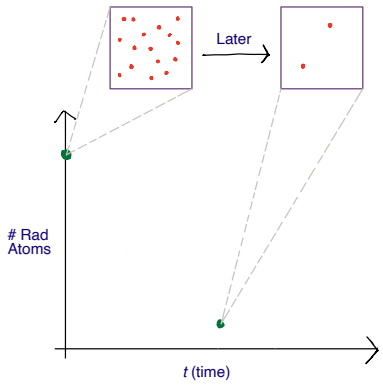


Figure 1.31 Time-Dependent Change in the Number of Radioactive Atoms. Top portion: Over time, the number of radioactive atoms in a sample (red circles in the box) decreases due to their decay. Note, non-radioactive forms of the atom or new elements generate from the decay process are not shown. Bottom portion: Plotting the number of radioactive atoms in the sample as a function of time for the two time points shown at the top.

fission. Finally, in some cases it is possible to directly emit protons or neutrons. It should also be pointed out that specific isotopes do not undergo only one type of decay process. Finally, the products of some decay processes are themselves unstable, especially in the case of larger elements. In these circumstances, a radioisotope can undergo a series of radioactive decays until a stable nucleus is formed (**Figure 1.30**).

1.13 Half-Lives

When radioactive isotopes decay, the speed at which they do so varies considerably (Table 1.1). Some are quite fast, taking much less than a second to effectively disappear. Others are quite slow, taking billions of years before a significant amount of the radioisotope has decayed. Nonetheless, the decay of all radioactive atoms has similar features that help us to describe and predict their behavior.

Spontaneous radioactive decay is a random process. That is, if we watched a particular radioactive atom, at any given moment there is a certain chance it will decay, but we can't be sure if it will. Still, if we watch a very large population of radioactive atoms, overall we can be confident in how much of the original amount of radioisotopes will still be present in a given amount of time. If we consider how that amount changes over time (we will discuss ways to describe amounts more thoroughly in the next chapter), qualitatively, we would expect it to decrease (**Figure 1.31**). We can describe the change in the amount over time more quantitatively. To do so, we can use the fact that the rate of decay of a radioisotope over a short time interval (for example how many atoms in a large sample decay in a second for a long-lived isotope), depends only on the current amount of radioisotope present (and not other factors like the temperature, whether the radioisotope is part of a molecule or not, etc.). This idea can be stated mathematically as follows:

$$\text{rate of isotope change} = \frac{dA}{dt} = -kA \tag{1.11}$$

This equation says that the rate of isotope change (the small change in the amount of radioisotope, dA, in a short interval of time, dt) is proportional to the current amount of the isotope, A. The negative sign is present because we expect a negative rate of isotope change, i.e. a decrease in the amount of isotope over time. k is a proportionality constant that depends on the radioactive atom of interest, as the same amount of two different radioactive atoms could have very different rates. This equation matches our intuition for how the rate of isotope change depends on the amount of isotope present. With a large amount (say before much decay has occurred), the rate of change will be greater than with a smaller amount (say after significant decay has occurred). This equation also says something about any function, $A(t)$, that relates the amount of radioisotope present at a given time. In the language of calculus, Equation 1.11 says for $A(t)$, its derivative, $dA(t)/dt$, has to give back that same initial function, $A(t)$, multiplied by $-k$. We can find this function, **Equation 1.12**, using a little integral calculus or by guessing what sort of function meets the criteria described by Equation 1.11:

$$A(t) = A_o e^{-kt} \tag{1.12}$$

This is an exponential decay function, where the amount of radioisotope at some given time, $A(t)$, depends on the time elapsed, t, the amount of radioisotope you started with, A_o ($A(t)$ when $t = 0$), as well as the rate constant specific to the radioisotope, k. The graph of this function is shown in **Figure 1.32**. You can see that it matches our prior intuition for how amount should change with time, as amount continues to decrease with time. You can also see that it matches our constraint from Equation 1.11. If you take the slope at any point along the curve, $dA(t)/dt$, you can see that the magnitude of the slope is greater (steeper) earlier in the curve, where the amount of radioisotope is

greater, compared to later in the curve, when the amount of radioisotope is less. If you know some calculus, you can even take the derivative of Equation 1.12 and see that it does give back $-kA(t)$, as dictated by Equation 1.11.

One use of Equation 1.12 is that if you know how much radioactive material you start with, as well as the rate constant for your radioisotope, you can predict how much will be present at any time after that. Alternatively, if you know how much you started and ended with, as well as the rate constants, you can determine how much time has elapsed (we'll see some examples of this in Subsection 1.14). Finally, if you measure how much radioisotope is present at various times, you can determine the rate constant for the isotope. The rate constants for various radioisotopes (Table 1.1) are a useful way to compare how fast they decay, with large values indicating fast rates of decay, and small values indicating slow rates of decay.

Although the rate constant gives a sense of how fast radioactive decay can proceed, a more intuitive way to think about these rates is the half-life of the decay process. Suppose you started with 100 radioactive atoms ($A_0 = 100$) with a certain rate constant of decay and wanted to know how long it takes for your atoms to be half decayed ($A(t) = 50$). With some algebra you could solve for t in Equation 1.12, the half-time of decay. If you repeated this calculation starting with 500 of the same radioactive atoms, and calculated how long it would take for them to decay to 250, you would find the same half-time of decay, a value we will call the half-life. This is a unique feature of exponential decay as described by Equation 1.12, and you can see that this is the case if you use $A_o/2$ to represent $A(t)$ for half of any initial amount of radioisotope, A_o. This means that if it took 10 minutes for some radioactive atom to decay half-way, its half-life would be 10 minutes. If we started with 400 of these atoms, in 10 minutes we would have 200. Ten minutes later we would have 100. Ten minutes after that, we would have 50, and so on (**Figure 1.33**).

If we wanted to calculate the half-life, $t_{1/2}$, of a radioisotope from its rate constant k, we could use Equation 1.12, plug in $A_o/2$ for $A(t)$, A_0 for A_0, and solve for t (which will be $t_{1/2}$). In so doing, we get the following formula:

$$t_{1/2} = \frac{ln(2)}{k} = \frac{0.693}{k} \qquad (1.13)$$

From this equation, we can see that the larger the value of k is (bigger rate constant of decay, i.e. faster decay), the smaller the half-life will be, which is what we would expect. Half-life values for various radioisotopes are shown in Table 1.1. As promised at the beginning of the section, there is a considerable range of values.

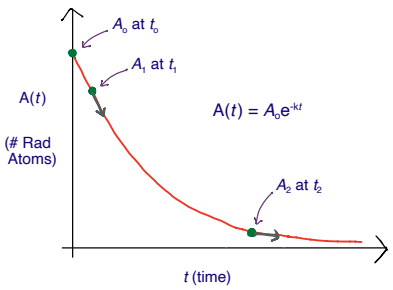


Figure 1.32 First-Order Exponential Decay Curve. Shown is a plot of Equation 1.12, where at any given time, t, the number of radioactive atoms is described by the value of $A(t)$. When the time is 0 seconds, t_o, this amount is A_o (an amount of radioactive isotope that will depend on a particular sample). Over time, A decreases, i.e. at the later time, t_2, the amount of radioisotopes, A_2, is less than it was at earlier time t_1, which had A_1 radioisotopes. Additionally, the magnitude of the rate of change of the radioisotope (the size of the slope at a point t) decreases with less A in accord with Equation 1.11 (the slopes at times t_1 and t_2 are represented by arrows, where a slope of zero is represented by an arrow parallel to the x-axis).

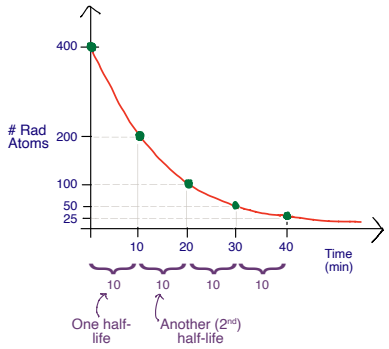


Figure 1.33 Exponential Decay and Half-Lives. A unique feature of exponential decay curves is that over a specific time interval, its half-life, the amount of radioactive isotope is halved. The amount of radioisotope will be halved after one half-life no matter where on the curve you start, or how many half-lives have already occurred. In the example shown, the half-life is 10 minutes, but the half-life values of different radioisotopes can vary considerably.

1.14 Uses of Radioactivity

There are many applications of radioactive atoms that take advantage of different aspects of the decay process. We will highlight a couple of examples from different categories.

Radioisotopes can be used to help determine the age of an object. Recall that for a radioactive isotope with a known half-life, if you know how much of the isotope you currently have and how much you started with, you can determine how much time has elapsed (Equation 1.12). In radiocarbon dating (**Figure 1.34**) the decay of carbon-14 is used to determine the age of plant- or animal-based materials that can be up to about 50,000 years old. Carbon-14 undergoes β^- decay (Figure 1.28) with a half-life of about 5,730 years (Table 1.1). This half-life is short enough that alone, effectively all carbon-14 would have decayed to nitrogen over the comparatively long lifespan of earth. However, carbon-14 is constantly being replenished in the atmosphere at low levels by bombardment of atmospheric nitrogen by energetic neutrons in cosmic rays. This atmospheric carbon can be incorporated into carbon dioxide, meaning that there

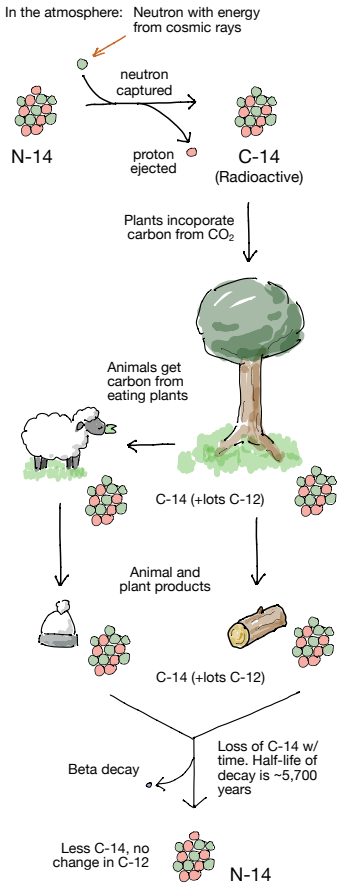


Figure 1.34 Schematic of Radiocarbon Dating. Incorporation of unstable carbon-14 into biological matter provides a way to determine its age: measuring how much carbon-14 remains relative to non-radioactive carbon-12.

is a relatively constant, albeit small, amount of carbon-14 relative to regular carbon-12 present in atmospheric carbon dioxide. Plants can use the carbon in carbon dioxide to make many biomolecules, so plants or animals (which ate plants or ate animals that ate plants), or human-made items containing plant or animal materials, contain biomolecules with some amount of radioactive carbon-14. Unlike in the atmosphere, the amount of carbon-14 in these items is not replenished when the organism dies, so by determining how much carbon-14 is left relative to non-radioactive carbon-12, the age of the item can be determined. A similar idea can be used with other elements and isotopes. For example, the most common form of uranium, uranium-238, has a half-life of about 4.5 billion years. The age of rocks containing trace amounts of uranium can be determined, and from such studies, the formation of the earth is thought to have occurred roughly 4.5 billion years ago.

Another use for radioisotopes is detection and imaging. These techniques take advantage of the fact that the particles produced by radioactive decay are high in energy and not produced by the non-radioactive atoms that predominate. This allows small amounts of a substance containing the radioisotope to be detected with high sensitivity. An additional advantage, as mentioned earlier in the chapter, is that radioisotopes of elements do not differ significantly in their chemical properties from their non-radioactive forms. This means that if a molecule can be made with a non-radioactive element, it can be made with a radioactive one, too. For example, biomolecules like DNA and RNA, which we will study later, contain a significant amount of phosphorus atoms. This means specific DNA or RNA molecules can be synthesized with a radioactive form of phosphorus, phosphorus-32 (Table 1.1). In the presence of other molecules, even small amounts of the synthesized DNA or RNA molecules can be detected, since they are the only molecules that generate a significant amount of beta particles. The electrons generated from decay are relatively high in energy and can be detected directly by their ability to darken photographic film or to be captured in phosphor-imaging plates that can be read out later (**Figure 1.35**). It should be mentioned that phosphorus-32 is not common naturally and has a relatively short half-life of about two weeks. This means it is impractical to isolate phosphorus-32 from natural sources and store it. Instead, radioactive ^{32}P is made and used when needed. This is the case for many radioisotopes that are used scientifically and medically, and such radioisotopes are typically synthesized by bombarding other elements with high energy neutrons or protons.

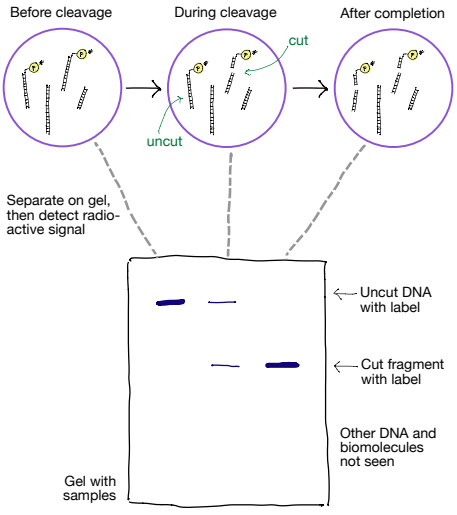


Figure 1.35 Example of Using Radiolabels with Nucleic Acids to Facilitate Their Detection. To probe the cleavage of a specific DNA, that DNA contains a phosphorus-32 radioisotope at one end (represented as a P in a circle with an asterisk). Other DNA molecules do not contain the radioactive label. During the course of the cleavage reaction (left to right), the DNAs present can be separated by length with a technique called gel electrophoresis, where smaller fragments of DNA migrate farther to the bottom of the gel. Exposure of the gel to a material that can detect radioactive phosphorus decay allows only the labeled DNA to be detected, even if its amount is small relative to the rest of the DNA (and other potential biomolecules) that are present.

An example of imaging using radioisotopes is PET (positron emission tomography) scans, such as that of the brain (**Figure 1.36**). Fluorine-18 is a form of fluorine that contains one less neutron than the stable fluorine-19 isotope and undergoes β^+ decay to become oxygen and releases a positively-charged electron antiparticle, a positron:

$$^{18}_{9}\mathrm{F} \longrightarrow {}^{18}_{8}\mathrm{O} + {}^{0}_{+1}\mathrm{e} + \textit{energy} \qquad (1.14)$$

A positron is very short-lived, because when it encounters an electron, the two particles are annihilated. This produces two gamma rays that travel in opposite directions.

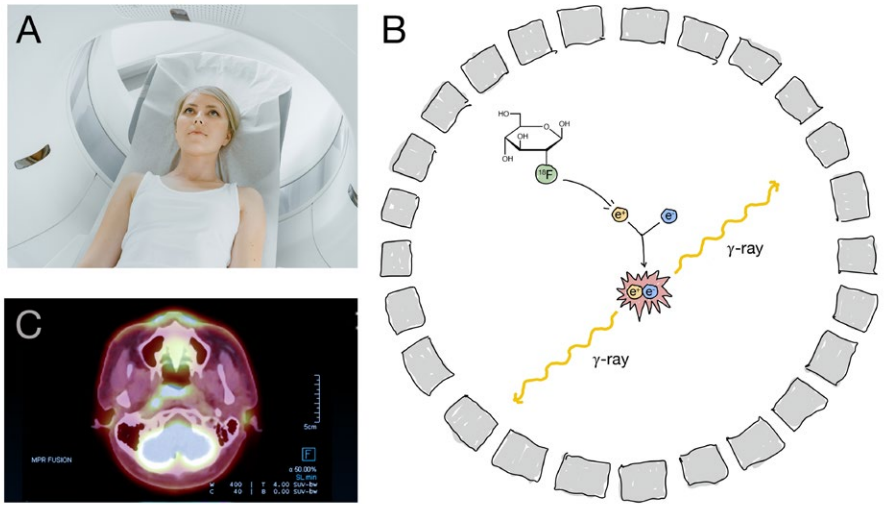


Figure 1.36 PET Scan of the Brain. PET (Positron Emission Tomography) scans are a method of producing 3-D images inside of the body, including in the brain. A) A patient is given glucose sugar containing radioactive fluorine-18, an element not present in normal glucose. They are then placed in an array of detectors that encircles their head. B) The decay of the fluorine ultimately results in signals that indicate where the decay occurred. C) Tabulation of the location and number of decays throughout the brain provides a map of the brain and its activity, as high activity requires more glucose.

By using an array of sensors that encircles the patient, the detection of the two gamma rays allows the position of the original fluorine-18 atom to be determined. Fluorine is not commonly present in biomolecules but can be incorporated into a modified form of the sugar glucose in which one oxygen atom is replaced by fluorine-18. When a patient is injected with the compound, the brain takes up this glucose analog much as it takes up regular glucose, and the PET-scan instrument can visualize where in the brain glucose goes. This provides not only an image of brain structure, but also of brain activity, since brain cells that are more active use more glucose for energy.

Radioactive decay can also be used therapeutically. The underlying idea is to target a radioisotope to a specific location in the body, where its high-energy emission can kill the cells in that area. An example of this is in the treatment of various thyroid conditions with iodine-131 (**Figure 1.37**). This isotope undergoes β^- and then γ decay. Iodine is not commonly incorporated into biologically relevant molecules. However, the thyroid, a gland found in the neck, uniquely produces two hormone molecules that contain iodine. When the thyroid is either overactive, a condition known as hyperthyroidism, or cancerous, thyroid cells can be killed with iodine-131. The iodine is naturally targeted to the patient's thyroid, and the high-energy particles of radioactive decay destroy the thyroid cells.

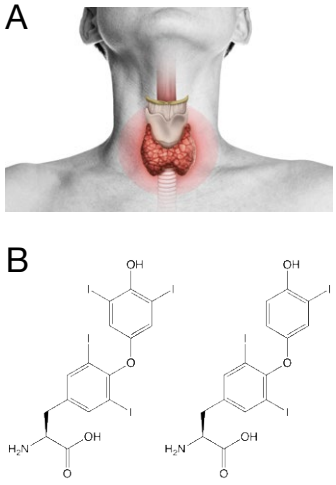


Figure 1.37 Unique Iodine Utilization in Thyroid Hormones. A) The thyroid (highlighted in red) is a gland found in the neck. B) The thyroid produces two hormone molecules that uniquely incorporate iodine into their structure (shown as the letter 'I'). Thus, dietary iodine, including radioactive forms, will be targeted to the thyroid to produce these iodine-containing hormones. This targeting can be exploited to visualize the thyroid or, as described in the main text, to kill undesirable thyroid cells.

In some applications, such as nuclear reactors and weapons, the goal is to use the large amounts of energy that are released from radioactive decay. The most common isotope of uranium is uranium-238, which undergoes very slow alpha decay (Equation 1.10 and Table 1.1). However, a different isotope of the element, uranium-235, when converted to a uranium-236 by bombardment of a neutron, can rapidly undergo a different type of decay, nuclear fission. This reaction produces two nuclei of relatively close mass, three neutrons, and a significant amount of energy, including gamma radiation (shown is one set of several possible fission products):

$$^{235}_{92}\mathrm{U} + {}^{1}_{0}\mathrm{n} \longrightarrow {}^{236}_{92}\mathrm{U} \longrightarrow {}^{141}_{56}\mathrm{Ba} + {}^{92}_{36}\mathrm{Kr} + 3\,{}^{1}_{0}\mathrm{n} + \textit{energy} \qquad (1.15)$$

A novel aspect of this reaction is that it requires a neutron to proceed, but produces three neutrons. Thus, the reaction of one uranium-235 isotope can facilitate the reaction

of up to three more uranium-235 atoms, which could then go on to cause fission in nine uranium atoms, and so forth (**Figure 1.38**). This process in which a reaction amplifies

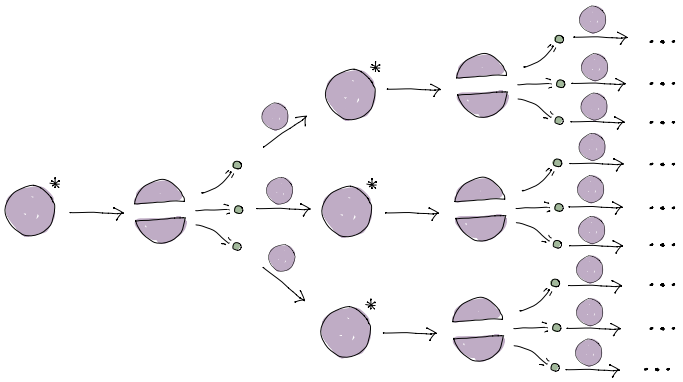


Figure 1.38 Schematic of a Chain Reaction of Uranium Fission. Starting from the left-hand side, a uranium-235 atom that has been bombarded by a neutron (purple circle with an asterisk) splits into two fragments, releasing three neutrons (small green circles), which can go on to repeat the process.

itself is known as a chain reaction and can release tremendous amounts of energy in a short time. Indeed, the first nuclear bombs were based on this principle, releasing the equivalent of over tens of thousands of tons of the conventional explosive TNT. In a less destructive application, the energy of this chain reaction can be released more slowly and in a controlled fashion within a nuclear reactor, such as light water reactors. These reactors take the nuclear energy released, to convert water to steam, to drive turbines, which in turn generate electricity.

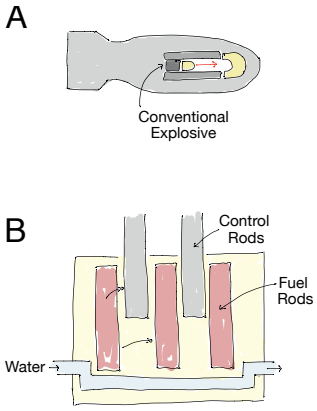


Figure 1.39 Different Ways to Control the Rate of Fission Reactions. A) Nuclear weapons go from not releasing energy to doing so at an extremely fast rate. Rapid fission of uranium-235 not only requires that this isotope is highly enriched (97% pure), but also other factors, including the amount of uranium. The critical mass is the minimum amount of radioisotope needed for the reaction to be self-sustaining. One way to achieve a critical mass that is conceptually similar to what was used in the first atomic bomb is shown: two portions of uranium (yellow) below the critical mass are combined to form a mass above this threshold, initiating rapid fission. B) In nuclear reactors the rate of energy release needs to be slower and controlled. In some reactors, fuel rods containing uranium-235 (3% pure) or other radioactive isotopes emit neutrons (green circles) that can facilitate fission in neighboring rods. Control rods containing molecules that can absorb neutrons are lowered between the fuel rods to control how fast fission occurs.

Naturally occurring uranium-235 is relatively rare, constituting slightly less than 1% of the uranium in mined uranium ore (Table 1.1). At this level, the uranium-235 atoms are too spread out to undergo a chain reaction. Various time-intensive methods have been developed to enrich the percentage of uranium-235, with enrichment levels of about 3% needed for nuclear reactors, and greater than 90% for nuclear weapons. Even at high enough enrichment, a certain amount of uranium-235 is required, a so-called critical mass. In early nuclear bombs, this provided a conceptually simple method to initiate the chain reaction: two masses of enriched uranium below the critical mass were brought together to generate a sample greater than the critical mass (**Figure 1.39A**). In nuclear power plants, such as light water reactors, the extent of nuclear fission is controlled a different way. Rods containing molecules that can absorb neutrons are introduced into the reactor core, and by raising and lowering the rods, the amount of fission can be adjusted (**Figure 1.39B**). Improper control of the fission process can potentially lead to a core meltdown, but it is not the only potential danger of nuclear reactors. After use, the uranium-235-containing fuel rods eventually become spent, but contain a number of products that are radioactive and/or otherwise toxic elements. This nuclear waste cannot be readily converted to safer substances and needs to be stored in some capacity.

It should be mentioned that the examples of nuclear reactors and weapons are but one approach to harnessing nuclear processes, and there are other strategies. Nuclear fusion, in which two lighter isotopes (such as deuterium and tritium) are fused into a new element (helium in this case) can produce even greater amounts of energy than the fission processes described. Indeed, nuclear fusion is the process that predominantly powers our sun. Nuclear weapons employing fusion have been developed and efforts to harness fusion for energy production are ongoing.

1.15 Radiation Damage and Safety

Radiation is everywhere, and we are constantly exposed to it by things like cosmic rays from outer space, medical instruments used for diagnostics, and even radioisotopes in the molecules of our own bodies (**Table 1.2**). Luckily, our total radiation exposure tends to be relatively low. Still, radiation can be damaging to biological systems.

Source	Ave Exposure (%)
Radon gas	55
Internal	11
Medical X-rays	11
Cosmic Rays	8
Other Human-made	7
Terrestrial	6
Other	2

Table 1.2 Breakdown of Common Sources of Radioactive Exposure. Shown are common natural and human-made sources of radioactive exposure and how much each contributes to an individual's average exposure, from highest percentage to lowest. Internal sources refer to naturally occurring radioisotopes in our own bodies. Terrestrial refers to radioactive isotopes found in the ground.

The alpha, beta, or gamma particles generated by radioactive decay are all forms of ionizing radiation: i.e. particles with sufficient energy to remove electrons from other atoms. This radiation can damage biological molecules directly, or do so indirectly, changing molecules (like water) that surround biological molecules into species that can react with biomolecules (**Figure 1.40**). Exposure to high levels of radiation leads to what are known as deterministic effects, where reaching a specific level of exposure and cellular damage leads to well-defined outcomes, such as radiation burns. Lower levels of radiation lead to what are known as stochastic effects that are generally tolerated, but which always have a chance of developing into more serious outcomes, especially with more incidents of exposures. For example, cells tend to be relatively effective in repairing DNA damage that arises from low levels of radioactivity, but repeated exposure to radioactivity increases the risk of unrepaired DNA damage. As we will learn later, DNA is a biomolecule that contains the instructions for cells, and its damage can lead to long-term changes. If this damage occurs in reproductive cells, genetic defects can be passed down to offspring. In other cells, DNA damage can lead to them becoming cancerous.

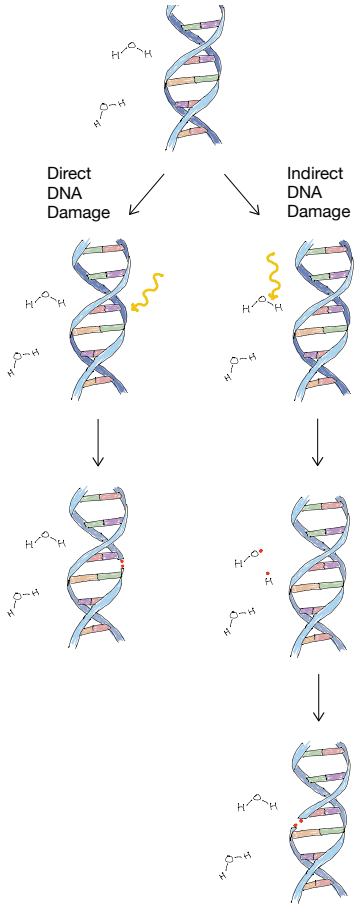


Figure 1.40 Examples of the Effects of Ionizing Radiation at the Molecular Level. Ionizing radiation (shown as yellow wavy arrows) has sufficient energy to break chemical bonds, potentially damaging biological molecules such as DNA. The damage can be direct, indicated by ionizing radiation generating a DNA molecule with a single-stranded break (left branch). Alternatively, damage can be indirect. For example, a water molecule (H_2O) can be affected by the ionizing radiation different ways (such as becoming a hydroxy radical). This reactive species can potentially interact with the DNA molecule, also creating a single-stranded break (right branch).

Since the effects of radiation exposure can range from relatively benign to severe, what dictates how dangerous it is? Practically, this is a challenging question to answer precisely, since many factors contribute, including: the type of radiation, the amount of exposure, and the exposure rate.

The type of radioactivity contributes to how potent its effects are. The energy of ejected particles can vary considerably. For example, the beta particle (electron) ejected by phosphorus-32 is roughly ten-fold more energetic than that of carbon-14, which itself is ten-fold more energetic than hydrogen-3 (**Figure 1.41A**). Further, the type of emitted particle varies in its ability to penetrate the body (**Figure 1.41B**).

Alpha particles are relatively non-penetrating, and are generally capable of being stopped by a sheet of paper. Thus, they can be stopped by a layer of dead skin and are not usually an external hazard. That said, inhalation or ingestion can be a problem. One example of a dangerous alpha emitter is radon, which on average constitutes an individual's greatest amount of exposure to radioactivity (about 55%, Table 1.2). Radon is a noble gas produced from natural decay of uranium in the soil and varies in its abundance from location to location. As a gas, radon is a component of the air. However, because of its large atomic weight, it is quite heavy and tends to accumulate in low areas, like basements of houses. When radon is inhaled, it becomes trapped in our tissues, irradiating them with biologically damaging alpha particles.

Beta particles are more penetrating than alpha particles (Figure 1.41B). In air, a beta particle with roughly half the energy of an ejected phosphorus-32 electron can travel 3-4

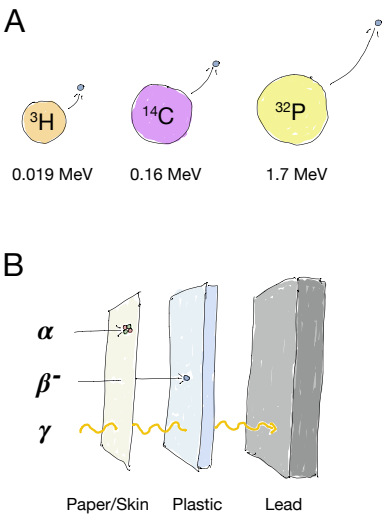


Figure 1.41 Differences in Energies and Penetration of Radiation. A) Comparison of energies of β^- decay for different elements. Shown are the maximum amounts of energy generated for tritium, carbon-14, and phosphorus-32 decays, with that energy predominantly going to the velocity of the ejected electron (small blue circle). B) Comparison of typical α-, β^-, and γ-decay in terms of their ability to penetrate materials with different composition and thickness.

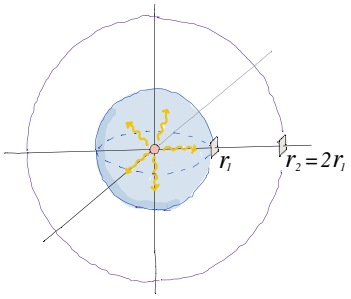


Figure 1.42 Radiation Exposure Decreases with Increased Distance from the Source. Shown at the origin is a source of radioactivity emitting radiation in all directions equally. Even if no radioactivity is absorbed, the amount of radiation reaching a target (shown as squares) decreases as the distance to the target increases, proportional to $1/r^2$. Exposure of the target at a distance r can be related to the fraction of radioactivity that reaches the target (its area) compared to the total amount of radiation at that distance (the surface area of the sphere at r, $4\pi r^2$). At twice the distance, $2r$, the area of the target would be the same, but the total radiation will be spread over a much larger sphere with four times the surface area ($4\pi(2r)^2$), significantly decreasing the fraction of radiation that reaches the target.

meters. In plastic, it travels roughly 1 cm. This means that beta emitters can be external hazards to the skin and eyes, as well as internal hazards due to inhalation or ingestion.

Gamma particles are the most penetrating of these radioactive decay products (Figure 1.41B) and can easily travel through the entire body, causing damage to internal tissues and organs. Additionally, inhalation or ingestion of gamma emitters is highly hazardous. While X-rays are not produced directly by radioactive decay, their effects on the body are the same as gamma rays (though gamma rays are generally more energetic), and so safety concerns about the two are often considered together. Both gamma- and X-rays can be stopped by materials made from heavy atoms with lots of electrons, such as lead. Indeed, I-125 gamma emission (0.03 MeV) can be effectively attenuated with 1/8" lead.

The number of radioactive decays that occur also contributes to the risk, with more decays being more dangerous. This number is proportional to the number of radioactive atoms. While the number of radioactive molecules found in the environment is generally low, it can be high naturally (for example accumulation of radon gas), and is usually high when working with enriched or synthetic radioactive materials (for examples in a medical or scientific context). Having more radioactive atoms will result in more decays. However, as described in the half-life section, the rate constant of decay for a given atom type will also contribute to how frequently the radioactive atoms decay.

Even with knowledge of the decay rate of a radioactive sample, this does not tell us how much of the emitted decay products reach a person. Distance affects radiation exposure, with fewer particles reaching a person the farther away they are from a radioactive source. The average exposure is inversely proportional to the square of the distance (**Figure 1.42**), meaning that compared to being say 1 meter away from a radioactive source, a person 2 meters away would experience 1/4th the exposure ($1/2^2$); a person 3 meters away would experience 1/9th the exposure ($1/3^2$); and so on. Additionally, as mentioned above, the penetration of different types and energies of radioactive decay particles differs, meaning that the amount of radioactive decay that reaches a person is also dictated by what is between them and the radiation source. For example, the exposure received by a medical technician working with diagnostic x-rays is different (and less) if they are wearing a lead apron.

Some final factors to consider include which tissue type is exposed and for how long. Tissues differ in their response to absorbing radiation, with some being more sensitive to exposure. This can extend to whole organisms, where fetal exposure is generally more serious than equivalent exposure in an adult. The time interval in which a dose is received is also important. Exposure to a dose of radiation in a short time is generally more damaging than the same amount of radiation exposure over a long time.

Type of Measurement	Composition	Units	Related Units
Activity (Frequency of decays)	Decays/Sec	Becquerels (Bq) (1 dps)	Curies (Ci) (3.7×10^{10} Bq)
Specific activity (Activity per amount)	Activity/Amount	Bq/g, Bq/mole	Ci/mg, Ci/mmol
Absorbed dose (Radiation energy absorbed per mass)	Energy/Mass	Gray (Gy)	Radiation absorbed dose (rad), Roetgen (R)
Effective dose (Relative biological damage in the body)	Absorbed dose adjusted for radiation type and biological tissue	Sieverts (Sv)	Roentgen equivalent man (rem)

Table 1.3 Common Ways to Quantify Radioactivity. Shown are different ways to measure amounts of radioactivity and radioactive dosages.

Quantitatively, the amount of radiation present can be described a number of different

ways, including directly reporting the activity for the amount of radioisotope present, describing it in terms of amount of decay per specific amount of radioisotope, or the dose of decay product that reaches a tissue. Different units of measure are used to describe each of these (**Table 1.3**), with more about units in the next chapter. Which measurements end up being used depends on which aspect of the decay is the focus.

While the factors dictating the severity of radiation exposure are complicated, any exposure could be harmful and should be taken seriously. That said, different levels of caution are required, as risks differ substantially with different dosages (**Table 1.4**).

Event	Exposure Time	Approx Dosage (μSv)
Airport security scan (backscatter X-ray)	< Min	0.1
Eating a banana	< Min	0.1
Dental X-ray	< Min	5.0
Background dose average person on average day	Day	10.0
Flight from New York to LA	Hours	40.0
Chest X-ray	< Min	100.0
Mammogram	< Min	400.0
Year dose per person from food	Year	400.0
US Gov yearly limit rad expose to public	Year	1,000.0
Spinal X-ray	< Min	1,500.0
Fukushima site day after disaster, 1 hour	Hour	1,500.0
Ave yearly dose natural background rad (varies wildly)	Year	2,400.0
Average CT scan	< Hour	10,000.0
Smoking 1.5 pack of cigarettes a day for a year	Year	36,000.0
Max yearly dose permitted for US rad worker	Year	50,000.0
Lowest annual dose w/evident increase lifetime cancer risk	Year	100,000.0
Max radiation level detected at Fukushima per hour	Hour	400,000.0
Temporary radiation sickness, not fatal	Hours	1,000,000.0
Highly targeted dose used in conventional radiotherapy	< Min	2,000,000.0
Severe dose – bleeding, hair loss, possible death untreated	Hours	4,000,000.0
Usually fatal within 2-4 weeks if untreated	Hours	6,000,000.0
Fatal dose, death within 2 weeks	Hours	10,000,000.0
Seizure and tremors, death within 48 hours	Hours	30,000,000.0
10 min exposure Chernobyl reactor core after meltdown	Mins	50,000,000.0

Table 1.4 Comparison of effective dosages from different radioactive events.

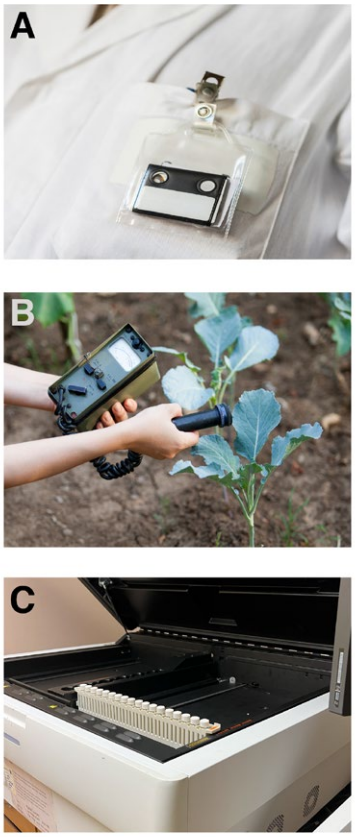


Figure 1.43 Examples of Devices Used to Monitor Radioactivity. A) Film Badge. The film (or related detection material) in a badge will darken with radioactive expose and can be used to provide a measure of cumulative radioactive exposure over time. B) Geiger Counter. Radiation with sufficient energy to ionize the gas inside of the detector can be detected by the current created by the ionized (charged) gas, providing a real-time measure of radiation levels. C) Scintillation Counter. Potentially radioactive samples are placed in proximity to a scintillation material (for example in a vial with scintillation fluid). Interaction of the emitted radioactive particles with the scintillant generates light, which can be detected to give a highly sensitive and accurate measure of the amount of radioactivity present.

Avoiding significant exposure as much as possible is a good idea, and that can be accomplished by proper storage, access, and disposal of radioactive materials. If exposure is necessary, its dangers can be minimized by maintaining distances from the radioactive source, using shielding to block the radiation, and keeping the time working with the radioactivity as short as possible. As a final cautionary note: our bodies have no way to sense radiation exposure before damage has already occurred. A number of devices can be used to monitor for exposure (**Figure 1.43**), and their use is an important component in safe usage of radioactivity.

F. Further Exploration - Atomic Orbitals

To better understand atoms, in this section we delve into a more accurate description of how electrons are distributed in atoms: atomic orbitals.

1.16 Quantum Weirdness

Earlier in the chapter we proposed a model in which the electrons of an atom surround the nucleus like planets orbiting the sun. While a useful simplification, this description is inaccurate. At the level of the very small, the quantum level, many of our intuitions about the nature and behavior of matter turn out to be incorrect.

From our experience, we expect that objects will have a well-defined spatial distribution. For example, for a planet in our solar system, we can describe exactly how wide it is and where it is located at any time in its orbit around the sun (**Figure 1.44A**). That is, at any given time there are places in space the planet is located and there are (many) places the planet isn't. Surprisingly, that isn't true of how an electron is distributed around its nucleus. Electrons are effectively spread out over space, with some places being more likely locations to find them, but with some non-zero (but potentially very small) probability of being found nearly anywhere (**Figure 1.44B**). Thus, instead of a well-defined particle with a specific trajectory, an electron is better thought of as a diffuse probability cloud. An electron's probability distribution is derived from the square of its wavefunction, where the name emphasizes that the electron has features similar to a wave rather than simply being a particle. Different electrons in an atom can occupy different wavefunctions, and therefore these electrons exist in different probability clouds.

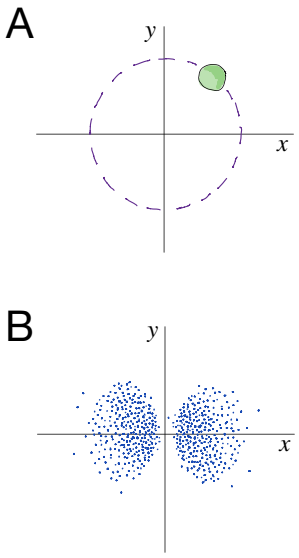


Figure 1.44 Where a Particle Might be Found at the Atomic and Non-atomic Scale. For simplicity, in both examples the particle (a planet or an electron) is shown on a two-dimensional plane with the central object (the sun or the atomic nucleus) not shown. A) The location of a planet orbiting the sun. The planet travels around the sun in well-defined orbit and has a specific position and velocity at a given time. B) An example of where an electron might be found around an atomic nucleus (specifically for an electron in a $2p_x$ orbital). The electron does not have a discrete position and velocity and is better described in terms of a complicated probability distribution, where areas of greater probability are represented by regions with more dots present.

1.17 Hydrogen Wavefunctions

What dictates the wavefunctions of an atom? Ultimately, any potential wavefunction must fulfill certain requirements regarding the energy of the system, described by what is known as Schrödinger's equation. While the details of the equation are too complicated to go over here, the equation has the following form for the simplest atom, hydrogen, which contains one electron and one proton:

$$\left\{\left(-\frac{\hbar^2}{2\mu r^2}\left[\frac{\partial}{\partial r}r^2\frac{\partial}{\partial r}+\frac{1}{\sin\theta}\frac{\partial}{\partial\theta}\sin\theta\frac{\partial}{\partial\theta}+\frac{1}{\sin^2\theta}\frac{\partial^2}{\partial\phi^2}\right]\right)+\left(-\frac{e^2}{4\pi\epsilon_o r}\right)\right\}\Psi(r,\theta,\phi)=E\,\Psi(r,\theta,\phi) \quad (1.16)$$

In this equation, an electron wavefunction for hydrogen, Ψ, is defined in terms of the potential position of the electron in spherical coordinates, r, θ, and ϕ. According to the equation, the sum of the kinetic energy of the electron (the terms in the first parenthesis operating on the wavefunction) and the potential energy of the electron (the terms in the second parenthesis operating on the wavefunction and describing the energy of attraction between the electron and the proton in the nucleus), must have some specific and constant value (the total energy, E). This requirement severely restricts what kind of wavefunctions are possible in a hydrogen atom. However, there are still numerous wavefunctions that can fulfill these constraints.

A feature of any possible hydrogen atom wavefunction is that the shape of the function depends on three values: n, the principal quantum number; l, the orbital angular momentum quantum number; and m_l, the magnetic quantum number. Each of these terms is an integer and can have certain values. The principal quantum number can be any positive, non-zero integer:

$$n = 1,\ 2,\ 3,\ 4,\ \ldots \quad (1.17)$$

The orbital angular momentum quantum number can independently be any positive integer or zero. However, its value cannot be equal to or greater than the principal quantum number for that wavefunction:

$$l = 0,\ 1,\ 2,\ 3,\ \ldots,\ (n-1) \quad (1.18)$$

The magnetic quantum number can independently be a positive, negative, or zero-valued integer. However, its value cannot be greater than the positive or negative value of the orbital angular momentum quantum number for that wavefunction:

$$m_l = -l, \ldots, -1, 0, 1, \ldots, l \tag{1.19}$$

We can specify a particular wavefunction using its quantum numbers as follows (note, we're not showing what the actual wavefunction equation would be, because that formula is too complex for our purposes):

$$\psi_{n,l,m_l}(r, \theta, \phi) = \psi_{n,l,m_l} \tag{1.20}$$

According to our rules, a valid hydrogen wavefunction could be $\Psi_{1,0,0}$, since n is a positive, non-zero integer, l is a non-negative integer that is less than n, and m_l is an integer no less than $-l$ and no greater than $+l$. Similarly, $\Psi_{2,1,-1}$ would be okay according to our rules. In contrast, $\Psi_{1,1,2}$ would not be a valid hydrogen wavefunction.

1.18 Hydrogen Atomic Orbitals

A property of the hydrogen atom wavefunctions is that any wavefunction with the same principal quantum number, n, has the same energy, while wavefunctions with larger n values have more energy. This means that n corresponds to our concept of electron shells, where an atom can have multiple electron shells (wavefunctions with different n values) and more than one electron can occupy a shell (multiple wavefunctions can have the same principal quantum number).

To better understand the wavefunctions of various shells, we can list all of the wavefunctions for the first couple of principal quantum numbers (**Table 1.5**). What can be seen is that for the first shell (n = 1), there is only one possible wavefunction, while four are available in the second shell (n = 2), and nine in the third (n = 3). This means that an electron in a hydrogen atom with low energy can occupy one wavefunction in the first shell. With more energy, it can occupy any of the four wavefunctions in the next shell, and so on. Under conditions we typically might encounter (such as a hydrogen atom at room temperature), the amount of energy needed to get to the second shell is much greater than what is available, so effectively all hydrogen atoms have electrons in the n = 1 wavefunction.

What does the wavefunction in this lowest energy shell look like? From Table 1.5 you can see that the wavefunctions in each shell can be grouped according to their orbital angular momentum quantum number, l. When l = 0 (the only option for n = 1), it turns out that the shape of the wavefunction depends only on its radial position and is independent of its angular position (i.e. θ and ϕ don't matter). This means these wavefunctions are spherically symmetric, i.e. they are the same at any angle for a given radius. Because of their spherical symmetry, these wavefunctions are called s orbitals: 1s for the first shell, 2s for the second, and so forth (Table 1.5). As mentioned above, the wavefunction ultimately describes the probability of finding an electron at a given position (i.e. at a specific radial position). It turns out that besides being in the nucleus, the electron has some probability of being at any radial position (Figure **1.45A**). However, there is a maximal probability of finding the electron at some specific distance, the Bohr radius. While such a probability distribution can be depicted in three-dimension (**Figure 1.45B**), drawings of the 1s orbital typically depict the electron density at the Bohr radius, making the orbital appear like the surface of a sphere (**Figure 1.45C**).

Although the wavefunctions for the second shell of hydrogen are generally not occupied, their shapes have relevance to other atoms and are therefore worth considering. When n = 2 and l = 0, we get the 2s orbital. This wavefunction is also spherically symmetric.

n	l	m_l	ψ_{n,l,m_l}	Atomic Orbital
1	0	0	$\psi_{1,0,0}$	1s
2	0	0	$\psi_{2,0,0}$	2s
2	1	-1	$\psi_{2,1,-1}$	$2p_x$, $2p_y$, $2p_z$
2	1	0	$\psi_{2,1,0}$	
2	1	1	$\psi_{2,1,1}$	
3	0	0	$\psi_{3,0,0}$	3s
3	1	-1	$\psi_{3,1,-1}$	$3p_x$, $3p_y$, $3p_z$
3	1	0	$\psi_{3,1,0}$	
3	1	1	$\psi_{3,1,1}$	
3	2	-2	$\psi_{3,2,-2}$	$3d_{xy}$, $3d_{xz}$, $3d_{yz}$, $3d_{x^2-y^2}$, $3d_{z^2}$
3	2	-1	$\psi_{3,2,-1}$	
3	2	0	$\psi_{3,2,0}$	
3	2	1	$\psi_{3,2,1}$	
3	2	2	$\psi_{3,2,2}$	

Table 1.5 Atomic Orbitals for a Hydrogen Atom. Shown is information about the possible atomic orbitals for a hydrogen atom with a principal quantum number (n) of up to three. l refers the orbital angular momentum quantum number and m_l the magnetic quantum number. The specific wavefunction for each set of quantum numbers is indicated with Ψ and alone or in combination make up the atomic orbitals indicated in the last column.

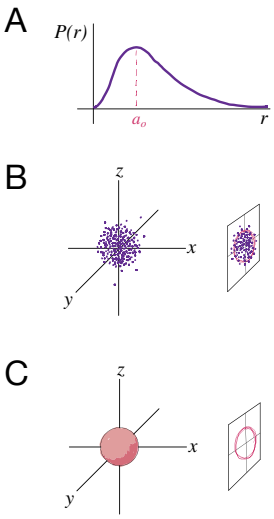


Figure 1.45 Representations of the Hydrogen 1s Orbital. A) Probability density of the 1s orbital in terms of radial position. The most probably radius (highest point in the probability density) is the Bohr radius, abbreviated as a_o. B) The three-dimensional representation of the 1s probability density distribution is shown on the left. A slice of this distribution through the yz plane is shown on the right. C) A simplified representation of the distribution from part B is shown, where the most probable radius (the Bohr radius) is shown as a surface.

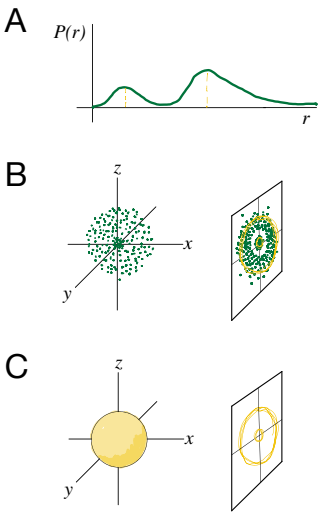


Figure 1.46 Representations of the Hydrogen 2s Orbital. A) Probability density of the 2s orbital in terms of radial position. B) The three-dimensional representation of the 2s probability density distribution is shown on the left. A slice of this distribution through the yz plane is shown on the right.) C) A simplified representation of the distribution from part B is shown, where the most probable radius is shown as a surface.

However, instead of a single radial position with a peak of probability, the 2s orbital has two (**Figure 1.46**). For n = 2, there is also a second possible orbital angular momentum quantum number, l = 1. The distribution of electrons in such an orbital does depend on angular position (θ and ϕ), as well as radial position (r). There are three such wavefunctions (m_l = -1, 0, and 1) and this magnetic quantum number defines the relative orientation of these wavefunctions. These wavefunctions alone or in certain combinations make up what are known as p orbitals pointing in different directions: $2p_x$, $2p_y$, $2p_z$. In appearance, these p orbitals have two lobes and there is no probability density in the nodal plane (**Figure 1.47**).

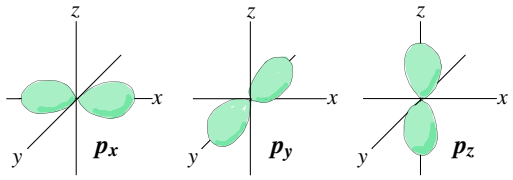


Figure 1.47 Representations of the Hydrogen 2p Orbitals. Shown are simplified three-dimensional representations of the three 2p orbitals.

In addition to one s and three p orbitals, the third electron shell has five d orbitals: $3d_{xy}$, $3d_{yz}$, $3d_{xz}$, $3d_{z^2}$, and $3d_{x^2-y^2}$. The shapes of these orbitals are more complicated still and are shown in **Figure 1.48**.

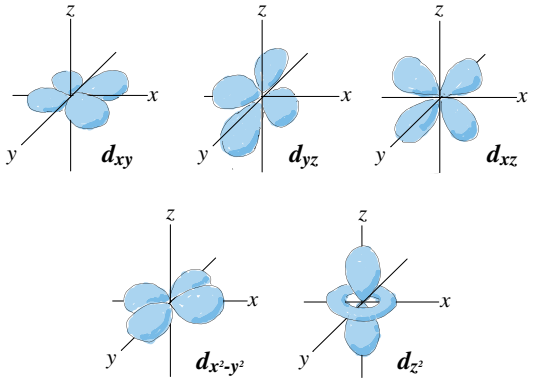


Figure 1.48 Representations of the Hydrogen 3d Orbitals. Shown are simplified three-dimensional representations of the five 3d orbitals.

1.19 Atomic Orbitals and the Periodic Table

Before we can apply our understanding of the electronic structure of the hydrogen atom to other elements, we need to introduce one more quantum number, the spin quantum number, m_s.

The spin quantum number does not directly fall out of the Schrödinger equation. However, a more complete and complex quantum mechanical description of the atom does produce this term. There are two possible values for the spin quantum number: +1/2 and -1/2. However, these two states are often referred to simply as spin up and spin down, and can be schematically represented as an arrow pointing up or down (**Figure 1.49**).

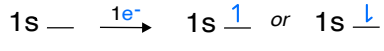


Figure 1.49 Representation of Electron Spin. An electron can be added to an orbital, such as a 1s orbital, either in a spin up state (left blue arrow) or spin down (right blue arrow).

Including the spin quantum number with the other three quantum numbers allows us

to fully specify the atomic orbital of any electron in an atom. For example, a hydrogen atom with 1 electron in its lowest energy 1s orbital could be described by quantum numbers: $n = 1, l = 0, m_l = 0$, and $m_s = +1/2$. This electron would occupy the wavefunction of $\Phi_{1,0,0,+½}$ (where the general form of a hydrogen wavefunction that includes spin is $\Phi_{n,l,m_l,m_s}(r,\theta,\phi) = \Phi_{n,l,m_l,m_s}$), or more simply, there would be a spin up electron in the 1s orbital (**Figure 1.50**). In the absence of an external magnetic field, the electron in a wavefunction with a -1/2 spin would have the same energy, and could have been occupied by our electron instead (1s with spin down).

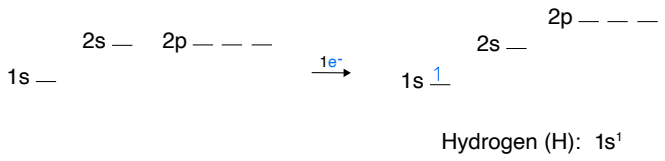


Figure 1.50 Orbital Energies for the n = 1 and n = 2 Shells. Left: In a one-electron atom, the 2s and 2p orbitals are equal in energy, Right: A spin-up electron placed in the 1s orbital (shorthand: $1s^1$); in multi-electron atoms, the occupied 1s causes the 2s to fall below the 2p orbitals.

In going from a hydrogen atom to other elements, the same atomic orbitals can be used. However, now we need to be able to add more than one electron to the orbitals. This can be done by adding one at a time, with some additional rules. One thing that turns out to be required is that no two electrons in an atom have the same set of quantum numbers, a rule called the Pauli exclusion principle. Thus, for a helium atom, the first electron, like hydrogen, can add to a 1s orbital, say spin up (with associated wavefunction $\Phi_{1,0,0,+½}$). For helium's second electron, it could not occupy the 1s orbital with the same spin state (wavefunction $\Phi_{1,0,0,+½}$), because this would violate the Pauli exclusion principle. However, it can occupy the 1s orbital with a spin down state (i.e. $\Phi_{1,0,0,-½}$) as seen in **Figure 1.51A**.

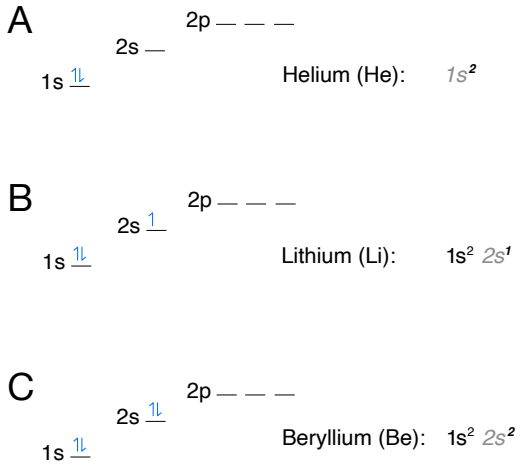


Figure 1.51 Electron Configurations of Elements that Fill the 1s and 2s Orbitals. Electron configurations of A) Helium (two electrons), B) Lithium (three electrons), and C) Beryllium (four electrons).

You might wonder if the second electron of the helium atom could have been in the 2s orbital instead of the 1s (either spin up or down, since the 2s is a different orbital than the already occupied 1s one and thus fulfills the Pauli Exclusion Principle). Indeed that is possible. However, recall that for the hydrogen atom, orbitals with a higher principal quantum number are higher in energy (Figure 1.50), and that the jump in energy between $n = 1$ and $n = 2$ is so large at room temperature as to be largely insurmountable. Thus, it makes sense to fill the lowest energy orbitals before filling the higher energy ones.

What happens if we want to add a third electron, say for the third element in the periodic table, lithium? With the orbitals in $n = 1$ filled (See Table 1.5 again), the next available orbitals are the 2s and 2p orbitals of $n = 2$. For our model of the hydrogen atom from the Schrödinger's equation with one electron total and no spin, the 2s and 2p orbitals have the same energy (Figure 1.50). However, the presence of electrons in the 1s orbital causes this to no longer be the case, with the 2s orbital now being lower in energy than the 2p orbital (Figures 1.50 and 1.51A). So the valence electron of lithium ends up occupying

the 2s orbital (**Figure 1.51B**). Adding the next electron for the element beryllium fills the 2s orbital — while leaving the three 2p orbitals unoccupied (**Figure 1.51C**).

When we get to the next element, boron (atomic number 5), the 2p orbital can begin to be occupied. The three 2p orbitals are actually equivalent in energy (**Figure 1.52A**), so the next electron can go into any of the 2p orbitals. Moving on to carbon we add one more electron. Where does it go: the same p orbital or a different one? It turns out that putting an electron in a different p orbital is less energetically costly than doubly occupying the original orbital. This idea that electrons preferentially stay unpaired to fill energetically equivalent sub-orbitals (like the p orbitals) before pairing electrons in an orbital is known as Hund's Rule (Figure **1.52B**). You can see its further application when one more electron is added for nitrogen (**Figure 1.52C**). However, with one more electron for oxygen, there are no longer any more unoccupied p orbitals, and so one of the p orbitals becomes doubly filled (Figure **1.52D**).

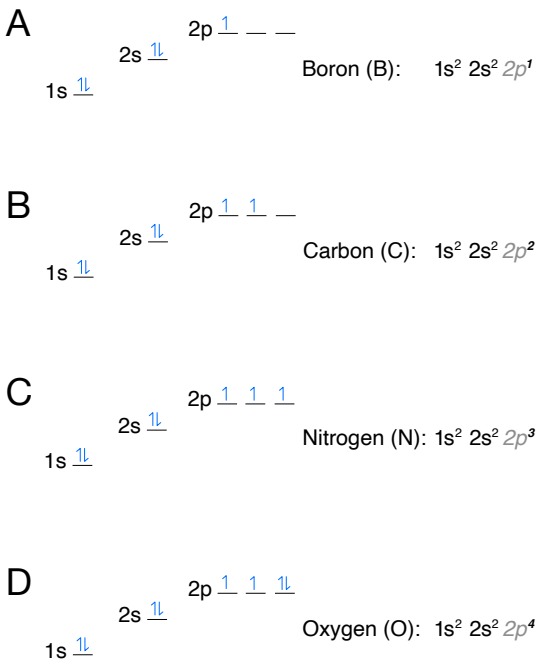


Figure 1.52 Electron Configurations of Elements that Fill the 2p Orbitals. Electron configurations of A) Boron (five electrons), B) Carbon (six electrons), C) Nitrogen (seven electrons), and D) Oxygen (eight electrons).

When elements have enough electrons to start occupying the third shell (**Figure 1.53**), similar to the second shell, the 3s orbitals are occupied first, and then the 3p orbitals.

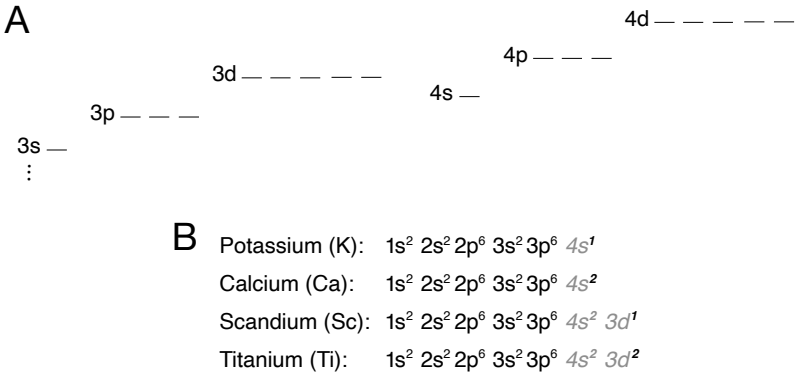


Figure 1.53 Filling of d Orbitals. A) Schematic of the energies of the n = 3 and n = 4 orbitals as orbitals are filled. Note, the 4s orbital has a lower energy than the 3d orbital, meaning that electrons fill the 4s orbital before the 3d orbitals are occupied. B) Electron configurations of selected elements.

However, after the 3p orbitals are filled, it turns out that the 4s orbitals are slightly lower in energy than the 3d orbitals, so they are filled first. So, for an element like potassium or calcium, they fill their 4s orbitals before the 3d orbitals. With more electrons, those 3d orbitals begin to be filled in elements such as Scandium and Titanium, creating the large blocks of atoms known as the transition metals.

Altogether, the presence of atomic orbitals and how they are filled explains the structure of the periodic table (**Figure 1.54**), where elements in the first row have only the 1s orbital available, which can hold up to two electrons, the second row fills the 2s orbital, before filling the 2p orbitals (for a total of 8 electrons in this row). The third row fills the 3s orbitals and then the 3p orbitals. In the fourth row, the 4s orbitals are filled before the 3d orbitals are filled, and so on.

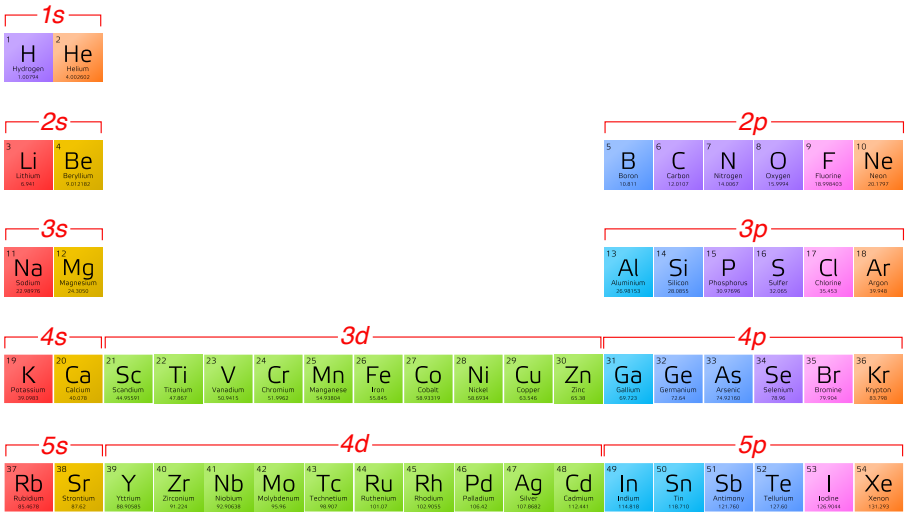


Figure 1.54 Structure of the Periodic Table in Terms of Orbitals. The first five rows of the periodic table are shown where filling of specific orbitals is highlighted.

The presence of atomic orbitals and how they are filled also explains many of the properties of these elements and the compounds that can be made from them. For the organic elements, one idea we will be coming back to is that hydrogen atoms only have an s orbital, but carbon, nitrogen, and oxygen atoms have s and p orbitals.



CHAPTER 2
Amounts and Concentrations

Motivation and Overview: The effects atoms or molecules have on a system often depend on how much of these particles there are. For example, when there is a saltier environment outside of a cell than inside (as detailed in the next chapter), the cell can shrivel up and die. Thus, it is important to have ways of quantitatively describing "how much" of something is present (for our example, the "saltiness" inside and outside our cell). In this chapter we first focus on different ways to describe the amount of particles. Because these amounts can be very large or very small, we examine strategies for dealing with such numbers. We then look at how conversion factors allow us to go between different types of amounts, leading us to consider the concept of a mole. Finally, because biological molecules are typically dissolved in water, we see how the idea of concentrations can be useful.



Figure 2.1 A tempting snack of milk and cookies.

A. Ways of Describing Amounts

There are many different ways we can describe the amount of something, and the milk and cookies pictured in **Figure 2.1** give us a simple way to explore a couple of them. Let's start with what is the most intuitive amount: the number.

2.1 Number

As a measure of amount, the number is just how many of a given object we can count. In our example from Figure 2.1, there are five cookies. We can apply this idea at the molecular level, too. While the composition of both the cookies and milk is highly complex (i.e. there are a lot of different kinds of molecules in each), we could describe the number of table sugar (sucrose) molecules found in our five cookies, or the number of water molecules in our milk (how we might get those numbers will have to wait for later in the chapter).

Knowing the number of something can be valuable by itself, but it is often more useful in relation to the number of something else. For example, suppose we know that one molecule of 'A' reacts in some way with one molecule of 'B' to make one molecule of 'C,' as shown in **Figure 2.2**. Knowing the number of 'A' and 'B' molecules that we have will determine how much of molecule 'C' we can make, and how much of 'A' and 'B' will be left over. For example, suppose we had 2 molecules of 'A' and 3 molecules of 'B.' Because we need 1 'A' and 1 'B' molecule to make 1 'C' molecule, the 'A' molecules are limiting and we can only make as much 'C' as we have 'A,' i.e. two molecules of 'C.' Since we started with 3 molecules of 'B,' but used up 2 to make 2 'C' molecules, we have 1 molecule of 'B' left.



Figure 2.2 Theoretical reaction of molecules A and B. The arrow means a transformation is taking place. Here molecules A and B react to become a new molecule, C. The ones in front of each molecule indicate that one A and one B molecule make one C molecule. These numbers are called the stoichiometric coefficients, and don't have to each be one. For example, a two in front of the B would mean that two molecules of B combine with one molecule of A to make one molecule of C. In this figure the ones are included to make the concept clear; in most chemical equations, stoichiometric coefficients of one are omitted.

2.2 Mass

Another way to describe the amount of something is its mass. The mass of an object is effectively how much it weighs (Note: technically, mass and weight differ in physics — but in everyday speech, 'weight' almost always means mass).

To quantify the mass of something, we need a unit of mass. We could choose any number of different units of mass: pounds, tons, atomic mass units, etc. However, for scientific measurements we use the metric system and the base unit of mass is a gram, abbreviated as 'g'. For a sense of what the mass of one gram is, a standard paper clip is about one gram (**Figure 2.3A**). Applied to our cookies example, each cookie has a mass just under 12 g, equivalent to roughly 12 paper clips (**Figure 2.3B**).

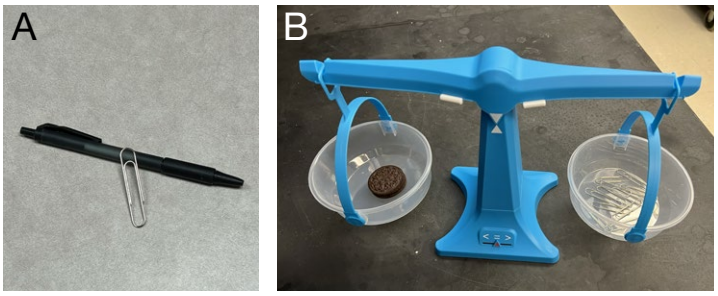


Figure 2.3 Mass of one paper clip and one cookie. A) One standard paper clip weighs about 1 gram. B) One cookie is about 12 grams, roughly the mass of 12 paper clips. Note: a traditional two-pan balance is shown; modern labs typically use a digital scale.

Thus, the five cookies accompanying our glass of milk in Figure 2.1 would have a total mass of about 60 g.

We can determine the mass of an object, like our cookies, using a scale. It is worth noting that the milk in our example also has a mass. However, being a liquid, measuring the mass of the milk is a bit more complicated than measuring a solid like our cookies. Still, if we subtract the mass of the empty glass, it can be done (**Figure 2.4**). As mentioned above, there are sucrose and water molecules in the cookies and milk. Individually, each of these molecules has a mass in grams. Collectively, there is a total mass of sucrose in a cookie or a total mass of water in a glass of milk.

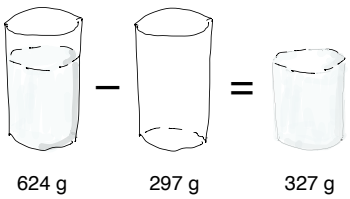
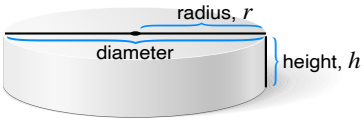


Figure 2.4 Measuring the mass of a liquid. The mass of the milk alone is the mass of the glass with milk in it minus the mass of the glass.

2.3 Volume

Volume is yet another way to describe the amount of something. The volume of an object is how much physical space an object takes up. For example, for one cookie we could use simple geometry to approximate its volume as a cylinder: We would measure the diameter of the top cookie wafer, use that information to determine the area of that circle, and then multiply that area by the height of the cookie to get a volume (**Figure 2.5**).



$$V_{cylinder} = (\pi \times r^2) \times h$$

Figure 2.5 Approximating the volume of one cookie as a cylinder. The width of a circle is its diameter, which divided by two is its radius. The circular area of the top of the cylinder is the square of its radius times the constant pi (roughly 3.14). Multiplying this area by the cylinder's height gives the cylinder's volume.

Volumes are especially easy to directly measure for liquids. For example, the volume of the milk in our glass could be determined by transferring it to a measuring cup, a marked beaker, a graduated cylinder, or even a syringe. The convenience of determining liquid volume makes it the most common way to describe liquid amounts.

The standard scientific unit for volume in the metric system is the liter, commonly abbreviated as 'L' or 'l' (the lower-case 'L'). An intuition for how much volume is taken up by a liter is that large bottled waters are often one liter (**Figure 2.6**). For those familiar with Imperial units, a liter is also roughly equivalent to a quart. In our milk and cookie example, our glass of milk would have a volume of about 0.33 L. The approximate volume of our cookie is 0.021 L. The fact that the volume of one cookie is considerably

less than our glass of milk makes sense, as many cookies would be needed to fill the same volume as our milk.



Figure 2.6 Volume taken up by one liter. Shown is a 1L bottled water.

B. Dealing with Big and Small Numbers

From the last section, the approximate volume of one cookie, 0.021 L, is a number that is a bit inconvenient to work with. However, many amounts are even worse. For example, the mass of the largest blue whale ever recorded was nearly 200,000,000 g (that's a lot of zeros and paper clips). Even less pleasant, an average *E. coli* bacterium in your guts has a mass of about 0.000000000001 g (**Figure 2.7**). Both of these numbers have so many zeros that it's not only inconvenient but also easy to lose track of how many there are. Such big or small numbers are not uncommon when working with molecules, so how do we deal with them? There are several possible strategies, and we will start by looking at how such numbers can be represented by scientific notation.

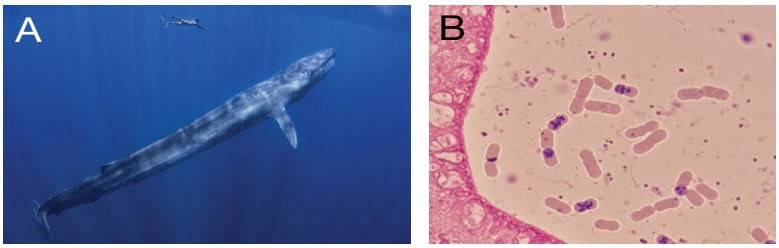


Figure 2.7 Some very large and very small things. A) A blue whale and a diver (at the top). Blue whales are the largest animal on earth, with females being larger and having an average length of about 24 m. B) An *Escherichia coli* bacterium is a relatively small organism. Average length is from 2–4 µm.

2.4 Scientific Notation

The mass of the largest blue whale ever recorded can be represented in scientific notation as such:

$$200{,}000{,}000 \text{ g} = 2 \times 10^8 \text{ g} \qquad (2.1)$$

The mass in scientific notation (right side of the equal sign) has a couple of components. Leftmost is always a number from one to less than ten (in this case, two). Following that is the multiplication sign and a value of ten raised to some power (ten to the eighth, here).

To see why the number has this form, it's useful to first review what raising a number to something means. When a number is raised to a power, that number is multiplied by itself that many times. For example, 10^2 is 10 times itself, 10 x 10 = 100, while 10^4 is 10 x 10 x 10 x 10 = 10,000. How does this power-of-ten term affect the first number? Suppose you were to multiply 2 by 10 (10^1). You would get 20. If you multiply 2 by 100 (10^2) you get 200. One way to think of this is that for every power of ten you multiply by, you move the decimal over that many places to the right (where there are always zeros that can be written after our first number). Consider 2 x 10^2:

$$2 \times 10^2 = 2.00 \times 10^2 = 2.\underset{\frown}{0}\,\underset{\frown}{0} = 200 \qquad (2.2)$$

In this, we see that 2 is equivalent to 2.00, and that multiplying that number by 10^2 results in moving the decimal place to the right two times, giving us 200. Going back to Equation 2.1, we see that 2.0 x 10^8 g gives us the original number, 200,000,000 g, by moving the decimal to the right eight times.

This shortcut for going from scientific notation to normal number representation can be used in reverse to go from a normal number to the scientific notation. For the number 200,000,000 we would need to move the (implied) decimal point eight times to the left to get 2, so the representation in scientific notation would be 2 x 10^8:

$$200{,}000{,}000 = 200{,}000{,}000.0 = 2\,\underbrace{0\,0\,0\,0\,0\,0\,0\,0}\,0. = 2.0 \times 10^{8} \qquad (2.3)$$

A couple of points worth noting. Up to this point, we have only used numbers with a bunch of zeros. However, things work exactly the same with more complicated numbers. For example, consider 325. In scientific notation we could move the decimal two places over to get 3.25×10^{2}.

Another thing to note is that numbers less than one can also be represented in scientific notation. For example, the approximate mass of an *E. coli* bacterium is:

$$0.000000000001\ \text{g} = 0.\underbrace{0\,0\,0\,0\,0\,0\,0\,0\,0\,0\,0\,1}\ \text{g} = 1 \times 10^{-12}\ \text{g} \qquad (2.4)$$

Here, to get the mass in scientific notation, we move the decimal to the right, instead of left (as we did in Equation 2.3), and we move it to the right of the first non-zero digit. In our example, we need to move the decimal twelve times to get to the right of the one. Because we have moved the decimal to the right, we raise the ten to a negative power, here ten to negative twelve. Indeed, when a number is smaller than one, its scientific notation representation will always have a negative power. In going from the scientific notation to the regular notation, a negative exponent indicates that instead of multiplying the initial digit by some power of 10 that will make the number bigger (for example multiplying by $10^{2} = 100$), we divide it by some power of 10 to make it smaller ($10^{-2} = 1/10^{2} = 1/100$). For our bacterial mass, we take 1.0 and divide it by 10 twelve times, that is, move the decimal place over to the left of 1 twelve times.

Various mathematical operations can be performed on pairs of numbers in scientific notation, and comparisons can be drawn between them. With two numbers, say the mass of a female blue whale, 2×10^{8} g, and an E. coli bacterium, 1×10^{-12} g, the larger number will be the one with the power of ten that is the greater, more positive integer (note, if the power of 10 is the same, just compare the number before the multiplication sign). In our example, $8 > -12$, so, unsurprisingly, a whale has more mass than a bacterium.

Suppose we wanted to know exactly how many times more massive the whale is compared to the bacterium. We need to divide the mass of the whale by the bacterium's mass. For any of the mathematical operations discussed in the rest of this section, we can always convert the numbers from scientific notation to normal representation, do the math operation, and then convert the result back to scientific notation. However, doing operations directly in scientific notation is not especially difficult. For our relative mass calculation, we can separately divide the numbers before the multiplication sign and those after. The division of the terms before the multiplication sign is straightforward: $2/1 = 2$. However, how do we deal with: $10^{8}/10^{-12}$? You may recall from algebra that when dividing exponents (the 8 and −12 terms) with the same base (10), you take the difference of their exponents: $8 - (-12) = 20$. That is, $10^{8}/10^{-12} = 10^{20.}$ So altogether:

$$(2 \times 10^{8})/(1 \times 10^{-12}) = (2/1) \times (10^{8}/10^{-12}) = 2 \times 10^{20} \qquad (2.5)$$

This says that the mass of the whale is over 20 orders of magnitude (powers of 10) greater than the bacterium, or that 1 whale has as much mass as 2×10^{20} bacteria.

An interesting wrinkle arises if we wanted to determine what fraction of the mass of a female blue whale one *E. coli* bacterium takes up, i.e. the reciprocal of what we just did: $(1 \times 10^{-12}\ \text{g})/(2 \times 10^{8}\ \text{g})$. As before, we can divide the terms before the multiplication sign, $1/2 = 0.5$, and those after, $10^{-12}/10^{8} = 10^{-20,}$ to get the number 0.5×10^{-20}. However, this number doesn't conform to what we said a number in scientific notation should be. Specifically, the first number, 0.5, isn't at least one (although it does fulfill the other requirement of being less than ten). How can we deal with this? If we multiplied the

first term by ten, 0.5 would become 5.0 and be in our desired range. There is a problem, though. We can't just take a number and multiply it by anything we want, unless the number we multiply by is one, since the product won't change. So when we multiplied the first term by 10, if we also divided the term after the multiplication sign by 10, we are effectively multiplying our number by one (multiply by ten, then divide by ten), which is okay. Doing so in our example, when we divide 10^{-20} by 10 (10^{1}) we just reduce the initial exponent by one, to get 10^{-21}. So to summarize:

$$0.5 \times 10^{-20} = (0.5 \times 10) \times (10^{-20}/10) = 5.0 \times 10^{-21} \quad (2.6)$$

This trick of adjusting a number can often be necessary when we do other basic mathematical operations on numbers in scientific notation (**Figure 2.8**).

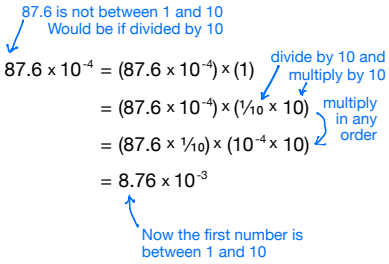


Figure 2.8 The logic of how to adjust a number to conform to scientific notation. In this example, the initial number does not conform to the format expected for scientific notation. However, adjusting the number before the multiplication sign coupled with compensating adjustments to exponent gives a number in the right format.

Multiplying two numbers in scientific notation is similar to division, except that the first terms are multiplied, and the second term exponents are added. The multiplication of the first terms might generate a number larger than ten, but as we've discussed, this can be dealt with by dividing the first factor by some factor of ten, and multiplying the second factor by the same factor of ten.

When adding or subtracting two numbers in scientific notation, if the power of ten terms are the same, the first terms can simply be added or subtracted, maintaining the same power of ten term in the answer. For example, in adding the mass of two bacteria:

$$(1 \times 10^{-12}) + (1 \times 10^{-12}) = 2 \times 10^{-12} \quad (2.7)$$

However, if the two terms have different powers of ten, you will have to adjust one of the numbers to make the power of tens match, and then proceed to add as above. Note, if your answer does not conform to the scientific notation requirements, it will have to be adjusted. As an example:

$$(2.35 \times 10^{3}) + (1 \times 10^{5}) = (0.0235 \times 10^{5}) + (1 \times 10^{5}) = 1.0235 \times 10^{5} \quad (2.8)$$

A summary of working with scientific notation is shown below (**Figure 2.9**):

Figure 2.9 Scientific notation guide.

1) **Going from regular notation to scientific notation**: Move the decimal until it is just after first digit and count how many places it moved. If moved to the left, the power of ten will be the number of places moved as a positive number. If moved to the right, the power of ten will be the number of places moved as a negative number.

   2,136 = 2.136×10^{3}

2) **Going from scientific notation to regular notation**: Move the decimal over as many places as the power of ten. If the power is positive, move the decimal to the right. If the power is negative, move the decimal to the left.

   3.9×10^{-4} = 0.00039

3) **Adding/Subtracting numbers in scientific notation:** Either convert to regular notation, do the operation, and convert back; or make sure both numbers are the same power of ten before adding/subtracting the values before the multiplication sign without changing the power of ten. Adjust answer to conform to scientific notation if necessary.

   $(2.1 \times 10^{2}) + (1.1 \times 10^{1}) = (2.1 \times 10^{2}) + (0.11 \times 10^{2}) = 2.21 \times 10^{2}$

4) **Multiplying/dividing numbers in scientific notation:** Either convert to regular notation, do the operation, and convert back; or multiply/divide the values before the multiplication sign, and multiply/divide the values after the multiplication sign (remember that multiplying tens to a power is just adding the exponent, dividing is subtracting). Adjust answer to conform to scientific notation if necessary.

   $(3 \times 10^{4}) \times (4 \times 10^{-2}) = 12 \times 10^{2} = 1.2 \times 10^{3}$.

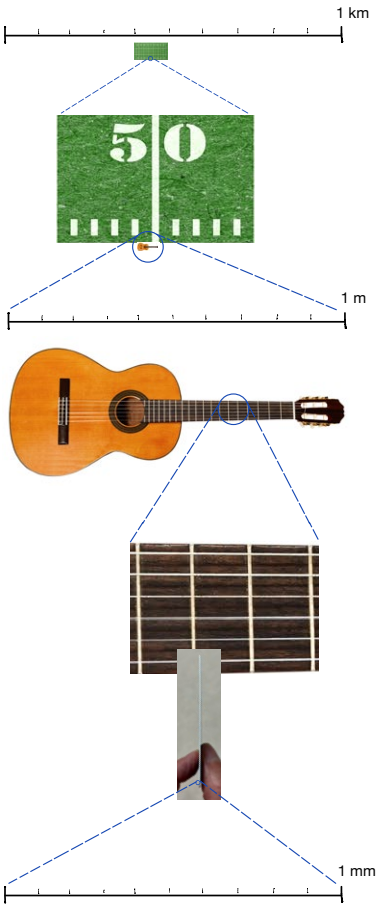


Figure 2.10 Lengths from 1 kilometer to 1 millimeter. Shown are jumps from 1 kilometer to 1 meter to 1 millimeter. Each is a one-thousand-fold jump, for a total of a one-million-fold difference in length. Example objects are shown to provide a sense of scale and include a football field (just under 100 m or ~1/10 km), a guitar (~1 m), and the edge of a credit card (~ 1 mm).

2.5 Prefixes on Units

Another approach, complementary to scientific notation, is using unit prefixes. In the metric system, there are prefixes to describe thousand-fold jumps in amounts. For example, 1,000 grams is 1 kilogram, and in the other direction, 1/1,000th of a gram is 1 milligram. Put another way, 1/1000th of a kilogram is 1 gram, and 1,000 milligrams make up a gram. These prefixes can be attached to any standard metric units and modify the base unit the same way. For example, 1 milliliter is 1/1,000th of 1 liter, or 1,000 milliliters make up 1 liter. In general, our brains tend not to be so good at internalizing how amounts compare when there are one-thousand-fold jumps. **Figure 2.10** tries to provide some context, as well as give some more practice with these prefixes.

In biological systems, we rarely use prefixes for amounts larger than kilos. However, we do often encounter amounts that are less than milli- amounts. For these smaller amounts, 1/1000th of a milligram is called a microgram and 1/1000th of a microgram is a nanogram. Prefixes are often abbreviated with a single letter, where decreasing in 1,000-fold increments of mass we have: 1 kg (one kilogram), 1 g (one gram), 1 mg (one milligram), 1µg (one microgram - µ is the Greek letter mu), and 1 ng (one nanogram).

One microgram is 1/1,000th of a milligram, which is itself 1/1,000th of a gram. So in terms of grams, 1 microgram is ((1/1000) x (1/1000)) = 1/1,000,000th of a gram. These relationships are easier to represent in terms of scientific notation, where 1/1,000th is 1 x 10^{-3}. Thus, 1 microgram would be 1 x 10^{-3} milligrams, which is itself 1 x 10^{-3} grams, so 1 microgram would be (1 x 10^{-3}) x (1 x 10^{-3}) = 1 x 10^{-6} grams. Using scientific notation to describe the relationship of all masses relative to the base unit of grams: 1 kg = 1 x 10^{3} g, 1 mg = 1 x 10^{-3} g, 1 µg = 1 x 10^{-6} g, and 1 ng = 1 x 10^{-9} g. Thus, if there are 3 x 10^{3} g, we have 3 kg; if there are 7.2 x 10^{-6} g, we have 7.2 µg; and if we have 1.0 x 10^{-8} g (which is equivalent to 10 x 10^{-9} g), we have 10 ng. A summary of how metric prefixes are used is shown in **Table 2.1**.

Prefix	Abbrev.	Relation to Base Unit (Standard Notation)	Relation to Base Unit (Scientific Notation)	Example (Volume)
kilo-	k-	x 1,000	x 10^{3}	1 kl = 1 x 10^{3} L
–	–	x 1	x 10^{0}	1 L
milli-	m-	x 0.001	x 10^{-3}	1 ml = 1 x 10^{-3} L
micro-	µ-	x 0.000001	x 10^{-6}	1 µl = 1 x 10^{-6} L
nano-	n-	x 0.000000001	x 10^{-9}	1 nl = 1 x 10^{-9} L

Table 2.1 Metric Unit Prefixes.



Figure 2.11 A package with an unknown number of cookies. While the number of cookies cannot be discerned without opening the package, the mass of the package is easily determined.

Before we go on, it is worth noting that one other prefix that we will use in the context of length is centi-. The base metric unit of length is a meter (m), and a centimeter (cm) is 1/100th of a meter (1 x 10^{-2} m), or 10 millimeters (10 mm). Centi- is not commonly used scientifically as a prefix for masses or volumes. Also, the metric prefixes do not apply to counts of particles directly, but Section D introduces an alternative unit for counting that does use these prefixes.

C. Converting Between Amounts, Units

Because the amount of something can be described in different ways (Section A), it is often useful to be able to convert between them. This is especially true if one type of amount is easier to measure than another. For example, suppose we had a pack of the cookies shown in **Figure 2.11** and wanted to know how many cookies there were. If we could not see through the packaging, nor were able to open it, we could not directly count the cookies. However, if we could determine the total mass of cookies in the pack

and knew the mass of one cookie, we could calculate the number of cookies in the pack. While this example is somewhat fanciful, for a collection of molecules it is often not possible to count them directly to determine their number. However, measuring their mass is often straightforward.

2.6 What are Conversion Factors and How Are They Used?

For the cookie example we just described, the key to converting between the mass of the pack of cookies and the number of cookies is the mass of one cookie. Suppose the mass of the pack of cookies was 404 g (where we will assume that the mass of the packaging is negligible). As we mentioned previously, the mass of one cookie is about 12 grams. Intuitively, we expect that dividing the mass of the pack of cookies by the mass of one cookie, 404 g/12 g, would give the approximate number of cookies in the pack, 34 cookies (actual number is 33). However, in many cases, it is not as obvious how to convert between our amounts, and a systematic approach that works in all circumstances would be helpful.

The mass of one cookie is the basis for what we will call a conversion factor. A conversion factor is a quantitative relationship between two different things. In the case of the cookie, the conversion factor is the relationship between the mass of one cookie (12g) and the number of cookies (1 cookie). This ratio of 12 g : 1 cookie can be represented as a fraction to make it a conversion factor, which is read as "12 grams per 1 cookie":

$$\frac{12\ \text{g}}{1\ \text{cookie}} \tag{2.9}$$

Also true is the ratio of 1 cookie : 12 g, which gives a different, but equally valid conversion factor of "1 cookie per 12 grams" (and is just our previous conversion factor flipped):

$$\frac{1\ \text{cookie}}{12\ \text{g}} \tag{2.10}$$

So how do we use a conversion factor to determine the number of cookies in a pack, and which conversion factor do we use? The first step in our calculation is to determine the type of amount we are starting with and the type of amount we want to end up with (**Figure 2.112**). Here, we are starting with a mass amount (404 grams), and want a number amount (an unknown number of cookies). What we want to do is take our starting amount and multiply it by our conversion factor to convert things to our desired amount units. Considering just the units, let's see what units we end up with when we multiply our original units by each conversion factor. For the conversion factor in Equation 2.9 we get:

$$\text{g} \times \frac{\text{g}}{\text{cookie}} = \frac{\text{g} \times \text{g}}{\text{cookie}} = \frac{\text{g}^2}{\text{cookie}} \tag{2.11}$$

For the conversion factor in Equation 2.10 we get:

$$\text{g} \times \frac{\text{cookie}}{\text{g}} = \frac{\text{g} \times \text{cookie}}{\text{g}} = \text{cookie} \tag{2.12}$$

For the first conversion factor (2.9), we don't end up with the desired units of cookies at the end. In contrast, with our second conversion factor (2.10), the gram units in the numerator and denominator end up canceling out, leaving just our desired amount unit, the number of cookies. Thus, the conversion factor in Equation 2.10 is the one we want to use to do our calculation:

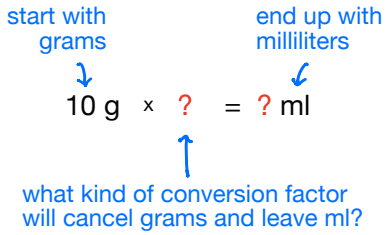


Figure 2.12 Strategy for converting from one unit to another using a conversion factor. In this example, you have 10.0 g of mercury and want to know how much volume it takes up in ml. From searching the internet, you find that there are 13.6 g of mercury per ml. To get an answer in ml, you need to use the conversion factor of 1 ml/13.6 g. This causes the gram units to cancel, leaving the answer in ml units (The answer is 10 g of mercury takes up 0.74 ml).

$$404\text{ g x }\frac{1\text{ cookie}}{12\text{ g}} = \frac{404\text{ g x }1\text{ cookie}}{12\text{ g}} = \frac{404\text{ x }1\text{ cookie}}{12} = 33.7\text{ cookies} \quad (2.13)$$

Although this approach may not seem easier than the intuitive one, it does give the same answer and can be applied to more complicated conversions, including multi-step conversions. Suppose we wanted to know how much volume is taken up by all of the cookies in a pack, but only knew the package of cookies weighed 404 g and that one cookie weighed 12 g and took up a volume of 0.021 L (mentioned in Section 2.3). We see that what we start with is in terms of g (404 g) and what we want to end up with is a volume (? L). The problem also gives us a couple of conversion factors: (1 cookie)/(12 g), (12 g)/(1 cookie), (1 cookie)/(0.021L), and (0.021L)/(1 cookie). Which conversion factors will allow us to go from grams to liters? With a little thought, we see the following gives us the desired final units:

$$\text{g x }\frac{\text{cookie}}{\text{g}}\text{ x }\frac{\text{L}}{\text{cookie}} = \text{L} \quad (2.14)$$

Notice grams cancel and cookies cancel, leaving just liters. Besides just trying different conversion factors, we could have gotten this by working forward. Since we start with grams, the only way to get rid of this is to use the conversion factor with grams in the denominator, which leaves us with cookies. To get rid of cookies and end up with liters, we can multiply this by the conversion factor with liters in the numerator, and cookies in the denominator.

Doing the calculation with our actual numbers and conversion factors, we find that the cookies in a package take up 0.71 L:

$$404\text{ g x }\frac{1\text{ cookie}}{12\text{ g}}\text{ x }\frac{0.021\text{ L}}{1\text{ cookie}} = 0.71\text{ L} \quad (2.15)$$

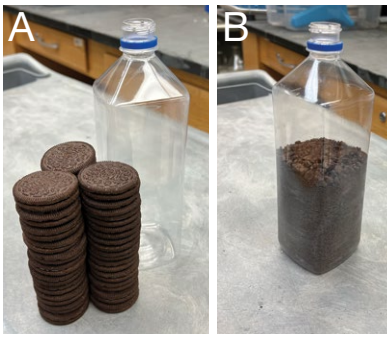


Figure 2.13 Volume of a bag of cookies. A) Three stacks of 11 cookies (one package) next to an empty 1-liter water bottle. B) All 33 cookies crushed up and dumped into the bottle. The estimated volume of the bag of cookies is 0.71 L. 1.0 L of water does not completely fill the water bottle (see Figure 2.6).

With any calculation, it is a good idea to assess whether the answer seems reasonable (calculator errors are easy to make). Our calculation says that a whole package of cookies would take up between 2/3 and 3/4 of a liter. Three cookies have roughly the same area as the bottom of the water bottle from Figure 2.6. So, if we divided the 33 cookies in the package into three stacks, their height should roughly correspond to the volume they would take up in the bottle (**Figure 2.13A**). To be more accurate, we can crush up all the cookies and put them in the bottle (**Figure 2.13B**). In doing so, we see that our volume estimate of 0.71 L is fairly decent, especially considering all of the approximations we made (weight of the cookies, dimensions of the cookies and bottle, treating each cookie as completely filling their volume, etc.).

2.7 Use of Conversion Factors With Unit Prefixes and Other Conversions

We just calculated that the total volume of all of the cookies in a package would be approximately 0.71 L. How many milliliters would that be? Intuitively, we know that there are many milliliters in a liter, so we know that the number of milliliters should be much larger than 0.71. A liter is 1000 ml (10^3 ml), so one quantitative approach to converting 0.71 L to ml would be to move the decimal point three places to the right to give a bigger number, resulting in an answer of 710 ml. Another way to approach the problem is to recognize that the relationship between milliliters and liters is a conversion factor: (1,000 ml)/(1 L). Calculating the volume in Equation 2.15 in terms of ml becomes:

$$404\text{ g x }\frac{1\text{ cookie}}{12\text{ g}}\text{ x }\frac{0.021\text{ L}}{1\text{ cookie}}\text{ x }\frac{1{,}000\text{ ml}}{1\text{ L}} = 710\text{ ml} \quad (2.16)$$

Suppose, for some reason, we wanted to calculate the volume of our package of cookies in nanoliters and all of our information had been in scientific notation. Here our conversion factor would be (1 x 10^9 nl)/(1 L), and the calculation would be as such:

$$4.04 \times 10^2 \text{ g} \times \frac{1 \text{ cookie}}{1.2 \times 10^1 \text{ g}} \times \frac{2.1 \times 10^{-2} \text{ L}}{1 \text{ cookie}} \times \frac{1.0 \times 10^9 \text{ nl}}{1 \text{ L}} = 7.1 \times 10^8 \text{ nl} \quad (2.17)$$

Conversion factors can be useful in other contexts, too. If you encounter amounts in the Imperial System where mass is in pounds (or ounces or tons), volume is in gallons (or cups, pints, quarts, or fluid ounces), and length is in yards (or feet, inches, or miles), you can convert them to metric units via conversion factors: (0.453592 kg)/(1 pound), (3.78541 L)/(1 gallon), and (0.9144 m)/(1 yard).

