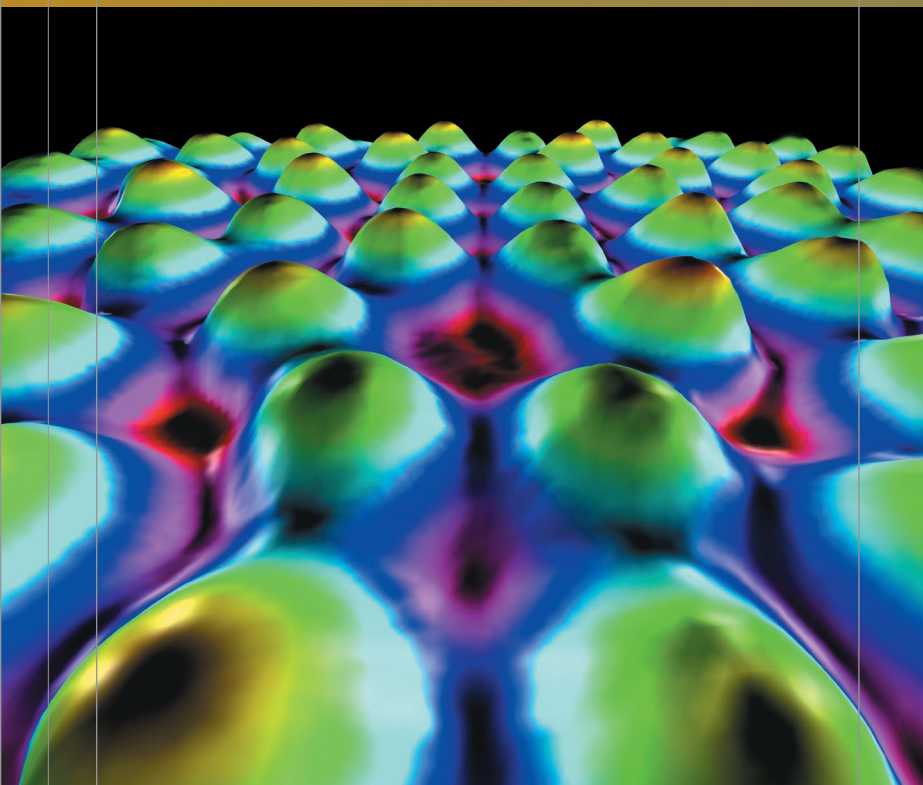


Chemical Composition of the Body and Its Relation to Physiology



Scanning tunneling micrograph of individual silicon atoms on a silicon chip. ©Andrew Dunn/Alamy Stock Photo

In Chapter 1, you were introduced to the concept of homeostasis, in which variables such as the concentrations of many chemicals in the blood are maintained within a normal range. To fully appreciate the mechanisms by which homeostasis is achieved, we must first understand the basic chemistry of the human body, including the key features of atoms and molecules that contribute to their ability to interact with one another. Such interactions form the basis for processes as diverse as maintaining a healthy pH of the body fluids, determining which molecules will bind to or otherwise influence the function of other molecules, forming functional proteins that mediate numerous physiological processes, and maintaining energy homeostasis.

In this chapter, we also describe the distinguishing characteristics of some of the major organic molecules in the human body. The specific functions of these molecules in physiology will be introduced here and discussed more fully in subsequent chapters where appropriate. This chapter will provide you with the knowledge required to best appreciate the significance of one of the general principles of physiology introduced in Chapter 1, namely that physiological processes are dictated by the laws of chemistry and physics. ■

2.1 Atoms

Components of Atoms

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Chapter 2 Clinical Case Study

2.1 Atoms

The units of matter that form all chemical substances are called **atoms**. Each type of atom—carbon, hydrogen, oxygen, and so on—is called a **chemical element**. A one- or two-letter symbol is used as an abbreviated identification for each element. Although more than 100 elements occur naturally or have been synthesized in the laboratory, only 24 (**Table 2.1**) have been clearly identified as essential for the function of the human body and are therefore of particular interest to physiologists.

Components of Atoms

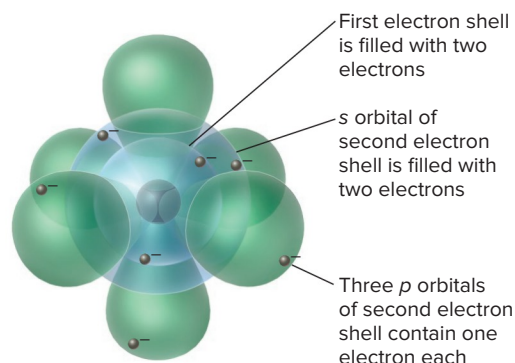
The chemical properties of atoms can be described in terms of three subatomic particles—**protons**, **neutrons**, and **electrons**. The protons and neutrons are confined to a very small volume at the center of

TABLE 2.1

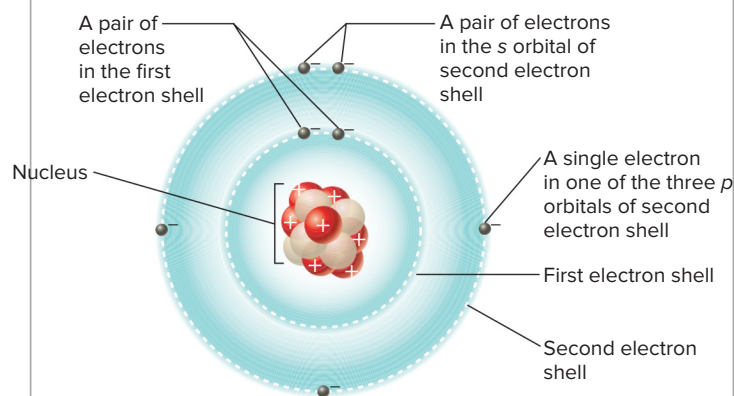
Essential Chemical Elements in the Body
(Neo-Latin Terms in *Italics*)

Element	Symbol
<i>Major Elements: 99.3% of Total Atoms in the Body</i>	
Hydrogen	H (63%)
Oxygen	O (26%)
Carbon	C (9%)
Nitrogen	N (1%)
<i>Mineral Elements: 0.7% of Total Atoms in the Body</i>	
Calcium	Ca
Phosphorus	P
Potassium	K (<i>kalium</i>)
Sulfur	S
Sodium	Na (<i>natrium</i>)
Chlorine	Cl
Magnesium	Mg
<i>Trace Elements: Less than 0.01% of Total Atoms in the Body</i>	
Iron	Fe (<i>ferrum</i>)
Iodine	I
Copper	Cu (<i>cuprum</i>)
Zinc	Zn
Manganese	Mn
Cobalt	Co
Chromium	Cr
Selenium	Se
Molybdenum	Mo
Fluorine	F
Tin	Sn (<i>stannum</i>)
Silicon	Si
Vanadium	V

an atom called the **atomic nucleus**. The electrons revolve in orbitals at various distances from the nucleus. Each orbital can hold up to two electrons and no more. The larger the atom, the more electrons it contains, and therefore the more orbitals that exist around the nucleus. Orbitals are found in regions known as electron shells; additional shells exist at greater and greater distances from the nucleus as atoms get bigger. An atom such as carbon has more shells than does hydrogen with its lone electron, but fewer than an atom such as iron, which has a greater number of electrons. The first, innermost shell of any atom can hold up to two electrons in a single, spherical (“s”) orbital (**Figure 2.1a**). Once the lone orbital of the innermost shell is filled, electrons begin to fill the second shell. The second shell can hold up to eight electrons; the first two electrons fill a spherical orbital, and subsequent electrons fill three additional, propeller-shaped (“p”) orbitals. Additional shells can accommodate further orbitals; this will happen once the inner shells are filled. For simplicity, we will ignore the distinction between *s* and *p* orbitals and represent the shells of an atom in two dimensions as shown in **Figure 2.1b** for nitrogen.



(a) Nitrogen atom showing electrons in orbitals



(b) Simplified depiction of a nitrogen atom (seven electrons; two electrons in first electron shell, five in second electron shell)

AP|R **Figure 2.1** Arrangement of subatomic particles in an atom, shown here for nitrogen. (a) Negatively charged electrons orbit around a nucleus consisting of positively charged protons and (except for hydrogen) uncharged neutrons. Up to two electrons may occupy an orbital, shown here as regions in which an electron is likely to be found. The orbitals exist within electron shells at progressively greater distances from the nucleus as atoms get bigger. The first electron shell contains only a single orbital; progressively distant shells may contain a different number of orbitals. (b) Simplified, two-dimensional depiction of a nitrogen atom, showing a full complement of two electrons in its innermost shell and five electrons in its second, outermost shell. Orbitals are not depicted using this simplified means of illustrating an atom.