As useful as conversion factors are, not every quantity can be related to another via a conversion factor. Conversion factors between quantities exist when one quantity is directly proportional to another, that is, the ratio of one quantity to another is always the same constant. Sometimes that is not the case (**Figure 2.14**), and for such quantities it is necessary to use a formula to relate them. For example, temperature in the Imperial system (degrees Fahrenheit, or ˚F) is related to the temperature in the metric system (degrees Celsius, ˚C) as such:

$$°C = \frac{5}{9}(°F - 32) \quad (2.18)$$

According to this formula: water freezes at 0 ˚C or 32 ˚F; it boils at 100 ˚C or 212 ˚F; and standard body temperature is 37 ˚C or 98.6 ˚F. In general, we will not use many formulas in the fundamentals sections of the books. However, many of the intuitions we will try to develop are based on relationships that are best described in formulas, and some formulas will be examined in the further exploration sections.

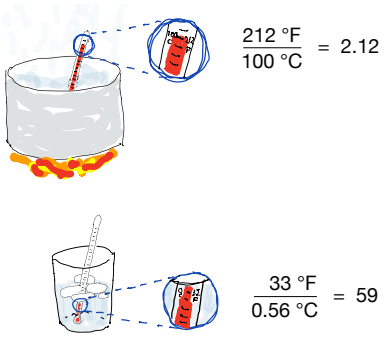


Figure 2.14 Temperatures in Celsius and Fahrenheit are not directly proportional to one another. Shown is a calculation of how many times greater the Fahrenheit temperature is relative to the Celsius temperature at the temperature water boils and just above where water freezes. Notice that this ratio is not the same at both temperatures, so using a simple conversion factor to convert between these units is not possible.

D. Concept of a Mole

Frequently we will be interested in how many copies of a specific atom or molecule are present in a sample. Because these particles are very small and their total numbers very large, it is usually not practical to count them directly. However, in many cases, such as a sample we have prepared, we will know the total mass of the particle of interest. As we saw last section in our cookie example, with the right conversion factor (cookies per gram), we can go from mass to the number. Every atom or molecule will have their own mass to number conversion factor, but let's consider the simplest atom first, a hydrogen atom. The mass of a hydrogen atom is about 1.66 x 10^{-24} g, meaning the conversion factors relating mass and number are 1 H atom/1.66 x 10^{-24} g and 1.66 x 10^{-24} g/1 H atom. Thus, if we had 100 hydrogen atoms, the mass of that collection of atoms would be about 1.66 x 10^{-22} g:

$$1.0 \times 10^2 \text{ H atoms} \times \frac{1.66 \times 10^{-24} \text{ g}}{1 \text{ H atom}} = 1.66 \times 10^{-22} \text{ g} \quad (2.19)$$

As another example, if we had 1.0 grams of hydrogen atoms, that would contain 6.02 x 10^{23} hydrogen atoms:

$$1.0 \text{ g} \times \frac{1 \text{ H atom}}{1.66 \times 10^{-24} \text{ g}} = 6.02 \times 10^{23} \text{ H atoms} \quad (2.20)$$

While these calculations are accurate, you will notice that the numbers of grams is quite small and the number of particles very large, making both unwieldy to work with. Further,

it is unclear how we might get a conversion factor for atoms and molecules besides the hydrogen atom. The solution to these issues can be found in the concept of a mole.

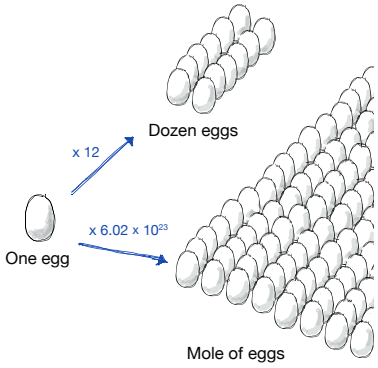


Figure 2.15 Two different possible ways to define a cluster of eggs. Twelve eggs is known as a dozen. Roughly 6.02 x 10^{23} eggs is known as a mole (only a small, small, small fraction of eggs in a mole are shown).

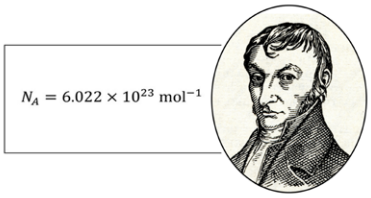


Figure 2.16 Avogadro's Constant. Avogadro's constant, sometimes abbreviated as N_A, defines the relationship between one mole and the number of particles in a mole (here shown as part of its full value). While Amedeo Avogadro did not actually determine the value of the constant that bears his name, it was named in his honor for Avogadro's contributions to science.

2.8 What is a Mole?

A mole is a certain number of objects or particles, similar to how a dozen is twelve objects/particles (**Figure 2.15**). However, a mole of particles is much, much, much more than a dozen particles. A mole of particles is defined as:

$$1.0 \text{ mole} = 6.02214076 \text{ x } 10^{23} \text{ particles} \tag{2.21}$$

For our purposes, we'll round this number to include three digits and consider it close enough:

$$1.0 \text{ mole} \approx 6.02 \text{ x } 10^{23} \text{ particles} \tag{2.22}$$

What this is saying is that if I had one mole of eggs, I would have 6.02 x 10^{23} eggs. Clearly this is much more than a dozen eggs, as we are saying that the number of eggs is roughly six followed by twenty-three zeros! If I had 2 moles of eggs, I would have 12.04 x 10^{23} eggs (just twice one mole of eggs). With 0.5 moles of eggs, I would have 3.01 x 10^{23} eggs.

With more complicated mole calculations, we can use a conversion factor. Our approximate definition of a mole (Equation 2.22) gives us the following conversion factors: 1 mole/6.02 x 10^{23} particles and 6.02 x 10^{23} particles/1 mole (**Figure 2.16**). So, if for some reason we had 4,230 moles of helium atoms, the number of helium atoms would be:

$$4{,}230 \text{ moles He x } \frac{6.02 \text{ x } 10^{23} \text{ He atoms}}{1 \text{ mole He}} = 2.55 \text{ x } 10^{27} \text{ He atoms} \tag{2.23}$$

We can also use our conversion factors to go the other way. Suppose we had 1.93 x 10^{15} water molecules, how many moles of water would we have?

$$1.93 \text{ x } 10^{15} \text{ molec x } \frac{1 \text{ mole water}}{6.02 \text{ x } 10^{23} \text{ water molec}} = 3.21 \text{ x } 10^{-9} \text{ moles water} \tag{2.24}$$

In our discussion of metric prefixes (Section 2.5) we noted that we don't use prefixes for the number of particles. In contrast, we can use prefixes for moles, where: 1 x 10^{3} moles = 1 kilomole = kmole; 1 x 10^{-3} moles = 1 millimole = mmole; 1 x 10^{-6} moles = 1 micromole = µmole; and 1 x 10^{-9} moles = 1 nanomole = nmole. Thus, for Equation 2.24, 3.21 x 10^{-9} moles of water is 3.21 nmoles of water molecules:

$$3.21 \text{ x } 10^{-9} \text{ moles water x } \frac{1 \text{ nmole water}}{1.0 \text{ x } 10^{-9} \text{ moles water}} = 3.21 \text{ nmoles water} \tag{2.25}$$

2.9 Atomic Mass and Moles

Although the number of particles in a mole may seem like an arbitrary number, it actually connects the number of particles to atomic mass. Consider a collection of hydrogen atoms. As we saw in Equation 2.20, one gram of hydrogen atoms is 6.02 x 10^{23} hydrogen atoms, and this number of atoms is a mole. Thus, one gram of hydrogen atoms is a mole of hydrogen atoms, with a conversion factor of 1 gram/mole of H atoms and 1 mole of H atoms/gram. For example, if we had two grams of hydrogen atoms, we would have 2 moles of hydrogen. If we had 0.5 moles of hydrogen, we would have 0.5 grams of hydrogen atoms.

Hydrogen is an element where the main isotope has a single proton, giving it an atomic mass of 1 amu (recall electrons are very small compared to protons, so we will ignore them for mass calculations). This means that the atomic mass of hydrogen is equal to its conversion factor of grams/mole and this relationship holds true for every element. The main isotope of carbon has an atomic mass of 12 amu (6 protons plus 6 neutrons). In atomic mass units, one carbon is 12-times more massive than a hydrogen (1 proton). Thus, 1 mole of carbon atoms would be 12 g of carbon. This also means that 2 moles would be 24 g, and 0.5 moles would be 6 g. As a more complicated example, if we had 50 g of carbon, we would expect it to be just a bit over 4 moles of carbon atoms (we would expect four moles of carbon to be 48 grams). More quantitatively:

$$50 \text{ g C} \times \frac{1 \text{ mole C}}{12 \text{ g C}} = 4.167 \text{ moles C} \qquad (2.26)$$

The bottom line is that for any element, if we want to get the conversion factor between mass and number of particles (in moles), we can just consult the periodic table and the element's atomic mass will also be how many grams of that element there are per mole.

This relationship between mass and particles can be extended to molecules. To determine the molar mass of any molecule (how many grams is in a mole of that molecule) we just need to add up the atomic masses of the atoms that comprise it (**Figure 2.17**). You are probably aware that water has the formula H_2O. This means that one water molecule is composed of two hydrogen atoms and one oxygen atom. Hydrogen has an atomic mass of 1 amu, and oxygen has an atomic mass of 16 amu. So a water molecule has a mass of 18 amu (2 x 1 amu + 1 x 16 amu), and its molar mass is 18 g/mole.

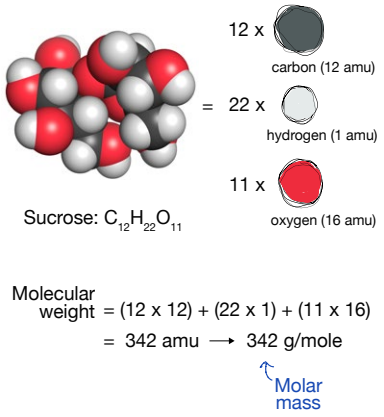


Figure 2.17 Molar mass of molecules. Because the molar mass of an element (how many grams are in a mole of an element), is equivalent to the element's atomic mass, the molar mass of a molecule (how many grams are in a mole of a molecule) is simply the sum of the atomic masses of all of the atoms that make it up. Shown is a space-filling model of table sugar (sucrose) with a molecular formula of $C_{12}H_{22}O_{11}$.

If we wanted to know how many moles are in one gram of water, we could just use its molar mass as a conversion factor:

$$1 \text{ g water} \times \frac{1 \text{ mole water}}{18 \text{ g water}} = \frac{1}{18} \text{ moles water} = 0.0556 \text{ moles water} \qquad (2.27)$$

This answer makes sense. We saw that one gram of hydrogen atoms is one mole of particles. A water molecule is 18-times more massive than a hydrogen atom, so we would expect that one gram of water molecules would have fewer molecules in it – in fact 1/18th as many.

If we wanted the actual number of water molecules in 1 g of water, we could just use the result from Equation 2.27 and the conversion factor relating moles to particles:

$$0.0556 \text{ moles water} \times \frac{6.02 \times 10^{23} \text{ water molec}}{1 \text{ mole water}} = 3.35 \times 10^{22} \text{ water molec} \qquad (2.28)$$

That said, generally we don't need to convert from moles to actual particle numbers. As mentioned in Section 2.1, particle number is mostly used to relate the number of different molecules, and mole units also allow us to do that. For example, if we know that we need 3 molecules of 'A' for every molecule of 'B,' it is equally true that we need 3 moles of molecule 'A' for every mole of molecule 'B.'

E. Concentration

In organisms, biological molecules typically "swim" in an environment made up of water. Thus, another useful way to quantify a molecule is to describe the amount of molecules found in a given volume of this watery environment, i.e. the concentration of the molecule. But before we dive into the details of calculating and using concentrations, we

need to understand the concept of a solution, as well as a number of terms associated with solutions.

2.10 Solutions

When two (or more) substances are combined (without reacting or binding to one another), the result is a mixture (**Figure 2.18**). Viewed at the molecular level, there are two kinds of mixtures. If there is an uneven distribution of the molecules, for example the molecules of one substance clump together, the mixture is a heterogeneous mixture (Figure 2.18, left). On the other hand, if all of the molecules of the two substances are evenly dispersed, the mixture is a homogeneous mixture (Figure 2.18, right). A homogeneous mixture goes by a special name, a solution.

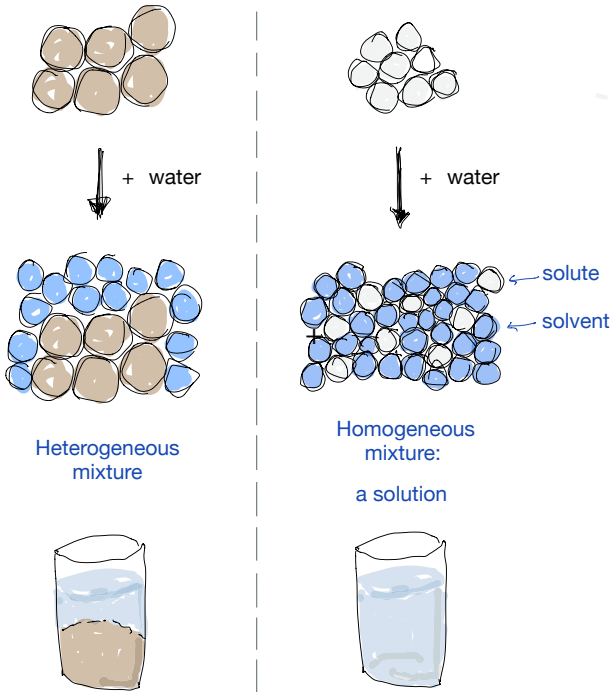


Figure 2.18 Mixtures. Shown at the top is what could happen when a substance made of many molecules is added to water (each molecule is depicted as a ball). On the left, the substance (composed of brown balls) does not dissolve into individual molecules in water (blue balls). On the right, the substance (composed of white balls) does dissolve, becoming evenly distributed among the water molecules. Below the schematics are an example of a heterogeneous mixture, sand in water, and a homogeneous one, sugar dissolved in water.

Atoms and molecules can exist in a number of different phases, the most familiar being solids, liquids, and gases. A solution can technically be any homogeneous mixture of two substances, where each can be in any phase. However, in this book and in common usage, the term solution refers to solids, liquids, or gases dissolved in a liquid. We will refer to the substance dissolved in the liquid as the solute, and the liquid that dissolves the solute as the solvent.

For example, when table sugar is dissolved in water, it forms a solution, where at the molecular level every sugar molecule is surrounded by water molecules and on average the sugar and water molecules are evenly distributed throughout (Figure 2.18, right). Here, the water molecules are the solvent and the sugar molecules are the solute. In this book, the solutions we discuss will generally use water as the solvent. Such solutions are called aqueous solutions (aqua being Latin for water), so our sugar solution is an aqueous sugar solution.

Because the sugar is dissolved by the water, it is said to be soluble in water. Substances that do not dissolve are called insoluble and form heterogeneous mixtures. A clear example of this is sand in water. By eye we can see individual grains of sand that ultimately settle to the bottom, indicating that the sand is neither dissolved in the water nor homogeneously distributed (Figure 2.18, bottom left). That said, being able to see discrete particles is not a requirement for a substance to be considered insoluble or a

heterogeneous mixture. In milk (seen in Figure 2.1), at the microscopic level fat molecules clump together to form small globules. This makes milk a heterogeneous mixture, despite the fact that these globules are not directly visible by eye.

The solubility of a substance describes how readily it dissolves in a liquid. It can be between the extremes of being fully soluble and fully insoluble, that is, be partially soluble. Even substances that are considered fully soluble in water may not be so under certain conditions. For example, at some point, continually adding sugar to water results in some undissolved sugar (**Figure 2.19**). Here, the solvent has dissolved as much solute as it can, and we say the solvent is saturated.

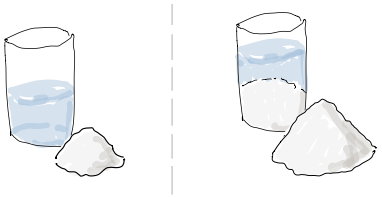


Figure 2.19 Differences in solubility due to the amount. At room temperature roughly 200 grams of sucrose (table sugar) can be dissolved in 100 ml of water. On the left is 100 grams of sucrose, and a solution made by adding 100 g of sucrose to 100 ml of water (about 100 g less sugar than the solubility limit). On the right is 300 g of sucrose, and the mixture that results from adding 300 g of sugar to 100 ml of water (about 100 g greater than the solubility limit).

For our discussion of concentrations in the rest of this chapter we will be assuming that we are dealing with solutions. That said, insolubility and heterogeneous mixtures are topics we will be coming back to in future chapters.

2.11 Qualitative Description of Concentration

Concentrations indicate how much solute is present in some volume of solution, and it is likely that you have some intuition for what this means. For example, if you made instant lemonade by adding a powder mix to water, how yellow the solution appears indicates how concentrated the lemonade is (**Figure 2.20**):

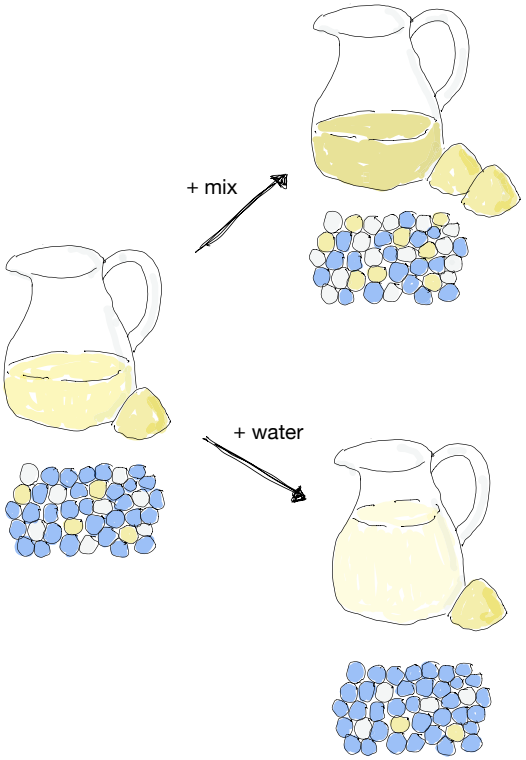


Figure 2.20 Differences in lemonade concentration, as demonstrated by how yellow the lemonade is. The top of each image shows lemonade solutions at different concentrations. The solution on the left comes from the addition of one scoop of instant lemonade mix to one liter or water. On the right, the lemonade concentration is either increased by adding an additional scoop mix, or decreased, by adding an additional liter of water. Below each of these pictures is a schematic image of the solutions at the molecule level. Sugar molecules are shown as white circles, yellow dye molecules in yellow, and water molecules in blue.

Adding more mix would make the lemonade more yellow, increasing its concentration. Additional water would make the lemonade less yellow, decreasing the lemonade concentration and making it more dilute. Lemonade mix is composed of many components including sugars, flavoring agents, and dyes. In lemonade, each component is dissolved in water and has its own concentration. At the molecular level, the difference in concentration for each component means that a different number of its molecules is found in the same solution volume. Most compounds that are soluble in water do not interact with visible light in a way that we can see them. However, dye molecules make a solution appear colored, meaning that increasing their concentration increases how colored they appear.

While describing the concentration of a solution using terms like more and less concentrated is intuitive and useful, it is also worth describing concentration in a more quantitative way.

2.12 Mass and Molar Concentrations

The concentration of a solution indicates the amounts of solute in a given solvent volume, and there are several ways the amount can be described. We will focus on two.

Mass concentration is the mass of solute found in a volume of solution. Because the base unit of mass is grams, and the base unit of volume is liters, mass concentration has the units of grams per liter or g/L. For example, if you had 10 g of table salt dissolved in water in a total volume of 1 L, the mass concentration of the solution would be 10 g/L. As a more complicated example, say for a 360 ml serving size of instant lemonade we use 37 g of lemonade mix. The mass concentration of the lemonade is 103 g/L:

$$37 \text{ g} \times \frac{1}{360 \text{ ml}} \times \frac{1{,}000 \text{ ml}}{1} \text{ L} = 103 \frac{\text{g}}{\text{L}} \tag{2.29}$$

Importantly, mass concentration is defined in terms of total volume of the solution, not the volume of solvent. Thus, for a solution that is 10 g/L we are not saying that there are 10 g of solute and 1 L of solvent. Instead we are saying there are 10 g of solute in a total solution volume of 1 L (the solution volume will include both the volume of solute and solvent). To prepare such a solution, we would weigh out 10 g of our solute, and transfer it to something we can measure a liter of volume. Then we would add solvent until the total volume reaches one liter. For this example, the volume of 10 g of solute would be pretty small compared to our final volume of 1 L, so adding 1L of solvent to it would give us pretty close to the same mass concentration as doing it the right way. However, in our lemonade example, 103 g of mix takes up a pretty significant volume, so just adding 1 L of water to it, would give it a total volume of more than 1 L, making the mass concentration less than 103 g/L (**Figure 2.21**):

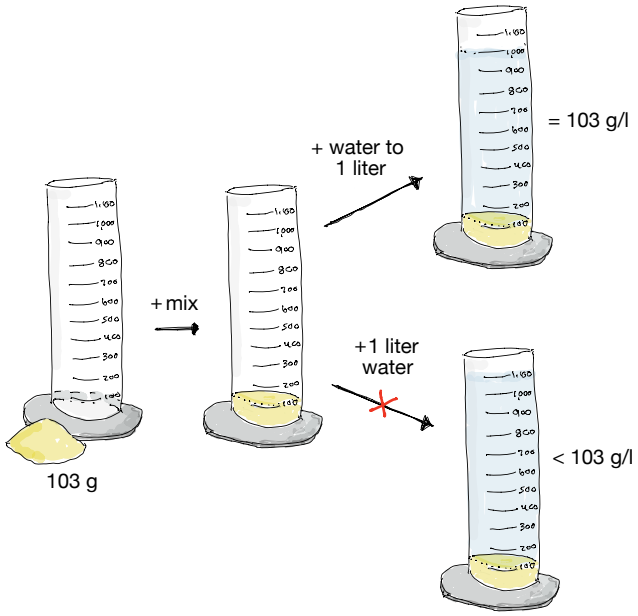


Figure 2.21 Making solutions to a specific concentration. If we want to make a 103 g/L solution of lemonade, we first add 103 g of lemonade mix, then bring the volume to 1 L, which involves adding less than 1 total liter of water. If we were to add 1 liter of water to our 103 g of mix, the final volume of the solution (mix and water) would be greater than 1 L and the final concentration would be less than 103 g/L.

An advantage of using mass concentration is that preparing such solutions is easy: weigh out some mass of solute and bring it up to a desired volume. We don't even need to know exactly what is in the solute (like in our lemonade mix example). However, one disadvantage of mass concentrations is that they do not explicitly tell us how many particles are in a given volume - in other words, the number concentration of the solute.

For example, if we have a 10 g/L solution of some compound 'A' and a 10 g/L solution of some compound 'B', would a liter of each solution have the same number of particles? Here we cannot tell, because we don't know the conversion factor from mass amount to number amount. Indeed, we can imagine a situation where the number concentrations of solution 'A' and 'B' are very different (**Figure 2.22**). Suppose a molecule of 'B' has a mass that is 10 times that of 'A'. Then for 10 grams of 'B', we would have 1/10th as many 'B' molecules as we would have in 10 grams of 'A'. So, while our 10 g/L solutions of 'A' and 'B' have the same mass concentration, the number concentration of solution 'A' would be ten-times higher than that of solution 'B'.

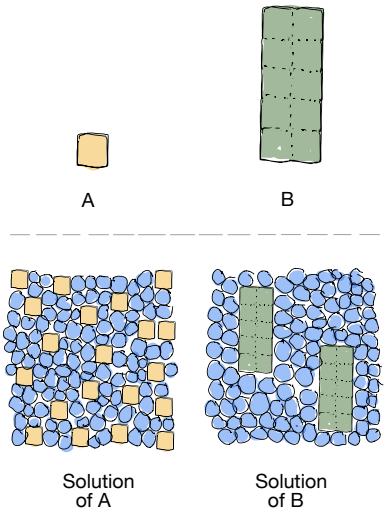


Figure 2.22 Difference between mass and molar particle/molar concentrations. In this fanciful example (top), the compound 'B' (green) has a mass ten times that of compound 'A' (orange), as shown schematically by making 'B' ten times bigger than 'A'. For potential solutions of 'A' and 'B' (bottom), the mass concentration can be the same (again, size of solute is a proxy for its mass). However, the number/molar concentrations are not the same – the solution of B is 10-times less.

Instead of using the number of particles to define a concentration, it is much more common to express the amount of solute in moles. This concentration is known as a molar concentration, and it has the units of moles/L. A solution with a molar concentration of 1 mole in 1 liter has its own concentration unit of 1 molar, abbreviated as 1 M:

$$1\ \frac{\text{mole}}{\text{liter}} = 1\ \text{molar} = 1\ \text{M} \tag{2.30}$$

Like other metric units of measure, molar concentrations can be modified by prefixes to indicate greater and lesser molar concentrations. For example: a 1 mM solution is 1/1,000th as concentrated as a 1 M solution (1×10^{-3} M); a 1 μM solution is 1/1,000,000th as concentrated as a 1 M solution (1×10^{-6} M).

Let's do some examples. Above we described an aqueous solution of table salt with a mass concentration of 10 g/L. What is its molar concentration? We start in units of g/L and want to end up in units of moles/L, so we need a conversion factor from grams of salt to moles of salt. The formula for table salt is NaCl with one sodium and one chlorine atom (technically both are ions, as we'll see next chapter, but that won't affect our calculation). Thus, for one mole of NaCl, we will have one mole of sodium and one mole of chlorine. The molar masses of sodium and chlorine are about 23 g/mole and 35.5 g/mole, respectively. So, the molar mass of table salt is 23 + 35.5 = 58.5 g/mole. We can plug this in to calculate our molar concentration:

$$10\ \frac{\text{g}}{\text{L}} \times \frac{\text{mole}}{58.5\ \text{g}} = 0.171\ \frac{\text{moles}}{\text{L}} = 0.171\ \text{M} = 171\ \text{mM} \tag{2.31}$$

This says that in this solution there are 0.171 moles of table salt per liter of solution. As we'll see next chapter, the situation is a bit more complicated than this, because in water the salt molecule splits into two parts.

Suppose we wanted to know how much salt we would need to add to make a solution with a particular molar concentration. For example, let's say we wanted to make the 171 mM salt solution in Equation 2.31. We saw that this solution is 10 g/L. If we wanted to make 1 liter of this solution, we would weigh out 10 grams of table salt, and dissolve it in enough water to bring its total volume up to 1 liter.

As a slightly more complicated example, suppose we wanted to make 200 ml of a 171 mM solution. 200 ml is 1/5th of a liter (1 L = 1000 ml), so intuitively we would need 1/5th as much salt as we needed for 1 L, so we would need 1/5th of 10 g of salt = 2 g of salt, for 200 ml. That said, sometimes it is easier to solve a problem like this with a conversion factor, and concentrations themselves are conversion factors. In this case, we know our desired volume (200 ml), and we want to end up with a mass amount of salt to use to make the solution. We can go from the volume to amount using the desired mass concentration as the conversion factor (and converting ml to liters):

$$200\ \text{ml} \times \frac{1\ \text{L}}{1000\ \text{ml}} \times \frac{10\ \text{g salt}}{\text{L}} = 2\ \text{g salt} \tag{2.32}$$

As a final example combining some of these ideas, suppose we wanted to make 2 liters of a 5 M aqueous solution of NaCl. How much table salt would we need?

$$2\text{ L} \times \frac{5\text{ moles}}{\text{L}} \times \frac{58.5\text{ g NaCl}}{\text{mole}} = 585\text{ g NaCl} \tag{2.33}$$

To make this 5 M NaCl solution, we would weigh out 585 grams of table salt and then add water until the solution had a volume of 2 liters. Again, it is important to stress that we would not just add 2 liters of water, as the table salt takes up a substantial volume of the solution.

2.13 Working With Concentrations

Concentrations describe the amount of a substance in a given volume. One way this can be useful is for comparing concentrations, especially molar concentrations. If the molar concentration of one solution is greater than another, it means that zooming into the same volume of each solution, the more concentrated solution will have more molecules than the less concentrated one (**Figure 2.23A**). That said, it is important to stress that concentration is a measure of amount per volume, not simply amount. Two solutions with the same molar concentrations could have different numbers of molecules if their volume were different, as demonstrated in **Figure 2.23B**. As a more quantitative example, you could have a 1 ml and a 1 L aqueous solution of table sugar at 1 M. Both solutions have the same concentration (ratio of sugar molecules to water), but the 1 ml solution clearly contains fewer sugar molecules than the 1 L solution (1,000x less, in fact).

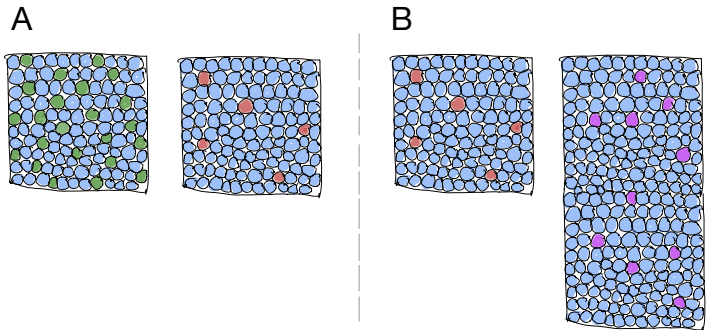


Figure 2.23 Comparing molar concentrations, molar amounts. A) Two solutions in containers with the same volume, where the molar concentration of the green molecules is greater than the red molecules. B) Two solutions, where the molar concentration of the red and purple molecules are the same, but the total moles of each particle is not. The volume of the container for the purple molecules is twice of the red molecule container.

The fact that concentration is amount divided by volume makes concentrations behave differently from simple amounts in several additional respects. If I had a gram of sugar and took half of it away, I would have half a gram of sugar left. In contrast, if I had 10 ml of a 1 g/L solution of sugar and took away half of the solution, the remaining solution would still have a 1 g/L mass concentration. If I wanted to change the concentration, say make it more concentrated, I could either add more sugar to it, or I could somehow reduce the volume (maybe evaporate off some of the water). Conversely, if I wanted to make the solution more dilute, I could somehow remove sugar from the solution, or more commonly, add more water to it (both of these ideas were explored in Figure 2.20). Diluting solutions is such a common thing to do, it's worth discussing it further.

Suppose I had 1 L of a 10 g/L solution and wanted to reduce the concentration of the solution by half to 5 g/L. Intuitively, we can see that doubling the total volume of our solution to 2 L would halve the sugar concentration to 5 g/L. Note, the 2 L for the 5 g/L is the volume of that solution. Since we started with 1L, we would bring that 1 liter to 2 liters by adding 1 liter to it (2 L final - 1 L initial = 1 L added), not by adding 2 liters to our original 1 L.

For calculation with more complicated dilutions, a similar approach can be taken, but other strategies can be used as well. One commonly used formula for dealing with dilutions is:

$$C_1V_1 = C_2V_2 \tag{2.34}$$

In this formula, C_1 and V_1 are multiplied and are the initial concentration and volume, respectively. C_2 and V_2 are also multiplied and represent the desired concentration and final volume. For a dilution problem, you plug in C_1, V_1, and C_2 and then solve for V_2. In our sugar dilution example, that would be:

$$\frac{10\text{ g}}{\text{L}} \text{ x } 1\text{ L} = \frac{5\text{ g}}{\text{L}} \text{ x } V_2 \tag{2.35}$$

Solving for V_2 gives a total final volume of 2 L, as before. This formula works because the initial concentration times the initial volume gives the total amount of solute present. This holds for both mass and molar concentrations. This amount of solute does not change during the dilution, so it is equal to the final concentration times the final volume.

A final concentration topic worth considering is what ranges of concentrations can be made. With regard to a lower concentration limit, there really is no bottom. If you have a molecule in solution at a given concentration, you can pretty much always reduce its concentration further by adding more solvent. The same isn't true of the maximum concentration of a solute. As mentioned earlier, the solubility of a molecule is its maximum solution concentration, and different molecules have different solubilities depending on the solvents and temperature. For example, a very water-soluble compound like table salt can be dissolved in room-temperature water up to about 357 g/L or 6.1 M NaCl. Beyond the solubility limit, there will be undissolved salt. At its maximum concentration, 357 g of table salt takes up a significant volume of a 1 L solution (**Figure 2.24**). A more fundamental upper limit that is independent of solubility, is simply how many molecules can fit in a given volume. A useful number in this regard is the "concentration" of water (i.e. how many moles of water can be fit into a liter). This concentration is about 55 M, suggesting that for most molecules, even if solubility is not an issue, it would not be possible to have a solution more concentrated than this.

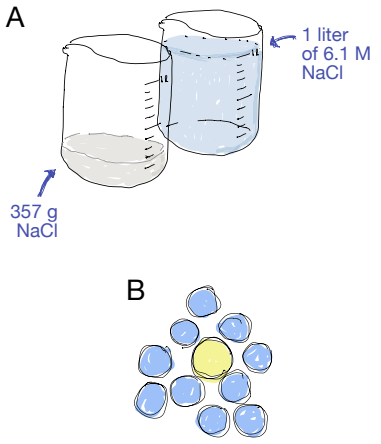


Figure 2.24 A solution of table salt at maximum concentration. A) The amount of table salt (NaCl) that is contained in 1 liter of a 6.1 M solution of NaCl. B) A zoom-in on roughly how many water molecules (blue) there are per sodium ion (yellow), which is roughly ten molecules to one (we are ignoring the chloride ions and will discuss ions more in the next chapter). Note, the particles shown here are depicted in a 2-dimensional plane, but actually exist in a 3-dimensional volume.

Where to from here: In this chapter we have introduced various ideas regarding amounts and concentrations. In the further exploration sections, we discuss how we can deal with uncertainty in measuring things like amounts and concentrations. We also look at other ways to measure concentration and properties related to concentration. In the next chapter we return to exploring atoms by examining atomic ions and salts, and see how concentrations can influence their behavior.

F. Further Exploration - Uncertainty in Measurements

In this section, we introduce the idea of uncertainty in measurements, then look at two different ways to handle uncertainty: significant figures and a probabilistic description.

2.14 What is Uncertainty in Measurements?

Values such as the mass of an object or the concentration of a solution, come from either a single measurement (using a scale to determine an object's mass), or a combination of measurements (calculating the mass concentration of a solution by weighing a solute and then dividing that by the measured volume of the solution made from that solute). In performing measurements, some degree of uncertainty is always present, where the uncertainty is a lack of confidence in the accuracy of a measured value beyond a certain digit place. The size of this uncertainty can be large compared to the number measured (for example, centimeters uncertainty in a length measurement that is in the range of centimeters) or it might be small (say micrometers uncertainty for the same measurement). However, the uncertainty is never zero.

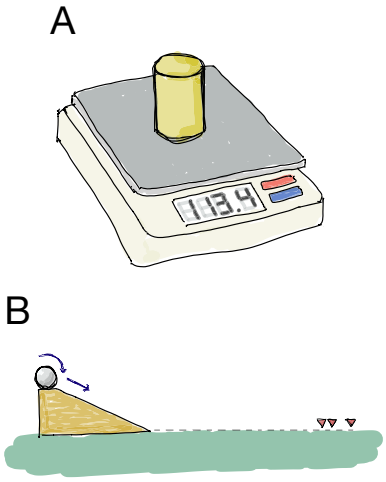


Figure 2.25 Examples of uncertainty in measurement. A) Digital scale that measures up to but not beyond a tenth of a gram. B) Potential distance travelled by a ball rolling down a ramp from the same initial position (end points indicated by red triangles).

Uncertainty in measurements can come from a variety of sources. Uncertainty may arise from the limitations of the measuring device used. For example, if we had a scale only capable of reporting mass to a tenth of a gram, we would only be certain of an object's mass to a tenth of a gram (**Figure 2.25A**). A more expensive scale might go to a thousandth of a gram and give us less uncertainty, but we would still be uncertain of any value beyond the thousandths place. Other potential sources of uncertainty include experimental factors that cause variations in a measurement. Say we were interested in the distance a ball travels after rolling down a ramp (**Figure 2.25B**). Even if we were very careful to start the ball at the same position every time, the total distance measured would not be exactly the same due to small differences in how the ball interacted with its surroundings during its travels. Across many measurements, the total distance might vary by a couple of centimeters. Here, the uncertainty would be on the order of centimeters. It would be inappropriate to report the uncertainty as being several millimeters, as that would be less uncertainty than observed. Similarly, we wouldn't want to report the uncertainty as being several meters, as that would overstate our uncertainty.

So altogether, having a way to describe the uncertainty of our measurements is important, because we have to know how much to trust the numbers we report. We don't want to claim we know a measurement to a greater degree of precision than we do, nor do we want to underestimate how much our measurement tells us. Further, because we will often take measurements and combine them with other measurements, we need to know how uncertainty compounds across these calculations. One relatively simple strategy for handling uncertainty is using significant figures.

2.15 Significant Figures

We can indicate the uncertainty of a measurement by how many significant figures we choose to present. For example, if we weigh an object and the scale shows a value of 113.4 grams (see previous Figure 2.25A), we report the mass to four total significant figures (all four digits), where the last significant figure is in the tenths of grams place (the 4). By writing the mass to four significant figures, we are saying that we are confident in all four digit places. We are also saying we are uncertain of values beyond that. Thus, we should not include any more or fewer digits. For example, for a scale that shows a mass of 113.4 g, we wouldn't report the mass as 113.427 g (six significant figures), because that number overstates how much certainty we have in the measurement. Similarly, we wouldn't report a mass of 113 g (three significant figures), because that would understate our certainty. These two examples may seem obvious, but would it be okay to report the mass as 113.400 g? If our scale only measured it to 113.4 g, it would not be appropriate to add the extra zeros, because 113.400 g indicates that we know the mass to six significant figures, i.e. we know the hundredths and thousandths values are zero (which we don't).

In general, identifying which figures in a measurement are significant, and therefore values we have confidence in, can be confusing. To address this, it is useful to consider some rules (**Figure 2.26**).

Things are pretty straightforward when we're talking about non-zero digits, as stated by rule one: All non-zero digits are significant. As we saw, if we reported a mass of 113.4 grams, all four digits are significant, and we are saying we have a relatively high certainty in all of those digits. If we reported a mass of 113 g, there would be three significant digits. We would only use that number if we had weighed the same object on a different, less precise scale.

When zeros are added to numbers, there are several cases to consider. Let's start with rule two: Any zero between non-zero digits is significant. For example, 302.4 g has four significant values. This rule makes sense, because like the non-zero digits, we know that zero in the tens place is exactly zero.

Number of Significant Digits

1) All non-zero digits are significant.

2) Any zero between non-zero digits is significant.

3) Zeros before the first non-zero digit are not significant.

4) For a number without a decimal point, zeros after the last non-zero digit are not significant.

5) For a number with a decimal point, all zeros after the first non-zero digit are significant.

Mathematical Operations

6) When adding or subtracting two or more numbers, the answer will have the same number of decimal place digits as the original number with the least decimal place digits.

7) When multiplying or dividing two or more numbers, the answer will only have as many significant figures as the original number with the smallest number of significant figures.

Figure 2.26 Rules for significant figures.

What if the zero is somewhere else? According to rule three: Zeros before the first non-zero digit are not significant. Not surprisingly, a weirdly written number like 0038 g only has two significant digits. Perhaps more surprisingly, a number like 0.0038 g also only has two significant figures, according to this rule. One way to see why this makes sense is that you could also write this mass as 3.8 mg, which clearly only has two significant figures. As these are the same mass, the number of significant digits has to be the same.

Rule four considers zeros at another location: For a number without a decimal point, zeros after the last non-zero digit are not significant. If we reported a mass of 300 g, we are saying there is only one significant digit, the three. Thus, we are uncertain of the values both in the tens and ones place. This makes sense if your scale only measured hundreds of grams and nothing below that. However, you might be wondering, what if the scale measured to the single gram place, and the object happened to weigh exactly 300 grams. There are several possible ways to indicate that the zeros are significant in this scenario: you could add an explicit trailing decimal point (300. g); you could put a bar above or below the last significant zero (i.e. $30\overline{0}$ g or $30\underline{0}$ g); or, you could write the number in scientific notation, 3.00×10^2 g, where the fact that the zeros are to the right of the decimal indicates they are significant (i.e. rule five).

A final zero to consider, rule five: For a number with a decimal point, all zeros after the first non-zero digit are significant. If we reported a mass of 113.400 g, we are saying all six digits are significant, and that the scale is precise enough to measure to the hundredths and thousandths place with certainty (again, if we weren't certain of those zeros, we would not write them).

Altogether, identifying the number of significant digits with these rules is something that comes easily with a bit of practice (**Figure 2.27**).

When mathematical operations are performed on numbers (such as addition, subtraction, multiplication, or division), the uncertainty of the numbers propagates through the calculation, and the uncertainty of one number can dominate the other. In practice, the mathematical operation is first performed without regard to significant figures. Then, the number of significant figures of the result is adjusted, rounding according to standard rules.

A) 426.89

B) 270

C) 0.00370210

D) 2030.0

Figure 2.27 Significant digits practice. For the numbers shown, try to determine how many digits are significant before looking at the following answers: A) 5, B) 2, C) 6, D) 5.

Let's consider addition and subtraction first. As described in rule six: When adding or subtracting two or more numbers, the answer will have the same number of decimal place digits as the original number with the least decimal place digits. This idea is easiest to understand with an example. Suppose I added 102.235 m to 2.4 m. The last significant digit for the first number is in the thousandths place, while the last significant digit of the second number only goes to the tenths place. Thus, the sum, 104.635 m, can only go to the tenths place. Since the number after the six (a three) is less than five, we round down, making the sum, 104.6 m. Why the rule works this way is reasonable. Since 2.4 doesn't have significant digits past the tenths place, adding the hundredths and thousandths place digits of 102.235 (3 and 5, respectively) to the unknown digits of 2.4 would give uncertain values, and therefore these digits should not be included in the answer.

For multiplication and division, rule seven is followed: When multiplying or dividing two or more numbers, the answer will only have as many significant figures as the original number with the smallest number of significant figures. As an example, if you were to multiply 102.235 m and 2.4 m, you would initially get a product of 245.364 m^2. 102.235 m has six significant figures and 2.4 m only has two. So, according to our rule, the product can only have two significant figures. In 245.364 m^2, the number after the second significant figure is a five, meaning the second significant figure should be rounded up, giving the result of 250 m^2 (which has the desired two significant figures according to rule four).

What is the logic behind how significant figures are handled for multiplication and division? Here, we see that the uncertainty for 102.235 m lies beyond the thousandths place. As a fraction of 102.235, the uncertainty is small. In contrast, for 2.4 m, there is uncertainty past the tenths place, and as a fraction of the entire number, the relative uncertainty is much larger. When multiplying or dividing numbers, the number with the greatest relative uncertainty dominates. This idea is more clearly illustrated if we varied the values of our two numbers slightly. Suppose the second length was 2.3 m instead of 2.4 m. The product of the first and second length (2.3 m x 102.235 m) would now be 235.1405 m^2, a change of about 10 m^2. What if instead of 102.235 m, the first length was 102.234 m? Here the product would be 2.4 m x 102.234 m = 245.3616 m^2, a much smaller change (about 0.002 m^2). Thus, in this multiplication the length that had the fewest significant digits (and therefore the greatest relative uncertainty), 2.4 m, has a disproportionate effect on the uncertainty of the product, making it necessary to not include more than two significant digits. This is why the least-precise factor governs the precision of the result.

A summary of the examples used to illustrate how significant figures propagate for various mathematical operations is shown in **Figure 2.28**:

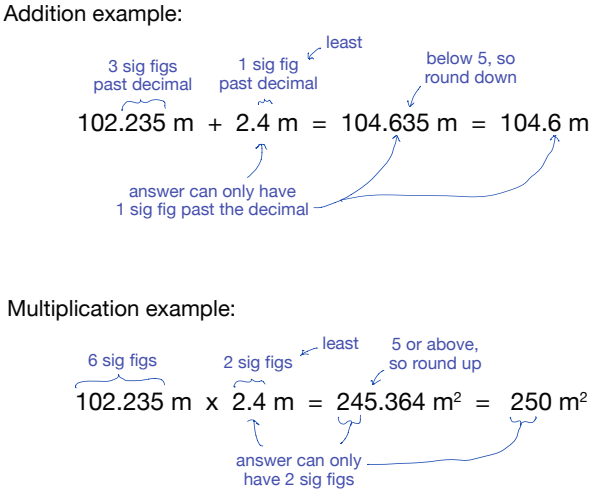


Figure 2.28 Summary of the math examples for propagating uncertainty with significant digits.

Beyond the rules described, there are a couple of additional wrinkles to consider when working with significant figures:

If a number in a calculation is a true integer (for example, the number of hydrogens in water is 2), that number should be considered to have infinite significant figures (i.e. 2.00000…).

When doing multiple mathematical operations in sequence, first do all steps without consideration of significant figures or rounding. Then, go back and proceed through the steps in the order of operation and take note of how many significant figures should be included. The number of significant figures and rounding are then applied once as a final step.

For more complex mathematical operations, such as raising values to powers, additional rules for handling significant figures are available, but beyond the scope of this text.

2.16 Probabilistic Descriptions of Uncertainty

Up to this point, we have been a bit vague in defining exactly what we mean by uncertainty. In this section we get more rigorous and root our treatment of uncertainty in probability and statistics, though we will only be able to scratch the surface of the topic. Let's start by examining the relationship between significant figures and uncertainty for a system we have already seen.

Earlier we considered an object that our scale displayed as having a mass of 113.4 g (previously shown in Figure 2.25A). This measured mass has four significant figures and there is clearly uncertainty for any values to the right of the tenths place. However, there is actually some uncertainty of the value in the tenths place, too. The actual mass could be as low as 113.35 g, as the scale would round the value up to 113.4 g (meaning the tenth's place could have been a 3 instead of a 4). At the top end, the mass could almost be as large as 113.45 g (say 113.44999 g), which would be rounded down to 113.4 g. A better description for the potential mass of our object would be a range of masses, 113.4 ± 0.05 g. Still, even this description is not complete. How do the possible masses fall in this range? For instance, is 113.41 g more likely than 113.44 g or are all values in the range equally probable?

For our object, we don't know if its mass is really 113.41 g, 113.44 g, 113.36723 g, or some other value between 113.35 g and 113.45 g. Indeed, any of the values in our range are equally likely based on the information we have. This can be summarized as a graph, where the x-axis shows the potential mass values, and the y-axis indicates what is known as the probability density (**Figure 2.29A**). For our object and scale, the function that relates these two variables is one in which the probability density is zero both below 113.35 g and above 113.45 g, as any of these values would not have resulted in a reading of 113.4 g. Between 113.35 g and 113.45 g, the probability density is all the same value, because all values in the range are equally likely. A graph that relates a particular value (such as a mass) to how often that value occurs is a distribution. When the probability of specific outcomes can be determined by the graph, the distribution is known as a probability distribution (a uniform probability distribution in this case).

A probability distribution provides a way to quantify measurement certainty as a probability For example, assuming the only uncertainty in the mass of our object is the decimal limit of the scale, what is the probability that our object has a mass between 113.35 g and 113.45 g? Intuitively, we expect this probability to be 1.0 (100%), since we have defined the allowable range to be between 113.35 g and 113.45 g. This can also be computed from the probability distribution (**Figure 2.29B**). The probability of a certain range of values is the area under the curve between those values. The area under the curve from 113.35 to 113.45 is 0.1 x 10 = 1.0 (where 10 is the height of

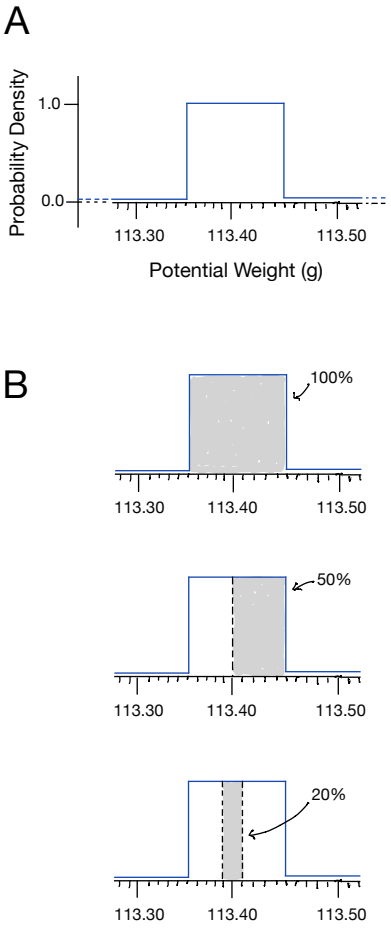


Figure 2.29 Uniform probability distribution of a measured mass and its use to calculate uncertainties. A) Shown is the distribution of potential masses for the object and scale shown in Figure 2.25A. The mass reading was 113.4 g with no additional information beyond the tenths of a grams digit. The actual mass of the object could be any value from 113.35 g to 113.45 g, with an equal probability for any of these values. B) Probabilities that the actual mass falls within a certain range, where the probability is represented by the shaded areas under the curve compared to the total area under the curve. The top probability is for values from 113.35 g to 113.45 g; the middle for values from 113.40 to 113.45 g; and the bottom for values within 0.01 grams of the observed value.

the distribution, since height × width must equal 1). As another example, what is the probability that our object mass is between 113.40 g and 113.45 g? This is just half of the area of the rectangle from our last problem, so the probability is 0.5 (50%). As a final example, how certain are we that the mass of our object is within 0.01 g of its reading, 113.40 g ± 0.01 g? As each unit of 0.01 g occupies 1/10th of the distribution, the area of the curve between 113.39 g and 113.41 g is two times 1/10th of the whole probability, or 2 x 0.1 x 1.0 = 0.2; so we are only 20% certain our actual mass is within 0.01 g of our measurement.

Probability distributions can be non-uniform. A commonly encountered distribution for experiments in which multiple measurements are taken is a normal distribution (also known as a Gaussian distribution or more informally as a bell-curve). In this distribution (**Figure 2.30A**), one value is most frequent (highest in terms of the y-axis). As we move away from this value in either direction on the x-axis, the frequency decreases - slowly at first, then more rapidly:

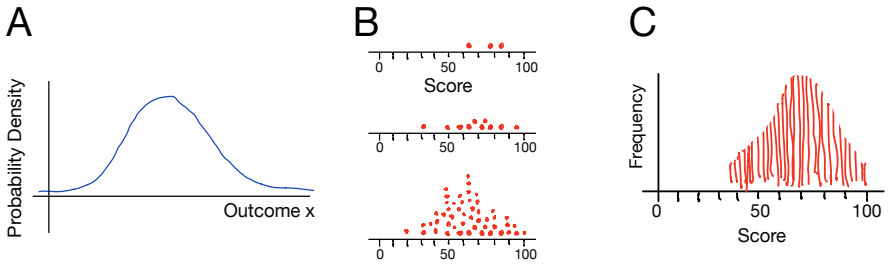


Figure 2.30 Normal distribution and examples. A) The shape of a generic normal probability distribution. B) Test score outcomes ranging from 0-100%, where a dot represents one score. Going down, the plots include increasing numbers of scores: 3,10, and 50 scores. C) Score distribution by single percentage for 500 students. The height of each bar represents how many students obtained that score.

One example where such a distribution might arise is student's scores on an exam. If we plotted how each student did on a test score number line, eventually, we might see a pattern, where more of the scores are clustered around a certain score, with fewer students with scores farther from this clustered value in either direction (**Figure 2.30B**). We could turn this into a frequency distribution, by counting how many student scores got a certain percentage (0%, 1%, 2%, …, 98%, 99%,100%). With enough student scores, this distribution might end up looking like the normal distribution (**Figure 2.30C**), though a score distribution certainly could be something besides normal. Dividing the frequency of each score by the total number of scores, the distribution becomes a probability distribution, where in this case the height of the bar for each percentage denotes the probability of having that score.

Because a probability distribution is a useful representation of what values a measurement can take and how probable they are (regardless of whether the distribution is uniform, normal, or something else), we could include a graph or equation of the distribution. However, this approach becomes unwieldy when there are many different measurements and difficult to use if measurements need to be combined. One alternative is to describe the distribution using two numbers, the average and standard deviation (**Figure 2.31**):

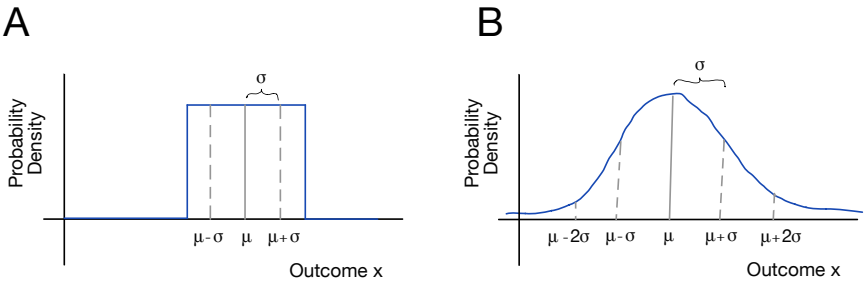


Figure 2.31 Average values and standard deviations for uniform and normal probability distributions. The average is represented by μ and a solid gray line. The standard deviation about the average is represented by σ and dotted gray lines (for the normal distribution, two standard deviations about the mean are shown). A) A uniform probability distribution with values from x_1 to x_2. 58% of the area of the curve is within one standard deviation of the average to either side. B) A normal probability distribution. 68% of the area of the curve is within one standard deviation of the average to either side. 95% is within two standard deviations.

The average (or mean) of a distribution is a concept you are probably familiar with. For our test scores, the average would be calculated by adding up all of the test scores,

and dividing it by how many test scores there are. This idea can be summarized in the following formula:

$$\mu = \frac{x_1 + x_2 + \ldots + x_n}{n} = \frac{1}{n}\sum_{i=1}^{n} x_i \tag{2.36}$$

where μ is the average measured value, x_i is the value for measurement i, and n is the total number of measurements taken. Applied to our first three test scores from Figure 2.30B, 47.0%, 64.2%, and 87.1%, their average would be (47.0 + 64.2 + 87.1)/3 = 66.1%. Applied to all 500 scores, we find that the average test score is 69.7% (**Figure 2.32A**):

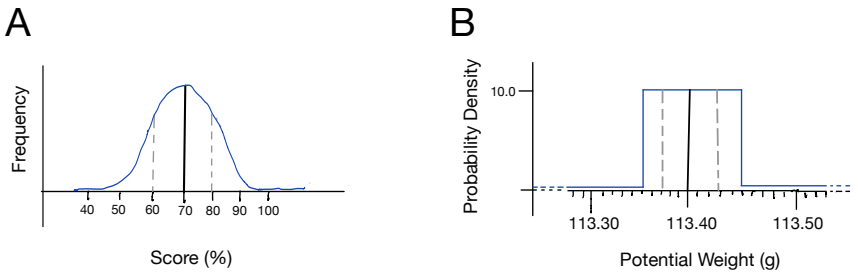


Figure 2.32 Averages and standard deviations for our example distributions. For both distributions, the average score is indicated by a solid black line, and one standard deviation from the average in either direction is shown as a gray dotted line. A) Test score distribution from Figure 2.30C. The average score is 69.7%. The standard deviation is 10.0%. B) Possible mass distribution from Figure 2.29A. The average mass is 113.40 g. The standard deviation is about 0.03 g.

For distribution curves that are described by a formula instead of a set of specific numbers, the underlying idea of Equation 2.36 can be applied using some calculus to get a formula for the average. For a uniform distribution, the average ends up being (x_2 + x_1)/2, and for our scale example that average is 113.40 g (**Figure 2.32B**). It's worth noting that in both the uniform and normal distribution, the average is in the middle of the distribution, but this isn't the case for all distributions.

While the average encapsulates information about a distribution, it does not capture all of it. For example, consider two normal distributions with the same average (**Figure 2.33**):

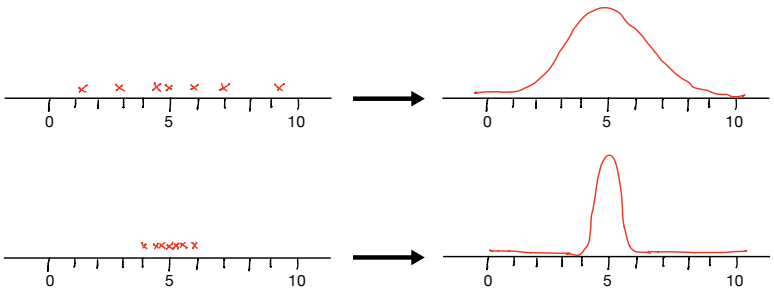


Figure 2.33 Two normal distributions with the same average, but different in how spread out they are. On the left is shown a sample of outcomes plotted on a number line for two different distributions that have the same average. On the right, the full distribution of each is shown.

Clearly the upper distribution is wider than the lower one. Can we find a number that describes how much the distribution spreads from the average? Indeed it is possible with a number called the standard deviation. The standard deviation is a measure of how much the values in a distribution vary from the average value, and can be calculated according to the following equation:

$$\sigma = \sqrt{\frac{(\mu - x_1)^2 + (\mu - x_2)^2 + \ldots + (\mu - x_n)^2}{n - 1}} = \sqrt{\frac{\sum_{i=1}^{n}(\mu - x_i)^2}{n - 1}} \tag{2.37}$$

Suppose we wanted to use this formula to calculate the standard deviation of our first three test score about their average (which we previously calculated to be 66.1%). We would first take the square of the difference between each of the scores and their average: $(66.1\text{-}47.0)^2$ = 364.8, $(66.1\text{-}64.2)^2$ = 3.6, and $(66.1\text{-}87.1)^2$ = 441.0; then "average" those values: (364.8 + 3.6 + 441.0)/2 = 404.7 (note, when we average the squared differences, we divide by one less than the total number of measurements for reasons that are beyond

the scope of this book); and finally take the square root of that average: $(404.7)^{1/2}$ = 20.1%. A similar procedure could be applied to all 500 of the test scores (a tedious process, but one well suited for a computer), giving a standard deviation of 10.0%. This standard deviation, 10.0%, provides a description of how wide the distribution of scores is around the average score, 69.7%.

Using the same basic idea as Equation 2.37, a formula for the standard deviation of a distribution curve can also be derived. For our uniform distribution, with a width of x_2 - x_1 (shown previously in Figure 2.31A), the standard deviation is:

$$\sigma_{uniform} = \sqrt{(x_2 - x_1)^2/12} \tag{2.38}$$

Applied to our example of an object weighed on a scale, the standard deviation ends up being about 0.03 g (shown previously in Figure 2.32B).

We can use our average and standard deviation to describe a distribution of x as:

$$x = \mu \pm \sigma \tag{2.39}$$

For our set of 500 test scores, we can say the distribution of scores is 69.7 ± 10%. For our scale measurement distribution, we can say our distribution of potential masses is 113.40 ± 0.03 g. Note, using the average and standard deviation gives us an approximation of the distributions, but it doesn't give us a full description, as the shapes of a normal and uniform distribution are different. Ideally the type of distribution (uniform, normal, etc.) should also be included with its average and standard deviation.

With this understanding of averages and standard deviations, we can relate these to the uncertainty in measurement. Let's start with the uniform distribution of masses measured on a scale, which in our example has a distribution of 113.40 ± 0.03 g. We would like to know what the actual mass of our object is, and how confident we are in that number. Of the possible range of mass values, 113.40 g is the average of those possible values. The standard deviation describes a range of values around this average from 113.37 g to 113.43 g. Because the distribution is uniform, this range is about 58% of the total possible range, meaning that there is roughly a 58% chance that the actual mass is within one standard deviation of the average. This is a general result for uniform distributions, where the probability of being within one standard deviation of the average (above or below) is 58% (for our specific example, we end up with a probability of 60% due to rounding).

We can define a new term, "the standard uncertainty," as a way of describing our confidence in a range of values around the average. We will abbreviate standard uncertainty as u. For any measurement then, a confidence interval about the mean is:

$$x = \mu \pm u \tag{2.40}$$

For our uniform distribution, the standard uncertainty of the distribution is equal to its standard deviation:

$$u_{uniform} = \sigma_{uniform} \tag{2.41}$$

Thus, for our scale example, we have a measurement of 113.40 ± 0.03 g, where the average actual mass is 113.40 g, with about a 60% probability of finding the actual mass within the standard uncertainty of 0.03 g to either side of the average value. One thing

to note: we have used the plus-minus sign in three different contexts, defining the range of possible values, the standard deviation, and now the standard uncertainty. Just from the numbers themselves, it is not clear which we are referring to, and it is important to be clear by stating which we are using.

So far, our standard uncertainty described the precision of a single measurement — one weighing on one scale. But sometimes we take multiple measurements and average them, hoping the average does a better job of tracking the true value than any single reading would. In that case, the standard uncertainty of the average reflects not the limits of the measuring device, but how representative our sample average is of the overall distribution. Let's take the example of our test score distribution. Suppose we wanted to perform a "measurement" on this distribution by taking one exam randomly from the distribution. We would get some score, and we might wonder, like with our mass measurement, about the uncertainty of this measurement. However, unlike the mass measurement, where there is an actual mass, there is no "actual" score to compare it to, just the distribution itself. So instead we might ask how confident we are that the measurement we took was close to the average of the scores. If we took one measurement, the chance it would fall within one standard deviation of the average for a normal distribution would be 68% (and within two standard deviations it would be 95%). What if we sampled three test scores and computed their average? We would expect that average would be closer to the actual score average than sampling a single score. In fact, if we sampled many test scores, like 50, we would expect the average of those measurements would likely be quite close to the actual average.

How do we relate this intuition to calculating the standard uncertainty of a measured average? Suppose we took some number of random samples from our distribution of 500 test scores, and then calculated the average of our sampled data. If we repeated this process over and over to obtain many different averages, we would ultimately have a distribution of the sample averages. **Figure 2.34** shows these distributions for n= 1, 3, and 10:

Number of scores sampled	Example sample (%)	Example average (%)
n = 1	59.5	59.5
n = 3	59.5, 61.2, 79.8	66.8
n = 10	59.5, 61.2, 79.8, 65.5, 53.2, 76.8, 87.4, 77.7, 72.2, 65.7	69.9

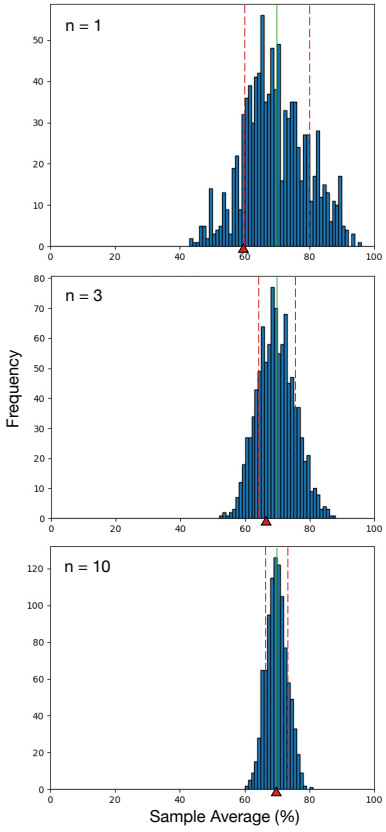


Figure 2.34 Distribution of sampled averages when the number of measurements used to calculate the sample average differs. All samples are taken from the test score distribution shown in Figure 2.30C. In that distribution, the average score is 69.7% with a standard deviation of 10.0%. On the left are examples of sampling, one, three, or ten scores and the resulting average. On the right is the distribution of averages, where the process on the left is repeated 1,000 times and plotted. A red triangle indicates where the specific average calculated on the left falls. The standard deviation for each of these distributions is shown with a dotted red line and is: 10.0% for n =1, 5.8% for n = 3, and 3.2% for n = 10.

What are some features of these distributions? 1) It turns out that distribution of averages generated from multiple samples becomes approximately normal, regardless of whether the original distribution sampled from was normal or not. 2) The average of these distributions is the average of the distribution sampled from. 3) The standard deviation of these distributions, which we will call the standard uncertainty of the sample averages, is related to the standard deviation of the distribution sampled from, σ, but also depends on how many samples, n, were used to calculate each sample average according to the following formula:

$$u_{average\ of\ a\ sample} = \frac{\sigma}{\sqrt{n}} \tag{2.42}$$

Matching our prior intuition, the standard uncertainty of the sample averages decreases when the number of samples used to calculate the sample average is increased. Thus, for our test score distribution with an average score of about 70% and a standard deviation of 10%, when we sample a single test score (n = 1), there is a 68% chance that this value will be within 10% of the actual mean of 70%. When we average a sampling of three test scores (n = 3), there is a 68% chance that this value will be within 5.8% of the actual average. Averaging a sampling of ten test scores, (n = 10), there is a 68% chance that this value will be within 3.2% of the actual average.

A problem with directly applying Equation 2.42 to actual sampled data is that we don't know the standard deviation of the distribution we are sampling from. Instead, we can calculate a standard deviation of the sampled data as an approximation. As an example, suppose we randomly chose three scores: 47.0%, 64.2%, 87.1%. We previously calculated the average and standard deviation for these scores, which had values of 66.1% and 20.1%, respectively. If we divide this by the square root of three, we get a standard uncertainty of 11.6%. That is, there is a 68% chance that the actual average of the scores is within 66.1% ± 11.6% - which in this case is true, since the actual average of the 500 scores is 69.7%. You will note, that the standard uncertainty was larger than the 5.8% shown in Figure 2.34 for n = 3. This is because two of the scores we happened to randomly sample: 47.0% and 87.1% both happened to be more near two standard deviations away from the mean value, making our guess at the true standard deviation of the full set of scores seem larger than it actually is. If we had sampled another seven scores to get a total of 10 scores: 47.0%, 64.2%, 87.1%, 81.4%, 68.7%, 78.0%, 69.2%, 67.3%, 69.5%, and 72.3%, we would calculate that the sample average is 70.5% with a standard uncertainty of 3.4%. This means there was a 68% chance that the actual average of the 500 test scores was within 3.4% of 70.5%.

These examples, and more generally Equation 2.42, indicate we can decrease the uncertainty that our sample average matches the actual average by repeating our measurement more times. However, to halve the uncertainty expressed by u, we need to quadruple n. To get to one fourth requires increasing n by a factor of sixteen, and thus it requires more and more measurements to continue to shrink the standard uncertainty.

With standard uncertainties, it is possible to propagate uncertainty across calculations, like we did with significant figures. However, the equations for propagating standard uncertainties are rigorous, while the rules for significant figures are really just an approximation of these equations.

If we added (or subtracted) some quantity A to B, with uncertainties of u_A and u_B, respectively, the sum would be $A+B$ with an uncertainty of u_{A+B}, calculated as such:

$$u_{A\pm B} = \sqrt{u_A{}^2 + u_B{}^2} \tag{2.43}$$

Suppose there were a relatively large difference in uncertainties between two values, such

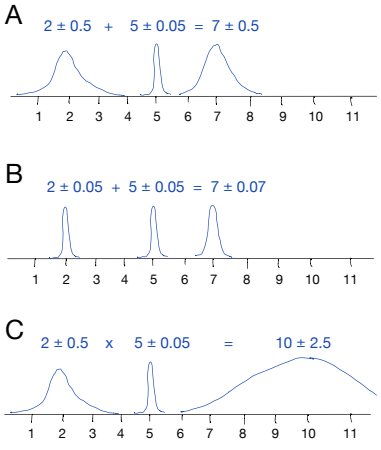


Figure 2.35 Examples of propagation of uncertainty. A) Adding two values, where one has a large uncertainty relative to the other. B) Adding two values with equal uncertainties. C) Multiplying two values, where one has a large uncertainty relative to the other.

as $u_A = 0.5$ and $u_B = 0.05$ (**Figure 2.35A**). We can see that u_{A+B} would end up dominated by the term with the larger uncertainty (0.5), just like in the case of significant figures. However unlike with significant figures, if both uncertainty terms are the same (**Figure 2.35B**), such as $u_A = u_B = 0.05$, there would still be an increase of uncertainty in the sum by a factor of a square root of two (in this example $u_{A+B} \approx 0.07$).

In multiplying (or dividing) A and B, again with associated uncertainties of u_A and u_B, the relationship of the product, $A \times B$, and the uncertainty of the product, $u_{A\times B}$ is:

$$\frac{u_{A\times B}}{A \times B} = \sqrt{\left(\frac{u_A}{A}\right)^2 + \left(\frac{u_B}{B}\right)^2} \tag{2.44}$$

By plugging values into this equation, $u_{A\times B}$ can be solved for. Unlike propagation of uncertainty in addition/subtraction, where the absolute uncertainties are the only contributors to the final uncertainty, in multiplication/division the relationship is between the relative uncertainties. Similar to significant figures, if the relative uncertainty of one of the terms dominates (fewer significant figures or large relative uncertainty), it will dominate in its contribution to the uncertainty of the answer (**Figure 2.35C**).

G. Further Exploration - Quantities Related to Concentration

Mass and molar concentrations relate the amount of solute to the total volume of the solution they are in. While these two quantities are the most common way to relate the amounts of solute, solvent, and solution, especially in biological systems, there are other ways to do so. In the first part of this section we will briefly explore some of these other quantities, including why they might be used. In the second part, we will focus on a quantity that has similarities to mass concentration, density.

2.17 Other Quantities Relating Amounts of Solute and Either Solvent or Solution

A quantity often confused with molarity is molality. Like molarity, molality is concerned with the number of moles of solute in a solution. However, instead of comparing this mole amount to the volume of the solution, molality compares the moles of solute to the *mass* of the *solvent* according to the following formula:

$$\text{molality} = \frac{\text{moles solute}}{\text{mass solvent}} \tag{2.45}$$

The difference between molarity and molality is illustrated in **Figure 2.36**:

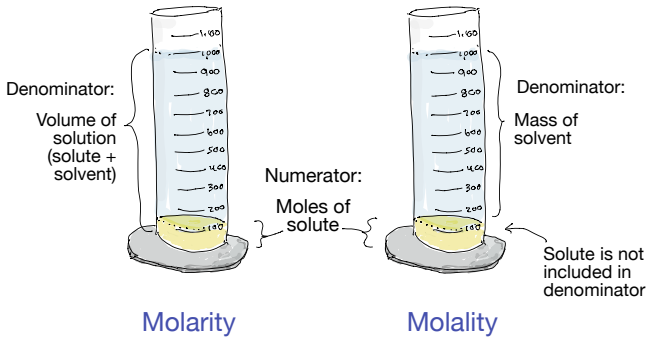


Figure 2.36 Molarity versus molality. Shown is lemonade mix and water, from Figure 2.21. In molarity (left), the number of moles of solute is compared to the volume of the solution. In molality (right), the number of moles of solute is compared to the mass of solvent.

In molality, solvent mass is measured in kilograms, making the units of molality moles per kg. A 1 mole per kg solution is a 1 molal (not molar) solution:

$$1 \frac{\text{mole}}{\text{kg}} = 1 \text{ molal} \tag{2.46}$$

Because the mass of one liter of pure water is 1 kg (something we'll discuss in the next section), dilute aqueous solutions tend to have nearly identical molarities and molalities. However, at high concentrations, where the volume of solute is a larger component of the solution volume, the two diverge. Besides knowing the difference between molarity and molality so as not to confuse them, molality tends to be used especially in situations where the volume of a solution might change, such as conditions of changing temperature or pressure (we'll explore why this might happen in the density section). The mass of a solvent will not change under such circumstances, making the molality of a solution constant with temperature and pressure. That said, in general, biological systems do not experience temperature or pressure changes large enough to affect solution volumes, making molarity suitable in most circumstances.

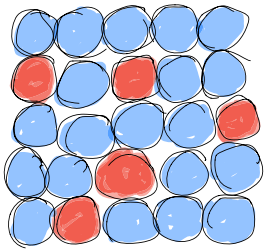


Figure 2.37 Example of a mole fraction. In this example solution, there is one molecule of 'A' (red) for every four 'B' molecules (blue). The mole fraction is 0.2, or 20%.

For molality, molarity, or mass concentrations, the units in the numerator and denominator are different. Sometime, however, it is useful to be able to compare apples to apples, as it were. For example, we might be interested in knowing the number of solute molecules in the solution compared to (i.e. divided by) the total number of solution molecules. This number is called the mole fraction or number fraction — using mole units or the corresponding particle counts in both numerator and denominator gives the same result. For example, a mole fraction of 0.2 of compound 'A' would mean that one out of every five molecules in the solution is an 'A' molecule (**Figure 2.37**). A mole fraction is defined in terms of the moles of one component compared to all components present:

$$\text{mole fraction} = \frac{\text{moles}_{\,component\ 1}}{\text{moles}_{\,all\ components}} \tag{2.47}$$

One useful feature of defining mole fraction this way is that it isn't limited to solutions, where all of the molecules are homogeneously distributed, and can be used to describe systems that are mixtures.

Fractions for comparing the amount of one component to all components aren't limited to moles. When applied to volumes, they describe a volume fraction:

$$\text{volume fraction} = \frac{\text{volume}_{\,component\ 1}}{\text{volume}_{\,all\ components\ before\ mixing}} \tag{2.48}$$

Note, the total volume in the denominator is the sum of the volumes for each of the components before mixing. The volumes of components can change upon mixing. If the total volume of all components after mixing is used in the denominator instead, the measurement is still a volume fraction, but sometimes called a volume/volume percent.

For masses, a mass fraction can be defined:

$$\text{mass fraction} = \frac{\text{mass}_{\,component\ 1}}{\text{mass}_{\,all\ components}} \tag{2.49}$$

For each of these quantities the fraction will be less than one, since the amount of the component in the numerator will always be less than the total amount of components in the denominator (which includes the component in the numerator).

In terms of units, the numerator and denominator have the same units (moles/moles, L/L, or g/g). These units cancel, making mole, volume, or mass fractions a unitless quantity. That said, a unit-like descriptor can often follow these fractional quantities. If the fraction is not much less than one, the number will often be multiplied by one hundred

and presented as a percent. For example, 300 ml of ethanol added to 700 ml of water have a volume fraction of 0.3, or 30%. If the fraction is much less than one, it might be labeled as parts per thousands (ppt), parts per million (ppm), or parts per billion (ppb). For example, the US Environmental Protection Agency's recommended standard for lead fraction in bare soil in play areas is 200 ppm by weight (**Figure 2.38**). This means that more than 0.000200 g of lead per 1 g of soil in play areas is considered dangerous.



Figure 2.38 Example of a mass fraction. For the soil on playgrounds, the EPA recommends no more than 1 g of lead atoms in any form per 5 kg of soil. This is a mass fraction of lead of 0.0002, or 200 parts per million (200 ppm).

The use of a mass fraction in this example illustrates some of its advantages. First, because mass fractions (and all of the fraction quantities described above) are not limited to solutions, they can be used to quantify features of complicated mixtures, like lead-containing compounds found within the many components of soil. Second, mass is an appropriate unit to use for the lead and for the soil. Multiple different lead compounds can be present in the soil. Determining their identity and molar or volume amount is difficult, while there are relatively straightforward ways of determining the total mass of lead of any form in a sample. For soil, determining what compounds are present — let alone how many moles of each — is quite challenging. However, weighing a soil sample is trivial.

In addition to mole, mass, and volume fractions, there are also related quantities called mole, mass, and volume ratios. In each of these ratios, the amount of a component is divided by the amount of all of the components besides the component of interest:

$$\text{mole ratio} = \frac{\text{moles}_{comp\ 1}}{\text{moles}_{all\ components} - \text{moles}_{comp\ 1}} \tag{2.50}$$

$$\text{volume ratio} = \frac{\text{vol}_{comp\ 1}}{\text{vol}_{all\ comp\ before\ mixing} - \text{vol}_{comp\ 1}} \tag{2.51}$$

$$\text{mass ratio} = \frac{\text{mass}_{comp\ 1}}{\text{mass}_{all\ components} - \text{mass}_{comp\ 1}} \tag{2.52}$$

Mole, volume, and mass ratios can be greater or less than one (greater than one, because you might have more of your component of interest than everything else in your sample). Like mole, volume, and mass fraction, the analogous ratios are unitless, but can be presented as percents or ppt, ppm, or ppb. Because all of these quantities are indistinguishable (is 10 ppm a mole fraction, a mass ratio, a volume fraction, …?), it is important to label what type of quantity the number is (10 ppm mass fraction).

Altogether, in this chapter we have presented many different ways to describe concentrations or quantities related to concentration. That said, we have not been exhaustive and will encounter some additional measures of concentration and related quantities, such as pH, later in the book.

2.18 Density

Concentrations describe the amount of something (a solute) in a given volume of something else (the solution). It can also be useful to describe the amount of a something in a given volume of itself. The volumetric mass density of a substance is the mass of a given volume of that substance (**Figure 2.39**). Volumetric mass density is commonly just called density and if often abbreviated with the Greek letter rho, ρ, making the formula for density:

$$\rho = \frac{m}{V} \tag{2.53}$$

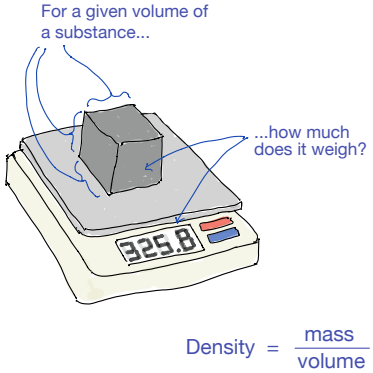


Figure 2.39 Definition of density. How much the substance weighs compare to its volume.

Density can be reported in different units, but a common unit of density is grams per

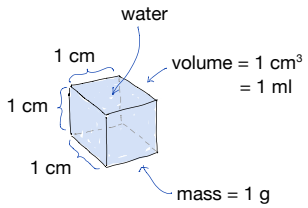


Figure 2.40 Density of water. The density of water is 1.0 g/ml, because 1 gram of water fills a cubic box with sides of 1 cm. The volume of this box, 1 cubic centimeter, is defined as 1 ml.

milliliter. As an example, liquid water, under the right conditions, has a density of 1.00 g/ml. This means that 1 gram of water takes up a volume of 1 ml. One milliliter is defined as the volume of 1 cubic centimeter (a cube with all sides being 1 cm long). So one cubic centimeter of water (1 cubic centimeter can be abbreviated as 1 cc or 1 cm^3) weighs 1 gram (**Figure 2.40**). As a side note, this convenience is not a coincidence — these relationships for water were deliberately chosen as the basis for the metric system.

Different substances can have different densities. Elemental lead is quite dense, with a density of 11.3 g/ml. In contrast, oxygen gas under standard conditions has a density of 0.00143 g/ml. This means that 1.00 ml liquid water, lead, and oxygen gas weigh 1.00 g, 11.3 g, and 0.00143 g, respectively, or that 1.00 g of these substances would take up a volume of 1.00 ml, 0.0886 ml, and 699 ml (densities can be used as conversion factors, and it's worth seeing if you can get these numbers yourself).

At the molecular level, why might the density value be large or small (**Figure 2.41**)?

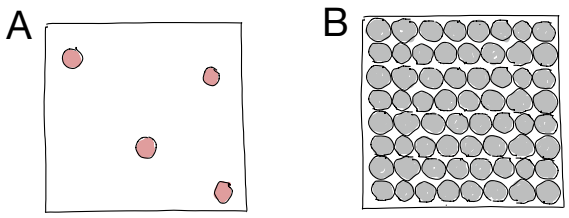


Figure 2.41 Molecular picture of density. A) A substance with a low density: Gaseous oxygen, O_2 (schematically represented by the red circles), has a greater mass than water (H_2O). However, at the molecule level the oxygen molecules are very far apart from one another. B) A substance with high density: elemental lead. Here the lead atoms (represented by the gray circles) are much heavier than water and are packed together tightly.

Let's consider a substance with a small density first. For a given volume of the substance, say 1 ml, in order for the density to be small, the mass of that substance in 1 ml would have to be small. This could either be due to the molecules making up the substance being light, there being relatively few molecules in the 1 ml volume, or both. Conversely, something with a high density might have heavy molecules and/or lots of molecules packed into the 1 ml volume. The mass of a molecule is just the sum of the masses of the atoms that make it up, and how heavy an atom is just depends on how many protons and neutrons it has. How many molecules are in a given volume depends on both the volume of an individual molecule (how big the atoms are, how atoms are arranged within the molecule) and how tightly individual molecules are packed against each other. This packing is often related to the phase of the molecule. Solids tend to have the molecules most densely packed, with liquids often being slightly less densely packed. Gases are much less densely packed, with lots of empty space between molecules. For our example compounds, lead is so much denser than water mostly because lead atoms are much heavier (atomic weight of 207 amu) than the oxygen (16 amu) and hydrogen (1 amu) that make up water (both lead, a solid, and liquid water are pretty tightly packed). Oxygen gas is much less dense than water, mostly because it is a gas, where there is a lot of empty space between oxygen molecules compared to tightly packed water (the mass of an oxygen molecule, O_2, is actually a bit more than for a water molecule, H_2O).

The density of a substance depends on the temperature and pressure at which it is measured, and these parameters should be reported as part of the density value. For example, water has a density of exactly one at 4 °C (39 °F) and 1 atmosphere (air pressure at sea level). Temperature and pressure affect density mainly by affecting how tightly packed molecules are, with higher pressures tending to push molecules closer together and higher temperatures giving molecules more energy to break free from potential forces holding them together. Densities for solids and liquids tend to not change significantly with normally encountered changes in temperature and pressure, unless the substances changes phase (goes from liquid to solid, from liquid to gas, and vice versa). On the other hand, gases, consisting of molecules that largely do not interact and surrounded by empty space, readily undergo compression and expansion, making their densities much more sensitive to changes in temperature and pressure.

One consequence of differences in densities is how buoyant substances are in water (**Figure 2.42A**). Substances with a density greater than water (i.e. greater than 1.0 g/ml) will sink when added to water (assuming it is not soluble in water). Substances less dense than water (less than 1.0 g/ml) will float. For example, a block of lead will sink in a tub of water, while a balloon filled with oxygen floats in water. Note, the mass of the balloon surrounding the oxygen gas contributes to the overall mass of the object, but still results in an overall density less than water. Even a lead balloon can float in water, if the total weight of the lead outside and gas inside relative to its volume is less than the density of water. The same principle explains how dense steel boats can float. The idea of accounting for the mass of all components of something when considering its density extends to solutions. Table sugar is more dense than water, and when an aqueous sugar solution is prepared, the solution is more dense than water. If pure water is carefully added to this solution, the sugar solution will form a separate layer on the bottom (**Figure 2.42B**). However, because the sugar solution and water are soluble in each other, eventually they will mix and form one solution. That said, more persistent separations of liquids are possible. As we will see in later chapters, oils are both insoluble in water and less dense, causing oils to float to the surface when added to water.

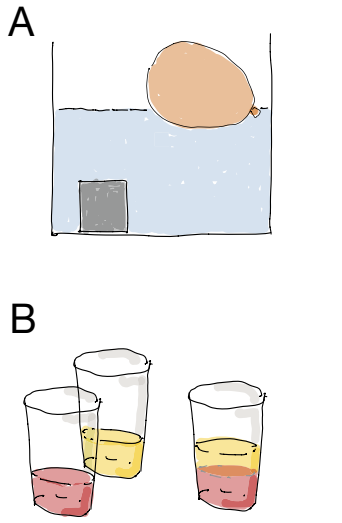


Figure 2.42 Buoyancy of objects in water. A) Shown are a block of lead and a balloon filled with oxygen in water. B) Water, colored with yellow dye, is less dense than a sugar solution colored with red dye.

As a final point, when the density of a substance is divided by the density of a reference substance, the result is called the specific gravity. Almost always the reference substance is pure water under conditions where the density is 1.00 g/ml. For such specific gravity values, they will have the same magnitude as the density, but will be unitless. For example, lead, with a density of 11.3 g/ml, has a specific gravity (with respect to water) of 11.3.



CHAPTER 3
Atomic Ions and Salts

Motivation and Overview: Atoms can gain or lose electrons. In this chapter we see how such changes generate charged species called ions. We also examine the ability of ions of opposite charges to come together to make salts, the distribution of specific ions in cells and other environments, and the roles that ions can play in biological systems.

A. Single Atom Ions

Atoms gain or lose electrons more readily than protons or neutrons; among an atom's electrons, those in the valence shell are particularly prone to gain or loss. For example, in Chapter 1 we saw that some atoms become more stable by losing or gaining one or more valence electrons to achieve a full electron shell. What are the ramifications of changing the number of electrons in an atom and how do we describe this process and its products?

3.1 Single Atom Ions are Charged

As we previously discussed, atoms contain positively charged protons (each having a +1 charge) and negatively charged electrons (each -1). In the atoms of elements, the number of protons and electrons is equal, making their net charge zero. However, when such an atoms loses or gains one or more electrons, this balance is thrown off and results in an atom with a non-zero net charge. For example (**Figure 3.1A**), an atom of elemental sodium metal contains 11 protons and 11 electrons. When it loses its one valence electron, it ends up with 10 electrons, giving it a net charge of +1:

$$\text{Charge of Na atom - } 1e^- = p^+ + e^- \text{ charges} = 11 \times (1) + 10 \times (-1) = +1 \qquad (3.1)$$

Similarly, a chlorine atom that gains an electron (**Figure 3.1B**) ends up with a net charge of -1:

$$\text{Charge of Cl atom + 1e- = p+ + e- charges} = 17 \times (1) + 18 \times (-1) = -1 \qquad (3.2)$$

While tabulating the total charges of an atom gives its net charge, an easier way is to focus on the change in charge. If an atom like elemental chlorine gains a negatively charged electron, its charge becomes -1. Similarly, if an elemental sodium atom loses an electron, it is left with a charge of +1. If multiple electrons are gained or lost, the charge on the atom changes that amount. For example, if an elemental magnesium atom loses two electrons, it will have a +2 charge. Similarly, if an elemental magnesium atom had gained two electrons, it would have a -2 charge.

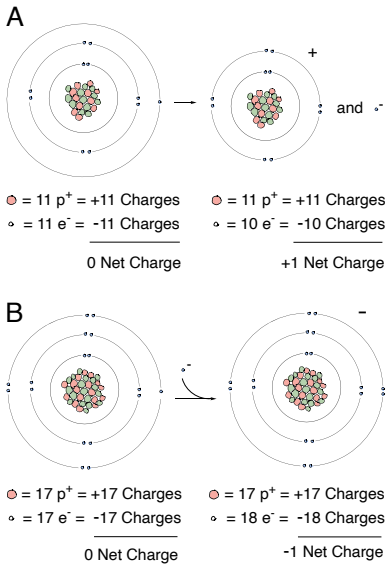


Figure 3.1 Single Atom Ions Have a Net Charge. A) Formation of a positively charged sodium ion from an elemental sodium atom. B) Formation of a negatively charged chloride ion from an elemental chlorine atom.

Any particle with a non-zero charge, such as a sodium atom with a +1 charge or a chlorine atom with a -1 charge, is called an ion. The presence of charge on single atoms can be indicated by writing the net charge as a superscript after the atom symbol. Thus, a sodium ion with a +1 charge would be Na^+ and a chloride ion with a -1 charge would be Cl^-. Note that for ions with a single charge, the number of charges is not included and is assumed to be one (such as Na^+ and Cl^-). However, if there are multiple charges, the number and type of charges is included. For example, a magnesium ion with a charge of +2 would be abbreviated as Mg^{2+}.

Just as losing two electrons from an elemental magnesium atom results in a Mg^{2+} ion, the reverse can be inferred: the presence of a Mg^{2+} ion indicates that an elemental magnesium atom must have lost two electrons sometime in its past. That said, we will often encounter single atom ions, like Mg^{2+}, and just take for granted that they are in that state, not worrying about when or where they lost their electrons.

3.2 Stability of Charged Atoms

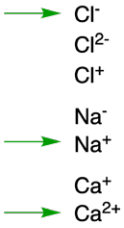


Figure 3.2 Potential Ions of Chlorine, Sodium, and Calcium. In theory, atoms of chlorine, sodium, and calcium can adopt different charge states by gaining or losing different numbers of electrons. However, the most common ions of these elements (indicated with a green arrow) correspond to atoms with a full valence.

Atoms can theoretically be in any number of different charge states (**Figure 3.2**). For example, a chlorine atom could be a Cl^- ion (gained one electron), a Cl^{2-} ion (gained two electrons), or even a Cl^+ ion (lost one electron). Nonetheless, not every one of these ions is equally likely to be seen. Since atoms are generally most stable when they have a full valence, they will tend to only gain or lose enough electrons to achieve a full valence shell. Of the possible ions of chlorine, Cl^- is ubiquitous, as gaining one electron gives chlorine a full valence. Encountering Cl^{2-} and Cl^+ ions is unlikely, because these species are further from having a full valence than Cl^- (the exception being situations where significant energy is available to generate the less stable species).

Based on stability, it is easy to predict the most common ions for the metals in the first two columns and for the halogens. For the elements we are most concerned with in those columns, they are Na^+, K^+, Mg^{2+}, Ca^{2+}, and Cl^-. Indeed, we will encounter these particular ions frequently throughout this chapter and in the rest of the book.

3.3 Ion Nomenclature

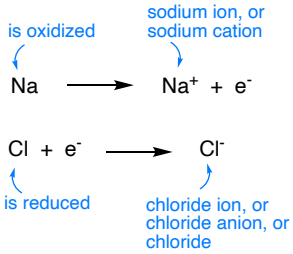


Figure 3.3 Terms Associated with Ions. When an atom or molecule loses one or more electrons it is oxidized, while it is reduced when gaining one or more electrons. Both processes shown also happen to be ionization reactions, where a neutral atom or molecule is converted to a charged particle by adding or removing electrons. An atom or molecule that ends up positively charged is a cation, while one that ends up negatively charged is an anion. Metal cations are known by the element's name followed by an indication of the ion (like sodium ion or sodium cation). Atomic anions are named with an -ide suffix to indicate it is an anion (like chloride).

Many terms are used for ions and the processes that generate them (**Figure 3.3**). Positively charged ions are known as cations and negatively charged ones as anions. Na^+ is a cation and can be referred to as a sodium cation or sodium ion. Cl^- is an anion, and single atom anions are designated by taking the atom's name and replacing the end portion with -ide. So, Cl^- would be a chloride (or more explicitly, a chloride ion or a chloride anion). As all the halogens can be anions, their ions are known as the halides and include the aforementioned chloride ion from chlorine, fluoride ion from fluorine, bromide ion from bromine, and iodide ion from iodine.

The fact that ions can have different numbers of charges can also be specified in their naming, and there are many ways to do so. One way is to explicitly state the number of charges. For example, Mg^{2+} could be referred to as the plus two ion of magnesium or magnesium plus two. Another approach is to use the term monovalent for a single charge, divalent for two, and trivalent for three. In this scheme, Mg^{2+} would be referred to as the divalent cation of magnesium. Often, when a single atom ion is in its most common charge state, it is just referred to as the ion without an indication of which charge it is. For example, Na^+ is often called a sodium ion, even though there are other possible charge states that ion could be. That said, some elements, especially the transition metals, readily adopt different charge states, making it necessary to specify their charge.

3.4 Electron Transfer Nomenclature

In processes where the number of electrons changes, there are ways to specify whether they are gained or lost (Figure 3.3). When an electron or electrons are added, we call

this a reduction reaction, and the species gaining electrons is reduced. Two examples are shown (**Equations 3.3** and **3.4**). In the first, an elemental chlorine atom gains an electron to generate the chloride anion - i.e. in this reduction reaction a chlorine atom is reduced to a chloride:

$$Cl + e^- \rightarrow Cl^- \quad (3.3)$$

In the second example, a sodium cation gains an electron to be reduced to an elemental sodium atom:

$$Na^+ + e^- \rightarrow Na \quad (3.4)$$

As seen in Equations 3.3 and 3.4, the term reduction makes sense, as the charge state after addition of the electrons is lower than when it started. Specifically, for Equation 3.3 the charge of the chlorine atom is reduced from 0 to -1 in the chloride anion. Similarly for Equation 3.4, the charge state of the sodium cation was reduced from +1 to 0 in the sodium metal.

The opposite process, in which an electron is removed, is known as an oxidation reaction and the atom or molecule that loses an electron or electrons is said to be oxidized. Two examples that reverse the previously shown reduction reaction are shown in **Equations 3.5** and **3.6**. In the oxidation reaction shown in Equation 3.5, an elemental sodium atom loses an electron to be oxidized to the sodium cation:

$$Na \rightarrow Na^+ + e^- \quad (3.5)$$

Similarly, in Equation 3.6, a chloride anion undergoes oxidation to be converted to an elemental chlorine atom:

$$Cl^- \rightarrow Cl + e^- \quad (3.6)$$

The term oxidation was coined when oxygen was the first recognized oxidizing agent (hence the name), but the concept has been generalized to include any electron-removal reactions.

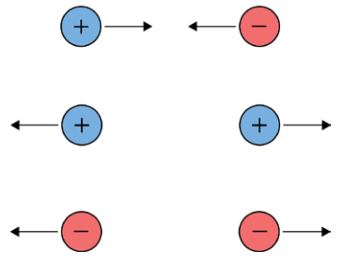


Figure 3.4 Electrostatic Attraction and Repulsion. Types of interactions exhibited between different pairs of charged particles.

B. Salts

When there is more than one ion present, they can interact in various ways. One way is to come together to form a compound known as a salt.

3.5 Interactions of Charged Particles and Salts

A charged particle can interact with other charged particles by electrostatic interactions (**Figure 3.4**). If two particles have the same type of charge (positive and positive, or negative and negative), they will repel each other. On the other hand, if they have opposite types of charges (positive and negative), they will attract one another. When this attraction is especially strong, ions of opposite charges will form a compound of interacting ions called a salt.

The prototypical salt you are probably familiar with (and previously mentioned in Chapter 1) is table salt, sodium chloride (**Figure 3.5**). Table salt is composed of sodium cations and chloride anions in a regular, tightly packed arrangement (Figure 3.5, right), where every sodium ion interacts with six neighboring chloride ions and every chloride ion interacts with six sodium ions (except at the edges of the crystal). This arrangement allows

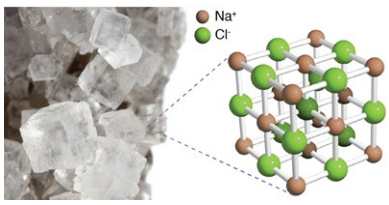


Figure 3.5 Structure of the Salt Sodium Chloride. On the right are the molecular details of the 3D packing of sodium cations (brown) and chloride anions (green) against one another in table salt. On the left are the macroscopic structures of salt crystals that results from the crystalline packing of ions shown on the right.

each ion to maximize its electrostatic interactions with the ion of the opposite charge. The geometry of packing at the molecular level extends in all directions to ultimately impart a cubic shape to the crystals of table salt (Figure 3.5, left). The close packing of ions is a common feature of salts, though the geometry of their arrangement will often differ and is based on the size and shape of the ions involved.

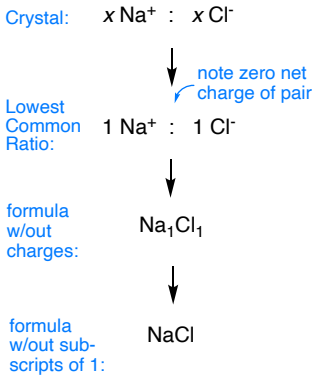


Figure 3.6 Chemical Formula of Sodium Chloride. In a crystal of salt there are many sodium cations and chloride anions, but the formula of the salt is written as the lowest common ratio of the two components, with the cation listed first. In a salt the ratio between an ion and its counterion must result in a net charge of zero. Because the charge of sodium ion is 1 and chloride is -1, there are equal numbers of each ion and the lowest common ratio is one of each and so the formula of the salt is written as NaCl.

3.6 Formulas and Names of Salts

When we write the formula of a salt, we first write the symbol for the cation followed by the symbol for the anion. For table salt (**Figure 3.6**), that is the sodium cation and then the chloride anion. The number of cations to anions is indicated by a subscript following the name of the ion. Although there are many individual cations and anions in a given salt crystal, the formula uses subscripts representing the lowest whole number ratio for each ion. For sodium chloride, that is 1 sodium ion to 1 chloride. If the subscript is a 1, it is typically not written. Additionally, in the formula of salts, the charges of the ions are not included. Putting this all together, the formula for table salt is NaCl.

In salts, an ion is paired with an ion of opposite charge, known as its counterion. For table salt, if we focused on the sodium cation, we would say that its counterion is the chloride anion. On the other hand, if we focus on the chloride, we would say its counterion is the sodium cation. In table salt, 1 sodium ion is matched with 1 chloride counterion. However, the number of ions and counterions in a salt does not have to be equivalent. Instead, the total charge of the salt has to be zero. For NaCl, that is the case with 1 Na^+ and 1 Cl^-, as the total charge is zero:

$$\text{total charge NaCl} = \text{cation} + \text{anion charges} = (+1) + (-1) = 0 \qquad (3.7)$$

However, for a salt made up of magnesium ions, Mg^{2+}, and chloride ions, Cl^-, 1 magnesium ion (+2) and 1 chloride ion (-1) do not add up to zero. To be able to make the total charge of magnesium and chloride ions add up to zero, we need two chloride ions for every magnesium ion:

$$\text{total charge } MgCl_2 = \text{cation} + \text{anion charges} = 1(+2) + 2(-1) = +2 -2 = 0 \qquad (3.8)$$

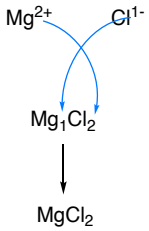


Figure 3.7 Shortcut for Generating a Salt's Formula From its Ions. Shown is the "crisscross" method applied to a salt of magnesium and chloride ions. The cation, Mg^{2+}, is listed first and the anion, Cl^-, second. In the salt, the number of charges of the cation (2) becomes the subscript of the anion, while the number of charges of the anion (1) becomes the subscript of the cation (that is, ion charges "crisscross"). Do not include any subscripts of 1 (i.e. not Mg_1), and make sure the subscripts reflect their lowest common ratio (not applicable here, but you wouldn't want subscripts of say 2 and 2).

Indeed, salts made from magnesium and chloride ions have two chlorides per magnesium ion, and, according to our rules, its formula is $MgCl_2$. While it's always possible to play with the subscripts in a salt's formula to get a total charge of zero, there is a shortcut for getting the correct subscripts by "crisscrossing" the ions' charges (**Figure 3.7**). It is also worth noting that there can be ions that consist of multiple atoms. Consequently, there can be salts in which one or both of its ions are not single atom ions.

Like the formula of a salt, a salt's name lists the cation component first and then the anion. The cation component is named without any ion designation (i.e. the element name is used alone, without adding the word 'ion' or 'cation'). If the anion is a single atom ion, the atom with the -ide suffix is used (without any additional ion designation). Thus, for a salt like NaCl, its name is sodium chloride (not sodium chlorine). For other salts composed of single atom ions, the number of cations to anions can be more complicated than the one-to-one case seen with sodium chloride. Nonetheless, these salts are named like sodium chloride without indicating how many of each ion is present (at least for the single atom ions we will focus on). So, a salt like $MgCl_2$ is simply called magnesium chloride.

3.7 Salts in Water

Within a salt, its ions are held together by attractive electrostatic interactions that are called ionic bonds (**Figure 3.8A**). Under many conditions (for example, table salt in a

salt shaker), these ionic bonds are quite strong. However, when some salts are added to water, these ionic bonds break and the salt dissolves (what water molecules are and why they can do this is covered in the next chapter).

For example, if a little table salt is added to water, it will fully dissolve (**Figure 3.8B**). At the molecular level, the individual sodium cations and chloride anions look like individual balls moving freely about in the water. Here, the attraction between an ion and its counterion is not strong enough to hold them together as a crystalline solid (again, for reasons explained in the next chapter). That is not to say that in water there is no electrostatic attraction between sodium cations and chloride anions or repulsions between same-charged ions. Indeed, on average sodium and chloride ions will spend a bit more time closer to one another than would be expected for non-interacting particles. Similarly, two sodium ions or two chlorides will tend to be farther apart from one another, on average, than would be expected by chance for two non-interacting particles.

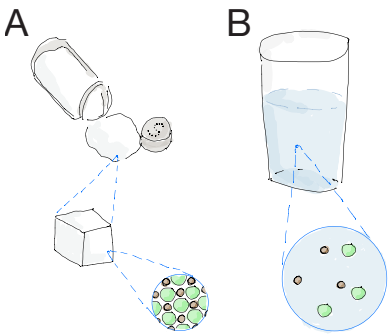


Figure 3.8 Table Salt in and out of Water. Shown is a schematic depiction of the molecular details of sodium chloride A) out of water, and B) after being added to water. Sodium cations are shown as brown balls, chloride anions as green ones. In the salt crystals, only a single layer of ions is shown for simplicity. Between the oppositely charged ions in the crystal are ionic bonds that are represented here as black lines. When sodium chloride is dissolved, these bonds break, and interactions with water molecules replace them. In the figure, water molecules are not shown, nor their interaction with the ions.

If a salt dissolves in water, there will be a certain concentration of cations and anions in the solution. If we know the initial concentration of the salt and that it fully dissolves, it is relatively easy to predict the ion concentration, though the value of the concentrations often surprises students the first time they see them. For example, if we were to make up a solution of table salt to 1 M NaCl, the solution would end up having a concentration of 1 M sodium cations and 1 M chloride anions. What does it mean to make up a salt solution to a certain concentration, and why do the ions end up at these concentrations?

Let's start with what it means to make a salt solution to a certain concentration. For a 1 M solution, we are describing a concentration of 1 mole of particles per liter of solution. For many particles, for example sodium ions, what a particle means is easy enough to understand. A one molar solution of sodium cations means one mole (6.02×10^{23}) sodium cations would be present in about one liter of water. For table salt, which has many sodium and chloride ions in one salt crystal and many salt crystals in a gram of the salt, what do we mean by a mole of particles? By convention, we consider a particle of salt equivalent to the formula of the salt. Thus, for table salt, NaCl, one mole of table salt would be one mole of NaCl's. To make 1 L of a 1 M solution of table salt (1M NaCl), we would first weigh out a mole of table salt, which is roughly 58.5 grams of table salt:

$$\frac{1 \text{ mole NaCl}}{1 \text{ L}} \times 1 \text{ L} \times \frac{58.5 \text{ g NaCl}}{1 \text{ mole NaCl}} = 58.5 \text{ g NaCl} \qquad (3.9)$$

Then, we would add water until the solution had a volume of 1 L, giving us our 1 M NaCl solution. As noted previously, once this salt is added to water, the ions fully dissociate into individual sodium and chloride ions. So what is the concentration of each? We know that every NaCl that was present before it was added to water will become one sodium cation and one chloride anion. Because each NaCl formula unit produces exactly one Na^+ and one Cl^-, the molar concentration of each ion in solution equals the original NaCl concentration.

If this doesn't seem intuitive, we can see the same thing using a conversion factor. Since 1 NaCl becomes 1 Na^+, 1 mole of NaCl becomes 1 mole of Na^+. We can use this information to create a conversion factor (choosing NaCl to be in the denominator):

$$\frac{1 \text{ mole } Na^+}{1 \text{ mole NaCl}} \qquad (3.10)$$

For a 1 M solution of NaCl, we can then use this conversion factor to calculate the sodium cation concentration in this solution:

$$\frac{1 \text{ mole NaCl}}{1 \text{ L}} \text{ x } \frac{1 \text{ mole } Na^+}{1 \text{ mole NaCl}} = \frac{1 \text{ mole } Na^+}{1 \text{ L}} = 1 \text{ M } Na^+ \qquad (3.11)$$

So, it should be clear that a 1 M solution of sodium chloride consists of a 1 M solution of sodium cations and a 1 M solution of chloride anions, while a fully dissolved 1 M solution of magnesium chloride ($MgCl_2$) is a 1 M solution of magnesium cations and a 2 M solution of chloride anions.

It's important to point out that not all salts dissolve fully in water, and even table salt might not fully dissolve in water under certain conditions. The factors that dictate the solubility of salts are discussed in Subsection 3.13 of this chapter and addressed more quantitatively in Chapter 5, Section F.

C. Abundance of Atomic Ions

As we will discuss in Section D, the concentration of an ion has a big impact on how it affects a biological system. Let's examine the average concentrations of common ions found in various solutions (**Table 3.1**).

Ion	Ocean	Tap Water	Blood Plasma	Human Cell*
Na^+	500 mM	2 mM	150 mM	10 mM
K^+	10 mM	0.1 mM	5 mM	100 mM
Ca^{2+}	10 mM	1 mM	2 mM	<< 0.1 mM free (2 mM bound)*
Mg^{2+}	50 mM	0.4 mM	1 mM	0.5 mM free (10 mM bound)
$Fe^{2+/3+}$	<< 0.1 mM	<< 0.1 mM	<< 0.1 mM	<< 0.1 mM
Cl^-	500 mM	2 mM	100 mM	10 mM

Table 3.1 Average Concentrations of Common Ions in Natural Solutions. Ion concentrations vary significantly within samples, so average concentrations are reported only to one significant digit. The asterisk indicates that where numbers for human cell were not available, the value was estimated from another eukaryotic organism, budding yeast. Most listed values are adapted from *R. Milo and R. Phillips, "Cell biology by the numbers," CRC Press, 2015*. Tap water ion concentrations are from United States averages reported in *"The mineral content of tap water in the United States household," K.Y. Patterson, P.R. Pehrson, and C.R. Perry, J Food Comp and Analysis, 31: 46-50, 2013*.

3.8 Sea and Tap Water

Water found in the ocean has relatively high concentrations of ions (Table 3.1), especially sodium and chloride ions. Both of these ions have concentrations of roughly 0.5 M. How do we think about such a concentration? Converted to a mass concentration, this corresponds to about 29 grams of NaCl per liter of water, a pretty substantial amount of salt. As mentioned in Subsection 2.13, the maximum concentration of sodium chloride in water at 25° C (77 ° F) is 6.1 M, meaning that the amount of sodium chloride dissolved in ocean water is almost 1/10th of the maximum that can be dissolved. Recall also that the "concentration" of water in pure water is about 55 M, meaning that for every sodium ion there are roughly 100 water molecules present. From experience, you may also be aware that the concentrations of sodium and chloride ions are quite high. If you have ever swum in the ocean and swallowed any water, it is aggressively salty. In fact, the commercially available form of table salt called sea salt is made from ocean water in which the largest component is sodium chloride.

While the concentrations of other ions in ocean water are less than sodium or chloride, they are still substantial. Magnesium ion (~50 mM) is about 1/10th as abundant as sodium. Potassium and calcium ions (~10 mM) are lower still, being about 1/5th the concentration of magnesium ion. Concentrations of iron ions are significantly lower.

Tap water, and other forms of fresh water, vary considerably in their ion concentrations depending on their source. Nonetheless, compared with ocean water, the concentration of ions in tap water tends to be substantially less, with no ion being at a concentration more than a couple of millimolar (Table 3.1). For example, sodium chloride, the ions with the highest concentration in ocean water (around 500 mM for each) still tends to be highest in tap water, but at a much lower level (around 2 mM). Other ions, such as the divalent cations of magnesium and calcium ions also are generally lower in concentration than in ocean water, though as a total fraction of ions present, they are more prominent. While the concentration of ions in tap water is low compared to ocean water, it is important to point out that the concentration is not zero, as is the case for "pure" water, or nearly so for distilled water. As we shall see, even lower levels of ions in tap water contribute to the properties of tap water.

3.9 Solutions Inside and Outside of Cells

The concentration of ions in biological solutions tends to be somewhere between that of ocean water and tap water. For solutions outside of cells, such as blood plasma (Table 3.1), sodium and chloride ions have the highest concentration (about 150 mM and 100 mM, respectively). They are just a bit more than 3-fold less than the concentration found in ocean water and almost 50- to 100-fold greater than in tap water. Besides magnesium, the trends in ion concentrations found in ocean water hold in blood plasma, though at 2- to 5-fold lower concentrations. For example, both blood plasma and ocean water have significantly lower concentrations of potassium ions compared to sodium ions.

Inside cells, the concentration of ions tends to be relatively high, like in blood plasma, but the relative amounts of specific ions are very different. For example, in both blood plasma and inside the cell, the total amount of cation present is somewhere between 100 mM and 200 mM. However, in blood plasma, the predominant contributor to this is sodium ions, with about 150 mM. In contrast, in cells the predominant contributor is potassium ions at about 100 mM. This difference has biological significance; how and why it occurs will be discussed in Subsection 3.12. Divalent cation concentrations also differ inside and outside the cell, though this analysis is complicated by the fact that inside the cell, many of these cations are bound, something we will discuss in Subsection 3.13.

3.10 Ions and Counterions in Solution

In undissolved salts, the total charge of an ion is matched by the total charge of its counterion. This is partly because the strong attractive force between an ion and its counterion makes it favorable to match them up. Further, the strong repulsive force between ions of the same charge makes an excess of one type of charge costly. When salts are dissolved in water, interactions are weakened - though still strong enough that a mismatch in cation and anion charges remains energetically costly. Thus, the total charge of most solutions will pretty much add up to zero, and that is largely the case with many of the solutions in Table 3.1. However, you will notice that this is not uniformly true, and is especially pronounced for solutions in human cells, where there is a large excess of various cations to chloride. Why is this the case? The major reason is not so much an exception as an incomplete accounting of ions: besides single atom ions, cells contain both small charged organic molecules and larger biomolecules that can serve as counterions. We'll introduce some of these molecules in Section D, and discuss them more fully in subsequent chapters. That said, a smaller contributor to the discrepancy between cations and anions in cells is that these charges are not perfectly balanced. As we pointed out, it is energetically costly for a system to not have a net zero charge. However, cells are willing to expend energy to generate a (small) imbalance, making the

positive charge outside of the cell just a bit greater than inside (or equivalently, making the inside of the cell more negative than the outside). Why a cell does this is discussed more in Subsection 3.12.

D. Ions and Biological Systems

Ions in solution affect cells, and cells in turn exploit ions. There are different ways to think about ions: as dissolved particles, as charged particles, and as particles with specific chemical identities. The effects of ions come from each of these aspects. In this section, we will explore three biologically relevant aspects of ion behavior, with our first topic, osmosis, focusing on ions as dissolved particles.

3.11 Osmosis

Osmosis is the bulk movement of water molecules that occurs when several requirements are met. First, there must be an unequal distribution of dissolved particles in the solution (i.e. osmosis can involve ions but can also happen with uncharged molecules). Second, this concentration difference needs to be maintained, say by some sort of barrier impermeable to the particles. Third, the water molecules in the solution must be able to pass through the barrier readily (or at least relatively easily). Under such conditions, water molecules will move from a region with fewer solute molecules to one with more, i.e. during osmosis, water flows across a barrier from the side of lower concentration of dissolved particles to the side of higher concentration (**Figure 3.9**).

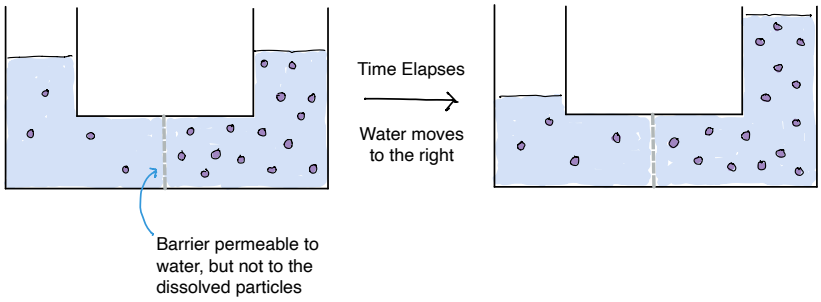


Figure 3.9 A System That Undergoes Osmosis. Two solutions are separated by a membrane that is permeable to water, but impermeable to the solute particles. Initially (left image), the system has equal volumes of water on both sides of the barrier, but the left solution has a lower concentration of solute particles than the one on the right. After time (right image), water has moved from the left side to the right (i.e. undergone osmosis), with the water level higher on the right than on the left. The water continues to move until the gravitational force on the excess water equals the force driving the water to move. Pressure can be applied to the right side to return the water levels to being equal, with the amount of applied pressure called the osmotic pressure.

Cells experience osmosis because their cell membranes are capable of allowing water to pass through them, yet are impermeable to many types of molecules (or only allow regulated passage of molecules across their membrane such that an uneven concentration inside and outside the cell is maintained). A clear demonstration of osmosis occurs when red blood cells are placed in different solutions (**Figure 3.10**). Blood cells are typically

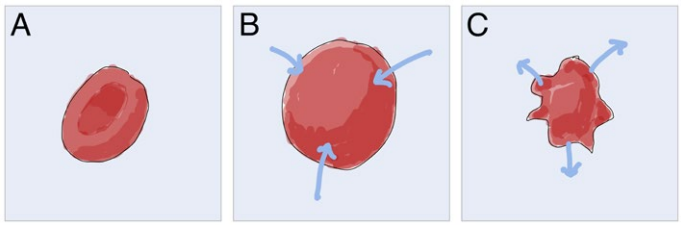


Figure 3.10 Red Blood Cells in Various Solutions. Shown are the effects of prolonged exposure of red blood cells to solutions of A) saline, B) distilled water, and C) ocean water. A saline solution has roughly the same solute concentrations as the cell (the solution is what is known as isotonic); Distilled water has a lower solute concentration (it is hypotonic); and ocean water has a higher solute concentration (it is hypertonic). Blue arrows indicate the direction of net water flow due to osmosis (water flow from regions of lower solute concentration to higher). Note, net flow doesn't mean that there is no flow in the other direction, just that the arrow represents the difference in flow. For the isotonic solution with no net flow, there is actually equal water flow in and out, resulting in zero net flow.

found in your circulatory system surrounded by blood plasma. As detailed in Table 3.1, while the composition of ions present in cells and in plasma differ, the overall ion concentration is comparable, meaning that there is not a significant amount of osmosis that occurs. If red blood cells are placed in a saline solution (Figure 3.10A), i.e. a solution of sodium chloride that has a total ion concentration similar to blood plasma, the cells will not undergo osmosis. In contrast, if the blood cells are placed into distilled water (Figure 3.10B), they will swell up and eventually burst. In this case, since the concentration of particles inside the cell is much higher than outside (Table 3.1), due

to osmosis, water will flow from the outside of the cell to the inside and increase the pressure exerted from the inside of the cell. If red blood cells are placed in a solution of ocean water (Figure 3.10C), they will eventually shrivel up and die. Here again, osmosis is to blame. Since the concentration of ions outside of the cell is higher than inside (Table 3.1), water flows from inside to outside of the cell, reducing the volume inside of the cell and allowing it to collapse.

Osmosis can be utilized to limit the growth of microbes, such as bacteria. Single celled organisms like bacteria commonly experience variations in the salinity (saltiness) and concentration of other molecules in their environment as they move about, and they have dedicated cellular machinery to deal with the resulting osmotic stress. However, if they experience prolonged exposure to high concentrations of particles, the stress becomes too much. In various types of salt curing of food products (**Figure 3.11A**), the concentration of salt proves too inhospitable to many of the bacteria that could cause us harm. Similarly, in many fruit jams and preserves, the presence of high concentrations of sugar molecules ultimately kills many bacteria (**Figure 3.11B**), despite the fact that these same sugar molecules are sources of energy for them (and us) at lower concentrations.

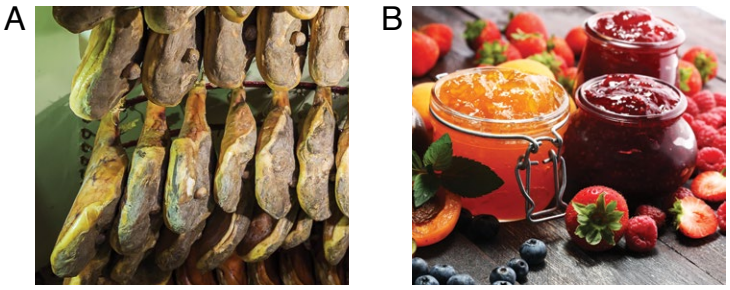


Figure 3.11 Using Osmosis to Preserve Food. A high concentration of salt or sugar can be used to A) cure meats or B) make fruit preserves. Organisms like bacteria lose water to their surroundings because of a concentration of dissolved particles greater than inside of their cells. These particles also affect the foods, but the effect can be more complicated than simply drying them out.

Too high of a concentration of ions can also affect people in various ways. Too much sodium ion in your body can result in fluid retention. This increases the pressure that the "tubes" that make up your circulatory system experience, and is thought to contribute to the condition of high blood pressure (**Figure 3.12A**). That is why a diet lower in salt is recommended for those with this condition.

Salt concentrations and osmosis are also important in proper kidney function. Your kidneys are organs that remove waste products and other undesirable molecules from your body in the form of urine (**Figure 3.12B**). To do so, the kidneys first filter molecules from the blood — including amino acids, small peptides, sugars, ions, and water — and then selectively reabsorb the ones the body needs. Proteins in the cells that make up the kidneys are responsible for removing most of the molecules (water being an exception, as discussed below). To remove water, at several stages the kidneys remove sodium ions into the surrounding tissue, raising its osmolarity. By osmosis, water follows, making what's left, the urine, more concentrated so you lose less water. That said, the kidneys are only able to remove so much sodium. If you ingest something with an extremely high concentration of sodium ions, such as ocean water, the kidneys cannot concentrate urine sufficiently to excrete the large salt load, so they must excrete more water than you drank, causing a net water deficit..

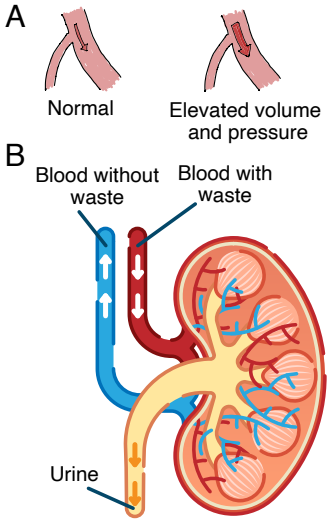


Figure 3.12 Osmosis in the Body. A) High levels of salt are thought to lead to an increase in extracellular fluid and volume of blood pumped by the heart, raising blood pressure. B) Your kidneys remove waste from your blood, excreting it as urine. To limit water loss, the kidneys use osmosis to concentrate your urine by removing water.

One final note about osmosis. Osmosis requires that water be free to travel between regions, while the concentrations of other components remain unchanged. Under certain circumstances this can be the case, but it is not uncommon for both water and solute to be free to move about. For example, suppose you begin with a system like the one shown in Figure 3.9, where the initial concentrations of a solute molecule differs across a barrier. However, instead of having a barrier permeable only to water, the barrier was permeable to both water and solute (perhaps the barrier had pores large enough for both water and solute to pass through) (**Figure 3.13**):

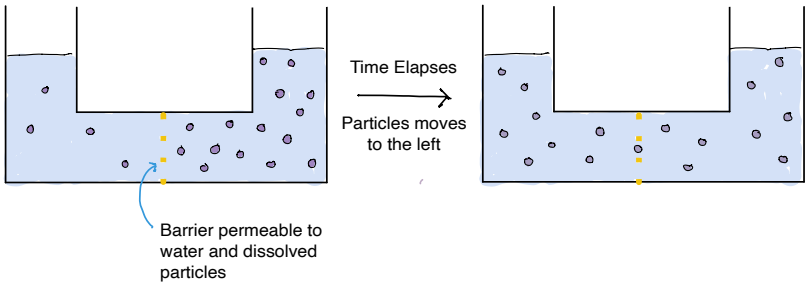


Figure 3.13 Example of a System with Movement of Both Solute and Water Molecules. A system is set-up similar to the one discussed in Figure 3.9 with the essential difference being that the barrier between the two solutions is permeable to water *and* solute molecules. In this system, the solute molecules move from a region of higher concentration to the lower until their concentration is identical on both sides.

Over time, both water and solute would pass through the barrier until the concentration of solute on both sides of the barrier was the same. If we focused on the solute, we would observe a net flow of solute molecules from the more concentrated side to the less concentrated one, until the concentrations were balanced. This phenomenon where molecules move from a region of higher concentration to a lower one is general, and we can even interpret osmosis as water effectively moving from a region of higher water concentration to a region of lower water concentration (with the other molecules unable to move).

3.12 Movement of Charged Particles

In Figure 3.13, we saw that dissolved particles can redistribute in response to an unequal concentration distribution. These particles do not have to be ions, indicating that charge isn't crucial to their movement. However, under certain circumstances, particles move because of their charge. For example, a positively charged particle placed near a stationary negatively charged object will be attracted to the object and, if possible, move toward it (**Figure 3.14**):

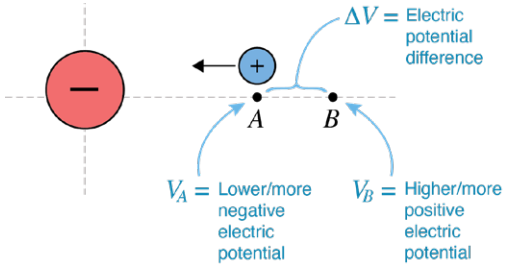


Figure 3.14 Electric Potential of a Positively Charged Particle Near a Negatively Charged Object. Shown are two possible points in space, A and B, that a positively charged particle could be relative to a stationary negatively charged object. Because there is an attraction between the particle and the object, moving the particle from A to B increases its electrostatic potential energy - i.e. the particle has more electrostatic potential energy at B than at A. The electric potential of a particle is its electrostatic potential energy divided by the particles charge (abbreviated as V), Thus, the positively charged particle has a higher electric potential at B (V_B) than at A (V_A). If the particle were held at B and then released, it would spontaneously move toward A to be at a lower electric potential. The difference in electric potentials between position A and B is the electric potential difference or voltage (ΔV). The sign of the voltage difference will contrast whether we are comparing going from A to B or B to A.

One way to understand this behavior (described more fully in Part E), is that a charged particle has differing amounts of electric potential (potential energy per unit charge) depending on the environment it is in. In our example (Figure 3.14), if the positive particle were moved further away from the negatively charged object, it would have more electric potential. Closer, it would have less. On its own, this charged particle will move from a position of higher to lower electric potential. This is like a dropped rock falling to the ground, where the rock goes from having more gravitational potential (gravitational potential energy per unit mass) to less. The difference in electric potential between two points is the electric potential difference, also known as the voltage, and can be measured in units of Volts . Various devices can generate a specific amount of electric potential difference. For a typical non-rechargeable AAA battery, there is a potential difference of 1.5 Volts between its two ends. A typical electrical outlet in a house in the US has an average (root-mean-square) potential difference of 120 Volts .

The voltage of such devices can be used to drive the movement of charged particles, which is called electrical current. When we think of electric currents, we often envision the movement of electrons. For example, when a wire is hooked up to a battery (**Figure 3.15A**), electrons flow through the metal of the wire. That said, electrons are not the only charged particles that can move when subjected to a voltage. Ions from dissolved salt

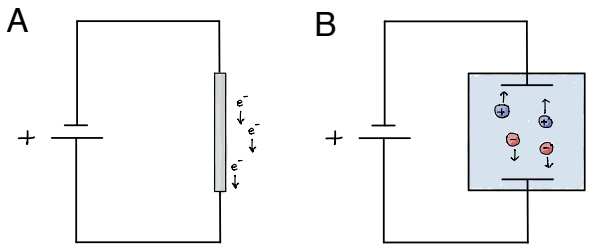


Figure 3.15 Effects of a Voltage on Charged Particles. A) When a metal wire is hooked up to the ends of a battery, the electric potential difference between the ends (its voltage) causes the negatively charged electrons in the wire to move toward the end of the battery with a more positive electric potential. This movement of electrons is an electrical current. B) When a salt solution is hooked up to the ends of the same battery, the voltage will cause the anions to move toward the end of the battery with the more positive electric potential, while the cations will move toward the end with the more negative electric potential. The movement of ions is also considered an electric current.

solutions can also travel through water as an electric current in response to an electric potential difference (**Figure 3.15B**). Because such solutions contain both negatively and positively charged particles and respond oppositely to a given voltage, the anions move in one direction and the cations move in the other. It should be noted that, with a large enough electric potential difference, electrons can also be induced to leave or join ions or surrounding water molecules, resulting in oxidation or reduction of these species.

Large electric potentials and currents pose a risk of electrocution. As we saw in Table 3.1, the fluids in our bodies have high ion concentrations. When we are subjected to a large electric potential difference, say coming in contact with a live wire (high electric potential) while standing on the ground (low electric potential), the voltage and induced current can have harmful effects on cells and organs: induced currents can rapidly release heat and cause electrical burns; high voltages can disrupt already established electric potentials (see next paragraph). Electrocution doesn't require direct contact between an individual and high or low electric potential sources. As we also saw in Table 3.1, tap water has dissolved ions and these concentrations are sufficient to conduct an ion-based current. This is why electrical devices, like hair dryers, include safety warnings not to use the device in or near water (**Figure 3.16**).



Figure 3.16 Hair Dryer Safety Warning. The ions in tap water can conduct electric current. This makes using electrical devices in or near water an electrocution hazard.

While electric potential differences and movement of charged particles can be hazardous, they can also be useful. In fact, we exploit them in our body's nervous system. The nervous system transmits signals between the brain and the rest of the body (**Figure 3.17A**), including signals for the voluntary movement of muscles in our limbs, the involuntary pumping of the heart, and the sensing of our surroundings. The nervous system is composed of nerve cells that mediate this signaling (**Figure 3.17B**), and a number of observations suggest that nerve signaling has an important electrical component. In the late 18th century, the Italian physician and physicist Luigi Galvani showed that electricity could cause a frog's legs to twitch, even in a non-living frog. Additionally, as mentioned earlier, electrocution can alter nerve signaling to the heart and skeletal muscles, thereby disrupting their normal contractions.

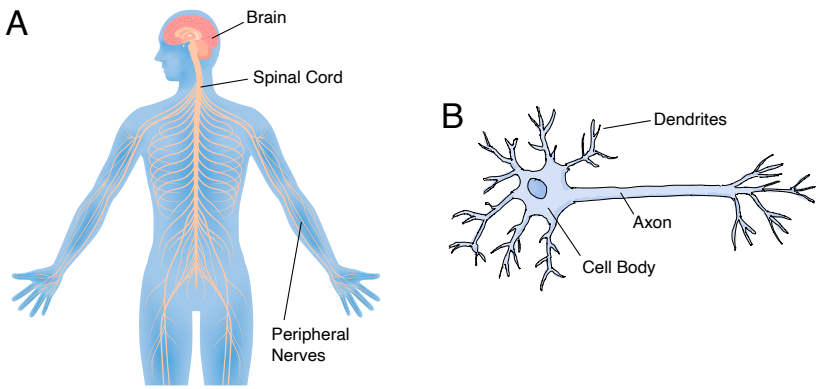


Figure 3.17 The Nervous System and Neurons A) A schematic of the body's nervous system including the brain, the spinal cord, and peripheral nerves. Signals from nerve cells (neurons) in the brain can be sent to peripheral motor neurons via nerve cells in the spinal cord to cause voluntary movements of skeletal muscles or involuntary functions of organs like the heart. Peripheral sensory neurons take information from sensory organs and send signals to the brain via the spinal cord neurons. B) Schematic of a typical neuron. Neurons vary considerably in their morphology, but often have a cell body that branches off into dendrites and axons. Dendrites receive signals from other nerve cells, while axons transmit signals to other nerve cells. In our brief exploration of nerve signaling, we will focus on transmission of signals down an axon. Axons of neurons above a certain diameter are typically surrounded by myelin, but that is not included in the figure for clarity.

What is the nature of the signal that nerve cells transmit? During signaling a voltage spike (known as an action potential) travels down the length of the majority of a nerve cell (**Figure 3.18**), and is created by movement of ions across its cell membrane. The entire process is quite complicated, but starts with the fact that all cells, including nerve cells,

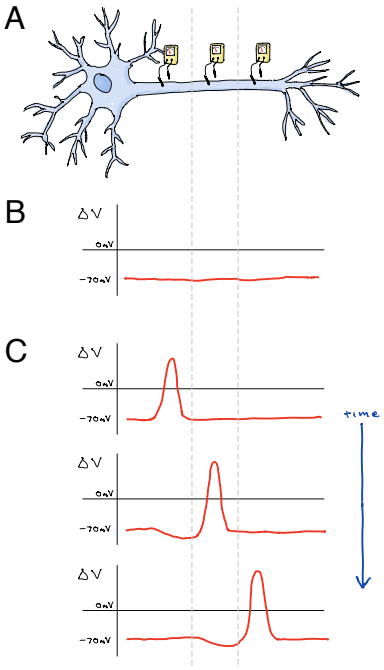


Figure 3.18 Progression of an Action Potential Down a Nerve Cell. A) Shown at the top is a neuron with probes that measure the electric potential difference between the inside and outside of the cell at three different locations in the axon. B) The measured voltage at the three positions shown in part A before a nerve signal is transmitted. All positions have the same resting potential of about -70 mV. C) The measured voltage at three positions shown in part A as nerve signaling is transmitted. The top panel shows that early on, there is a spike of voltage near the first detector, but not at the other. After some time (middle panel), the spike has moved down the axon to the second detector. A bit after that (bottom panel), the voltage spike has traveled to the end of the axon.

have a potential difference between their inside and outside. This potential difference is known as the cell's membrane potential. For resting nerve cells, this potential difference is about -70 mV, due to a slight excess of positive charge outside of the cell and a slight excess of negative charge inside (**Figure 3.19A**, right). This membrane potential value means that a cation placed outside of the cell has a higher electric potential than inside the cell, and all else being equal, would move inside to be at a lower electric potential.

Recall from our previous discussion of ion concentration (Table 3.1) that the concentration of sodium ions outside of the cell, including nerve cells, is 10-15 times higher than inside (Figure 3.19A, left). Why do sodium cations stay outside of a cell when moving inside would reduce the electric potential (as well as moving down their concentration gradient as described in Figure 3.13)? While there is a significant driving force for this movement, the cell membranes of nerve cells in their resting state are relatively impermeable to sodium ions, preventing this migration (and to the extent there is some leakage, there are systems that export sodium ions back out of the cell to maintain this imbalance).

However, the situation changes when nerve signaling is initiated (**Figure 3.19B**). Channels are found throughout the cell membrane that are only permeable to sodium ions (voltage-gated sodium channels). Starting at one end of the cell, the channels open, allowing the sodium ions to enter both to reduce their electric potential and to dissipate their concentration imbalance. As the sodium ions add positive charge to the more negative interior of the cell, the membrane potential inside goes from negative to more positive (and in fact proceeds to become positive, because the concentration gradient of sodium ions is sufficient to create an excess of positive ions inside the cell). An interesting feature of these sodium channels is that their opening is sensitive to the membrane potential, where a membrane potential of roughly -55 mV is sufficient to cause them to open. This means that when sodium ions rush in through one channel, increasing the local membrane potential, this triggers neighboring voltage-gated sodium channels to open (**Figure 3.19C**). This process repeats, causing this spike of voltage to propagate down to the other end of the nerve cell (Figure 3.18).

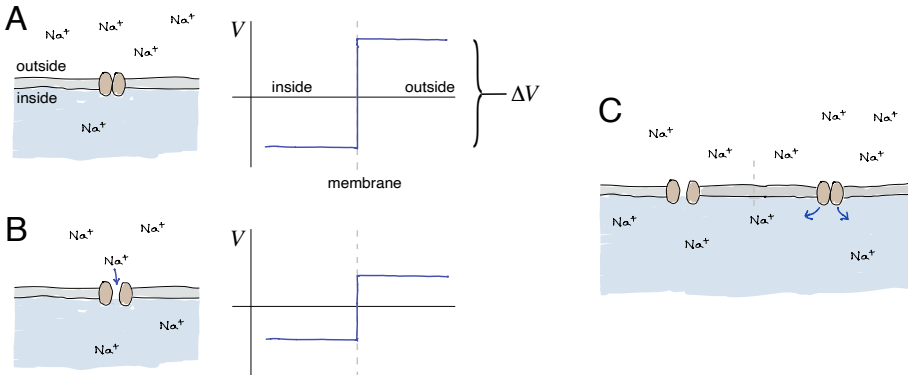


Figure 3.19 Role of Sodium Ions in Creating and Propagating Action Potentials. A) Resting potential. Left: Before a voltage spike occurs, there is an excess of sodium ions outside of the neuron, and membrane-embedded voltage-gated sodium channels that could allow sodium ions to pass (brown) are closed. For simplicity, no other ions are shown. Right: The cell has more positive charge outside of the cell than inside, making the resting potential negative (defined as potential inside minus outside). Note, the source of this potential difference is mostly due to non-sodium ions and is discussed later. Because sodium ions are in a region of higher positive electric potential, as well as the existence of a sodium ion concentration difference outside versus inside, these ions would have a lower free energy inside the cell. However, because they cannot readily pass through the membrane, they stay outside. B) Initial phase of the action potential. Left: Initiation of a voltage spike occurs when the sodium channel opens and lets only sodium ions through. Right: This increase in positive charge neutralizes the negative potential inside of the cell, causing the membrane potential difference to change. As shown, at this stage the potential difference is still negative, but less so than previously. Ultimately, the high concentration of sodium ions on the outside of the neuron can drive enough sodium ions into the cell to make the membrane potential positive (not shown). C) Propagation of the action potential down the axon. A feature of voltage-gated sodium channels is that they go from a closed state to an open state when the membrane potential rises above about -55 mV. Thus, the increase in membrane potential that occurs when one channel allows sodium ions in (left of the dotted line) triggers a neighboring voltage-gated sodium channel to open (right of the dotted line), propagating the nerve signal further down the neuron. Note that while accurate, this model is incomplete and does not address how the membrane potential returns to a resting potential, why the sodium channels open in the first place, and other complications (some of which are addressed in Figure 3.20).

It should be noted that while sodium ions and voltage-gated sodium channels are a crucial part of nerve signaling, creating the full action potential spike and establishing and reestablishing a resting membrane potential also involve other ions and ion channels (**Figure 3.20**). These include pumps that use energy to initially establish the excess of sodium ions outside of the cell (concomitant with an excess of potassium ions inside the cell), as well as various potassium channels that function to establish much of the initial resting membrane potential and to quickly decrease the voltage in the action potential spike.

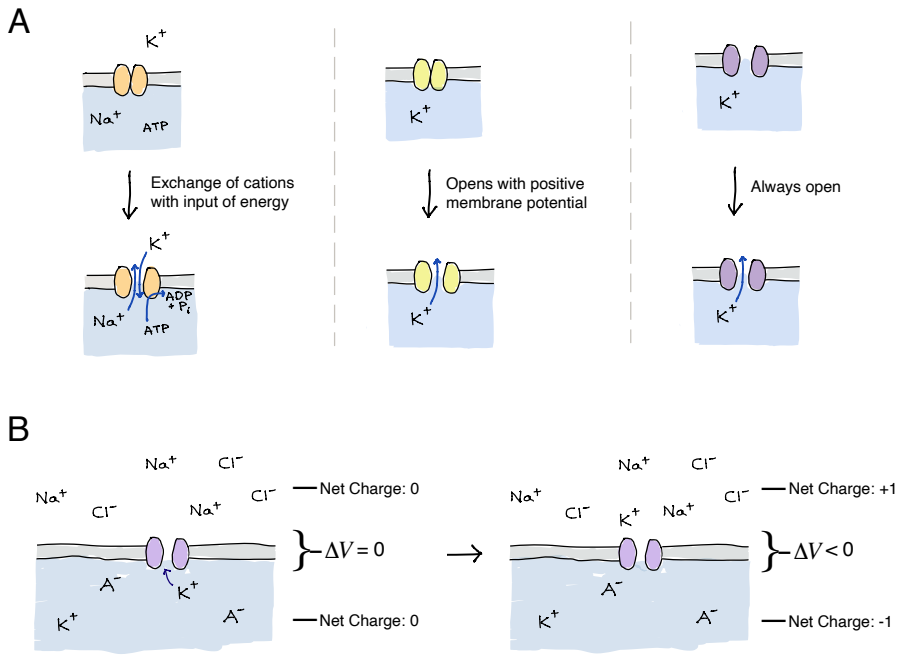


Figure 3.20 More Details About Action Potentials. A) Some of the other ion channels and pumps involved in nerve signaling. Light blue regions depict the inside of the neuron throughout. Left: The sodium/potassium pump. This molecule uses energy (from the molecule ATP) to establish and maintain excess sodium ions outside of the cell and potassium ions inside. For simplicity, the image depicts one sodium and one potassium ion being exchanged per ATP consumed in a single step, but in fact, two potassium ions are imported for every three sodium ions exported and the process occurs in multiple steps. Middle: The voltage-gated potassium channel. This channel opens in response to the rise in membrane potential in the initial phase of the action potential and allows potassium ions to move from inside the neuron to outside. This movement counteracts the positive membrane potential caused by open voltage-gated sodium channels, thereby helping to reestablish the resting potential. Right: The potassium leak channel. This potassium-specific channel is always open and allows free movement of potassium ions between the inside and outside of the cell and has a role in establishing the resting membrane potential as described next. B) Model of how the distribution of potassium ions largely creates the resting membrane potential of the cells. The action of the sodium/potassium pump (not shown) creates an unequal balance of sodium and potassium cations inside and outside the cell. This imbalance does not necessarily create an excess of charge across the membrane (i.e. a non-zero membrane potential), as every cation can still be neutralized by an anion. In this situation, both sodium and potassium ions would like to move across the membrane to relieve their concentration gradient. This is only possible for potassium ions, since (mostly) the only open channels are the potassium-specific leak channel. When a potassium ion moves across the membrane, it increases the positive charge outside by one and decreases the positive charge inside by one, since other ions cannot move to offset the movement of the potassium ion. This excess of charge creates an electric potential difference that makes it progressively harder for more potassium ions to leave the cell. In fact, it turns out that relatively few potassium ions compared to their total internal concentration need to leave to create a membrane potential sufficient to counteract more potassium ions from leaving. Thus, most of the resting membrane potential of the neuron results from a small number of potassium ions that have moved to the cell exterior. Note, the model as shown is an oversimplification, but is qualitatively correct.

3.13 Association of Charged Molecules

A final way that charged molecules can be biologically important is through the association of ions and their counterions. We have seen that sodium cations and chloride anions can associate strongly to form crystalline salt. However, when added to water, these ions will generally not be associated with each other. Like sodium ions and chloride, many charged particles do not form tight associations in water. That said, many do. In biological solutions the strength and duration of ion interactions varies considerably, and biological systems utilize both strong and weak interactions.

What dictates how strongly ions interact? Let's consider some factors that affect the attraction of oppositely charged ions (**Figure 3.21**): One factor is the total amount of charge a particle has, which affects its interactions, with more charge leading to stronger attraction. Another factor is the number of charged particles, which also has an effect, with high concentrations of ions driving association. As mentioned previously, water tends to neutralize the charge of ions, weakening association, and the presence of other counterions in solution can similarly shield some of the charge. Finally, the chemical composition and structure of the charged molecule plays an important role in the

strength of associations. In each of these factors, the effective amount of charge either increases or decreases, making the attraction to the opposite charge stronger or weaker. With interactions of similar charges, the increase or decrease similarly strengthens or weakens repulsion.

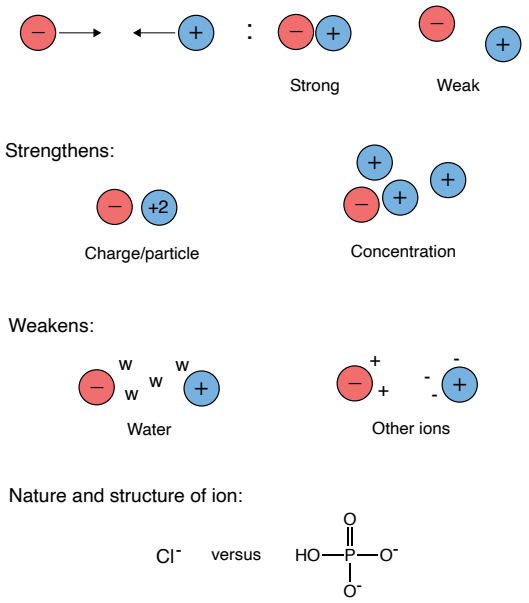


Figure 3.21 Factors That Can Influence Attractive Electrostatic Interactions. Attractive interactions between oppositely charged ions can be strong or weak, with numerous factors contributing. These same factors can also affect repulsion between ions with the same charge.

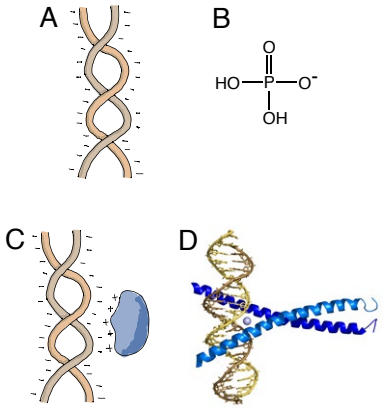


Figure 3.22 Strong Electrostatic Interactions between DNA and a DNA-binding protein. A) Cellular DNA is a rope-like molecule composed of two strands twisted around one another. Each strand is highly negatively charged. B) The negative charge of DNA comes from a component similar to a phosphate ion that occurs regularly throughout each strand. C) Schematic depiction of a transcription factor protein binding to DNA. Transcription factor proteins generally have surfaces with a high density of positive charges, facilitating DNA binding via attractive electrostatic interactions. D) More detailed structure of an actual DNA-protein complex, in this case between DNA and a human transcription factor called CREB-1 (PDB 1DH3). The structures of DNA-binding proteins vary considerably and further volumes will explore DNA, proteins, and their potential interactions.

Let's see these factors in action, starting with a simple system, table salt. As previously described, in the absence of water the sodium cations and chloride anions make multiple strong attractive electrostatic interactions that lock the ions tightly into a crystalline solid (Figure 3.8A). When a salt crystal is added to water (Figure 3.8B), the water molecules surround each ion and shield its charge. With the attractive electrostatic interactions between sodium and chloride ions weakened (though not entirely neutralized), the ions disperse relatively randomly throughout the solution. As more salt crystals are added to the water, this process can continue, but cannot do so indefinitely. At some point, the solubility limit of the salt is reached, and the water molecules cannot overcome all of the attractive interactions of the salt ions, leaving some of the salt undissolved. For table salt, this concentration threshold is substantial (roughly 6 M of NaCl), but in many salts it is much lower. Overall, higher salt concentrations tend to disfavor dissolving of the salt, as the higher density of ions in solution favors their re-association.

Water molecules significantly reduce the attractive electrostatic interactions between ions, weakening the attraction between ions. Nonetheless, their attraction can still be significant if the total charge of the interacting molecules is large. Molecules such as DNA and DNA-binding proteins, like transcription factors, can form tight interactions, where a significant portion of their binding (though certainly not all) comes from attractive electrostatic interactions. DNA is the material in which an organism's genetic information is stored. It is a long, thin molecule composed of two linear pieces that are twisted around each other, not unlike a rope made from two strands (**Figure 3.22A**). The chemical composition of the DNA strands is quite complicated, but one component repeated throughout its length is a negatively charged group of atoms similar to a phosphate ion (**Figure 3.22B**). This makes the exterior surface of the DNA molecule highly negatively charged. Some proteins in the cell are designed to bind to DNA. Like DNA, the composition of proteins is quite complicated, but these molecules often adopt a well-defined shape. For DNA-binding transcription factors, the surface of the protein is typically highly positively-charged, allowing it to form strongly attractive interactions with the high negative charge density of the DNA (**Figure 3.22C** and **D**).

Water molecules are not the only species capable of weakening the electrostatic attraction between oppositely charged molecules, like DNA and DNA-binding protein. As we have seen, the interior of the cell contains a high concentration of atomic ions: cations such as potassium, sodium, and magnesium ions; anions like chlorides. These ions are attracted to biomolecules with opposite charges and can compete with other biomolecules for binding. For example, potassium cations in solution are attracted to the negative charge of DNA (**Figure 3.23**), while chloride ions are attracted to the positive surface charge found in DNA-binding proteins. This attraction is not sufficiently strong (in water) for these single-atom ions to bind to the biomolecules, but does cause them to be localized near the DNA and protein, creating a sort of cloud of ions surrounding each. This partially neutralizes the charge of the DNA and protein, making the attraction between these biomolecules weaker than they would be otherwise. From an experimental perspective, this is an important fact to remember, as the scientific literature has many studies where DNA-protein interactions were probed in solutions without physiological ion concentrations, potentially resulting in much stronger binding interactions than are actually present in the cell.

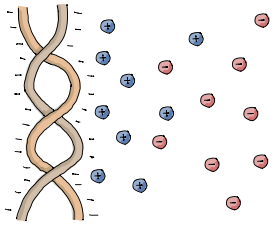


Figure 3.23 How Other Ions Can Reduce Attractive Electrostatic Interactions. When DNA is in a water solution with a high concentration of ions, such as potassium ions (shown schematically as circles with pluses), the negative charge of DNA attracts the potassium cations without binding them. The increased density of positive charge near the negatively charged DNA weakens binding of molecules like transcription factor proteins shown in Figure 3.22.

Monovalent sodium and potassium ions are not commonly associated with biomolecules in cells, but there are indeed biologically relevant examples of weak and/or shorter-lived associations. In our discussion of nerve cells, we discussed cation membrane channels like the voltage-gated sodium channel that allows sodium ions to rapidly pass through the cell membrane of neurons during the initiation of an action potential. Though the structure of cation channels is very complicated, the initial region that the cation passes through is effectively a thin tube lined with both negatively charged and partially negatively charged oxygens (**Figure 3.24**). Favorable but transient electrostatic interactions of sodium cations with these oxygens facilitate the targeting and rapid transit of the ions through the channel's initial pore. Past this region the ions emerge first into a larger water-filled region of the protein and then ultimately move into the interior of the cell, where sodium cation concentration is lower. These interactions also help explain why these channels selectively pass sodium ions but exclude the larger potassium ions.

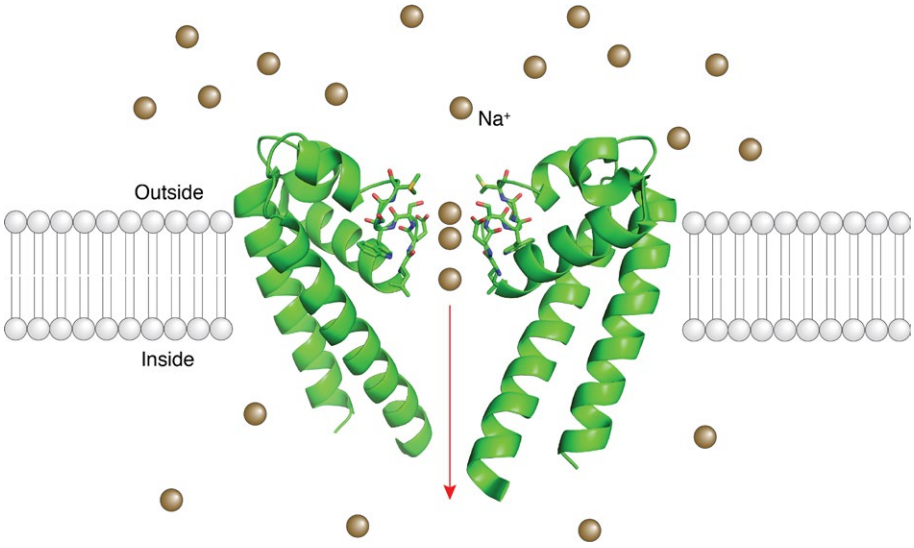


Figure 3.24 Structure of a Sodium Channel in Association with Sodium Ions. Shown is a side-on view of part of a protein channel (green) embedded in the cell membrane (components of which are shown schematically in gray). The channel is composed of four identical subunits, but only two are shown for simplicity. Most of the protein's structure is shown schematically, but the atoms that line the region known as the selectivity filter are shown in greater detail in the center of the image. In this region green represents carbon atoms, blue nitrogens, yellow sulfur, and red oxygens (hydrogens not shown). Sodium ions are depicted as brown balls (the three sodium ions in the channel are part of the channel structure, with the others added for illustration). The oxygen atoms can be fully or partially negatively charged and provide transient interactions with the positive sodium ions to facilitate their passage through the membrane.

While both sodium and potassium cations have a charge of +1, a key difference between them is their size. Since potassium is one row below sodium on the periodic table, potassium ions are larger than sodium ions. As the tunnel described in Figure 3.24 just fits a sodium ion, it is too small for a potassium ion to pass through. The selectivity filter of a potassium channel is precisely sized for potassium ion, coordinating it snugly with specific chemical groups. Sodium ions are too small to fill that coordination geometry

well, so they are not effectively stabilized and remain excluded (though the full mechanism is more nuanced than this).

Divalent cations like magnesium and calcium ions tend to act differently than sodium and potassium ions and can form relatively strong associations with the right kind of counterions. Indeed, as indicated in Table 3.1, much of intracellular calcium and magnesium is bound.

A non-biological example of a tight interaction with calcium cations occurs in tap water. Tap water can vary in its magnesium and calcium concentration depending on where it is from, and higher concentrations of these ions are what makes water considered "hard." A non-atomic ion that can be present in water is carbonate, which in one resonance structure bears negative charges on two of its three oxygens (**Figure 3.25A**). Carbonate anions and calcium cations can come together as calcium carbonate and this association is sufficiently strong in non-acidic water to form an insoluble crystalline solid (**Figure 3.25B**). Calcium carbonate is the main component of limescale (**Figure 3.25C**), a hard, chalky deposit found in faucets and shower outlets that is probably familiar to anyone who has lived in an older home or in areas with untreated hard water. There are a number of factors that make the interaction between these two ions strong, including the divalent charge on both components, the geometry of the multiple oxygens in the carbonate, and the nature of the calcium-oxygen interaction.

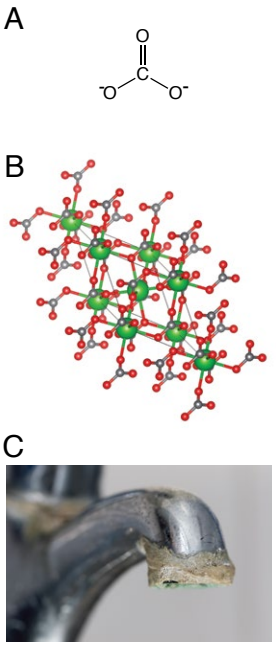


Figure 3.25 Calcium Carbonate. A) The structure of a carbonate anion. B) Calcium carbonate, $CaCO_3$, can adopt several different crystalline forms and the form shown is for calcite. The unit cell is indicated by thin black lines and is repeated in the crystal. Green spheres are calcium. Red and gray ones are oxygen and carbon, respectively. C) Limescale. Limescale is composed predominantly of calcium carbonate, but also include other ions. Limestone rock, chalk (a form of limestone), as well as marble, are also predominantly calcium carbonate, with differences in the type and size of their crystals.

Interestingly, many biological systems, including humans, utilize crystalline interactions involving calcium and phosphates (structure of a phosphate ion shown in Figure 3.22B). Calcium and phosphates, combined with lesser amounts of other ions, form the hard material that constitutes 70% of bone by weight. Both calcium ions and phosphates are plentiful in milk (as well as many other nutrients) and help to explain why milk and other dairy products are often recommended for proper bone growth and maintenance.

While divalent cations can form very stable crystalline products, in cells most of these ions form one-to-one associations with biological molecules that are strong, but reversible. For example, magnesium ions are often coordinated by anion oxygens drawn from multiple phosphate groups (**Figure 3.26A**). Similarly, calcium ions are tightly but reversibly held in complexes involving analogous chemical groups (**Figure 3.26B**).

Though less common, sodium and potassium ions can form complexes in proteins, and their generally weaker interaction can be offset by the high concentration of monovalent cations inside and outside cells.

Finally, it should be noted that some biomolecules can associate with transition metal ion, such as iron ions (**Figure 3.26C**). Because of the complicated electronic structures of transition metals (See Section 1F), these associations can result in structures with complex geometries and chemical properties. The groups coordinating the metal ions can be dynamic, and the inherent reactivity of the metal center can be utilized by the biomolecules to achieve their function.

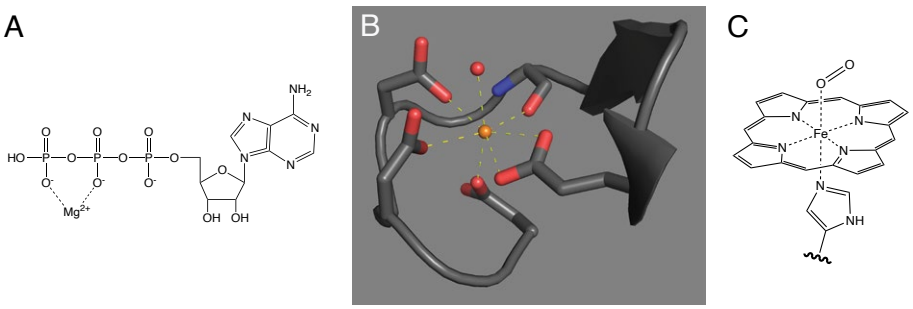


Figure 3.26 Examples of Single Atom Ions Coordinated by Biological Molecules. A) Structure of a Mg^{2+} ion coordinated by the oxygen anions of phosphate groups in the energy molecule ATP. Note, in aqueous solution the magnesium ion shown would also be coordinated to water molecules that are not shown. The complex shown can also be bound by proteins, which makes additional interactions with the magnesium ion. B) Coordination of a Ca^{2+} ion by the protein calmodulin. The central calcium ion is shown as an orange ball and the surrounding protein and water atoms are shown in red for oxygen atoms, blue for nitrogens, and dark gray for carbons. C) Fe^{2+} ion in a hemoglobin protein, where the iron is coordinated by four nitrogens in the porphyrin ring that surrounds it, a nitrogen from the hemoglobin protein, and a molecule of oxygen.

Where to from here: In this chapter we have examined various aspects of single atom ions. In the further exploration section, we get more quantitative in our understanding of electrostatic interactions and introduce the idea of systems in equilibrium. In the next chapter we begin studying multi-atom molecules, looking at the structure and properties of water.

E. Further Exploration - More on Electrostatic Interactions

In the previous section we saw that electrostatic interactions are an important contributor to the behavior of ions (though not the only one). So far our description of these interactions has been qualitative: particles with opposite charges attract, particles with the same charge repel. In this section, we examine this interaction more quantitatively. Doing so provides us with predictive power and new insights into electrostatic interactions. Further, in later chapters we will be introducing other types of molecular interactions and electrostatic interactions can serve as a model for addressing them.

3.14 Electrostatic Forces in a Simple System

Let's start with a simple system of a charged object and a charged particle with charges q_1 and q_2, respectively. If the charged particle is some distance, r, away from the charged object, the charged particle will experience a force, F, according to the formula known as Coulomb's Law:

$$F = k\frac{q_1 q_2}{r^2} \tag{3.12}$$

where k is a constant with a value of about 9 x 10^9 Nm^2C^{-2} when the charge is in the units of Coulombs (C) and the distance is in meters (m). A positive charge has a positive value of q, and a negative charge has a negative value of q, so when the charges are both positive or negative, the force has a positive value and is repulsive.When the charges are opposite, the force has a negative value and is attractive. One thing that falls out of this equation, a fact we previously discussed, is that the strength of the attraction or repulsion changes with the magnitude of the charge: doubling of a charge (say a cation going from +1 to +2) results in doubling the force of interaction. Something we hadn't previously discussed is that the force of attraction or repulsion between the charges decreases with their distance. In fact, it drops off relatively rapidly with the square of the distance (**Figure 3.27**). This means that if the distance between two charged particles was doubled, the force of interaction between them would drop to 1/4th its previous value.

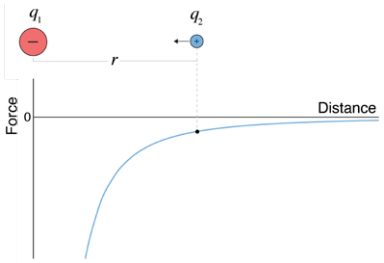


Figure 3.27 Electrostatic Force as a Function of Distance. Shown on top is a stationary negatively charged object with charge q_1, and a positively charged particle with charge q_2 some distance, r, away from it. As the force exerted on q_2 is attractive and in the direction of q_1, the force vector is negative (i.e. pointing in direction opposite from the direction the radius increases). At any given radius, the force experience by q_2 can be determined by Equation 3.12, and those values are plotted below.

Force is a vector quantity that has a magnitude and a direction. For a charged object (say one that is negatively charged), we could visualize the forces on different charged particles at different positions around our charged object as shown in **Figure 3.28**. If our charged particle was also negatively charged (Figure 3.28A), according to Equation 3.12 the forces would be directed away from our negatively charged object (effectively a push away from it) and the force experienced by our particle would die off the farther away it was from our object. Conversely, a charged particle with a charge equal in magnitude to our negative particle but opposite in charge (i.e. positive, not negative), would have a distribution of force vectors similar in magnitude, but oppositely directed (Figure 3.28B) - here the arrows would point from the potential position of the positively charged particle toward the negatively charged object (a pull toward the charged object in the center). In both cases, the magnitude of the force (the length of the vector arrow) decreases the farther the particle is from the object and can be calculated explicitly by Equation 3.12. This picture of electrostatic attraction closely resembles that of the gravitational force the earth exerts on a nearby object, where in Equation 3.12 masses replace charges, the constant is different, and only attractive forces are possible.

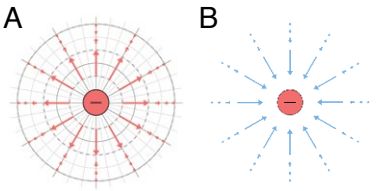


Figure 3.28 Vector Representation of Electrostatic Force. Forces experience by a charged particle at selected positions around a negatively charged object, where the charged particle is either A) negatively charged, or B) positively charged. On the left, different angles and radial positions are indicated with solid gray lines, and radii of 1, 2, and 3 units by dashed lines. In this depiction, the negatively charged particle is positioned at the base of the force vector. On the right, the positively charged particles are at the same position as the particles in part A. To emphasize that the magnitude of the force is the same, yet oppositely directed, the tip of the force arrow indicates the position of the positively charged particles.

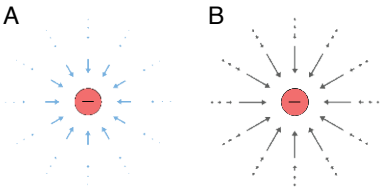


Figure 3.29 Difference between Electrostatic Force and the Electric Field. A) If the amount of charge on the positively charged particle in Figure 3.28B were halved, the force experienced would be halved (position of these positively charged particles are at the tip of the arrows, like Figure 3.28A). B) In contrast, the electric field around the negatively charged object shown is the same regardless of how much charge a particle surrounding the object has, or whether the particle is positively or negatively charged. To get from the electric field back to the electrostatic force, the field vectors are simply multiplied by the charge of a specific particle. To get the forces shown in part A, the field vectors in part B are multiplied by one half q_2. To get the force vectors shown in Figure 3.28A, the field vectors in part B are multiplied by negative q_2.

3.15 The Electric Field of Our Simple System

The depiction of forces shown in Figure 3.28 depends on the amount of charge of the object and the particle, and if the charge of the particle shown in Figure 3.28B were halved, the size of the force vectors would be halved (**Figure 3.29A**). Sometimes it is useful to have a description of how attractive or repulsive an object is independent of what the particle near it happens to be (i.e. independent of the sign and magnitude of the charge of a nearby particle). This can be accomplished by dividing the force in Equation 3.12 by the charge the particle, q_2. This gives what is known as the charged object's electric field, E:

$$E = \frac{F}{q_2} = k\frac{q_1}{r^2} \tag{3.13}$$

The electric field for the charged object q_1 is the same for any charged particle, q_2, regardless of q_2's magnitude or sign (**Figure 3.29B**). To get the force exerted on a particle from an object's electric field (i.e. go from Figure 3.29B back to 3.29A), you would multiply the field strength at the position of the charged particle by the magnitude (and sign) of the particle's charge:

$$F = q_2 E \tag{3.14}$$

3.16 The Electric Potential of Our Simple System

Instead of the force exerted on a charged particle, it is often useful to consider the potential energy of a particle in an electric field - especially when the position of the particle changes, causing its associated potential energy to change.

In general, the change in potential energy (ΔU) of an object in a field is related to the to the work done moving the object a displacement Δd against (or with) the force (F) exerted by the field:

$$\Delta U = -F \cdot \Delta d \tag{3.15}$$

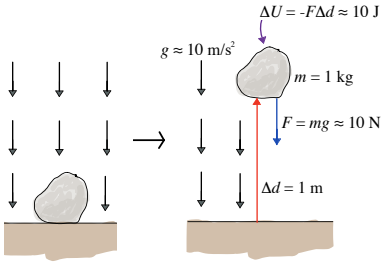


Figure 3.30 Potential Energy Stored in a Rock Lifted in a Constant Gravitational Field. Shown is a 1 kg rock lifted from the ground to a height of one meter. Work was done to lift the rock. That energy is stored as potential energy in the rock and is about ten joules.

For example, suppose you had a 1.0 kg rock and wanted to lift it 1.0 m (**Figure 3.30**). In the earth's gravitational field, this object would be subjected to a constant gravitation force, mg, of 9.8 Newtons directed toward the ground. Assuming we defined up as the positive direction, this means our force would be negative (down) and have a value of -9.8 N. The displacement of our rock (its change in height, h) would be 1.0 m up, that is positive 1.0 m. Thus, the amount of work we would need to supply to move the rock over that distance would be about 10 Joules of energy, and the object would store that energy as potential energy (i.e. at its final position relative to its initial, its potential energy increased, making it a positive potential energy change):

$$\Delta U = -(mg)h = -(-9.8\text{ N})(1.0\text{ m}) = 9.8\text{ J} \tag{3.16}$$

You would be able to see that the rock had that stored energy, because if you released it, it would fall back to the ground. While falling, it would speed up, converting its potential energy to kinetic energy. Just before it reached the ground, all of the stored potential energy would have been converted, predominantly to kinetic energy. When the rock hits the ground, that kinetic energy would be transferred to the ground and end up moving and heating up the ground a little, generating sound, etc. Thus, compared to its raised position, the rock on the ground would have lower potential energy.

Just like the rock, a charged particle at different positions within the electric field of

a charged object can have higher or lower potential energy than where it started. Take our simple model system with a negatively charged object at its center and a positively charged particle at some position around it. To move the positively charged particle, we would either be working against the attractive forces when moving the particle away from the object from A to B or working with the attractive forces when moving the particle toward the object from B to A (**Figure 3.31**). We could calculate the potential energy stored or released in our particle, just like our previous rock example. However, a key difference is that for our rock, the force was constant at all positions, while we have seen with Equation 3.12 that the force is continually changing depending on exactly where the particle is. How do we deal with that going from A to B? It turns out we can calculate the very small change in potential energy, dU, in moving a very small distance, dr (instead of Δr), using Equation 3.15, where the force is described by Equation 3.12. We can then use some integral calculus to add up the small change in potential energy that happens in these small steps and evaluate them in going from radius position A to B to determine the overall change of potential energy of the particle:

$$\Delta U_{A\to B} = \int_{r_A}^{r_B} dU = \int_{r_A}^{r_B} (-F \cdot dr) = -\int_{r_A}^{r_B} \left(\frac{k\,q_1 q_2}{r^2}\right) dr = \frac{k\,q_1 q_2}{r}\Bigg|_{r_A}^{r_B} = k\,q_1 q_2\left[\frac{1}{r_B} - \frac{1}{r_A}\right] \qquad (3.17)$$

Does this equation qualitatively match our intuition? If our stationary object is negatively charged ($q_1 < 0$) and the moved particle is positively charged ($q_2 > 0$), the terms outside of the bracket are negative. If the particle moves away from the object in going from A to B (i.e. $r_B > r_A$), then the value inside the bracket will also be negative. Together, these make the change in potential energy positive, meaning that the particle increased its potential energy. This makes sense: moving the positive particle away from the attractive negative object takes work to accomplish and this work is stored as potential energy. As r_B grows, $1/r_B$ term approaches zero, so the bracket $[1/r_B\text{-}1/r_A]$ changes by smaller and smaller amounts, meaning the potential energy continues to rise but by increasingly small increments.

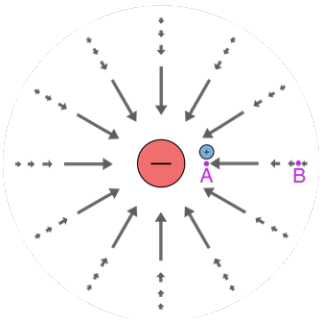


Figure 3.31 Stored Energy Moving with and Against an Electric Field. Shown is the electric field of a negatively charged object, and two possible positions where a charged particle could reside, positions A and B. If the charged particle is positive, the force vectors will be proportional to the size of the field vectors shown, and in the same direction. In this case, moving the particle against the field from A to B would require external energy to be supplied, which the particle would store as potential energy. If the particle was let go at position B, it would spontaneously move with the electric field to position A (and beyond), releasing potential energy to the system and lowering its potential energy. Note, at every point from A to B or B to A, the force vectors have a slightly different magnitudes, so determining the energy change is more complicated than an object moved in a constant field (like in the last figure).

The change of potential energy of the particle is defined relative to some initial position, r_A. If we decided to always start with the charged particle infinitely far away from the charged object, where effectively there would be no attraction or repulsion, the $1/r_A$ term would be zero, and we could consider the potential energy the particle has at r_B (which will now just call r) to be its absolute potential energy:

$$U = \frac{k\,q_1 q_2}{r} \qquad (3.18)$$

We can examine the graph of this function for our system with negative q_1 and positive q_2 values (**Figure 3.32A**). What you can see is that moving our positively charged particle away from our negatively charged object (increasing the distance r on our graph), increases the potential energy of the particle because we have to exert energy to "roll" it up the energy hill against the attractive forces (which the particle stores as potential energy). That said, when we are far enough away (to the far right of the graph), the energy landscape flattens out and we have to exert less energy to go further and increase in potential energy becomes less. Going the other direction, the positively charged particle will spontaneously roll down the energy hill to lower its potential energy and get closer to the attractive negative object.

If we consider the same (negatively charged) object with a negatively charged particle,

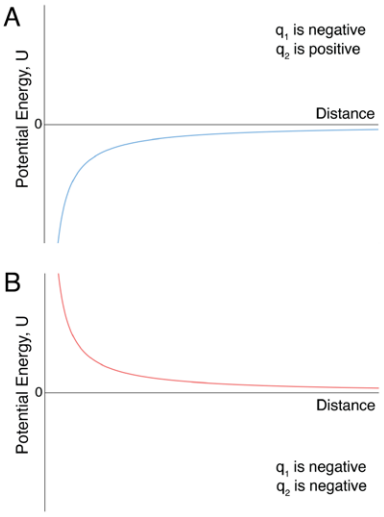


Figure 3.32 Absolute Potential Energy of Charged Particles Near a Negatively Charged Object. In the graphs the absolute potential energy, U, is shown for A) a positively charged particle, or B) a negatively charged particle, at some distance, r, away from a negatively charged object. The shapes of the curves conform to Equation 3.18. Note, the change in potential energy for a positively charged particle (part A) is not as steep as its change in its attractive forces as depicted in Figure 3.27.

the potential energy graph is reflected about the x-axis (**Figure 3.32B**). Now our particle has high potential energy when it is near the negatively charged object (r close to zero), due to all the energy it took to bring the particle close to the object it was repelling. Rolling down the curve (i.e. moving away from the object) lowers the particle's potential energy, though far enough away, the decrease in potential energy becomes small due to weaker repulsion further away.

Just as we could describe the electric field of an object independent of any particular charged particle near the object, we can re-express the electric potential energy of any particle around our object, independent of the magnitude or sign of the particle's charge. This is the electric potential of our object (not to be confused with the electric potential energy of the particle, though they are unfortunately very similarly named). We will abbreviate the electric potential of an object as V. Similar to how we derived the electric field of an object, the formula for electric potential can be obtained from Equation 3.18 by dividing it by the charge of the particle, q_2:

$$V = \frac{U}{q_2} = \frac{k q_1}{r} \tag{3.19}$$

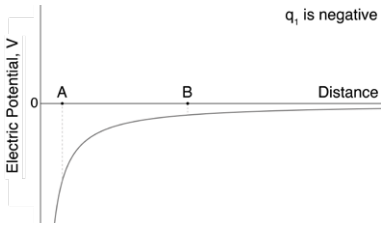


Figure 3.33 Electric Potential of a Negatively Charged Object. Shown is the electric potential , V, experienced by any charged particle some radial distance from negatively charged object. Two potential distances, labeled as points A and B, are highlighted.

A graph of the electric potential of the negatively charged object we have been examining so far would look like the curve depicted in **Figure 3.33**. This graph would be the same regardless of whatever positive or negatively charged particle we brought near it, which is convenient because it generalizes to any particle the object encounters. To generate the potential energy curves of Figure 3.32, we would simply multiply Equation 3.19 by the actual charge of the particle, with a positive charge giving a graph like Figure 3.32A and a negative charge giving a graph like Figure 3.32B:

$$U = q_2 V \tag{3.20}$$

In Figure 3.33, in which the electric potential of a negatively charged object is shown, we can see that a positively charged particle would prefer to be in a region of lower/more negative electric potential (point A) than a region of higher/more positive electric potential (point B), because from Figure 3.32A, point A corresponds to the particle having lower potential energy. On the other hand, a negatively charged particle would prefer to be in a region of higher/more positive electric potential (point B) than a region of lower/more negative electric potential, because as can be seen in Figure 3.32B, point B corresponds to a region of lower potential energy than point A. This observation is general, and is easy to remember because it mirrors our intuition about oppositely charged particles: a positively charged particle will prefer to be in a region of more negative/lower electric potential, while a negatively charged particle will prefer to be in a region of more positive/higher electric potential.

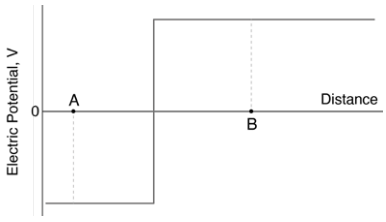


Figure 3.34 An Arbitrary Electric Potential Curve. In this graph, the electric potential is constant and negative in the region that point A resides in and constant and positive in the region point B resides in. A positively charged particle would prefer to be in a region of negative/lower electric potential and will move from point B to point A, if possible. Conversely, a negatively charged particle would prefer to be in a region of positive/higher potential and will move from point A to point B, if possible.

This observation does not require our electric potential function to look like one depicted in Figure 3.33. Consider the electric potential curve shown in **Figure 3.34**. Point A is in a region of negative electric potential while point B is in a region of positive electric potential, and so point A is in a region of lower/more negative electric potential than point B, and equivalently point B is in a region of higher/more positive electric potential than point A. This situation resembles the membrane potentials shown previously in Figure 3.19A, where the electric potential outside of the nerve cell is higher than the electric potential inside the cell. A positively charged particle, like a sodium cation, placed outside the cell in region B of more positive electric potential would have much more potential energy than if it were able to be inside the cell at position A with a more negative electric potential. Indeed, the lowering of electric potential energy by moving the positively charged particle from B to A is one of the driving forces that causes sodium ions to rush into nerve cells during the initiation of an action potential (the other driving force is movement of the sodium ions from a region of high concentration outside the

cell to lower concentration inside, where both driving forces favor movement of the sodium ions from outside to in).

Like a change in potential energy for a particle at different positions, we can talk about the electric potential difference, ΔV, between varying positions. This difference is also known as the voltage difference between two points (or voltage) and has the units of volts :

$$1 \text{ V} = 1 \text{ volt} = (1 \text{ joule})/(1 \text{ coulomb}) \tag{3.21}$$

The sign of the electric potential difference depends on which point we measure relative to. In Figure 3.33 if we were interested in the electric potential difference in going from point A to point B, we would subtract the electric potential of the initial point (A) from the final point (B). Since the electric potential at point B is a small negative number (close to zero) and the electric potential at point A is a large negative number, their difference is a small negative number minus a large negative number, which is positive. Thus, there is a positive electric potential difference in going from A to B. The potentials shown in Figure 3.34 resemble those found in resting nerve cells, where B would be a point outside of the cell and A a point inside. The membrane potential of a cell is defined as the inside potential minus the outside potential, giving a net negative value. This agrees with the measured membrane potential of a resting nerve, about -70 mV.

3.17 Electrostatic Properties of More Complicated Shapes

In the previous sections, we considered the electrostatic interaction of a charged particle with a charged object that occupies a single point in space. In many cases the situation is more complex, such as the charged object having a more complicated three dimensional shape. One approach to describing the electric field for such an object is to first use Coulomb's law for electric fields (Equation 3.19) to relate how the charge of a small portion of the object, *dq*, contributes a small part of the electric field, *dE*, experienced by a charged particle some distance away, *a*:

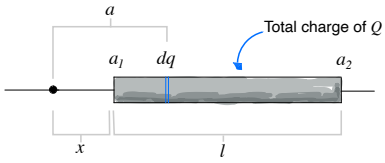
$$dE = k\frac{dq}{a^2} \tag{3.22}$$

If the charge density of the object at every point can be expressed as a function of its distance from the particle, $\lambda(a)$, it is possible to add up the contributions of the electric field over every part of the object using some calculus (that is integrating over the entire object from a_1 to a_2):

$$E = \int dE = k\int \frac{dq}{a^2} = k\int_{a_1}^{a_2} \frac{\lambda(a)da}{a^2} \tag{3.23}$$

A relatively simple application of this equation is to determine the electric field experienced by a charged particle separated from a charged rod along the rod's long axis (**Figure 3.35**). Similar methods can be used to describe the electric field for other situations, such as that of a charged particle at some distance perpendicular to the long axis of a charged rod, a charged ring, or a charged disk.

A charged particle that is not far from the surface of a charged disk, or equivalently when the charged disk is extremely large, presents an interesting situation in which the electric field above the charged surface in either direction is constant (**Figure 3.36A**). This limiting case is analogous to the gravitational field we experience. As mentioned earlier, the gravitational force between two objects is described by an equation similar in form to Coulomb's law. When we are considering the gravitational field of a large



$$\lambda(a) = \frac{Q}{l} \quad \text{for } x < a < x + l$$

$$\text{so, } dq = \lambda(a)da = \frac{Q}{l}da$$

$$E = \int_{a_1}^{a_2} \frac{k\,dq}{a^2} = \frac{kQ}{l}\int_x^{x+l} \frac{da}{a^2} = -\frac{kQ}{l}a^{-1}\Big|_x^{x+l}$$

$$= -\frac{kQ}{l}\left(\frac{1}{x+l} - \frac{1}{x}\right) = \frac{kQ}{(x)(x+l)}$$

Figure 3.35 Electric Field of a Rod Along Its Long Axis. It is possible to calculate the total electric field that a charged particle experiences when interacting with a charged rod using Equation 3.23. In this specific case, the rod is oriented relative to the charged particle as shown, is a distance x away from the charged particle, has a total length of l, and has a total charge of Q that is uniformly distributed across the rod. Not surprisingly, the electric field that the charged particle experiences depends on the total charge of the rod (Q) and how long and far away the rod is (l and x, respectively). It is worth noting, if the rod is very far away (x >> l), the equation becomes equivalent to Equation 3.13. This is expected, because when the rod is very far away, the rod effectively seems like a point charge to the charged particle.

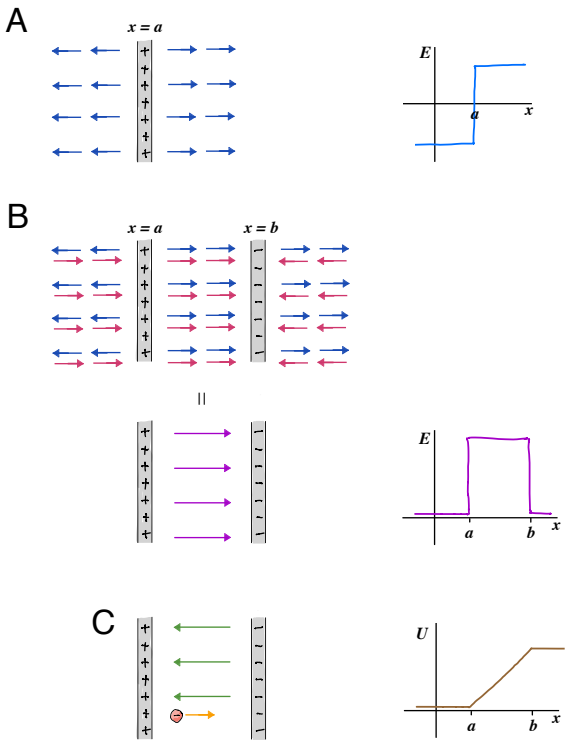


Figure 3.36 Electric Fields and Potential Energies for Charged Plates. A) The electric field of a charged plate. Such a system can be approximated as an "infinite" charged disk with a constant field above it. For the example shown on the left, the plate is positively charged and on its side, so the field "above" the plate is directly to the right or left (blue arrows). The value of the field, E, as a function of position, x, is plotted on the right. B) The electric field of a capacitor. This system has a positive and negative plate, each with its own electric fields (blue and red arrows, respectively, top figure). The image directly below shows the net electric field (purple arrows) that results from adding the fields of the positive and negative plates. In this idealized situation the fields between the plates add and those outside of the plates cancel, creating the plot of the electric field shown to the right. C) The potential energy of a particle moved between the plates of a capacitor. In this example, a negative charge is moved toward the negative plate (orange arrow). The force experienced by the negative charge is shown in green. This force is in the opposite direction of the electric field in part B, because the force is derived from the electric field times the charge, which is negative. Because this force is constant and opposes the movement of the charge (it moves away from the attractive positive plate and toward the repulsive negative plate), the particle stores more and more potential energy as it moves from one plate to the other (shown on the plot on the right).

object, like the earth, the surface of the earth is effectively an infinitely extended disk for a small object (like a rock), and the gravitational field value it experiences, g, is constant (Figure 3.30).

Large charged surfaces are found in capacitors, in which two oppositely charged plates face one another and the distance between them is relatively small compared to the area of the plates. Here, a charged particle experiences a constant force anywhere between the two plates, one side pushing the particle away from it and the other toward it (**Figure 3.36B**). If a charged particle is moved from the side of the plate with the opposite charge toward the other plate, the work done moving against the constant opposing force causes the potential energy of the particle to increase linearly (**Figure 3.36C**). Outside of the plates, there is no additional force in the limiting case, since the constant fields from each plate cancel each other out. This means that the potential energy of a charged particle doesn't change outside of the plates, creating two regions of constant, but different, electric potential.

The electric potential of a capacitor is similar to a neuron's membrane potential, as there is a potential difference in going from one side to the other. Further, the electric potential of both changes when a number of particles move from one side to the other (**Figure 3.37A**). The axon of a neuron can be modeled by combining capacitors with other electronic components (**Figure 3.37B**). Although the analysis of such a system is involved, it offers a number of insights, including how rapidly action potentials can be created, and how action potentials are propagated at maximum speed and signal strength. In reality, the distribution of ions in a resting neuron and the associated electric potential are more complicated than shown at the top of Figure 3.37, but can be described using other physical models (**Figure 3.38**).

3.18 Ionic Bonds

Coulomb's law was discovered from experiments with macroscopic objects, and we have seen that the behavior of matter at the atomic level can be very different (Section 1.17). Nonetheless, equations describing macroscopic electrostatic interactions are directly applicable to the atomic-scale with some additional considerations.

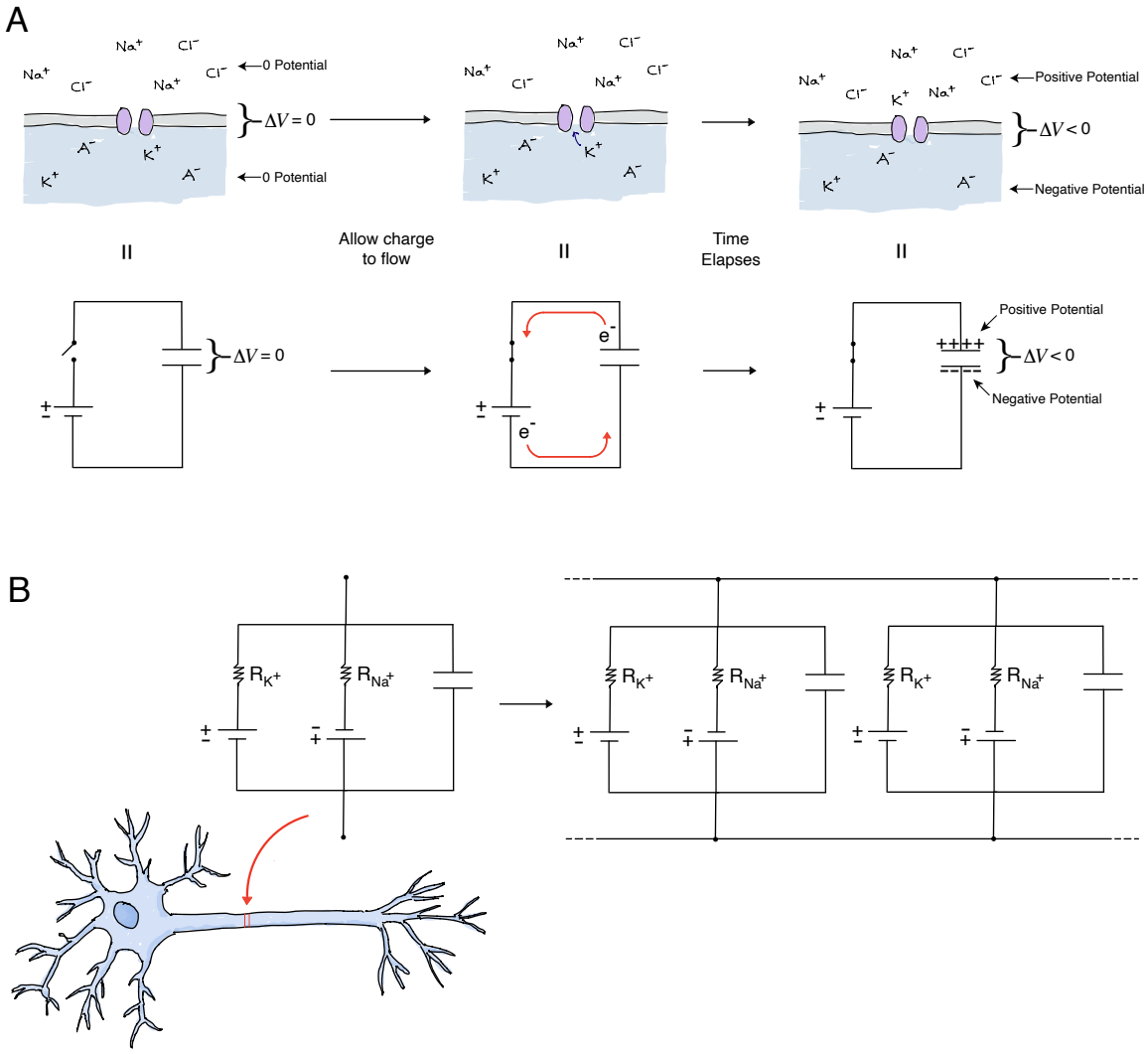


Figure 3.37 Simplified Models of Neurons based on the Hodgkin-Huxley Model. A) Establishment of a neuron's resting potential using both a cell- and a circuit-based model (top and bottom, respectively). On the top left panel is a situation where no electric potential difference has been established. Here, the cell has an excess of sodium ions outside the cell and potassium ions inside, but their charge is offset by an equivalent number of counterions, making the electric potential inside and outside the membrane zero, and the potential differences across the membrane zero. Within the cell membrane is a potassium-specific leak channel that can let potassium freely pass, but no other ions. Because there is an excess of potassium ions inside, there is a concentration driving force for potassium ions to move outside the cell. While the potassium leak channel is always open, for the purposes of our example, potassium ions have not yet begun to move. In the analogous circuit below, there is a battery (long and short lines on the left) with an end with a positive electric potential (the longer line) and an end with a negative electric potential (the shorter line). This battery represents the driving force of potassium ions due to their concentration difference across the membrane. The battery cannot act on the circuit because there is an open switch, representing the situation before potassium ions flow. On the right side of the circuit is a capacitor that represents the membrane potential. Because there has not been current flow in the system, the capacitor has no charges built up on its plates and the potential difference is zero, like the situation for the cell membrane. In the top middle panel, potassium ions begin to flow from the inside of the cell to the outside to relieve their concentration gradient. In the circuit model, the switch is closed. Electrons in the circuit (negatively charged) move to a region of higher electric potential, such as from one side of the capacitor plate (zero potential) toward the side of the battery with the positive potential (the cathode) and away from the side of the battery with the negative potential (the anode) to the other capacitor plate (zero potential). After time, as shown on the top right, no more potassium ions can flow to the outside, because the excess of positive charge outside the cell and negative charge inside the cell has created a membrane potential difference sufficient to counteract the potassium concentration gradient driving force (In the figure the relative amount of potassium ions that moves out of the cell is exaggerated for effect. In reality, only a small fraction of potassium ions moves across). At this point, the cell has a negative membrane potential (inside potential minus outside) of about -70 mV, the neuron's resting potential. In the circuit diagram, similarly, charge builds up on the capacitor plates until the electric potential on each plate is equivalent to electric potential at that end of the battery preventing any more electron movement. At this point, the capacitor is fully charged and has a significant electric potential difference. B) A more complete model of a neuron. On the left, a small portion of a neuron's axon is approximated by a circuit like the one shown in part A. However, channels are now represented by resistors, which can have different resistance values over time. When resistance is very high, there is no electron flow, analogous to the open switch. Low resistance will result in high current flow. In addition to a potassium channel (resistor) and potassium concentration difference driving force (battery), there is also a sodium channel resistor and a sodium concentration driving force battery. Note, because the driving force for sodium ions is from outside the cell to inside, the battery is oriented in the opposite direction. To model the entire axon, the components on the left are repeated numerous times and connected to each other, so that current can also flow down the axon.

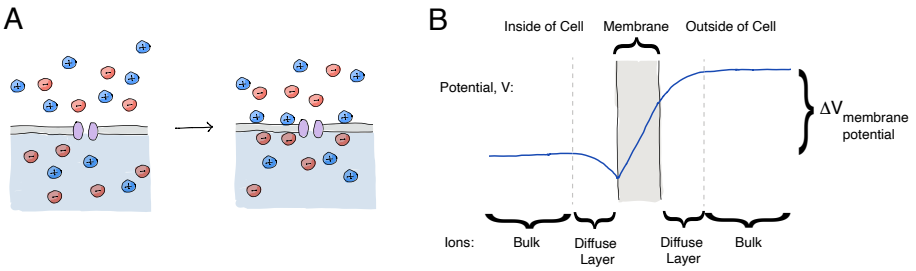


Figure 3.38 A More Complete Model of a Neuron's Resting Potential. A) The figure on the left shows the situation described at the top right of Figure 3.37A but focuses only on the charge of each ion. Because there are more positive ions outside of the cell and more negative ones inside, positive ions are attracted to the outer surface and negative ions are attracted to the inner one, causing ions to be effectively associated with the membrane (shown on the right). This attraction is offset by the concentration gradient created and ultimately results in a "diffuse layer" of ions that is not as concentrated in ions as at the membrane, but still more concentrated than the bulk solution farther out. B) The electric potential in and around the membrane after the ions rearrange on the surface and beyond. The diffuse layer of ions is relatively thin and voltages are typically measured in the bulk region to determine the membrane potential V_m. Adapted from *"The Heat of Nervous Conduction: A Thermodynamic Framework ," A.C.J de Lichtervelde, J. P. de Souza, M.Z. Bazant, Phys. Rev. E 101, 022406, 2020*.