An atom is most stable when all of the orbitals in its outermost shell are filled with two electrons each. If one or more orbitals do not have their capacity of electrons, the atom can react with other atoms and form molecules, as described later. For many of the atoms that are most important for physiology, the outer shell requires eight electrons in its orbitals in order to be filled to capacity.

Each of the subatomic particles has a different electrical charge. Protons have one unit of positive charge, electrons have one unit of negative charge, and neutrons are electrically neutral. Because the protons are located in the atomic nucleus, the nucleus has a net positive charge equal to the number of protons it contains. One of the fundamental principles of physics is that opposite electrical charges attract each other and like charges repel each other. It is the attraction between the positively charged protons and the negatively charged electrons that serves as a major force that forms an atom. The entire atom has no net electrical charge, however, because the number of negatively charged electrons orbiting the nucleus equals the number of positively charged protons in the nucleus.

Atomic Number

Each chemical element contains a unique and specific number of protons, and it is this number, known as the **atomic number**, that distinguishes one type of atom from another. For example, hydrogen, the simplest atom, has an atomic number of 1, corresponding to its single proton. As another example, calcium has an atomic number of 20, corresponding to its 20 protons. Because an atom is electrically neutral, the atomic number is also equal to the number of electrons in the atom.

Atomic Mass

Atoms have very little mass. A single hydrogen atom, for example, has a mass of only 1.67×10^{-24} g. The **atomic mass** scale indicates an atom's mass relative to the mass of other atoms. By convention, this scale is based upon assigning the carbon atom a mass of exactly 12. On this scale, a hydrogen atom has an atomic mass of approximately 1, indicating that it has one-twelfth the mass of a carbon atom. A magnesium atom, with an atomic mass of 24, has twice the mass of a carbon atom. The unit of atomic mass is known as a dalton. One dalton (d) equals one-twelfth the mass of a carbon atom.

Although the number of neutrons in the nucleus of an atom is often equal to the number of protons, many chemical elements can exist in multiple forms, called **isotopes**, which have identical numbers of protons but which differ in the number of neutrons they contain. For example, the most abundant form of the carbon atom, ^{12}C , contains six protons and six neutrons and therefore has an atomic number of 6. Protons and neutrons are approximately equal in mass, and so ^{12}C has an atomic mass of 12. The radioactive carbon isotope ^{14}C contains six protons and eight neutrons, giving it an atomic number of 6 but an atomic mass of 14. The value of atomic mass given in the standard Periodic Table of the Elements is actually an average mass that reflects the relative abundance in nature of the different isotopes of a given element.

Many isotopes are unstable; they will spontaneously emit energy or even release components of the atom itself, such as part of the nucleus. This process is known as radiation, and such isotopes are called **radioisotopes**. The special qualities of radioisotopes

are of great practical benefit in the practice of medicine and the study of physiology. In one example, high-energy radiation can be focused onto cancerous areas of the body to kill cancer cells. Radioisotopes may also be useful in making diagnoses. In one common method, the sugar glucose can be chemically modified so that it contains a radioactive isotope of fluorine. When injected into the blood, the cells of all of the organs of the body take up the radioactive glucose just as they would ordinary glucose. Special imaging techniques such as **PET (positron emission tomography) scans** can then be used to detect how much of the radioactive glucose appears in different organs (**Figure 2.2**); because glucose is a key source of energy used by all cells, this information can be used to determine if a given organ is functioning normally or at an increased or decreased rate. For example, a PET scan that revealed decreased uptake of radioactive glucose into the heart might indicate that the blood vessels of the heart were diseased, thereby depriving the heart of nutrients. PET scans can also reveal the presence of cancer—a disease characterized by uncontrolled cell growth and increased glucose uptake.