As we saw for the simplest atom, the hydrogen atom, the electrostatic potential energy between the negatively charged electron and the positively charged proton in the hydrogen nucleus is part of the energy (Hamiltonian) operator term that forms the Schrödinger equation (Equation 1.16). That said, this operator also includes a kinetic energy-like term. Unlike the kinetic energy we envisioned for a rock in free fall or a charged particle in a field, this term takes a very different mathematical form. Further, the electrostatic energy term of the Schrödinger equation applies to the electron's wavefunction, instead of applying to a charged particle with a discrete position and trajectory.

The interaction of an ion and a counterion could similarly be characterized in its entirety by the Schrödinger equation: say between a single sodium cation and a chloride anion with no other molecules around. However, even in such a simple system, solving the Schrödinger equation including all of the charged particles in the ions is largely intractable and invites an alternative approach. As a sodium cation approaches a chloride anion from far away, the potential energy decreases (**Figure 3.39A**), as would be expected for attractive electrostatic interactions between ions. Indeed, this trend is well-described using Coulomb's law (**Figure 3.39B**, dashed red line), and the sodium ion "rolls" down the potential energy hill to get closer to the chloride. However, at some point in this approach, the potential energy of the system begins to rise steeply (Figure 3.39A). What is the source of this increase?

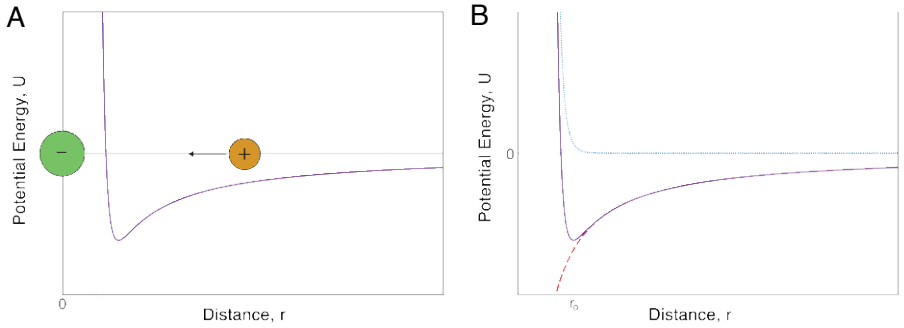


Figure 3.39 Ionic Bonding Energy Curve for Singly Charged Ions. A) A negatively charged ion (such as a chloride) is fixed at the origin and the absolute distance to a positively charged ion (such as a sodium ion) is shown along the positive x-axis. At each distance the corresponding potential energy is displayed along the y axis as the solid curve. B) The curve shown in part A is composed of the sum of the potential energy of electrostatic attraction between the ions (dashed red line), and their repulsion energy due to electrostatic repulsion and the Pauli Exclusion principle (solid blue line). The overall potential energy curve (solid purple line) has a lowest point, r_o, that is the optimal distance between the oppositely charged ions (indicated with the dotted gray line). The potential energy value of zero is set as the energy of the ions when they are maximally separated and does not account for whether forming each of these ions is energetically favorable or not.

While it is often useful to think about our sodium and chloride ions as balls with a single charge, it is important to recognize that these ions are actually atoms. Atoms have a nucleus with a significant and concentrated amount of positive charge, as well as many electrons that form a diffuse cloud of negative charge surrounding the nucleus, with the valence electrons being especially far from the nucleus. While the net charge of these atoms causes them to be attracted to one another, as they get close, the negatively charged electron clouds (and positively charged nuclei) can start repelling one another electrostatically. However, another important, if not the major, contributor to the short-range repulsive energy between ions is a quantum mechanical phenomenon.

Recall that in any atom with more than two electrons, the electrons cannot all occupy the same (1s) atomic orbital, due to Pauli's exclusion principle (which ultimately has to do with the type of particle electrons are). After the first two electrons fill the lowest energy orbital, additional electrons occupy higher-energy orbitals. Similarly, when filled

valence orbitals begin to overlap in ions, the electrons need to access higher energy orbitals to obey Pauli's exclusion principle, raising the potential energy of the system.

The repulsive interactions end up generating a very steep energy curve that decreases rapidly as atoms are separated (Figure 3.39B, solid blue line). When combined with the electrostatic potential energy curve, these two together create an ionic bonding energy curve with a potential energy valley (Figure 3.39, solid purple line). When the sodium ion settles into this valley, it is more stable at this position than closer or farther away from the chloride, and indeed the distance predicted by such a curve is close to the observed distance between sodium and chloride ions.

At this position, a sodium ion and a chloride ion are held in an ionic bond and the lower potential energy of the pair compared to when the ions are separated explains why the bond forms. However, the energy gained from forming one ionic bond per sodium-chloride ion pair isn't sufficient to explain why elemental sodium and chlorine can form a salt. For an uncharged sodium atom and chlorine atom in isolation from all other molecules, it is energetically favorable for a chlorine atom to accept an electron, but energetically unfavorable for sodium to lose one, making the overall process net unfavorable. This is made even worse by the fact that additional energy must be spent to convert elemental form of sodium and chlorine (sodium metal and diatomic chlorine gas) to individual sodium and chlorine atoms. While the energy of one ionic bond partly offsets this total unfavorable energy cost, it does not do so fully. Making multiple ionic bonds per ion fully offsets this energy cost. The attractive electrostatic force of an ion is spherically symmetrical, meaning that it comes from all directions (**Figure 3.40A**). When an ionic bond is formed between one sodium and one chloride ion, this doesn't preclude either ion from forming more ionic bonds with a counterion (**Figure 3.40B**). Ultimately, with more of these interactions, the total energy gained from making ionic bonds exceeds the energy of making ions from elemental forms of sodium and chlorine.

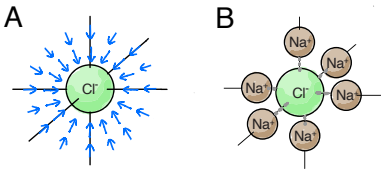


Figure 3.40 Ionic Bonds to a Chloride ion in Table Salt. A) The electric field of a chloride ion is spherically symmetrical, creating attraction for cations in all directions in space. B) Arrangement of sodium cations around a chloride. Chloride ions can make ionic bonds with six sodium cations to maximize electrostatic interactions. Each sodium cation can also make ionic bonds to six chloride anions (not shown).

In general, salts maximize the number of ionic bonds they can form. This process is constrained by the need to have a net neutral charge, as well as the size, shape, and charge of the ions. These factors ultimately dictate the arrangement and distance between ions in the crystalline solid that is a salt.

3.19 Water, Other Solvents, and Other Molecules

In the previous section we saw that in the absence of other molecules, the electrostatic attraction between ions of opposite charges is substantial, allowing salts with an extensive network of ionic bonds to be formed. However, in the cellular context water molecules are ubiquitous and attenuate the interaction of the ions in salts like sodium chloride to the point that these ions are typically fully dissociated. As said before, we will have to wait until the next chapter to explore the structure of water to understand this effect. Still, we can incorporate the shielding effect of water into our quantitative description of electrostatic forces. To do so, we can introduce a parameter called the relative permittivity, ε_r (formerly called the dielectric constant). The relative permittivity can be included in Coulomb's law as follows:

$$F = k\frac{q_1 q_2}{\varepsilon_r r^2} \tag{3.24}$$

The value of the relative permittivity factor, ε_r, is always a number one or greater, and differs for various solvents and conditions. For example, in a vacuum (i.e. no other molecules around) the relative permittivity constant is 1. Under these circumstances Equation 3.24 just reduces to our previous version of Coulomb's law (Equation 3.12) and accounts for the strong ionic bonds for table salt in air. Unlike in a vacuum, water has a large relative permittivity factor which at room temperature is roughly 80. You can see that with 80 in the denominator, the force exerted between ions is significantly

decreased (though not eliminated). For sodium and chloride ions in water, this force is generally too weak to overcome the many potential interactions with water, resulting in dissociation of the ions.

The relative permittivity values of various substances are shown in **Table 3.2**. You can see that for some solvents, such as hexane, the relative permittivity is quite low. As will be discussed in later chapters, the environments in certain regions of the cell or in the interior of some biomolecules can have compositions and relative permittivities similar to these solvents. Consequently, the strength of electrostatic interactions within these environments will be significantly stronger than that in water.

Substance	Relative Permittivity
Air/Vacuum	1.0
n-Hexane	1.9
Ethanol	24.3
Methanol	32.7
Water	78.4

Table 3.2 Relative Permittivities of Selected Substances. Adapted from *"Relative Permittivity." Wikipedia, Wikimedia Foundation, 11 May 2023, en.wikipedia.org/wiki/Relative_permittivity*

In the cell, there are many different types of ions present, each potentially interacting with one another independently. Some of these ions can have complex structures and the electrostatic environment of the cell can be complicated. Rigorous treatments of such systems can be challenging, but many approaches are possible. In some cases, molecules or systems of molecules can be simplified to uniform fields, or approximated with shapes or components described earlier (Section 3.17). More complex treatments of the average energetic behavior of collections of particles can also be applied (a result of such a treatment was shown in Figure 3.38B). A somewhat different approach is to directly simulate the molecules in a system (or approximations of those molecules) using computer models. In such a simulation, the initial positions and energies of molecules can be defined. Then, with discrete time steps, their interaction can be calculated using potential functions similar to those shown in Section 3.18 (adjusting for the effect of the solvent, as detailed in this section). In response to these interactions, molecules in the system will move, and over time their behavior can be tracked.

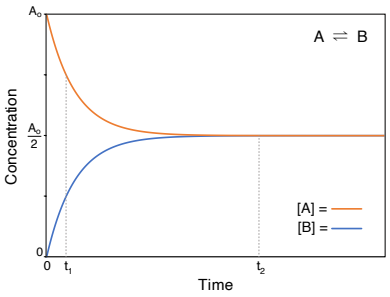


Figure 3.41 Equilibrium Between Two Interconverting Molecules, A and B. Shown is the change in concentrations of compounds A (orange line) and B (blue line) over time, where initially only compound A is present. Several timepoints are noted: time 0, where the concentration of A is A_o and the concentration of B is 0; t_1, when some A has been converted to B, but the system is not at equilibrium; and t_2, where the system has reached equilibrium. In this example, the concentrations of A and B are equal at equilibrium, but that does not have to be the case.

F. Further Exploration - Equilibrium

Up to this point, we have not discussed the concept of equilibrium, a topic important for understanding the behavior of chemical and biochemical systems. In this section we introduce what equilibrium is, how we can tell if a system is in equilibrium, and how to quantitatively describe such a system.

3.20 The Idea of Equilibrium

Given enough time, chemical and biological systems will settle into an equilibrium, where the concentrations of the components in the system remain relatively constant. Consider a simple theoretical chemical reaction involving compounds "A" and "B":

$$A \rightleftharpoons B \tag{3.25}$$

In this equation, the half-arrow to the right indicates that compound A can be converted to compound B, while the half-arrow to the left indicates that compound B can be converted to compound A. If we started with only compound A, over time compound B would be generated from A. However, as compound B was formed,

it would start to generate compound A. At some point, the system would reach an equilibrium, where the concentrations of A and B were relatively constant (**Figure 3.41**). As an example, consider diffusion — a process mentioned earlier — where the same molecule simply moves between two locations rather than being chemically converted. Suppose we had a tank of water with a permeable barrier in the middle and initially the left side of the tank had some solute molecules present, say dissolved sugar molecules, as shown in **Figure 3.42** (left panel).

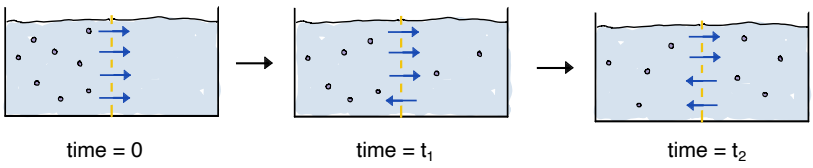


Figure 3.42 Diffusion of Sugar Molecules. A tank of water is separated into two sections of equal volume by a barrier permeable to sugar molecules. Initially (left image), all sugar molecules are on the left. When the system reaches equilibrium (right image), the sugar concentration is equal on both sides. Arrows represent the number of sugar molecules that would flow across the barrier, with equal amount of flow from both sides at equilibrium. The time points shown below each image corresponds to the timepoints shown in Figure 3.41, where the orange line represents the concentration of sugar molecules on the left side of the barrier, the blue line, sugar molecules on the right.

Because the left-hand side has a higher concentration of solute molecules than the right-hand side, the solute molecules would begin moving past the barrier to the right-hand side (Figure 3.42A middle). This "reaction" could be described as follows:

$$\text{Sugar}_{left} \rightleftharpoons \text{Sugar}_{right} \tag{3.26}$$

As in the theoretical case, as the concentration of sugar builds up on the right side, some of that sugar could randomly move back to the left. Eventually, when there were equal concentrations of sugar on the right and left sides, the flow of sugar in each direction would be matched, and the concentration of sugar would not change — the system would have reached equilibrium (Figure 3.42, right).

It is important to point out that being at equilibrium does not mean that the reaction in either direction stops — just that their rates are matched so that no further change in concentration occurs. In our sugar example, that means that at equilibrium, there are molecules of sugar moving from the right side of the tank to the left, as well as sugar molecules moving from the left side to the right. Because both sides of the tank have the same sugar concentration, the number of molecules moving in each direction is matched and there is no net change of concentration (Figure 3.42, right image). All systems in equilibrium are dynamic like this.

When our tank of sugar solution reaches equilibrium, equal concentrations of components are present. That can occur for any system in equilibrium, but it need not be and usually is not the case. Consider the following reaction mentioned earlier (Figure 3.22C and D), where a DNA-binding protein binds to DNA to make a DNA-protein complex. This process can be described with the following equilibrium equation, where the complex between the DNA and the protein is indicated by a hyphen connecting them:

$$\text{DNA} + \text{Protein} \rightleftharpoons \text{DNA-Protein} \tag{3.27}$$

In this system, two molecules (one DNA and one DNA-binding protein) come together to make one DNA-protein complex. Conversely, one molecule of DNA-protein complex can dissociate into two molecules. If only individual DNA and protein molecules are present initially, when they encounter each other they can form the bound complex. Over time, some of these complexes will dissociate back into unbound DNA and protein molecules. This back and forth of binding and unbinding will continue until the system reaches equilibrium. For many DNA-binding proteins, binding to their target sequences is quite tight. Thus, if we started with reasonable initial concentrations of DNA and protein, at equilibrium we would expect more products to be present than reactants (i.e. more DNA-protein complex than unbound protein or DNA). One way we could represent this in our equilibrium equation is as follows:

$$\text{DNA} + \text{Protein} \rightleftharpoons \text{DNA-Protein} \tag{3.28}$$

Here the longer half-arrow to the right compared to the shorter one to the left indicates that formation of product from starting materials occurs to a greater extent than formation of the starting materials from product (i.e. binding of DNA and protein dominates over unbinding of the complex components). Indeed, if one direction in the equilibrium reaction completely dominates over the other, we can denote this with a single arrow, showing here that product formation is effectively irreversible:

$$\text{C} \rightarrow \text{D} \tag{3.29}$$

That said, no system is truly irreversible, even when the amount of back reaction that occurs is so small as to be effectively zero. It should also be pointed out that the forward arrow is often used simply to indicate a chemical reaction, and it should not be assumed that it indicates an irreversible reaction.

3.21 Equilibrium Criteria

How do we know a system has reached equilibrium? One indicator is that the concentrations of components stop changing over time. For example, in our system with DNA and DNA-binding protein, if we have some way to measure the formation of the DNA-Protein complex, after mixing the individual components, we can monitor the system until the concentration of the DNA-Protein complex does not change. A word of caution, though. There is no guarantee that a system will reach equilibrium rapidly, and the reactions may proceed so slowly as to seem like no change in concentration occurs over the time sampled.

Another test takes advantage of the dynamic nature of equilibrium systems. If components are isolated from a system at equilibrium, they should be able to reestablish an equilibrium state. For our DNA-protein system, suppose that when equilibrium was reached there were measurable amounts of unbound DNA and DNA-binding protein. If some of the DNA-protein complex is removed from the system and placed in a new container, that isolated sample will partially dissociate over time to reestablish equilibrium, generating small amounts of unbound DNA and DNA-binding protein (exactly how much unbound DNA and protein should remain at equilibrium will be addressed in the next section).

Beyond the issue of timescale, a variety of other factors can hinder a reaction from reaching equilibrium. Other reactions involving the reactants or products can affect the concentrations of these components. If all of the reactions reach equilibrium, the components of interest will still maintain their original equilibrium distributions. However, if these other reactions do not, they can continually alter the concentrations of the components of interest. For example, if a reactant rapidly and irreversibly forms an undesirable side-product, the reactant will be continually diverted and not generate significant product. Such side reactions need not be deleterious. In metabolic pathways, reactants and products of interest can be rapidly generated and consumed by other reactions in the pathway, preventing the components of interest from achieving equilibrium. Equilibria can also be perturbed by components not directly involved in the reaction of interest. Changes in reaction conditions like the temperature, ion concentration, and pH (discussed in Chapter 6) can all alter where the equilibrium lies.

3.22 Equilibrium Expressions and Constants

All reactions at equilibrium have stable concentrations of starting materials and products, but the relationship between these concentrations varies from system to system. In some systems, the equilibrium concentrations of reactants and products are the same, like the distribution of sugar molecules between the two sides of the tank shown in Figure 3.42.

In others, the equilibrium concentration of the products exceeds those of the reactant, like the formation of DNA-protein complex relative to free DNA and free DNA-binding protein (Equation 3.28). Yet other systems favor reactants over products at equilibrium. Where the equilibrium lies for a given reaction can be described quantitatively using an equilibrium expression that includes a factor called the equilibrium constant, K_{eq}.

An equilibrium expression can be written from any balanced chemical equation. A balanced chemical equation is one in which the count for every atom on the reactant side is the same on the product side - i.e., no atoms are created or destroyed in going from reactants to products. This can be ensured by assigning an appropriate number in front of every reactant and product, their stoichiometric coefficients. Suppose we had the following balanced chemical equation for a generalized reaction of "a" molecules of "A" reacting with "b" molecules of "B" to generate "c" molecules of "C" and "d" molecules of "D":

$$aA + bB \rightleftharpoons cC + dD \tag{3.30}$$

The equilibrium expression for this reaction is:

$$K_{eq} = \frac{[C]_{eq}^{c}[D]_{eq}^{d}}{[A]_{eq}^{a}[B]_{eq}^{b}} = \frac{[C]^{c}[D]^{d}}{[A]^{a}[B]^{b}} \tag{3.31}$$

In this expression, the value of K_{eq} is equal to the multiplied value of all of the equilibrium concentrations of products (C and D) raised to their stoichiometric coefficients (c and d, respectively), divided by the multiplied value of all of the equilibrium concentrations of reactants (A and B) raised to their stoichiometric coefficients (a and b, respectively). In the middle part of Equation 3.31, the fact that the concentration of each component is its equilibrium concentration is indicated by including the "eq" subscript outside of the concentration brackets. However, it is much more common not to include this subscript, as shown on the right. In this representation, the fact that these concentrations are equilibrium concentrations is implied. Indeed, this expression is only equal to a given equilibrium constant when all of the component concentrations are at their equilibrium concentrations.

As an example, we could write the equilibrium expression for our tank of sugar molecules with the permeable barrier (Figure 3.42 on the right, and Equation 3.26) as follows:

$$K_{tank} = \frac{[\text{Sugar}_{right}]}{[\text{Sugar}_{left}]} \tag{3.32}$$

This equilibrium expression conforms to our general expression in Equation 3.31, in that the "products" of the reaction shown in Equation 3.26 are sugar molecules that have moved to the right side of the tank and thus occupy the numerator as their equilibrium concentration. Similarly, the equilibrium concentration of sugar on the left side of the tank is in the denominator. Because the stoichiometric coefficients of the equation for sugar on either side of the tank are one, the equilibrium concentrations in the equation are each raised to the power of one (and not shown).

For our example of DNA and DNA-binding protein coming together to make a DNA-protein complex (Figure 3.22D and Equation 3.27), the equilibrium expression is as follows:

$$K_{DNA-Protein} = \frac{[\text{DNA-Protein}]}{[\text{DNA}][\text{Protein}]} \tag{3.33}$$

Here the numerator contains the equilibrium concentration of the bound DNA-Protein complex (to the first power), and the denominator contains both the equilibrium concentration of unbound DNA and the equilibrium concentration of unbound DNA-binding protein (again, each to the first power).

In any equilibrium expression, the equilibrium constant is a specific number, and this number can be very different for different reactions (which is why the equilibrium constants shown in Equations 3.32 and 3.33 were given different subscripts). What might the value be for a given equilibrium constant, and what does its magnitude mean? Let's consider the equilibrium expression for our tank of sugar (Equation 3.32). We saw that if we started with a high concentration of sugar on the left side of the tank and no sugar on the right (say 1.0 M and 0.0 M, respectively), when the sugar reaches equilibrium, the concentration of sugar on both sides would be the same (both 0.5 M in this example). If we plug the equilibrium concentrations into Equation 3.32 (0.5 M for the numerator, 0.5 M for the denominator), we see that the value of the equilibrium constant is 1.0:

$$K_{tank} = \frac{[\text{Sugar}_{right}]}{[\text{Sugar}_{left}]} = 1.0 \tag{3.34}$$

This equilibrium expression gives us predictive powers. If we know our tank is at equilibrium with respect to sugar, and the concentration of the sugar on the left side of the tank happens to have a value like 0.2 M, we can plug that into Equation 3.32 and see that the concentration of sugar on the right side of the tank must also be 0.2 M. Indeed, this will be applicable for any equilibrium concentration of sugar that happens to be in our tank. However, that is not the case if our system is not at equilibrium. For example, if we started with 1.0 M sugar on the left side, and 0.0 M sugar on the right, plugging those values into Equation 3.34 would not give a value of 1.0, because the system is not in equilibrium. Nonetheless, we could find the equilibrium concentrations from the initial concentrations using some algebra. If we started with 1.0 M sugar on the left side, at equilibrium some x molar amount of sugar will have moved over to the right side. This would mean the molar equilibrium concentration of sugar on the right would be x (since the left side lost x molar sugar that went to the right side, which had no sugar to start with). The left side at equilibrium would have a concentration of 1-x molar sugar (again, this side started with one molar sugar and lost x molar). We can plug these into Equation 3.34 (x in the numerator, 1-x in the denominator). If we solve for x, we find that its value is 0.5 M. The equilibrium concentration of sugar on the right is x, so the concentration on the right is 0.5 M. The equilibrium concentration on the left is 1-x, which is also 0.5 M. Admittedly, we could have reasoned this to be the case, where a 1M solution that starts only on the left had to be diluted into both the right and left chambers equally at equilibrium, reducing its final concentration by half. However, as we will see, sometimes the situation is more complicated.

In the case of our tank, the equilibrium constant of 1.0 tells us something about the relative concentrations of products and reactants in our system at equilibrium (specifically that in the way we've set up our system, they have to have equal concentrations at equilibrium to conform to a K_{tank} of 1.0). What about for other systems? For the DNA binding protein and DNA, if binding is relatively tight (which it often is) and we start with substantial and equal concentrations of protein and DNA, we would expect that at equilibrium the concentration of DNA-protein complex might be significantly greater than that of unbound DNA and protein molecules. From Equation 3.33, that would indicate that the equilibrium constant should be a large positive number. What that number is will depend on the specific DNA-binding protein and DNA, but a value like 1.0×10^9 is reasonable.

$$K_{DNA-Protein} = \frac{[\text{DNA-Protein}]}{[\text{DNA}][\text{Protein}]} = 1.0 \times 10^9 \tag{3.35}$$

(As a side note - although you might expect this equilibrium constant to have units of M^{-1}, since in the equilibrium expression there are two concentration terms in the denominator versus one in the numerator, for reasons too technical to delve into here, all equilibrium constants are actually unitless). Like our previous example, this equilibrium constant constrains the concentration of each component at equilibrium. To get a value of 1.0×10^9 you might have relatively high concentrations of DNA-protein complex and a low concentration of free DNA and DNA-binding protein. For example, if you knew that at equilibrium your concentrations of unbound DNA and unbound protein were each 1.0 μM (1.0×10^{-6} M), the concentration of DNA-protein complex would have to be 1.0 mM (1.0×10^{-3} M). This agrees with our intuition that binding would be relatively tight, as at equilibrium the ratio of DNA-protein complex to unbound DNA (or protein) is 1,000 to 1.

Even though the equilibrium concentration of unbound species is the same in the example we just discussed, that doesn't have to be the case. For an equilibrium concentration of 1.0 mM DNA-protein complex that we described previously, unbound DNA and protein concentrations of 1.0 nM and 1.0 mM, respectively, would still give the equilibrium constant shown in Equation 3.35.

From these examples, we can see that many different equilibrium concentrations of starting materials and products will be consistent with the equilibrium constant shown in Equation 3.35. Given that, how can we predict what concentrations will actually be present at equilibrium?

If we know the equilibrium constant and the equilibrium concentrations of two species, it is always possible to use Equation 3.35 to solve for the equilibrium concentration of the third. Directly measuring the concentrations of various components to do so is sometimes possible. However, it is more common to only know the initial concentrations of species, such as how much DNA and DNA-binding protein were present before they were mixed and formed the complex. For example, suppose we started with a solution of 1.0 μM of DNA, 1.0 μM of DNA-binding protein, and no DNA-protein complex. Because this system is not at equilibrium, we can clearly see that plugging the initial concentrations into Equation 3.35 does not give the expected equilibrium constant. Still, we can determine the equilibrium concentration of the species using some algebra (**Figure 3.43**), similar to what we did for our sugar system:

	DNA	+	Protein	⇌	DNA-Protein
Initial:	1×10^{-6} M		1×10^{-6} M		0 M
Change:	$-x$		$-x$		$+x$
Equilibrium:	$(1 \times 10^{-6}\ \text{M}) - x$		$(1 \times 10^{-6}\ \text{M}) - x$		x

$$K_{eq} = \frac{[\text{DNA-Prot}]}{[\text{DNA}][\text{Prot}]} = \frac{x}{(1 \times 10^{-6} - x)(1 \times 10^{-6} - x)} = 1 \times 10^{9}$$

$$(1{,}000{,}000{,}000)x^2 + (-2{,}001)x + 0.001 = 0$$

$$x = 0.97 \times 10^{-6}\ \text{M} \Rightarrow [\text{DNA-Prot}]_{eq} = 0.97\,\mu\text{M (97\% bound)}$$

$$[\text{DNA}]_{eq} = 0.03\,\mu\text{M}$$

$$[\text{Prot}]_{eq} = 0.03\,\mu\text{M}$$

Figure 3.43 Example of Determining Equilibrium Concentrations from Initial Concentrations. In this example, we are trying to find the equilibrium concentration of DNA-Protein complex that is formed starting with 1.0 μM DNA, 1.0 μM DNA-binding protein, and no DNA-protein complex, where the equilibrium constant for this association is 1.0×10^9. The strategy is to fill in the initial amounts of each component, how much they change to get to equilibrium (plus or minus x), and the equilibrium concentration. The collection of all of these values is often called an ICE (Initial, Change, Equilibrium) table. The equilibrium values are plugged into the equilibrium expression and simplified to a quadratic expression in terms of x. Using the quadratic formula, we can determine potential values of x and use those values to determine the equilibrium concentrations (using only the value of x that gives equilibrium concentrations that are all positive). Since we started with 1.0 μM of DNA and DNA-binding protein, the most DNA-Protein complex we could have formed was 1.0 μM. Our calculations show that for our conditions, we formed 0.97 μM of DNA-Protein complex, so at equilibrium 97% of the possible complex is formed. For the equilibrium values calculated, we can check our work by plugging those equilibrium concentrations back into the equilibrium expression and making sure they match our equilibrium constant (always a good idea). Doing so returns the given equilibrium constant, within rounding error (in our calculations, we assumed our initial values were accurate to two significant figures).

Using this strategy we predict equilibrium concentrations of 0.03 μM free DNA, 0.03 μM free DNA-binding protein, and 0.97 μM DNA-protein complex. These values indicate that for our initial concentration, most (but not quite all) of the reactants are converted into product. As we have mentioned previously, the magnitude of equilibrium constant tells us something about the relative concentrations of products and reagents at

equilibrium, with a K_{tank} of 1.0 in Equation 3.34 indicating equal concentrations of sugar on both sides of the tank in our sugar example, and a $K_{DNA\text{-}Protein}$ of 1.0 x 10^9 in Equation 3.35 indicating that DNA-protein complex can dominate over unbound DNA and DNA-binding protein. As also previously stated, the value of the equilibrium constant can vary for different pairs of DNA and DNA-binding proteins, and it is instructive to see how that affects how much complex formed. With an initial concentration of DNA and DNA-binding protein both at 1.0 μM and a $K_{DNA\text{-}Protein}$ of 1.0 x 10^9 we were able to determine the equilibrium concentration of the DNA-protein complex (0.97 μM), and that represents 97% binding (0.97 μM of a maximum 1.0 μM amount of complex formed). Using the same initial concentrations, but different values of the equilibrium constant, we can calculate and plot the percent binding (**Figure 3.44**). From this figure, we can see that changing the value of the equilibrium constant does change the percent binding, with some (smaller) values of $K_{DNA\text{-}Protein}$ causing the fraction of DNA-protein complex to drop to very low levels for this initial concentration of DNA and DNA-binding protein: that is, for a given initial concentration of reagents, the magnitude of the equilibrium constant will dictate on which side of the equilibrium a reaction lies.

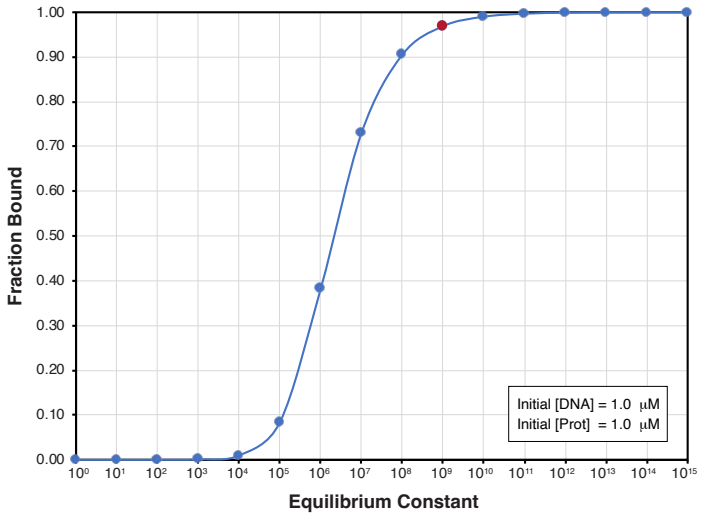


Figure 3.44 Changes in the Extent of DNA-Protein Complex Formation with Different Equilibrium Constant Values. Starting with 1.0 μM DNA and 1.0 μM DNA-binding protein, the fraction that forms DNA-Protein complex at equilibrium is shown for different values of the equilibrium constant for DNA-Protein association. On the graph, the magnitude of the equilibrium constants increases 10-fold with every tick mark. A value of 0.97 fraction bound (97%) was previously determined when the equilibrium association constant was 1 x 10^9. On the plot, that data point is highlighted with a red circle.

It is also instructive to look at percent binding when the equilibrium constant is held constant, but the initial concentrations of DNA and DNA-binding protein are varied (**Figure 3.45**). What we see is that over a range of initial concentrations of starting material, roughly 1 μM and higher, the percent binding is close to 100%. However, if we start with low enough concentrations of DNA and DNA-binding protein, the percent binding is close to zero: for example starting with 0.01 nM of DNA and DNA-binding protein (1 x 10^{-11} M), the percent binding is just under 1%. This means that the extent of binding doesn't just depend on the magnitude of the equilibrium constant, but also depends on the initial concentrations of the reagents, with some concentrations of starting materials being too low to drive complex formation, even if binding is considered tight.

These insights about equilibrium constants and binding apply to more than just DNA and protein binding, and we will see many biological examples of two molecules coming together to form a bound complex. In fact, the equilibrium expression of Equation [3.31] applies broadly to chemical reactions and binding processes, not just to the DNA-protein association we have been discussing. In Chapter 6 (Section 6E, for example), we will see an example of this in describing the equilibrium of deprotonation of an acid. Biological processes and reactions involving greater or fewer numbers of starting materials or products can be described using an adapted form of Equation 3.31, and then applied to determine and predict equilibrium concentrations. It should be mentioned, however, that this is not true in all cases. The derivation of Equation 3.31 assumes that all components in the reaction are free to move about and that there are no external fields affecting the molecules. In almost all of the processes and reactions we examine,

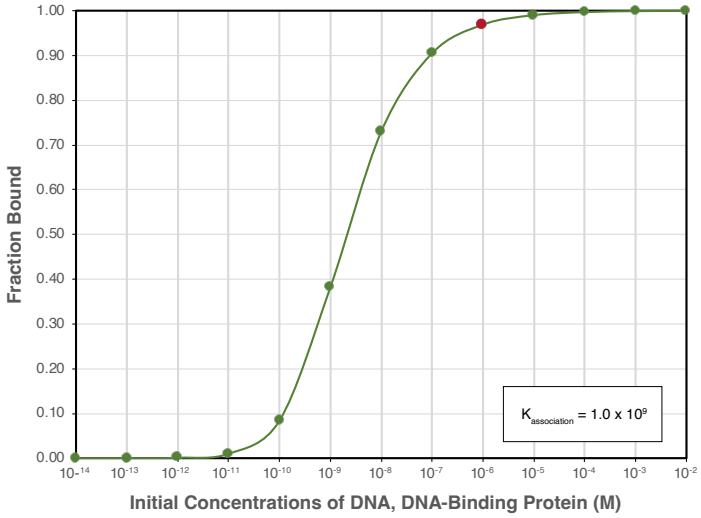


Figure 3.45 Changes in the Extent of DNA-Protein Complex Formation with Variations in the Initial DNA and DNA-Binding Protein Concentration. For a DNA and DNA-binding protein pair with an equilibrium association constant of 1 x 10^9, the fraction of DNA-Protein complex formed at equilibrium is calculated for various initial concentrations of the DNA and DNA-binding protein (which are identical). Lowest concentrations of DNA and DNA-binding protein start on the left and increase to the right, and each tick mark is a 10-fold increase in molar concentration. A value of 0.97 fraction bound (97%) was previously determined when the starting concentrations of DNA and DNA-binding protein were both 1.0 μM. On the plot, that data point is highlighted with a red circle.

this will be the case. Nonetheless, we have already seen one example of a system that does not fulfill this criterion. Recall that in the resting state of nerve cells, there is an uneven distribution of potassium ions across the membrane (Figure 3.20B and 3.37A) and this is effectively an equilibrium state. Unlike the sugar-tank example — where the two sides were identical and K = 1 arose from symmetry — the resting nerve cell involves an electric field that the standard equilibrium expression cannot capture. This is because unlike the sugar in that example, not all of the ions in the system are equally free to move. In fact, in our simple model of the resting nerve cell, only potassium ions can move, not other cations like sodium, and importantly, not anions that can counteract the charge of the potassium ions that do move out of the cell. This movement creates an electric potential difference between the inside and outside of the cell, and the higher net positive charge outside the cell (and corresponding negative charge inside) creates a field that opposes further movement of potassium ions out. The potential created by such a field can be incorporated in an equation that describes such systems (known as the Nernst equation). However, because this equation is somewhat complicated and will not be used in the rest of the book, we only note that it exists.

CHAPTER 4
A Covalent Compound - Water

Motivation and Overview: One way atoms achieve a full valence is to share their electrons in covalent bonds, thereby forming molecules known as covalent compounds. In this chapter we focus on one such compound, water. Examining this biologically essential and ubiquitous molecule provides insights into the nature of covalent bonds, as well as the structures of compounds composed of covalent bonds. An important property of a water molecule is its ability to make strong interactions with other water molecules. We look at how these interactions arise and their implications for water as a solvent, water's phases, and its cohesion and adhesion.

A. Covalent Bonds and Water

The molecular formula of water is H_2O - that is, one molecule of water is made up of two hydrogen atoms and one oxygen atom. Each atom wants a full valence. Unlike atoms that accomplish this by gaining or losing electrons to form ions, the hydrogen and oxygen atoms in water share electrons to complete their valences. To understand how this sharing works, let's start by considering the elements that comprise water.

4.1 Hydrogen

Hydrogen is the simplest of the elements, with one proton and one electron (**Figure 4.1A,** left). An especially useful way to depict atoms that form covalent compounds is to show them as electron dot structures (also called Lewis dot structures). In such a representation, the atom's valence electrons are shown as dots, one per electron, and the atom's symbol stands in for the rest of the atom. So for a hydrogen atom, its electron dot structure is an H with one dot (Figure 4.1A, right). Atoms with more valence electrons have correspondingly more dots surrounding their atomic symbol (**Figure 4.1B** and **C**).

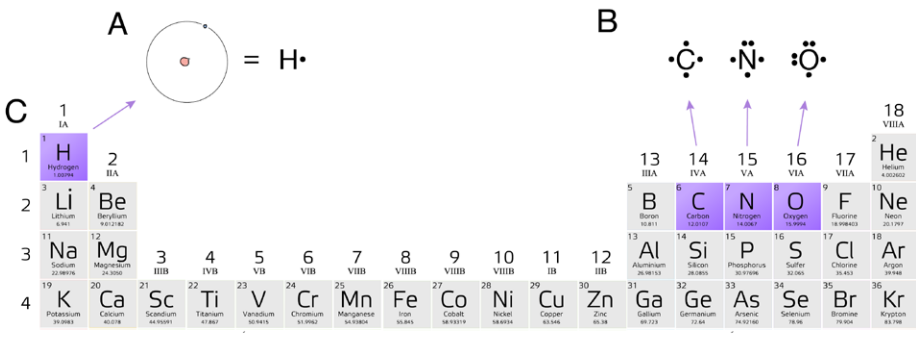


Figure 4.1 Electron Dot Structures of Hydrogen and Other Elements. A) Different depictions of a hydrogen atom. To the left, the hydrogen atom is shown as in previous chapters, where the proton in the nucleus is red and the electron surrounding it is in blue. To the right is the electron dot structure representation, where the one valence electron of the atom is shown as a dot, and the rest of the atom (just the nucleus in this case) is the letter 'H'. B) Electron dot structures of other atoms: carbon, nitrogen, and oxygen. The positions of the electrons shown in electron dot structures are somewhat arbitrary, though no position contains more than two electrons. C) Part of the periodic table is shown with the elements shown in parts A and B highlighted in purple.

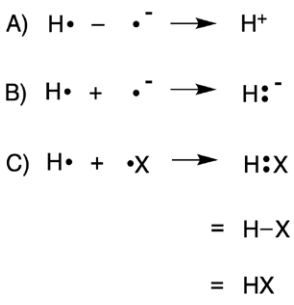


Figure 4.2 Ways for a Hydrogen Atom to Achieve a Full Valence. Hydrogen, in the first row of the periodic table, can have up to two valence electrons and can A) lose, B) gain, or C) share its electron.

To achieve a full valence, hydrogen has several options (**Figure 4.2**): A hydrogen atom can lose its electron (Figure 4.2A), gain another one (Figure 4.2B), or share an electron with some other atom (Figure 4.2C). All of these possibilities are feasible in biological systems, and we will see examples of hydrogen cations in the next chapter and hydrogen anions in a later volume. A simple example of hydrogen sharing electrons is hydrogen gas, H_2, which is the most common form of elemental hydrogen on earth. In this molecule, one hydrogen atom achieves a filled valence of two electrons by sharing its electron with another hydrogen atom:

$$H\cdot + \cdot H \rightarrow H{:}H = H{-}H = H_2 \qquad (4.1)$$

As you can see in Equation 4.1, when two hydrogens with a total of two electrons (left side of the arrow) come together, they can share these electrons, giving each hydrogen a full valence of two electrons. Such sharing of electrons is known as a covalent bond. The covalent bond can be shown as two dots (compound to the right of the arrow). However, it is much more common to use a solid line to represent a covalent bond (compound to the right of the first equal sign). Conversely, when you see a solid line between atoms in a compound, it represents two shared electrons. Hydrogen gas (also called molecular hydrogen or diatomic hydrogen) can also be depicted simply as two hydrogens, H_2. Although the covalent bond is not shown in such a representation, it is implied by the nature of the compound.

At this point, we have seen two different types of bonds that hold atoms together: ionic bonds and covalent bonds. In ionic bonds, the ions that make up the compound are held together by electrostatic attraction between charges of opposite signs. In covalent bonds, what holds the two atoms together is a bit more complicated and ultimately includes a contribution that is quantum mechanical in nature (detailed further, for those interested, in Further Exploration Section 5.16).

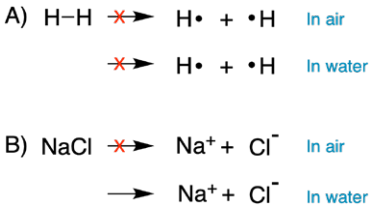
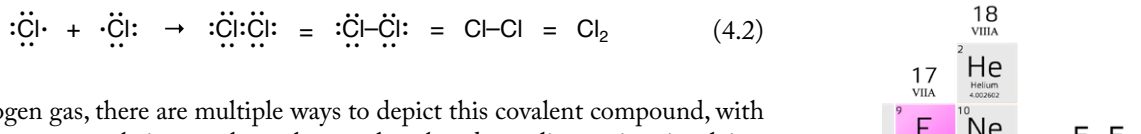


Figure 4.3 Differences between Ionic and Covalent Bonds in Air and in Water. A) Tendency of diatomic hydrogen to not dissociate in either air or water. B) Tendency of sodium chloride to not dissociate in air, but to dissolve in water.

When not in aqueous solution, both ionic and covalent bonds tend to be strong, meaning that it takes a substantial amount of energy to pull apart the atoms in such a bond. Consequently, under normal conditions, it is rare for these bonds to spontaneously break. For example (**Figure 4.3A**, top), for hydrogen gas at room temperature, it is very uncommon for the reverse of the reaction shown in Equation 4.1 to occur: a molecule of diatomic hydrogen splitting back into two atoms of hydrogen. Similarly, for a salt like sodium chloride sitting in a salt shaker, sodium and chloride ions do not individually break away from the salt crystal they are in (**Figure 4.3B**, top).

The effective strengths of ionic and covalent bonds in aqueous solution can be quite different. While covalent bonds tend to remain intact in water, ionic bonds can be broken. For example, while hydrogen gas is not very soluble in water, those that do enter the water remain diatomic molecules (Figure 4.3A, bottom). In contrast, for a salt like sodium chloride, its addition to water generally results in full dissociation of the ionic compound into individual sodium cations and chloride anions (Figure 4.3B, bottom). It's worth pointing out that, as we saw in the last chapter, not all ionic bonds are broken in water, with some salts not being very soluble in water, and even very soluble salts, like table salt, remaining undissolved when too much is added to water.

We can justify diatomic hydrogen forming from hydrogen atoms because the individual atoms are each just one electron away from achieving a full valence. As we saw in Chapter 1, the halogens are also one valence electron away from a full valence. Thus, like hydrogen, they can form a single covalent bond to obtain a full valence (**Figure 4.4**). For example, two chlorine atoms can come together to form the elemental form of chlorine, diatomic chlorine gas:



As with hydrogen gas, there are multiple ways to depict this covalent compound, with the most common ways being to show the covalent bond as a line or just implying its presence in the molecular formula. One difference from diatomic hydrogen is that diatomic chlorine has more valence electrons than are involved in forming a covalent bond. Such electrons are typically shown paired together, and each pair is referred to as a lone pair of electrons. Thus, in diatomic chlorine, each chlorine atom has three lone pairs of electrons, with six lone pairs of electrons in the molecule. As we will see, lone pairs of electrons are important for a molecule's overall structure and properties. However, it is pretty common not to include them in the depiction of a molecule for convenience and clarity (such as the last two structures shown in Equation 4.2). In these structures, the presence of the lone pair electrons is implied. Under such circumstances, if you want to know how many valence electrons are present that are not involved in covalent bonds, take the number of electrons found in the atom's full valence and subtract the number of electrons in its covalent bonds. Dividing this number by two gives you the atom's number of lone pairs of electrons (**Figure 4.5**).

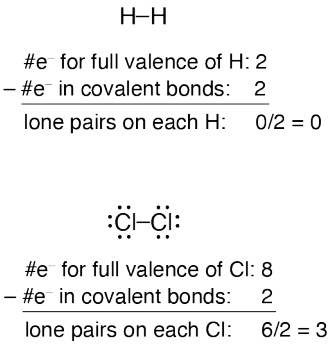


Figure 4.5 Examples of Determining an Atom's Number of Lone Pairs of Electrons. Shown is how the number of lone pairs of electrons can be calculated for each hydrogen and chlorine atom in diatomic hydrogen and chlorine, respectively.

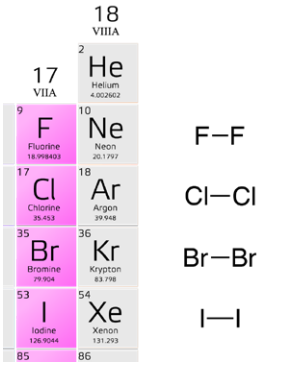
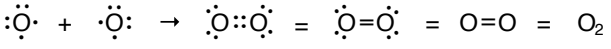


Figure 4.4 Diatomic Halogen Compounds. Selected halogens in the periodic table are highlighted in magenta. The corresponding diatomic halogen molecules are shown on the right. Under standard conditions, diatomic fluorine and chlorine are gases, diatomic bromine is predominantly a liquid, and diatomic iodine is predominantly a solid. We have seen that chlorine atoms can be part of a covalent compound or an ionic one. What dictates whether chlorine will form diatomic chlorine, sodium chloride, or some other compound? Ultimately, it depends on what atoms are present and whether a pathway exists to get to a specific product. Chlorides in sodium chloride are more stable than the chlorine atoms in diatomic chlorine. However, if no sodium metal is present, chlorine atoms will react with other chlorine atoms to make diatomic chlorine.

4.2 Oxygen

Besides hydrogens, water contains an oxygen atom. Oxygen possesses six valence electrons and could achieve a full valence, at least theoretically, in several ways (**Figure 4.6**): It could lose six electrons (Figure 4.6A), gain two electrons (Figure 4.6B), or share two electrons (Figure 4.6C). Losing six electrons is very unlikely, as oxygen is a very electronegative atom with a high ionization energy and removing even a single electron from an oxygen atom is energetically costly. Because oxygen is so electronegative, you might expect it to commonly gain two electrons. However, in biologically relevant molecules, this form of oxygen is not generally encountered. In fact, in organic compounds, even the less extreme form, an oxygen with a single negative charge, is not nearly as common as those containing a neutral oxygen (though we see some examples of such oxygen anions in coming chapters). Neutral oxygen-containing compounds can be formed when oxygen shares electrons, and one example of such a compound is oxygen gas, O_2:



Here, two oxygen atoms, each with six valence electrons, come together. By sharing two of their valence electrons, each oxygen atom is able to achieve a full valence of eight electrons. Each shared pair of electrons is a covalent bond, so oxygen gas (also known as molecular oxygen or diatomic oxygen) has two covalent bonds, or what is called a double bond. This is in contrast to diatomic hydrogen and chlorine, which are linked via a single bond. Note: the true electronic structure of O_2 is more complex than shown here, and is addressed more accurately in Further Exploration Section 5.17.

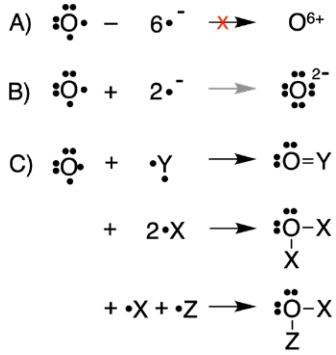


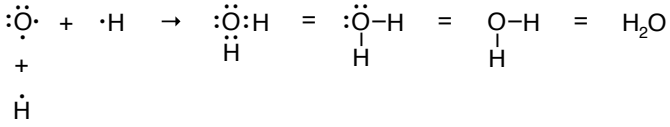
Figure 4.6 Potential Ways for an Oxygen Atom to Achieve a Full Valence. Oxygen, with six valence electrons, can lose, gain, or share electrons. In biologically-relevant molecules, sharing of electrons with one or more atoms is the most common way for oxygen to achieve a full valence.

A double bond can be depicted in terms of its shared electron dots (structure to the right of the arrow in Equation 4.3). However, as with the covalent compounds previously discussed, it is much more common to depict a covalent bond as a line between atoms, making the double bond appear as two parallel lines between the oxygen atoms (structure to the right of the first and second equals signs). Like diatomic chlorine, not all of the valence electrons in diatomic oxygen are used in forming the double bond, resulting in two lone pairs of electrons per oxygen. These lone pairs can be explicitly shown (structure to the right of the first equal sign), or omitted but implied (structure to the right of the second equal sign). Again, the structure on the right neither shows the covalent bonds nor the lone pairs, but their presence is implied.

The fact that an oxygen atom in diatomic oxygen makes two bonds and has two lone pairs of electrons left over is a general phenomenon for covalent compounds containing an uncharged oxygen. Indeed, it is useful to commit to memory how many bonds each organic atom makes, as well as how many lone pairs of electrons are left over. So for the organic atoms we have discussed: a hydrogen makes one bond and has no lone pairs electrons; an uncharged oxygen atom makes two bonds (either two single bonds or one double bond) and has two lone pairs of electrons.

4.3 Covalent Bonds in Water

With what we now know about hydrogen and oxygen, we can tackle how these atoms come together to form a molecule of water, H_2O. The oxygen in water wants to make two bonds, while the two hydrogens each want to make one bond. These requirements are satisfied if oxygen makes a single bond to each hydrogen:



(4.4)

In addition to having two single bonds to hydrogens, the central oxygen of water has two lone pairs of electrons. Like our prior examples, the depiction of the lone pairs is optional.

B. Three-Dimensional Structure of Water

Our analysis from the last section indicated that water links a central oxygen atom to two hydrogen atoms. However, this analysis does not tell us how these atoms are arranged in space relative to each other, and there are many possibilities (**Figure 4.7A**). For example, in Equation 4.4, water is shown having a geometry in which the angle made from going from one hydrogen to the oxygen to the other hydrogen is 90°. But is this correct? Could the angle between these atoms be 180° to make their arrangement linear? Could it be close to 0°? Or is it something else in between? Could there even be a collection of structures that water adopts with interconversion between them?

Experimental data shows that water actually has an average bond angle of 104.5° between hydrogens with relatively little deviation from this value over time (**Figure 4.7B**). Why does water adopt this geometry and could we have predicted it?

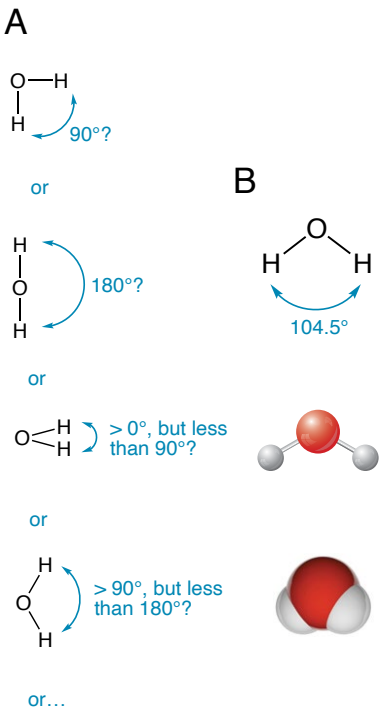


Figure 4.7 Possible and Actual Bond Angles in Water. A) Some possible bond angles between hydrogens in water. B) The actual bond angle of hydrogens in water. The top image shows the molecule in terms of electron dot structures. The middle image is a ball and stick model. The bottom image depicts a space filling model. In ball and stick and space filling models, it is typical for hydrogens to be shown as white spheres and oxygens as red ones.

4.4 VSEPR Theory

As we will discuss in later volumes, many compounds do not have an absolutely fixed three-dimensional structure. Nonetheless, most adopt a single major structure (or at least a set of structures that are pretty similar to one another). VSEPR theory is a simple approach that does a surprisingly good job at predicting the predominant geometries of many compounds, including water.

VSEPR theory stands for valence shell electron pair repulsion theory, and its underlying idea is simple: in a molecule, groups of electrons get as far away from each other as possible in three-dimensional space in order to minimize electrostatic repulsion between these groups. VSEPR theory can be applied to a molecule using several steps (**Figure 4.8A**). Before we apply them to water, let's examine those steps.

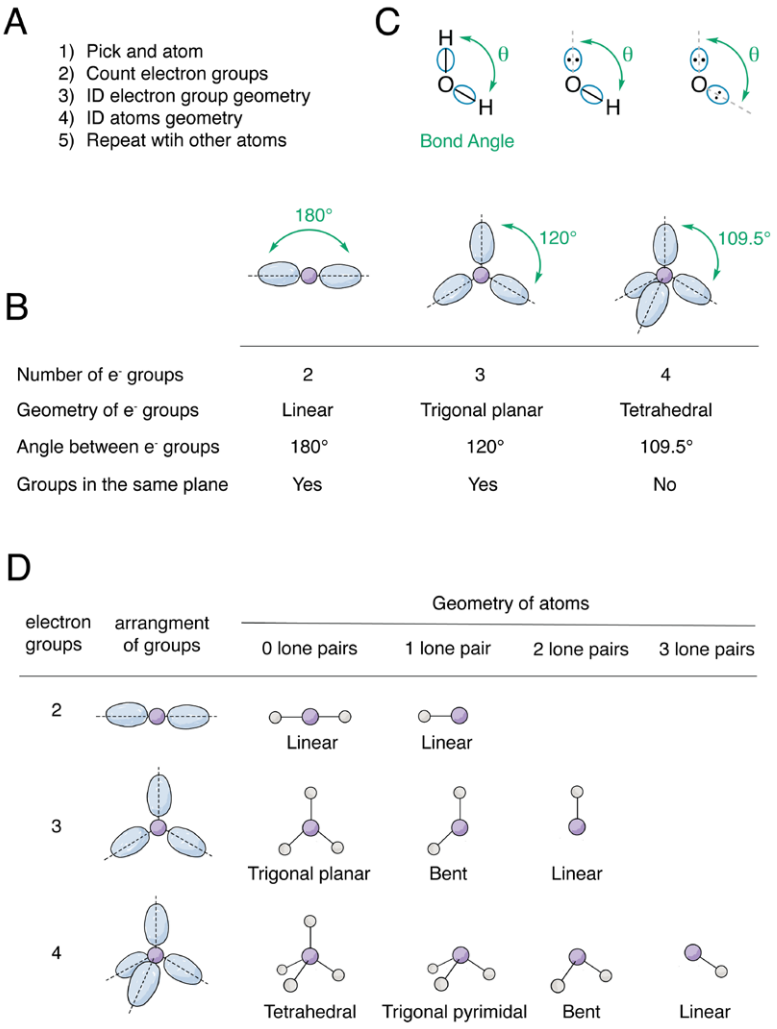


Figure 4.8 VSEPR Theory. A) Steps in applying VSEPR theory. B) Possible electron group geometries with two, three, or four electron groups. C) The "angle between groups" is the angle between the line from the central atom to one group and the line from the central atom to another group. This angle, shown in the figure as θ, could be between two bonds to atoms (left), a bond and a lone pair of electrons (center), or two lone pairs of electrons (right). When the angle is between two bonds to atoms, the angle is called the bond angle. D) Possible atom geometries, where the central atom has anywhere from zero to three lone pairs of electrons.

Step one is to choose an atom to focus on. If there is a central atom in a molecule, it is usually a good idea to start there. If there are multiple such atoms, pick one and come back to the others later.

Step two is to count how many groups of electrons the atom has. An electron group is any set of electrons occupying a covalent bond or a lone pair. If the atom of interest has a bond to another atom, those electrons are counted as one group. This is true whether the bond is a single, double, or triple bond. For example, if an atom of interest has a double bond to one atom, and a single bond to another, it would have two groups of electrons. In terms of lone pairs of electrons, you simply count each as a group. So if an atom had three lone pairs of electrons (i.e. six valence electrons not involved in a covalent bond), that would be three groups of electrons due to lone pairs. The total number of groups of electrons would then be the sum of groups of bonds and lone pairs. For our entirely contrived example, the number of groups would be five: two from bonds (the one single and one double bond) and three from lone pair electrons.

Step three is to identify the geometry of the electron groups that positions the groups

in three-dimensional space as far away from each other as possible (illustrated on the left side of **Figure 4.8B**). For every specific number of electron groups, there is only one possible arrangement:

When there are two groups connected to the atom of interest, the groups will be farthest away from each other when the groups and the central atom all fall on a straight line. This geometry is called linear, and the angle between groups is 180° (**Figure 4.8C** shows how this angle is defined for different combinations of bonds and lone pairs that come off of the central atom).

With three groups, the groups and the atom of interest will all be in the same plane. The atom of interest will be in the center of an equilateral triangle with the groups as the vertices. In this arrangement, the angle between any two groups is 120°, and the geometry of the groups in this arrangement is known as trigonal planar.

With four groups, the atom of interest and its associated groups adopt a slightly more complicated arrangement known as a tetrahedral geometry. In this arrangement, the atom of interest is again in the center, and the groups are arranged in a way that the three groups at the bottom make a tripod (with the atom of interest at the point where the three legs meet), and the group on the top points above the atom of interest to make a kind of stem on top of the tripod. In the tetrahedral geometry, the angle between any two groups is 109.5°.

It is possible for an atom in a molecule to have more than four groups, but most of these compounds are not organic compounds, so we will not concern ourselves with those here.

Knowing the geometry of the electron groups around our atom of interest allows us to proceed to the fourth step of applying VSEPR theory - defining the geometry of the atoms (not groups) surrounding our atom of interest. In this step, we are effectively just tracing the connection between atoms, or equivalently, ignoring the lone pairs. If none of the groups surrounding the atom of interest are lone pairs of electrons, the geometry of atoms is equivalent to that determined in the previous step (Figure 4.8B). On the other hand, with each lone pair of electrons that is present, there is a different name for the geometry of atoms (linear, bent, and trigonal pyramidal with one lone pair, as shown in column four of Figure 4.8D; linear and bent for two lone pairs, as shown in the fifth column of Figure 4.8D).

If there are no atoms beyond those attached to the atom of interest you identified in step 1, there are no additional steps, and the name of the geometry of the atoms found in step 4 is the molecular geometry (**Figure 4.9A**). If that is not the case, you can move on to the other atoms and repeat the process. In this case, the result of steps 1-4 describes the arrangement of atoms around each atom of interest. For example, suppose you had a compound with two carbons, each with a different number of groups. The arrangement of atoms around one carbon could be tetrahedral, while the arrangement around another carbon could be trigonal planar (**Figure 4.9B**). In such a case, there is not one name that can be given to describe the arrangement of the atoms for the entire molecule.

Understanding these rules is much clearer when applied to specific molecules, so let's see what VSEPR theory predicts about the molecular structure of water.

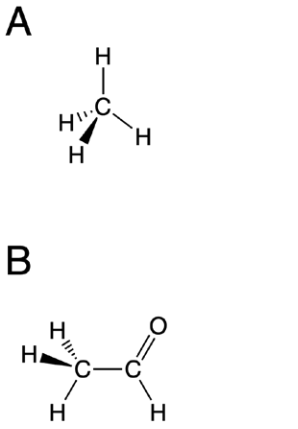


Figure 4.9 Examples of Different Molecular Geometries. A) According to VSEPR theory, the arrangement of four hydrogens around a carbon is tetrahedral (the fact that the bottom three hydrogens are arranged like a tripod is indicated by one hydrogen pointing slightly out of the plane of the image (bond with a solid triangle), one hydrogen pointing slightly behind the plane of the image (bond with a dotted triangle), and one hydrogen in the plane of the image (bond with the straight line). As there are no additional atoms beyond the hydrogens connected to the central carbon, the arrangement of atoms is also its molecular geometry: i.e. this compound (called methane) has a tetrahedral molecular geometry. B) According to VSEPR theory, the arrangement of atoms around the left carbon is tetrahedral, while the arrangement around the right carbon is trigonal planar. The overall molecular geometry of this compound (called acetaldehyde) does not have a name. Instead, it has a portion that is tetrahedral and a portion that is trigonal planar.

4.5 Three-Dimensional Structure of Water

As we saw in Equation 4.4, a central oxygen bridges two hydrogens, making the oxygen a good candidate to focus on in step 1 of our application of VSEPR theory (**Figure 4.10A**). In step two, we can identify how many electron groups are associated with the oxygen (**Figure 4.10B**). There are the two single bonds to hydrogen, so the number of electron groups due to covalent bonds is two. In terms of lone pairs, we can see in Equation

4.4 that there are two lone pairs of electrons surrounding the oxygen (remember, an uncharged oxygen always has two lone pairs of electrons in its valence after making two bonds). Thus, the total number of electron groups is four: two groups in bonds plus two groups in lone pairs. In step 3, we consult the chart in Figure 4.8B (or just remember) that the way to get four groups of electrons as far away from one another as possible is to have them adopt a tetrahedral geometry (**Figure 4.10C**). In step 4, since some of these groups of electrons are lone pairs, we ignore them in describing the arrangement of the atom. Specifically, we ignore two lone pairs for the oxygen of water. What we are left with when we trace the trajectory from the first hydrogen to oxygen to the second hydrogen is an overall 'V'-like shape, called bent. Because there are no other atoms in water past the hydrogens, we are done with our analysis. Overall, our water molecule can be described as being bent.

With our knowledge about the tetrahedral geometry, we would predict the bond angle of hydrogens in water is 109.5°. As stated earlier, the measured bond angle is 104.5°, a value that is pretty close, though not exactly the same. Why is there a discrepancy? In VSEPR theory, all groups of electrons — whether lone pairs or bonds — are treated as roughly equivalent in their effect on geometry. However, lone pair electrons are in practice slightly more repulsive than bond electrons, which is why the measured bond angle of water (104.5°) is somewhat less than the predicted tetrahedral angle (109.5°). Nonetheless, for such a simple algorithm, VSEPR theory is quite effective in predicting molecular structures, and we will be applying it to a range of compounds in the next chapter. Still, before we move on to examine water molecules more deeply, it is worth looking at VSEPR predictions for the diatomic compounds we have seen.

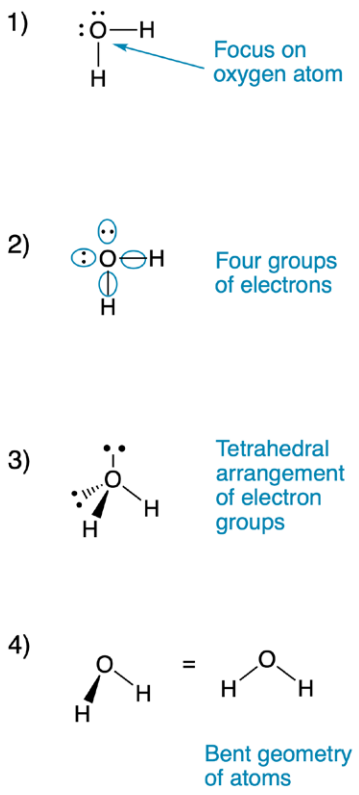


Figure 4.10 Application of VSEPR Theory to Water. VSEPR theory predicts that water is a bent molecule with a bond angle of 109.5°. This bond angle is close to, but not exactly, the experimentally observed bond angle of 104.5°.

4.6 Three-Dimensional Structures of Diatomic Molecules

Diatomic hydrogen (Equation 4.1) has two hydrogens, each with one covalent bond and no lone pair electrons (**Figure 4.11A**). With only one group, this means the molecule must be linear.

Slightly more complicated are the diatomic halogens (Figure 4.4), such as chlorine gas (**Figure 4.11B**). In this molecule (Equation 4.2), each chlorine has one covalent bond and three lone pairs of electrons, bringing the total number of electron groups for each chlorine atom to four. Four groups of electrons are arranged in a tetrahedral geometry, according to VSEPR theory. This means that the three lone pairs and the bond to the other chlorine adopt a tetrahedral arrangement; since we describe geometry only in terms of atoms, diatomic chlorine is linear.

As a final diatomic example, consider molecular oxygen (Equation 4.3 and **Figure 4.11C**). Each oxygen is connected to another oxygen in a double bond, constituting one group of electrons (remember, any covalent bond, whether it is a single, double, or triple bond, is considered one group for the purposes of VSEPR theory). Oxygen is an atom that forms a double bond with the other oxygen — counting as one electron group — and has two lone pairs of electrons left over. Thus, each oxygen has three groups of electrons. The geometry of three groups is trigonal planar, meaning that for a given oxygen, its two lone pairs of electrons are in the same plane as the oxygen-oxygen double bond and are 120° (1/3 of a full rotation) away from the double bond and each other. Again, the geometry of the entire molecule does not depend on the lone pair electrons, so focusing on the oxygen atoms and their connection, we see that oxygen gas is also a linear molecule.

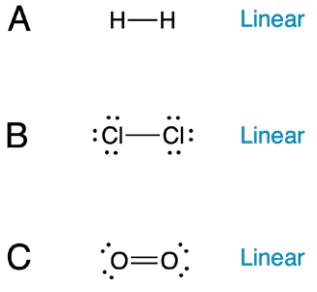


Figure 4.11 Structure of Diatomic Molecules. Electron dot structures and molecular geometries for A) diatomic hydrogen, B) diatomic chlorine, and C) diatomic oxygen.

C. Uneven Distribution of Electrons in Bonds and Molecules

The electrons in covalent bonds are shared between atoms, but they may or may not be shared equally. In diatomic molecules where both atoms are the same, like hydrogen,

chlorine, and oxygen gas, the electrons are shared equally since both atoms have the same electronegativity. In water, the atoms involved in its bonds are not the same. What does this mean for how electrons are shared in this molecule?

4.7 Polar Covalent Bonds

Consider the different ways oxygen and hydrogen could "share" electrons in a water molecule (**Figure 4.12**). At one extreme, like diatomic hydrogen or oxygen, these electrons could be shared entirely equally between the two atoms (Figure 4.12, electron dot structure farthest to the left). However, this situation seems unfavorable, because oxygen is a substantially more electronegative atom than hydrogen. If instead, you took oxygen's affinity for electrons to its extreme, oxygen could take hydrogen's electron entirely for itself (Figure 4.12, electron dot structure farthest to the right). This would make oxygen an anion and hydrogen a cation. As we mentioned earlier, despite being electronegative, oxygen atoms associated with other organic atoms tend not to adopt a full negative two charge. Thus, neither extreme is ideal. An intermediate option is for oxygen and hydrogen to share the pair of electrons, but to do so unequally. As oxygen is the more electronegative element, it would "own" the electrons to a greater degree than hydrogen (Figure 4.12, electron dot structure in the middle).

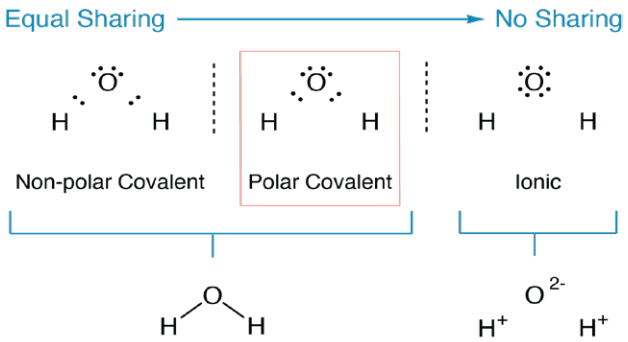


Figure 4.12 Potential Ways of Sharing Electrons in Water. On the upper left, the two electrons in the O-H covalent bonds are shared equally. Moving to the right, the oxygen "owns" the electrons more than the hydrogens, where at the most extreme, oxygen has fully taken the electrons previously belonging to the hydrogens. Actual water molecules share electrons unequally (red box) in what is called a polar covalent bond.

This kind of unequal sharing of electrons is still considered a covalent bond, but is called a polar covalent bond. This distinguishes them from what are known as non-polar covalent bonds, in which electrons are either shared equally or shared mostly equally. This distinction is not simply about nomenclature, for as we will see, compounds with polar covalent bonds (often shortened to polar bonds) can have very different properties from those with non-polar covalent (non-polar) bonds. A polar covalent bond is also different from an ionic bond, in that in ionic bonds, the electrons belong exclusively to one of the atoms, making the atoms ions. In the continuum from non-polar covalent to ionic bonds, polar covalent bonds represent a middle ground (Figure 4.12).

4.8 Bond Dipoles

One ramification of the unequal sharing of electrons in an O-H bond is that there is an uneven distribution of charge between oxygen and hydrogen. As we saw in imagining water going from a non-polar covalent form of an O-H bond to a fully ionic one (Figure 4.12), oxygen goes from having no charge to having a negative two charge. This can be understood in terms of how many electrons the oxygen has at each of these extremes. An oxygen atom with six valence electrons has no charge: the eight positively charged protons of oxygen are offset by two negative electrons in its first shell and six electrons in its second (valence) shell. In a theoretical form of water containing non-polar bonds with equal sharing of electrons (Figure 4.12, left electron dot structure), oxygen makes two non-polar covalent bonds and has four lone pair electrons. Since we have proposed that the bond electrons are shared equally, oxygen "owns" one electron from the bond, meaning that with its lone pair electrons, it has six valence electrons, just like a neutral elemental oxygen atom. For a theoretical ionic form of water, oxygen takes an electron

from each hydrogen. This gives it eight total valence electrons, two more than it normally would have, causing oxygen to have a negative two charge. In the actual form of water, in which the electrons are shared with hydrogens in polar covalent bonds, oxygen does not fully "own" the electrons from hydrogen, but it does not share them equally, either. This means that the oxygen in water has a partial negative charge. Similarly, hydrogen has a partial positive charge, because it has possession of less than its usual valence electron.

The depiction of water's covalent bond as a line does not communicate an uneven distribution of charge, but this distribution can be shown several different ways (**Figure 4.13**). One is to directly label the partial charges on the oxygen and hydrogen (Figure 4.13, middle). Here the lower case delta, δ, indicates a partial charge, such as the partial negative charge, δ-, on the oxygen. Another way to indicate the uneven charge distribution is to use an arrow with a bar at its base (Figure 4.13, bottom). In this depiction, the arrow points toward a region of increased electron density (i.e. more electrons toward the oxygen), while the bar represents a region of electron depletion (which results in a partial positive charge on hydrogen, with the plus charge echoing the plus made by the bar).

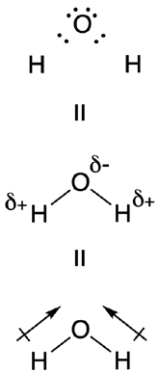


Figure 4.13 Depicting Unequal Electron Sharing and Charge Distributions in a Water Molecule.

This arrow symbol also indicates that this distribution of electrons is an electrical dipole. You may be familiar with another kind of dipole, a magnetic dipole, that is present in a bar magnet that has a north and south end (**Figure 4.14A**). An electric dipole occurs when two equal charges of opposite signs are separated by some distance (i.e. something has a positive and negative end). In water, the polar covalent O-H bond represents an electric dipole, a bond dipole, where charges of δ- and δ+ are separated by the distance between the oxygen and hydrogen atoms (**Figure 4.14B**). Electric dipoles can be described more quantitatively as vectors, which are typically represented as arrows. A vector describes some quantity that has a magnitude and direction. For an electric dipole, its magnitude (shown as the length of the arrow) depends both on the size of the charge at either end of the dipole, and the distance separating them. The direction (where the arrow points) is simply the orientation of the dipole in three-dimensional space.

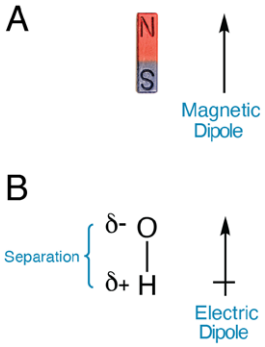


Figure 4.14 Examples of Dipoles. A) A bar magnet (left) has a magnetic dipole that can be represented by a vector (right). B) An OH bond (left) has an electric dipole called a bond dipole. This dipole arises from separation of equal, but opposite, charges and the dipole can also be represented by a vector (right).

4.9 Molecular Dipoles

Water has two bond dipoles, and these electric dipoles can be combined to generate a molecular electric dipole, which we'll just call a molecular dipole (**Figure 4.15A**).

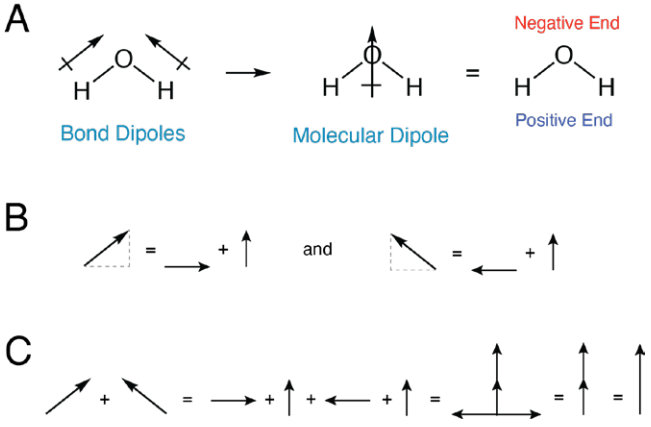


Figure 4.15 Molecular Dipole of Water. A) The bond dipoles of water can be combined to form a net dipole, water's molecular dipole. B) Decomposition of each of water's bond dipoles into component x- and y-vectors. C) Vector addition of water's bond dipoles is equivalent to the addition of the component vectors of the bond dipoles and results in a net vector that only has a y-component.

That is, the water molecule itself has an overall electric dipole, where the negative end of the molecular dipole is the oxygen, and the positive end is the end with the hydrogen. We can understand how this molecular dipole arises from doing some simple vector addition. In general, a compound's molecular dipole results from adding together all of its bond dipoles. For water, that specifically means adding the two bond dipole vectors. These two vectors point in directions that are neither the same nor opposite, making their addition complicated. However, a nice property of vectors is that they can be decomposed into perpendicular component vectors, such as the component of the

vector in the x-direction and the component in the y-direction (**Figure 4.15B**). These components can then be added up individually and used to construct a new vector. As shown in **Figure 4.15C**, the y-components of each bond vector are the same size and point in the same direction. This means they can be added together to get a new vector pointed along the y-axis. The x-component vectors of the bond dipoles are the same size but are oppositely directed. This means adding them together cancels them out. Thus, the sum of the two bond vectors results in a new molecular vector pointed toward the oxygen, with its positive end located between the two hydrogen atoms.

It's important to note that water's bond dipoles and particular three-dimensional shape are both needed for water to have a molecular dipole. The requirement for bond dipoles is not surprising, as a molecular dipole can't arise unless there is at least one bond dipole that contributes an uneven distribution of charge. Still, the presence of bond dipoles does not guarantee that a compound will have a molecular dipole. Suppose instead of having a bent shape, water were a linear molecule (**Figure 4.16**). In this case, the two bond dipoles would be equal in their magnitude but pointed in opposite directions, canceling each other out. As a result, water would not have a positive and negative end. Asymmetry in the orientation and/or magnitude of bond dipoles is necessary for a compound to have an overall molecular dipole.

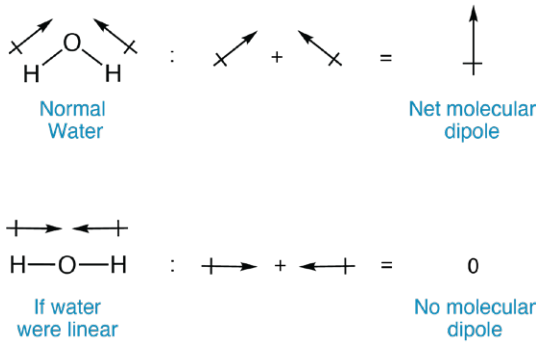


Figure 4.16 Importance of a Compound's Geometry in its Molecular Dipole. A bent water molecule has a molecular dipole, while a theoretical linear water molecule would not.

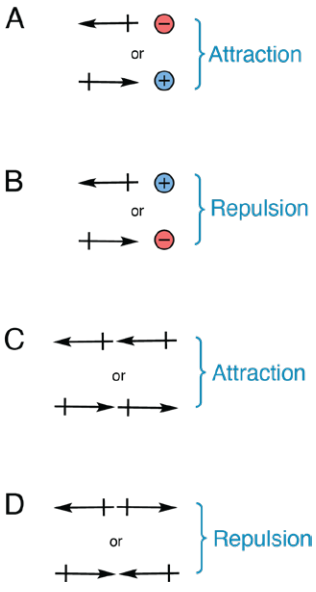


Figure 4.17 Electrostatic Interactions with a Dipole. The interaction of a dipole with a charged particle (A and B) or another dipole (C and D) can be attractive (A and C), or repulsive (B and D).

Compounds with molecular dipoles can interact with other compounds electrostatically. This includes interaction between a compound with a molecular dipole and a charged particle, where attractive interactions can form between the positively charged end of the dipole and a negatively charged particle or the dipole's negatively charged end and a positively charged particle (**Figure 4.17A**). Repulsive interactions can occur when the end of the dipole and charged particle have the same charge (**Figure 4.17B**). Dipoles can also interact with other dipoles. Similar to a bar magnet, which has a magnetic dipole with a north and south end, molecular dipoles interact favorably when oppositely charged ends are lined up (**Figure 4.17C**), but unfavorably when their ends have the same charge (**Figure 4.17D**).

4.10 Hydrogen Bonds

The partial positive charge on hydrogen — due to its polar bond with oxygen — allows it to interact with lone pair electrons on another electronegative atom, a type of interaction known as a hydrogen bond. For example, water molecules can form hydrogen bonds with other water molecules. Shown below is a single hydrogen bond (dashed line) formed between two water molecules, where the hydrogen of the left water molecule interacts with the lone pair electrons of an oxygen in the right water molecule:

$$HO–H + :OH_2 \rightarrow HO–H\text{- - -}:OH_2 \qquad (4.5)$$

Compared to the covalent bond between oxygen and hydrogen within a water molecule,

the hydrogen bond between these same atoms is considerably weaker. Indeed, a dashed line is used to represent a hydrogen bond in part to emphasize this fact. Nonetheless, hydrogen bonds are strong enough to be a significant contributor to many of the properties of water.

Before examining those properties, it's worth noting that water molecules can form hydrogen bonds with compounds other than water — as we'll see in examples later in the chapter. Further, hydrogen bonds can be formed between molecules containing atoms other than just oxygens and hydrogens — something we'll see in the next chapter. In general, interactions between molecules (or even within molecules) that are not mediated by covalent bonds are known as non-covalent interactions, and hydrogen bonds are just one type of non-covalent interaction. Attractive electrostatic interactions, such as those between oppositely charged ions, ions and dipoles, and between dipoles, are other examples of non-covalent interactions, and in later chapters we will learn of other non-covalent interactions that are important in biological systems.

D. Properties of Water

Water has many unique properties that arise from its ability to make dipole and hydrogen bond interactions. In this subsection we will see how these features help us to understand what dissolves in water and what doesn't; how water forms solids, liquids, and gases; and what are the effects of water sticking to itself and other compounds.

4.11 Water as a Solvent

Water is a very effective solvent for some substances and not so effective for others (**Table 4.1**). What dictates these differences? A major factor is to what extent water can make favorable interactions with the molecules of a substance.

Compound Name	Type	Solubility (g/L)
Table Salt	Salt	360
Glucose	Polar Compound	909
Motor Oil*	Non-polar Compound	<< 1*

Table 4.1 Water Solubility of Selected Compounds. Solubility is measured at 25 °C at 1 atmosphere of pressure. *Motor oil is a mixture of predominantly non-polar compounds and all components are soluble to much less than 1 g/L.

In general, water is good at dissolving charged particles. For example, the solubility of a salt like sodium chloride is quite high (up to 360 g/L or 6.2 M at 25 °C). In the dissolved salt, the molecular dipole of water allows it to orient itself around the salt's components (**Figure 4.18A**), where water's partially negatively charged oxygen can make favorable electrostatic interactions with the positive charge of a sodium ion, and the partially positive charge of water's hydrogens can do so with the negative charge of the chloride. Similar to the ions in table salt crystals, dissolved ions can interact with more than one charged particle, creating a shell of multiple water molecules directly surrounding the ion. Because there is some residual charge that is not neutralized by the waters, and because the water molecules orient themselves such that the end pointing outward has the same charge as the ion, the hydration shell can extend past a single layer of waters (**Figure 4.18B**). That said, attraction weakens as the hydration shell grows in size, and at some point additional water molecules are not held to a significant extent, causing them to be randomly oriented like the bulk solution of pure water.

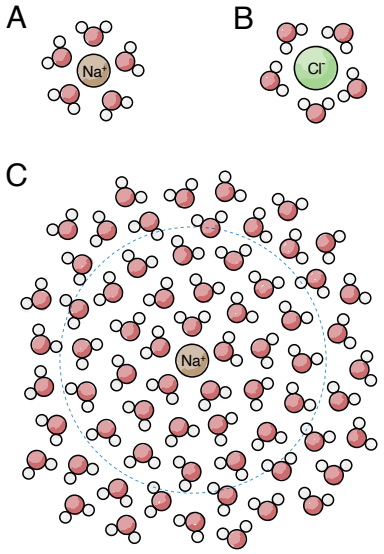


Figure 4.18 Molecular Details of Table Salt Dissolved in Water. A) Electrostatic interactions between water molecules and a sodium ion (left) or a chloride ion (right) B) The hydration shell of an ion. Water molecules in the hydration shell are within the dotted blue lines. In A and B, molecular details have been exaggerated and simplified for clarity.

Water is also good at dissolving polar compounds, molecules with a preponderance of polar covalent bonds. For example, the polar sugar molecule glucose (**Figure 4.19A**)

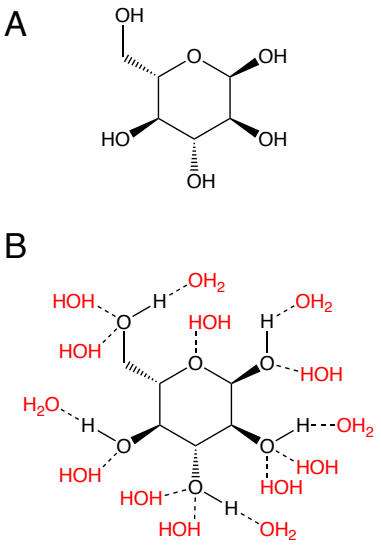


Figure 4.19 Solubility of Glucose in Water. A) Representation of a glucose sugar molecule, $C_6H_{12}O_6$. B) Some of the hydrogen bonds a glucose molecule can form with water. For clarity, the water molecules are depicted in red and not all possible hydrogen bonds between glucose and water molecules are shown.



Figure 4.20 Insolubility of Oil in Water. A) When motor oil is added to water, the motor oil will form a separate layer, because the two substances are immiscible. B) A potential component in motor oil (octane). This molecule is highly non-polar, as electrons are shared evenly in the compound's C-C covalent bonds and relatively evenly in its C-H covalent bonds.

has a high solubility in water (up to 909 g/L or 5.0 M at 25 °C). Although we don't yet have enough background to understand the structure of glucose, we can see that it is a molecule that contains five -OH groups that resemble the -OH group in water and that contain polar covalent bonds. In the absence of water, glucose can adopt a crystalline structure, where glucose molecules are held together with other glucose molecules via hydrogen bonds among their -OH groups. When glucose is added to water, the polar -OH groups in glucose can make hydrogen bonds with water (**Figure 4.19B**), surrounding the glucose molecule with water molecules and removing individual glucose molecules from the sugar crystal, i.e. dissolving them.

Water is not very good at dissolving compounds that are categorized as being non-polar (compounds predominantly with non-polar bonds). For example, the major components of motor oil are a mixture of non-polar compounds that are very insoluble in water (much less than 1 g/L at 25 °C). When they are mixed with water, the oil initially forms small droplets. Over time these droplets coalesce into a layer of oil that floats above the water (**Figure 4.20A**). While we will have to wait until later in the book to more fully understand why the water and oil don't mix (as well as what compounds are present in the oil), one reason is that non-polar molecules (like the one shown in **Figure 4.20B**) tend not to have an uneven distribution of charge in their bonds. Thus, interactions with water molecules via dipole interactions or hydrogen bonds are not as readily made as with other compounds. This prevents water molecules from surrounding and dissolving the compounds in the oil in the same way that water does with salt ions or glucose molecules.

A useful shorthand for predicting the solubility of compounds is the saying: "like dissolves like." The underlying idea is that solvents with a specific polarity tend to dissolve compounds with the same polarity. As we have seen, polar water molecules with concentrated regions of charge are a good solvent for dissolving polar sugar molecules and charged salt ions. Similarly, non-polar compounds in motor oil can dissolve the other non-polar components in the oil (in this case, all of the motor oil components are liquids, so we say that they are mutually soluble, or are miscible). Implied by "like dissolves like" is that compounds that are unlike in their polarity tend to not dissolve each other. This was seen with polar water and non-polar motor oil. These components are not mutually soluble, and are described as immiscible.

Two terms commonly used to describe solubility in water are hydrophilic and hydrophobic. Compounds that are hydrophilic, meaning "water-loving," are ones that readily dissolve in water. They are typically molecules that are predominantly polar or charged. Compounds that are hydrophobic, meaning "water-fearing," are those that do not readily dissolve in water. They are molecules that are predominantly non-polar.

Having some sense of the polarity of a compound can be very useful in understanding whether it will dissolve in a given solvent. That said, polarity and solubility of compounds can be complicated, with the polarity of compounds often existing on a spectrum. As we will see, molecules can also contain both regions that are polar and regions that are non-polar. Sometimes, one will dominate over the other, making the substance effectively polar or non-polar. In other cases, compounds, like some biomolecules, are not entirely soluble in either polar or non-polar solvents, leading to interesting behaviors that we will examine in a later volume.

4.12 Phases of Water

Water is commonly encountered in one of three phases of matter (**Figure 4.21**, top): a solid (ice), a liquid (liquid water, or often just water), or a gas (water vapor). At the molecular level, one way to think about the difference between such phases is how much the molecules "stick" to one another (Figure 4.21, bottom).

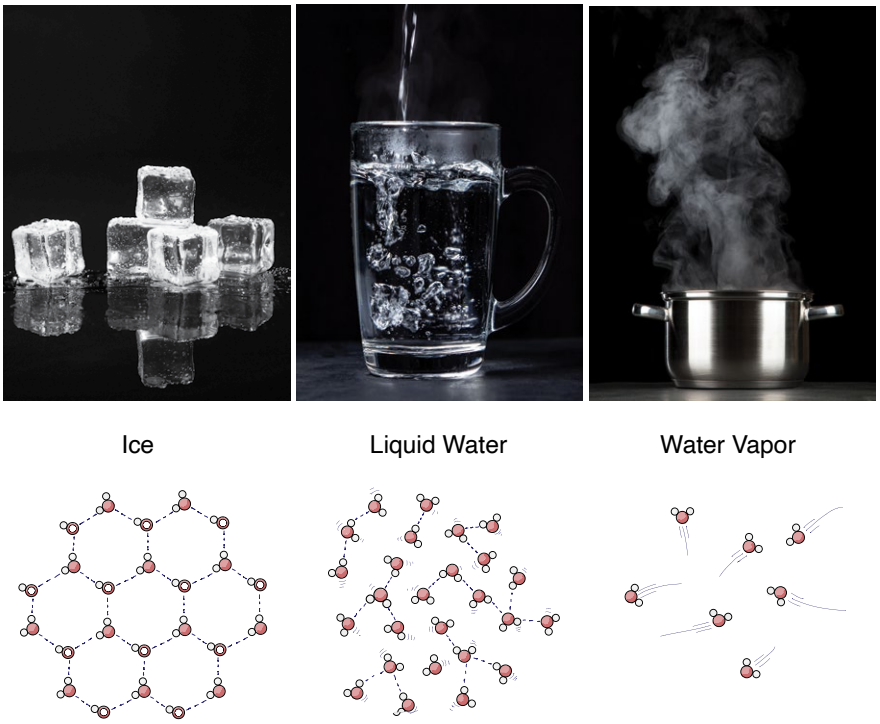


Figure 4.21 Phases of Water. Shown are the common phases of water at the macroscopic (top) and microscopic (below) level. Water vapor is not actually visible macroscopically. What is seen is an aerosol of small, condensed droplets of liquid water. In the microscopic depictions of ice, only a single sheet of water molecules is shown and they are not in the same plane. For liquid water and steam, the molecules are shown as if they were in two dimensions.

In the gas phase, water molecules do not stick to each other at all. They move rapidly through space, and the distance between them is large relative to the molecule's size. In the liquid phase, water molecules stick together enough to coalesce into a substance that is too heavy to remain in the air. Nonetheless, these molecules do not stick so tightly that they are held rigidly in place, and this allows them to move past each other and flow. In the solid phase, water molecules stick to one another tightly and do not move to a significant degree. This creates a substance that has a well-defined shape.

One of the factors that dictates a molecule's phase is its temperature. What is temperature? For molecules in the gas phase, temperature can be thought of as the molecules' average energy of motion. For a simple gas molecule resembling a sphere, this energy is simply related to its translational motion, that is, how fast it is moving (**Figure 4.22A**). For a more complicated gas molecule, say a gaseous water molecule, it would also include its rotational motion (how rapidly the molecule is tumbling in space) and internal vibrational motions (how fast various atoms in the molecule move relative to one another, constrained by the bonds between them) (**Figure 4.22B**). If more energy is provided to the gas molecules (say we heat water vapor in a fixed-volume container), the average energy of motion of the gas, its temperature, will increase (water molecules will move faster on average, rotate more, and potentially vibrate more).

The "stickiness" of intermolecular forces, like hydrogen bonds, can counteract the motion of the molecules. To see this, let's suppose we had a collection of relatively small molecules at room temperature with no intermolecular interactions. These molecules would act as a gas, moving rapidly. If we had the ability to introduce interactions between the molecules and somehow dial up their strength, at some point, the energy of attraction between molecules would exceed their energy of motion. At this point, this excess of attractive energy would allow them to start coming together. Near this transition, the interaction energy wouldn't be enough to prevent the molecules from undergoing translation relative to one another, but multiple transient interactions per molecule would be sufficient to keep the molecules close to one another, making the collection of molecules a liquid. If we continued to increase the strength of molecular interactions, we would ultimately

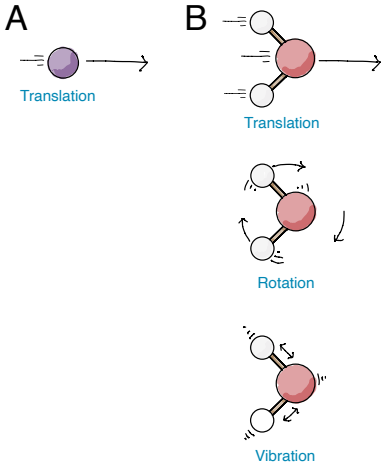


Figure 4.22 Types of Molecular Motion. A) A monoatomic (one atom) gas, like helium, can undergo translational motion in all three dimensions. B) A polyatomic (multiple atom) gas, like water vapor, can undergo translational, rotational, and vibrational motions. Multiple modes of each of these motions in three dimensions are possible.

freeze the molecules in place relative to one another — fully limiting their translational motion and making the collection of molecules some sort of solid.

For water at room temperature (say 20 °C), hydrogen bonds between water molecules are sufficiently strong to make water a liquid, but not sufficiently strong to make water a solid, i.e. ice. Each water molecule can make multiple hydrogen bonds, but in the liquid phase, hydrogen bonds are rapidly being made and broken. If we added energy to our system by heating it, the temperature of the water would go up, and at 100 °C, the water molecules would have so much energy of motion that things like collisions between molecules would knock them loose from hydrogen bonds, causing water to enter the gas phase as individual molecules. Conversely, if instead of adding heat to water at room temperature, we took it away and cooled the system, water would move more slowly and start to stick together with more and better-oriented hydrogen bonds. When the water reached 0 °C, the water molecules would have so little energy of motion that hydrogen bonding between the molecules would dominate, causing water to form a crystalline solid, ice, that maximizes the number and strength of the hydrogen bonds.

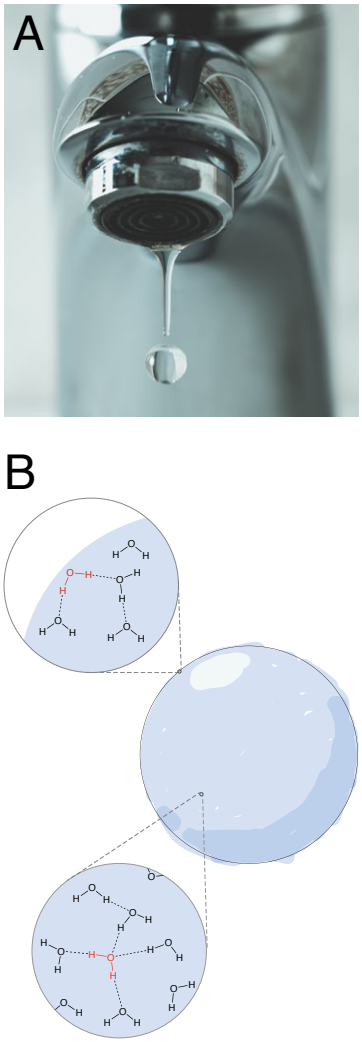


Figure 4.23 Cohesion and Water Droplets. A) Example of a water droplet. B) Comparison of the hydrogen bonding network of two water molecules (colored red). One is on the surface of the droplet (top left). The other is in the droplet's interior (bottom left)

The volume occupied by many substances shrinks in going from a gas to a liquid and from a liquid to a solid, as the molecules are pulled closer together because their interactions grow stronger. Water is an exception to this trend. While the volume taken up by water molecules decreases significantly in going from the gas to liquid phase, in becoming a solid it increases slightly (Figure 4.21, bottom). This occurs because, in order for the water molecules in ice to maximize the number and strength of hydrogen bonds, they have to be arranged slightly farther apart from one another than in liquid water.

One sign that ice takes up more volume per molecule than liquid water is that ice floats above liquid water (Figure 4.21, top). In liquid water, one gram of water takes up 1 cubic centimeter of volume, i.e. 1 ml. This water has a density of 1.0 grams per ml. For ice, the same amount of water molecules, 1.0 gram, takes up slightly more than 1 ml of volume, making the density of ice less than 1.0 gram per ml (about 0.92 g/ml). Since the ice is less dense than the liquid water, it floats to the surface of liquid water. This fact has had, and continues to have, important consequences for life on Earth. Because ice floats in water, it forms a layer above bodies of water like lakes. This layer protects the water below from freezing to some degree, allowing life to persist below the surface during cold times. If ice were denser than water, during winters, ice would sink to the bottom of bodies of water and they would freeze solid more readily, making life harder to sustain.

Another distinctive feature of water is that it is a liquid at room temperature. Hydrogen bonds are stronger than many other non-covalent intermolecular forces, so a small molecule like water can remain a liquid at room temperature where a relatively small molecule relying only on weaker forces (such as diatomic oxygen) would be a gas. The prevalence of liquid water on our planet has been crucial to life. Liquids, like the interior of our cells, are especially good for providing a medium in which the numerous molecules needed for life can be packed close enough to one another to function, but are not held so rigidly that they cannot move about and interact.

4.13 Cohesion and Adhesion of Liquid Water

Liquid water's extensive network of hydrogen bonds makes it a highly cohesive substance — one that tends to stick together. This cohesion leads to a number of water's physical properties.

Cohesion causes water to ball up into spherical droplets, as can be seen in raindrops or in the water that drips from a faucet (**Figure 4.23A**).Why does water adopt this

shape? Within the interior of a droplet, a water molecule is surrounded by other water molecules and can maximize the number of favorable hydrogen bonding interactions (**Figure 4.23B**). In contrast, on the surface of the droplet, air constitutes a significant part of a water molecule's environment. Water cannot make hydrogen bonds with air, meaning potential favorable interactions are lost (Figure 4.23B). Thus, an ideal shape for a collection of water molecules maximizes its interior (volume), while minimizing its exterior (surface area). A sphere is a shape that does just this, and so, water will tend to form spherical droplets when possible.

Cohesion also leads to the relatively high surface tension of water. Surface tension is a measure of the amount of energy required to increase the surface area of a liquid. Such an increase occurs when an object enters the liquid, because molecules formerly in the liquid's interior become part of the new surface that surrounds the object (**Figure 4.24A**). In water, the hydrogen bonds between molecules make this relatively costly, since some of these strong interactions in the interior are lost. Some organisms, such as water striders, take advantage of water's high surface tension, using it, in part, to stay above the surface of water (**Figure 4.24B**). On their feet are hairs that do not interact favorably with water. This distributes the weight of the insect over a larger area, lowering the pressure each leg exerts. This makes the energy required to push a leg through the surface greater than the gravitational energy the insect would gain by sinking, so it remains above the water.

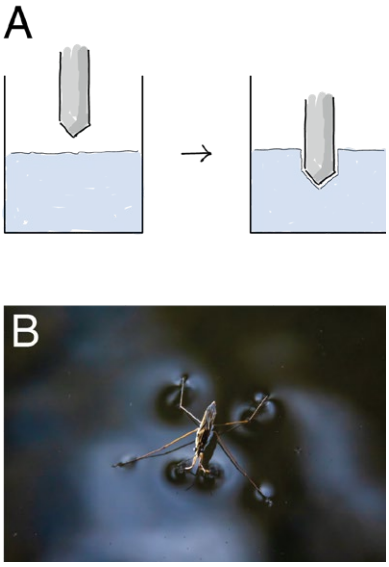


Figure 4.24 Surface Tension of Water. A) Plunging an object into water increases the surface area of the liquid. For water, this is energetically costly due to the disruption of hydrogen bonds and is reflected in water's relatively high surface tension. B) A water strider staying above the surface of the water. Water striders exploit the high surface tension of water, as well as their hydrophobic legs, to keep from sinking.

Adhesion of liquid water is the ability of water to stick to the surface of other objects. As water is a polar liquid, it tends to adhere most strongly to objects with polar or charged surfaces, making hydrogen bond and/or dipole interactions with the surface (**Figure 4.25A**, top). Water adheres weakly to those with non-polar surfaces, being unable to make the same interactions as strongly (**Figure 4.25B**, top). As an example, when the hood of a car is freshly waxed, the compounds in the wax are non-polar in nature. Thus, water exhibits weak adhesion, readily running off the hood or beading up into small droplets (Figure 4.25B, bottom). An unwaxed or dirty car tends to be coated with more polar and charged compounds, and water is able to spread out more over the surface of the car to make favorable interactions (Figure 4.25A, bottom).

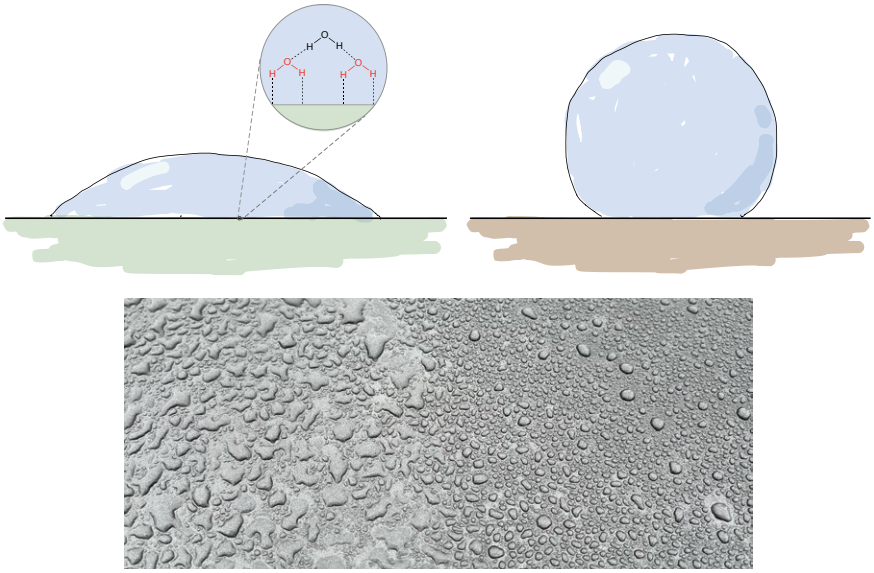


Figure 4.25 Adhesion of Water to Surfaces. The bottom picture shows a car hood with water on it. The right side was washed and waxed. The left side was not. Above the picture on the left is a schematic of a water droplet with strong adhesion to the unwaxed (polar) surface. Potential hydrogen bonds between the water and a polar surface are depicted, though interactions with a charged surface via water's molecular dipole are also possible. The schematic on the top right is of a water droplet with weak adhesion to the waxed (non-polar) surface.

Adhesion (as well as cohesion) are also important in what is known as capillary action. In capillary action, a liquid, such as water, can flow into a narrow space and can even act counter to external forces. For example, if the open end of a narrow glass tube is placed in water, water can rise up in the tube, seemingly counter to gravity (**Figure 4.26A**). The reason for capillary action (**Figure 4.26B**) is that most glass surfaces develop a negative

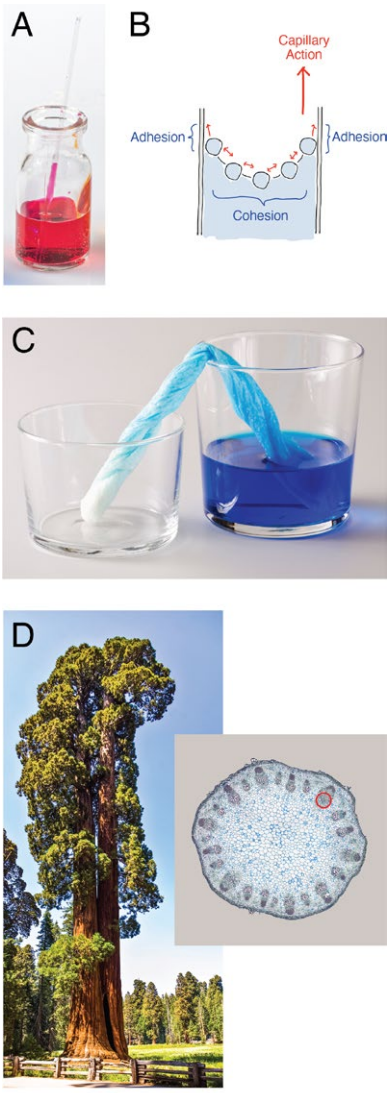


Figure 4.26 Capillary Action of Water. A) An example of capillary action, where colored water is drawn into a narrow glass tube. B) Basis of capillary action in A due to adhesion of the water to the glass surface and cohesion of the water molecules that are dragged along. C) Colored water being drawn into a paper towel by capillary action. D) A redwood tree (left) supplies water from its roots to its leaves. Plants employ capillary action, in part, to accomplish this with bundles of narrow "tubes", known as xylem. The xylem is visible in a plant stem cross-section (right), where one bundle of xylem is indicated by the red circle.

charge in water. By adhesion, water can flow up the walls of the tube due to favorable dipole-ion interactions. Since the tube is relatively narrow, the cohesion between water molecules can pull up water molecules not directly interacting with the sides of the tube.

Another example of capillary action is using a paper towel to clean up a spill. Even without pressing the towel into the spill, the liquid soaks up into the paper towel over time (**Figure 4.26C**). Paper towels are made of fibers with many narrow channels between them. The fibers consist of molecules like cellulose, a compound that we will see in later chapters links together many glucose molecules. As we saw (Figure 4.19), glucose is a very polar molecule with many -OH groups capable of making hydrogen bonds with water. In paper towels, water molecules can adhere to the cellulose (via its glucose-derived -OH groups), driving the water to spread into the paper towel.

As a final example, many plants utilize capillary action, in part, to transport water from the soil to their leaves (**Figure 4.26D**). Within the stems and trunks of plants are structures known as xylem. The xylem of a plant contains long, narrow tube-like structures that go from the roots to the top of a plant and are composed of substances like cellulose. As water can make favorable interactions with the components of the xylem, capillary action allows water to move counter to gravity, providing a way for the plant to transport water (and ions) that can be plentiful in the soil to regions of the plant that have less direct access.

Where to from here: In this chapter we examined water with respect to its covalent bonds and molecular structure. We saw how these features combine to give water unique properties that are biologically important. In the further exploration section, we delve into the concepts of dipoles and hydrogen bonds in more depth. We also look at the properties of gases on their own and when dissolved in water. In the next chapter, we consider covalent compounds beyond water.

E. Further Exploration - Dipoles and Hydrogen Bonds

4.14 Dipoles

Because of the difference in electronegativities between oxygen and hydrogen atoms, the OH groups of water are bond dipoles (bonds with a positive and negative end), and these bond dipoles combine to give water a molecular dipole (a molecule with a positive and negative end). Many biologically relevant compounds contain OH moieties or other groups with an uneven distribution of charge, meaning that individual bond dipoles or combinations of them are common in biological molecules. As objects with a single charge have interesting electrostatic properties (Section 3E), so too do objects containing dipoles. In this section, we will examine some of those properties.

A dipole is any object in which an equal amount of charge of opposite signs, a charge value of Q, is separated by some distance, d. This dipole can be represented mathematically by a vector (**Figure 4.27A**). The direction of the vector is along the axis separating the positive and negative charge and is pointed in the direction of the negative charge. The magnitude of the vector is the charge value times the distance ($Q \times d$) and is known as its dipole moment, μ. Dipole moments are measured in units of Debyes (D), where 1 Debye is about 3.34×10^{-30} Coulomb-meters. For reference, if a dipole has a charge value equal to one proton and the charges are separated by 1 angstrom (roughly the order of magnitude of most covalent bond lengths), it would have a dipole moment of 4.80 D. A molecule of water has a molecular dipole moment of about 1.84 D, while hydrogen chloride has a molecular dipole moment of about 1.08 D (**Figure 4.27B**).

Recall that an object with a single charge has an electric field, and this field either attracts or repels other charged particles. For example, if a positively charged particle is brought near a positive object, it experiences a repulsive force pushing the charged particle away

(**Figure 4.28A**, left). Conversely, the same positively charged particle around a negative object would experience an attractive force pulling the charged particle toward the object (Figure 4.28A, right).

A dipole also has an electric field (**Figure 4.28B**). This field is more complicated than that for the singly charged object but is ultimately just the sum of the electric fields of the two charges that make up the dipole. To get a qualitative sense of the forces experienced by a charged particle near a fixed dipole, suppose a positive charged particle is placed somewhere along the dipole axis (Figure 4.28B, dotted gray line). If the positively charged particle is placed at position A, it is relatively close to the positive charge of the dipole and relatively far from the negative one. This means it would largely experience the field of the positive charge, pushing it away. That said, the force would be slightly less than if the negative charge of the dipole were absent, as the negative charge slightly counteracts the repulsive force of the positive charge with attractive force. If the position of the positively charged particle was flipped to position B, it would largely experience an attractive force toward the dipole's negative end, offset slightly by the repulsive force from the positive end of the dipole. If the charged particle was somehow between the two charges at position C, it would be both repelled by the positive end of the dipole and attracted by the negative end, resulting in a greater force than would be experienced at the same position relative to the equivalent positive or negative charge alone. Altogether this means a charged particle can be attracted to a dipole, but it is attracted to the end of the dipole with the opposite charge.

In the previous chapter (Subsection 3.16), we saw that moving a charged particle to a position near an object with the same charge took energy to overcome the repulsive forces between them, and this energy is stored in the particle as potential energy. Conversely, energy is released in moving a negatively charged particle near a positively charged object, resulting in a decrease in potential energy for the particle. This potential energy can be described quantitatively (**Table 4.2**, first row). In this equation, the strength of the interaction is dictated by the numerator, depending both on the amount of charge on the object (Q) and particle (q). The range of this interaction is dictated by the denominator, decreasing as the distance between them, r, increases.

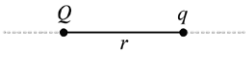
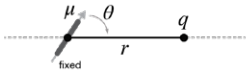
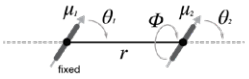
Type of Interaction	Schematic of Interaction	Interaction Energy
Charge-Charge		$\frac{Qq}{kr}$
Dipole-Charge		$-\frac{\mu q \cos\theta}{kr^2}$
Dipole-Dipole		$-\frac{\mu_1\mu_2[2\cos\theta_1\cos\theta_2 - \sin\theta_1\sin\theta_2\cos\phi]}{kr^3}$

Table 4.2 Electrostatic Interaction of Pairs of Charged Objects. Adapted from *J. Israelachvili "Intermolecular and Surface Forces" 2nd ed. Academic Press Inc. London 1995, p.28.*

A charged particle brought near a dipole also either stores or releases a certain amount of potential energy, and it is possible to derive an equation for the magnitude of this interaction energy (Table 4.2, second row). The dipole-charge equation differs from the charge-charge equation in several important ways. First, for a dipole, the potential energy of a nearby charged particle depends on the angle between the particle and the dipole's axis, with the interaction energy being positive if a positively charged particle is nearer the positive end of the dipole, and being negative near the dipole's negative end. Second, the strength of the dipole interaction energy depends on the dipole moment of the dipole, μ. This means that like a singly charged object, the amount of charge in the dipole, Q, is important. However, the distance separating the charges in

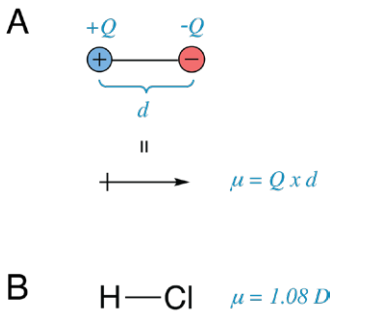


Figure 4.27 Electric Dipole and Dipole Moments. A) An electric dipole is one in which an equal amount of opposite charge is separated by some distance (top). This dipole can be represented as a vector, where the magnitude of this vector, its dipole moment μ, is the product of the charge value and distance (bottom). B) An example of a simple molecular dipole is a molecule of hydrogen chloride gas (which dissolved in water is known as hydrochloric acid). Hydrogen chloride, HCl, consists of a hydrogen atom linked to a chlorine atom via a single covalent bond. This bond is polar covalent, as chlorine has a significantly higher electronegativity (3.16) than hydrogen (2.20). The bond length of the molecule is roughly 1.3 Å and each atom has roughly 17% of a full charge, giving the molecule an observed dipole moment of 1.08 D.

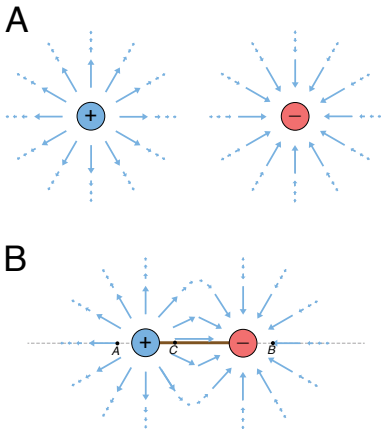


Figure 4.28 Electrostatic Force Experienced by a Positively Charged Particle. A) The particle experiences a repulsive force around a positively charged object (left) and an attractive force around a negatively charged object. B) The particle can experience either an attractive or repulsive force around a dipole. Near the negative charge (right side in parts A and B), the tip of the force arrow indicates the position of the positively charged particle to emphasize that the magnitude of the force is the same, yet oppositely directed.

the dipole, *d*, also contributes. Third, the range of the dipole-charge interaction energy is inversely proportional to the square of the distance between the center of the dipole and the charged particle ($1/r^2$). This means that the interaction energy between a charged particle and a dipole dies more quickly with increasing distance than with a charged object ($1/r$). In general, decreasing interaction energy with increasing distances makes sense, as the farther a charged particle is away, the less it "sees" the charged object or dipole. For a dipole, this decrease happens more quickly, because from a distance, the dipole with both a positive and negative charge "looks" uncharged, with the opposite charges counteracting each other.

Dipoles can also interact with dipoles, and the interaction energy between a fixed dipole and another dipole is given in Table 4.2, third row. Although this equation is even more complicated than for a dipole-charge interaction, some features can be discerned. The equation shows that two dipoles achieve their lowest potential energy when the positive end of one dipole lines up with the negative end of the other and the highest potential energy occurs when two positive or two negative ends of the dipoles line up. This situation is similar to the poles of a magnet, where lining up a north and south pole is strongly favorable, while a north-to-north or south-to-south is strongly unfavorable. The equation indicates that the strength of the interaction energy depends on the dipole moments of both dipoles. It also shows that the range of interaction energy decreases even more rapidly with distance ($1/r^3$). Altogether, this equation indicates that dipole interactions can be strong. However, the dipoles need to be properly oriented and relatively close to one another for this to be the case.

While these equations for interaction energies are useful for simple systems, things become much more complicated at the molecular level. For example, in trying to understand why a crystal of table salt dissolves in water, before the salt is added to water there are electrostatic interaction energies between all of the charged ions. In the fully dissolved system, there are charge-dipole interactions between the ions and molecule dipoles of water, as well as some dipole-dipole interactions between water molecules in the hydration shell. Altogether, it is not unreasonable to assume that NaCl dissolves in water because the interaction energies of the ions in the crystal are at least mostly offset by the interaction energies that form in the hydrated ion. That said, there are other factors involved. The fact that there are many more ways to arrange the dissolved ions in solution compared to the undissolved ions in the crystal is also important, and this gives an additional driving force for dissolving (though there is also ordering of water molecules to solvate the ions that has some cost). Consideration of how "ordered" a system is before and after a process is something we'll explore later (Chapter 11).

Another complication in quantifying the interaction of dipoles is that in the equations we have considered so far (Table 4.2), we have kept the orientation of at least one dipole fixed in space. However, in many cases, a dipole is free to rotate. Many molecules in the liquid and gas phase at room temperature exhibit random translational and rotational motion. Dipoles in solution or in the gas phase will have some randomness in orientation relative to one another, but will also have some degree of at least transient ordering. This can be thought of as a trade off between the energy in the system, related to the temperature, orienting the dipole randomly versus the interaction forces and energies causing them to line up. Greater randomness can come from higher temperatures and/or weaker dipole-dipole interaction energies, while greater organization can come from lower temperatures and/or stronger dipole-dipole interaction energies (molecules with larger dipole moments and/or smaller average distances between molecules).

How might we think about dipoles changing their orientation in response to an external electric field? Consider a simple situation in which a dipole starts in an orientation perpendicular to a uniform electric field (**Figure 4.29**). The positive end of the dipole will experience a force pushing it in the direction of the field, while the negative end of

the dipole will be pushed in the opposite direction. These forces, each acting at a distance from the center of the dipole, produce a net torque that rotates it. The lowest energy state of the dipole has its dipole moment antiparallel to the applied field

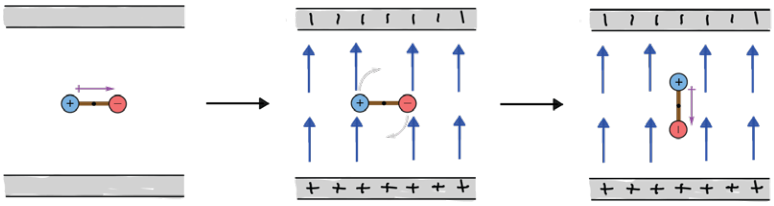


Figure 4.29 Effect of a Uniform Electric Field on an Unconstrained Dipole. The dipole begins in the absence of an electric field (left). When a uniform electric field is applied in the direction perpendicular to the dipole moment (here from a capacitor), the dipole experiences a torque (middle). This results in the reorientation of the dipole, where ultimately its dipole moment is antiparallel to the applied field (Note: some texts define the dipole moment vector in the opposite direction, from the negative to the positive end, which gives a parallel rather than antiparallel lowest-energy orientation.)

As an example, suppose we have two metal plates that become charged by a voltage, i.e. a capacitor (**Figure 4.30**). The opposite charges on the two plates will generate a constant electric field between them (see Subsection 3.17). If between the plates we put a container filled with randomly oriented water molecules, what would happen? As water molecules are molecular dipoles, they would respond to the capacitor's electric field, reorienting to oppose it. Not all of the water molecules would be oriented the same way (the overall kinetic energy of the water molecules, characterized by the water's temperature, would mean that some molecules would have enough energy to adopt other orientations). Nonetheless, enough water molecules would be oriented opposite to the external electric field as to decrease its net strength. How much water attenuates the electric field of a capacitor is effectively how its relative permittivity ($\varepsilon_r = 80$) is measured.

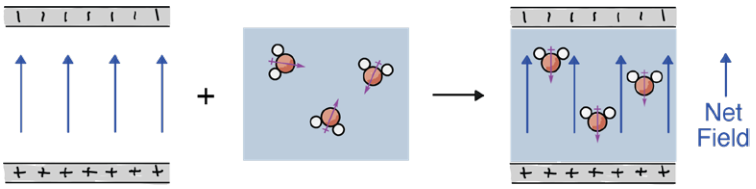


Figure 4.30 Effect of a Uniform Electric Field on Water Molecules. When randomly oriented water molecules are placed in the uniform electric field of a capacitor, the molecular dipoles of the water molecules will orient to oppose the field. If the total charge on the plates cannot change, the net field across the capacitor is reduced.

Similarly, the ability of water molecules to reorient their dipoles in response to the electric field of an ion, like a sodium ion, helps explain why the interaction energy between water and the cation is favorable. Shells of oriented water molecules attenuate the electric field of the sodium ion and explain why the Coulombic attraction between a sodium cation and a counterion, like a chloride anion, becomes relatively weak in table salt dissolved in water.

4.15 Hydrogen Bonds

Water molecules stick to each other and to other compounds via hydrogen bonds. Here, we delve into hydrogen bonds more deeply, starting with what constitutes a hydrogen bond and what kinds of compounds can form them.

While water is a prototypical example of a compound that can form hydrogen bonds, hydrogen bonds are a broader phenomenon than just compounds containing polar covalent bonds between oxygen and hydrogen. In general, the formation of a hydrogen bond can be described as follows:

$$\text{X–H} \quad + \quad \text{Y} \quad \rightarrow \quad \text{X–H- - -Y} \tag{4.6}$$

This reaction requires two components. The first is a compound where a hydrogen is covalently bonded to an atom, X, and this hydrogen is depleted in electron density due to X. The second is a compound that contains an atom, Y, that is rich in accessible electrons.

Together these components interact to form a hydrogen bond (depicted by the dashed line), where X-H is the source of the hydrogen (what we will refer to as the hydrogen bond donor), and Y is the recipient of the hydrogen (the hydrogen bond acceptor).

Technically, a number of different atoms can be X and Y, if they fulfill the criteria described above. However, for biological systems, the most commonly encountered atoms involved in hydrogen bonds are the electronegative atoms oxygen or nitrogen, where X and Y can both be oxygen, both be nitrogen, or some combination of oxygen and nitrogen. Since we have not yet discussed covalent compounds of nitrogen, the rest of our discussion will focus on hydrogen bonds that contain oxygen. As we saw with water (Equation 4.5), the hydrogens in water are involved in a covalent bond with the much more electronegative oxygen atom, depleting the hydrogen of electron density and making the OH group a suitable hydrogen bond donor. The oxygen in water is electron rich, due to the unequal sharing of electrons with the hydrogens. This allows the lone pairs of the oxygen in a different water molecule to act as hydrogen bond acceptors.

What is the nature of the hydrogen bond? Surprisingly, despite being proposed over a century ago, its nature is still not fully understood. Electrostatic interactions between the H in the hydrogen bond donor and the O in the acceptor are thought to be the major contributor to hydrogen bonding, where the partial positive charge on the hydrogen attracts the partial negative charge on the neighboring oxygen. However, other factors, such as covalent bonds, are thought to also contribute to the hydrogen bond. It is possible to think of the covalent nature of the hydrogen bond being similar to covalent bonds we have previously discussed: that is, two atoms sharing two electrons. In this case, the hydrogen and oxygen share a pair of electrons that comes exclusively from the oxygen atom.

Although hydrogen bonds have some covalent character, they tend to be considerably weaker than covalent bonds, and they are longer and less constrained in their geometry. When hydrogen bonding between water molecules is optimal, the distance between H and O atoms is roughly twice that of an O-H bond within a water molecule, and the bond angle from oxygen to hydrogen to oxygen is 180° (**Figure 4.31A**). Such optimal hydrogen bonds can be observed in ice crystals (**Figure 4.31B**).

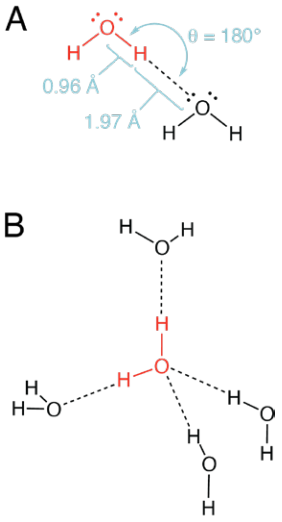


Figure 4.31 Details of Hydrogen Bonding in Water. A) Optimal bond lengths and angles in hydrogen bonds between one water molecule (red) and another (black). B) Three-dimensional orientation of water molecules (black) around a water molecule (red) in an ice crystal. For clarity, only waters attached to the central water are shown.

For different hydrogen bonds, the strength of the interaction can vary, with many factors contributing. One factor is the particular atoms involved. As we will see next chapter, hydrogen bonds between only nitrogen atoms are generally considerably weaker than those containing just oxygen. Additionally, the substituents connected to the non-hydrogen atoms in a hydrogen bond can influence the strength of the interaction.

The strength of hydrogen bonds can also vary depending on the number of hydrogen bonds made and whether they are positioned optimally. A single water molecule can make up to four hydrogen bonds: each of its hydrogens serving as hydrogen bond donors and each lone pair serving as hydrogen bond acceptors (Figure 4.31B). In ice, each water molecule makes four hydrogen bonds with optimal distances and bond angles (Figure 4.31 and Figure 4.21 bottom left). Because of the large number of optimal hydrogen bonds in ice and the relatively low kinetic energy of the molecules, the bonds in ice are stable and long lived.

In contrast, in liquid water, hydrogen bonds are generally sub-optimal, with hydrogen bond lengths that can be slightly longer than in ice, and O to H to O bond angles smaller than 180°, though rarely less than 120°. Due to the suboptimal hydrogen bonds and relatively high kinetic energy at room temperature, hydrogen bond formation in liquid water is transient with the average lifetime of a hydrogen bond being only about 1 picosecond (1×10^{-12} s). Nonetheless, these transient interactions are sufficient to keep water in a non-gaseous, condensed state at room temperature (Figure 4.21, bottom middle). Moreover, the transient nature of the hydrogen bonds allows them to flow past one another, keeping water a liquid and not a solid.

F. Further Exploration - Gases

Most biologically relevant molecules are in the liquid or solid phase, but some, such as diatomic oxygen, can be in the gas phase. In this section we examine some of the properties of gas phase molecules, as well as the extent to which such molecules dissolve and diffuse into the solutions that comprise and surround cells.

4.16 Properties of Gases

Molecules in the gas phase have large-scale (macroscopic) properties that can be observed and measured, including: volume, amount, temperature, and pressure. What are these quantities and how do they arise from molecular-scale (microscopic) features of gases? To address these questions, let's consider a system of gas molecules contained in a closed box (**Figure 4.32**). To keep things simple, we will consider the gas molecules to be "ideal." That is, they are rapidly moving, small, hard spheres that effectively take up no space and are widely spaced from one another. Additionally, these spheres bounce off of one another and the walls of the box without sticking to any significant degree.

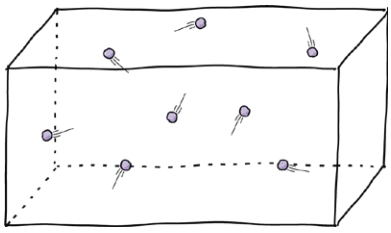


Figure 4.32 A Simple Model of a Gas and Its Properties. Shown are gas molecules in a closed container, where the gas molecules behave ideally (rapidly moving point spheres that experience only elastic collisions). The volume of the gas, V, is equivalent to the volume of the container. The amount of gas, n, is the number of gas particles in the container (in moles). The temperature of our simplified system, T, is proportional to the average translational kinetic energy of the gas particles. The pressure of the gas, P, is the force per unit area exerted by the gas molecules on the container and depends on the strength and frequency of collisions.

One macroscopic property of our system is the volume of the gas, which we will abbreviate as V. The volume of the gas is equivalent to the volume of the box that contains it, because at the microscopic level, the gas molecules move rapidly and randomly in all directions and do not stick together or to the walls. The only things that constrain how much space the gas molecules take up are the walls of the box.

Another property of our system is the amount of gas, which could be the weight of the gas in the box or the number of gas particles. Both of these amounts are directly related to the number of gas molecules, which is simply the total count of molecules in the box. The weight of the gas is the number of gas molecules times how much each molecule weighs. In this section, we will focus on the number of gas molecules in a system. Because there will be many particles in all but the smallest box, we will describe the number of particles in terms of moles and abbreviate it as n.

Our collection of gas molecules will also have a certain temperature, T. This temperature is how "hot" the system is and can be quantified simply by placing a thermometer in the box. For our simplified gas molecules of spheres, temperature is proportional to the average translational kinetic energy of the molecules - that is, the faster the molecules are moving about on average (v), the greater the average kinetic energy they possess ($\frac{1}{2}\, mv^2$) and the higher the temperature (T).

Finally, the gas in the box has a certain pressure, P. The pressure of a gas can be thought of as how much the molecules are "pushing" against the walls of the box. From your own experience, you are probably comfortable with the idea that a balloon or tire with more air in it is at a higher pressure than when it is less inflated. At the microscopic level, pressure arises from gas molecules bouncing off the walls of the box. With each collision, the gas molecule exerts a force on the wall by imparting some change in momentum in some period of time. The total amount of force a wall experiences will depend on the average number of molecules that hit the wall and on average how "hard" the molecules hit (the force of a given collision will depend on the mass of the gas molecule and its velocity, which will vary in a population of gas molecules). The pressure of a gas is related to the force its molecules exert on the walls, but is not equivalent to it. Pressure is the force exerted on an area divided by the area:

$$P = \frac{F}{A} \tag{4.7}$$

You may have experienced the difference between force and pressure, if you have had a toddler rest in your lap. If they put their weight on your lap (the force) using just

their elbows (small area), the pressure you experience is much greater than them laying across your lap (lesser pressure, because the same force is spread out over a larger area).

4.17 Ideal Gas Law

Any sample of a gas will have a certain temperature, amount, pressure, and volume, and it turns out that these properties are interrelated. That is, the value of any one property depends on the value of the others. For an ideal gas, the relationship between pressure, volume, amount, and temperature is relatively simple:

$$PV = nRT \tag{4.8}$$

Equation 4.8 is known as the ideal gas law. It allows us to determine one gas parameter from the other parameters or to predict how changing one parameter might affect another parameter, if the remaining parameters are unchanged. Before we look at how to use this equation, we need to consider the units for each parameter.

For volume, *V*, the most commonly used unit is liters. For the number of molecules, *n*, moles are typically used. The temperature of the gas, *T*, needs to be in units of Kelvins. Kelvin degrees have the label K and are related to Celsius degrees, where the temperature in Kelvins is 273 more than the Celsius temperature:

$$\text{Kelvin Temp} = \text{Celsius Temp} + 273 \tag{4.9}$$

For example, water at its freezing temperature (0 °C) is at 273 K (0 + 273).

Pressure can be reported in many different kinds of units, which will be explored more in Subsection 4.18. For now we will use the units of atmospheres (atm). 1.0 atmosphere represents the average pressure of the air at sea level at 15 °C (59 °F). A pressure greater than 1.0 atm means the pressure is greater than atmospheric pressure. For example, at a depth of about 20 meters in the ocean, the pressure a person would experience would be about 3.0 atm.

The last units to consider are for the parameter *R*. *R* is a constant known as the ideal gas constant, and varies in its value and units depending on what units are used for *P*, *V*, *n*, and *T*. For the units we have described, *R* has a value of about 0.0821 and has units of $L \cdot atm \cdot K^{-1} \cdot mol^{-1}$. You can see these units make sense from considering the ideal gas law in Equation 4.8. On the right side of the equation, you see that *R* (units of $L \cdot atm \cdot K^{-1} \cdot mol^{-1}$) is multiplied by *n* (units of mol) and *T* (units of K). The amount and temperature units cancel, leaving only units of L•atm. These are the units of volume times pressure and match the units generated on the left side of the ideal gas law equation, *PV*.

Let's see if we can apply the ideal gas law to determine one parameter from knowledge about the others. Suppose we have 1.00 moles of diatomic oxygen at 1.00 atmosphere at 20° C (68 °F) and want to know the volume it would take up. Before we plug these numbers into Equation 4.8, we should address a couple of questions: Does the ideal gas law apply to our system? Even though diatomic oxygen is not an ideal gas (it is not a near volume-less sphere, it can make weak interactions), under the conditions described, it acts pretty much ideally, so using Equation 4.8 is okay; For a gas that is just floating around, what do we mean by it having a pressure of 1.0 atmosphere, and how do we think about its volume under those conditions? In problems with gases, it is often helpful to imagine the gas contained in a box in which one side can be adjusted to match an external pressure (**Figure 4.33**). In this problem, we imagine our box is filled with a mole of oxygen molecules at 20 °C (293 K). Outside the box is just our normal

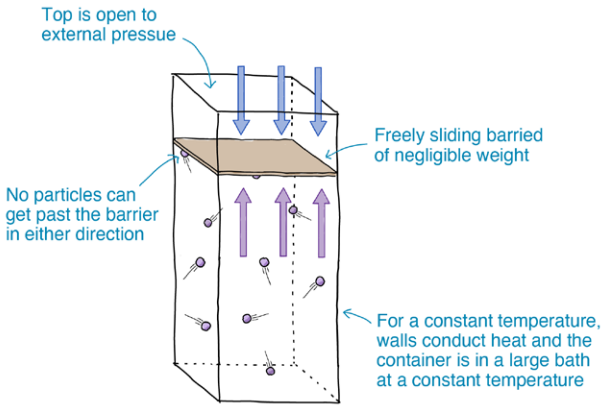


Figure 4.33 Box of Gas That Adjusts Its Volume to Match the External Pressure. In this container of gas, one end of the box can move freely up or down. It will settle at a specific height (and therefore constrain the gas to a specific volume) when the pressure of the gas inside the container (pushing the adjustable end upwards) matches the external pressure (pushing the adjustable end downward). The external pressure could be from the gas of the atmosphere, weights sitting on the adjustable end, or someone pushing down. For our purposes, the weight of the adjustable end itself is considered negligible. If the amount and temperature of the gas remains constant (box doesn't leak, box has heat conducting sides and is put in a large bath with a constant temperature), as the edge is pushed down, the volume of the gas will decrease (box becomes smaller), but its pressure will increase (more particles hit the walls with the smaller volume than when the volume was larger and the particles were more spread out).

atmosphere, pressing down on the box's adjustable side with a pressure of 1 atm. Under these circumstances, the pressure of the gas inside the box must ultimately also be 1 atm, because, if the pressure inside was greater than 1 atm, the push from the inside would be more than from the outside, and the adjustable side would move up. Similarly, if the pressure were less inside the box, the pressure from outside the box would cause the box to compress. Thus, we want to know the volume of our gas that would exert a pressure to match the outside pressure.

To determine the volume for our system, we can rearrange Equation 4.8 to isolate V on one side, and then plug in the information we have:

$$V = \frac{nRT}{P} = \frac{(1.00\ \text{mol})(0.0821\ \text{atm•L•mol}^{-1}\text{•K}^{-1})(293\ \text{K})}{1.00\ \text{atm}} = 24.1\ \text{L} \qquad (4.10)$$

This says that one mole of oxygen gas at atmospheric pressure and 20°C will have a volume of 24.1 L. It's worth noting that this result is true of any ideal gas, not just oxygen. So the idea that 1 mole of gas (at near room temp and atmospheric pressure) will occupy roughly 24 liters is a useful fact to keep in your back pocket (though you may also see 22.4 L quoted, which is the value at 0 °C).

How big of a box is this? In terms of milliliters, 24.1 L is 24,100 ml, and since one milliliter is one cubic centimeter (cc or cm3), this is also a volume of 24,100 cm^3. If the gas were in a box with sides of equal length (a cube), the volume of a cube is the length of a side cubed. A box with a 24,100 cm^3 volume would have sides of length $(24{,}100\ cm^3)^{(1/3)}$, or almost 30 centimeters (28.9 cm).

What can we say about the density of gases? The diatomic oxygen in our box would weigh about 32 g (16 g/mol x 2 x 1 mol). A mole of other gases weighs different amounts, such as 2 g for diatomic hydrogen or 71 g for diatomic chlorine. Recall that density is the mass of a substance in a given volume (Subsection 2.38). Since a mole of each gas has a different mass but the same volume (24.1L at 1atmosphere and 20°C), their densities differ: hydrogen gas has a much lower density (8.3×10^{-5} g/ml) than air, which has a density similar to oxygen (1.3×10^{-3} g/ml). Thus, a balloon filled with hydrogen (or helium gas) is more buoyant than air and floats.

How does the volume of one mole of gas compare to a mole of liquid under similar conditions? Consider water. A mole of water (H_2O) weighs 18.0 g. The density of water is about 1.00 g/ml, meaning that one mole of water takes up about 18 ml. This is less than 1/1,000th of the volume a mole of oxygen molecules takes up, reflecting the fact that gas molecules have a lot more empty space around each molecule. A cube of 18.0 ml of water would contain 18.0 cc, with sides 2.62 cm. This means comparing a cube containing a mole of water molecules compared to a mole of oxygen gas molecules, the

sides of a cube of water would be just a bit less than 1/10th the size of the cube with oxygen gas.

In addition to allowing us to calculate properties, the ideal gas law can help us predict how a gas will change when a property is varied, especially when we limit changes to two of its properties. For example, suppose we doubled the pressure of the sample of diatomic oxygen we've previously discussed (Figure 4.33). What would happen to the volume if nothing else changed, i.e. the amount remained 1.00 mole and the temperature remained 20 ˚C? Such a situation might arise, if the box was leak-proof (no change in moles of gas) and could exchange heat with an environment at 20 ˚C (i.e. the temperature of the gas in the box could ultimately equilibrate with its surroundings to remain at the same temperature). Doubling the pressure outside of the box would push down on the box until the pressure inside the box was the same (the pressure inside the box had doubled so it was pushing equally hard from inside the box as the surroundings from the outside). Intuitively, we would reason that the volume of the box under these circumstances would decrease, as the same number of molecules moving at the same speed (assuming the oxygen molecules were acting as an ideal gas) would make more collisions with the walls in a smaller box, increasing the pressure. We could see this more quantitatively by plugging our new numbers into the expression for volume from Equation 4.10, where pressure has changed to 2.00 atmospheres:

$$V = \frac{nRT}{P} = \frac{(1.00\text{ mol})(0.0821\text{ atm•L•mol}^{-1}\text{•K}^{-1})(293\text{ K})}{2.00\text{ atm}} = 12.05\text{ L} \quad (4.11)$$

Here, we can see that doubling the pressure from our original value (1.00 atm to 2.00 atm) decreased the volume by 1/2 (24.1 L to 12.0 L). Another way to approach this quantitatively is to directly inspect the ideal gas law, $PV=nRT$. We know that nothing on the right side of the equation, nRT, is going to change. If we double the pressure on the left side, the only way that everything on the left side, PV, does not change (so it is still equal to the unchanged right side) is for V to be reduced by 1/2 (2 x 1/2 = 1).

Yet another way to see this: suppose we consider our initial conditions as state 1. The ideal gas law for state 1 could be expressed as:

$$P_1V_1 = n_1RT_1 \quad (4.12)$$

After something changes about our gas, our final conditions would be state 2, and we could now express the ideal gas law as such:

$$P_2V_2 = n_2RT_2 \quad (4.13)$$

In our example, neither the amount of gas nor the temperature changes ($n_1 = n_2$ and $T_1 = T_2$, respectively). This means the right sides of Equations 4.12 and 4.13 are the same, meaning we can equate the left sides of these equations:

$$P_1V_1 = P_2V_2 \quad (4.14)$$

We can use this relationship to solve for V_2 and see that if pressure doubles ($P_2 = 2P_1$), V_2 is half of the original volume:

$$V_2 = \frac{P_1}{P_2}V_1 = \frac{P_1}{2P_1}V_1 = \frac{1}{2}V_1 \quad (4.15)$$

as was seen comparing Equation 4.10 to 4.11. If instead, pressure had gone down by half (P_2 = 0.5 atm), the final volume would end up double ($V_2 = 2V_1$). If we knew that under constant amount and temperature, the volume of a gas doubled, the pressure would be half of its original value ($P_2 = 0.5\ P_1$).

What if we have a gas in which volume and temperature don't change, but amount does (say add more gas to a fixed size box)? What happens to the pressure in this case? Intuitively, we would expect the pressure to increase, as there would be more molecules with the same energy colliding with the walls of the box. From examining the ideal gas law (Equation 4.8), we can see that holding everything else constant, increasing n will increase P proportionally: that is, if we double the amount of particles, the pressure will double. What if in the same system, we don't increase the amount, but the temperature? In this case, we would also expect the pressure to increase, as the same number of molecules are moving faster (increase of temperature increases average kinetic energy, raising velocity), which results in more and harder collisions with the walls of the box, raising the pressure. Quantitatively, from the ideal gas law we see that doubling the temperature will double the pressure, all else staying the same. Remember though, that temperature for the ideal gas law is in Kelvin, not Celsius. So if our gas was originally at 20 °C (68 °F, 293 K), the gas temperature to double the pressure would not be 40 °C (104 °F, 313 K), but would need to be 313 °C (595.4 °F, 586 K). If our gas doubles in temperature, but the amount and pressure stay the same, we can see that the volume doubles (more energy in the gas molecules pushes the wall of the box out to increase its volume until gas molecules become sufficiently diluted to match pressure outside of the box, say 1 atm throughout).

Incidentally, Equation 4.14 is known as Boyle's law and predates the formulation of the ideal gas law. Similar manipulations of the ideal gas law, keeping two parameters constant each time, can generate other relationships with special names that can predict how the other parameters change with respect to each other.

Something to keep in mind is that to use the ideal gas law, the gas has to be ideal. That is, the gas molecules are point particles with negligible volume, and when the spheres bounce off of one another and the walls, they do not stick to either to a significant degree. As we have mentioned before, under most circumstances and for most gases (though not all) this will be the case. Some conditions where the ideal gas law breaks down include: very small volumes where molecular size becomes significant; very strong gas–gas interactions; or temperatures low enough or pressures high enough that even weak interactions affect behavior.

4.18 Other Aspects of Gas Pressure

In our examples, pressure was expressed in terms of atmospheres. However, a number of other units are possible (**Table 4.3**):

Pressure Unit	Alternative names/units	Standard atmosphere
atm	atmospheres	1 atm
Pa	pascals, N/m^2	101,325 Pa
bar	100 kPa	1.01325 bar
psi	pounds per square inch, lbf/in^2	14.7 psi
mm Hg	millimeters of mercury, torr*	760 mm Hg*
in H_2O	inches of water	406.78 in H_2O

Table 4.3 Different Units of Pressure. *A torr is not actually equivalent to 1 mm of mercury anymore, but the difference is about 0.000015%, so the units are effectively the same.

Some units are based on the definition of pressure itself: force over a given area (Equation

4.7). For example, the scientific units for force and area are Newtons (N) and square meters (m^2), respectively, so 1 N of force applied to 1 square meter would be 1 N/m^2, which is also known as a Pascal (Pa). One standard atmosphere is 101,325 Pa. Since this is a large number, gas pressures are often reported in thousands of Pascals (kPa) or 100,000s of Pascals (a bar). Non-metric analogs of N/m^2 include pounds per square inch (psi), or more accurately pound-force per square inch (lbf/in^2).

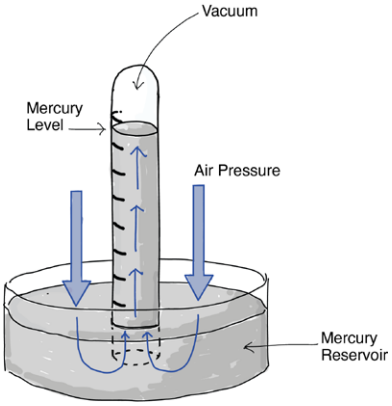


Figure 4.34 Schematic of a Mercury Barometer. In a mercury barometer, the height of the mercury in the bulb reflects the atmospheric pressure, where standard atmospheric pressure is 760 mm of mercury.

Other units of pressure are based on how it is measured. Atmospheric pressure can be determined with a barometer, such as one in which a tube is filled with mercury (**Figure 4.34**). One end is open to the atmosphere, while the other end is closed and has a vacuum (no gases at all). Because the open end will experience the pressure of the atmosphere pushing down on the mercury, while the vacuum end will experience no pressure, the mercury will rise until the force from the weight of the mercury column is equal to the force exerted by the atmosphere. At this point, the mercury will have a certain height, which can be expressed in terms of millimeters of mercury (mm Hg). A millimeter of mercury was also originally defined as a torr, which is effectively equivalent. One atmosphere of pressure is 760 mm Hg, which is also 760 torr. Mercury is not the only type of liquid that can be used to measure pressure, nor are metric units. Sometimes you might encounter pressure in units of inches of water.

Under certain circumstances, gas pressure can be used as a proxy for concentration. If you rearrange the ideal gas law (Equation 4.8) in terms of pressure, you can see that the pressure of an ideal gas is related to its concentration, C (moles of molecules per liter):

$$P = \left(\frac{n}{V}\right)RT = CRT \tag{4.16}$$

If you are measuring the pressure of different systems at the same temperature (T is constant), then the pressure is directly proportional to the concentration. This is why sometimes the concentration of a gas will be reported as its pressure, where double the pressure indicates double the concentration.

To this point we have considered vessels containing only a single gas, such as our box filled with diatomic oxygen. However, mixtures of gases are possible, and in fact the air in our atmosphere is a mixture of gases (discussed more in the next chapter). What are the volume and pressure of the gases that make up a mixture? If each gas behaves ideally, each will fill the entirety of its container - that is, each gas will have the same volume. Each gas will then exert its own pressure based on the amount of that gas and its temperature, based on the ideal gas law (Equation 4.8). The total pressure of the mixture will then simply be the sum of the pressures of the individual gases. For example, a mixture of 1 atm of diatomic oxygen and 0.5 atm of diatomic hydrogen would have a total pressure of 1.5 atm. Consequently, each gas in a mixture has a certain partial pressure, the pressure it would exert if it were the only gas present in a container. The partial pressure of a gas relative to the total pressure of the gas mixture also reflects the relative fraction of molecules in the mixture. In our oxygen/hydrogen example, if the partial pressure of diatomic hydrogen is 0.5 atm compared to a total pressure of 1.5 atm, 1/3 (0.5 atm/1.5 atm) of the molecules in the gas mixture are diatomic hydrogen.

4.19 Solubility of Gases in Water

Most compounds that are gases at room temperature have poor solubility in water. This is because they generally do not have dipoles or the capacity to form hydrogen bonds, the main ways water molecules are able to interact with compounds. For example, diatomic oxygen, a non-polar compound, is not very water soluble. In fresh or salt water, it dissolves to just under 0.01 g/L at 25 °C and 1 atm, significantly less than the solubility of table salt (360 g/L) or glucose (909 g/L).

As discussed in later chapters, diatomic oxygen is used to efficiently harvest energy from food, and many organisms need oxygen to survive. In larger organisms, cells in their interior do not have direct exposure to the oxygen present in their environment. A common way to address this issue is to employ a circulatory system, where oxygen is transported to cells by pumping blood throughout the body. How can this be done effectively, if oxygen gas is not very soluble in water, the main constituent of blood? Blood contains a molecule, hemoglobin, that is both water soluble and capable of forming a strong but reversible interaction with diatomic oxygen (**Figure 4.35**). By binding oxygen, hemoglobin greatly increases the total amount of oxygen that blood can carry.

The poor solubility of diatomic oxygen in water can also make it difficult to acquire enough oxygen for organisms that "breathe" water. Organisms like fish address this issue with their gills. Gills are organs that expose a large surface area over which a substantial amount of water can be rapidly passed. This allows more oxygen molecules to be encountered and transferred to the fish's circulatory system. Low amounts of environmental oxygen are less of an issue for terrestrial organisms, as air has roughly 30 times greater concentration of oxygen than water (more details on air composition in Chapter 5). However, in larger organisms like us, our lungs are still designed to have large surface areas (although this area is fractal and irregular, estimates of its area range from 50-140 m^2, which is roughly up to half the size of a tennis court!). This large area promotes rapid uptake of oxygen, and breathing rates rise when our need for oxygen increases.

The solubility of a gas in water is affected by temperature and tends to decrease with increasing temperature, a trend opposite of many liquids and solids. This change in gas solubility can be understood in terms of the molecule's kinetic energy. At higher temperatures, gases have greater amounts of molecule motion, which tend to disrupt any favorable interactions between dissolved gas molecules and water. For a gas like oxygen, which isn't very soluble to begin with, decreasing the amount of dissolved oxygen can be problematic for aquatic organisms. Warming of waters due to waste heat from industrial processes and global warming can lead to an environment less hospitable to fish and other wildlife. It should be noted that heating of water is not the only way that deoxygenation can occur. When algae and plants bloom, and then die and decompose, the decomposing microbes consume much of the available soluble oxygen. This can occur from eutrophication, the increasing concentrations of nutrients in the water, which can arise for various reasons, some human caused, such as runoff of fertilizers or sewage.

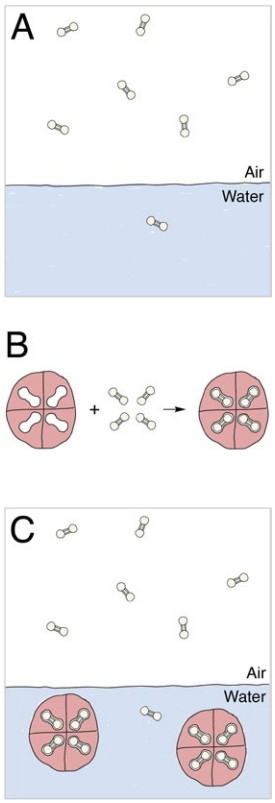


Figure 4.35 Hemoglobin Increases Oxygen Concentration in Blood. A) Oxygen gas is not very soluble in water. B) The blood protein hemoglobin binds four oxygen gas molecules tightly, but reversibly. C) Because hemoglobin is very water soluble (and constitutes most of the interior of red blood cells), binding of oxygen by hemoglobin significantly increases the concentration of oxygen in blood.

The pressure of a gas above an aqueous solution also affects gas solubility, with increased pressure generally increasing the amount of gas dissolved. Microscopically, greater pressures mean more gas molecules entering the water, increasing the number of gas molecules that can interact with the water and be retained. Commercial preparation of carbonated (but non-fermented) drinks takes advantage of this. The gas carbon dioxide is introduced to the beverage at high pressure, allowing more to dissolve than at atmospheric pressure.

When gases (or other substances) that are dissolved in solution are in equilibrium, as much of that substance is dissolved as possible. If the conditions change (for example, a liquid exposed to high pressure of a gas goes to normal atmospheric pressure, or a cold solution is suddenly warmed up), the equilibrium will ultimately adjust to the new conditions. For example, when scuba divers descend to great depths in the ocean, the amount of gases, such as nitrogen, that are dissolved in their blood increases. If they return to the lower pressure of the surface too fast, they can suffer from what is known as the bends, where the gases rapidly bubble out of their blood. This can result in the blockage of blood flow and the stretching and tearing of blood vessels and nerves.

It is important to note that equilibration of a system to new conditions does not have to occur right away, and can even take a long time (an idea discussed in Subsection 3.21). In this case there can be a higher concentration of dissolved gas (or other substances)

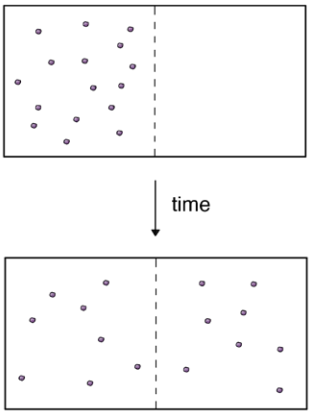


Figure 4.36 Diffusion of a Gas. Gas molecules held entirely on one side of a container and then released (top), will diffuse throughout the container until the entire volume is filled and the concentration throughout the container is effectively equal (bottom). The top is a non-equilibrium system, while the bottom represents a system at equilibrium (and the distribution of particles can be described by an equilibrium expression as described in Section 3F).

than would normally be the case, i.e. the solution is what is known as supersaturated. For example, when a bottle of carbonated soda is opened and the gas pressure is reduced, the soda does not typically go flat immediately. This is because loss of the gas is more rapid when gas molecules come together to form bubbles that are buoyant enough to escape, but initiation of bubble formation can be slow.

4.20 Diffusion of Gases

At the microscopic level, both gas molecules and particles in solution are constantly in motion, moving randomly through space. When a concentration difference exists, this random motion produces a net movement of particles from regions of higher concentration to regions of lower — a process called diffusion. For example, gas molecules exclusively on one side of a container will spread to the other side, filling the container and ultimately equalizing the concentration throughout the container (**Figure 4.36**). During this process, how rapidly particles move through a given area from one region to another is dictated by two main factors (**Figure 4.37**): the concentration difference between the regions, with larger differences speeding up diffusion; and the diffusion constant of the particle, with larger diffusion constants resulting in more rapid diffusion.

Gas molecules are generally quite small and do not differ significantly in their size. When gas molecules are in the air, the viscosity is low and the temperature reasonably high, making the diffusion coefficient relatively large. If a large concentration difference of gas molecules exists, diffusion can be quite rapid. For example, an odorant molecule released in one corner of a room can spread rapidly throughout the room.

In contrast, gas molecules in water diffuse much more slowly. This is due to the high viscosity of water compared to air, since in water, a gas molecule is constantly bumping into water molecules, significantly slowing how rapidly it will spread out on average. This is not to say that gases will not diffuse through water, but how much they do so depends on both the length scale and the amount of time considered. On a length scale of a cell, roughly several μm, gases diffuse through rapidly. This is why single-celled organisms in water can get oxygen from their environment, as dissolved oxygen will diffuse into a cell quickly. For organisms like us, we also take advantage of this rapid diffusion, as oxygen in the air sacs in our lungs can readily diffuse into our circulatory system. That said, diffusion isn't sufficient to distribute oxygen throughout our body. The distances oxygen has to travel from our lungs to our extremities can be on the order of a meter, and diffusion in liquid over that length is quite slow (and even slower when bound to much larger hemoglobin molecules). That is why all vertebrates have hearts, a hollow muscular organ that pumps blood. By pushing blood through the circulatory system, oxygen can reach cells that need it much faster than by diffusion alone.

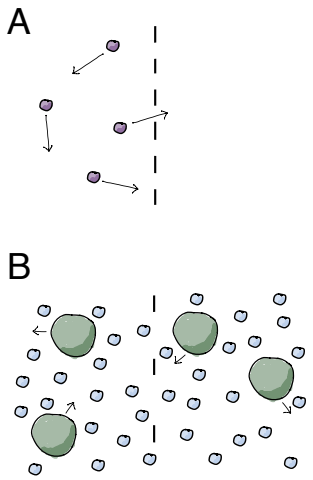


Figure 4.37 Factors Affecting Net Diffusion. Shown are factors that favor A) fast net diffusion, versus B) slow net diffusion. Concentration differences between regions affect net diffusion. In part A, all particles are on one side. Diffusion is random, so the particles can go in any direction. However, the chance that some particle will diffuse from the left to the right is much higher than the chance some particle will move from the right to the left (since there are no particles on the right). In part B, if we track the green particle, we see the concentrations on the right and left are the same. This means that the chance of a particle on the left diffusing right is the same as the chance of a particle on the right diffusing left. Overall, the two will cancel each other out, leading to no net diffusion. That said, this system, which is in equilibrium with respect to concentration, is a dynamic equilibrium: the particles are still constantly in motion, moving from one side to the other, there is just no net flow of particles from one region to another. Besides a concentration difference, diffusion rates are dictated by features of the particles and their surrounding molecules. In part B, the diffusion of the green particle is further slowed, compared to part A, because these particles (for example protein molecules) have other molecules to move past (the blue particles representing something like water molecules). The green particle's large size and the presence of the other particles slow its movement. In contrast, the particles on the top are small and have relatively few surrounding molecules (say if the particles were gas molecules). Thus, they can diffuse rapidly in an unhindered fashion.



CHAPTER 5
More Covalent Compounds, Molecular Ions

Motivation and Overview: Last chapter we saw how one atom of oxygen and two atoms of hydrogen form covalent bonds to make a molecule of water. In this chapter we build on this foundation and examine a sampling of covalent compounds made from the organic atoms, with a particular focus on C, N, O, and H. In the first section, we explore covalent compounds with only single bonds. In the second, some that have double bonds. In the third section, we see how charged covalent compounds can be made, i.e., molecular ions. In the fourth section, we look at some of the biologically important covalent compounds that comprise air. For all of these compounds, we touch on their three-dimensional structures and properties, utilizing ideas introduced in our examination of water.

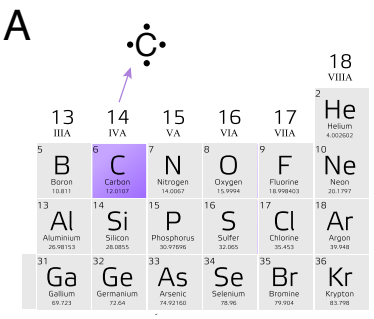
A. Some Covalent Compounds with Single Bonds

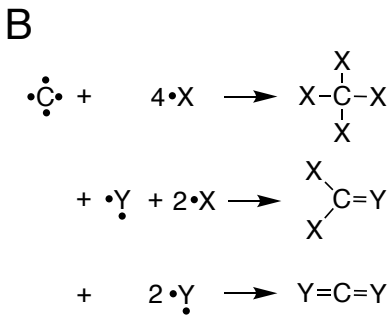
Many different covalent compounds can be generated by linking together some combination of carbon, hydrogen, nitrogen, and oxygen atoms via single bonds. Carbon often forms the core scaffold of organic and biological molecules (**Figure 5.1**), so let's begin with carbon-containing compounds. We start with the simplest possible stable compound that can be made from single bonds of carbon and hydrogen, methane.

5.1 Methane

Methane, CH_4, is composed of one atom of carbon and four atoms of hydrogen. In the previous chapter, we saw that hydrogen can form one bond with no lone pair electrons left over. What can we say about carbon?

In the periodic table, carbon is in the 4th column of its row, meaning it has four valence electrons (**Figure 5.2**). To have a complete valence, it needs eight total electrons. If it can form four covalent bonds (share each of its valence electrons with valence electrons from one or more other atoms), it achieves a full valence. Thus, carbon is an atom that can form four bonds and have no lone pairs of electrons left over.





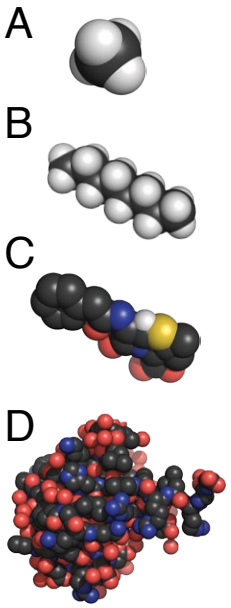


Figure 5.1 Examples of Carbon-containing Compounds. Carbon is the scaffold on which organic and many biologically-relevant molecules are built. Shown are space-filling models of: A) a compound with a single carbon, methane; B) a component of gasoline, octane; C) the antibiotic benzylpenicillin; D) the small protein ubiquitin. Carbons are shown as black spheres, hydrogens as white ones, oxygens as red, nitrogens as blue, and sulfurs as yellow. The four structures are not shown at the same scale, though the sphere used for each atom type is the same size. Hydrogens are largely omitted from the structures shown in C and D for clarity.

Figure 5.2 Properties of Carbon. A) Carbon has four valence electrons and needs four more for a full valence. It can do so by making four covalent bonds, with no lone pair electrons left over. B) A couple of theoretical ways carbon could make four covalent bonds.

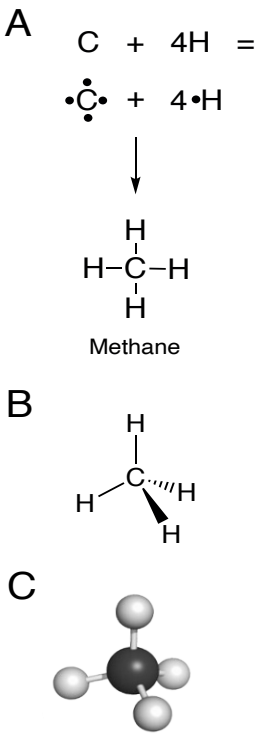


Figure 5.3 Structure of Methane. A) In methane, four hydrogen atoms form four covalent bonds with a single central carbon atom. This molecule has a tetrahedral geometry, which can be depicted in B) a perspective drawing, or in C) a ball-and-stick structure.

Methane has one carbon and four hydrogens, where each hydrogen wants to make one bond, and the carbon wants to make four bonds. These requirements can be met by having the central carbon make four single bonds to hydrogens (**Figure 5.3A**).

What is the three-dimensional shape of methane? Like we did with water, we can apply VSEPR theory (Subsection 4.4). From the central carbon, there are four groups of electrons from the four single bonds, with no additional groups from lone pair electrons. The arrangement of four groups of electrons that spaces them farthest apart is tetrahedral. To go from the arrangement of electron groups to the arrangement of atoms, we ignore any lone pair electrons. Since carbon has no lone pair electrons, the molecular shape of the molecule is the same as the shape of its electron groups. That is, methane is a tetrahedral molecule. This arrangement can be depicted several ways. In the perspective drawing shown in **Figure 5.3B**, you can see that the central carbon sits atop three bonds to hydrogens that form the legs of a tripod, where one hydrogen is in the plane of the page (solid line), one hydrogen is pointed out in front of the plane of the page (dark triangle), and one hydrogen is pointed behind the plane of the page (dotted line). The fourth bond to hydrogen is above the carbon and is in the plane of the page (solid line). This geometry can be hard to visualize, and the ball-and-stick depiction in **Figure 5.3C** gives a clearer sense of the arrangement, with the black ball in the center being carbon (carbon is frequently depicted as either gray or black), and the hydrogens as the smaller white balls (hydrogen is often depicted in white in such models).

Water has a molecular dipole. Does methane? A first requirement for a molecular dipole is that the molecule have at least one bond dipole. What can we say about the polarity of the C-H bond? Recall that polar bonds are those in which the electrons are shared unevenly due to a large difference in electronegativities between the atoms involved in the bond. In a polar O-H bond, oxygen is much more electronegative than hydrogen. Carbon is a much less electronegative atom than oxygen, so we would not expect a C-H bond to be as polar as an O-H bond. In fact, while carbon is more electronegative than hydrogen, the difference is not sufficient for the bond to be considered polar, making C-H bonds non-polar. With no polar bonds, methane cannot have a molecular dipole (Incidentally, its symmetry would have prevented it from being a dipole anyhow: four equivalent bonds in a tetrahedral arrangement cannot have a positive and negative end).

As a non-polar compound, methane would not be very soluble in a polar solvent like water (like dissolves like). The non-polar nature of methane also explains why it exists as a gas at room temperature. Methane has about the same molecular weight as water. However, water is a very polar molecule capable of forming hydrogen bonds, which allow it to remain a liquid at room temperature. Methane cannot form such strong interactions. This difference in interaction strengths is reflected in the difference in boiling points between the two compounds as seen in **Table 5.1**. Note, as we will see in Chapter 8 of Volume II, non-polar molecules, like methane, do have a type of interaction they can form. However, on a per atom basis, this interaction is much weaker than a hydrogen bond.

Compound	Boiling Point	Phase
Water	100° C	Liquid
Methane	-162° C	Gas
Ethane	-89° C	Gas
Methanol	65° C	Liquid
Ammonia	-33° C	Gas

Table 5.1 Physical Properties of Various Compounds. The boiling points and phase are reported for a standard atmospheric pressure of one atmosphere. Phase information is for room temperature (20-25 °C).

Water has a boiling point of 100 ˚C (under standard pressure), meaning that the temperature has to be above 100 ˚C for water to be in the gas phase. Since room temperature (typically 20-25 ˚C) is below water's boiling point, water is a liquid at room temperature. Methane has a boiling point of -162 ˚C (under standard pressure). This means the temperature needs to be below -162 ˚C for it to be a liquid, and therefore methane is a gas at room temperature.

Methane is important in a number of different contexts. It is the major component of natural gas (about 85% by volume, on average), which generates a large amount of energy when burned and is relatively easy to obtain and transport. Natural gas has a number of uses, including cooking for gas stoves (**Figure 5.4A**), heating homes in gas furnaces and water heaters, and generating electricity at gas-fired power plants (estimated currently to provide almost a quarter of the world's electricity).

Methane is also a greenhouse gas. Greenhouse gases are compounds that, when present in the atmosphere, result in greater retention of heat energy within Earth's atmosphere (**Figure 5.4B**). If enough of this energy is trapped, it can increase the average temperature of the planet. Greenhouse gases such as carbon dioxide are more plentiful in the atmosphere and better known — and will be discussed later in the chapter. However, levels of atmospheric methane are also a serious concern, because methane is roughly 30 times as potent as carbon dioxide in trapping heat in the atmosphere.

There are many potential sources of methane. Most supplies of natural gas (as well as other fossil fuels, such as petroleum and coal) originate from carbon-based organic matter that was present on the earth hundreds of millions of years ago. Before the organic matter decayed, it became buried. Over time, heat and pressure converted this material to fossil fuels, which humanity learned to recover as a rich source of energy and of raw materials for organic compounds. Methane is also being continuously generated by the action of microbes. Bogs and swamps are environments conducive to oxygen-free digestion and fermentation of plant and animal matter to make methane. Additionally, microbes in the guts of ruminants, such as cows (**Figure 5.4C**), are a source of methane that is present in their burps (and a little in their flatulence). In the US, about 2% of atmospheric methane is due to cows, with about 4% due to all ruminants. Worldwide, up to 20% of atmospheric methane comes from livestock.

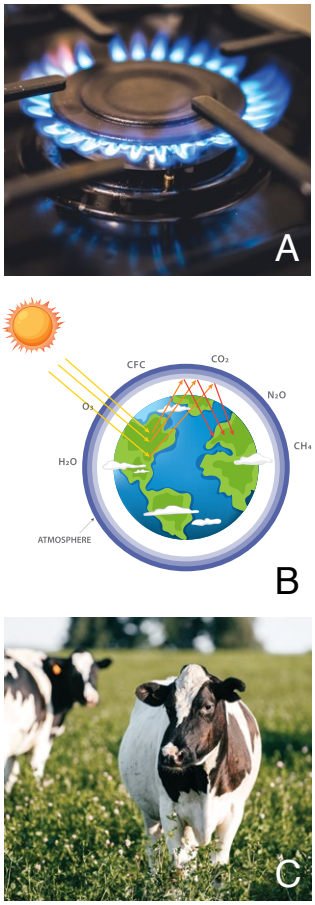


Figure 5.4 Significance and Sources of Methane. A) Methane is the main component of natural gas, which can be burned for various purposes, including cooking. B) Methane is also a greenhouse gas that can trap heat originally from the energy of sunlight. C) Besides fossil fuels, methane can be produced naturally by microbes, including those found in the guts of ruminants like cows.

5.2 Ethane

Ethane, C_2H_6, is a molecule that is slightly more complicated than methane, having two carbons and six hydrogens. How are these atoms attached and arranged (**Figure 5.5A**)? We know that carbons want to make four bonds. With six hydrogen, we can make three single bonds to hydrogens for each carbon. This leaves each carbon wanting one more bond. If we make a single bond between the two carbons, this gives all of the atoms a full valence. You'll notice that the two halves of the molecule resemble a methane molecule, in that they have a carbon with four bonds, though in this case only three of those are to hydrogen. We will call this arrangement of atoms a methyl group, so an ethane molecule can also be thought of as two methyl groups connected to one another.

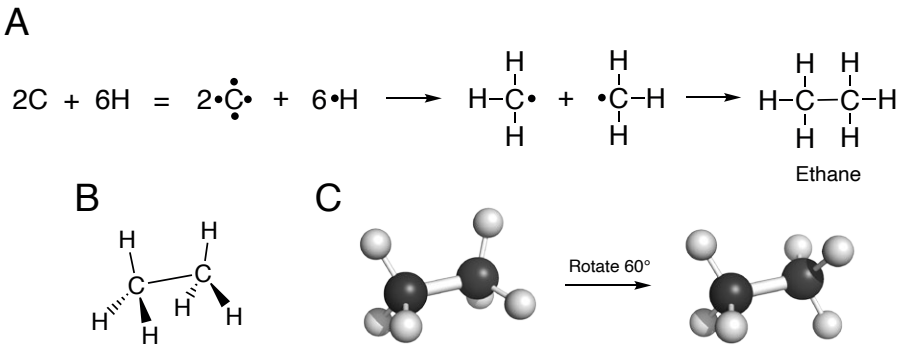


Figure 5.5 Structure of Ethane. A) In ethane, two carbons and six hydrogens are attached to each other so that each carbon has three single bonds to hydrogens and one single bond connecting the carbons. Half of an ethane molecule can be called a methyl group. It should be noted, the scheme shown is not meant to imply how ethane molecules form, but instead as a way to understand why the atoms in ethane are connected in the way they are. B) The three-dimensional structure of ethane shown in a perspective drawing, where each carbon has a tetrahedral geometry. C) A ball-and-stick representation of ethane showing that rotation around the carbon-carbon bond can generate a structure in which the methyl groups of ethane are in a different orientation.

What is the three-dimensional structure of ethane? Each carbon is tetrahedral, making ethane like two tripods (carbons with three C-H legs) that share a stem (the C-C single bond), as seen in **Figure 5.5B**. How are the two C-H tripods, i.e. the two methyl groups, oriented relative to one another? It turns out that atoms tend to be relatively free to rotate around a single bond, meaning that the methyl groups can swivel around their shared C-C bond and adopt many different orientations (**Figure 5.5C**). As we shall see in Chapter 8 of Volume II, some of these orientations are slightly more favorable than others. However, for now, we'll just assume that there is free rotation around the carbon-carbon bond, where the methyl groups are constantly spinning relative to one another to adopt slightly different structures.

Because ethane is structurally similar to methane, it shares many of the same properties. Ethane is a non-polar molecule: As we saw with methane, C-H bonds are considered non-polar, and carbon-carbon bonds share electrons equally, making them non-polar. Because ethane is non-polar and small, it does not stick to itself strongly, making it a gas at room temperature and standard pressure (Table 5.1), like methane. Ethane's boiling point, -89 °C, is higher than methane's, but we won't explore why until Chapter 8 of Volume II. Ethane is a less abundant component of natural gas (2-5% by volume) and is present in, or generated from, fossil fuels.

5.3 Methanol and Ethanol

If we add an oxygen atom to carbons and hydrogens, one of the compounds we can generate is called an alcohol. The simplest alcohol is known as methanol, with a molecular formula of CH_4O.

To understand the arrangement of atoms in methanol, we could do what we've done for methane and ethane and consider the valence requirements of each atom and determine what bonds will fulfill those requirements. However, let's consider another approach. To this point we've seen a number of atoms or groups of atoms that form single bonds. The first are hydrogen atoms, such as those in water and in methane (**Figure 5.6A**). The second is the methyl group in ethane (**Figure 5.6B**). The third is the -OH group in water, which we will call a hydroxyl group (**Figure 5.6C**). As a way to imagine possible new compounds, we could imagine swapping out one group that forms a single bond for another. Although not all such molecules are stable, this approach gives us a useful tool for imagining new compounds. For example, if we had methane and swapped a single bond to a hydrogen for a single bond to a methyl group, we end up with the compound ethane.

What happens if we swap the single bond to a hydrogen in methane for a single bond to a hydroxyl group? Or equivalently, if we start with a water molecule and swapped a

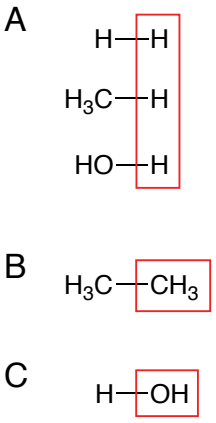


Figure 5.6 Groups That are Attached to a Molecule via a Single Bond. A) A hydrogen in diatomic hydrogen, methane, and water. B) A methyl group in ethane. C) A hydroxyl group in water.

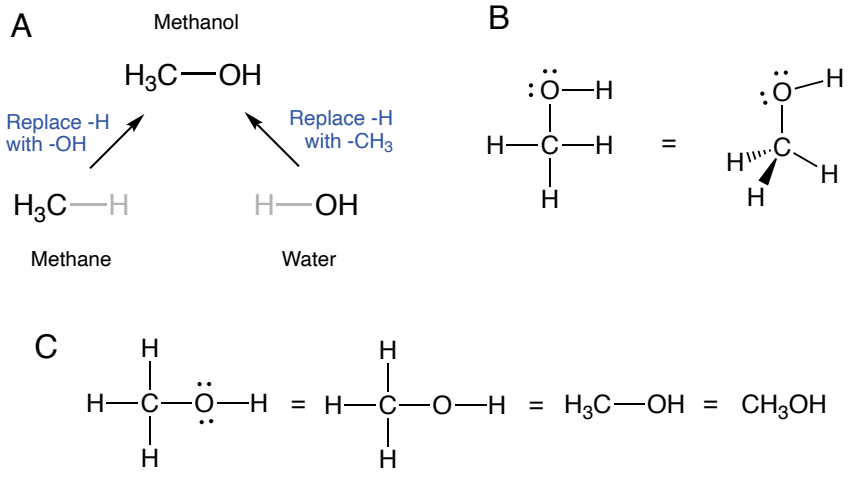


Figure 5.7 Structure of Methanol. A) Methanol, with a molecular formula of CH_4O, can be thought of as coming from: a methane where one of its hydrogens has been replaced by a hydroxyl group; or from water, where one of its hydrogens has been replaced by a methyl group. B) VSEPR theory predicts that the atoms around the carbon of methanol are arranged tetrahedrally, while the arrangement of groups around the oxygen has a bent geometry. C) Different ways of depicting the structure of methanol.

single bond to hydrogen with a methyl group. In both cases (**Figure 5.7A**), we generate the compound methanol, with the molecular formula of CH_4O. Does this compound fulfill our requirements for each atom? Hydrogen wants to form a single bond with no lone pair electrons left over. The four hydrogens in methanol are each attached to an atom via a single bond, with three hydrogens on the carbon, and one hydrogen on the oxygen. Carbon wants to form four bonds with no lone pairs left over. In methanol, the carbon forms three single bonds to hydrogen, and one single bond to oxygen. Finally, oxygen wants to form two bonds with two lone pairs of electrons left over. In methanol, oxygen makes a single bond to a carbon and a hydrogen, and has two lone pairs of electrons on its oxygen.

Using VSEPR theory, we can say something about the three-dimensional arrangement of the atoms in methanol (**Figure 5.7B**). The four single bonds around the carbon of methanol cause those atoms to be arranged around the carbon in a tetrahedral geometry. For the two bonds and two sets of lone pair electrons around oxygen, the arrangement of atoms around the oxygen is bent.

The structure of methanol, as well as most organic molecules, can be depicted in many different ways (**Figure 5.7C**). Lone pair electrons on methanol's oxygen can be shown (first structure from the left) or implied (second structure). Just the C-O bond can be shown (third structure), emphasizing the methyl and hydroxyl groups of the molecule. The molecule can be shown without any bonds (fourth structure). In this case, the methyl and hydroxyl groups are still shown separately. However, by convention, the methyl group in such a structure is written with the carbon preceding the hydrogens. These structures all refer to the same molecule and can be useful in different contexts depending on what aspect of the molecule is being emphasized and to what extent you want to present a simplified structure.

Compounds having a hydroxyl group attached to a carbon that is only attached to other carbons or hydrogen are known as alcohols, so methanol is a type of alcohol. Methanol's name reflects this combination: methan-, related to the methyl group, and -ol for the alcohol hydroxyl group. These groups are also apparent in another common name for methanol: methyl alcohol. Methanol was originally isolated from the destructive distillation of wood, giving it the common names wood alcohol and wood spirits.

Methanol's dual character — a polar hydroxyl group from water, a non-polar methyl group from methane — has direct practical implications for its properties.

Because methanol has a polar hydroxyl group and a non-polar methyl group, its overall polarity is somewhere between water and methane. This polarity and the ability of methanol's hydroxyl group to form hydrogen bonds allow it to stick to itself strongly, making methanol a liquid at room temperature (**Figure 5.8**). However, because one of the hydrogens of water has been replaced by a methyl group that does not form hydrogen bonds, there are fewer interactions between methanol molecules. This contributes to methanol having a boiling point (65 °C) lower than water (100 °C), though methanol's boiling point is significantly higher than methane's (-162 °C).



Figure 5.8 Methanol is a liquid. Shown is a bottle of commercially available methanol. Methanol is a liquid at room temperature because methanol molecules hydrogen bond to other methanol molecules via hydroxyl groups.

The dual polarity of methanol also affects methanol's solubility in water and its ability to act as a solvent. Because water can form hydrogen bonds with the hydroxyl group of methanol, methanol is highly soluble in water even though it has a non-polar methyl group. Methanol also turns out to be a relatively good solvent for a wide range of compounds. The polar hydroxyl group allows methanol to dissolve polar compounds, and to some degree salts (though less effectively than water), while the non-polar methyl group allows methanol to dissolve some non-polar compounds.

A different alcohol can be generated if one of the hydrogens of ethane is replaced by a hydroxyl group (**Figure 5.9A**). This makes the compound ethanol, sometimes also called

ethyl alcohol. Ethanol's polar hydroxyl group allows it to form hydrogen bonds with other ethanol molecules, making ethanol a liquid (**Figure 5.9B**). The hydroxyl group of ethanol can also form hydrogen bonds, making it soluble in water. You are likely familiar with ethanol as an important component of a number of drinks, collectively called alcoholic beverages: wines, beers, and liquors (**Figure 5.9C**). In fact, the liquor vodka is largely just ethanol (around 40% by volume) in water, with trace impurities and flavorings.



Figure 5.9 The Structure and Properties of Ethanol. A) The alcohol ethanol conceptually comes from an ethane molecule in which a hydrogen is replaced by a hydroxyl group. B) Ethanol is a liquid because of interactions of its hydroxyl group. It is a good solvent for both polar and non-polar substances, due to its hydroxyl and ethyl groups, respectively, and ethanol is a component of some "rubbing" alcohols, though isopropyl alcohol is more common. C) Ethanol is a component of wines, beers, and liquors.

5.4 Ammonia, Methylamine, and Ethylamine

Let's look at some compounds that contain nitrogen. As an element, nitrogen has five valence electrons, needing three more to achieve a full valence (**Figure 5.10**). It can do so by making three covalent bonds, leaving one group of lone pair electrons.

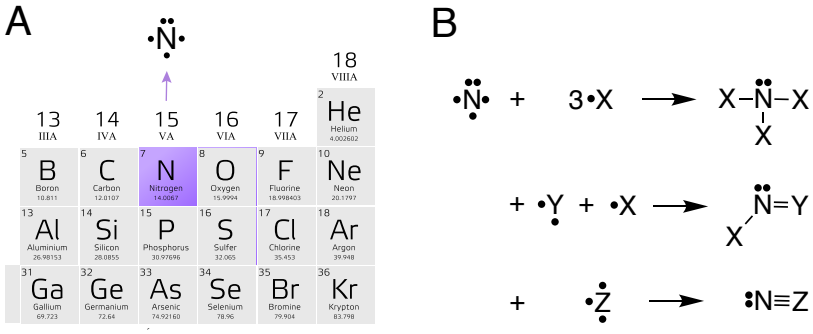


Figure 5.10 Properties of Nitrogen. A) Nitrogen, found between carbon and oxygen in the periodic table, has five valence electrons and needs three more to achieve a full valence. It can do so by making three covalent bonds, with a lone pair of electrons left over. B) Several theoretical ways nitrogen could make three covalent bonds.

Ammonia, a simple compound with one nitrogen and three hydrogens, NH_3, can satisfy the valence requirements for both the nitrogen and hydrogens by having the nitrogen make three single bonds to each hydrogen (**Figure 5.11A**). The three dimensional structure of ammonia is trigonal pyramidal (**Figure 5.11B**). Here, the three bonds to hydrogens and the lone pair of electrons are arranged tetrahedrally around nitrogen. When only atoms are included, they make a tripod-like shape without a stem.

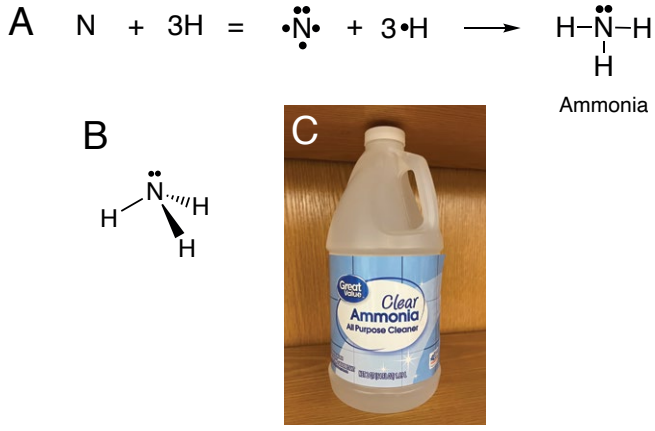


Figure 5.11 Structure and Properties of Ammonia. A) Ammonia is a molecule in which a central nitrogen is connected to three hydrogens by single bonds. B) Ammonia adopts a trigonal pyramidal geometry, where the lone pair of electrons on ammonia's nitrogen sit atop the apex of the pyramid. C) Pure ammonia is a gas at room temperature but is readily dissolved in water to serve as a common household cleaner.

Nitrogen is between carbon and oxygen on the periodic table (Figure 5.10A), making it more electronegative than carbon, but less so than oxygen. Nitrogen's electronegativity is sufficient to make an N-H bond polar covalent, but it is less polarized than an O-H bond. Consequently, the hydrogens of ammonia can form hydrogen bonds with the lone pair electrons on nitrogen in other ammonia molecules, but the interaction is weaker. A relatively weak interaction, coupled with fewer total hydrogen bonds, means pure ammonia tends to exist as a gas at room temperature, with a boiling point of -33 °C (Table 5.1). Ammonia can also form hydrogen bonds with water, making aqueous solutions of ammonia possible. You are probably familiar with ammonia in this form as a household cleaning product (**Figure 5.11C**), which is typically a 4-7% solution of ammonia in water.

As we saw previously, we can replace one of the hydrogens in methane or ethane with a hydroxyl group and generate the alcohols methanol and ethanol, respectively. A similar substitution can be done using a fragment of ammonia — an amino group — in place of the hydrogen. This generates compounds that are known as amines (**Figure 5.12**). When one of the hydrogens of methane is replaced with an amino group, it makes the amine compound methylamine. Similarly, substituting one of the hydrogens of ethane with an amino group makes the amine ethylamine. Like ammonia, both of these amines are gases at room temperature and standard pressure, and both compounds are soluble in water.

Before we go on to describe other compounds, it is worth summarizing what we've learned about the most common organic atoms (**Table 5.2**). For a neutral atom in a compound, hydrogen forms 1 covalent bond with no lone pairs of electrons left over; carbon forms 4 bonds with no lone pairs of electrons left over; oxygen forms 2 bonds with 2 lone pairs of electrons left over; and nitrogen forms 3 bonds with 1 lone pair of electrons left over.

Atom	# Bonds	# Lone Pairs
H	1	0
C	4	0
O	2	2
N	3	1

Table 5.2 Bonds and Lone Pairs of Organic Atoms.

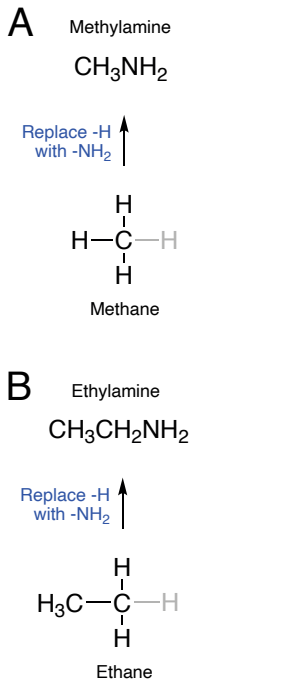


Figure 5.12 Methylamine and Ethylamine. A) Methylamine can be thought of as a methane molecule in which a hydrogen has been replaced by an amino group. B) Similarly, ethylamine can be thought of as an ethane molecule in which a hydrogen has been replaced by an amino group.

B. Some Covalent Compounds with Double Bonds

Carbon makes four bonds to fill its valence, but not all of these bonds need to be single bonds. In this subsection, we look at a number of compounds in which carbon makes a double bond to another carbon or to an oxygen.

5.5 Ethene

Consider the covalent compound ethene, C_2H_4. How are the atoms in this molecule connected? Like ethane, ethene is composed of only carbons and hydrogens, and it has two carbons. However, ethene has two fewer hydrogens than ethane (four versus six). Suppose we started with the compound ethane, and removed two hydrogens, i.e., broke two of ethane's C-H bonds (**Figure 5.13A**). In the resulting compound, each carbon would only have three bonds and contain an unpaired electron — a situation that doesn't give carbons a full valence. A simple fix would be to make a new bond with the unpaired electrons. This gives each carbon four bonds (a full valence) and two covalent bonds between the carbons. So, whereas ethane is a compound with a carbon-carbon single bond, ethene is one with a carbon-carbon double bond.

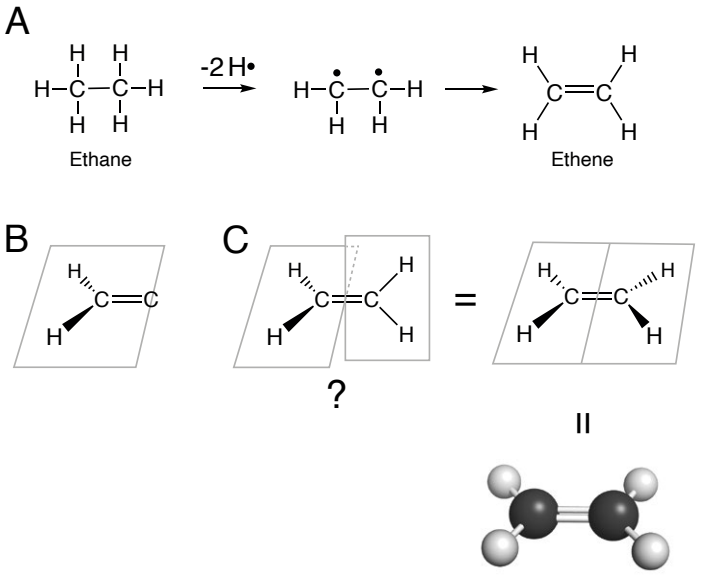


Figure 5.13 Structure of Ethene. A) Ethene, C_2H_4, can be theoretically generated from ethane, C_2H_6, via the removal of two hydrogens and formation of a double bond. B) Orientation of atoms around a carbon in ethene is trigonal planar: i.e., in the same plane separated by 120°. C) All of the atoms in ethene reside in the same plane.

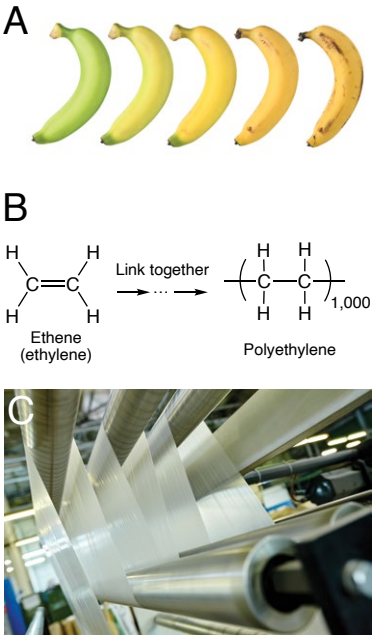


Figure 5.14 Uses of Ethene, Also Known as Ethylene. A) Some plant tissues produce ethylene, a gaseous plant hormone that facilitates ripening in fruits such as bananas. B) The common plastic polyethylene can be made from many individual ethene units covalently linked together into a polymer chain that can be millions of carbons long. Polyethylene polymers can vary in length, degree of branching, and cross-linking between chains, all of which give the plastic different properties. Shown is a simple linear polyethylene polymer made from 1,000 ethene molecules. C) Polyethylene film being made for packaging.

What is the three dimensional structure of ethene? From VSEPR theory, the arrangement of three groups of electrons around each carbon (two single bonds to hydrogens, a double bond to the other carbon) is trigonal planar. This means the three atoms surrounding a carbon are in the same plane and spaced apart by 120° (**Figure 5.13B**). What is the relative orientation of the two planes surrounding each carbon (**Figure 5.13C**)? Recall that for ethane, there is relatively free rotation around its C-C single bond, meaning that many different orientations of atoms are possible. That is not true for the C-C double bond in ethene. Why not? Suppose two atoms were styrofoam balls, and each bond between them were a wooden dowel. For a single bond in a molecule like ethane, it would be easy to rotate the atoms around the wooden dowel, allowing the methyl groups to adopt any orientation. In contrast, for a double bond in a molecule of ethene, the two dowels prevent free rotation. Obviously, atoms are not styrofoam balls, nor bonds wooden dowels. Still, the same principle applies to real double bonds: rotation around a C-C double bond is restricted (a more rigorous treatment of this idea is discussed in the Further Exploration Section on bonding in Subsection 5.18). Thus, the two planes of the atoms at each end of ethene are in a fixed orientation relative to one another. But what orientation? It turns out that all of the atoms in ethene are in the same plane, making ethene a flat molecule. (The reasons for this are complicated, but also addressed in Subsection 5.18).

Ethene often goes by the common name ethylene and is encountered in several different contexts. Ethylene is a plant hormone that facilitates ripening of some fruits, like bananas (**Figure 5.14A**). Being a compound with only non-polar C-H and C-C bonds, ethene, like ethane, is very non-polar and exists as a gas at room temperature. This fact can be exploited to speed up ripening. When bananas are stored in a bag, ethylene gas builds up and causes them to ripen faster than they would otherwise. Ethylene is also a precursor chemical for making various forms of polyethylene, some of the most commonly used plastics in the world (**Figure 5.14B** and **C**). In these compounds, ethene units are covalently linked together, with or without branches and crosslinking. This makes a long chain of repeating units known as a polymer.

5.6 Formaldehyde and Acetone

Carbons can make double bonds with other atoms, such as oxygen. The simplest of such compounds is formaldehyde, CH_2O (**Figure 5.15A**). How are the atoms in formaldehyde connected? Just as we can take two hydrogens from the C-C bond of ethane to make ethene, if we take one hydrogen from the carbon and one from the oxygen (i.e., the hydroxyl

hydrogen) in methanol, the single bond becomes a double bond, yielding formaldehyde (**Figure 5.15B**). Formaldehyde is a polar compound, because of the molecule's polar C-O bond, as well as for reasons we'll discuss in Volume II, Chapter 9. Formaldehyde is a gas under standard conditions, but dissolves in water. Aqueous solutions of formaldehyde are used as preservatives, and you may have seen organs or organisms preserved in formaldehyde in classrooms or museums (**Figure 5.15C**).