The **gram atomic mass** of a chemical element is the amount of the element, in grams, equal to the numerical value of its atomic mass. Thus, 12 g of carbon (assuming it is all ^{12}C) is 1 gram

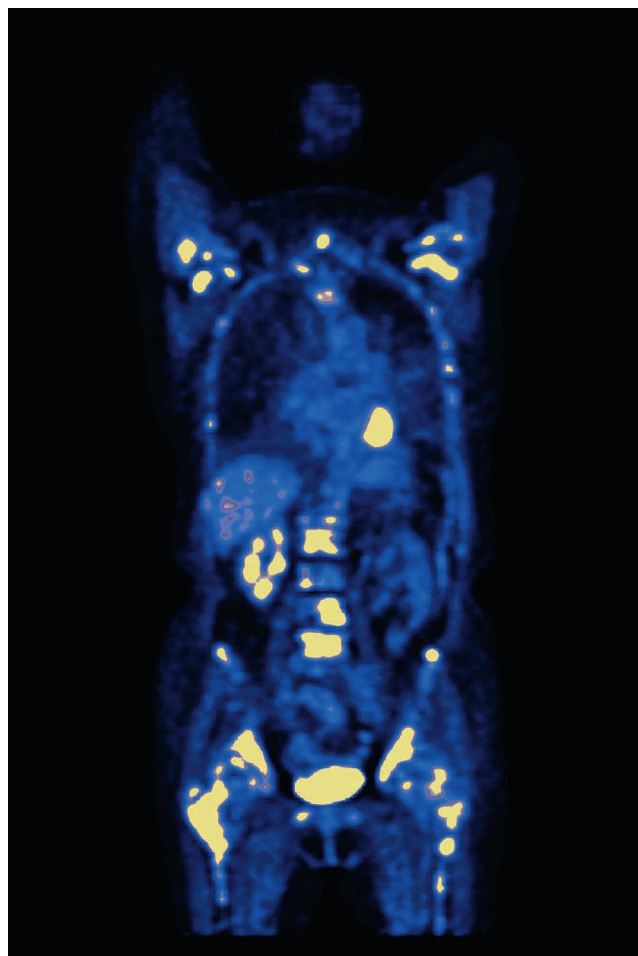


Figure 2.2 Positron emission tomography (PET) scan of a human body. In this image, radioactive glucose that has been taken up by the body's organs appears as a false color; the greater the uptake, the more intense the color. The brightest regions were found to be areas of cancer in this particular individual. ©Living Art Enterprises/Science Source

atomic mass of carbon, and 1 g of hydrogen is 1 gram atomic mass of hydrogen. *One gram atomic mass of any element contains the same number of atoms.* For example, 1 g of hydrogen contains 6×10^{23} atoms; likewise, 12 g of carbon, whose atoms have 12 times the mass of a hydrogen atom, also has 6×10^{23} atoms (this value is often called Avogadro's constant, or Avogadro's number, after the nineteenth-century Italian scientist Amedeo Avogadro).

Ions

As mentioned earlier, a single atom is electrically neutral because it contains equal numbers of negative electrons and positive protons. There are instances, however, in which certain atoms may gain or lose one or more electrons; in such cases, they will then acquire a net electrical charge and become an **ion**. This may happen, for example, if an atom has an outer shell that contains only one or a few electrons; losing those electrons would mean that the next innermost shell would then become the outermost shell. This shell is complete with a full capacity of electrons and is therefore very stable (recall that each successive shell does not begin to acquire electrons until all the preceding inner shells are filled). For example, when a sodium atom (Na), which has 11 electrons, loses one electron, it becomes a sodium ion (Na^+) with a net positive charge; it still has 11 protons, but it now has only 10 electrons, two in its first shell and a full complement of eight in its second, outer shell. On the other hand, a chlorine atom (Cl), which has 17 electrons, is one electron shy of a full outer shell. It can gain an electron and become a chloride ion (Cl^-) with a net negative charge—it now has 18 electrons but only 17 protons. Some atoms can gain or lose more than one electron to become ions with two or even three units of net electrical charge (for example, the calcium ion Ca^{2+}).

Hydrogen and many other atoms readily form ions. **Table 2.2** lists the ionic forms of some of these elements that are found in the body. Ions that have a net positive charge are called **cations**, and those that have a net negative charge are called **anions**. Because of their charge, ions are able to conduct electricity when dissolved in water; consequently, the ionic forms of mineral elements are collectively referred to as **electrolytes**. This is extremely important in physiology, because electrolytes are used to carry electrical charge across cell membranes; in this way, they serve as the source of electrical current in certain cells. You will learn in Chapters 6, 9, and 12 that such currents are critical to the ability of muscle cells and neurons to function in their characteristic ways.

Atomic Composition of the Body

Just four of the body's essential elements (see Table 2.1)—hydrogen, oxygen, carbon, and nitrogen—account for over 99% of the atoms in the body.

The seven essential **mineral elements** are the most abundant substances dissolved in the extracellular and intracellular fluids. Most of the body's calcium and phosphorus atoms, however, make up the solid matrix of bone tissue.

The 13 essential **trace elements**, so-called because they are present in extremely small quantities, are required for normal growth and function. For example, iron has a critical function in the blood's transport of oxygen, and iodine is required for the production of thyroid hormone.

Many other elements, in addition to the 24 listed in Table 2.1, may be detected in the body. These elements enter in the foods we eat and the air we breathe but are not essential for normal body function and may even interfere with normal body chemistry. For example, ingested arsenic has poisonous effects.

2.2 Molecules

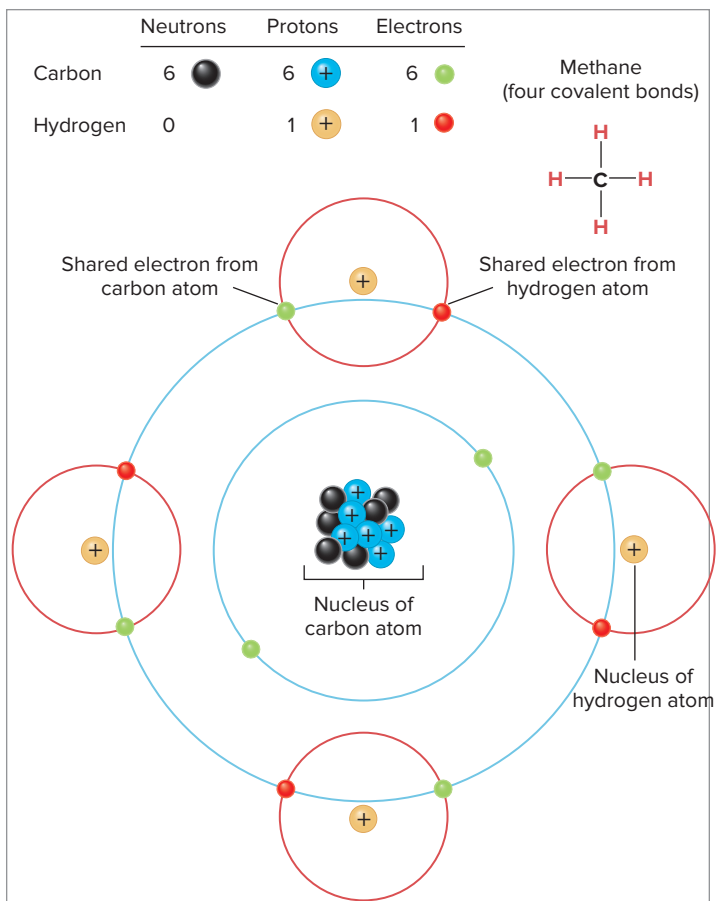
Two or more atoms bonded together make up a **molecule**. A molecule made up of two or more different elements is called a compound, but the two terms are often used interchangeably. For example, a molecule of oxygen gas consists of two atoms of oxygen bonded together. By contrast, water is a compound that contains two hydrogen atoms and one oxygen atom. For simplicity, we will simply use the term *molecule* in this textbook. Molecules can be represented by their component atoms. In the two examples just given, a molecule of oxygen can be represented as O_2 and water as H_2O . The atomic composition of glucose, a sugar, is $\text{C}_6\text{H}_{12}\text{O}_6$, indicating that the molecule contains 6 carbon atoms, 12 hydrogen atoms, and 6 oxygen atoms. Such formulas, however, do not indicate how the atoms are linked together in the molecule. This occurs by means of chemical bonds, as described next.