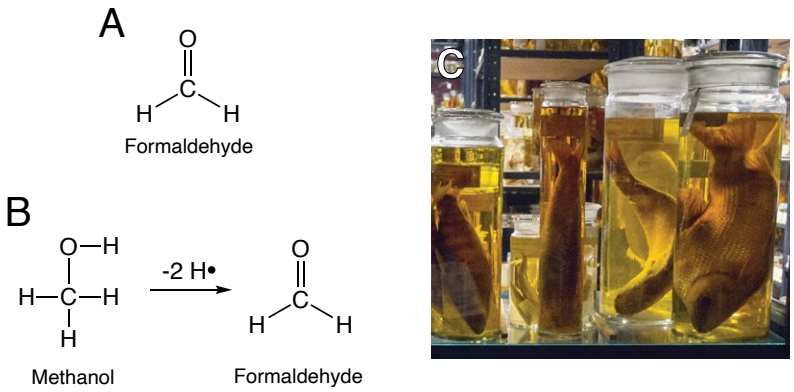


Figure 5.15 Structure and Uses of Formaldehyde. A) Structural formula of formaldehyde. B) You can imagine formaldehyde being generated from methanol by removing two hydrogens. C) Fish preserved in an aqueous formaldehyde solution.

Formaldehyde has two carbon-hydrogen single bonds, and the bond to the hydrogens can be swapped with other groups to make new compounds containing a carbon-oxygen double bond. If both hydrogens are replaced by methyl groups, we get the compound acetone (**Figure 5.16A**). Acetone is a liquid that is a good solvent for both polar and non-polar compounds, because the molecule has both polar and non-polar character. Acetone is one of the main (and sometimes only) components of nail polish remover (**Figure 5.16B**). Acetone is also one of the three ketone bodies produced by the body from fats during starvation or carbohydrate restriction, though it is present in smaller amounts than the other two.

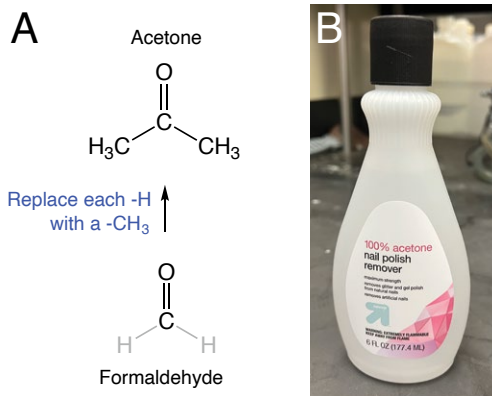


Figure 5.16 Structure and Uses of Acetone. A) Structural formula of acetone. Acetone can be thought of as being related to formaldehyde if both hydrogens in formaldehyde are replaced by methyl groups. B) Acetone is commonly found in nail polish removers and is a good solvent of polar and non-polar compounds.

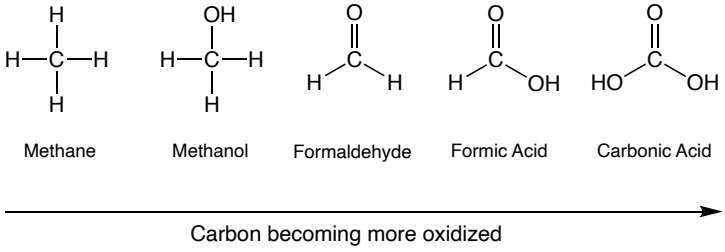


Figure 5.17 Oxidized Forms of Carbon. With more bonds to oxygens, a carbon is more oxidized. The increase in carbon oxidation formally reflects a change in its oxidation number (-4 for methane; -2 for methanol; 0 for formaldehyde; +2 for formic acid; and +4 for carbonic acid - An explanation of oxidation number is found in a Further Exploration Section of Chapter 12 of Volume II). While changes in oxidation number do not have to involve bonding to oxygen, in this case they do.

A side note on some terminology. When an atom, like carbon, gains more bonds to oxygens, it is considered more oxidized (**Figure 5.17**). Thus the carbon in methanol (1 single bond to oxygen) is more oxidized than methane (0 bonds to oxygen), while the

central carbon of formaldehyde is more oxidized (1 double bond to oxygen) than methanol. (It's worth pointing out that how "oxidized" an atom is isn't limited to how many oxygens it's bonded to, and instead depends on the atom's oxidation state or number. If you are interested in learning more, consult the Further Exploration section on Redox Chemistry in Chapter 12 of Volume II). Let's consider some compounds that have a carbon even more oxidized than formaldehyde or acetone.

5.7 Acetic, Carbonic, Sulfuric, and Phosphoric Acids

From formaldehyde, if instead of replacing both hydrogens with methyl groups, we replaced one hydrogen with a methyl group, and one with a hydroxyl group, we get the compound called acetic acid (**Figure 5.18A**). Acetic acid is highly oxidized (3 total bonds to oxygens) and is a liquid that is very polar and dissolves well in water. Acetic acid is the main ingredient of most vinegars, after water. Indeed, white vinegar is just acetic acid diluted in water: 4-7 % acetic acid by volume with 93-96% water (**Figure 5.18B**).

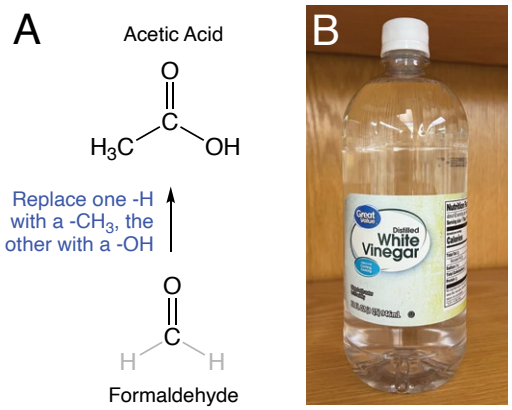


Figure 5.18 Structure and Uses of Acetic Acid. A) Structural formula of acetic acid. Acetic acid is related to formaldehyde if one of the hydrogens in formaldehyde is replaced by a methyl group and the other by a hydroxyl group. B) Acetic acid is commonly found in vinegars, such as white vinegar.

It is possible to derive even more oxidized compounds from formaldehyde. If both hydrogens in formaldehyde were replaced by hydroxyl groups, we generate the compound carbonic acid (**Figure 5.19A**). Carbonic acid is an important compound in our body and will be discussed more in the next chapter. The carbon in carbonic acid is highly oxidized (4 total bonds to oxygens), but other atoms can also exist in highly oxidized forms.

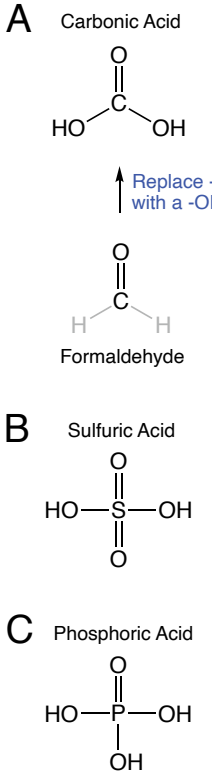


Figure 5.19 Structure of Various Highly Oxidized Acids. A) Structural formula of carbonic acid. Carbonic acid can be thought of being related to formaldehyde if both hydrogens are replaced by hydroxyl groups. Structural formulas of B) Sulfuric acid, and C) Phosphoric acid.

Sulfuric and phosphoric acid both resemble carbonic acid, in that a central atom is attached to multiple oxygen atoms in single and double bonds (**Figure 5.19B** and **C**). Sulfuric acid has two sulfur-oxygen double bonds and two hydroxyl groups off of its central sulfur. Phosphoric acid has one phosphorus-oxygen double bond, and three hydroxyl groups off of its central phosphorus. It's worth pointing out that the central sulfur and phosphorus atoms in these compounds do not appear to adhere to our rules that atoms want a full valence, seemingly having too many electrons from all of their bonds. There are reasons these atoms might be able to have more electrons, as well as reasons to consider whether the structures drawn accurately depict the number of bonds around the central atom. However, both of these ideas are beyond the scope of what we've covered so far.

At this point we have learned a number of simple covalent compounds: water, methane, ethane, methanol, ethanol, ammonia, methylamine, ethylamine, ethene, formaldehyde, acetone, acetic acid, carbonic acid, phosphoric acid, and sulfuric acid. Knowing the structure of these compounds will be useful going forward, so it is recommended you commit them to memory.

C. Molecular Ions

In Chapter 3, we saw that single atoms can be charged — species like sodium cations

and chloride anions. The covalent compounds we have discussed so far are not. Can covalent compounds be charged, and if so, what is the nature of such molecular ions?

5.8 Protons and Covalent Compounds

Single atom ions are usually generated by losing or gaining negatively charged electrons (**Figure 5.20A**). For example, when atoms in a sodium metal lose an electron, they are converted to sodium cations. When chlorine atoms gain an electron (or diatomic chlorine molecules gain two electrons), chloride anions are produced. While covalent molecules can directly lose or gain electrons, a more common way to change their charge is to lose or gain a hydrogen cation. That is, they lose or gain a proton (**Figure 5.20B**). When a neutral covalent compound loses a proton, its overall charge decreases and it becomes an anionic molecule. In contrast, when a neutral covalent compound gains a proton, the positive charge of the proton increases the charge of the molecule, making it a cationic molecule.

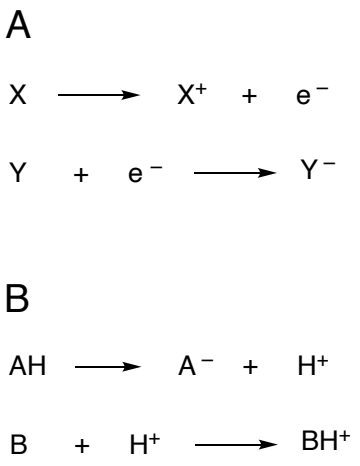


Figure 5.20 Potential Ways for a Molecule to Become Charged. A) Lose or gain an electron. B) Lose or gain a proton.

Proton loss or gain is easiest to understand with some examples. If an acetic acid molecule loses a proton from its hydroxyl group, it goes from a neutral molecule to a negatively charged one: the molecular ion acetate (**Figure 5.21A**). If an ammonia molecule gains a proton on the lone pair of its nitrogen, it goes from being a neutral molecule to a positively charged one: an ammonium ion (**Figure 5.21B**).

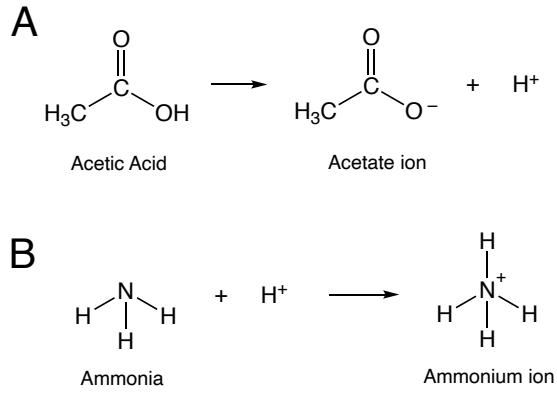


Figure 5.21 Examples of Covalent Compounds Becoming Ions. A) Acetic acid loses a proton to become a negatively charged acetate. B) Ammonia gains a proton to become a positively charged ammonium ion.

5.9 Acids and Molecular Anions

Not every covalent compound can readily gain or lose a proton. Which can and why? Let's start with those that can lose protons. Molecules that do so are known as acids (**Figure 5.22A**). Minimally, an acid requires a hydrogen that can be lost, and we've seen the structure of several acids: acetic acid (**Figure 5.22B**), carbonic acid, phosphoric acid, and sulfuric acid (Figure 5.19). Let's examine acetic acid.

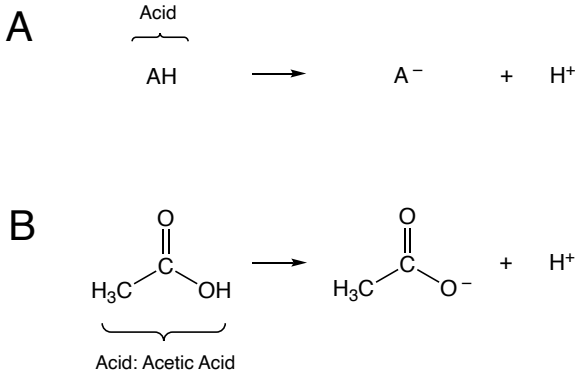


Figure 5.22 Acids are Molecules That Lose a Proton. A generic acid, HA, is shown in part A), while an example acid, acetic acid, is shown in part B).

Acetic acid has a hydroxyl group that contains a polar covalent bond between the

oxygen and hydrogen (**Figure 5.23A**, left of the arrow). The uneven sharing of electrons in this bond can be represented a number of different ways, such as showing its bond dipole or the partial charges on each atom. However, depicting the bond between the oxygen and hydrogen as a pair of electrons is most instructive (Figure 5.23A, bottom left). Here, the pair of electrons is shared, but shared unevenly. Oxygen, being more electronegative, pulls the electrons closer to itself, but has not "won" this tug of war. If oxygen is able to pull the electrons fully to itself (Figure 5.23A, right of the bottom arrow), it breaks the covalent bond, making itself an oxygen anion and the hydrogen a cation (the proton). This process resembles how a salt like sodium chloride dissociates into chloride and sodium ions (**Figure 5.23B**), and both processes occur most easily in water.

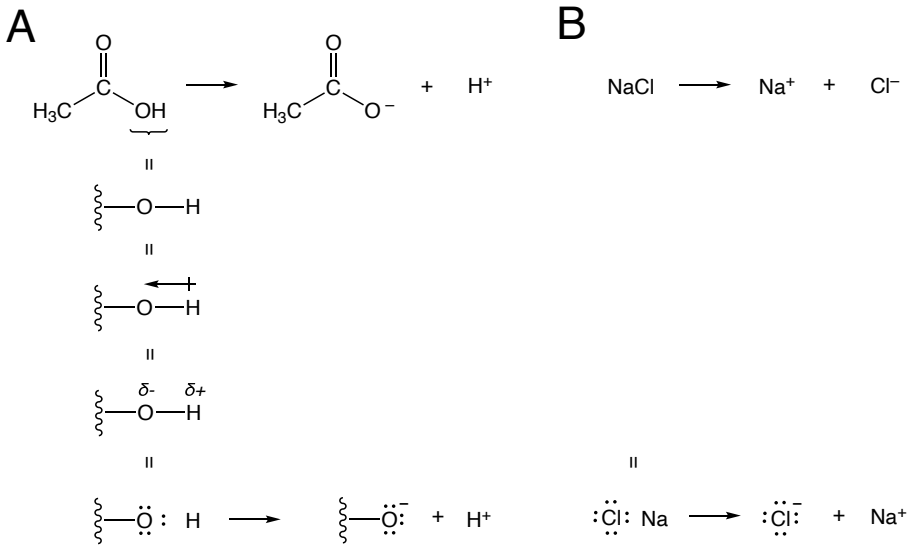


Figure 5.23 Dissociation of Neutral Molecules into Pairs of Oppositely Charged Particles. A) The polar covalent bond between the oxygen and hydrogen in acetic acid can be broken unevenly, such that the electrons in the bond go to the oxygen. This generates a negatively charged oxygen species and a positively charged proton. B) The ionic bond between a sodium and chloride ion in sodium chloride salt can be broken, generating a negatively charged chloride and a positively charged sodium ion.

Because oxygen is so much more electronegative than hydrogen, many OH-containing compounds readily lose a proton to become molecular anions (**Figure 5.24**). This loss of a proton is also called deprotonation. Besides the deprotonation of acetic acid's hydroxyl group to generate an acetate ion with a charge of -1 (Figure 5.24A), the two hydroxyl groups of carbonic acid can be deprotonated (Figure 5.24B). When the first proton is lost, the ion generated with a single negative charge is known as bicarbonate. When both protons are lost, this anion with a -2 charge is known as a carbonate ion. Sulfuric acid can lose two protons from its hydroxyl groups, generating a bisulfate ion (-1 charge) and a sulfate ion (-2 charge), respectively (Figure 5.24C). Up to three protons can be lost from the hydroxyl groups, generating phosphate ions with -1, -2, or -3 charges (Figure 5.24D). Even the OH in water can potentially lose a proton to form a hydroxide ion with a charge of -1 (Figure 5.24E).

While many biologically relevant acids lose protons from OH groups, there are acids with other electronegative atoms besides oxygen. Hydrogen chloride (HCl) is a covalent compound that when found in water (known then as hydrochloric acid), dissociates into a proton and a chloride anion (Figure 5.24F).

A couple of things to note about these anions: Chloride, bicarbonate, and phosphate ions are some of the most common small-molecule anions found in biological systems and serve as many (but not all) of the counter ions for cellular cations. Recall (Subsection 3.10) that when we considered only chloride in cells, there was a large discrepancy between the concentration of cations and chloride ions. The molecular ions of bicarbonate and phosphate provide some of those "missing" ions. Carbonate is an ion we've seen before. When it encounters Ca^{2+} ions found in hard water, the two form the major component of limescale (Subsection 3.13). Finally, how easily the molecular anions described can be formed by deprotonation of their acidic form

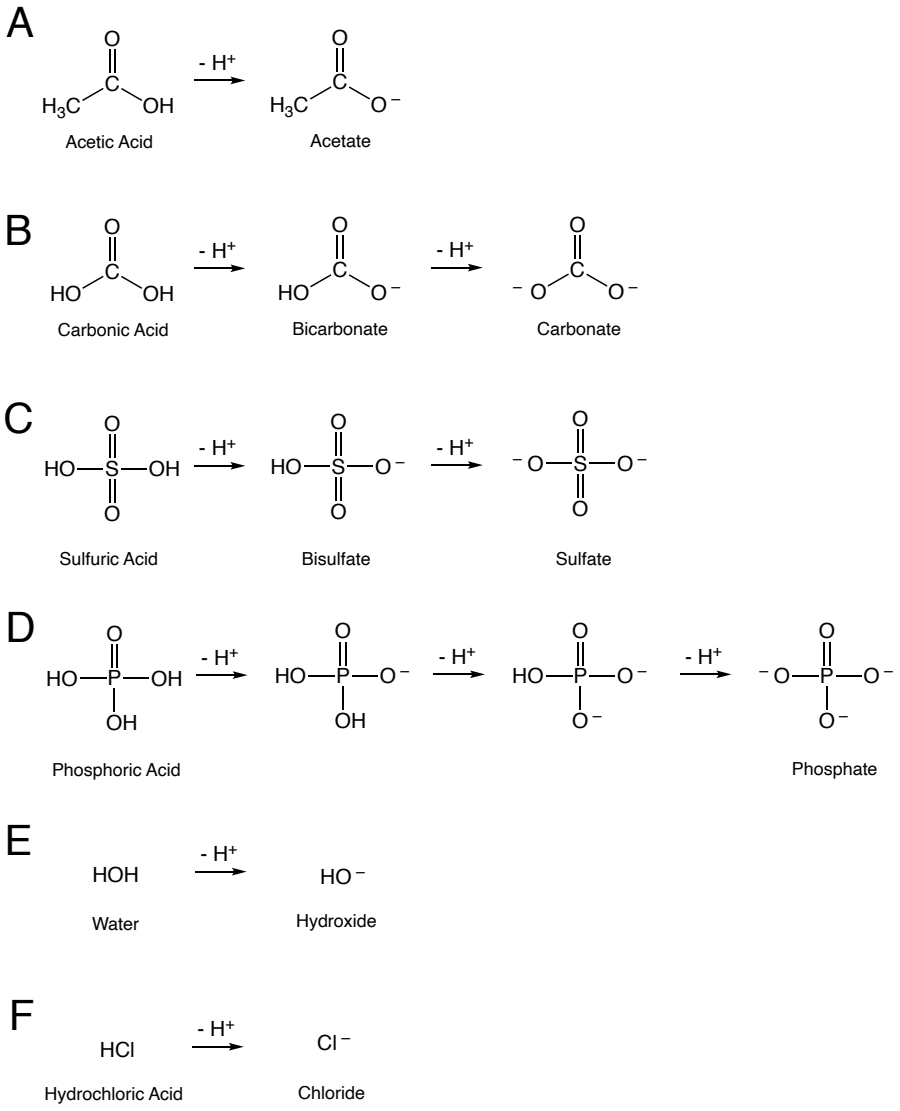


Figure 5.24 Various Acids Losing One or More Protons to Generate Anions. A) Deprotonation of acetic acid generates an acetate ion. B) Carbonic acid can lose up to two protons. Loss of the first proton generates the ion known as bicarbonate. Loss of the second proton generates a carbonate ion. C) Sulfuric acid can lose up to two protons, with the singly deprotonated anion known as a bisulfate ion and the fully deprotonated anion known as a sulfate ion. D) Phosphoric acid can lose up to three protons, with the fully deprotonated anion known as a phosphate ion. E) Water can lose a proton to become a hydroxide ion. F) Deprotonation of hydrochloric acid generates a chloride ion.

varies, with some being easy to form in water and some being difficult. A more complete discussion of this will be addressed in the next chapter.

5.10 Bases and Molecular Cations

What kind of compounds pick up a proton to become a cation and why? Compounds that have atoms with lone pair electrons (like nitrogen and oxygen) can gain a proton and are known as bases (**Figure 5.25A**). For example, ammonia is a base that can gain a proton to make the cation known as an ammonium ion (**Figure 5.25B**). In this process, known as protonation, the hydrogen cation makes a covalent bond with the lone pair

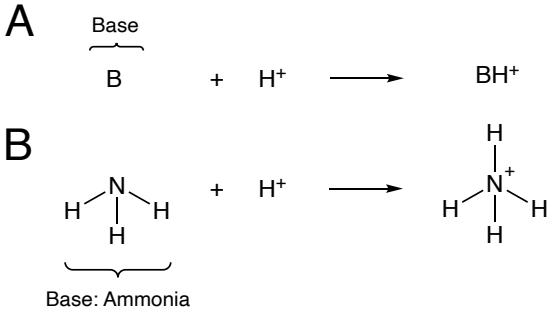


Figure 5.25 Bases are Molecules that Gain a Proton. A) A generic base, depicted as the molecule B. B) A specific example of a base, ammonia.

electrons of the nitrogen in ammonia. Note, in this situation, the shared electrons in the covalent bond both originate from one atom, as opposed to other covalent bonds we've previously looked at, in which one electron was provided by each atom. Nonetheless, as two electrons are shared between two atoms, this fulfills our criteria for a covalent bond.

Because there is a conservation of charge, the proton (+1) and the neutral ammonia become the +1 charged ammonium ion. This charge formally resides on the nitrogen in the ammonium cation. Why? When ammonia forms a covalent bond with a proton (**Figure 5.26A**), the lone pair of electrons that previously belonged exclusively to ammonia's nitrogen is now being shared. This formally reduces the nitrogen's number of negative electrons by one, making it +1. On the other hand, the hydrogen cation picks up an electron from the covalent bond, formally decreasing it from a +1 charge to 0. The formal charge an atom acquires upon protonation helps explain why ammonia is a better base than water, though both can act as bases. When water picks up a proton, the oxygen gains a formal +1 charge (**Figure 5.26B**). Oxygen is an extremely electronegative atom, so depleting its electrons to become positively charged is energetically costly. While it is still relatively costly for the nitrogen in ammonia to gain a +1 formal charge, because nitrogen is significantly less electronegative than oxygen, this ends up being less of an issue. In fact, under physiological conditions, nearly all of the ammonia in water is protonated to form ammonium ions.

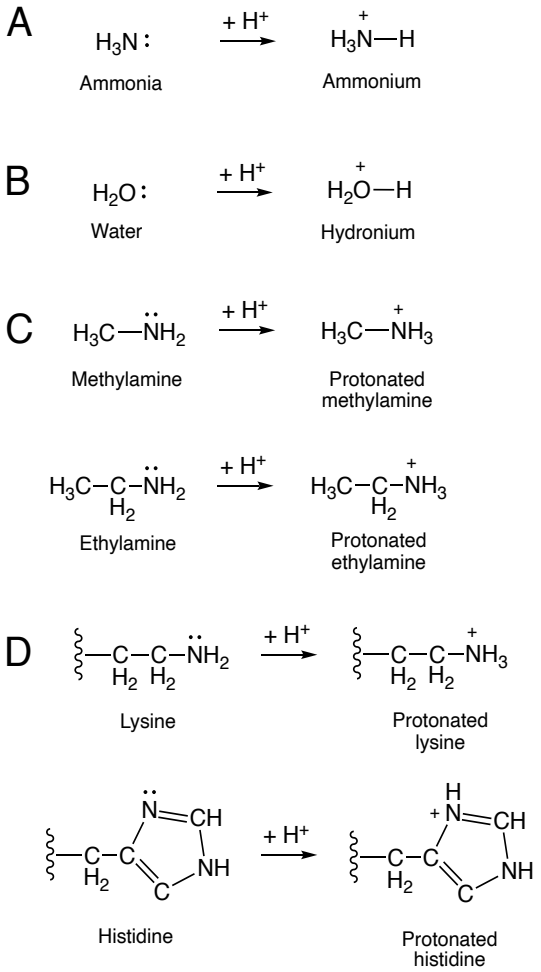


Figure 5.26 Various Bases Gaining a Proton to Generate a Cation. Protonation of A) ammonia, B) water, C) methylamine and ethylamine, and D) lysine and histidine. Lysine and histidine are two of several amino acids with basic side chains found in proteins. Lysine resembles an ethylamine with a longer carbon chain, while the structure of histidine is more complicated.

Like the nitrogen in ammonia, the nitrogen in amines like methylamine and ethylamine can be protonated, making them bases as well (**Figure 5.26C**). The protonated forms of these amines are called protonated methylamine and protonated ethylamine. Many biologically relevant bases have amines or amine-like groups (**Figure 5.26D**).

5.11 Salts and Molecular Ions

In Chapter 3, we saw that atomic ions with opposite charges, like sodium and chloride ions, can come together to form a salt. Molecular ions can do so as well. For example, an acetate anion can form a salt with a sodium or potassium ion, generating sodium acetate or potassium acetate, respectively (**Figure 5.27A**). Similarly, an ammonium ion

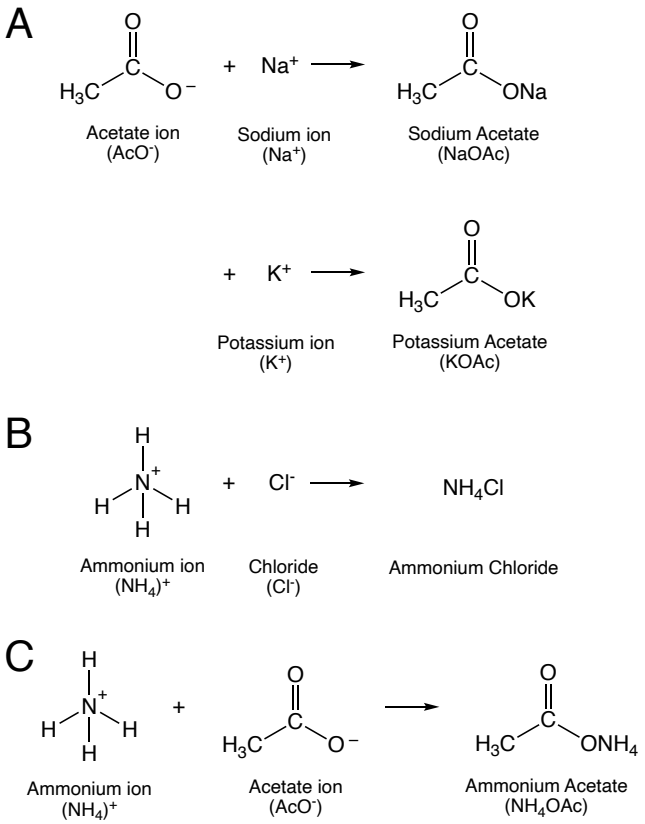


Figure 5.27 Salts of Molecular Ions. A) Acetate ion (abbreviated as $^{-}$OAc or AcO^{-}) can form a salt with cations such as sodium ions or potassium ions. B) Ammonium ion can form a salt with ions such as chloride ions. C) Acetate and ammonium ions can also form a salt. D) Crystals of ammonium chloride salt. This salt has white crystals, like many salts involving molecular ions, non-transition metal ion, and/or halides.

can associate with a chloride ion to make ammonium chloride salt (**Figure 5.27B**). It is even possible for both of the ions in a salt to be molecular ions: an acetate anion can be paired with an ammonium ion to get the salt, ammonium acetate (**Figure 5.27C**). Like sodium chloride, each of these particular salts is a white, crystalline solid (ammonium chloride is shown in **Figure 5.27D**). When put into water, each salt largely dissociates into its respective ions (reverse of the reactions shown in Figure 5.27A-C). That said, not all salts are equally soluble in water. Whether a salt dissolves fully, partially, or not at all depends on the ions it contains. More information about the atomic and molecular ions that can make up salts, as well as qualitative

and quantitative ways of describing their water solubility, can be found in Further Exploration Section F of this chapter.

D. Compounds in the Air

Most biologically relevant covalent compounds are solids or liquids. However, some gas molecules play important biological roles, including those found in the air that surrounds us and that we breathe. In this section we examine air and the compounds that compose it.

5.12 Air Properties and Composition

Air is a gas, meaning that its constituent molecules are rapidly moving particles with lots of space between them. These microscopic features give gases macroscopic properties that differ from solids and liquids — properties like low density, high compressibility, and rapid diffusion. These topics were discussed previously (Subsection 2.18 and Further Exploration Section F of Chapter 4); reviewing them will help you better understand air's physical properties.

Air is a homogeneous mixture of gas molecules (**Table 5.3**). Diatomic nitrogen constitutes the majority of air molecules (close to 4 of 5 molecules), while diatomic oxygen is the next most plentiful (around 1 in 5). The amount of water vapor in the air varies depending on the location and time, but it ends up being a relatively small fraction (less than 1 in 30). The rest of the gases in the air make up an even smaller fraction. Nonetheless, some of these less plentiful gases, like carbon dioxide, have an important impact on living and non-living things. Let's look at some of these molecules in greater depth.

Molecule	Percent
Diatomic nitrogen	78%
Diatomic oxygen	21%
Carbon dioxide	0.04%
Water vapor	0 - 3%
Others	< 1%

Table 5.3 Composition of Air. Percentages for N_2, O_2, and CO_2 are given for dry air; water vapor content varies by location and conditions.

5.13 Diatomic Oxygen

Molecular oxygen is the second most abundant molecule in the air, constituting roughly 21% of its molecules. As we discussed last chapter (Subsection 4.2), molecular oxygen, O_2, is a linear diatomic molecule with a non-polar covalent double bond between the oxygens (**Figure 5.28A**).

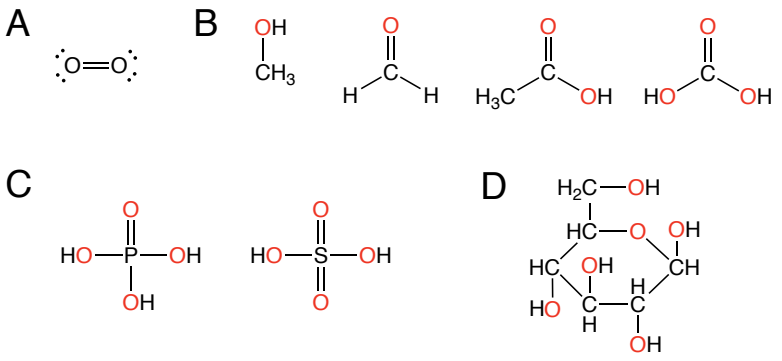


Figure 5.28 Molecular Oxygen and Oxygen-containing Compounds. A) Structure of diatomic oxygen. B) Carbon-containing and C) Non-carbon containing covalent compounds with one or more oxygen atoms. D) The biologically important sugar molecule glucose, containing many oxygen atoms.

Molecular oxygen is quite reactive. Although each oxygen formally achieves a full valence by sharing electrons equally in a double bond, oxygen is highly electronegative. If an oxygen atom can share its electrons with an atom less electronegative than itself, it is generally energetically beneficial to do so (there is actually more to the story of O_2 reactivity, which the Further Exploration Section will reveal). Because of this inherent reactivity, and facilitated by the large number of oxygen molecules in Earth's atmosphere, diatomic oxygen reacts with many atoms and molecules. That is, there are many atoms and molecules that are oxidized to form new compounds with oxygen bonds. Previously discussed carbon-containing examples include methanol, formaldehyde, acetic acid, carbonic acid (**Figure 5.28B**), and others. Oxygen also combines with non-carbon atoms, and we have seen highly oxidized forms of sulfur, in sulfuric acid, and phosphorus, in phosphoric acid (**Figure 5.28C**). Pretty much all of the biomolecules that we will be discussing in Volume III contain at least one oxygen, and some, like sugars (**Figure 5.28D**), contain many oxygens.

We can see oxygen's reactivity in action when we burn carbon-containing organic compounds, like methane, or more complex substances that contain many kinds of organic compounds, like wood (**Figure 5.29A**). This rapid reaction of organic compounds and oxygen to form carbon dioxide and water is an example of a combustion reaction (shown for methane combustion):

$$CH_4 + 2\,O_2 \rightarrow CO_2 + 2\,H_2O + \text{Energy} \qquad (5.1)$$

In this reaction, carbon dioxide and water are more stable than methane and molecular oxygen — that is, the products are lower in energy (Figure **5.29B**). Going from higher-energy to lower-energy molecules, this energy is released and is observable as light and heat. As we will see in later chapters, the reactivity of oxygen is also why we breathe molecular oxygen. This molecule allows us to "burn" the food we eat. How this happens is different from how a wooden log is burned, but overall, both processes produce energy that can be captured and used.



Figure 5.29 Combustion Reactions Involving Oxygen. A) Combustion of natural gas, which contains methane (top), and of wood, which consists of a wide range of carbon-containing compounds. B) Internal energy of methane and diatomic oxygen compared to carbon dioxide and water. The lower energy of the products means energy is released during the combustion process.

5.14 Diatomic Nitrogen

The most abundant molecule in air is molecular nitrogen, N_2, making up roughly 78% of its molecules. Nitrogen is an atom that forms three bonds with one lone pair of electrons left over, so two nitrogen atoms can achieve a filled valence by forming a triple bond to each other, making a linear diatomic molecule (**Figure 5.30A**).

Unlike molecular oxygen, molecular nitrogen is unreactive. For living organisms this presents an issue. Many biological molecules contain nitrogen atoms that have to come from somewhere. Air is an abundant source of nitrogen, but most living organisms cannot convert nitrogen gas into a form of nitrogen that can be used in biomolecules.

Some microorganisms, such as a group of bacteria known as rhizobia (**Figure 5.30B**), are able to "fix" molecular nitrogen, converting it into ammonia with a net input of electrons, protons, and energy:

$$N_2 + 8\,e^- + 8\,H^+ + \text{Energy} \rightarrow 2\,NH_3 + H_2 \qquad (5.2)$$

Legume plants, including beans, peas, soy, and clover, are able to form a symbiotic relationship with rhizobia. In these plants, the rhizobia reside in nodules of the legume's roots (**Figure 5.30B**). The legume provides the rhizobia with compounds that are a source of carbon and are energy rich, while the bacteria provide the plant with nitrogen in the form of ammonia or nitrogen-containing biomolecules. When grown as crops, legumes benefit directly from the nitrogen fixed by rhizobia, which also increases the amount of nitrogen fixed in the soil.

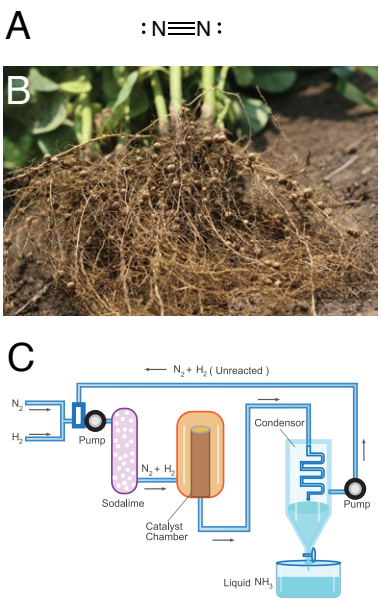


Figure 5.30 Molecular Nitrogen and Its Conversion to Ammonia. A) Structure of diatomic nitrogen. B) Rhizobia bacteria and legumes can form a symbiotic relationship, where the rhizobia reside in nodules in the plant's roots. The rhizobia bacteria are capable of converting nitrogen gas to ammonia. C) Industrial conversion of diatomic nitrogen to ammonia.

Conversion of diatomic nitrogen to ammonia can also be achieved industrially (**Figure 5.30C**). In the Haber-Bosch process, developed in the early part of the 20th century, hydrogen and nitrogen gas are subjected to high heat and pressure in the presence of an iron-based catalyst to generate ammonia:

$$N_2 + 3\,H_2 \rightarrow 2\,NH_3 \qquad (5.3)$$

The Haber-Bosch process has had a profound impact on society, as it made ammonia available as a plant fertilizer for the first time, significantly increasing agricultural yields and helping to feed the world. To this day, there is widespread use of processes very similar to that developed by Haber and Bosch, and the use of ammonia or ammonia-derived compounds in fertilizers continues to be an essential source of nitrogen for crops.

5.15 Carbon Dioxide

Carbon dioxide, CO_2, is a linear triatomic gas molecule with a central carbon linked to two oxygens by double bonds (**Figure 5.31A**). Although its relative abundance in the atmosphere is low (0.04% or 1 of 2,500 of the molecules present in air), carbon dioxide is important in a number of ways, and the production and consumption of carbon dioxide are part of what is known as the carbon cycle (**Figure 5.31B**).

Carbon dioxide can be formed from the reaction of oxygen with carbon-containing compounds. As discussed earlier, such a reaction happens during combustion (Equation 5.1), where burning of organic materials, such as natural gas, petroleum products, or wood, generates the highly oxidized carbon product, carbon dioxide, as well as water, and energy. Also mentioned previously, organisms "burn" organic materials, like food, during metabolism. This process also requires oxygen and similarly produces carbon dioxide, water, and energy. Atmospheric carbon dioxide also can result from geological events, such as eruptions of volcanoes.

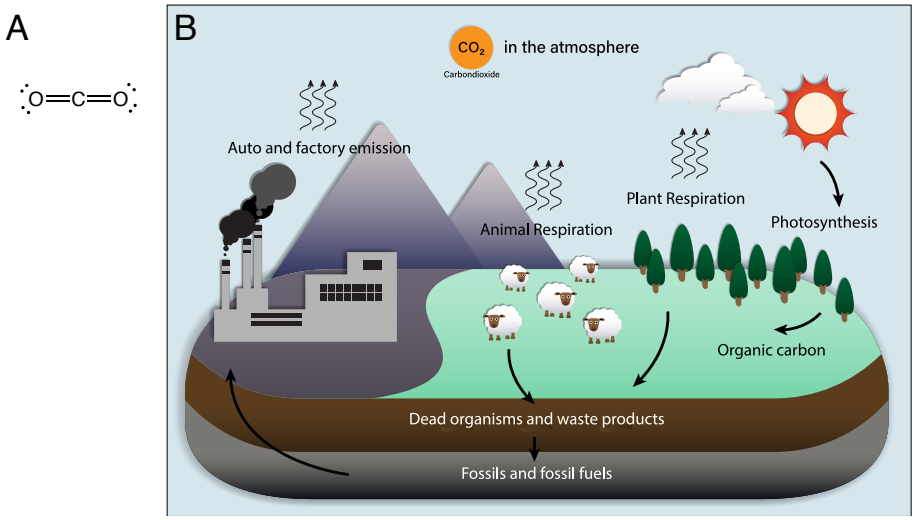


Figure 5.31 Carbon Dioxide and the Carbon Cycle. A) Structure of carbon dioxide. B) Schematic representation of the carbon cycle.

Carbon dioxide can be removed from the atmosphere by different natural mechanisms. One of special significance to all living things is that carbon dioxide is utilized by plants and other organisms to make carbon-containing biomolecules. These compounds serve as a source of energy and raw materials for making other organic molecules not only in plants, but also in the organisms that consume them (and organisms that consume those organisms). Thus, the conversion of carbon dioxide to biological molecules serves as a foundation for all biological molecules in living things.

For over a century, the levels of carbon dioxide have been rising in response to increasing

human-caused emissions. The effects of this increase in atmospheric carbon dioxide concentration are complicated, but are having impacts on the earth's environment. Carbon dioxide is a greenhouse gas that absorbs and radiates heat. Carbon dioxide, in concert with other greenhouse gases, has been responsible for increases in the average global temperature and has led to changing weather patterns. As we will see in the next chapter, carbon dioxide can also dissolve in water and react with it, changing a property of water known as its pH. The ultimate effect of all of these changes is not entirely clear, but the current changes that are due to increased carbon dioxide levels are serious enough that efforts to reduce carbon dioxide levels are needed.

Where to from here: In this chapter we examined a wide range of covalent compounds and ions made from atoms common to organic and biological molecules. In the further exploration sections, we delve into more sophisticated models of the covalent bonds that form these molecules, and we consider the solubility of salts made up of atomic and molecular ions. Next chapter, the acidic and basic compounds introduced in this chapter are investigated further.

E. Further Exploration - Bonding

Up to now, we have used relatively simple ideas to understand how atoms come together to form covalent bonds and the structure of the resulting molecules: atoms tend to "want" full valences; if the electronegativity of two atoms is not too different, they achieve a full valence by sharing electrons in a covalent bond; and groups of electrons around an atom try to space themselves as far apart as possible. These precepts are sufficient for understanding the organic and biochemical topics presented in subsequent volumes. However, they do not always accurately predict the bonding and structure of molecules, nor are they grounded in the more accurate quantum mechanical model of atoms. In this section we will explore some other models of bonding and see how they can provide additional insights into molecules we have discussed so far. These models also offer a way of understanding other kinds of compounds, such as transition metal complexes, that will be discussed at the end of the section.

5.16 Bonding in Diatomic Hydrogen

Let's start our discussion of covalent bonds with a simple covalent compound, H_2, diatomic hydrogen. This compound is composed of two hydrogen atoms, which individually are well described using quantum mechanics (Subsection 1.17-1.19). For a hydrogen atom, we saw its sole electron is distributed around its proton nucleus in some form of an electron "cloud." The probable locations of the electron are dictated by wavefunctions called atomic orbitals, and under standard conditions, the electron resides in its lowest energy atomic orbital, the 1s orbital (**Figure 5.32**). The s orbital is spherically symmetric, meaning its wavefunction has a similar distribution along any axis.

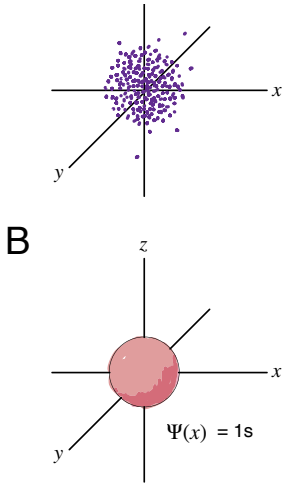


Figure 5.32 The Hydrogen 1s Atomic Orbital. Representation of the probable locations of an electron in a 1s orbital. The hydrogen nucleus is located at the origin of the graph. A) Each dot marks one possible position of the electron, placed randomly with probability proportional to $|\psi|^2$, so denser regions indicate higher probability. This graph emphasizes that the probability of finding an electron is greater closer to the nucleus than farther away and that there is no difference in the probability distribution along any possible radial axis. B) The electron probability distribution shown in part A arises from a spherically symmetric wavefunction, the 1s orbital, which can be represented schematically as a sphere.

The hydrogen electron has this particular wavefunction (as well as other higher-energy ones), because the wavefunction fulfills the criteria dictated by its Schrödinger equation (Equation 1.16). Specifically, the 1s orbital meets requirements for the kinetic energy of the electron and the electrostatic potential energy between the electron and the nucleus (**Figure 5.33A**). For diatomic hydrogen, the expectation is that this molecule will have its own wavefunction describing how the electrons from both hydrogen atoms are distributed, and this wavefunction will have a lower overall energy than the wavefunctions of the individual hydrogen atoms (hence making the formation of a covalent bond favorable). As done with the hydrogen atom, the Schrödinger equation can be used to determine the wavefunction for diatomic hydrogen. However, compared to the hydrogen atom, there are many more energy terms to consider, including the kinetic energy of the four particles in diatomic hydrogen (two protons and two electrons) and the electrostatic attractions and repulsions between these particles (**Figure 5.33B**).

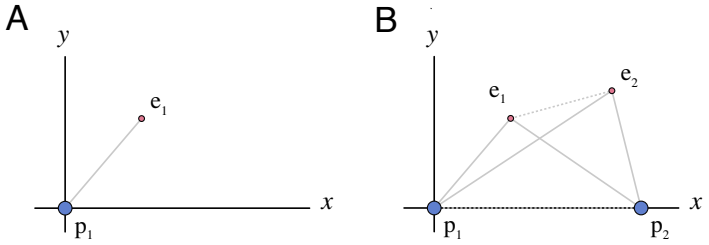


Figure 5.33 Potential Electrostatic Interaction in H and H_2. A) In a hydrogen atom, the only electrostatic interaction is an attractive one (solid gray line) between a proton nucleus (p_1) and an electron (e_1). For simplicity, all components are depicted in a single plane, here and for diatomic hydrogen. B) In a diatomic hydrogen molecule, there are attractive electrostatic interactions (solid gray lines) from each electron (e_1 and e_2) to each nucleus (p_1 and p_2), as well as repulsive electrostatic interactions (dotted gray lines) between the two electrons and the two nuclei. The full Schrödinger equation for diatomic hydrogen has to include these terms for electrostatic potential energy as well as for the kinetic energy of each of the components (not shown).

Finding exact wavefunctions that fulfill the Schrödinger equation is not possible. None theless, very accurate approximate wavefunctions can be found. From the perspective of chemical intuition, building approximate wavefunctions from atomic orbitals has been extremely useful, and we will examine two such approaches: valence bond theory and molecular orbital theory.

In valence bond theory, pairs of electrons in atomic orbitals come together to form new bonding orbitals. The appeal of such an approach is that it is analogous to the model of covalent bonds that we have seen with electron dot structures. In an early application of this idea, each hydrogen in H_2 maintains its electron in its 1s orbital, but these electrons have some overlap with the 1s orbital of the other hydrogen (**Figure 5.34**). This overlap (as well as exchange of which electron belongs to which hydrogen) results in stabilizing interactions between the atoms - that is, bonding.

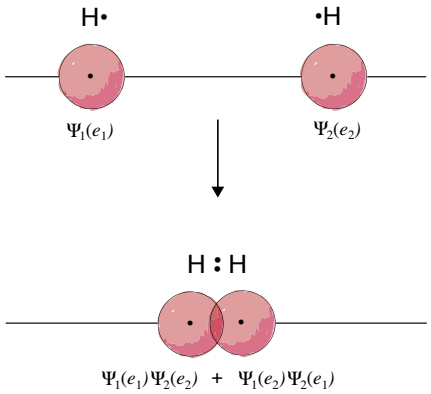


Figure 5.34 A Valence Bond Model of Diatomic Hydrogen. Shown is a schematic of the Heitler and London model from 1927. At the top are the 1s atomic orbitals of each hydrogen electron, with a dot in the wavefunction to emphasize that the orbital is occupied by one electron. After being brought together, the new wavefunction is the sum of two terms: the product of each individual wavefunction, and an equivalent product in which the electrons are swapped. Using a Schrödinger equation that includes all but the kinetic energy term for the nuclei, stabilization energy is obtained at a certain distance between nuclei from attractive electron interactions with the opposite nuclei and especially "exchange" energy that comes from the equivalent wavefunction in which the electrons are swapped.

In molecular orbital theory, two or more atomic orbitals combine to form molecular orbitals, and then electrons are placed within these molecular orbitals. The simplest application of this idea to diatomic hydrogen is that a lower energy bonding orbital can be formed from the sum of two 1s orbitals (as well as a higher energy antibonding one) (**Figure 5.35A and B**). Like filling the atomic orbitals of elements beyond hydrogen, the two electrons in H2 fill the bonding molecular orbital, creating a covalent bond (**Figure 5.35C**).

In their simplest forms, neither valence bond theory nor molecular orbital theory fully captures the nature of H_2's covalent bond. In the valence bond model, constraining each electron to one of the 1s hydrogen orbitals underemphasizes the potential contribution of both electrons being near one hydrogen nucleus (i.e. having some ionic character). In the molecular orbital model, allowing each electron to independently occupy a molecular orbital discounts the cost of repulsive interactions between the electrons. Ultimately, the full picture of covalent bonding is complicated, consisting of trade-offs between lowering the kinetic energy of the electrons by allowing them to spread out, attractive electrostatic interactions between the electrons and nuclei, and repulsive interactions between similarly charged particles. Additional contributions to valence bond and molecular orbital models improve their accuracy and make them complementary perspectives on the nature of covalent bonding.

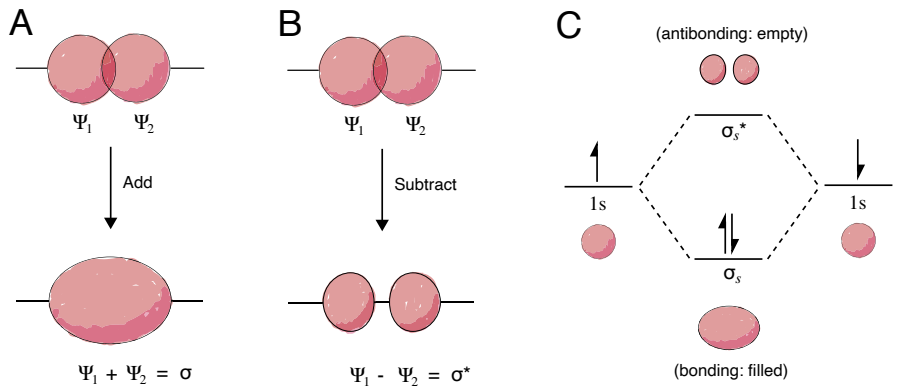


Figure 5.35 A Molecular Orbital Model of Diatomic Hydrogen. Shown is a schematic of a molecular orbital model of diatomic hydrogen, originally developed by Hund, Mulliken, and others in the late 1920s and 1930s. A) At the top, two hydrogen 1s atomic orbitals are shown near one another. At the bottom, a new wavefunction is made from the sum of the two atomic orbitals (a bonding molecular orbital, σ). A Schrödinger equation that includes the kinetic energy of the electron, its interaction with each nucleus, and the electrostatic interaction of the nuclei indicates that this molecular orbital is stabilized relative to the atomic orbitals. B) The difference in two 1s atomic orbitals results in an antibonding molecular orbital, σ_s^*. This molecular orbital is destabilized relative to the original atomic orbitals. C) A schematic of the energetics of the atomic and molecular orbitals of two hydrogens. Each orbital can accommodate up to two electrons, and the electron from each hydrogen (shown as arrows) fills the lower-energy bonding molecular orbital to stabilize an H_2 molecule. The antibonding orbital is empty in H_2.

5.17 Other Diatomic Molecules

Atoms beyond hydrogen have additional electrons and can access non-1s orbitals, such as: 2s and 2p orbitals; 3s, 3p and 3d orbitals; and so forth (Subsection 1.20). How are these electrons and orbitals involved in the formation of covalent bonds? For simplicity, let's start with diatomic molecules from the second row of the periodic table — atoms that have valence electrons in 2s and 2p orbitals.

In molecular orbital theory, the idea is to combine one or more atomic orbitals to make molecular orbitals, and then to fill these orbitals with the electrons of the atoms. As we saw with diatomic hydrogen, combining two 1s orbitals created two new orbitals: a bonding and an antibonding orbital. This phenomenon is general, in that combinations of atomic orbitals result in the same total number of molecular orbitals, and these orbitals are either higher or lower in energy than the starting atomic orbitals (bonding or antibonding). Thus, when two atoms from the second row come together, their one 1s, one 2s, and three 2p orbitals can be combined to form various molecular orbitals.

Accounting for all the possible combinations of atomic orbitals is complicated, but can be simplified using several guidelines: Atomic orbitals with similar energies mix most; atomic orbitals combine more effectively when they have good spatial overlaps; and for atomic orbitals to mix, they have to have the same symmetry. Delving into the symmetry of molecular orbitals is beyond the scope of this section, but the other guidelines are relatively easy to apply.

In considering possible molecular orbitals for a diatomic second row molecule, each atom's 2s and 2p orbitals extend farther from the nucleus than the 1s orbital. This means that when two atoms are brought together, these 2s and 2p orbitals will tend to overlap more easily than the 1s orbitals, making the contribution of the 1s orbitals relatively unimportant. This is similar to the idea that valence electrons are the ones we have to consider in making bonds, and, in general, molecular orbital theory considers only the valence orbitals.

For second row atoms, the 2s orbital is lower in energy than the 2p orbital (which is why electrons fill the 2s orbital before the 2p orbitals), and for elements with more electrons in their valence shell, this energy difference is relatively significant. As atomic orbitals with similar energy mix most effectively, to a first approximation this means that 2s atomic orbitals mix with 2s orbitals and 2p orbitals mix with 2p orbitals.

Combining two 2s orbitals works the same way as combining two 1s orbitals: a lower energy bonding orbital is generated, as well as a higher energy antibonding orbital. Mixing of the 2p orbitals is a little more complicated. Recall that in a p orbital, the electron density consists of two lobes pointed in opposite directions (**Figure 5.36A**). There are three p orbitals, and each is mutually perpendicular to the other two (**Figure**

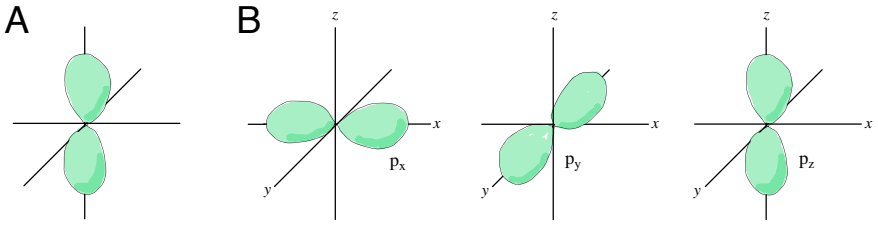


Figure 5.36 Atomic p Orbitals. A) Unlike the spherically symmetric s orbitals, the distribution of electron probability in a p orbital has an angular component, with the greatest electron density found in two lobes pointing in opposite directions. B) An electron can occupy any of three mutually perpendicular p orbitals with the orbitals aligned along: the x-axis, p_x; the y-axis, p_y; or the z-axis, p_z.

5.36B). For convenience, we will define these orbitals as being oriented along the x-, y-, and z-axis. For bonding to occur, there must be overlap between orbitals. Suppose that two atoms approach one another along the z-axis so that there can be overlap between the p_z orbitals. This will create a lower-energy bonding molecular orbital and a higher-energy antibonding one (**Figure 5.37**). This overlap of $2p_z$ orbitals occurs along the axis the atoms approach each other, similar to overlap of the 1s and 2s orbitals. Such bonding orbitals are called sigma orbitals (σ orbitals) and the bonds are known as sigma bonds (σ bonds).

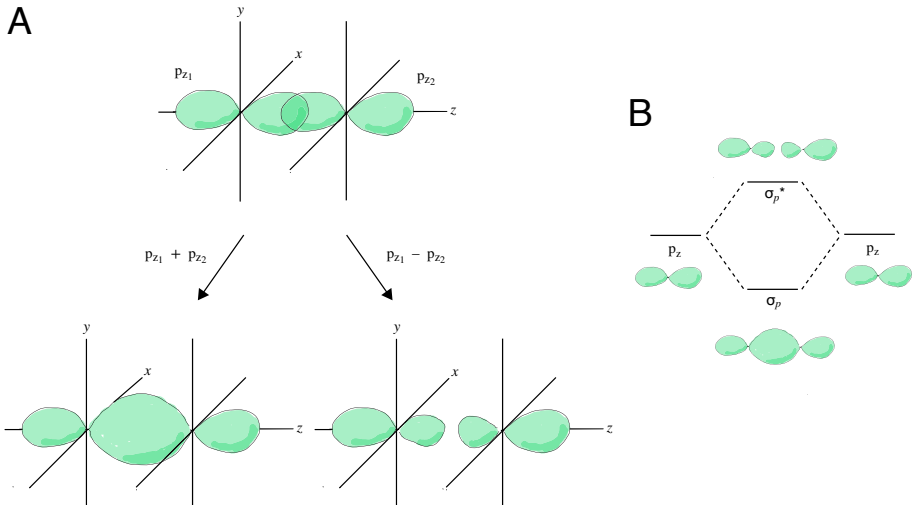


Figure 5.37 Formation of a Sigma Bond from Two p Orbitals. A) When two p_z atomic orbitals are aligned along the z-axis and in close proximity, their sum results in a bonding molecular orbital. In this wavefunction, called a sigma (σ) orbital, the electron density between the atoms increases. The difference of p_z orbitals results in an antibonding orbital. In this wavefunction, called a sigma star (σ*) orbital, the electron density between the atoms decreases. Note in both the σ and σ* orbitals, the wavefunction is symmetric around the z-axis. B) Focusing on the energetics of the process in part A: combining two p_z orbitals of the same energy results in a lower energy bonding orbital and a higher energy antibonding orbital.

When two $2p_z$ orbitals form a sigma bond, the $2p_y$ orbitals can also overlap to form a bond (**Figure 5.38A**). Unlike the $2p_z$ orbitals, whose lobes point directly at each other along the bond axis, the lobes of the $2p_y$ orbitals do not point directly at one another. This means that the electron density of this bond is found on either side of the internuclear axis (and above and below a sigma bond). Such a bond is known as a pi bond (π bond),

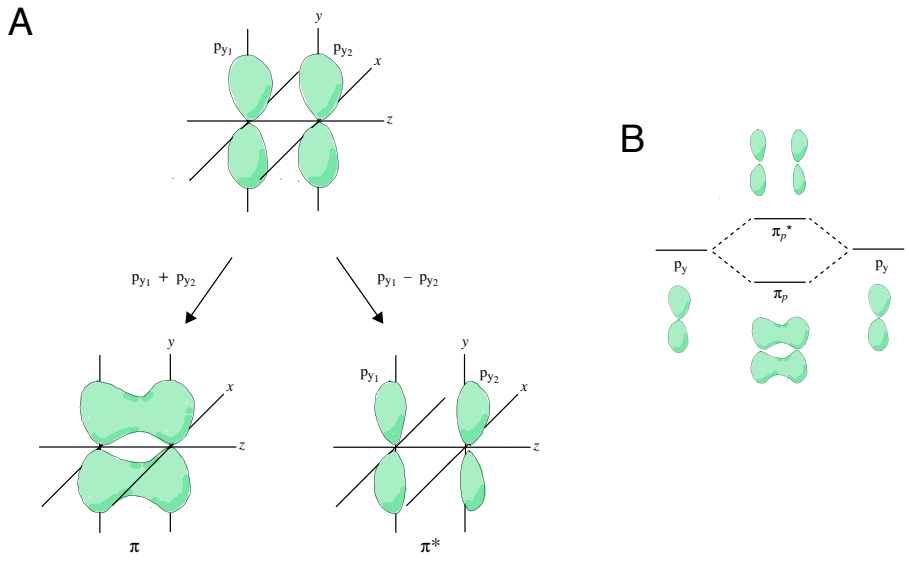


Figure 5.38 Formation of a Pi Bond from Two p Orbitals. A) The sum of proximal p_y atomic orbitals produces a pi (π) bonding molecular orbital with increased electron density between the atoms. The difference produces a pi star (π*) antibonding orbital with decreased electron density between the atoms. Unlike sigma orbitals, the pi orbitals are not symmetric all around the z-axis. B) Energetics of pi bonding and antibonding molecular orbitals. Pi bonds are not as stabilized as sigma bonds, nor pi antibonds as destabilized.

and the bonding orbital is known as a pi orbital (π orbital). In a pi bond, the overlap of atomic orbitals is less than in a sigma bond. Consequently, the bonding orbital formed is not as stabilized as in a sigma bonding orbital (but is still lower than the original $2p_y$ orbitals) (**Figure 5.38B**). Mixing of atomic orbitals also produces antibonding orbitals, and combining two $2p_y$ orbitals creates a pi antibonding orbital, with this orbital less destabilized than the sigma antibonding orbital.

$2p_x$ orbitals combine to form pi orbitals in a manner identical to $2p_y$ orbitals. So altogether, when two atoms from the second row of the periodic table come together, their 2s atomic orbitals form a bonding and antibonding sigma orbital, and their three 2p orbitals form one sigma and two pi bonding orbitals, and one sigma and two pi antibonding orbitals (**Figure 5.39**). Let's now see how these molecular orbitals fill for various elements. We'll start with the end of the row (Ne) and work our way back (going in this direction may seem strange, but the reason will become apparent).

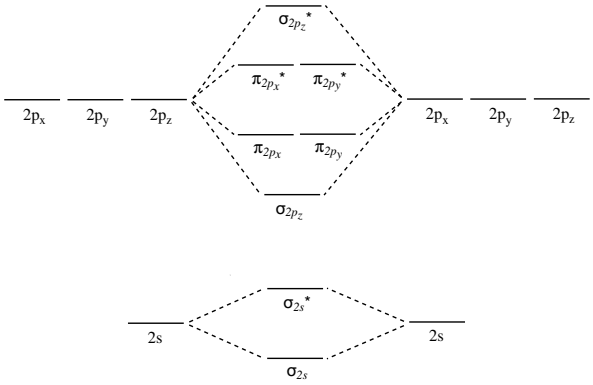
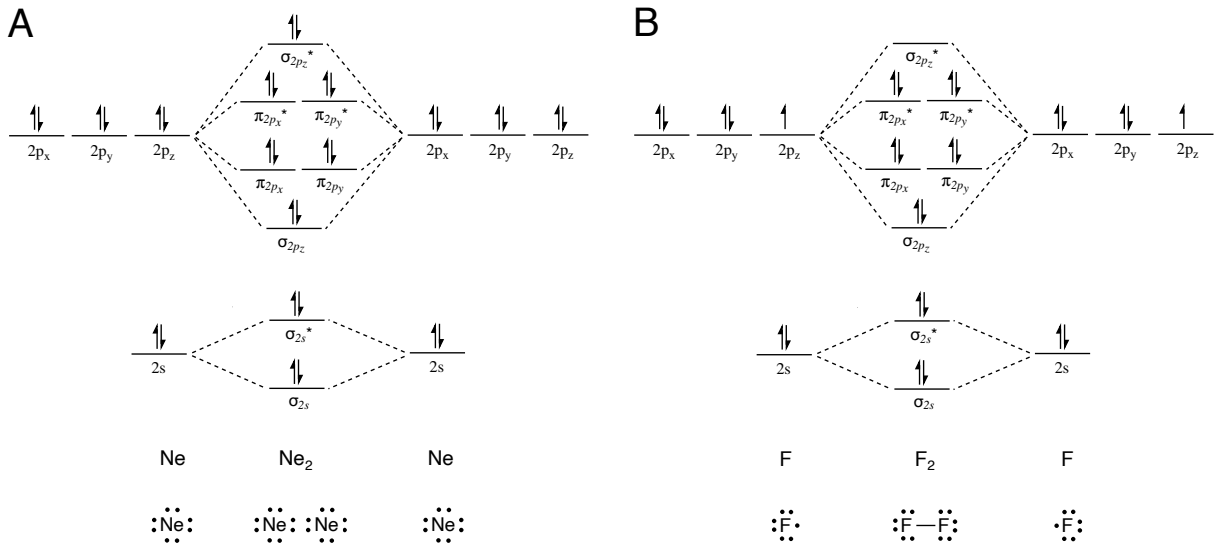


Figure 5.39 Potential Molecular Orbitals Generated by Combining Second Shell Atomic Orbitals. Shown are the molecular orbitals for second row diatomic elements with a large number of valence electrons: oxygen, fluorine, and neon. These elements have a large separation in energy between their 2s and 2p atomic orbitals, and those orbitals mix independently. For the arrangement of molecular orbitals of elements with fewer electrons, see Figure 5.42.

A neon atom has eight valence electrons, so a theoretical diatomic Ne_2 molecule would have 16 valence electrons. We can use these electrons to fill the molecular orbitals in Figure 5.39 according to Pauli's Exclusion Principle (no orbital can have more than two electrons) and Hund's Rule (if orbitals are the same, or relatively close, in energy, electrons will maximize the number of unpaired electrons). When we do this (**Figure 5.40A**), we see that all of the molecular orbitals are filled for Ne_2. This means that for every filled bonding orbital there is a filled antibonding orbital offsetting any bonding stabilization. Thus, diatomic neon is not favorable to form, as we previously predicted based on the fact that neon is a noble gas with a filled valence shell.

When we do the same analysis with diatomic fluorine, each with 7 valence electrons,

Figure 5.40 Molecular Orbital Diagrams for Ne_2 and F_2. A) Diatomic Neon. B) Diatomic Fluorine. Below the molecular orbital diagrams are the analogous electron dot diagrams for the atoms coming together.



we see that not all of the antibonding orbitals are filled (**Figure 5.40B**). This leaves one net sigma bond (σ_{2p_z}), and results in F_2 having a single (sigma) bond, consistent with our electron dot structures for F_2.

Up to this point, molecular orbital theory has not provided us with any insights that we could not gain from electron dot diagrams. That is not the case with diatomic oxygen

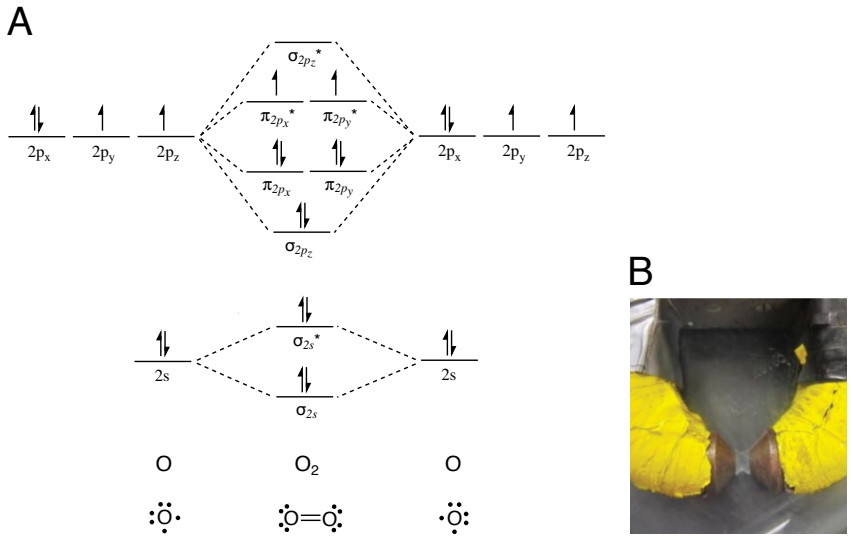


Figure 5.41 Diatomic Oxygen and its Properties from a Molecular Orbital Perspective. A) Molecular orbital diagram for diatomic oxygen. Note that the molecule contains unpaired electrons in the pi antibonding orbitals. The electron dot diagram for diatomic oxygen is shown below. B) Diatomic oxygen is magnetic due to its unpaired electrons. Shown is liquid oxygen trapped by the field of a magnet.

with a total of 12 valence electrons (**Figure 5.41A**). O_2 has a net sigma bond and a net pi bond. This indicates that oxygen has a double bond, as expected, but the bonds are not the same in terms of where the electrons are located nor in the relative strengths of the bond (something not discernible from the electron dot structure). Further, the molecular orbital diagram of O_2 indicates that the molecule has two unpaired electrons. Unpaired electrons make compounds magnetic, and indeed, oxygen has a magnetic moment and can interact with a magnetic field (**Figure 5.41B**). Additionally, oxygen often reacts as a diradical, that is, a compound with two unpaired electrons. Oxygen possessing unpaired electrons is not apparent from the electron dot structure.

As a last example, consider diatomic nitrogen (**Figure 5.42**). N_2 has ten total valence electrons. Four of the ten valence electrons fill the 2s-derived bonding and antibonding orbitals, which cancel each other out. The remaining six fill all three p-orbital bonding

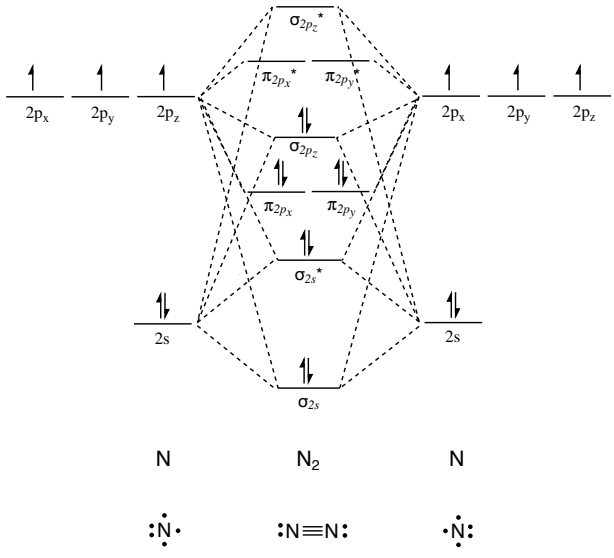


Figure 5.42 Diatomic Nitrogen. Shown are the molecular orbital diagram (top) and electron dot diagram (bottom) for diatomic nitrogen. Note, the ordering of molecular orbitals for diatomic nitrogen differs from those shown earlier (Figures 5.39—41). Specifically, the pi bonding orbitals generated from the 2p atomic orbitals are more stable than the sigma bonding orbitals generated from the 2p atomic orbitals. This particular ordering of molecular orbitals is also true of all second row elements with fewer valence electrons than nitrogen.

orbitals — one sigma and two pi — without occupying any p-derived antibonding orbitals. This gives N_2 a triple bond with one sigma bond and two pi bonds. One thing to note about the molecular orbitals of N_2 is that the stabilities of the sigma and pi bonding orbitals are swapped from those of diatomic oxygen, fluorine, and neon. This is because the energy separation between the 2s and 2p orbitals decreases when atoms have fewer valence electrons, allowing these orbitals to mix and altering the stability of the bonding and antibonding molecular orbitals. Specifically, for nitrogen and other lighter second-row elements, the sigma bonding orbitals from the 2p atomic orbitals can mix with the 2s sigma bonding orbital, stabilizing the 2s sigma bonding orbital. However, this comes at the cost of the stability of the 2p sigma bonding orbital, raising its energy to the point that the 2p pi orbitals are more stable.

5.18 Polyatomic Organic Compounds

Not surprisingly, understanding the bonding of a compound with multiple different atoms is more complicated than a molecule with two of the same atoms. Consider the relatively simple polyatomic compound of methane, in which one carbon is bound to four hydrogens (**Figure 5.43**). By using an electron dot structure, applying VSEPR theory, and considering the atoms' electronegativities, we found that methane is a molecule in which each of carbon's four valence electrons can be shared with the valence electron of a hydrogen in a non-polar covalent bond. These bonds to hydrogens are identical and are spaced evenly apart to give methane a tetrahedral structure.

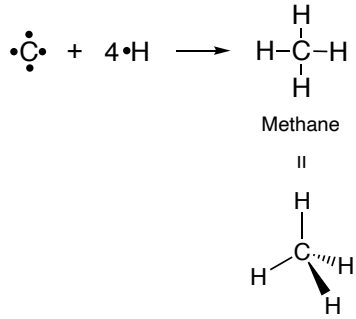


Figure 5.43 Structure of Methane from an Electron Dot and VSEPR Approach. The carbon of methane shares its four valence electrons with four hydrogen atoms in four single covalent bonds. VSEPR theory predicts that for these bonds to be as far away from each other as possible, the molecule adopts a tetrahedral geometry.

Starting from the same spatial arrangement of atoms, we can describe the bonding in methane from a molecular orbital perspective. Each hydrogen atom has one s orbital, while carbon has one s orbital and three p orbitals in its outermost shell. With eight total atomic orbitals, we expect to be able to generate eight molecular orbitals, four bonding and four antibonding (**Figure 5.44A**). We can combine the carbon 2s orbital with all four hydrogen 1s orbitals to give one bonding molecular orbital in which there is overlap between all atoms (**Figure 5.44B**, top). At a higher energy, the four hydrogen 1s orbitals can combine with each of carbon's 2p orbitals to make three bonding orbitals, where the energies of each of these molecular orbitals is the same, but which orbitals are involved in the overlap is different (Figure 5.44B, bottom). All eight of the valence electrons from the atoms in methane fill bonding molecular orbitals, corresponding to four total bonds (Figure 5.44, bottom left). However, the nature of these bonds and

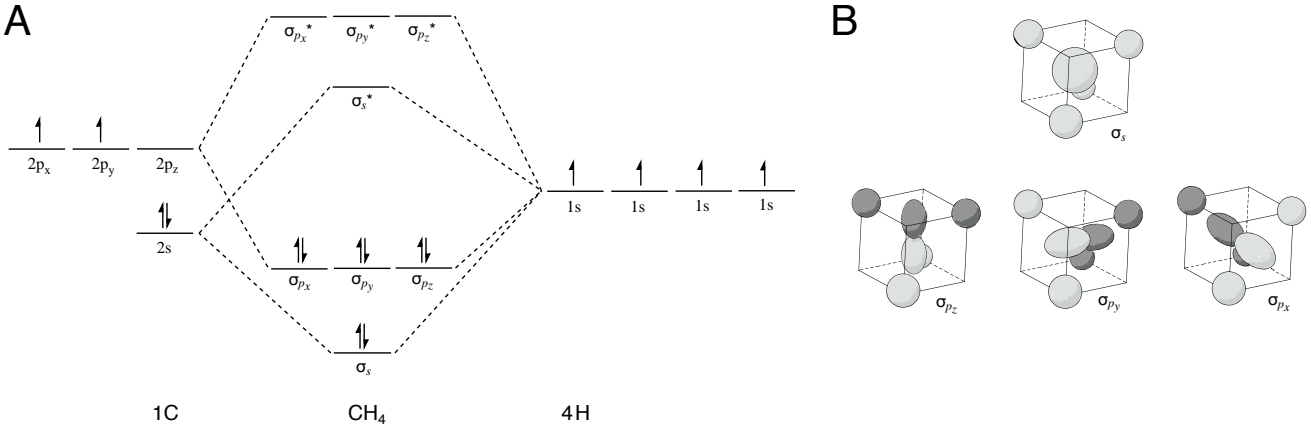


Figure 5.44 A Molecular Orbital Model of Methane. A) The four valence orbitals of carbon (one 2s and three 2p orbitals) combine with four valence orbitals of hydrogen (four 1s orbitals) to form eight molecular orbitals (four bonding, four antibonding). B) The lowest energy bonding molecular orbital for methane, σ_s, comes from the sum of carbon's 2s orbital with all four hydrogen 1s orbitals (top image). The next lowest energy bonding molecular orbitals are three σ_p orbitals. These come from the combinations of each of the carbon's 2p orbitals (bottom three images), where pairs of hydrogen 1s orbitals (spheres with the same color) interact with one of the lobes of one of carbon's 2p orbitals. An aspect of the p orbital we have not discussed is the fact that the two lobes of a 2p orbital are out of phase with one another (indicated by the different colors). 1s orbitals exist in one phase. For two wavefunctions to constructively overlap, the overlap portion has to be in the same phase. Hence, in the σ_p orbitals, two hydrogen 1s orbitals are in one phase to overlap with one lobe of the carbon's 2p orbital (dark color), while the other two hydrogen orbitals are in the opposite phase to overlap with the other lobe of the carbon's 2p orbital (light color).

their energies are different from those in the electron dot structure. In the lowest energy bonding orbital, the electron density is spread out amongst all of the atoms, instead of being between one carbon and one hydrogen atom. Even in the higher energy bonding orbitals, the electron density is not directly between one carbon and one hydrogen. Instead it is between pairs of hydrogens and one of the lobes of a p-orbital (dark colored orbitals together and light colored orbitals together). Spectroscopic studies do suggest that the electrons in methane occupy different bonding levels. However, the chemical intuition gained from the electron-dot model is lost.

A valence bond description of methane provides an orbital-based picture analogous to the electron-dot model. Carbon has four valence orbitals in which it can potentially form bonds (one 2s and three 2p orbitals). That said, for a single atom of carbon, two of its electrons fill its 2s orbital, two of the 2p orbitals have one electron, and one 2p orbital is empty. This situation only provides two orbitals with one electron (two of the p orbitals) from which to form a covalent bond with an electron from a hydrogen. However, if all of carbon's atomic orbitals are mixed to form new orbitals, and with the electrons redistributed, carbon can then make four bonds with four hydrogens. This mixing of orbitals is called hybridization, and different types and numbers of hybrid orbitals are formed when different numbers and types of atomic orbitals are combined.

Before getting to methane's hybrid orbitals, let's consider the simpler case of combining one s and one p orbital. By combining these two atomic orbitals in different ways (**Figure 5.45A**), we can get two sp hybrid orbitals (note, the hybrid orbital is called an sp hybrid orbital because it comes from one s and one p orbital). Each sp hybrid orbital has a similar, prominent lobe pointed in one direction. However, the two sp hybrid orbitals are oriented in opposite directions, i.e. 180° (**Figure 5.45B**, top). If we were to take combinations of one s and two p atomic orbitals, we would generate three sp^2

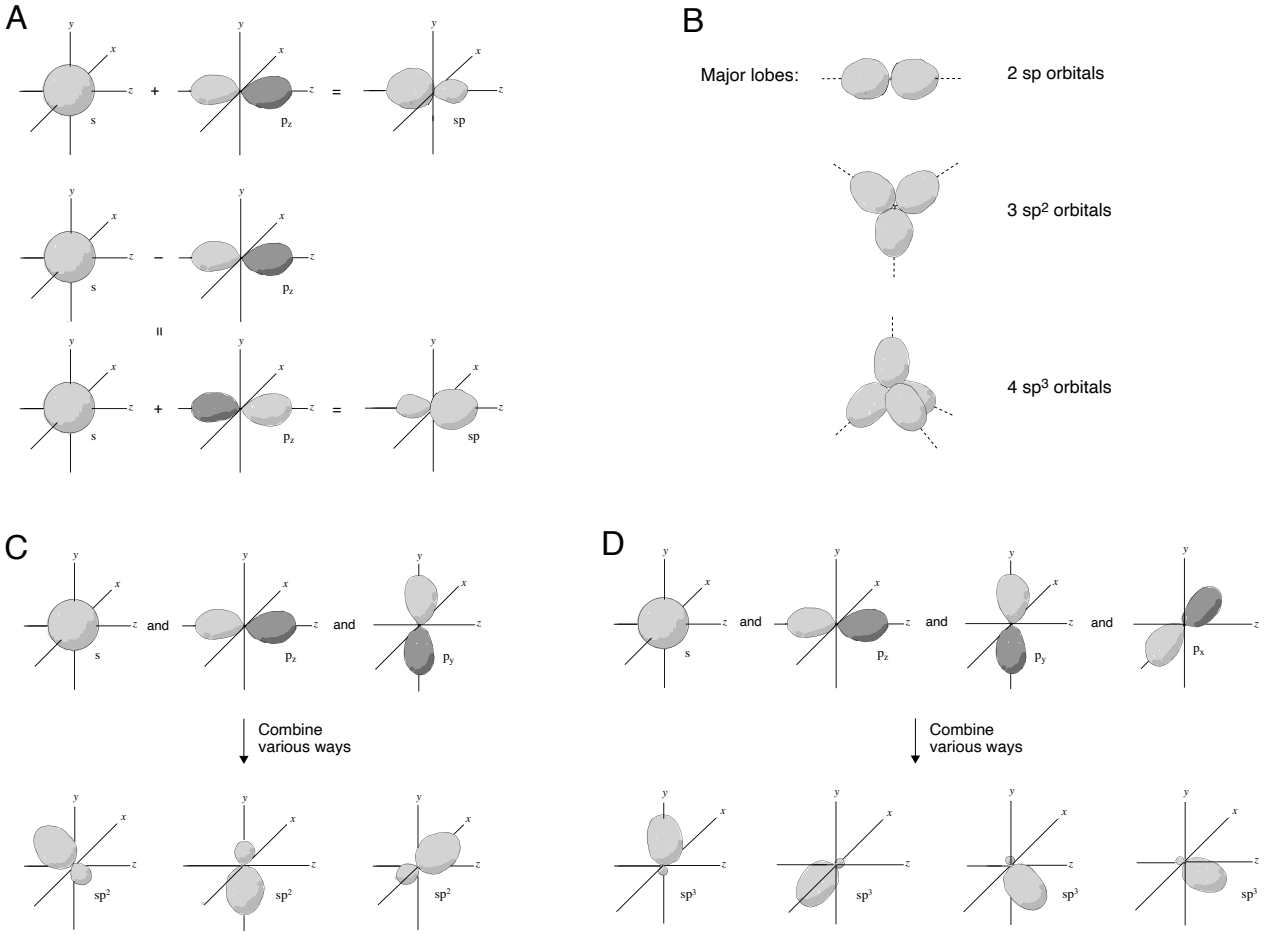


Figure 5.45 Various Hybrid Orbitals. A) How two sp hybrid orbitals can be formed from combining one s and one p orbital. B) Summary of hybrid orbitals, including the major lobes of the hybrid sp orbitals shown in A. C) Three sp^2 hybrid orbitals can be generated from a combination of one s and two p orbitals. How the atomic orbitals are combined is more complicated than for generating the sp orbitals and involves combining fractions of the p orbitals. This is done to both generate the geometry consistent with a three-bonded atom and to fulfill certain general requirements for orbitals. D) Four sp^3 hybrid orbitals can be generated from a combination of one s and three p orbitals. It should be noted that hybrid orbitals are used to explain a given molecular geometry in terms of contributions of atomic orbitals, and not as a justification of an observed geometry.

hybrid orbitals (**Figure 5.45C**). These orbitals are more directional than the sp hybrid orbital, because they have a higher p character than sp hybrid orbitals (2 parts p to 1 part s, compared to the equal 1:1 mix in sp hybrid orbitals). They are also in the same plane and are pointed 120° from one another (Figure 5.45B, middle). If we combine one s orbital with three p orbitals, we get four sp^3 hybrid orbitals, where each orbital is highly directional and pointed 109.5° away from each other (**Figure 5.45D** and Figure 5.45B, bottom).

In methane, carbon's four atomic orbitals can be thought to have been hybridized into four sp^3 orbitals, each with one of carbon's four valence electrons. These hybrid orbitals can each then overlap with a 1s orbital from a hydrogen, and the two electrons in those overlapping orbitals form a shared covalent bond (**Figure 5.46**). The overlap of orbitals is along the axis of approach, so the bonds made between the sp^3 and s orbitals are considered sigma bonds. Because carbon's sp^3 hybridized orbitals are arranged tetrahedrally around the atom, the molecule made with the hydrogens is also tetrahedral.

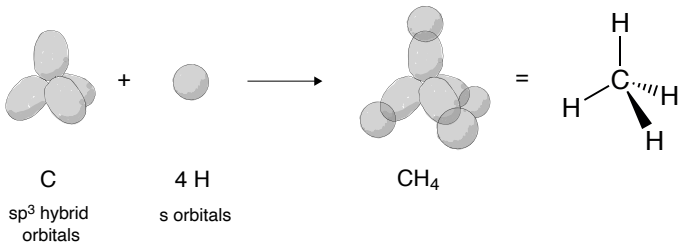


Figure 5.46 The Structure of Methane in Terms of Hybrid Orbitals. The four valence electrons of the carbon in methane are hybridized into four sp^3 orbitals. These orbitals overlap with the one electron s-orbitals of four hydrogens to generate four sigma bonds arranged in a tetrahedral geometry.

An organic molecule like ethane can be understood in terms of hybrid orbitals very similarly to methane (**Figure 5.47A**). The difference is that instead of all four sp^3 hybrid orbitals on each carbon forming bonds with hydrogens, one sp^3 orbital on each carbon forms a bond with the other carbon. The resulting C-C covalent bond is a sigma bond, in which each methyl group can rotate while maintaining this orbital overlap.

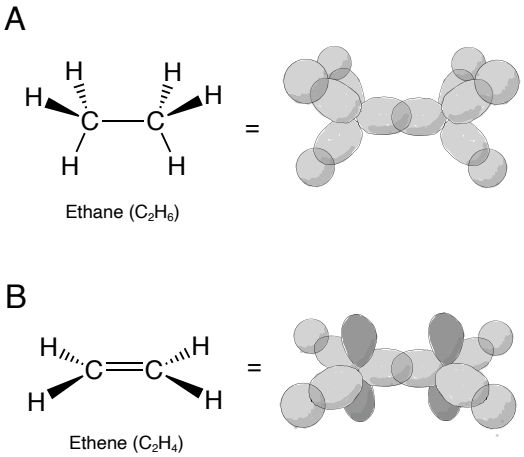


Figure 5.47 Comparison of Valence Bond Models of Ethane and Ethene. A) The carbons of ethane resemble the carbon of methane, having sp^3 hybridization. Between the two carbons, sp^3 hybrid orbitals overlap to make a sigma bond between the atoms. B) The carbons in ethene each have three electrons in sp^2 hybrid orbitals and one electron in a p orbital. Between the carbons, one pair of sp^2 hybrid orbitals can overlap to form a sigma bond and one pair of p orbitals can overlap to form a pi bond (p orbitals shown in darker color and without overlap for clarity). Thus, the double bond in ethene consists of one sigma and one pi bond.

For ethene, each carbon is bonded to only three other atoms. With only three bonds to form, each carbon uses sp^2 hybridization — made by combining one s and two p orbitals into three hybrid orbitals, with one p orbital left over. The three sp^2 orbitals form sigma bonds: one between the two carbons and two with hydrogens (**Figure 5.47B**), arranged in a trigonal planar geometry. The remaining p orbital on each carbon is perpendicular to this plane. It cannot overlap with the other carbon's p orbital along the bond axis to form a sigma bond, but it can overlap side-by-side to form a pi bond — giving ethene a carbon–carbon double bond.

Altogether, we have seen that molecular orbital and valence bond theory can provide a

deeper understanding of simple covalent compounds. As we explore organic compounds in the next volume, we will see that these theories can be useful in understanding the behavior of more complex compounds. Additionally, these theories are quite useful for understanding more complicated inorganic molecules, as we will see in our next section.

5.19 Transition Metal Complexes

In these volumes, we will focus on organic compounds made mostly from elements in the first two rows of the periodic table (C, H, N, and O), with occasional compounds including elements from the third row (S and P). That said, compounds can be made from other elements in the periodic table, and molecules containing transition metals can have important biological roles.

Transition metal elements begin in the fourth row of the periodic table, occupying columns 3 through 12 (**Figure 5.48A**). These metals have access to more than just the s and p orbitals we have examined so far and can have anywhere from 1-10 electrons in d orbitals. For example, a transition metal in the fourth row has access to nine orbitals: one 4s orbital, five 3d orbitals, and three 4p orbitals (**Figure 5.48B**). From molecular orbital theory, we've seen that every atomic orbital can potentially form a bonding orbital with another atom, so a metal with nine orbitals could potentially form up to nine bonds. That said, most transition metal complexes cannot do so. This is because there is usually not enough space to accommodate that many bonds, and because many metals fill some of these nine orbitals with their own electrons. A notable exception is the anionic metal complex ReH_9^{2-} (**Figure 5.48C**). Because rhenium is a large atom in the sixth row of the periodic table, and hydrogen atoms are small, there is enough space in this complex to accommodate nine bonds. Additionally, in the complex, rhenium is assigned a +7 oxidation state, meaning it is formally considered to have lost all seven of its outermost

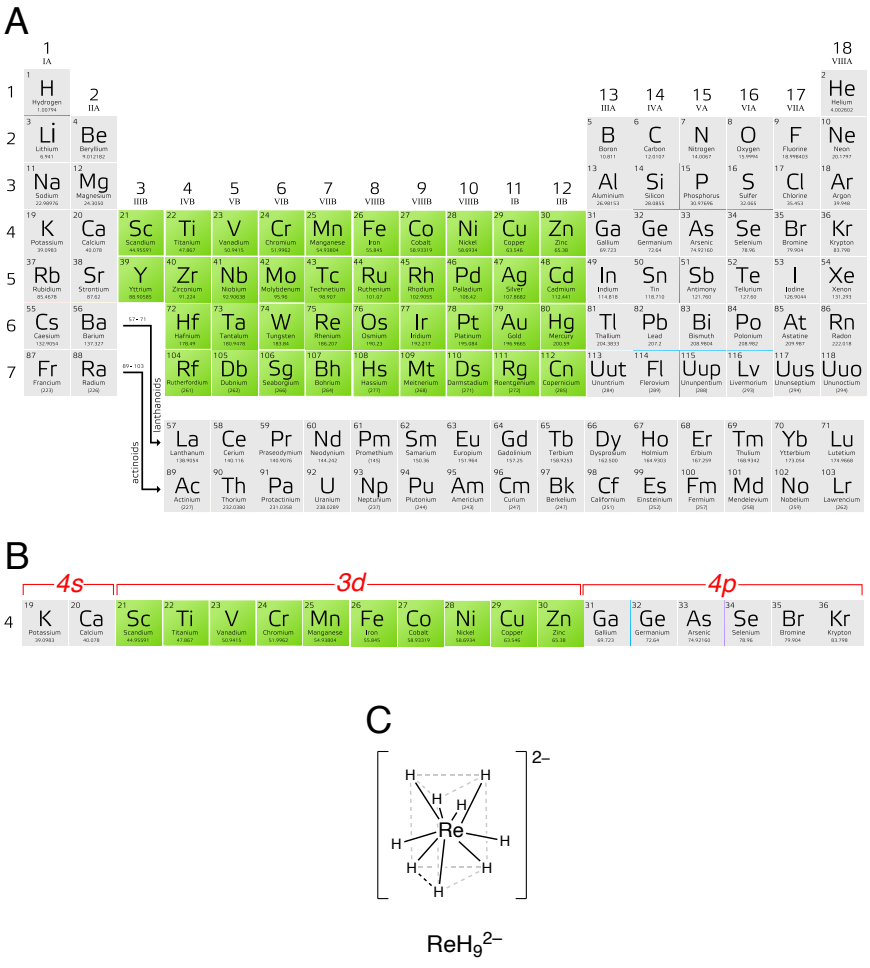


Figure 5.48 Transition Metals and Possible Bonds. A) Portion of the periodic table containing the transition metals is in green. B) Outer atomic orbitals associated with elements in the fourth row of the periodic table. C) Structure of the transition metal complex ReH_9^{2-} containing nine bonds.

electrons (oxidation state is described more in depth in Volume II, Chapter 12). All nine of its outer orbitals are then used to form bonds with hydride atoms: an H^- ion, or a hydrogen with two electrons. The net -9 charge of the nine hydrides gives the complex an overall charge of -2 (7 - 9 = -2).

In transition metal complexes, the groups attached to the metal center are known as ligands, and complexes with four or six ligands arranged in various possible geometries are common. Such complexes can be relatively simple, like those shown containing a single type of ligand in Figure **5.49A**. Other complexes are more complicated with different kinds of ligands, such as some biologically relevant complexes shown in Figure **5.49B**.

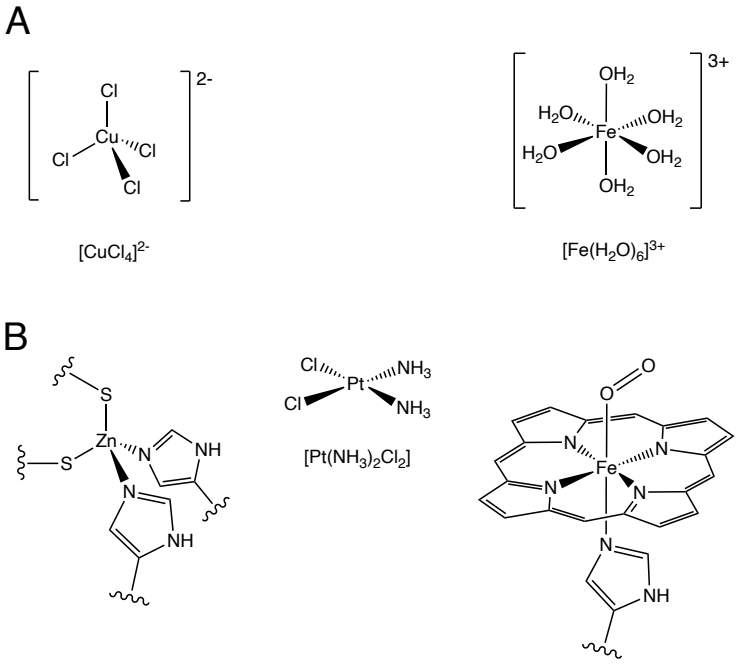


Figure 5.49 Example of Transition Metal Complexes. A) Complexes with a single type of ligand. The compound on the left, tetrachlorocuprate(II) is a complex with four chloride ligands arranged around a copper in a tetrahedral geometry. The complex on the right, hexaaquoiron(III) ion is an iron complex with six water ligands and adopts an octahedral geometry. B) Biologically relevant complexes with multiple ligands. The complex on the left is a zinc coordinated by two histidine and two deprotonated cysteine side chains within a protein. The four ligands adopt a tetrahedral geometry. This motif, a zinc finger, is found in some proteins that bind DNA. The complex in the center is cisplatin, in which platinum is coordinated by two ammonia ligands and two chloride ligands in a square planar geometry. Cisplatin is a potent chemotherapeutic agent for treating cancers. The complex on the right is found in four copies in the oxygen-transporting protein, hemoglobin. The iron has six ligands arranged in an octahedral geometry. Four of the ligands come from a nitrogen ring system called a porphyrin (which has been simplified for clarity). One ligand comes from a histidine side chain from the protein. The last ligand is reversibly bound to diatomic oxygen.

How do we understand how many bonds a metal forms, the arrangement of these bonds, and other properties of the complex? The complicated electronic structure of transition metals doesn't allow us to simply apply the idea of forming covalent bonds to achieve a full valence. Further, factors besides repulsion of electronic groups make VSEPR theory inadequate to predict the geometry of transition metal complexes. In general, the structure and properties of a transition metal complex depend on the metal, its oxidation state, and the ligand, where specific metals favor certain oxidation states, coordination states, and ligands.