Covalent Chemical Bonds

Chemical bonds between atoms in a molecule form when electrons transfer from the outer electron shell of one atom to that of another, or when two atoms with partially unfilled electron orbitals share electrons. The strongest chemical bond between two atoms is called a **covalent bond**, which forms when one or more electrons in the outer electron orbitals of each atom are shared

TABLE 2.2 Ionic Forms of Elements Most Frequently Encountered in the Body

Chemical Atom	Symbol	Ion	Chemical Symbol	Electrons Gained or Lost
Hydrogen	H	Hydrogen ion	H^+	1 lost
Sodium	Na	Sodium ion	Na^+	1 lost
Potassium	K	Potassium ion	K^+	1 lost
Chlorine	Cl	Chloride ion	Cl^-	1 gained
Magnesium	Mg	Magnesium ion	Mg^{2+}	2 lost
Calcium	Ca	Calcium ion	Ca^{2+}	2 lost

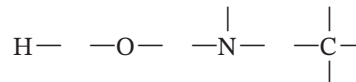


AP|R Figure 2.3 A covalent bond formed by sharing electrons. Hydrogen atoms have room for one additional electron in their sole orbital; carbon atoms have four electrons in their second shell, which can accommodate up to eight electrons. Each of the four hydrogen atoms in a molecule of methane (CH_4) forms a covalent bond with the carbon atom by sharing its one electron with one of the electrons in carbon. Each shared pair of electrons—one electron from the carbon and one from a hydrogen atom—forms a covalent bond. The sizes of protons, neutrons, and electrons are not to scale.

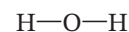
between the two atoms (Figure 2.3). In the example shown in Figure 2.3, a carbon atom with two electrons in its innermost shell and four in its outer shell forms covalent bonds with four hydrogen atoms. Recall that the second shell of atoms can hold up to eight electrons. Carbon has six total electrons and only four in the second shell, because two electrons are used to fill the first shell. Therefore, it has “room” to acquire four additional electrons in its outer shell. Hydrogen has only a single electron, but like all orbitals, its single orbital can hold up to two electrons. Therefore, hydrogen also has room for an additional electron. In this example, a single carbon atom shares its four electrons with four different hydrogen atoms, which in turn share their electrons with the carbon atom. The shared electrons orbit around both atoms, bonding them together into a molecule of methane (CH_4). These covalent bonds are the strongest type of bonds in the body; once formed, they usually do not break apart unless acted upon by an energy source (heat) or an enzyme (see Chapter 3 for a description of enzymes).

As mentioned, the atoms of some elements can form more than one covalent bond and thus become linked simultaneously to two or more other atoms. Each type of atom forms a

characteristic number of covalent bonds, which depends on the number of electrons in its outermost orbit. The number of chemical bonds formed by the four most abundant atoms in the body are hydrogen, one; oxygen, two; nitrogen, three; and carbon, four. When the structure of a molecule is diagrammed, each covalent bond is represented by a line indicating a pair of shared electrons. The covalent bonds of the four elements just mentioned can be represented as



A molecule of water, H_2O , can be diagrammed as



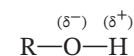
In some cases, two covalent bonds—a double bond—form between two atoms when they share two electrons from each atom. Carbon dioxide (CO_2), a waste product of metabolism, contains two double bonds:



Note that in this molecule the carbon atom still forms four covalent bonds and each oxygen atom only two.

Polar Covalent Bonds Not all atoms have the same ability to attract shared electrons. The measure of an atom’s ability to attract electrons in a covalent bond is called its **electronegativity**. Electronegativity generally increases as the total positive charge of a nucleus increases but decreases as the distance between the outer electrons and the nucleus increases. When two atoms with different electronegativities combine to form a covalent bond, the shared electrons will tend to spend more time orbiting the atom with the higher electronegativity. This creates a polarity across the bond (think of the poles of a magnet; only in this case the polarity refers to a difference in charge).

Due to the polarity in electron distribution just described, the more electronegative atom acquires a slight negative charge, whereas the other atom, having partly lost an electron, becomes slightly positive. Such bonds are known as **polar covalent bonds** (or, simply, polar bonds) because the atoms at each end of the bond have an opposite electrical charge. For example, the bond between hydrogen and oxygen in a **hydroxyl group** ($-\text{OH}$) is a polar covalent bond in which the oxygen is slightly negative and the hydrogen slightly positive:



The δ^- and δ^+ symbols refer to atoms with a partial negative or positive charge, respectively. The R symbolizes the remainder of the molecule; in water, for example, R is simply another hydrogen atom carrying another partial positive charge. The electrical charge associated with the ends of a polar bond is considerably less than the charge on a fully ionized atom. Polar bonds do not have a *net* electrical charge, as do ions, because they contain overall equal amounts of negative and positive charge.

Atoms of oxygen, nitrogen, and sulfur, which have a relatively strong attraction for electrons, form polar bonds with hydrogen atoms (Table 2.3). One of the characteristics of polar bonds that is important in our understanding of physiology is that molecules that contain such bonds tend to be very soluble in

TABLE 2.3

Examples of Polar and Nonpolar Covalent Bonds

Polar Covalent Bonds	$\text{R}-\overset{(\delta^-)}{\text{O}}-\overset{(\delta^+)}{\text{H}}$	Hydroxyl group (R-OH)
	$\text{R}-\overset{(\delta^-)}{\text{S}}-\overset{(\delta^+)}{\text{H}}$	Sulfhydryl group (R-SH)
	$\begin{array}{c} \text{H}^{(\delta^+)} \\ \\ \text{R}-\text{N}^{(\delta^-)}-\text{R} \end{array}$	Nitrogen-hydrogen bond
Nonpolar Covalent Bonds	$\begin{array}{c} \\ -\text{C}-\text{H} \\ \end{array}$	Carbon-hydrogen bond
	$\begin{array}{cc} & \\ -\text{C} & -\text{C}- \\ & \end{array}$	Carbon-carbon bond

water. Consequently, these molecules—called **polar molecules**—readily dissolve in the blood, interstitial fluid, and intracellular fluid. Indeed, water itself is the classic example of a polar molecule, with a partially negatively charged oxygen atom and two partially positively charged hydrogen atoms.

Nonpolar Covalent Bonds In contrast to polar covalent bonds, bonds between atoms with similar electronegativities are said to be **nonpolar covalent bonds**. In such bonds, the electrons are equally or nearly equally shared by the two atoms, such that there is little or no unequal charge distribution across the bond. Bonds between carbon and hydrogen atoms and between two carbon atoms are electrically neutral, nonpolar covalent bonds (see Table 2.3). Molecules that contain high proportions of nonpolar covalent bonds are called **nonpolar molecules**; they tend to be less soluble in water than those with polar covalent bonds. Consequently, such molecules are often found in the lipid bilayers of the membranes of cells and intracellular organelles. When present in body fluids such as the blood, they may associate with a polar molecule that serves as a sort of “carrier” to prevent the nonpolar molecule from coming out of solution. The characteristics of molecules in solution will be covered later in this chapter.

Ionic Bonds

As noted earlier, some elements, such as those that make up table salt (NaCl), can form ions. NaCl is a solid crystalline substance because of the strong electrical attraction between positive sodium ions and negative chloride ions. This strong attraction between two oppositely charged ions is known as an **ionic bond**. When a crystal of sodium chloride is placed in water, the highly polar water molecules with their partial positive and negative charges are attracted to the charged sodium and chloride ions (**Figure 2.4**). Clusters of water molecules surround the ions, allowing the sodium and chloride ions to separate from each other and enter the water—that is, to dissolve.