Ligands in transition metal complexes are attached to their metal centers through a dative covalent bond — also called a coordinate bond. In a dative bond, two electrons from the ligand are shared with the metal by placing them into an empty metal orbital. This is similar to the situation we have seen with other covalent bonds, but instead of each atom contributing an electron to share, both electrons come from the ligand. We have seen an example of a dative bond in protonation of a base, such as protonation of ammonia to an ammonium ion. In this reaction (**Figure 5.50A**), the proton, H^+, has an empty 1s orbital that can be filled with two electrons contributed by the lone pair electrons of ammonia.

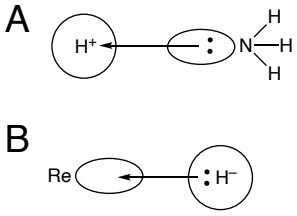


Figure 5.50 Examples of Dative Bonds. A) the lone pair electrons of an ammonia molecule form a dative bond with the empty atomic orbital of a proton, leading to protonation of the ammonia. B) A pair of electrons in a hydride ion ligand (hydrogen with an extra electron) forms a dative bond with an empty orbital of the rhenium ion (one of nine such dative bonds formed in the ReH_9^{2-} transition metal complex).

In transition metal complexes, the metal cation, like the proton of the previous example, can make a dative bond with a ligand containing a lone pair of electrons. However, in transition metal complexes, there are more empty orbitals available, allowing more ligands to be bound. As an example, in the previously described ReH_9^{2-} anion complex (Figure 5.48C), we saw that the metal is formally a +7 ion (+7 oxidation state), thereby

having nine empty valence orbitals (one 6s orbital, five 5d orbitals, and three 6p orbitals). Hydrogen in the form of a hydride, H^-, has a lone pair of electrons that can form a dative bond with the orbitals of the metal (**Figure 5.50B**). Because the hydride is small and Re large, all nine of rhenium's empty orbitals can be filled by forming dative bonds with the hydrides, leaving no additional electrons to account for.

In other metal complexes, not all of the atomic orbitals are used for formation of dative bonds and some of these orbitals are occupied with the metal's electrons. Let's look at octahedral complexes, like those of the iron in hexaaquoiron(III) ion (Figure 5.49A right).

One way to understand the dative bonds in an octahedral complex is using valence bond theory. If you hybridize one s orbital, three p orbitals, and two of the five d orbitals, specifically $d_{x^2-y^2}$ and d_{z^2}, you end up with six equivalent sp^3d^2 orbitals (**Figure 5.51**). These orbitals end up oriented in the direction of the six ligand bonds, and each such orbital is filled by the lone pair electrons of the ligands. This leaves the electrons of the metal to fill the other orbitals.

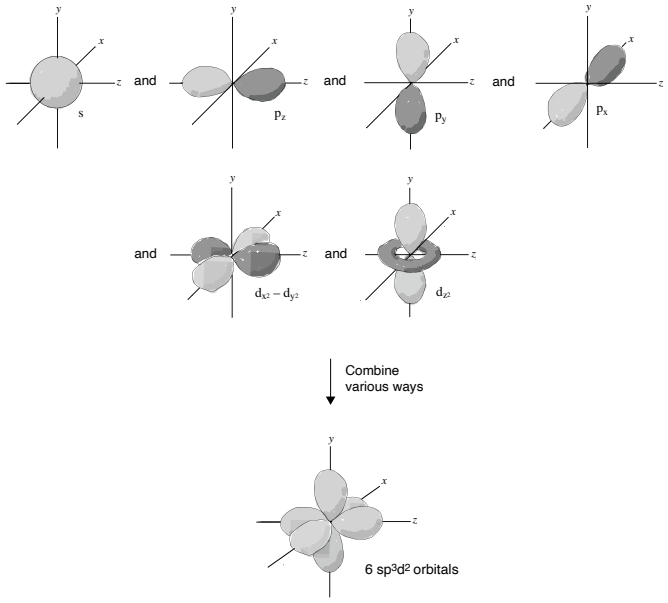


Figure 5.51 Hybridization of Atomic Orbitals in Octahedral Complexes. Combination of an s, three p, the $d_{x^2-y^2}$, and the d_{z^2} orbitals produces six sp^3d^2 hybrid orbitals that can form dative bonds with six ligands, like the hexaaquoiron(III) ion complex shown in Figure 5.49.

While a valence bond model provides an intuitive way to understand the dative bonds of the octahedral complex, a molecular orbital model provides a more accurate way to understand where extra metal electrons end up in metal complexes and the properties they impart. For a basic molecular orbital model of octahedral complexes (**Figure 5.52A**), the atomic orbitals combine in a more complicated way with the ligand orbitals to create six bonding molecular orbitals that are filled by the twelve lone pair electrons from the six ligands. As in the valence bond picture, three d orbitals (the t_{2g} orbitals) do not participate in bonding and remain unchanged. The next highest orbitals are two antibonding orbitals called e_g^* orbitals. The five orbitals in the t_{2g} and e_g^* orbitals are where up to ten of the metal's electrons are placed. These electrons fill these orbitals according to Pauli's Exclusion Principle and Hund's Rule, where sometimes electrons will fill the e_g^* orbitals to maintain unpaired electrons, if the energy gap between the t_{2g} and e_g^* orbitals is small (**Figure 5.52B**). The number of unpaired electrons contributes to whether the metal complex is magnetic or not, and the difference in energies between the highest occupied molecular orbital and the lowest unoccupied molecular orbital relates to how the complex can absorb light energy.

For octahedral complexes like the four iron centers found in hemoglobin (Figure 5.49B, right), the molecular orbital model is more complicated. However, the light-absorbing and magnetic properties of different forms of hemoglobin can partly be explained by its

molecular orbital configuration. Additionally, when one iron coordination complex releases oxygen to become a five-coordinate complex, the changes in the complex's geometry are responsible for a larger structural rearrangement in the hemoglobin protein, which alters oxygen binding by the other three iron centers of hemoglobin.

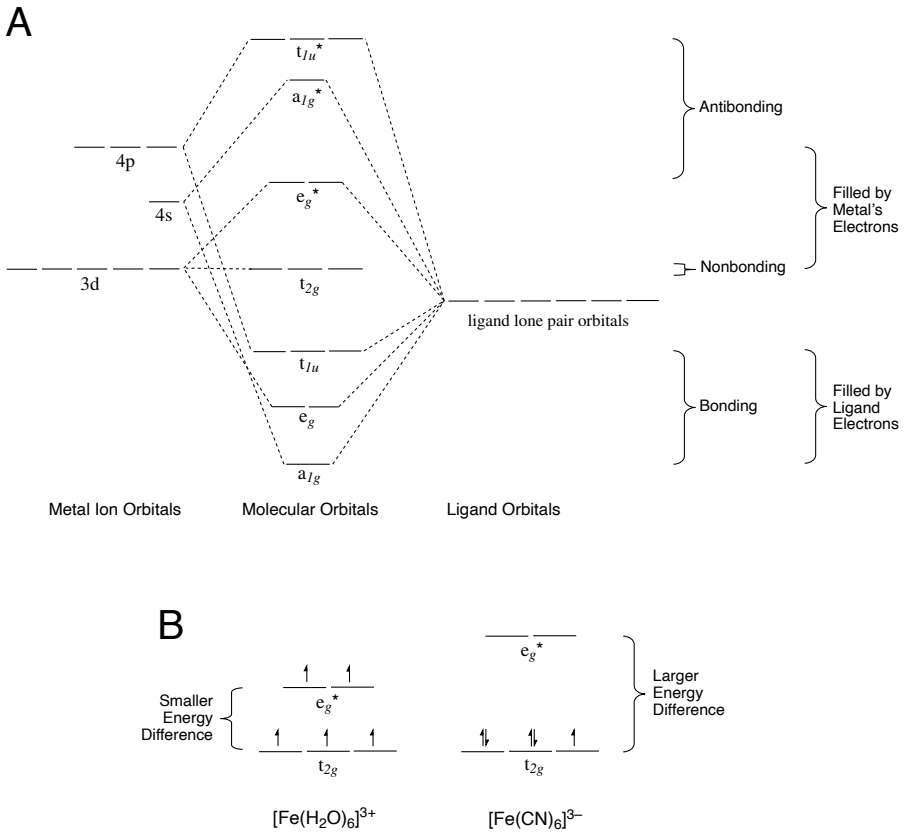


Figure 5.52 Electrons in Octahedral Metal Complexes. A) A Molecular Orbital Diagram of an Octahedral Metal Complex. The twelve electrons of six ligands fill the six molecular orbitals with the lowest energy. The electrons of the metal ion potentially fill the non-bonding orbitals (t_{2g}) and first antibonding orbitals (e_g^*). B) Examples of various ways the t_{2g} and e_g^* molecular orbitals are filled in two different iron(III) octahedral metal complexes. In both complexes, the iron has five electrons to distribute in the t_{2g} and e_g^* molecular orbitals. For hexaaquoiron(III) ion complex (left), one electron is placed in each orbital, to give a high spin complex (five unpaired electron spins). Although the e_g^* orbitals are higher in energy than the t_{2g} orbitals, that energy difference is less than the cost of pairing the electrons in the t_{2g} levels. For a hexacyanoferrate(III) complex, the energy gap between the t_{2g} an e_g^* orbitals is greater. The iron's five electron fill the t_{2g} orbitals, leaving one electron spin unpaired, making it a low spin complex.

F. Further Exploration - Ion Solubility

As mentioned previously, an ion and its counterion may not be soluble in water, limiting its availability to biological systems. In this Further Exploration section, we examine ion solubility of both atomic and molecular ions more in depth. After introducing several new ions, we look at a qualitative approach for describing ion solubility and some more quantitative techniques.

5.20 More Molecular Ions

In addition to the atomic and molecular ions we have previously discussed, many other possible ions can exist in solution. One interesting set of anions is nitrites and nitrates (**Figure 5.53**). These compounds are reminiscent of some of the other molecular anions we've looked at, in that nitrite and nitrate ions have a central atom (here a nitrogen) that is highly oxidized. Specifically, nitrite contains two oxygens (NO^{2-}) and nitrates three (NO^{3-}). Although we will not be discussing these ions after this chapter, they do have an important role in the nitrogen cycle. Bacteria produce these molecules from ammonia generated by nitrogen fixation or decomposition, and for plants, these compounds serve as alternatives to ammonia for nitrogen acquisition. Indeed, nitrates are a common component of plant fertilizers.

Another biologically relevant anion is oxalate. Oxalate is a highly oxidized two-carbon compound ($C_2O_4^{2-}$ or $O_2CCO_2^{2-}$) that looks a bit as though the oxidized carbons from two acetic acid molecules were jammed together (**Figure 5.54**). Oxalates are produced in your own body and are found in many vegetables, fruits, nuts, and grains. Spinach,

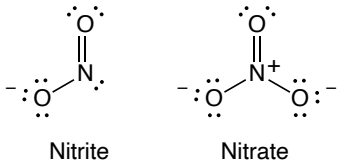


Figure 5.53 Nitrite and Nitrate Ions.

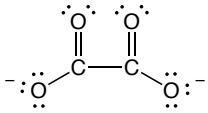


Figure 5.54 An Oxalate Ion.

soy, almonds, potatoes, beets, navy beans, raspberries, and dates are especially high in oxalates. As we will see, oxalates can form insoluble salts with certain cations, and too much oxalate has the potential to remove certain nutrients from food and promote formation of kidney stones (which can also form from other anions). For most people, oxalate levels are not an issue, because the amount of water they drink is sufficient to reduce the concentration of oxalates in their diet, and because certain native gut bacteria metabolize oxalates. However, chronic dehydration, disruption of a body's gut flora, or genetic conditions can make an individual more susceptible to the ill effects of oxalates.

Transition and post-transition metal cations are not plentiful in the body (99% of the human body by weight is oxygen, hydrogen, nitrogen, carbon, calcium, and phosphorus, with sulfur, potassium, sodium, chlorine, and magnesium accounting for an additional ~0.85% of body mass) — nor are they typically abundant in seawater or drinking water. Nonetheless, the body requires trace amounts of many of these cations (or in the case of iron, several grams per person). For other cations, even trace amounts can have detrimental effects.

How much of an ion is present in solution is dictated in part by what counterions are present and to what extent they are soluble. Let's consider the solubility of various ions.

5.21 Solubility Tables

A qualitative way to address the solubility of ions is a solubility table (**Table 5.4**):

	NH_4^+	Na^+	K^+	Mg^{2+}	Ca^{2+}	Al^{3+}	Fe^{3+}	Cu^{2+}	Ag^+	Zn^{2+}	Pb^{2+}
F^-	Sol	Sol	Sol	Ins	Ins	Sol	Slt	Sol	Sol	Sol	Ins
Cl^-	Sol	Sol	Sol	Sol	Sol	Sol	Sol	Sol	Ins	Sol	Sol
Br^-	Sol	Sol	Sol	Sol	Sol	Sol	Sol	Sol	Ins	Sol	Slt
I^-	Sol	Sol	Sol	Sol	Sol	Sol	Rec	Rec	Ins	Sol	Ins
OH^-	Sol	Sol	Sol	Ins	Slt	Ins	Ins	Ins	Slt	Ins	Ins
SO_4^{2-}	Sol	Sol	Sol	Sol	Slt	Sol	Sol	Sol	Slt	Sol	Ins
CO_3^{2-}	Sol	Sol	Sol	Ins	Ins	Rec	Rec	Rec	Ins	Ins	Ins
NO_3^-	Sol	Sol	Sol	Sol	Sol	Sol	Sol	Sol	Sol	Sol	Sol
PO_4^{3-}	Sol	Sol	Sol	Ins	Ins	Ins	Ins	Ins	Ins	Ins	Ins
CH_3COO^-	Sol	Sol	Sol	Sol	Sol	Slt	Sol	Sol	Sol	Sol	Sol
$O_2CCO_2^{2-}$	Sol	Sol	Sol	Ins	Slt	Ins	Ins	Ins	Ins	Slt	Ins

Table 5.4 Ion Pair Solubility Table. "Sol" means soluble, with a solubility of > 1g/100 ml water. "Slt" means slightly soluble, with between a 0.1-1.0 g/100 ml water solubility. "Ins" means insoluble and reflects a solubility of < 0.1 g/100 ml water. "Rec" indicates the compound is reactive and unstable in water. OH^- is hydroxide, SO_4^{2-} is sulfate, CO_3^{2-} is carbonate, NO_3^- is nitrate, PO_4^{3-} is phosphate, CH_3COO^- is acetate, and $O_2CCO_2^{2-}$ is oxalate.

In this table, an ion and a counter ion are selected, and their solubility is read out. For example, if you were interested in whether calcium phosphate is soluble in water, you would find calcium in the list of cations and phosphate in the list of anions and determine that this pair is insoluble. That is, if you had solid calcium phosphate and put it into water, it would only dissolve to a very small extent:

$$Ca_3(PO_4)_2\,(s) \rightleftharpoons 3\,Ca^{2+}\,(aq) + 2\,PO_4^{3-}\,(aq) \qquad (5.4)$$

Note, this indicates the results of the reverse reaction as well. If any significant amount of calcium and phosphate ions are added into a solution, the vast majority of the species will precipitate as solid calcium phosphate:

$$3\,Ca^{2+}\,(aq) + 2\,PO_4^{3-}\,(aq) \rightleftharpoons Ca_3(PO_4)_2\,(s) \qquad (5.5)$$

This insolubility is in contrast to some other possible salts containing either calcium or phosphate ions. For example, solid calcium nitrate salt would be expected to dissolve well in water, as it is listed as soluble on the solubility table:

$$Ca(NO_3)_2\,(s) \rightleftharpoons Ca^{2+}\,(aq) + 2NO_3^-\,(aq) \quad (5.6)$$

Similarly, potassium phosphate salt is water soluble:

$$K_3(PO_4)\,(s) \rightleftharpoons 3\,K^+\,(aq) + PO_4^{3-}\,(aq) \quad (5.7)$$

Because plants need nitrogen, phosphorus, calcium, and potassium (amongst other elements), application of a fertilizer solution containing calcium nitrate (Equation 5.6) and a solution containing potassium phosphate (Equation 5.7), would be a good way to provide these nutrients. However, it would be important to keep these solutions separate. As we saw, calcium phosphate is not very water soluble (Equation 5.4). Thus, if we mixed the calcium nitrate and potassium phosphate solutions, we would lose the calcium and phosphate due to their ability to form a water insoluble salt (not balanced for simplicity):

$$3Ca^{2+}(aq) + NO_3^-(aq) + K^+(aq) + 2PO_4^{3-}(aq) \rightleftharpoons Ca_3(PO_4)_2\,(s) + K^+(aq) + NO_3^-(aq) \quad (5.8)$$

From studying the solubility table, we can identify several trends. The cations listed with a +1 charge (Na^+, K^+, and NH_4^+) are soluble with all of the anions listed. For sodium, potassium, and ammonium ions, this is generally true for any anion, meaning that these ions tend to exist free in aqueous solution. Similarly, several anions are pretty much soluble with all of the cations listed: nitrate is soluble with all of the listed cations; acetate is fully soluble with all the listed cations except aluminum, with which it is slightly soluble; and chloride is soluble with all but silver cations.

Several anions are largely insoluble in water in the presence of the Group 2 cations (Mg^{2+} and Ca^{2+}) and the transition/post-transition metal cations shown (Al^{3+}, Fe^{3+}, Cu^{2+}, Ag^+, Zn^{2+}, Pb^{2+}): Phosphate is insoluble with all of these cations; carbonate is insoluble with these cations, except being slightly soluble with the copper cation; amongst these cations, hydroxide is only slightly soluble with calcium and silver cations; and for oxalate, this anion is insoluble with most of the Group 2 and transition/post-transition metal cations shown, with the exception that it is slightly soluble with calcium and zinc ions.

As previously discussed, there are ramifications of the insolubility of particular ion pairs: The insolubility of phosphate with calcium makes it a good material for the mineral portion of bones (Subsection 3.13); the insolubility of carbonate with calcium (and magnesium) ions in hard water contributes to formation of limescale (Subsection 3.13); and the fact that calcium oxalate is only slightly soluble in water means that too much calcium, too much oxalate, or too little water can result in the formation of kidney stones (Subsection 5.20).

5.22 Equilibrium Expressions and Constants

Solubility tables give a qualitative sense of how soluble a pair of ions will be, but a quantitative description is often useful. One way to do so is to use the solubility concentration of a salt. Solubility concentrations are typically reported as the mass of a salt that can be dissolved in a given volume under certain conditions.

As an example, let us consider the salt calcium oxalate monohydrate, $Ca(O_2CCO_2)\cdot H_2O$ (when calcium oxalate crystallizes, it typically includes one or more molecules of water. The monohydrate, with one water molecule, is the most common form of calcium oxalate

in kidney stones). Calcium oxalate monohydrate is soluble to 0.736 mg in 100 ml of water at 25°C (Table 5.5). This means that for 1 L of water, if there is more than 7.36 mg of the salt present, there will be undissolved calcium oxalate monohydrate. Below that amount, all of the salt will dissolve.

Compound	Anion	Solubility Concentration	K_{sp}
$Ca(O_2CCO_2)\cdot H_2O$	Oxalate	0.736 mg/100 ml	2.54×10^{-9}
$Ca_3(PO_4)_2$	Phosphate	0.0035 mg/100 ml	2.1×10^{-33}

Table 5.5 Solubility Concentrations and K_{sp} Values for Calcium Oxalate and Phosphate.

What is the concentration of the dissolved calcium oxalate in terms of molar concentration? The molecular weight of calcium oxalate monohydrate is 146.1 g/mol, so 0.00736 g of salt in 1L is 50.4 μM. That would be the concentration of calcium oxalate monohydrate molecules, if they were to dissolve in that form. However, the salt dissolves such that for every molecule of calcium oxalate monohydrate, one molecule of calcium cation is generated, one molecule of oxalate is generated, and one water molecule is released. Since the conversion is one to one, there will be up to 50.4 μM of calcium ions and 50.4 μM of oxalate ions in a saturated solution of the salt. For salts with a more complicated stoichiometry, the concentrations would differ. For example, the saturation concentration of tricalcium phosphate, $Ca_3(PO_4)_2$, is 0.0035 mg in 100 ml of water at 25°C (Table 5.5). This corresponds to a molar concentration of 0.114 μM of dissolved tricalcium phosphate. Since every dissolved molecule of this salt generated 3 calcium ions and 2 phosphate ions (Equation 5.4), the molar concentration of the dissolved components is 0.342 μM Ca^{2+} (3 x 0.114 μM) and 0.228 μM of PO_4^{3-} (2 x 0.114 μM).

As discussed in Section F of Chapter 3, systems can exist in an equilibrium between species, such as the equilibrium between dissolved and undissolved salt particles. For a salt like tricalcium phosphate, the dissolution reaction is given by Equation 5.4, and the equilibrium expression for that reaction is:

$$K = \frac{[Ca^{2+}]^3[PO_4^{3-}]^2}{[Ca_3(PO_4)_2]} \tag{5.9}$$

One of the components of this equilibrium expression is a solid, undissolved $Ca_3(PO_4)_2$ salt. It turns out that a solid in equilibrium expressions can be ignored by setting its "concentration" to 1, which generates an equilibrium constant called the solubility product constant, K_{sp} (Why we can do this is beyond the scope of this book, but I will mention that the concentration terms in an equilibrium expression are not actually concentrations, but something called activities. For dilute solute molecules, activities generally have the same value as their concentrations — hence they appear directly in the expression. In contrast, the contribution of the activity of a solid does not change with the amount of solid present, so that term is set to 1).

$$K_{sp} = \frac{[Ca^{2+}]^3[PO_4^{3-}]^2}{[\ 1\ ]} = [Ca^{2+}]^3[PO_4^{3-}]^2 \tag{5.10}$$

For tricalcium phosphate, we can plug in the equilibrium concentrations of the ions we previously calculated to determine the value of K_{sp} for this salt:

$$K_{sp} = [0.342 \times 10^{-6}]^3[0.228 \times 10^{-6}]^2 = 2.07 \times 10^{-33} \tag{5.11}$$

Instead of using measured equilibrium ion concentrations to calculate a solubility product constant, the K_{sp} values of many salts are published and readily available.

With K_{sp} values and the stoichiometry of dissolution, we have another way to calculate the equilibrium concentration of the ions. For example, for tricalcium phosphate, if the concentration of dissolved salt at equilibrium is x, then the solubility product constant is:

$$K_{sp} = [3x]^3[2x]^2 = 2.07 \times 10^{-33} \tag{5.12}$$

Solving for x, we get that the equilibrium concentration of dissolved salt is 0.114 μM, meaning the equilibrium concentration of Ca^{2+} is 0.342 μM (3 x 0.114 μM) and the equilibrium concentration of PO_4^{3-} is 0.228 μM (2 x 0.114 μM).

Another way a solubility product constant can be useful is to predict the concentration of a salt's ion when the concentration of the counterion is known. For example, suppose we added tricalcium phosphate salt to a 100 μM solution of calcium chloride, $CaCl_2$. How much phosphate dissolves? Calcium chloride is fully soluble in water, so the equilibrium concentration of calcium ion before the tricalcium phosphate salt is added is 100 μM, and would not change significantly, even if the tricalcium phosphate dissolved to its fullest extent. Thus, we can plug that value into Equation 5.12, with tricalcium phosphate's K_{sp}:

$$K_{sp} = [Ca^{2+}]^3[PO_4^{3-}]^2 = [100 \times 10^{-6}]^3[PO_4^{3-}]^2 = 2.07 \times 10^{-33} \tag{5.13}$$

We can solve for the phosphate concentration, and see that it is 0.0000455 μM. This is roughly 5,000 times less phosphate than is present compared to when the calcium in the calcium chloride solution was not present (PO_4^{3-} without $CaCl_2$ was 0.228 μM). With the calcium chloride, all of the excess calcium ultimately suppresses the ability of the tricalcium phosphate to dissolve, a phenomenon known as the common ion effect.



CHAPTER 6
Acids and Bases

Motivation and Overview: Too much acid or base is deleterious to biological systems. In this chapter, we explore why that is the case and how organisms deal with such a threat. In the process, we examine how the presence of acids and bases in water generates protons and hydroxide ions, ways to describe and measure the concentrations of these species, and how various acids and bases differ in their ability to produce protons and hydroxide ions.

A. Effects of Acids and Bases on Living Things

In the previous chapter we saw that acids give up protons and bases take them. When biological molecules interact with such compounds, the biomolecules are frequently changed in ways that can harm the organism. Let's look at some examples of how and why this is the case.

6.1 Organismal Effects

Most organisms do not thrive when their environment becomes highly acidic - that is, when there is a large excess of protons. Exposure to extremely acidic solutions, like a concentrated sulfuric acid solution, can cause burns to the skin, eyes, and throat and can lead to permanent damage or death. Such solutions can be found in lead-acid batteries used in many vehicles with combustion engines (**Figure 6.1A**). Sulfuric acid, as well as other acids, can also be found at lower concentrations in acidic rainwater known as acid rain. Acid rain occurs when specific pollutants are present in the air. During the 1980s, acid rain was prevalent enough to cause significant environmental damage, and it led to the local elimination of fish from Scandinavian surface waters and forest damage in Europe (**Figure 6.1B**). Regulation of industrial emissions of pollutants like sulfur dioxide — which forms sulfuric acid after oxidation in the atmosphere — has significantly reduced these compounds in the air and has largely eliminated the problem of acid rain. Nonetheless, slow acidification of ocean waters continues and is largely due to increases in global concentrations of carbon dioxide (described more in Subsection 6.13). This acidification is believed to have contributed to problems such as reduced calcification in corals and shellfish, as well as broader disruption of marine food webs.

Just as living organisms cannot handle exposure to high levels of acidity, they cannot handle high levels of basicity. The extremely basic conditions of concentrated sodium hydroxide solutions can cause severe burns to the skin, eyes, and throat (**Figure 6.1C**). Such conditions are present in some cleaning products, such as drain cleaners. Additionally, they can be a byproduct of commercial processes that make cement, steel, batteries, and electricity at coal-fired fuel plants. These byproducts can be dangerous if not properly disposed of.

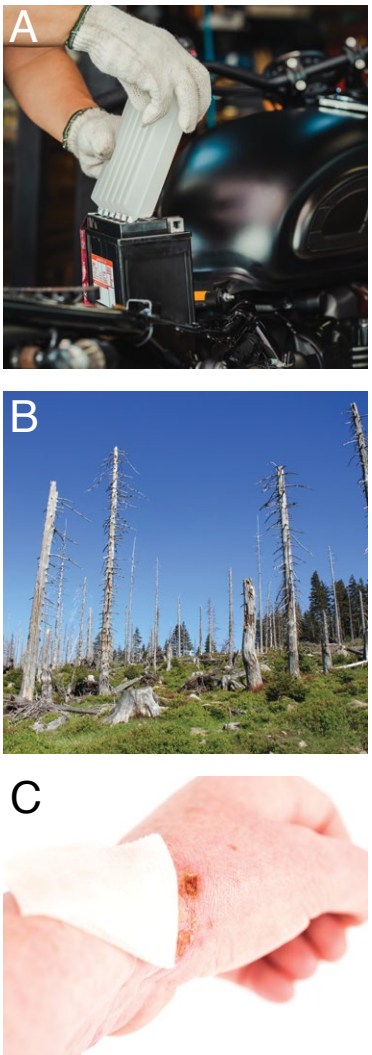


Figure 6.1 Highly Acidic or Basic Solutions and Their Effects. A) Battery acid in a rechargeable lead-acid battery is composed of 30-50% sulfuric acid in water and is very acidic. Shown is battery acid being added to a motorcycle battery. B) Polish forest damaged by acid rain. C) Chemical burn due to a highly basic sodium hydroxide solution.

6.2 Molecular Effects

Highly acidic and basic solutions affect biological molecules in many complicated ways. As a simple example, let's consider what they can potentially do to the structure of a protein. Proteins are the workhorses of the cell, performing a range of structural and functional tasks. As we will detail later (Chapter 15 of Volume III), proteins are long, linear strings of chemical compounds called amino acids, and most proteins fold up into specific, well-defined shapes to perform their cellular roles (**Figure 6.2A**). Acidic and basic groups are frequently found on the surface of folded proteins, and when proteins are exposed to large amounts of protons in solution, the protein's basic groups can pick up these protons, increasing the overall positive charge of the protein (**Figure 6.2B**). As positive charges repel other positive charges, this can disrupt the protein's structure, leading to its unfolding and loss of its ability to function properly. Exposing proteins to highly basic conditions leads to deprotonation of their acidic groups and to an overall increase in the negative charges in a protein (**Figure 6.2C**). This also disrupts protein structure, leading to loss of its function.

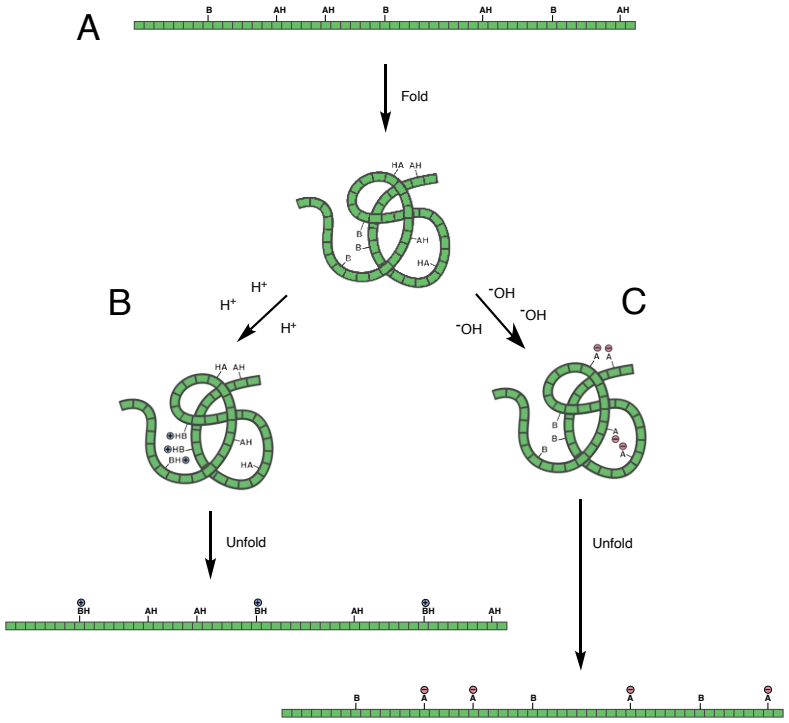


Figure 6.2 Schematic of Acid or Base Mediated Unfolding of Proteins. A) A protein is a linked series of amino acids, some of which can have acidic groups, HA (with some shown oriented in the opposite direction: AH), or basic groups, B. This linear chain can fold up into a specific three-dimensional shape, where adopting this shape is required for the protein to perform its functions. B) Addition of protons from an acid can protonate the basic group, causing them to be more positively charged. The protein can unfold to minimize the repulsion between these charges. C) Addition of base molecules, here hydroxide ions, can remove protons from the protein's acidic groups. This creates regions of greater negative charge and can also lead to unfolding of the protein. In an unfolded state, proteins can no longer perform their functions, and additionally may become aggregated or degraded.

B. pH

As protons influence the behavior of biological systems, it is important to be able to describe quantitatively how much is in solution. The standard way to do so is using the pH scale. However, before we delve into that, it's useful to consider proton concentrations in molar terms.

6.3 Molar Concentrations of Protons

In Chapter 2 we introduced molar concentration: the number of dissolved particles of a substance (in moles) in a given volume of liquid (such as a liter of water). We saw that we could use this idea to quantify how much sodium ion is present in various solutions (Table 3.1). In seawater, sodium ion concentration is roughly 0.5 M (0.5 moles of sodium cations per 1 liter of seawater, or about 3×10^{23} sodium ions per liter of seawater). This concentration is quite high, as roughly 1 in every 100 molecules in seawater is a sodium ion, and this is about 1/10th of the maximum concentration of sodium ions that can be dissolved in water. In tap water, the molar concentration of sodium ions is substantially

lower (and variable). A concentration of 0.002 M (2 mM) Na^+ is typical and is roughly 1/250th the amount found in the same volume of seawater.

Protons are cations, like sodium ions, and their concentration in various solutions can be described in molar terms (**Figure 6.3**). A 1.0 M solution of protons is considered a highly acidic solution and would need to be handled with care. Cola sodas are fairly acidic, having proton concentrations between 0.001-0.010 M (1-10 mM). Pure water has quite a low acidity, having a proton concentration of 1 x 10^{-7} M (0.1 μM).

Describing proton concentration in molar terms is entirely valid, and in many contexts it is the clearest approach. Nonetheless, partly by convention, partly for practical reasons, the pH scale is widely used. What is it?

6.4 Understanding a Log Scale

Before we define the pH scale, let's motivate its creation with an example. Suppose we were interested in how stable a compound is at different proton concentrations. So we start with a solution with a relatively high proton concentration, 0.1 M H^+, and make 10-fold dilutions of this solution to test: 0.01 M, 0.001 M, 0.0001 M, 0.00001 M.

We get our results and want to plot them on a graph. The first issue that arises is: how do we do that? If the x-axis is going to be our molar proton concentration, we could make the distance between each tick marks be 0.1 M (**Figure 6.4A**). In this case, we quickly

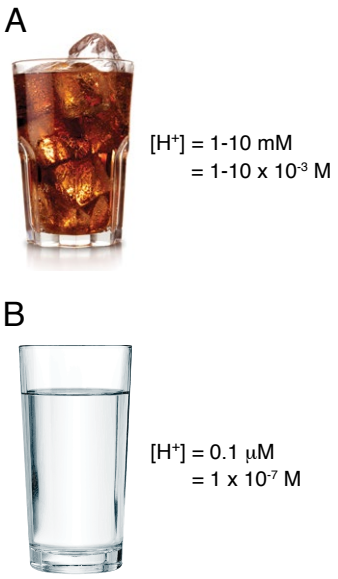


Figure 6.3 Molar Proton Concentrations of Colas and Pure Water. A) Cola beverages have molar proton concentrations between 1-10 mM. This is 10,000 to 100,000 times greater than B) the molar proton concentration of pure water, which is about 0.1 μM.

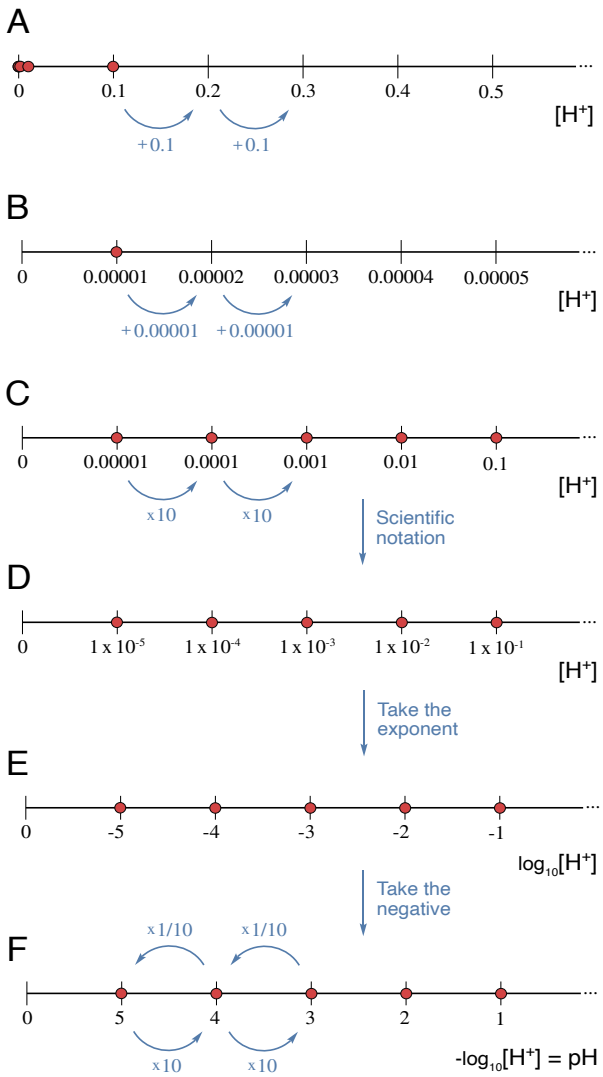


Figure 6.4 Different Ways to Plot Proton Concentrations. Five molar proton concentrations (red circles): 0.1 M, 0.01 M, 0.001 M, 0.0001 M, and 0.00001 M are shown on different concentration scales. A) A linear scale with each tick mark being an increase in 0.1 M. B) A linear scale with each tick mark being an increase in 0.00001 M. C) A logarithmic scale with each tick mark being a 10-fold increase in concentration. D) The same scale as shown in part C, but in scientific notation units. E) The same scale as shown in part D, but using only the exponent. This is equivalent to taking the log base 10 value of the concentrations shown in D. F) The same scale as part E, but multiplied by -1 to make all values positive. Somewhat confusingly, in this scale, the pH scale, the most concentrated proton solution has the lowest number, and concentration decreases 10-fold in going from 1 to 2, 2 to 3, etc.

find that we can't really distinguish between the 0.001 M, 0.0001 M, and 0.00001 M data points. We decide instead to use a tick-mark spacing matching the smallest concentration we want to represent, with each tick being 0.00001 M apart (**Figure 6.4B**). This works fine for our lowest concentration, but to put our highest concentrations on the same graph requires a very long graph. In fact, on the scale of Figure 6.4B, the graph would have to be more than 123 meters to contain the highest proton concentration of 0.1 M. Clearly this isn't practical. One way to solve this problem is not to use a linear scale for our x-axis. Instead of each tick representing some additional increment of a given amount (+0.1 M in Figure 6.4A, +0.00001 M in Figure 6.4B), each tick mark could represent a multiplicative increment. In this specific case, we could make each tick mark represent a 10-fold increase in molar concentration (**Figure 6.4C**). On such a graph, all five data points could be represented on a single well-spaced graph.

Having solved that problem, we might worry about a secondary problem: The units on our graph are a bit unwieldy — 0.00001 M has a lot of zeros; and the numbers are easily confused - did the last data point have 3 or 4 zeros before the 1? One way to simplify things slightly is to convert all of our concentrations to scientific notation, making them: 1×10^{-1} M, 1×10^{-2} M, 1×10^{-3} M, 1×10^{-4} M, and 1×10^{-5} M (**Figure 6.4D**). Simpler yet would be just to use the exponent alone (**Figure 6.4E**). Since folks tend not to like negative numbers, let's take the exponent, but drop the sign. Now our values are: 1, 2, 3, 4, and 5 (**Figure 6.4F**). In this graph the last point (pH 1) represents a concentration of 0.1 M, and moving one unit along the graph (say from 1 to 2, or from 2 to 3) represents a 10-fold decrease in proton concentration, and the lowest value has the highest proton concentration. What we created is the pH scale.

We can formalize what we have done as an equation. From the proton concentration in molar units (Figure 6.4D), we took the exponent of the power of 10 representation of that concentration (Figure 6.4E): for example, the power of 10 for 1×10^{-1} is -1. This is equivalent to taking the log base 10 of the concentration ($\log_{10}[H^+]$, which is typically written just as $\log[H^+]$). Because almost all proton concentrations we encounter will be less than 1 M, their log values will be a negative number: for a 0.1 M proton solution, the $\log[H^+]$ will be $\log[0.1] = \log[1 \times 10^{-1}] = -1$. To ensure that these values are positive, we can take the negative of what we just calculated (Figure 6.4F): the -1 we got from our 0.1 M proton solution becomes 1 when we multiply it by a negative. The new quantity we have calculated is the pH of the solution:

$$\mathrm{pH} = -\log[\mathrm{H}^+] \tag{6.1}$$

To summarize, the pH scale is just a proton concentration scale in which a change in a single pH unit corresponds to a 10-fold change in molar proton concentration, and increasing values of pH indicate more dilute proton concentrations. To make sure we have a good feel for these ideas, it's useful to do some example problems.

6.5 pH Calculations

Suppose we have a cola that has a proton concentration of 0.001 M. What is its pH? To apply the pH equation (Equation 6.1), we need to follow three steps (**Figure 6.5A**): first, make sure our proton concentration is in molar units; second, take the log base ten of this concentration; and third, multiply the value by negative one. For our cola, the concentration, 0.001 M, is already in molar units, and its value in scientific notation is 1×10^{-3} M. At this point, we need to take the log of the concentration. While this could be done on a calculator, just by inspection we can see that the power of 10 that will give us 1×10^{-3} is simply -3 (more generally, if we have a concentration in the form of 1×10^{x}, the log base ten of that concentration will be x). All we have left to do is multiply -3 by -1 to get a pH value of 3. It should be noted that pH values are almost never negative. If you end up with one, make sure you didn't forget this last step.

A) Proton Concentration to pH

1) Express proton concentration in molar units
2) Take $\log_{10}$ of proton concentration
3) Take the negative value

B) pH to Proton Concentration

1) Take the negative of the pH
2) Raise 10 to this power
3) Adjust to desired concentration units from molar units

Figure 6.5 Steps for Calculating pH from Proton Concentration and Vice Versa.

As another example, we saw that typical colas range in proton concentrations from 0.001 M to 0.01 M (Figure 6.3). We just calculated the pH of the 0.001 M proton concentration. What is the pH for the 0.01 M concentration? This solution's molar concentration is 1 x 10^{-2} M, meaning that its pH will be 2. Thus, typical colas have pH values between 2 (0.01 M) and 3 (0.001 M). Note, these two pH values differ by 1 pH unit (pH 3 versus 2) and correspond to a 10-fold difference in molar proton concentrations (0.001 M versus 0.01 M, respectively). Additionally, because the negative log of molar proton concentration is used to calculate pH, increasing pH values correspond to lower proton concentration, and conversely, a lower pH indicates a higher proton concentration. Indeed, the molar proton concentration at pH 2 (0.01 M) is greater than that at pH 3 (0.001 M).

Both of our pH calculations so far have been relatively straightforward, as the concentrations have started in molar units and can be written in the form of 1 × 10^{x}. Let's consider a slightly more complicated example. Suppose we had a 43 μM solution of protons. What would its pH be? The first step is to express the concentration in molar units. 1 μM is 1 x 10^{-6} M, so this proton concentration would be 43 x 10^{-6} M, which is equal to 4.3 x 10^{-5} M (divide 43 by 10 and then multiply 10^{-6} by 10). At this point, we want the negative log of the concentration and could directly plug this into a calculator. Before doing that, though, let's estimate the answer. 4.3 x 10^{-5} M is more than 1 x 10^{-5} M and less than 10 x 10^{-5} M — which is equal to 1 x 10^{-4} M. The pHs for these values are 5 and 4, respectively. Thus, we expect the pH of 4.3 x 10^{-5} M to be somewhere between a pH of 4 and 5. When we use a calculator to determine the pH of 4.3 x 10^{-5} M, we get a value of 4.4, which is within our estimated range.

If we have a pH and want the proton concentration, we effectively reverse the steps we took to calculate the pH (**Figure 6.5B**): reverse the sign of the pH value and then raise 10 to that value. For example, if the pH is 1.0, we convert that to -1.0 and raise ten to -1.0, i.e. 10^{-1}. 10^{-1} M is 0.1 M so a pH of 1.0 corresponds to a 0.1 M solution of protons. As a slightly more complicated example, if we had a pH of 6.2, we would raise 10 to -6.2 to get $[H^+] = 10^{-6.2}$ M = 6.3 x 10^{-7} M = 0.63 μM.

6.6 Protons, Water, and Hydroxide Ions

As we just discussed, as the pH of a solution goes down, the number of protons present increases and the solution is considered more acidic. Equivalently, when the pH of a solution increases, the concentration of protons in solution decreases and the solution is considered less acidic. Aqueous solutions with increasing pHs are also considered more basic. What do we mean by being more basic, and why does an increase in "basicity" occur?

Consider a sample of pure water, that is, water in which nothing else is present. If we measured the pH of such a sample at room temperature, the pH would be very close to 7. This means that the concentration of protons in pure water is approximately 1 x 10^{-7} M. Where do these protons come from? As mentioned in Chapter 5, water is considered an acid - a compound that can lose a proton:

$$H_2O \rightleftharpoons H^+ + {}^-OH \tag{6.2}$$

This deprotonation reaction does not proceed to a significant extent, as only a small concentration of protons (1 x 10^{-7} M) is generated compared to the concentration of the water molecules (roughly 55 M). Nonetheless, some protons are made. It is important to note that in this process another ion is generated, a hydroxide ion. Here, the concentration of hydroxide ion (1 x 10^{-7} M) is the same as the proton concentration, because when one proton is generated by the dissociation of a water molecule, one hydroxide ion is left behind.

Just as we could use pH to describe the proton concentration of a solution, an analogous term, the pOH, can be used to characterize the hydroxide ion concentration in solution. Indeed, the definition of pOH is nearly identical to that of pH, where instead of the molar proton concentration, we use the molar hydroxide concentration:

$$\text{pOH} = -\log[\text{OH}^-] \tag{6.3}$$

For our sample of pure water with 1 x 10^{-7} M hydroxide ions, the pOH would be 7. Hydroxide ion is a base, as it can readily pick up a proton in the reverse of Equation 6.2:

$$H^+ + {}^-OH \rightleftharpoons H_2O \tag{6.4}$$

Thus, an excess of hydroxide ions in aqueous solution causes the solution to be considered basic. In pure water, the fact that there are an equal number of protons and hydroxide ions means that the basicity of the hydroxide ions is offset by the acidity of the protons. Hence, the solution is considered neutral.

If a solution is not neutral, how much hydroxide ion is present? It turns out, for reasons detailed in Further Exploration Section E, there is a relationship between the proton and hydroxide concentrations that holds in all aqueous solutions: the pH and pOH add up to a constant value of 14 at room temperature:

$$\text{pH} + \text{pOH} = 14 \tag{6.5}$$

We can see this is the case for pure water: the pH and pOH are 7, adding up to 14.

What about a solution that is very acidic, like one with a pH of 1? According to Equation 6.5, if the pH is 1, the pOH of that solution must be 13. In such a solution, there is a very large proton concentration (1 x 10^{-1} M) and a very small hydroxide concentration (1 x 10^{-13} M).

What about a solution that has a very high hydroxide concentration, such as one with a pOH of 1? Using Equation 6.5 we see that the pH of that solution must be 13, meaning that there is a very low proton concentration (1 x 10^{-13} M) and a very large hydroxide concentration (1 x 10^{-1} M).

In general (**Figure 6.6**), Equation 6.5 says that when proton concentrations are high, hydroxide concentrations will be low, and vice versa. Thus, when the pH of a solution is below 7, the solution is considered acidic, because proton concentration exceeds hydroxide

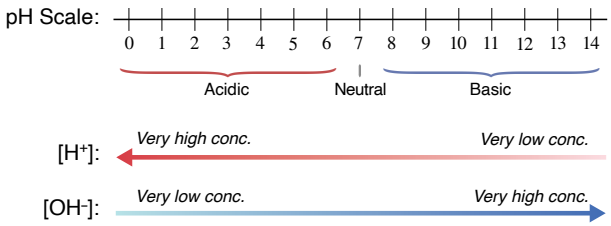


Figure 6.6 Relative Amounts of Protons and Hydroxides Across the pH Scale. Note, the pH scale can be negative or exceed 14.

concentration. When the pH of a solution is above 7, the solution is considered basic, because the hydroxide concentration exceeds the proton concentration. And at pH 7, where the proton and hydroxide concentrations are equal, the pH is considered neutral. The lower the pH value, the more acidic the solution. The higher the pH value, the more basic. It should be mentioned that the informal term alkaline is often used in place of basic; note that alkalinity has a more precise meaning in quantitative chemistry that we will not cover here. Thus, if a solution is described as being highly alkaline, it is a very basic solution with a high concentration of hydroxide ions.

6.7 Measuring pH and Common Values

Now that we have a better sense of what the pH scale describes, how is it measured? Most techniques reporting pH do so by utilizing the protons present in solution in some way. One versatile and quantitative way to measure pH in a laboratory setting is a pH meter (**Figure 6.7A**). Here, a pH probe is able to exploit the difference in proton concentration inside and outside of the probe to create an electrical potential difference whose magnitude can be correlated to the pH. A less quantitative but potentially more portable approach is to use pH indicator dyes in solution or bound to paper (**Figure 6.7B**). These compounds change color at specific pH values depending on their own proton-binding properties. With combinations of dyes, the color of the dye solution or paper can roughly indicate the solution pH.

Interestingly, we all happen to carry a pH detector with us, our tongue (**Figure 6.7C**). Specific protein receptors in some of our taste buds are sensitive to protons, and we perceive solutions with high concentrations of protons (low pHs) as being sour. Although we do not appear to have receptors in our mouths for high concentrations of hydroxide ions, there are receptors that are sensitive to a number of compounds that are basic, such as those containing nitrogen. These compounds register as being bitter tasting, and it is thought that the ability to detect these compounds evolved to discourage their ingestion, as many are produced in plants as defense molecules and are toxic in high doses.

What are typical pH values for various substances? As shown in **Table 6.1**, in the low pH range are highly acidic substances, such as stomach acid (pH 1.5-2.0), which is full of hydrochloric acid, and sour beverages, like lemonade (pH 2.6), that have a high concentration of citric acid. Pure water is neutral (pH 7.0), and tap water varies near neutrality depending on what other substances are dissolved in it (pH 6.5-8.5). Biological fluids tend to be slightly more basic than pure water, with the interior of the cell having a pH around 7.2 and blood having a pH of 7.35-7.45. At the higher end of the pH scale are solutions

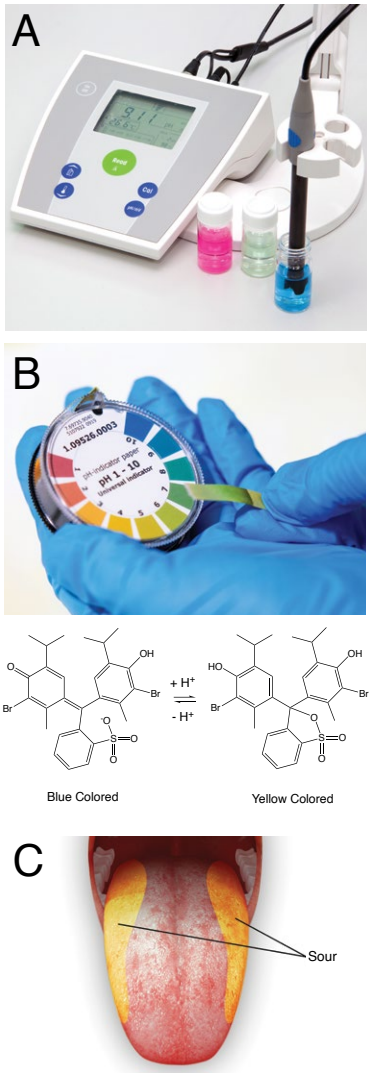


Figure 6.7 Methods of Measuring pH. A) A pH meter reads the pH of a solution with a pH probe. This probe is made of two separate electrodes – one held at a constant pH and one exposed to the pH of the solution via a membrane that is selectively permeable to protons. When a difference in proton concentration exists between the electrodes, protons will move into or out of the membrane in response, creating a potential difference (See Section 3.16). This potential difference is measured by the meter and, when calibrated against known pH standards, correlated to a specific pH value. B) pH paper (top) can be dipped into a solution to determine its pH. The pH paper has one or more pH-sensitive dyes in it (the pH paper shown has multiple dyes), where changing the protonation state of the dye molecule changes its color. For example (bottom), the dye bromothymol blue is blue when significantly deprotonated (roughly pH 7.5 and above), but is yellow when predominantly protonated (roughly pH 6.0 and below). Between these pH values a mixture of protonated and deprotonated dye is present, giving the solution a greenish appearance. Other dyes change protonation state and color at other pH values. Note, in the chemical structure of bromothymol blue, we use some shortcuts for representing the molecule that we will not discuss until Chapter 7 of Volume II. C) Taste receptor cells in taste buds capable of detecting sour taste contain receptor proteins, such as Otop1. This proton-selective ion channel allows movement of hydrogen cations across the cell membrane, similar in concept to the way that sodium and potassium ion channels can allow their respective ions to pass through membranes.

Substance	pH
Stomach Acid	1.5-2
Cola Drink	2-3
Lemonade	2.6
Tap Water	6.5-8.5
Pure Water	7.0
Cell Interior	7.2
Blood	7.35-7.45
Ammonia Solution	11
Drain Cleaner	14

Table 6.1 Typical pH Values of Various Substances.

of ammonia, where this basic compound brings the pH to 11. A very basic, and corrosive, solution of sodium hydroxide can be found in some drain cleaner preparations, and the pH of these solutions is very high, having pHs around 14.

C. Strengths of Acids and Bases

When protons are added to water, their concentration increases and the pH of the solution drops. Where might these protons come from? We've seen that acids are defined as compounds that can donate a proton to solution, so adding an acidic compound to a solution will lower the solution's pH. However, not all acids are equally effective in releasing protons.

6.8 Acids With Different Strengths

As an example of an acid that generates a significant amount of protons, suppose we add concentrated hydrochloric acid to pure water to an initial concentration of 0.1 M HCl. After a little bit of time and mixing, we could measure the solution's pH with a pH meter and see that it is about 1.0. From this pH, we can calculate the concentration of protons present and find that $[H^+]$ = 0.1 M. This is the same concentration of HCl initially present, so every molecule of HCl added dissociated into one proton and one chloride. That is, the extent of acid deprotonation is 100% (**Figure 6.8A**).

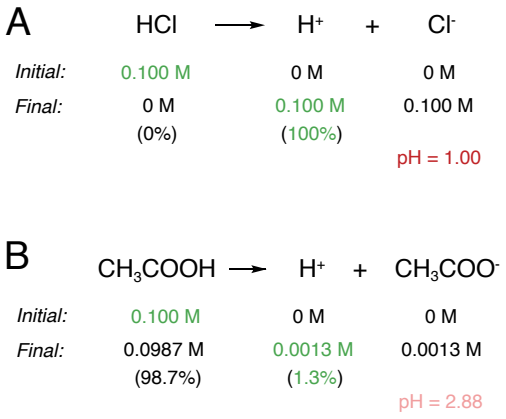


Figure 6.8 Extent of Dissociation of Different Acids. Starting from a 0.1 M solution of A) hydrochloric acid, or B) acetic acid, the hydrochloric acid dissociates fully (100%), while the acetic acid dissociates only to a limited extent (~1.3%).

In contrast, consider what happens when we add acetic acid to pure water at an initial concentration of 0.1 M. The pH of this solution is 2.88 - significantly less acidic. In fact, when we calculate the molar proton concentration, we find that it is only 0.0013 M. This represents an extent of dissociation of only 1.3%. That is, for every 100 acetic

acid molecules we started with, about 1 becomes deprotonated in water, while about 99 remain protonated (**Figure 6.8B**).

As an even more extreme example, recall that in pure water the concentration of protons is 1 x 10^{-7} M. These protons came from dissociation of a water molecule into a proton and hydroxide ion (Equation 6.2). As the concentration of water molecules in pure water is about 55 M, this means that only 1 in about half a billion water molecules gives up a proton in solution, an extent of proton dissociation of about 0.0000002%.

These examples clearly demonstrate that acids can be better or worse at donating a proton. This situation is similar to the water solubility of salts that we have discussed in previous chapters. For example, a salt like sodium chloride fully dissociates into its ions when added to water (**Figure 6.9A**). On the other hand, the salt, calcium carbonate, almost does not dissociate at all when the same amount is added to water (**Figure 6.9B**).

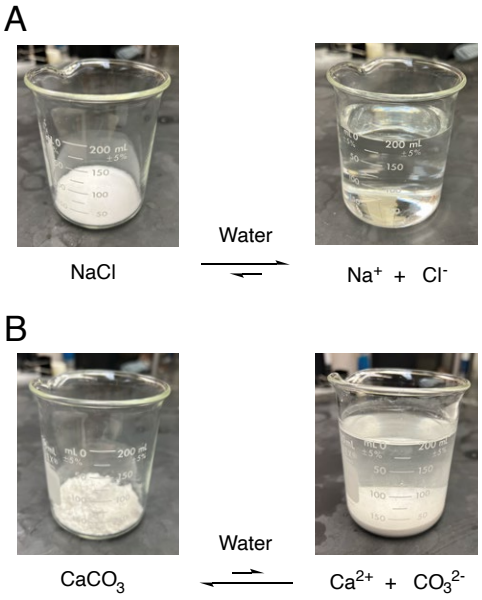


Figure 6.9 Extent of Dissociation for Different Salts. 200 ml of water were added to 20 grams of either A) sodium chloride or B) calcium carbonate. The sodium chloride fully dissolves/dissociates, while the calcium carbonate barely does (some remains undissolved and suspended in the water, giving it a slightly cloudy appearance). Sodium chloride is the main component of table salt, while calcium carbonate is a major component of limescale, chalk, and marble.

To understand why various acids are better or worse at giving up their proton, we will have to develop some additional concepts and wait until Chapter 11 in Volume II. Nonetheless, we can group acids (and bases) into categories, based on their behavior.

6.9 Strong and Weak Acids and Bases

We can classify any acid that fully dissociates in water as a strong acid. There are only a handful of such acids, and for those we've discussed, there are only two: hydrochloric acid, and the first deprotonation of sulfuric acid (**Table 6.2**).

Any acid that isn't a strong acid can be considered a weak acid. That is, the extent of proton dissociation of these acids is less than 100%. This can include acids like acetic acid, water, carbonic acid, and phosphoric acid.

It should be noted that weak acid is a pretty broad category, and there are significant differences in how "weak" these acids are (Table 6.2). As we saw (Subsection 6.8), acetic acid qualifies as weak, because it is dissociated to only a couple of percent in water. However, water itself is a really weak acid, as only a minuscule fraction of water molecules end up releasing a proton in solution. Ranking weak acids like carbonic and phosphoric acid is slightly more complicated, because they have multiple acidic sites. Carbonic acid can donate two protons, but both sites are effectively less acidic than acetic acid and more acidic than water. The first acidic group of phosphoric acid is relatively strong, as it dissociates to a

substantially greater extent in water than acetic acid. Phosphoric acid's second acidic group is a weak acid similar in strength to the first site of carbonic acid, and the third acidic group is in the same general range as the second site of carbonic acid, though modestly weaker. Exactly how "weak" various acids are can be made quantitative, and if you are curious, that is something discussed in Further Exploration Section E of this chapter.

Acid	Acid Strength	Conjugate Base
HCl	Strong	Cl^-
H_2SO_4	Strong, Weak	HSO_4^-, SO_4^{2-}
CH_3COOH	Weak	CH_3COO^-
H_2O	Weak	^-OH
H_2CO_3	Weak	HCO^{3-}, $CO3^{2-}$
H_3PO_4	Weak	$H_2PO_4^-$, HPO_4^{2-}, PO_4^{3-}

Base	Base Strength	Conjugate Acid
NaOH	Strong	H_2O
KOH	Strong	H_2O
NH_3	Weak	NH_4^+
CH_3NH_2	Weak	$CH_3NH_3^+$
$CH_3CH_2NH_2$	Weak	$CH_3CH_2NH_3^+$

Table 6.2 The Strength and Conjugates of Various Acids and Bases.

The addition of acids to a solution lowers the pH by generating protons. Bases raise the pH of an aqueous solution by generating hydroxide ions. Thus, if a strong acid delivers a proton for every acid molecule, a strong base would be one that makes a hydroxide for every base molecule added. The only strong bases we will be concerned with are the hydroxide salts, sodium hydroxide and potassium hydroxide. These compounds are strong bases, because when they are dissolved in water, they fully dissociate into a hydroxide ion and a singly charged cation.

The other bases that we have dealt with are all weak bases, in that the base does not generate a hydroxide ion for every base added. For example, when the bases ammonia, methylamine, or ethylamine are added to water, they do increase the pH of the solution, showing that hydroxide ions are being generated. However, the magnitudes of the pH change indicate incomplete water deprotonation by these nitrogen-containing compounds. For example, a 0.1 M ammonia solution has a pH of about 11 (pOH of 3), instead of a pH of 13 (pOH of 1) that would be expected if every ammonia molecule added to the water became protonated.

6.10 Conjugate Acids and Bases

The number of acids and bases we know doubles, if we include what are known as conjugate acids and conjugate bases. Let's see why with an example.

If we add acetic acid to water to a concentration of 0.1 M, we have seen that it will spontaneously, though incompletely (Figure 6.8B), dissociate into a proton and an acetate ion:

$$CH_3COOH \rightleftharpoons H^+ + CH_3COO^- \qquad (6.6)$$

This process is reversible — if an acetate ion and a proton encounter each other, they can combine to form an acetic acid molecule. In this reverse reaction, the acetate acts as a

base, picking up a proton. This is a general phenomenon, in that any deprotonated acid can pick up a proton as a base. We call the deprotonated form of an acid the conjugate base of the acid, or simply the conjugate base. Thus, every acid has a conjugate base (**Figure 6.10A**). For acetic acid, its conjugate base is acetate (**Figure 6.10B**). A list of the conjugate bases of the acids we have discussed is shown in Table 6.2.

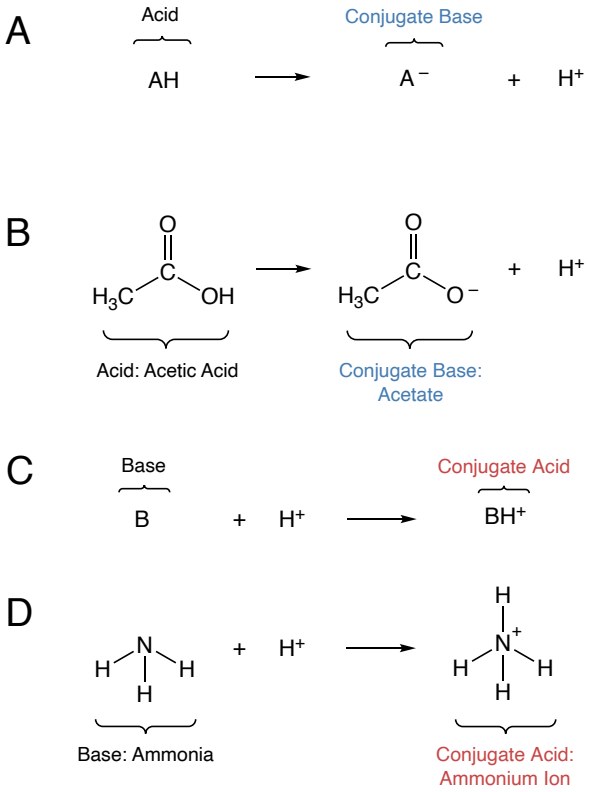


Figure 6.10 Acids, Bases, and Their Conjugates. A) Deprotonation of an acid produces its conjugate base, such as B) the dissociation of acetic acid to make acetate. C) The protonation of a base produces its conjugate acid, such as D) the protonation of ammonia to make ammonium ion.

A similar logic applies to bases. When a base becomes protonated, the protonated form can lose that proton. This protonated form of a base is its conjugate acid (**Figure 6.10C**). For example, for the base ammonia, its conjugate acid is ammonium ion (**Figure 6.10D**). That is, when ammonia becomes protonated, it has the capacity to donate that proton as an acid. A list of conjugate acids for the bases we have discussed is shown in Table 6.2.

The strength of a given acid or base allows us to make predictions about the strength of its respective conjugate base or acid. Specifically, for a strong acid or strong base, its conjugate form will be very weak, and vice versa. This is easiest to see with examples for each case.

A strong acid has a very weak conjugate base: The strong acid HCl has chloride as its conjugate base, a very weak base:

$$HCl\ \textit{(strong acid)} \rightleftharpoons H^+ + Cl^-\ \textit{(very weak conjugate base)} \qquad (6.7)$$

The fact that the chloride ion is a weak conjugate base follows directly from the definition of a strong acid. In water, the proton and chloride generated from HCl do not significantly re-associate. If they did, HCl dissociation would not be complete and hydrochloric acid would not be considered a strong acid. That is, a strong acid wants to give up its protons, so its conjugate base does not want to pick them back up. It can also be shown experimentally, and perhaps intuitively, that chloride ions are very weak bases. If table salt, sodium chloride, is added to water, it fully dissociates into ions without

raising the pH. The presence of chloride ions doesn't remove protons from water to generate hydroxide ions:

$$Cl^- \text{ (very weak base)} + H_2O \rightleftharpoons HCl \text{ (strong conjugate acid)} + {}^-OH \quad (6.8)$$

Thus, a chloride ion, the conjugate base of a strong acid, is a very weak base.

A very weak base has a strong conjugate acid: In the previous example, we saw that chloride ions are very weak bases (Equation 6.8), and so we predict that the conjugate acid of the chloride ion would be strong. Indeed this is the case. The protonated form of chloride is hydrochloric acid, and hydrochloric acid is a strong acid (formation of HCl from H^+ and Cl^- is simply the reverse of Equation 6.7). The fact that a very weak base has a strong conjugate acid makes sense intuitively. A very weak base is not good at picking up a proton. Thus, if it manages to do so, it readily loses that proton.

A strong base has a very weak conjugate acid: The hydroxide ion of sodium hydroxide is a strong base. The conjugate acid of hydroxide ion is its protonated form, water (Equation 6.4). Water is a pretty terrible acid, spontaneously dissociating into a proton and a hydroxide ion about once for every half a billion molecules. Hence, water qualifies as a very weak conjugate acid. Overall, the intuitive idea here is that if a base is strong, it really wants protons. Once it is protonated to form its conjugate acid, it really doesn't want to lose those protons and consequently is classified as a very weak acid.

A very weak acid has a strong conjugate base: As we just discussed, water is a very weak acid. If it manages to give up a proton, its conjugate base is the resulting hydroxide anion (Equation 6.2). As we've already seen, hydroxide ion is a strong base that wants a proton much more than its protonated form, water, wants to give it up.

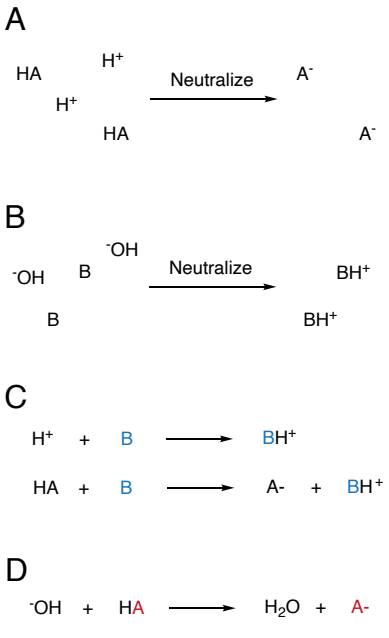


Figure 6.11 Neutralization Reactions. The effects of neutralization reactions on A) protons and acids, or B) hydroxide ions and bases. Neutralization reactions require a neutralizing agent, and for C) protons and acids, this agent is a base (blue). D) For hydroxide ions and bases the neutralization agent is an acid (red).

What can we say about the strength of the conjugate forms of weak acids and bases (i.e. acids or bases that are neither strong nor very weak)? In general, the conjugate form of a weak acid or base is also weak. A weak acid can give up protons but not strongly enough to do so fully. Consequently, its conjugate base (the deprotonated form) can take some protons from water to a very small degree, but does not deprotonate water molecules to a significant extent. A similar argument can be made for the conjugate acid of a weak base.

As an example, consider acetic acid and acetate. If we start with a 0.1 M solution of acetic acid, we've seen that slightly more than 1% becomes the deprotonated form, acetate, making the acid a weak acid (Figure 6.8B). If we start with a 0.1 M solution of the base sodium acetate, it turns out that about 0.01% ends up in the protonated form, acetic acid, making the base a weak base. As acetate is the conjugate base of acetic acid, and acetic acid is the conjugate acid of acetate, these results agree with our rule of thumb: The conjugate base of a weak acid is weak, and the conjugate acid of a weak base is weak.

D. Buffers

At extreme pHs, high concentrations of protons or hydroxide ions are dangerous to organisms, because they can damage biological molecules by changing their protonation state (Figure 6.2) and/or facilitate chemical reactions that effectively would not occur at a neutral pH. Thus, it is crucial for living systems to have means of removing protons and hydroxide ions, and potentially the acids and bases that generate them. One way to do so is to utilize what is known as a pH buffer system. But before we can delve into what that is, we need to consider what are known as neutralization reactions (**Figure 6.11**).

6.11 Neutralization Reactions

In a neutralization reaction, species that can change the pH of a solution are eliminated, i.e., neutralized. In an acid neutralization reaction, a proton or the proton of an acid is eliminated (Figure 6.11A). In a base neutralization reaction, a hydroxide ion or the group of a base capable of generating a hydroxide ion is eliminated (Figure 6.11B). Acid neutralization requires a base (Figure 6.11C), while base neutralization requires an acid (Figure 6.11D).

Let's consider neutralization of protons with a strong base. Suppose you had an acidic solution at pH 1.0 — i.e., a 0.1 M solution of protons, perhaps from a 0.1 M solution of HCl. To neutralize these protons, you could add a strong base, such as a solution of sodium hydroxide:

$$H^+ \xrightarrow{NaOH} H_2O + Na^+ \qquad (6.9)$$

We have seen that hydroxide reacts with a proton to form a water molecule (Equation 6.4). Moreover, this reaction is largely irreversible, as sodium hydroxide is a strong base, and the resulting water molecule is a very weak acid. Thus, every hydroxide ion we add to our acidic solution can remove one proton, neutralizing that proton and raising the pH (**Figure 6.12**). This will continue as we add more sodium hydroxide solution until we run out of protons from our HCl. At this point, there are effectively no protons or hydroxide ions in solution, just the protons and hydroxide ions spontaneously generated by pure water. Our solution is fully neutralized and has a neutral pH, a pH of 7. Note, if we continue adding sodium hydroxide past this point, the pH will continue to go up, as now we have unneutralized hydroxide ions making the solution basic.

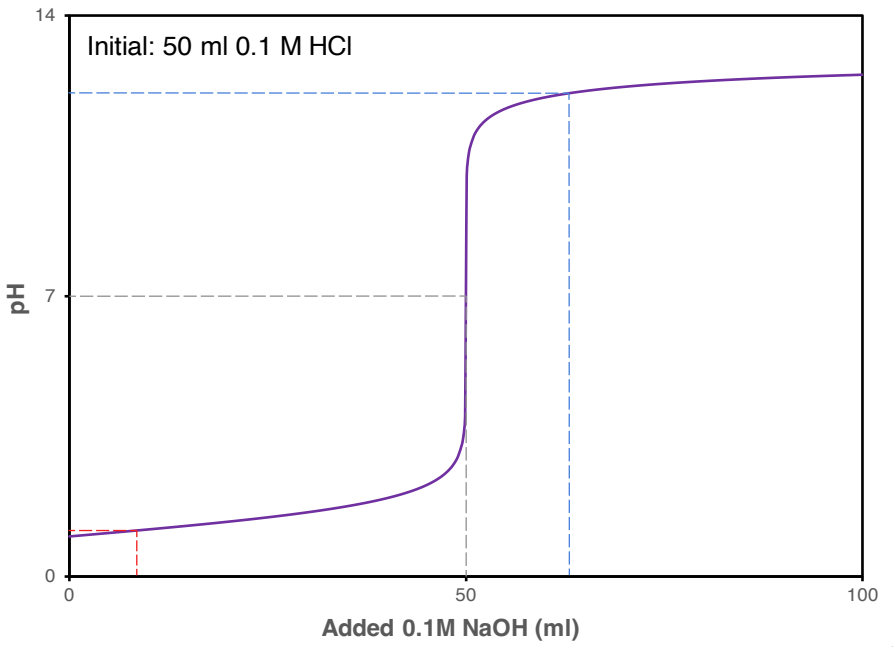


Figure 6.12 pH Effect of Neutralizing Protons in Solution. Initially, hydrochloric acid is added to 50 ml of water to a concentration of 0.1 M. As HCl is a strong acid, it fully dissociates, making the proton concentration 0.1 M and resulting in a very low pH (leftmost point on the purple curve). Adding a 0.1M solution of OH^- changes the pH of the solution (purple curve). When a relatively small volume of the base is added (dotted red line), it neutralizes some of the protons and raises the pH. However, because there is a significant amount of protons left over, the pH is still acidic. When exactly enough OH^- ions have been added to fully neutralize all of the HCl protons (dotted gray line), there is not a significant concentration of protons or hydroxide ions, making the pH neutral. After that, adding more of the hydroxide solution leads to an excess of hydroxide ion, making the pH basic (dotted blue line). A more detailed treatment of this neutralization process is discussed in Subsection 6.19.

A weak acid can also be neutralized by a strong base like sodium hydroxide. Suppose we added the weak acid acetic acid to pure water to a concentration of 0.1M. As we saw in Subsection 6.8, this solution would have some protons (about 0.0013 M) and substantially more protonated acetic acid molecules (about 0.0987 M). As sodium hydroxide was added to this solution, the hydroxide ions would neutralize the small amount of protons present. It would also neutralize the protonated acetic acid molecules, producing an acetate and water molecule for each acid molecule:

$$CH_3COOH \xrightarrow{NaOH} H_2O + CH_3COO^- + Na^+ \quad (6.10)$$

This process largely goes to completion because the hydroxide ion is a stronger base than the acetate ion: i.e., in the battle for who ultimately "owns" the proton, the hydroxide ion "wants" it more than the acetate. Like our example with protons in solution, we can continue neutralizing acetic acid molecules until all of the protons free in solution or attached to acetic acid molecules are neutralized. This will leave a solution of about 0.1 M acetate ions. As these molecules are slightly basic, the pH of this fully neutralized solution will be above 7 (**Figure 6.13**). Again, if we go past this point and add an excess of hydroxide ions, the pH will rise further.

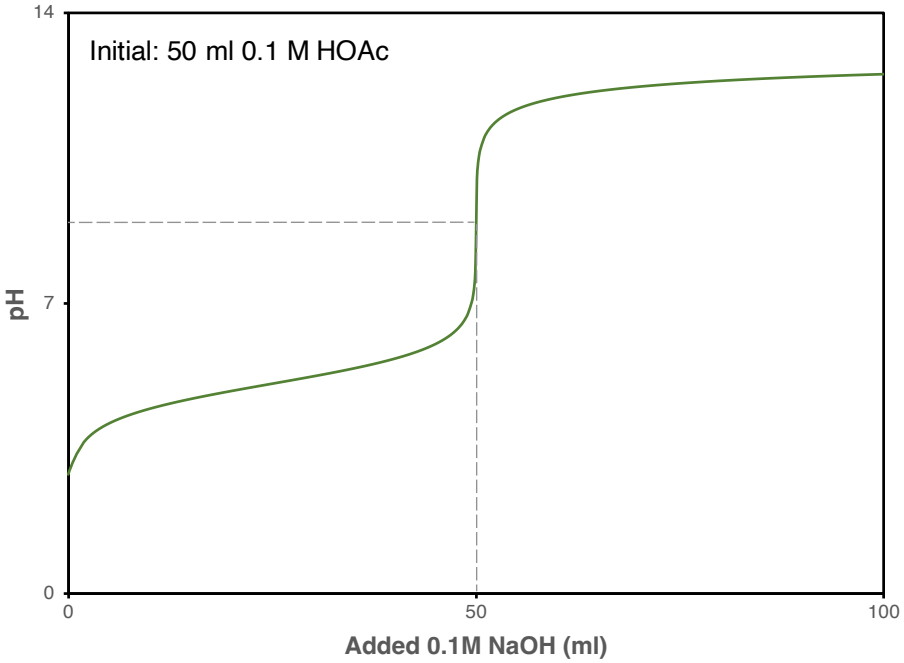


Figure 6.13 pH Effect of Neutralizing Acetic Acid in Solution. Acetic acid is added to 50 ml of water to a concentration of 0.1 M. When increasing volumes of a 0.1 M solution of OH- are added, acetic acid is neutralized to acetate and the pH rises (green curve). When all of the acetic acid molecules have been neutralized (dotted gray line), they will be in the form of acetate. Acetate is a weak base, so to a small degree, it is able to remove some protons from water, and raise the pH above neutral. Beyond this point, any added hydroxide is not neutralized, resulting in further pH increases.

Sodium hydroxide effectively neutralizes protons and acids, because it is a strong base. However, even weak bases can neutralize protons and acids in the right circumstances. Let's return to an acidic solution containing free protons in solution and suppose we have a 0.1 M solution of protons. What happens if we add ammonia molecules to a concentration of 0.1 M? Ammonia is a weak base and not particularly great at abstracting protons from water. However, it is not tremendously weak, and if it encounters protons in solution, it will largely accept them to form ammonium ions:

$$NH_3 \xrightarrow{H^+} NH_4^+ \quad (6.11)$$

With an equal amount of protons and ammonia molecules, we can imagine the solution becoming entirely ammonium ions (i.e. 0.1 M NH_4^+). This protonated species is a conjugate acid. While it is not a strong acid, it does give up some protons. Thus, when the proton solution is fully neutralized by ammonia, the pH will be below 7.

A weak base like ammonia can even neutralize a weak acid like acetic acid:

$$CH_3COOH \underset{}{\overset{NH_3}{\rightleftharpoons}} CH_3COO^- + NH_4^+ \quad (6.12)$$

Ammonia is a stronger base than acetate, so it will become protonated preferentially. As the difference in basicity between acetate and ammonia is not as dramatically different as that

between acetate and hydroxide ion, deprotonation is less complete, and the exact amounts of acetate, ammonium ions, acetic acid, ammonia, protons, and hydroxide ions that are present in the final solution are a bit more complicated. Nonetheless, the point remains that for this particular pair of acids and bases, ammonia can largely neutralize acetic acid.

Just as protons or acids can be neutralized by bases, hydroxide ions or bases can be neutralized by acids. A 0.1 M solution of hydroxide ions (perhaps generated by dissolving sodium hydroxide salt to a concentration of 0.1 M), can be fully neutralized by a strong acid, like a hydrochloric acid solution. This solution can also be neutralized by a weak acid like acetic acid, to generate almost entirely a 0.1 M solution of acetate ions. Weak bases can also be neutralized by acids, as long as the acid is stronger than the protonated form of the base. A 0.1 M solution of acetate (say from sodium acetate salt that is added to a concentration of 0.1 M), can be almost fully protonated by a 0.1 M solution of hydrochloric acid (hydrochloric acid is a much stronger acid than acetic acid).

That said, if we tried to neutralize a 0.1 M acetate solution with a 0.1 M solution of ammonium ion (say from ammonium chloride salt added to a concentration of 0.1 M), to a large extent, the acetate molecules would not be neutralized. What we are trying to do is the reverse of Equation 6.12, where formation of acetate and ammonium ion largely went to completion. This behavior can be rationalized by the fact that acetic acid is a stronger acid than ammonium ion and therefore ammonia will preferentially take the proton from acetic acid. Note, this is equivalent to our previous argument that ammonia is a stronger base than acetate, leading to preferential protonation of ammonia over acetate.

Altogether, we can see that if a base is sufficiently strong, it can neutralize protons and acid solutions, and if an acid is sufficiently strong, it can neutralize hydroxide ions and base solutions.

6.12 Buffer Mixtures

How can we exploit the neutralization power of acids and bases to protect cells from added hydroxide ions/bases or protons/acids — thereby maintaining the pH of the cells? Suppose we wanted to protect a cell from added hydroxide ions (**Figure 6.14A**).

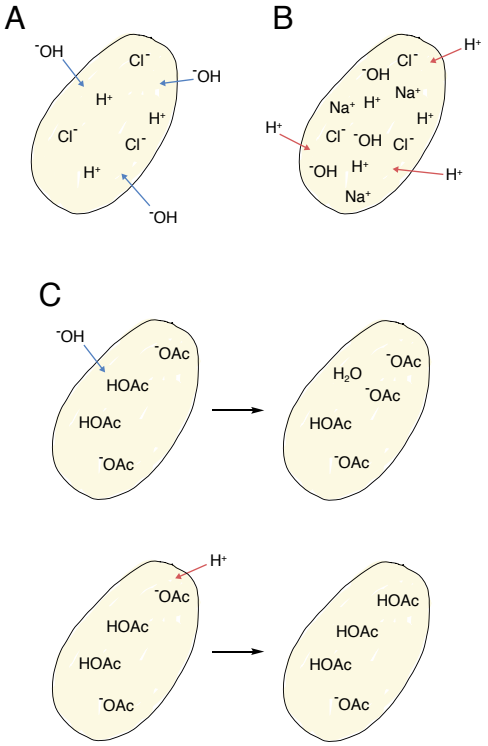


Figure 6.14 Theoretical Ways a Cell Could Protect Itself from Protons and Hydroxide Ions in Their Environment. A) A cell with a high internal concentration of protons would be able to neutralize external hydroxide ions coming into the cell (blue arrows), but would not protect against protons. The cell would also have a low internal pH. B) A cell with a high internal concentration of hydroxide ions and protons could protect against external protons (red arrows) and hydroxide ions (not shown). However, unless the cellular protons and hydroxide ions were sequestered, they would neutralize each other. C) Presence of an equal mixture of a weak acid and its conjugate base inside the cell could potentially neutralize external hydroxide ions (blue arrow) or protons (red arrow) and the pair would not neutralize each other. Shown is an example of using a buffer of acetic acid and acetate. This system exists in equal amounts at pH 4.76 and would be best suited for maintaining the cell at that pH (i.e. not the near neutral environment that most cells need).

One possibility would be for the cell to have lots of hydrogen chloride present. As a strong acid, this acid would completely neutralize the added hydroxide ions. However, there are two potential issues. First, the hydrogen chloride itself would lower the pH of the cell and potentially cause problems. Second, if protons were added instead of hydroxide ions, the hydrogen chloride in the cell would do nothing to protect against that.

Let's ignore the first issue and deal with the second. Suppose that in addition to hydrogen chloride, we had sodium hydroxide in our cells (**Figure 6.14B**). This could allow us to deal with externally added hydroxide ions or protons. But this creates a new issue. Unless we are able to keep the protons from the hydrogen chloride separate from the hydroxide ions from the sodium hydroxide, those components will neutralize each other to become water.

Having a freely-floating mixture of acids and bases capable of neutralizing added protons or hydroxide ions, but not capable of neutralizing each other, would be ideal. Consider what happens if we were to add an equal amount of a weak acid, like acetic acid, and its conjugate base, acetate. Although this acid is weak, it is still strong enough to donate its proton to a hydroxide ion and neutralize it (**Figure 6.14C**, top). Similarly, while acetate is a weak base, it is strong enough to neutralize protons (Figure 6.14C, bottom). Further, the acids and conjugate bases in this mixture don't neutralize each other. If an acetic acid molecule protonates an acetate ion, the result is simply one acetate ion and one acetic acid molecule. The net composition of the mixture is unchanged.

We call a mixture of acid and conjugate base a buffer system, and the buffer components prevent pH perturbations from added protons/acids or hydroxide ions/bases.

It should be noted that buffer systems have limits. Because each buffer component can only neutralize one molecule, if the added acid (or base) outnumbers the available buffer molecules, some of the added acid or base will be left unneutralized and the pH will change dramatically. The amount of acids/bases a buffer system can absorb is its buffering capacity, and the greater the total concentration of the acid/conjugate base, the greater the buffering capacity.

The effectiveness of a buffer also depends on its relative concentration of acid to conjugate base, where an equal amount of each (a 1:1 mixture) is ideal. Under these conditions, there is enough acid in the buffer to neutralize added bases, and enough conjugate base to neutralize added acids. Unfortunately, achieving such a ratio is not always possible, as the relative amount of the buffer components depends on the desired pH of the buffer and the nature of the acid/conjugate base. To get an intuition of how pH affects the ratio of an acid/conjugate base in solution, let's consider the following examples of acetic acid/acetate solutions at various pHs.

Suppose we had 10 liters of a very basic solution with a pH of 13 (say 0.1 M NaOH). If we added 1 ml of a 0.1 M acetic acid/0.1 M acetate buffer solution, the high relative amount of hydroxide would deprotonate all of the acetic acid, making our buffer solution only acetate, and the overall pH of the solution would be unchanged (**Figure 6.15A**). That is, in a very basic solution at pH 13, acetic acid would exist almost exclusively as acetate ions.

If instead we started with 10 liters of a very acidic solution at pH 1 (say 0.1 M HCl) and added 1 ml of our 0.1 M acetic acid/0.1 M acetate buffer solution, all of the acetate molecules in our buffer solution would become acetic acids (**Figure 6.15B**). In this case, a very acidic solution at pH 1, acetic acid would almost exclusively exist in its protonated form.

If we had 10 liters of a somewhat acidic solution with a pH of 4.8 and added 1 ml of our buffer solution, it turns out that the amount of acetic acid and acetate would remain about 0.1 M (**Figure 6.15C**). How do we think about this? Recall that a 0.1 M solution of acetic acid in pure water ended up deprotonated to a bit over one percent, but was still sufficient to drop the pH to 2.88. If the pH were raised a bit, but not too

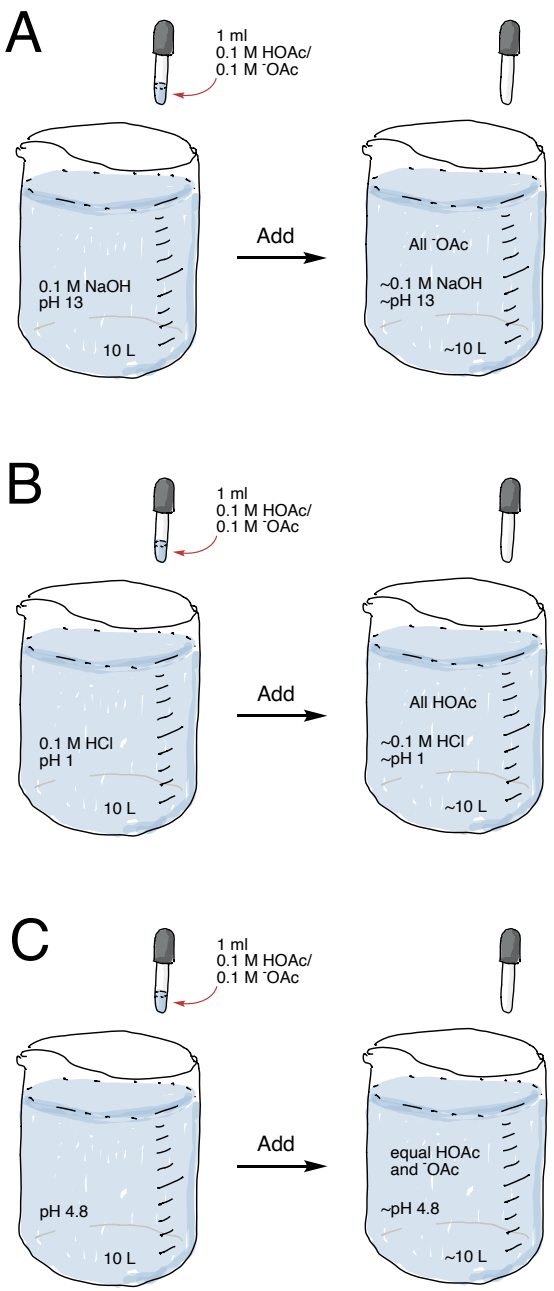


Figure 6.15 Change in the Protonation State of an Acetic Acid/Acetate Mixture as a Function of pH. In these examples, a small volume of a 0.1M acetic acid, 0.1 M acetate solution are added to a large volume of a solution at A) high pH (pH 13), B) low pH (pH 1), or C) some intermediate pH (pH 4.8). Because there is a large excess of molecules maintaining the pH of the large solutions, adding the small volume of acetic acid/acetate mixture does not change the pH of the overall solution. However, the protonation state of the acetic acid/acetate mixture is affected. At the pH extremes, the added molecules end up almost fully protonated or fully deprotonated. However, at pH 4.8, the balance between protonated and deprotonated is maintained.

much, that could deprotonate roughly half of the acetic acid molecules. For acetic acid, that pH ends up being around 4.8 (and is different for different acids). An acetic acid/acetate buffer solution would be especially good to maintain a pH near 4.8 (maybe ± 1 pH unit), but would not be well suited to buffer a solution at other pHs (a more quantitative description of how the ratio of specific acids/conjugate bases depends on pH can be found in Further Exploration Section E, Subsections 6.15-6.16).

If specific acid/conjugate base pairs are well suited for particular pHs, how do we know which acid/conjugate base pairs to choose, and which are best suited for buffering solutions near pH 7 — the pH most cells want to be at?

There is a number that describes the acidity of a molecule, its pK_a (more details in Further Exploration Section E, Subsections 6.14-6.16). pK_a values for various acids are shown in **Table 6.3**, where, if an acid can lose more than one proton, the pK_a for

each deprotonation is shown separately. pK_as are useful for determining an acid's ideal buffering pH. Specifically, the pK_a of an acid is the pH at which there will be an equal amount of acid and conjugate base. So for example, you can see that because the pK_a of acetic acid is about 4.8, it is best at buffering solutions that need to be maintained at a pH of 4.8. A bit less optimally, acetic acid can be used to buffer solutions with a desired pH as low as about 3.8 or as high as about 5.8 (i.e. roughly ±1 pH unit from the acid's pK_a).

Compound	pK_{a_1}	pK_{a_2}	pK_{a_3}
Sulfuric Acid	-3*	1.99	
Hydrochloric Acid	-7*		
Phosphoric Acid	2.15	7.20	12.35
Acetic Acid	4.76		
Carbonic Acid	6.3**	10.3	
Ammonium ion	9.25		
Protonated methylamine	10.6		
Water	14.0		

Table 6.3 pK_a Values for Selected Acids. *The pK_a of strong acids is hard to measure accurately and there are reported values above and below these values. **This is the apparent pK_a of carbonic acid, while the actual value is about 3.6. This discrepancy is addressed in Subsection 6.13.

For a cellular pH of about 7, what acid/conjugate base pairs are best suited as buffers? From Table 6.3 we see that some acids have pK_a values near 7, including phosphoric acid. Deprotonation of the second proton of phosphoric acid has a pK_a value of 7.2, so a mixture of doubly protonated phosphate (acid) and singly protonated phosphate (conjugate base) would be effective for maintaining a neutral pH.

In the laboratory, buffered solutions are important for well-controlled experiments. A mix of doubly and singly protonated phosphate molecules can be used when the pH of an experiment needs to be maintained near pH 7.0. Phosphate buffers do have some drawbacks, though. They can sequester various metal ions and make the ions unavailable, with binding sometimes being very tight (Subsection 5.21-5.22). Phosphate ions can also interfere with processes that utilize biomolecules that include phosphate groups. For most biochemistry experiments, pH buffering is accomplished with other compounds that are described in the Further Exploration Section F, Subsection 6.21.

In cells, pH is maintained near neutrality using a number of compounds. Phosphate and phosphate-related biological compounds are an important source of pH buffering. Metabolites and proteins provide additional buffering capacity. It should be noted that control of cellular pH is also regulated actively by pumping protons into and out of cells using proteins that, at least conceptually, are related to some of the ion transporting membrane proteins described in Subsection 3.12.

Your blood is maintained at a slightly alkaline pH, generally being in the narrow range of pH from 7.35-7.45. One of the major buffering agents used in blood is bicarbonate. However, how this reagent maintains the desired pH is a bit involved, as will be described next.

6.13 Reactions of Carbonic Acid

Besides carbonic acid's ability to lose one or two of its protons, carbonic acid can lose a whole water molecule to become a molecule of carbon dioxide:

$$H_2CO_3\,(aq) \rightleftharpoons H_2O + CO_2\,(aq) \rightleftharpoons CO_2\,(gas) \qquad (6.13)$$

Conversion of carbonic acid to carbon dioxide gas is favorable: In the first step, carbonic acid is less stable than its products, water and dissolved carbon dioxide, so in water carbonic acid will generally undergo this decomposition; In the second step, because carbon dioxide is not very water soluble, carbon dioxide will typically exit the solution into the air.

You have likely seen this reaction, though you may have been unaware of it. A common science demonstration is to make a "volcano" that spews "lava" (**Figure 6.16A**). This occurs when sodium bicarbonate (baking soda) and vinegar (a 4-7% solution of acetic acid) are mixed (usually in the presence of some red food coloring to make the "lava" red, and some dish soap to make it more foamy). Bicarbonate is sufficiently basic relative to acetic acid to transfer the proton from acetic acid to bicarbonate to convert it to carbonic acid. The carbonic acid then decomposes into water and carbon dioxide, releasing the carbon dioxide as a gas that rapidly bubbles out of the solution.

This reaction has practical applications for making a number of baked goods (**Figure 6.16B**). In cakes, baking powder is a standard ingredient. Baking powder typically contains a solid mixture of sodium bicarbonate salt and two solid acids: one that releases protons immediately when the baking powder is dissolved in water, and one that only does so when heated. Thus, when a liquid batter is made and then cooked, the bicarbonate and the acids in baking powder (and potentially other acids in the batter) react to make carbonic acid, which is quickly converted to carbon dioxide gas. This gas gets trapped in the batter and then in the baked cake as tiny bubbles that make the cake spongy and light. Without any leavening agent, baked goods would tend to be flat and dense, like unleavened flatbread.

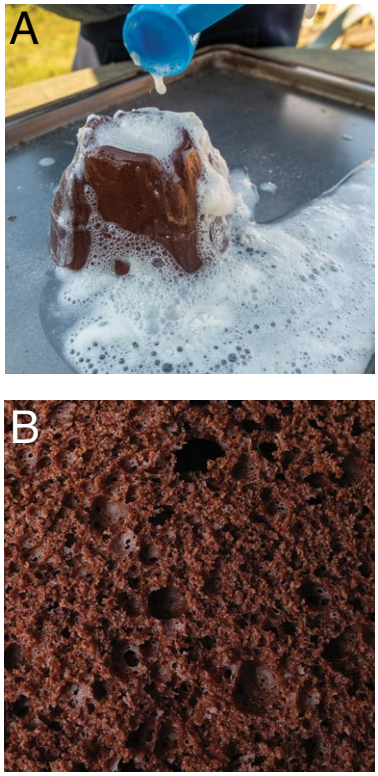


Figure 6.16 Examples of the Instability of Carbonic Acid. A) Demonstration volcanoes exploit the fact that carbonic acid generated from neutralization of bicarbonate decomposes into carbon dioxide gas. This gas allows the "lava" to bubble out of the "volcano." B) Leavening in baking can be achieved using baking powder, where neutralization of the bicarbonate in baking powder produces carbon dioxide gas that becomes trapped in the baked product.

The reverse reaction occurs, too, though usually only to a small degree. Atmospheric carbon dioxide can dissolve in water and make some carbonic acid. This species can give up a proton to become the more stable bicarbonate species, lowering the pH of the solution in the process. Rainwater generated in the presence of atmospheric carbon dioxide tends to be somewhat acidic, with an average pH of 5.6, though this acidity tends to be neutralized by soil compounds before reaching freshwater and ocean environments. Over the last two centuries, the amount of atmospheric carbon dioxide has increased, resulting in more dissolved carbon dioxide in the ocean. This generates more carbonic acid that can decrease the pH of the oceans. Prior to the industrial revolution, the surface pH of the ocean was about 8.2, and currently the pH is around 8.1. On an absolute level, this isn't a large difference in pH, but the 0.1 decrease in pH corresponds to about a 26% increase in the molar proton concentration. This ocean acidification is already believed to have had effects. If nothing is done and projections are correct that the pH of the ocean drops to as low as 7.7-7.8 by the end of the century, it is likely to cause major disruptions and damage to a number of ocean ecosystems.

Part of our motivation for discussing carbonic acid is the fact that it is used as part of a buffer system in blood. In light of the relative instability of carbonic acid, how do we understand this role?

Recall that an ideal buffer system is one in which there are roughly equal amounts of an acid and its conjugate base, and that different acids/conjugate base pairs are better suited for different pHs. For example, an equal mix of doubly/singly protonated phosphoric acid is a good buffer near pH 7, and acetic acid/acetate is well suited for buffering solutions near a pH of 5. Using the true pK_a of carbonic acid (~3.6, rather than the apparent value of 6.3 shown in Table 6.3), carbonic acid is a stronger acid than acetic acid. Consequently, we might expect that an equal mixture of carbonic acid and bicarbonate would be good for buffering solutions at pHs lower than 5, as we would need a more acidic solution to keep the system half protonated. However, carbonic acid/bicarbonate are used to buffer much more basic systems, with pHs between 7 and 8. Why is this the case?

The ability of a carbonic acid/bicarbonate system to buffer higher pHs than expected

arises directly from the instability of carbonic acid. In the buffer solution, bicarbonate can pick up a proton to generate carbonic acid. The reverse can occur, too: carbonic acid can be depleted by giving up a proton. However, because carbonic acid can also be lost by becoming carbon dioxide and bubbling out of solution, the balance between bicarbonate protonation and carbonic acid deprotonation is thrown off, causing bicarbonate to pick up more protons than if carbonic acid were not removed as carbon dioxide gas. This extra ability to pick up a proton makes bicarbonate effectively more basic than it would have been otherwise. Put differently, because carbonic acid is continuously being lost from the system, the bicarbonate-to-carbonic acid ratio stays high even at relatively basic pHs — meaning the 1:1 ratio that marks the optimal buffering point isn't reached until a much higher pH than the true pK_a of carbonic acid would suggest.

From a laboratory perspective, a carbonate/bicarbonate system is not a practical buffer for experiments at physiological pH. Ultimately the amount of a carbonic acid/bicarbonate mixture that can be present in solution depends on the amount of carbon dioxide above the solution, and unless high pressures of carbon dioxide gas are used, the concentration of carbonic acid is going to be too low to provide much buffering capacity.

The situation is different in blood. As we will discuss in depth in Chapter 22 of Volume IV, cellular metabolism generates a significant supply of carbon dioxide in solution. Conversion of aqueous carbon dioxide to carbonic acid can be slow, but in your body there is a protein called carbonic anhydrase that practically makes this interconversion instantaneous. Thus, there is a significant and renewing supply of carbonic acid that can be used to buffer your blood. This system also provides a way to transport carbon dioxide out of your body. Instead of the less soluble gas, carbon dioxide is converted into the more soluble forms of carbonic acid and bicarbonate in your blood. When your blood reaches your lungs, where the overall atmospheric concentration of carbon dioxide is low, carbonic anhydrase rapidly converts carbonic acid back to carbon dioxide, which is then released to the air.

Where to from here: In this chapter we introduced many concepts related to acids and bases, and how those concepts relate to the pH of solutions. From a qualitative perspective, we discussed the fact that some acids or bases are stronger than others. In the Further Exploration sections, we investigate: how to turn this qualitative description of the acidity or basicity into something more quantitative, a pK_a or pK_b; how these values can be used to understand the pH of solutions of acids and bases; and how to choose appropriate buffers for a given pH.

This chapter concludes our tour of general chemistry. In the next volume, we will build on the ideas we have developed in order to investigate and understand organic compounds. Many simple organic compounds are directly relevant to biological systems, and others will provide a foundation from which to understand the more complex organic molecules that are cellular biomolecules.

E. Further Exploration - pK_as

Every acid has a number that describes its acidity, its pK_a. In this section, we explore what this number means, where it comes from, and how to use it to determine the extent to which it is protonated at a given pH and the basicity of its conjugate base.

6.14 Qualitative Meaning of pK_a Values

Every molecule that can give up a proton (i.e. an acid) has an associated pK_a value (Table 6.3). For example, acetic acid, which can lose one proton to become an acetate, has a pK_a value of 4.76. If a compound can give up multiple protons, each deprotonation is associated with a specific pK_a value. This can be seen with phosphoric acid, which can lose three protons en route to becoming a phosphate ion, and it has pK_a values of 2.15, 7.20, and 12.35.

For a molecule with one acidic group, its pK_a can be interpreted as a rating of the acid's strength. On this scale, the lower the pK_a value, the stronger the acid. Conversely, the higher the pK_a, the weaker the acid. This is reminiscent of lower pH values indicating more acidic conditions and higher pHs indicating less acidic conditions.

Consider acetic acid and hydrochloric acid, with pK_a values of 4.76 and -7, respectively (Table 6.3). As HCl's pK_a value is lower than that of acetic acid (being even negative, in this case), hydrochloric acid is a stronger acid than acetic acid. This is in agreement with what we've previously learned: hydrochloric acid is a strong acid and fully dissociates into protons and chloride ions in water; acetic acid is a weak acid and undergoes limited dissociation when added to water.

The fact that a lower pK_a indicates a stronger acid also allows us to assign specific pK_a values to the deprotonation states of an acid that can lose multiple protons. For phosphoric acid, the pK_a of 2.15 indicates the most acidic group of the three deprotonations. This is the first deprotonation, as typically, removing subsequent protons becomes harder.

$$H_3PO_4 \underset{+H^+}{\overset{-H^+}{\rightleftharpoons}} H_2PO_4^- \underset{+H^+}{\overset{-H^+}{\rightleftharpoons}} HPO_4^{2-} \underset{+H^+}{\overset{-H^+}{\rightleftharpoons}} PO_4^{3-} \qquad (6.14)$$

The pK_a of the first deprotonation (pK_{a1} = 2.15) is lower than that for acetic acid (4.76), but higher than that of hydrochloric acid (-7). This indicates that phosphoric acid loses its first proton more readily than acetic acid, yet not as easily as hydrochloric acid.

The second deprotonation, pK_{a2}, going from a phosphate with two protons to a species with one (Equation 6.14) proceeds to a lesser degree than the first deprotonation (pK_as of 7.20 vs 2.15), with the doubly protonated phosphate being a weaker acid (pK_a of 7.20) than acetic acid (pK_a of 4.76). The third deprotonation (Equation 6.14) is weaker yet, with a pK_a value of 12.35.

There is another way to interpret the pK_a values of an acid. A pK_a of a compound indicates the pH at which its acidic group is half protonated. Above this pH, the group is more deprotonated than protonated. Below this pH, the group is more protonated than not. Let's consider a simple example, acetic acid, with a single acidic group, and a pK_a of 4.76. If we had a solution of acetic acid at a pH of 4.76, half of the molecules would be acetic acid molecules, and half would be acetate molecules. If we had the same solution, but the pH was 7.0 (much more basic), the majority of the acetic acid molecules would be in the form of acetate. If the solution were at a pH of 3 (much more acidic than our original solutions), almost all of our molecules would be protonated in the form of acetic acid.

How about for phosphoric acid? Suppose we started with a solution of phosphoric acid at a pH of 0 (1 M [H^+]) and continually raised the pH (**Figure 6.17**). The pH of our starting point is below the pK_a values of all three phosphoric acid groups (2.15, 7.20, 12.35), so fully protonated phosphate, phosphoric acid, would predominate. As we raised the pH, around a pH value of 2 we would have roughly an equal amount of phosphoric acid and singly deprotonated phosphoric acid (pH = pK_{a1}, pH < pK_{a2}, pH < pK_{a3}). As we continued to raise the pH, we would continue to deprotonate the molecules. At a pH of about 7, we would have about half of our molecules in the form of phosphates with two protons, and phosphates with one proton (pH > pK_{a1}, pH = pK_{a2}, pH < pK_{a3}). When we reached a pH of 12, we would have half phosphates with a single proton and half fully deprotonated phosphate ions (pH > pK_{a1}, pH > pK_{a2}, pH = pK_{a3}). If we wanted a solution with only deprotonated phosphate ions in it, we would need to increase the pH of the solution to even more basic conditions — i.e., significantly above 12.

This interpretation of pK_a helps us understand what pH an acid/conjugate base is well-suited for buffering. A buffer solution is most effective when it has roughly an equal concentration of an acid and its conjugate base. That is, the acid is half protonated and

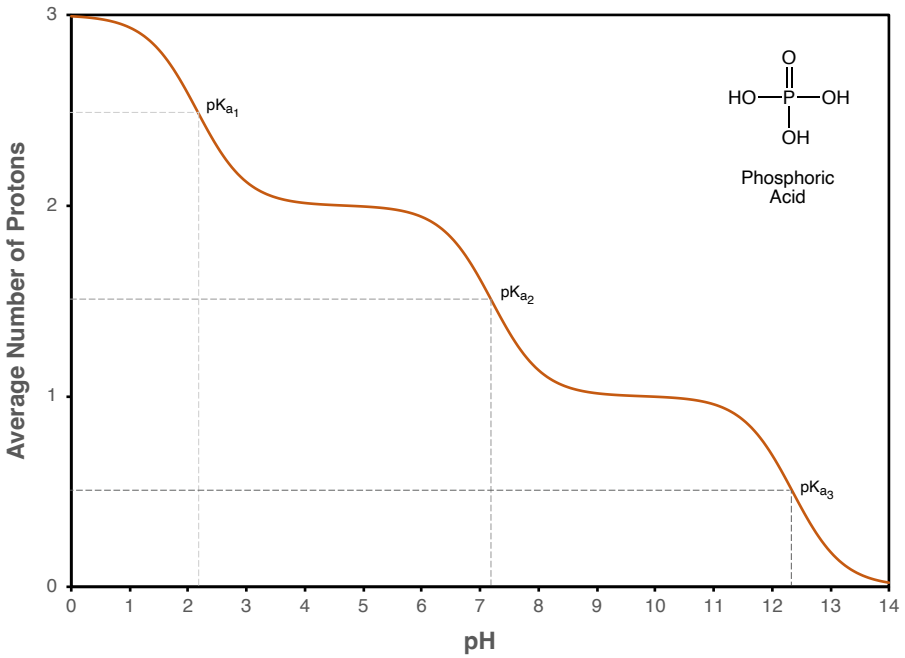


Figure 6.17 Average Number of Protons on Phosphoric Acid as a Function of pH. As the pH gets more basic, up to three protons can be lost from phosphoric acid, where the average number of protons is indicated by the orange line. Fifty percent loss of each of the three protons (average proton numbers of 2.5, 1.5, and 0.5) occurs at a pH corresponding to one of the three pK_a values for phosphoric acid (pK_{a1} = 2.15, pK_{a2} = 7.20, and pK_{a3} = 12.35) and are indicated by the gray dashed lines.

half deprotonated. Since this occurs when the pH is equal to the pK_a, the pK_a of an acid is its most effective buffering pH. For acetic acid with a pK_a of 4.76, it would be most effective at buffering solutions around a pH of 4.76. Phosphoric acid could potentially be used to buffer three different pHs. Most commonly, though, it is used to buffer around pH 7.20, where the concentration of singly and doubly protonated phosphate ions is equal.

It's important to point out that using a solution's pH to predict an acid's protonation state only works when the pH is known after the acid is added. For example, if I start with a solution at pH 7 and add acetic acid to a concentration of 0.1 M, just because the initial pH of 7 is significantly higher than the pK_a of the acid, 4.76, it does not mean that the acetic acid will end up mostly deprotonated. The addition of the acid will perturb the pH of the solution. As previously discussed (Figure 6.8B), when the initial solution is pure water (pH 7.0), addition of acetic acid to a concentration of 0.1 M results in a final pH of 2.88, because some of the acetic acid molecules release a proton. Now knowing the pH of the solution after the acid has been added, we can apply our rule of thumb. Since the pH of the solution, 2.88, is significantly lower than the pK_a of the acid, 4.76, we expect the acid to be mostly protonated. This matches what we have previously discussed, where acetic acid is a weak acid and when added to a solution of pure water, only a bit more than 1% of the acetic acid molecules deprotonate to become acetate ions.

When can we be certain about a solution's final pH? For textbook problems, the trivial answer is when we are told that the pH is the final pH. More practically, in real life there are several ways to know the final pH of a solution. We could measure the pH of the solution after the acid has been added and thoroughly mixed, like our example of acetic acid added to pure water. Alternatively, if we know the initial pH of a solution, the solution is buffered, and the buffering capacity of the solution exceeds the amount of acid we add, the final pH will be very close to the initial pH (i.e. the buffer prevented the addition of the acid from changing the pH). As an example of this situation, suppose we had a pH 7.2 phosphate buffered solution that contained 0.1 M doubly protonated phosphate and 0.1 M singly protonated phosphate. If we added acetic acid to a concentration of 0.001 M, this amount of acetic acid could be handled by the buffering agents and the final pH would still be close to 7.2. In this case, since the final pH is significantly higher than the pK_a of the added acid, we would expect most of the added molecules to be in their deprotonated form, acetate. Here, the singly protonated phosphate ions in the buffer are strong enough bases to largely neutralize or deprotonate all of the added acetic acid molecules and there are enough singly protonated phosphate ions left over

to continue to maintain the pH of the solution. A final way that we can be confident in knowing the final pH of a solution given an initial pH, is if we calculate the final pH using the pK_a value of the added acid. We'll see how to do this in the next subsection.

There are a couple more things to mention regarding the protonation state of an acid in solution. Even when the pH is much greater or much less than the pK_a of the acid, deprotonation or protonation of the acid is never complete. As we will calculate in Subsection 6.16, when the pH of a solution is 1 pH unit higher than the acid's pK_a, it will be 91% deprotonated, and 9% protonated. One pH unit below its pK_a, the acid will be 91% protonated and 9% deprotonated. At 2 pH units from the pKa, the ratios become 99% and 1%. At 3 pH units, they become 99.9% and 0.1%. This trend continues with further changes to the pH. While 0.1% is a small fraction of molecules, when we are talking molar amounts, this number can still be significant. Further, deprotonation and reprotonation are dynamic processes that tend to be fast, so even under conditions where an acid is 99.9% protonated, there will be times it is deprotonated, albeit for only a short while (0.1% of the time). For acids with multiple acidic groups, if their pK_a values are relatively close, it can be difficult to determine which groups are protonated or deprotonated at a given time. That said, in the polyprotic acids we have considered so far, all acid groups are chemically identical and the difference in pK_as for subsequent deprotonations is relatively large, so this is not a major issue.

6.15 pK_as and K_as

Why do pK_as indicate the relative acidity of a compound, and its protonation state at a given pH? To answer these questions, we need to step back and look at the equilibrium behavior of acids.

Suppose I have some acid, HA, that in water can give up one proton to become the A^- anion:

$$HA \rightleftharpoons H^+ + A^- \tag{6.15}$$

When HA is first added to water, all HA molecules are protonated. However, over time some HA molecules dissociate, donating their proton to the solution (more accurately, protonating water as a hydronium ion, H_3O^+). As this process continues, the concentration of protons in solution increases. However, when the proton concentration is high enough, some protons are able to come off their water molecules, to protonate A^- molecules and reform HA. When the two opposing processes have stabilized (but not stopped), the system has reached equilibrium, a concept we have explored in other contexts (Section F of Chapter 3).

A system at equilibrium can be described by its equilibrium constant, which is the equilibrium concentrations of products raised to their stoichiometries, divided by the equilibrium concentrations of their starting materials raised to their stoichiometries (Equations 3.30 and 3.31). For the reaction shown in Equation 6.15, the stoichiometries are all one, so the equilibrium constant, which we will call K_a, simplifies to the following:

$$K_a = \frac{[H^+][A^-]}{[HA]} \tag{6.16}$$

K_a will always be a positive number whose magnitude depends on the acid. From Equation 6.16, we can see that this magnitude depends on the equilibrium ratio of the HA concentration in the denominator, compared to the concentration of dissociated HA species, H^+ and A^-. Suppose we had a very weak acid that dissociated very little in water. At equilibrium, the numerator terms would be close to zero, making K_a close to zero. On the other hand, if we had a very strong acid, where HA in the denominator

was close to zero, K_a would be a very large number. Thus, the bigger the K_a value, the stronger the acid.

How does this relate to pK_as and acid strength? By definition, the pK_a of an acid is related to its K_a in a manner similar to how we define pH relative to a solution's molar proton concentration. That is:

$$pK_a = -\log(K_a) \tag{6.17}$$

If an acid is strong, i.e. its K_a is a large positive number (say 1,000,000), the log-base 10 of the K_a is also a positive number (6), and the negative of that, its pK_a (-6), will be a negative number. Hydrochloric acid has a pK_a of -7, which is in agreement with what you would expect for a strong acid with a large K_a. If we had a weak acid with a small K_a (say 0.00001), the pK_a we would get from Equation 6.17 would be 5. Acetic acid has a pKa of 4.76, which is in agreement with what you would expect for a weak acid with a small K_a.

Equation 6.17 allows us to plug in K_a values of an acid to get its pK_a. The equation can also be used to go the other way to get the K_a value from a pK_a:

$$K_a = 10^{-(pK_a)} \tag{6.18}$$

For hydrochloric acid, its K_a is 10^7 = 1.0 x 10^7. For acetic acid, its K_a is $10^{-4.76}$ = 1.74 x 10^{-5}.

6.16 Calculating The Extent of Protonation/Deprotonation with K_as and pK_as

With the K_a of an acid, it's possible to calculate exactly how much proton, protonated acid, and deprotonated acid are present at equilibrium.

Consider the situation where we add an acid to a solution of pure water: for example, adding acetic acid to a concentration of 0.1 M. To calculate the equilibrium concentration of protons in solution, we could use the strategy we employed in Figure 3.43. Initially, we would have 0.1 M acetic acid in solution, and 0 M proton or acetate. However, the acetic acid would lose some protons, until the system reached equilibrium. At equilibrium, there would be some unknown concentration of protons from acetic acid dissociation, x, an equal concentration of acetate ion, x, and a decreased concentration of acetic acid, 1-x. These equilibrium concentrations could be plugged into Equation 6.16, including the K_a value for acetic acid, 1.74 x 10^{-5}, that we calculated in the last subsection. After some algebra we would have a quadratic equation in terms of x. We could directly solve for x using the quadratic formula, or make some approximations. Either way, x, the equilibrium concentration of protons, ends up being about 0.00131 M. This corresponds to a pH of 2.88. This is exactly the value we described in Subsection 6.9, where acetic acid was added to pure water to a concentration of 0.1 M, resulting in only about 1.3% of acetic acid molecules releasing a proton into solution.

The previous example used a K_a value to calculate the equilibrium concentrations of the protonated and deprotonated form of the acid, as well as the proton concentration. This calculation was a bit complicated, because we started from pre-equilibrium concentrations and had to extrapolate to the equilibrium concentrations. On the other hand, if we know the equilibrium concentration of one of the components, it is relatively easy to calculate the concentration of the others. Let's look at an example where we know the equilibrium proton concentration. Suppose we started with a 0.001 M solution of acetic acid, and at equilibrium the pH of the solution is 7.0 (perhaps we are in a buffered phosphate solution buffered to pH 7.0, or maybe we added hydroxide ions to our solution until a

pH meter showed the pH was 7.0). Into Equation 6.16, we can directly substitute the K_a for acetic acid, 1.74 x 10^{-5}, and the molar proton concentration for pH 7.0, 1 x 10^{-7} M:

$$K_{a\ acetic\ acid} = 1.74\ x\ 10^{-5} = \frac{(1\ x\ 10^{-7})[A^-]}{[HA]} \tag{6.19}$$

Rearranging we get:

$$1.74\ x\ 10^2 = 174 = \frac{[A^-]}{[HA]} \tag{6.20}$$

Since we started with 0.001 M acetic acid (HA), at equilibrium the concentration of HA + A^- has to equal 0.001 M. If the equilibrium concentration of A^- is *x*, the equilibrium concentration of HA is 0.001-*x*. We can plug those values into Equation 6.20 and solve for *x* and 0.001-*x*. We find that the acetic acid concentration has dropped to 0.006 mM, while the equilibrium concentration of acetate has risen to 0.994 mM. That is, nearly all of our initial acetic acid has been deprotonated to acetate. This matches our rule of thumb that if the final pH of a solution (7.0), is significantly greater than the pK_a of our acid (4.76), our acid will predominantly be deprotonated.

It should be noted that often we aren't interested in the exact amount of protonated and deprotonated acid in solution and are instead interested in their ratio. Equation 6.20 gives us this ratio. It says that for every 174 molecules of deprotonated acetate we have in solution at pH 7, we have 1 protonated acetic acid molecule.

In the previous example, we determined the ratio of deprotonated to protonated acid from the final pH of the solution and the acid's pK_a. To do this calculation, we needed to convert the pH and pK_a to molar proton concentration and K_a, respectively. Is there a way to calculate this directly from pH and pK_a values? Let's start with Equation 6.16 and take the negative log-base 10 of both sides of the equation. Applying some properties of logarithm, we get the following:

$$-\log(K_a) = -\log\left(\frac{[H^+][A^-]}{[HA]}\right) = -\log[H^+] - \log\left(\frac{[A^-]}{[HA]}\right) \tag{6.21}$$

Negative log of K_a is pK_a and the negative log of molar proton concentration is pH. Substituting those terms in and rearranging we get:

$$pH = pK_a + \log\left(\frac{[A^-]}{[HA]}\right) \tag{6.22}$$

This equation is known as the Henderson-Hasselbalch equation. We can use it to solve our previous example using pH and pK_a value directly. If we have acetic acid in a pH 7.0 solution, we see that:

$$7.0 = 4.76 + \log\left(\frac{[A^-]}{[HA]}\right) \tag{6.23}$$

Solving, we see that the log of the equilibrium ratio of acetate to acetic acid at this pH is 2.24. To get rid of the log, we can raise 10 to 2.24, to get that the ratio of acetate to acetic acid is 174, just as we did in Equation 6.20.

More generally, the Henderson-Hasselbalch equation reveals how the protonation of any acid changes with the final pH of a solution. If the final pH is equal to the pK_a of the acid, the ratio of the conjugate base to acid is one. That is, there is an equal

amount of acid and its conjugate base. This shows why an acid and its conjugate base are most effective at buffering a solution when the pH is equal to the acid's pK_a. If the final pH of a solution is above an acid's pKa (pH - pK_a > 0), we can see that the deprotonated acid form will predominate. Similarly, a final pH below an acid's pK_a (pH - pKa < 0) means the protonated acid form will predominate. In fact, according to Equation 6.22, every change in one pH unit results in a 10-fold change in the ratio of acid to conjugate base.

6.17 K_w of Water

As discussed in Subsection 6.6 and shown in Equation 6.2, water is an acid that generates a proton and a hydroxide ion. As an acid, water has a K_a:

$$K_{a\ of\ water} = \frac{[H^+][OH^-]}{[H_2O]} \tag{6.24}$$

Similar to the reasons given in Subsection 5.22 for why solids do not contribute to the equilibrium expression, the water "concentration" term can be set to 1. This equilibrium constant is known as K_w, which has a value of 10^{-14}:

$$K_W = [H^+][OH^-] = 10^{-14} \tag{6.25}$$

This expression says that any increase in proton concentration in a solution must be offset by a decrease in hydroxide concentration, and vice versa (for example, if the proton concentration increases 2-fold, the hydroxide concentration must end up one half of where it started). This follows our intuition that at low pH values (high proton concentrations), the hydroxide concentration is very low, while at very high pH values, the proton concentration is very low and the hydroxide concentration is very high. Indeed, Equation 6.25 becomes Equation 6.5 when we take the negative log of both sides of the equation:

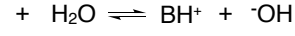
$$-\log([H^+][OH^-]) = -\log([H^+]) + -\log([OH^-]) = pH + pOH = 14 \tag{6.26}$$

As we've seen, this expression allows us to relate pH and pOH in solutions, and it will be useful in describing basicity more quantitatively in the next subsection.

6.18 K_bs and pK_bs

K_as and pK_as provide a quantitative way to describe the strengths of acids and a way to predict their protonation state. How do we do the same for bases? One approach is to consider their conjugate acids. The pK_as for these species are often found in tables of acids, and this indirectly tells us something about the base. For example, if the conjugate acid of a base is quite weak (i.e. has a large pK_a value), the base is relatively strong. For example, ammonium ion is quite a weak acid with a pK_a of 9.25. This makes it a worse acid than acetic acid (pK_a of 4.76) or the second proton of phosphoric acid (pK_a of 7.20), and so ammonia is a stronger base than acetate or doubly deprotonated phosphate. However, the pK_a of ammonium ion (9.25) is less than the third proton of phosphoric acid (12.35) or of water (14.0), so ammonia is less basic than fully deprotonated phosphoric acid or hydroxide ion.

What if you want to predict how much hydroxide ion a base produces when added to water? The reaction of a base with water can be described as follows:



(6.27)

An equilibrium expression, K_b, can be written for this equation:

$$K_b = \frac{[BH^+][OH^-]}{[B]} \tag{6.28}$$

Note, like we did for deriving the K_w of water (Equation 6.25), the K_b does not include the "concentration" of water into the equilibrium constant.

The equation for K_b resembles K_a (Equation 6.16) in form: Both equilibrium expressions have one species in the denominator and two in the numerator. In the K_a, one of the species in the numerator is the equilibrium concentration of protons. In the K_b, the corresponding species is the hydroxide concentration. Since K_a is a measure of acid strength, K_b is a comparable measure of base strength. Further, this K_b value can be used to calculate the concentration of hydroxide ion in solution from an initial concentration of base, just as was done with a K_a value and an initial acid concentration (Subsection 6.16).

Tables with K_b values are available for some bases, but many are not. More common are the pK_a values for the conjugate acid of the base. Luckily, there is a straightforward relationship between a base's K_b value and its conjugate acid's K_a. If we multiply the equilibrium expression of K_b (Equation 6.28) by the equilibrium expression of K_a (Equation 6.16 - where the terms have been adjusted to the conjugate acid of B), we see that we end up with K_w (Equation 6.25):

$$K_b \times K_a = \frac{[BH^+][OH^-]}{[B]} \times \frac{[H^+][B]}{[BH^+]} = [H^+][OH^-] = K_w = 10^{-14} \tag{6.29}$$

Thus, the K_b of a base and the K_a of its conjugate acid have to have a product of 10^{-14}.

The relationship in Equation 6.29 can also be expressed in terms of the pK_b of a base and the pK_a of its conjugate acid. The pK_b of a base is simply the negative log of its K_b:

$$pK_b = -\log(K_b) \tag{6.30}$$

If we take the negative log of the K_b, K_a, and 10^{-14} terms in Equation 6.29, after some substituting and rearranging, we get the following expression:

$$pK_a + pK_b = 14 \tag{6.31}$$

Let's use Equation 6.31 to better understand the base ammonia. The pK_a of ammonia's conjugate acid, ammonium ion, is 9.25. Thus, the pK_b of ammonia is 14 - 9.25 = 4.75. Ammonia's pK_b is nearly identical to acetic acid's pK_a (4.76). This suggests that ammonia is about as good at generating hydroxide ions from water as acetic acid is at generating protons. Let's see if this is correct. Recall that for a 0.1 M solution of acetic acid in pure water, the pH ended up being 2.88, corresponding to about 1.3% of initial acetic acid molecules giving up a proton (i.e. 1.3% is acetate ion). If we start with a 0.1 M solution of ammonia, do we end up with roughly the same percent of ammonium ion? From the pK_b of ammonia, 4.75, we can raise ten to the negative power of the pK_b to get a K_b of 1.78×10^{-5}. At equilibrium, the concentration of ammonium ion and hydroxide ion will be some value x, while the concentration of ammonia will be 0.1 - x. Plugging these values into Equation 6.28 and doing some algebra to solve for x, we find that the predicted equilibrium concentrations of ammonium ion and hydroxide ion are 0.0013 M, and the concentration of ammonia is 0.0987 M. This means at equilibrium about 1.3% of the initial ammonia molecules took a proton from water to generate ammonium and hydroxide ions. This extent of deprotonation of pure water by ammonia is the same as the extent of proton release by acetic acid, confirming the idea that in water ammonia is as good at generating hydroxide ions as acetic acid is at generating protons.

F. Further Exploration - Buffers Revisited

As discussed in Subsection 6.12, buffer systems resist changes in pH. These systems consist of a mix of a weak acid and its conjugate base, and different acids are better suited for particular pHs. In the previous section we explored some quantitative approaches for understanding acids, like pK_as and the Henderson-Hasselbalch equation. In this section, we use these tools to better understand how buffers work and to prepare more effective ones.

6.19 pH Titrations

To understand buffers, let us begin by examining some pH titration examples. In a titration experiment, defined amounts of a compound are added to a solution containing some other compound. As more compound is added, some change in a property of the solution is measured. In our pH titration examples, increasing amounts of a 0.1 M solution of sodium hydroxide base are added to 50 ml of a solution of 0.1 M acid, and the pH of the solution is noted.

As a first example (**Figure 6.18**) consider the case in which we add the hydroxide solution to a 50 ml solution lacking any acid: i.e., a 50 ml solution of pure water. Before we add any base, the pH of the pure water is 7.0 (left-most point in Figure 6.18). If we add 5 ml to the 50 ml solution, we expect the pH of the solution to rise, as we are increasing the hydroxide concentration of the solution from very low initial levels. While this rise will be substantial, it will not reach the pH of the NaOH solution added (pH 13), as the hydroxide ions in this 5 ml are diluted throughout the 55 ml of the solution (50 ml of the original solution plus the 5 ml of the hydroxide solution). The exact pH can be calculated, where 0.0005 moles of hydroxide (0.1 moles/L x 0.005 L) in 0.055 L gives a molar hydroxide concentration of 0.0091 M, a pOH of 2.04, and a pH of about 12. Adding more and more 5 ml aliquots of hydroxide increases the pH, though the rise levels off, as the difference in pH between the solution added and the mixture becomes smaller and smaller.

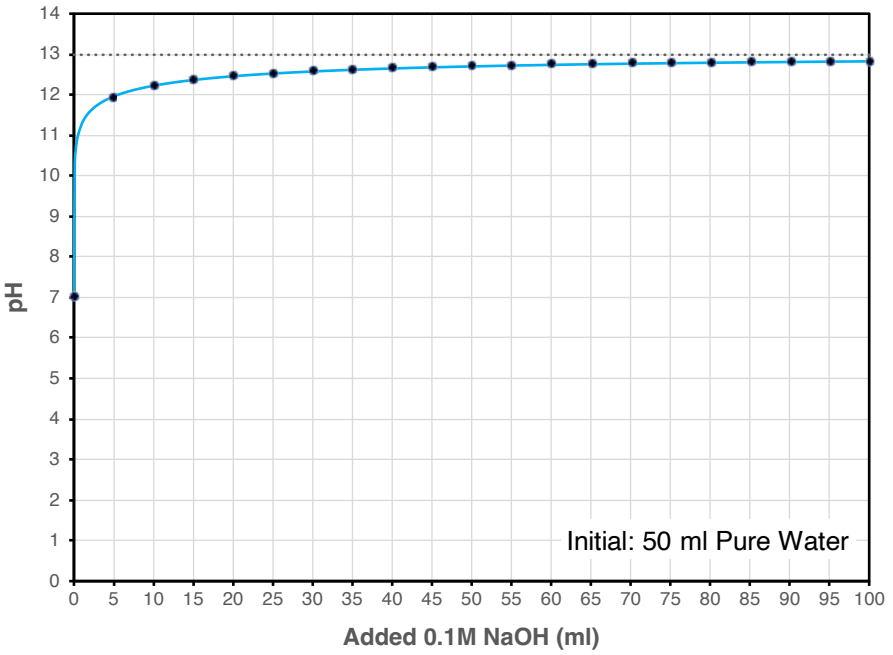


Figure 6.18 Calculated Results for the Base Titration of a Pure Water Solution. 5 ml aliquots of a 0.1 M NaOH solution are added to 50 ml of pure water. After each addition, the pH of the solution is determined (solid circles). The maximum possible pH for the experiment, pH 13, is indicated by the horizontal dotted gray line.

Let's now examine a base titration in which we start not with pure water, but with a 50 ml solution of 0.1 M HCl (**Figure 6.19**). Before any base is added, the pH of the solution is very low. HCl, being a strong acid, is fully dissociated, and the proton concentration of the solution is 0.1 M (pH 1.0). What happens when we add 5 ml of our

0.1 M hydroxide solution? The 0.0005 moles of hydroxide fully neutralize an equivalent amount of protons, producing water. This leaves 0.0045 moles of protons in 55 ml, for a pH of 1.09. Although a large fraction of protons have been neutralized, enough remain in solution that the log-based pH scale shows only a modest change. Even as we add more and more 5 ml aliquots of 0.1 M NaOH, the pH remains relatively flat and low. This continues until nearly all of the protons have been neutralized, i.e., 50 ml of total 0.1 M NaOH solution have been added to the original 50 ml volume of 0.1 M HCl. Here we have reached what is known as the equivalence point. At this point we have neither excess of protons nor hydroxide ions, so the pH is 7.0. When we add hydroxide ions past the equivalence point, the pH rises rapidly. This is analogous to the case when we added the hydroxide solution to pure water, as we have significant free hydroxide ions that perturb the pH of the solution into the highly basic range.

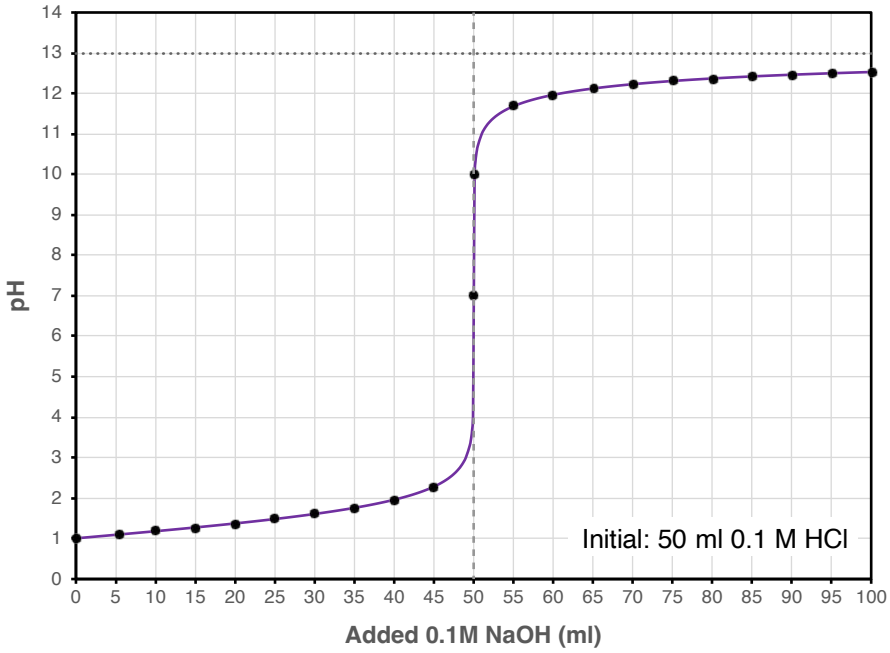


Figure 6.19 Calculated Results for the Base Titration of a Strong Acid Solution. 5 ml aliquots of a 0.1 M NaOH solution are added to a 50 ml solution of 0.1 M HCl. After each addition, the pH of the solution is determined (solid circles). The maximum possible pH for the experiment, pH 13, is indicated by the dotted horizontal gray line. The equivalence point (equal amount of added base to the amount of acid) is indicated by the dashed vertical gray line.

What does the base titration of a weak acid look like? Consider a 0.1 M solution of acetic acid before we add any sodium hydroxide (**Figure 6.20**). As we have discussed previously, the pH of this solution will be 2.88, as only about 1.3% of the original acetic acid molecules release a proton (Subsections 6.8 and 6.16). This causes the pH of this weak acid solution to start at a higher pH (less acidic pH), relative to a strong acid solution of the same initial acid concentration. What happens when we add 5 ml of the 0.1 M hydroxide solution? The 0.0005 moles of base neutralize an equivalent amount of protons, either free in solution or on acetic acid, since it is a much stronger base than acetate, the conjugate base of acetic acid. Thus, there are 0.0005 moles of acetate in solution and 0.0045 moles of acetic acid. According to the Henderson-Hasselbalch equation (Equation 6.22), with these equilibrium concentrations of A^- and HA, as well as a pK_a of 4.76 for acetic acid, we can calculate the pH, and get a pH of 3.81, a relatively large jump up in pH. However, if we continue to calculate the pH as we add more 5 ml aliquots of hydroxide ion, we see that as we approach the half-neutralization point of the acid (when 25 ml of 0.1 M NaOH has been added to the original 50 ml of 0.1 M acetic acid solution), that titration curve flattens out somewhat and the pH approaches the pK_a of the acid, 4.76, in this case. This flatter region continues as more than half of the acetic acid is neutralized, until it starts rising again more rapidly, especially as it nears the equivalence point (50 ml of 0.1 M NaOH added). Past this point, like the strong acid, the pH rapidly rises.

Let's look at the base titration of another weak acid solution, 50 ml of a 0.1 M solution

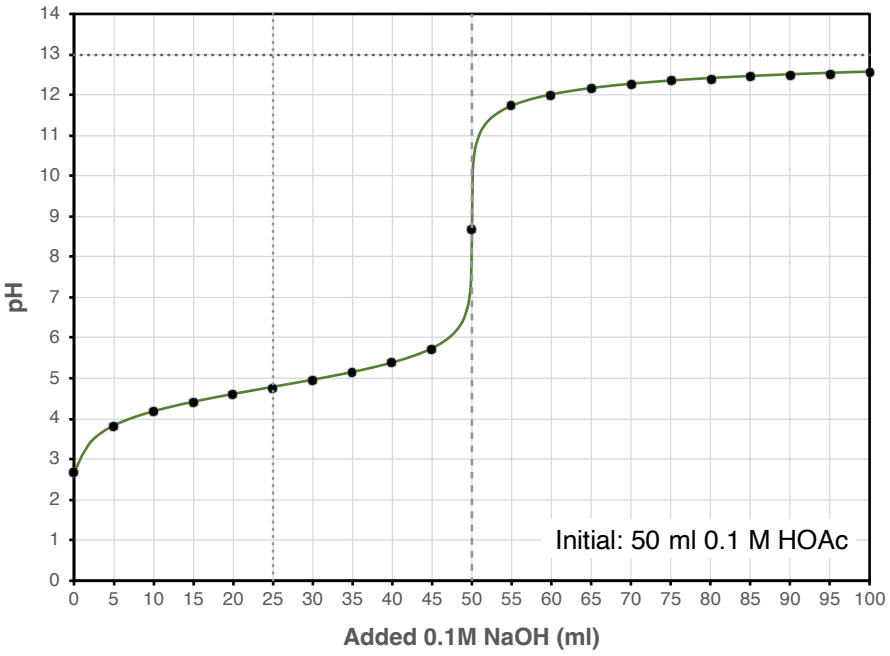


Figure 6.20 Calculated Results for the Base Titration of a Weak Acid, Acetic Acid. 5 ml aliquots of a 0.1 M NaOH solution are added to a 50 ml solution of 0.1 M acetic acid. After each addition, the pH of the solution is determined (solid circles). The maximum possible pH for the experiment, pH 13, is indicated by the horizontal dotted line. The half-neutralization point is indicated by the dotted vertical line. The equivalence point is indicated by the dashed vertical line.

of ammonium ion (**Figure 6.21**). A solution of ammonium ion, the conjugate acid form of ammonia, can be made from solid ammonium chloride salt dissolved to a concentration of 0.1 M (giving roughly 0.1 M ammonium ion and 0.1 M chloride). As ammonium ion is an acid, like acetic acid, it will deprotonate to some extent before any sodium hydroxide is added. That said, ammonium ion is an even weaker acid than acetic acid (justifiable from their pK_a values of 9.25 and 4.76, respectively, or from the fact that ammonia is a stronger base than acetate). Thus, if ammonium ion is added to pure water, the pH will be less than 7.0, but greater than 2.88 (the pH for acetic acid). From the pK_a of ammonium ion, we can calculate that the pH of this solution in pure water is 5.12 (leftmost point of Figure 6.21), corresponding to just under 0.01% dissociation (about 1 in 13,000 ammonium ions give up a proton). When we begin adding 5 ml aliquots of 0.1 M NaOH, the hydroxide ion is still a strong enough base that it effectively neutralizes every ammonium ion it encounters. This results in various ratios of ammonia to ammonium ion in solution, and we can again use the Henderson-Hasselbalch equation (Equation 6.22) to determine the pH is at each point along the titration

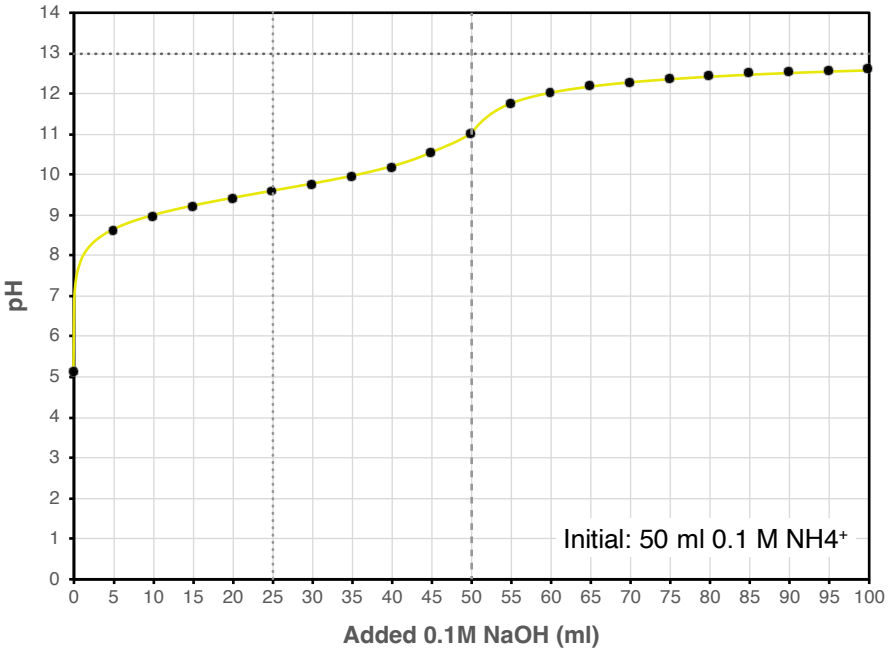


Figure 6.21 Calculated Results for the Base Titration of a Weak Acid, Ammonium Ion. 5 ml aliquots of a 0.1 M NaOH solution are added to a 50 ml solution of 0.1 M ammonium ion. After each addition, the pH of the solution is determined (solid circles). The maximum possible pH for the experiment, pH 13, is indicated by the horizontal dotted line. The half-neutralization point is indicated by the dotted vertical line. The equivalence point is indicated by the dashed vertical line.

curve (Figure 6.21). Of note, when the ammonium ion is half deprotonated (25 ml 0.1 M NaOH added to the original 50 ml 0.1 M NH_4^+ solution), the pH is 9.25, the pK_a of the ammonium ion. Near the equivalence point, where all of the ammonium ion is neutralized, (50 ml 0.1 M NaOH added to the original 50 ml 0.1 M NH_4^+ solution), the pH begins to rise more rapidly.

It's worth comparing the acetic acid and ammonium titration curves. At many points in the titrations the extent of neutralization is the same. For example, when 5 ml of 0.1 M NaOH was added to the 50 ml solutions of either 0.1 M acetic acid or 0.1 M ammonium ion, 10% of the acids are neutralized and 90% are still protonated. This means the titration curve will have the same shape in those regions (the log([A-]/[HA]) portion of Equation 6.22). However, the pH over which this occurs is not the same, because their pK_as differ.

Other acids can be titrated — for example, the polyprotic acid, phosphoric acid (**Figure 6.22**). As the first proton of phosphoric acid is relatively acidic, 50 ml of a 0.1 M solution of phosphoric acid starts at a low pH (leftmost point of Figure 6.22). As 5 ml aliquots of 0.1 M NaOH are added, the pH rises, as the first, second, and third protons are neutralized in turn, where the three deprotonation steps effectively behave like three independent acids with distinct pK_as.

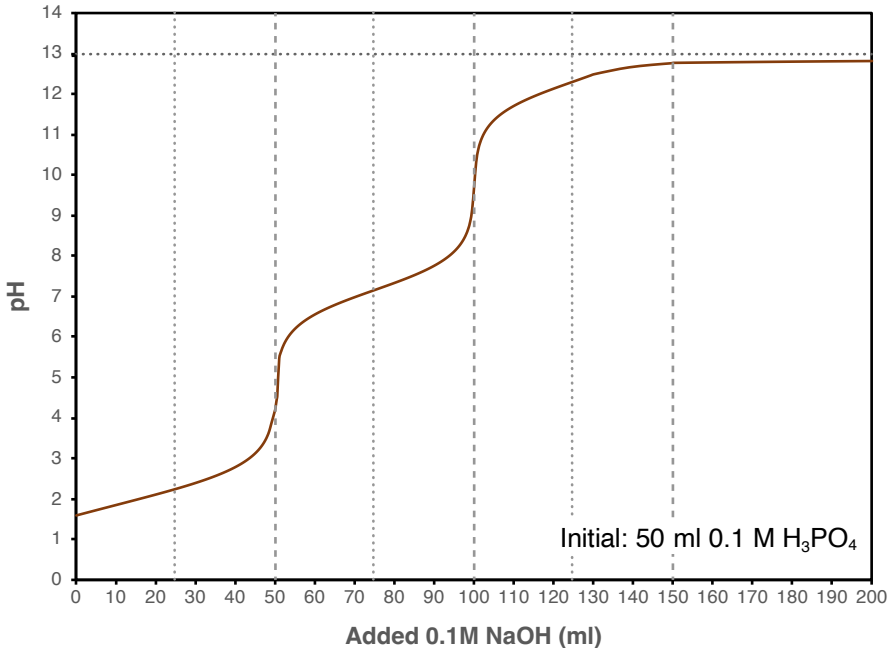


Figure 6.22 Calculated Results for the Base Titration of a Polyprotic Acid, Phosphoric Acid. Increasing amounts of a 0.1 M NaOH solution are added to a 50 ml solution of 0.1 M phosphoric acid and the pH determined. The maximum possible pH for the experiment, pH 13, is indicated by the horizontal dotted line. The three half-neutralization points are indicated by the three dotted vertical lines. The three equivalence points are indicated by the dashed vertical lines.

Just as we can titrate various acids with a strong base, we can titrate various bases with a strong acid — here a 0.1 M solution of HCl. The titration curves that result (**Figure 6.23B**) resemble our previous titration curves (**Figure 6.23A**), but with the pH progression reversed: All base solutions begin at a pH above 7, become neutralized, and then drop to a low pH past their equivalence points. Like the weak acids acetic acid and ammonium ion, their conjugate bases, the weak bases acetate and ammonia, don't start at the same pH and have different titration curves, as these bases have different pK_bs. Importantly, the pH of half neutralization for either acetic acid or acetate (or ammonium ion or ammonia) is equal to one another, as they both have the same equilibrium ratio of acid and conjugate base.

6.20 pH of Buffering and Buffering Capacity

The titration curves from the previous subsection show why weak acids and their conjugate bases are used as pH buffers. For an acid like acetic acid, you can see that if

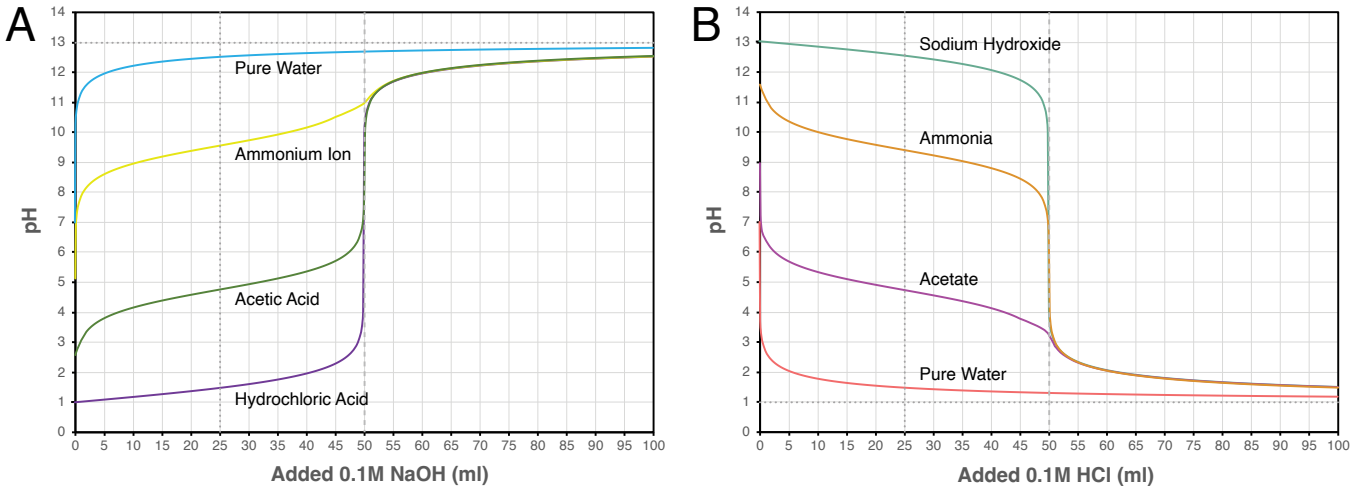


Figure 6.23 Comparison of Base Titrations of Various Acids with Acid Titrations of Various Conjugate Bases. A) A summary of the NaOH titrations of acids or pure water described in Figures 6.18-6.21. B) Acid (HCl) titrations of the conjugate bases of the weak acids from part A. In both parts, the maximum pH obtainable are indicated with horizontal dotted lines, the half-neutralization points by vertical dotted lines, and the equivalence point by vertical dashed lines.

you start at the point of half-deprotonation and add a small amount of hydroxide ion (Figure 6.23A, to the right of the midpoint on the HOAc curve), the pH changes less than any other portion of the curve. Similarly, if you add a small amount of protons instead (Figure 6.23B, to the right of the midpoint of the $^{-}$OAc curve), the pH changes relatively little and changes less than at any other point on the curve. The titration curves also show that different acid/base pairs differ at which pH they are most effective at buffering. Acetic acid is best suited to resist pH changes near a pH of 4.76 (acetic acid's pK_a), while ammonium ion does so around a pH of 9.25 (its pK_a).

The titration curves also provide insights into the buffering capacity of a buffer system. A buffer's buffering capacity reflects how many added protons or hydroxide ions it can neutralize. This depends both on the ratio of the buffer's acid to conjugate base, and on the total concentration of the buffer components. To illustrate the former, consider a 50 ml solution of an acetic acid/acetate buffer, where the buffer contains an equal amount of each of these components and their total concentration is 0.1 M. We could add up to 25 ml of 0.1 M NaOH before the buffer was fully neutralized (midpoint of HOAc curve in Figure 6.23A to the equivalence point). Similarly, we could add up to 25 ml of 0.1 M HCl before the buffer was neutralized (midpoint of $^{-}$OAc curve in Figure 6.23B to the equivalence point). Now consider an acetic acid/acetate buffer system where the total concentration of components is still 0.1 M, but the concentration of acetic acid exceeds the concentration of the acetate (some point to the left of the midpoint of Figure 6.23A, or some point to the right of the midpoint of Figure 6.23B). While this buffer system would be able to neutralize more added NaOH before reaching its equivalence point, the amount of HCl needed to reach the equivalence point would be less. Because we want our buffer to be equally good at resisting changes in pH in either direction, our original system with an equal amount of acid and conjugate base would have a greater buffering capacity and be superior.

The total concentration of buffering compounds in a buffer also influences its buffering capacity, with a larger concentration of buffer resulting in a greater buffering capacity. This makes intuitive sense. If our buffer has a greater concentration of acetic acid and acetate, it will be able to neutralize more hydroxide ions and protons, respectively. We can see this more concretely in **Figure 6.24**. Figure 6.24A shows the original titration curve for our 0.1 M acetic acid/acetate buffer, focusing on the region from starting with an equal amount of acetic acid and acetate (the midpoint) to when enough volume of 0.1 M NaOH has been added to fully neutralize the buffer (the equivalence point), i.e. 25 ml 0.1 M NaOH added. If the buffer solution contained half as much acetic acid/

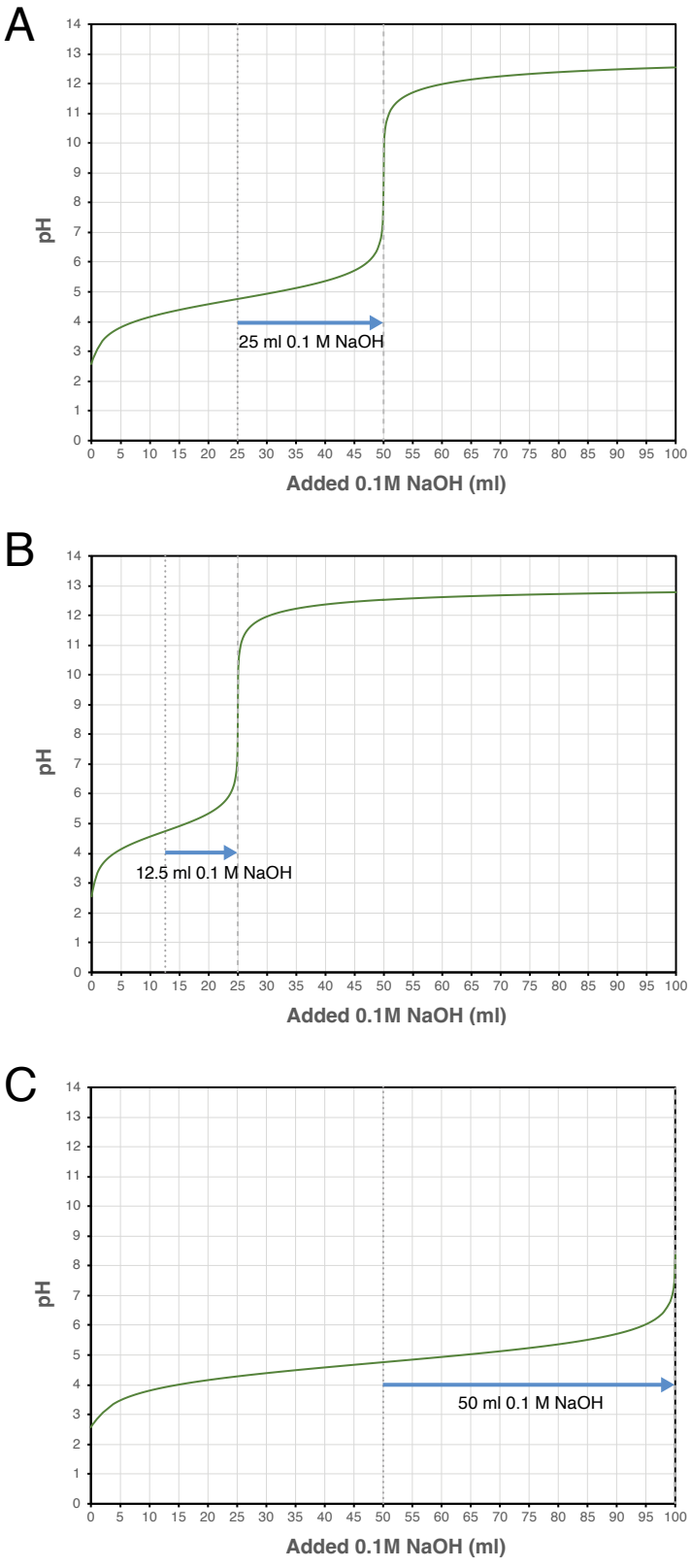


Figure 6.24 Comparison of Buffering Capacities. Three buffer solutions with an equal amount of acetic acid and acetate are made from a 50 ml solution of A) 0.1 M, B) 0.05 M, or C) 0.2 M acetic acid by neutralizing them with the addition of 0.1 M sodium hydroxide. From this point, each solution can absorb a different total amount of added base until all of the acetic acid in the buffer is neutralized (volume of 0.1 M NaOH absorbed indicated by the length of the blue arrow). In all graphs, the half-neutralized point is indicated by the dotted vertical line, and the equivalence point is shown with the dashed vertical line. Note, buffers are not typically made quite this way, with details described in Subsection 6.21.

acetate (Figure 6.24B), the volume of 0.1 M NaOH needed to reach the equivalence point would be half as much as for the more concentrated buffer (12.5 ml compared to 25 ml). That is, the buffer with the lower buffer concentration has a lower buffering capacity, because it cannot accommodate as much added hydroxide solution as the original buffer. Similarly, if we double the buffer concentration (Figure 6.24C), we can now absorb twice as much hydroxide as before.

6.21 Buffer Preparation and Ionic Strength

If an optimal pH buffer has an equal amount of acid and conjugate base, how do you prepare such a solution? Let's say you wanted to make 500 ml of a pH 4.76 buffer containing 0.1 M acetic acid/acetate. The titration curves from Figure 6.23 suggest two possible ways to do so. Figure 6.23A shows that if you start with a solution of acetic acid and add the right amount of NaOH, you can get to a point where you have half neutralized the acetic acid, i.e. you have equal concentrations of acetic acid and acetate.

Practically, to prepare the initial acetic acid solution, you would weigh out enough acetic acid so that in 500 mL it would have a concentration of 0.1 M. This corresponds to 0.05 moles of acetic acid (0.1 mole/l x 0.5 l = 0.05 moles). Pure acetic acid is 60.05 g/mol, so you would add 3.00 g to a beaker. Pure acetic acid is a liquid; while the equivalent volume (2.86 ml) could in principle be measured, it is highly viscous and difficult to dispense accurately, so weighing is the preferred approach. Then you would add pure water to a volume below 500 ml (perhaps add 450 ml). At this point, you are ready to half-neutralize the acetic acid. By analogy with Figure 6.20, you might imagine adding enough of a 0.1 M NaOH solution to do so. However, there are two problems. The first problem is that adding the necessary 250 ml of 0.1 M NaOH to our 450 ml acetic acid solution would bring the total volume to 700 ml, far exceeding the desired final volume of 500 ml. Although we can solve this problem by initially adding less water to the acetic acid, the second problem is that it's hard to be certain that we will hit the desired 1:1 ratio of acetic acid and acetate. If either the amount of acetic acid we measured or the concentration of the hydroxide solution is off, the ratio, and therefore final pH, could be wrong. One way we can get around this is to measure the pH with a pH meter as we add our hydroxide solution (with vigorous mixing). When the pH of the solution is 4.76, we can be confident that the ratio of acetic acid and acetate is equal. Often we start with a more concentrated hydroxide solution to add to the solution (1.0 or 10 M NaOH). When we get close to the target pH, we switch to a more dilute NaOH solution. At this point, our total volume may not be 500 ml (and therefore the final buffer concentration would not be 0.1 M). As long as we didn't add too much volume, we can add pure water to bring the solution to a final volume of 500 ml.

As an alternative to half-deprotonating an acetic acid solution with a strong base, Figure 6.23B suggests we could instead half-protonate an acetate solution with a strong acid, like HCl. The procedure would be similar to making 500 ml of a 0.1 M acetic acid/acetate buffer at pH 4.76: an appropriate amount of acetate would be weighed out, say in the form of sodium acetate salt (0.05 moles x 82.03 g/mol = 4.10 g sodium acetate); the salt would be dissolved in 450 ml of pure water, and then hydrochloric acid would be added until a pH of 4.76 was reached; water would be added to bring the buffer to a final volume of 500 ml.

Yet another way to prepare such a buffer would be to add an appropriate amount of acetic acid and acetate together. For 500 ml of buffer, we would want half as much acetic acid and acetate as we started with when we used just one component (1.50 g acetic acid and 2.05 g sodium acetate). The acid/conjugate base pair would be dissolved in water and the pH adjusted as required to reach the desired pH of 4.76.

In all of these strategies, the final ratio of acid to conjugate base is the same, suggesting that the solutions are identical. However, the solutions differ in their ionic strength. Ionic strength is a measure of the concentration of all ions in a solution that also depends on the total charge of the ions. Let's consider how ions are introduced into our buffers. Consider the case where we start entirely with the neutral molecule acetic acid, which by itself only dissociates into charged particles to a small degree when added to pure water. If we want to half-neutralize this solution, we add a sodium hydroxide solution, which provides a hydroxide ion and a sodium ion. The positively charged sodium ion isn't involved in the neutralization, but remains in solution as a charged particle. The

negatively charged hydroxide ion is consumed during the neutralization, becoming water. In the process, however, it converts a neutral acetic acid molecule to a negatively charged acetate. So, for every molecule of NaOH added, we end up with a positive ion (Na^+) and a negative ion (acetate). At half-neutralization of an initial 0.1 M solution of acetic acid, we've added 0.1 M of ions (0.05 M sodium cation, 0.05 M acetate anion). Compare this to when we start with 0.1 M sodium acetate and half-neutralize it with an HCl solution. Here, initially we have a solution of the fully dissociated salt that is composed of two ions, a sodium and acetate ion, for a total ion concentration of 0.2 M (0.1 M sodium cation and 0.1 M acetate anion). When we half-neutralize this solution with HCl, a negatively charged acetate ion is converted to a neutral acetic acid. This loss of a negative charge is offset by the negative chloride ion that was added, so there is no net change in the total number of ions in solution. Thus, the 0.1 M acetic acid/acetate buffer prepared from sodium acetate has twice the ion concentration (and ionic strength) as the one prepared from acetic acid.

How much do solutions with different ionic strength matter? For any solution in which ions are present (in our examples, all of the buffers we've made), it is worth keeping in mind the presence of the ions, as ions can have an effect on many biological processes (see Chapter 3). If you are comparing different solutions, say buffering a protein at different pHs to study the effect of pH, it is best to maintain an equal ionic strength between solutions, so any changes observed can be attributed to the difference in pH and not the change in ionic strength. The magnitude of ionic strength also depends on the charge of the ions, not just their number; separately, the chemical identity of the ions can matter as well.

6.22 Buffering Compounds

Different acid/conjugate base pairs have different pK_as and are useful for buffering different pHs. However, as we have discussed, not all buffering agents are appropriate for experiments, and the range of pHs is limited for the buffering agents described so far. Luckily, there are many commercially available compounds with a wide range of pK_a values (**Table 6.4**), meaning that most conceivable pHs can be buffered by one of these compounds. Although we will not have the tools to understand the chemical structure and properties of these compounds until later chapters, in general, the compounds have been developed to be well-behaved in an experimental setting. Unlike the issue of equilibration with carbon dioxide in bicarbonate buffers, or the ability of phosphate buffers to react with some ions or mimic some biomolecules, these buffers tend to be soluble, stable, and non-reactive. Potential exceptions to this are Tris and glycine buffers that are used for biochemical assays because they are relatively inexpensive. These compounds are related to amines like methylamine and ethylamine and can occasionally react with compounds that have carbon-oxygen double bonds, like formaldehyde and acetone. Additionally, their p$K_a$values can fluctuate with temperature more than most other buffers. That said, in many applications, they are good enough to use as buffering agents.

Compound	pK_a
Bis-Tris	6.5
PIPES	6.75
MOPSO	6.9
MOPS	7.2
HEPES	7.48
HEPPSO	7.80
TRIS	8.06
Gly-Gly	8.20
Bicine	8.35
TAPS	8.40

Table 6.4 Some commercially available buffering agents with pK_as between 6.5 and 8.5. Note, many other buffering agents are available within and outside of the pK_a range shown.

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Chapter 6: Acids and Bases

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About the Author

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Glossary

This glossary is focused on the essential terms found in the book, not every term. It does not include terms from the Further Exploration sections, nor the chemical compounds used to illustrate core concepts (both are available in the Index of Volume I). This glossary can serve as a good study guide for the materials presented - if you can explain each term in your own words, you have mastered the core vocabulary of the volume.

Acids: Compounds capable of giving up a proton, such as hydrochloric acid and acetic acid. Adding an acid to an aqueous solution will increase the solution's proton concentration.

Adhesion: The ability of a liquid to stick to a surface. Water, because of its polar nature, adheres strongly to surfaces with polar or charged groups via hydrogen bonds and dipole interactions, which is why water can climb the walls of a narrow tube (capillary action).

Anions: Particles with a negative charge. Anions can be a single atom or a molecule and can carry charges of -1, -2, -3, and so on.

Atomic Mass: The "weight" of an atom. A common unit is amus (atomic mass units), where protons and neutrons each weigh approximately 1 amu, and an atom's atomic mass is very roughly the sum of its number of protons and neutrons. Another unit of atomic mass is grams/mole, where an atom's amu value translates into that many grams per mole of the atom (its molar mass).

Atomic Nucleus: The subatomic particles (protons and neutrons) found at the center of an atom. For example, the nucleus of the most common isotope of carbon contains six protons and six neutrons. The atomic nucleus constitutes a small fraction of an atom's total volume.

Atomic Number: A number that uniquely identifies an element and is equal to the number of protons in its atom. For example, carbon, with six protons, has an atomic number of six.

Atomic Structure: The arrangement of subatomic particles in an atom. Protons and neutrons are found in the nucleus, while electrons are found outside of the nucleus in particular electron shells.

ATP: An organic biomolecule (adenosine triphosphate) that is the main energy currency for all living things. ATP is produced from the breakdown of food, and consumed to power processes like muscle contraction and protein synthesis.

Avogadro's Constant: The number of particles in a mole: 6.02×10^{23}. This number is so large that even a tiny mass of a substance contains an almost unfathomable number of atoms or molecules.

Bases: Compounds capable of picking up a proton, such as sodium hydroxide and ammonia. Adding a base to an aqueous solution reduces the proton concentration of the solution and increases its hydroxide concentration.

Biological Molecules: Organic molecules used by living organisms to perform cellular functions, such as supplying energy, providing cellular structure, facilitating chemical reactions, and storing genetic information. Some example biological molecules (also called biomolecules or organic biomolecules) include amino acids, sugars, nucleotides, lipids, ATP, and NADH.

Bond Angle: The angle between two covalent bonds in a molecule. For example, water has two O-H bonds and the bond angle for the molecule (the H-O-H angle) is 104.5°. Bond angles can theoretically be of any value from just over 0° to 180°.

Bond Dipole: A covalent bond that has a positive and negative end, such as the O-H bond in a hydroxyl group. A bond dipole occurs when two atoms with significantly different electronegativities make a covalent bond, causing the shared electrons of the bond to reside predominantly near the more electronegative atom. In an O-H bond, the bond electrons reside more on the oxygen, making the O partially negatively charged and the H partially positively charged.

Buffer (Buffer System): Compounds in solution (an acid and its conjugate base) that allow the solution to resist changes in pH. The acid of the buffer provides protons to neutralize bases added to the solution, while the conjugate base of the buffer neutralizes added acids. Different buffer systems are optimal for different pH values. For example, a buffer solution containing an equal concentration of acetic acid and acetate ions is well suited to maintaining a pH of about 4.76.

Capillary Action: A phenomenon where a liquid moves into the narrow spaces of an object even against gravity, due to adhesion to the object's surface. Water demonstrates capillary action when it climbs the walls of a capillary tube or is drawn into the narrow channels in paper towels.

Cations: Particles with a positive charge. Cations can be a single atom or a molecule and can carry charges of +1, +2, +3, and so on.

Cohesion: The ability of a liquid to stick to itself. Water, because of its polar nature, coheres strongly to itself via hydrogen bonds, which is why water tends to form droplets and has a high surface tension.

Compounds: A substance formed from two or more atoms that are bound together in a fixed proportion. Examples include table salt (NaCl, where Na^+ and Cl^- ions are held together by ionic bonds), and water (H_2O, where one O and two H atoms are held together by covalent bonds). NaCl is an ionic compound, and H_2O is a covalent compound.

Concentration: The amount of a substance dissolved in a given volume. A concentration is "high" when lots of something (solute) is dissolved in a liter of solution, and low if there is relatively little dissolved in the same volume. Concentrations can be described in different ways, including mass concentrations (g/L) and molar concentrations (moles/L).

Conjugate Acids and Conjugate Bases: When a base gains a proton, it becomes a conjugate acid. This is because the protonated form of the base is capable of losing the proton that it just gained, making it a (conjugate) acid. As an example, the conjugate acid of ammonia is an ammonium ion. When an acid loses a proton, it becomes a conjugate base. This is because the deprotonated form of the acid can gain back its proton, making it a (conjugate) base. As an example, the conjugate base of acetic acid is acetate.

Conversion Factors: A factor used to convert a number from one set of units to another, where the original number is multiplied by the conversion factor to get the value in the new units. For example, if I had driven 5.00 miles and wanted to know the distance I had traveled in kilometers, I could use the conversion factor of 1.61 km/mile (5.00 miles x 1.61 km/mile = 8.05 kilometers). Note that a conversion factor can only be used if there is direct proportionality between the units.

Counterion: An ion that counteracts another ion of opposite charge. For example, in table salt, NaCl, the counterion of the sodium ion (Na^+) is the chloride ion (Cl^-). Similarly, if I was focused on the chloride, its counterion would be the sodium ion. In general, the total charge of an ion is offset by its counterion (or counterions) to yield a net zero charge.

Covalent Bonds: The sharing of valence electrons between two atoms, where one, two, or three pairs of electrons can be shared. Examples include the bonds between hydrogens in H_2 gas, or between hydrogens and oxygen in water (H_2O). A covalent bond (two shared electrons) is often depicted as a line - so a single bond would have one line between atoms; a double bond, two; and a triple bond, three. If sharing of electrons between the atoms is equal or nearly equal, the covalent bond is considered a non-polar covalent bond. If the sharing is substantially unequal, the covalent bond is classified as a polar covalent bond.

Density: A property of a substance that describes how much mass is packed in a given volume. The units of density are g/ml, g/cm^3, or g/cc (all equivalent), with liquid water having a density of 1.0 g/ml at 4° C. A substance with a greater density than water will weigh more per milliliter than water, and will sink in water. Conversely, substances less dense than water will be buoyant and float.

Deprotonation: Removal of a proton (H^+) from a covalent compound. For example, deprotonation of acetic acid converts it to an acetate ion. Bases can facilitate the deprotonation of acids.

Diatomic Molecules: A molecule composed of two atoms linked by covalent bonds. The two atoms can be the same type, like diatomic hydrogen gas, H_2, or can be different, like hydrogen chloride gas, HCl. Diatomic molecules can have a single covalent bond (e.g. Cl_2), a double bond (e.g. O_2), or a triple bond (e.g. N_2).

DNA: The genetic storage material of all living things. At a molecular level, DNA consists of two long, thin strands of negatively charged units (nucleotides) wound together into a double helix, where the sequence of nucleotides encodes the instructions for making proteins.

Electric Dipole: An object with a positive and negative end. A covalent compound can have an electric dipole in the bond between two atoms (bond dipole) or it can have an overall electric dipole (molecular dipole).

Electron Dot Structures: A way of depicting covalent compounds that shows all valence electrons. In an electron dot structure, the valence electrons of an atom are presented by either dots (such as lone pairs) or lines (such as covalent bonds). Everything else in the atom (its nucleus and non-valence electron shells) is represented by the atom's symbol. For example, in the electron dot structure of water, H_2O, a central O is connected to two Hs by a single line (bond). The O also has two sets of two dots (lone pair electrons).

Electron Shells: Locations where an atom's electrons can reside, where each shell can accommodate multiple electrons. Electron shell occupancy is dictated by the element's position in the periodic table, and its outermost occupied shell is known as its valence shell. For example, oxygen has two electrons in its first shell and six in the second shell, its valence shell.

Electronegativity: A number that describes how strongly an atom attracts bonding electrons toward itself in a covalent bond, where the larger the number, the more electronegative the element is. Electronegativity tends to increase as we go left to right across a row in the periodic table (ignoring the elements in the last column), and decreases as we go down a column. Thus, fluorine is the most electronegative element. Of the atoms we will commonly encounter in this volume, both chlorine and oxygen are very strongly electronegative.

Electrons: Negatively-charged subatomic particles of negligible mass (compared to protons and neutrons) that reside outside of the atom's nucleus. The number of electrons of an element is equal to its number of protons (its atomic number), but electrons can be gained or lost in becoming an ion or

shared in a covalent compound. An atom's valence electrons are the most important for understanding its reactivity and stability.

Electrostatic Interactions: Force exerted between two charged particles that can be attractive (particles with opposite charges are pulled toward each other) or repulsive (particles with the same charge are pushed away from each other). Electrostatic interactions are the basis of interactions like ionic bonds, where the oppositely charged ions in table salt (Na^+ and Cl^-) come together to form NaCl due to their attractive electrostatic interactions.

Elements: A substance made from atoms sharing the same number of protons. Each element has a unique position and atomic number in the periodic table, and all matter is composed of individual elements or combinations of elements.

Gram: Fundamental metric unit of mass. One gram weighs approximately the same as a regular paper clip.

Halogens: Elements in the second-to-last column of the periodic table, such as fluorine and chlorine. These elements tend to be very electronegative and only need one more electron to achieve a full valence. To achieve a full valence, they will often undergo reduction to anions, like Cl^- (generally very stable) or form a covalent bond with another atom of comparable electronegativity, like Cl_2 (generally reactive species).

Hydrogen: The simplest of all elements, with the most common isotope consisting of one proton, one electron, and no neutrons. Hydrogen can lose its single electron to leave behind a bare proton (H^+), which is what acids donate and bases accept. This makes hydrogen central to acid-base chemistry, pH, and formation of hydrogen bonds.

Hydrogen Bonds: A non-covalent interaction between two molecules mediated by the hydrogen of one molecule and a lone pair of electrons on the other. In this volume, we will focus on hydrogen bonds associated with oxygens or nitrogens. While hydrogen bonds are much weaker than covalent bonds, they are the strongest of the non-covalent interactions covered in this volume. Water is an example of a compound that can form hydrogen bonds, and these bonds are responsible for many of the unique properties of water, including high surface tension, capillary action, and high freezing and boiling points.

Hydrophilic: A compound that is water soluble is considered hydrophilic. These compounds tend to contain many polar or charged groups and relatively few non-polar groups. Examples of hydrophilic compounds include methanol, acetic acid, acetate, and ammonia.

Hydrophobic: A compound that is not water soluble is considered hydrophobic. These compounds tend to contain many non-polar groups with few polar or charged groups. Examples of hydrophobic compounds include methane and ethene.

Hydroxyl Group: A portion of a molecule containing an oxygen with a single bond to a hydrogen (i.e., an -OH). Example compounds that contain a hydroxyl group include water, methanol, and acetic acid. Hydroxyl groups are polar and impart polar character to compounds that contain them. Compounds with hydroxyl groups can form hydrogen bonds, and many biological acids contain hydroxyl groups as the source of their protons.

Ionic Bonds: Force holding together oppositely charged particles, such as the ions that make up table salt (Na^+ and Cl^-). Ionic bonds are electrostatic in nature and increase with the magnitude of the charges on the ions. Ionic bonds are weakened by compounds that can shield their charge, such as water.

Ions: Particles with a net positive or negative charge. Ions can be a single atom (Na^+) or a molecule (acetate). The charge of an ion can be any positive or negative integer (..., -3, -2, -1, +1, +2, +3, ...). Cations refer specifically to positively-charged ions, while anions refer to negatively-charged ones.

Isotopes: Forms of an element that differ by their number of neutrons. For example, the single-proton element hydrogen has several naturally-occurring isotopes. The most common is hydrogen with one proton and no neutrons. Less common is hydrogen with one proton and one neutron (deuterium), or one proton and two neutrons (tritium). For the elements we focus on in this volume, the most common isotope tends to have roughly equal numbers of protons and neutrons.

"Like Dissolves Like": Phrase used to predict the solubility of compounds, where the underlying idea is that polar (or charged) compounds tend to dissolve well in polar solvents (for example, the sugar glucose in water) and non-polar compounds tend to dissolve well in non-polar solvents (such as the non-polar compounds that make up motor oil). An extension of this idea is that a mismatch between the polarity of a compound and a solvent causes them not to be soluble (motor oil and water).

Liter: Fundamental metric unit of volume. Many reusable water bottles store one liter of liquid.

Logarithmic Scale: A number scale where each step along the scale represents a change by some multiple (often a factor of ten change, but not always). pH is an example of a proton concentration scale that is logarithmic. Every change of pH by one unit represents a 10-fold change in molar proton concentration. For example, a solution at pH 2 (0.01 M proton) is 10-fold different than one at pH 3 (0.001 M proton). Note that the pH scale is a little weird, in that a one-unit decrease in pH represents a 10-fold increase in proton concentration. Thus, a solution with a pH of 2 has 10 times more protons than one with a pH of 3.

Lone Pair of Electrons: Pairs of valence electrons that are not involved in making covalent bonds. For example, when oxygen is part of a neutral compound (such as water), two of its six valence electrons make covalent bonds (for water, two single bonds to hydrogens). The remaining four valence electrons

end up as two sets of lone pair electrons. Lone pair electrons determine the molecular geometry of a compound (VSEPR theory), make hydrogen bonds, and accept protons in bases.

Mass: The amount of matter in an object. In everyday usage, mass and weight are used interchangeably, but they are technically different: mass is an intrinsic property of an object, while weight depends on gravity. The standard scientific unit of mass is the gram.

Mass Concentration: A concentration of a solution defined in terms of how many grams of a substance are present in some volume of the solution. Has units of g/L (or sometimes g/ml or g/cc). Note that the volume used in mass concentrations is for the entire solution, i.e., it includes the volume taken up by the dissolved substance (solute) and the volume of solvent added.

Metals: Elements in the columns on the left and middle of the periodic table. Metals have relatively low electronegativities and generally will undergo oxidation to cations to achieve a full valence. Metal cations from the first column (such as Na^+ and K^+) and the second column (like Mg^{2+} and Ca^{2+}) tend to be very stable.

Metric Prefixes: Modifiers placed in front of metric amounts (grams, liters, meters, etc.) to indicate some fold-increase or decrease in the base amount. The metric prefix that indicates more than the base amount is kilo- (k-), which represents 1,000 times the base amount. For example, one kilogram (1 kg) is 1,000 grams. The metric prefixes that indicate less than the base amount are: milli- (m-), which represents 1/1,000th of the base amount; micro- (μ-), which represents 1/1,000,000th of the base amount; and nano- (n-), which represents 1/1,000,000,000th of the base amount. For example, one millimeter (1 mm) is 1/1,000th of a meter, one micrometer (1 μm) is 1/1,000th of a mm, and one nanometer (1 nm) is 1/1,000th of a micrometer.

Mixture: A combination of two or more substances, where the substances maintain their chemical identity (i.e., they do not react). The components of a mixture may all be in the same phase, or differ. If the molecules of the components are equally distributed throughout the mixture, it is a homogeneous mixture. If they are not, it is a heterogeneous mixture. Solutions are examples of homogeneous mixtures.

Molar Concentration: A concentration of a solution defined in terms of how many moles of a substance are present in some volume of the solution. Has units of moles/L or M - where 1 M (1 molar) is 1 mole/L. Molar concentration can be derived from a mass concentration by using molar mass (how many grams are in a mole) as a conversion factor. Note that the volume used in molar concentrations is for the entire solution, i.e., it includes the volume taken up by the dissolved substance (solute) and the volume of solvent added.

Mole: A term used to denote 6.02×10^{23} particles (Avogadro's constant). A mole is used in describing the amount of something, similar to how a dozen would be used (though a mole of something is a lot more than twelve of the item). The number of moles of a substance that are present in a given mass can be determined using the substance's molar mass as a conversion factor (atomic mass for atoms, molecular mass for molecules).

Molecular Dipole: A molecule that has a positive and negative end (i.e., the molecule is an electric dipole). An example of a compound that is a molecular dipole is water, with oxygen being partially negatively charged, and the hydrogens being partially positively charged. To be a molecular dipole, a compound must have at least one bond dipole (water has two), and it must have a molecular geometry in which the bond dipoles do not cancel each other out (because water is bent, its dipoles add to form a non-zero net dipole – the molecular dipole).

Molecular Geometry: The three-dimensional shape of a covalent compound. The spatial arrangement of groups of atoms can often be predicted by VSEPR theory. These arrangements have specific names, such as linear, trigonal planar, bent, trigonal pyramidal, and tetrahedral. If a molecule contains just one of these groups, its molecular geometry is named for the group. For example, the carbon of methane has a tetrahedral arrangement of bonds to hydrogen and the molecule itself is tetrahedral. If the molecule is more complex, the shapes of portions of the compound can be identified. For example, the arrangement of groups around methanol's oxygen (a hydrogen and methyl group) is bent. The groups around methanol's carbon (three hydrogens and one hydroxyl group) are tetrahedral.

Molecular Mass: The "weight" of a molecule. A common unit is amus (atomic mass units), where a compound's molecular mass is the sum of the atomic masses of all of its atoms. Another unit of molecular mass is grams/mole, where the molecule's amu value translates into that many grams per mole of the molecule (its molar mass).

Neutralization Reactions: A proton transfer reaction in which an acid and a base react to form weaker, less reactive conjugates. If the base is hydroxide-based (as with NaOH), water will be generated as a neutralization product. For example, HCl (strong acid) + NaOH (strong base) → $Na^+ + Cl^- + H_2O$. The acid and conjugate base present in buffer systems neutralize added bases or acids, thereby maintaining the pH of the solution.

Neutrons: Neutral subatomic particles with a mass approximately equal to that of a proton. Along with protons, neutrons are found in an atom's nucleus. The number of neutrons in an atom is often close to the proton number, but does not have to match. Isotopes of an element are atoms of that element with different numbers of neutrons. Neutrons generally do not have much impact on the reactivity of biologically-relevant molecules. However, they do affect the molecular mass of a compound.

Non-covalent Interactions: Interactions between atoms, both attractive and repulsive, that are not driven by formation of

covalent bonds. Examples of non-covalent interactions covered in this volume include hydrogen bonds (like water with itself), electrostatic interactions of ions (for example, between Na^+ and Cl^-), and dipole interactions with ions (such as between H_2O molecules and Na^+ ions).

Organic Elements: The elements that organic and biological molecules are made of: carbon, hydrogen, nitrogen, oxygen, phosphorus, and sulfur (CHNOPS). These elements form covalent bonds and carbon often forms the structural skeleton of the molecules. Some groups of organic molecules that have been covered so far are alcohols and amines.

Osmosis: Spontaneous movement of water molecules from a region of lower solute concentration to one with a higher concentration. Osmosis requires that any barrier between these regions does not allow solute to pass, but water is free to do so. Such a barrier is called a semi-permeable membrane, and cell membranes are generally permeable to water, but not to ions or polar molecules, which generally require transport proteins to cross.

Oxidation: Loss of one or more electrons from an atom. The molecule that loses the electrons is oxidized, and the atom that takes the electrons is an oxidizing agent. An example of oxidation is when sodium metal loses one electron to become a sodium ion: $Na \rightarrow Na^+ + e^-$. Note that oxidation can formally occur without full transfer of an electron, but this is not covered in this volume.

Periodic Table: A table containing all possible chemical elements - currently 118 elements. Elements are organized into rows and columns, and elements in specific regions of the periodic table are often grouped together (metals, organic elements, halogens, noble gases) and share chemical properties.

pH: A measure of proton concentration that is on a logarithmic scale, which means that a single-unit change in pH indicates a 10-fold change in molar proton concentration. pH is defined as the negative log-base-ten of the solution's molar proton concentration (for example, a 0.1 M solution of protons would have a pH of 1). On the pH scale, larger molar concentrations of protons result in a lower pH value, and vice versa. When the pH of a solution is below 7.0, it is considered acidic (more protons than hydroxide ions in solution). When the solution's pH is above 7.0, it is basic (more hydroxide ions than protons in solution). At a pH of 7.0, the solution is neutral (equal amounts of protons and hydroxide ions, each with a concentration of about 1×10^{-7} M).

Phases of Matter: Different physical forms a substance can exist in, distinguished by how the molecules of the substance are arranged. The most commonly encountered phases are solids, liquids, and gases, and for water, those correspond to ice, liquid water, and water vapor. Which phase a substance adopts depends on a number of factors, including the strength and nature of intermolecular interactions between molecules of a compound, as well as the temperature and pressure of the system. The temperature of transition from solid to liquid (melting point) and liquid to gas (boiling point) vary for different substances, and are quite high for water because of its ability to form numerous, strong intermolecular hydrogen bonds.

Polar Covalent Bonds: A covalent bond in which the electrons aren't shared equally between the two atoms that make up the bond, such as the O-H bond of a hydroxyl group. Because the more electronegative atom ends up "owning" more of the bond electrons, it ends up partially negatively charged, while the atom depleted of electrons ends up partially positively charged. This bond dipole can interact with other dipoles and individual charges, and contributes to the ability of partially negatively charged atoms (such as an oxygen or nitrogen) to make hydrogen bonds.

Proteins: Workhorse "machines" that perform a wide range of cellular functions, like forming muscle fibers, facilitating chemical reactions, and transducing signaling information from the outside of a cell to the inside. At a molecular level, proteins are composed of a string of amino acids, where their sequence dictates how this string of amino acids folds up and functions. The surfaces of proteins tend to be polar or charged, allowing proteins to have positive, negative, or neutral surface charges.

Protonation: Addition of a proton (H^+) to a covalent compound. For example, protonation of ammonia converts it to an ammonium ion. Acids can facilitate the protonation of bases.

Protons: Positively-charged subatomic particles with a mass approximately equal to that of a neutron. Along with neutrons, protons are found in an atom's nucleus. The number of protons in an atom defines what element it is and corresponds to its atomic number. See Hydrogen for the proton's central role in acid-base chemistry.

Reduction: Gain of one or more electrons by an atom. The molecule that gains the electrons is reduced, and the atom that gives the electrons is the reducing agent. An example of reduction is when a chlorine atom gains one electron to become a chloride ion: $Cl + e^- \rightarrow Cl^-$. Note that reduction can formally occur without full transfer of an electron, but this is not covered in this volume.

Salts: Compounds composed of two or more ions that are held together by a network of ionic bonds. In naming a salt, the positive component (cation) is listed first, and then the negative component (anion) second. If the anion is a single atom, the end of its name is changed to -ide. For example, NaCl, sodium chloride, is a salt composed of a sodium cation and a chloride (not chlorine) anion. The net charge of a salt has to be zero, meaning that the stoichiometry of cations to anions may not be 1:1 - like in $MgCl_2$, which has two -1 chlorides to match the +2 charge of the magnesium ions. While water generally interacts strongly with ions, depending on the nature of the ions, different salts have different solubilities in water.

Scientific Notation: A way of representing numbers that is composed of two parts: the first is a number greater than zero, but less than ten, such that when it is multiplied by the second part, ten to some power, the original number is reproduced. For example, 12,345 in scientific notation is 1.2345×10^4. Scientific notation can be an especially convenient way of representing very large or very small numbers.

Solubility: A description of how much of a substance (solute) can be dissolved in a liquid (solvent). This description can be qualitative (terms like insoluble, slightly soluble, soluble) or quantitative (a specific amount of solute can dissolve in a given volume of solvent). When no more of a substance can be dissolved in solution, the substance has reached its solubility limit. The solubility of a substance in a liquid is dictated by a number of factors, including the type of interactions that can be made between the solute and solvent, and the temperature of the solution.

Solutions: A homogeneous mixture of one or more substances dissolved in a liquid. The dissolved components are known as the solutes. The liquid dissolving the solutes is the solvent. Different solutes have different solubilities in a given solvent.

Strong Acid and Strong Base: A strong acid is one that fully dissociates when added to water (for every acid molecule added, one proton is generated). Two strong acids discussed are hydrochloric acid and sulfuric acid (which acts as a strong acid only for its first proton). A strong base is one that generates one hydroxide ion for every base molecule added. Two strong bases that have been discussed are sodium hydroxide and potassium hydroxide.

Surface Tension: A measure of how difficult it is to "break" the surface of a liquid (or more accurately, the energetic cost of creating more surface area for a liquid). Water has a high surface tension, because plunging an object into the liquid breaks many hydrogen bonds. An example of an organism exploiting this property of water can be seen in the water strider, which is able to maintain itself above the surface of the water.

Temperature: A property of a system that describes the average kinetic energy of the molecules in the system. In general, as the temperature of a system rises, the molecules have greater energy and more motion. There are two standard scientific units of temperature: Celsius and Kelvin. In the Celsius scale, water freezes at 0° C and boils at 100° C. The Kelvin scale is offset from Celsius by 273 degrees, such that water freezes at 273 K, boils at 373 K, and 0 K is absolute zero, the lowest possible temperature.

Valence Electrons: Electrons found in the outermost electron shell of an atom. For elements, the number of possible valence electrons is indicated by the number of columns in their row in the periodic table, with the actual number of valence electrons dictated by which column the element occupies within the row. For example, carbon has 4 valence electrons out of a possible 8. Valence electrons are especially important for the properties and reactivities of elements, with many atoms being "happiest" when they achieve a full valence. This simple model explains why the noble gases in the last column are relatively inert (their valence is full), while halogens like chlorine (7 out of 8 valence electrons) and metals like sodium (1 out of 8 valence electrons) are quite reactive.

Volume: The amount of space an object takes up. The standard scientific unit of volume is the liter. Volume is used throughout chemistry to express concentration (the amount of a substance dissolved per unit volume) and to convert between mass and density.

VSEPR Theory (Valence Shell Electron Pair Repulsion Theory): A simple model for predicting the 3D arrangement of atoms around a central atom. In VSEPR theory, groups of electrons (those in covalent bonds or lone pairs) try to get as far away from each other as possible: a linear arrangement for two groups around a central atom, a trigonal planar arrangement for three groups, a tetrahedral arrangement for four. From this configuration, focusing on only the atoms and bonds gives the molecular geometry of the group of atoms (linear, trigonal planar, bent, trigonal pyramidal, and tetrahedral).

Water: A simple covalent compound, H_2O, that is ubiquitous in cells. Water is a highly polar, bent molecule that is a molecular dipole and that can form hydrogen bonds with itself and other compounds. These features define many of the unique properties of water, including its ability to be a good solvent for polar and charged compounds (including many biomolecules), its high melting and boiling temperatures, and its strong cohesion and adhesion properties.

Weak Acid and Weak Base: A weak acid is an acid that is not strong - i.e., one that generates less than one proton for each acid molecule added to water. Examples of weak acids include acetic acid, ammonium ions, and water. Similarly, a weak base is a base that is not strong - less than one hydroxide ion is generated for every base molecule added to solution. Examples of weak bases include ammonia, amines, and acetate. The designation of an acid or base as weak encompasses a wide range of behavior. For example, when acetic acid is added to water, it usually dissociates around 1% (i.e., roughly 1% becomes acetate, while 99% remains acetic acid). That said, acetic acid is a much stronger acid than water, where in a liter of water, about 1 in half a billion water molecules spontaneously dissociate into a proton and a hydroxide ion.

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About the Author



Chemistry and biology have always fascinated me. As an undergraduate at Stanford University, I majored in chemistry, and then went on to pursue a PhD at Caltech in organic chemistry. As a post-doc, curious about how chemical structure leads to function in more complicated systems, I became fascinated by chromatin's role in regulating the DNA it packages, as well as in biochemistry more generally. These interests have continued in my independent research career as a professor of biochemistry at Iowa State University, and recently I have focused on how to impart my excitement for biochemistry and biophysics to students of all types. Outside of my scientific interests, I enjoy reading, cooking, puzzle-making, and programming. Feel free to contact me at knaak@iastate.edu.

About This Book

Biologically relevant molecules are everywhere you look, and understanding them is crucial to grasping how the world works.

What is this book?

Introduction to Biology at the Molecular Level is a textbook series for understanding how biological systems work at the molecular scale. The books in the series are designed to be high-quality and affordable, with full-color figures throughout. This volume, the first, presents the general chemistry topics most relevant to living things. Subsequent books build on this foundation to explore larger and more complex molecules and systems. Specifically, the second volume focuses on organic molecules, the third on biological molecules, and the fourth on the interaction and function of biological molecules.

Who is this book for?

This series is intended for anyone wanting to learn about biology at the molecular level. The book assumes comfort with algebra at the high-school level and basic science concepts, but is otherwise intended for a wide audience, including: non-biochemistry college majors whose training requires an introduction to chemistry as it relates to biology; biochemistry and biochemistry-adjacent majors and graduate students looking for a concise refresher of biochemistry-related topics; and advanced high-school students, or others in technical and non-technical fields, wanting to know more about biological systems.

How is this book organized?

Each chapter in this book is aimed at exploring a general chemistry topic in a clear, concise, and well-motivated fashion. Chapters are divided into subsections, where the initial ones focus on material that is essential for understanding biological systems. Concluding subsections are optional and explore more specialized topics that may be of particular relevance in certain fields. This book is not meant to be an exhaustive treatment of general chemistry. Nonetheless, it will expose the reader to the chemical principles that animate biological systems and provide a strong foundation for further study.

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