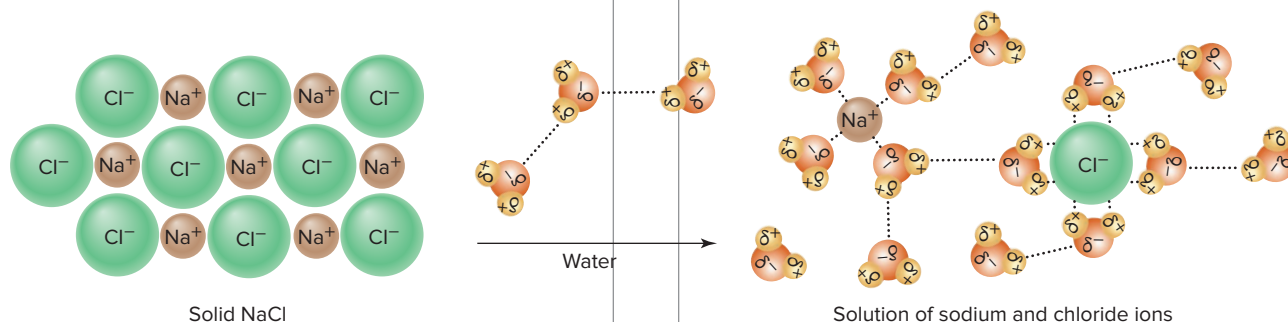
Hydrogen Bonds

When two polar molecules are in close contact, an electrical attraction may form between them. For example, the hydrogen atom in a polar bond in one molecule and an oxygen or nitrogen atom in a polar bond of another molecule attract each other forming a type of bond called a **hydrogen bond**. Such bonds may also form between atoms within the same molecule. Hydrogen bonds are represented in diagrams by dashed or dotted lines to distinguish them from covalent bonds, as illustrated in the bonds between water molecules (**Figure 2.5**). Hydrogen bonds are very weak, having only about 4% of the strength of the polar covalent bonds between the hydrogen and oxygen atoms within a single molecule of water. Although hydrogen bonds are weak individually, when present in large numbers, they have an extremely important function in molecular interactions and in determining the shape of large molecules. This is of great importance for physiology, because the shape of large molecules determines their functions and their ability to interact with other molecules. For example, some molecules interact with a “lock-and-key” arrangement that can only occur if both molecules have precisely the correct shape, which in turn depends in part upon the number and location of hydrogen bonds.

Molecular Shape

As just mentioned, when atoms are linked together they form molecules with various shapes. Although we draw diagrammatic structures of molecules on flat sheets of paper, molecules are three-dimensional. When more than one covalent bond is formed with a given atom, the bonds are distributed around the atom in a pattern that may or may not be symmetrical (**Figure 2.6**).

Molecules are not rigid, inflexible structures. Within certain limits, the shape of a molecule can be changed without breaking the covalent bonds linking its atoms together. A covalent bond is



AP|R Figure 2.4 The electrical attraction between the charged sodium and chloride ions forms ionic bonds in solid NaCl. The attraction of the polar, partially charged regions of water molecules breaks the ionic bonds and the sodium and chloride ions dissolve.

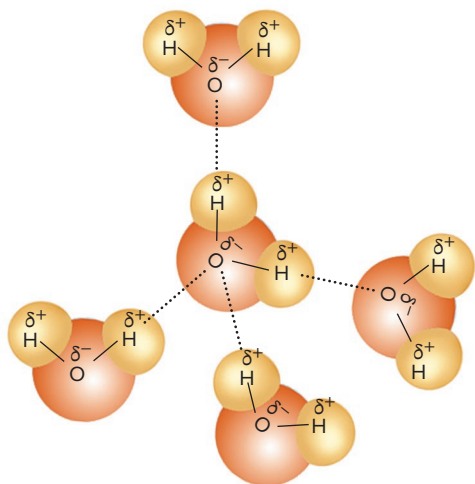


Figure 2.5 Five water molecules. Note that polar covalent bonds link the hydrogen and oxygen atoms within each molecule and that hydrogen bonds occur between adjacent molecules. Hydrogen bonds are represented in diagrams by dashed or dotted lines, and covalent bonds by solid lines.

PHYSIOLOGICAL INQUIRY

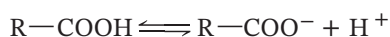
- What effect might hydrogen bonds have on the likelihood that liquid water becomes a vapor?

Answer can be found at end of chapter.

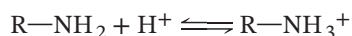
like an axle around which the joined atoms can rotate. As illustrated in **Figure 2.7**, a sequence of six carbon atoms can assume a number of shapes by rotating around various covalent bonds. As we will see in subsequent chapters, the three-dimensional, flexible shape of molecules is one of the major factors governing molecular interactions, and reflects the general principle of physiology that structure is a determinant of—and has coevolved with—function.

Ionic Molecules

The process of ion formation, known as ionization, can occur not only in single atoms, as stated earlier, but also in atoms that are covalently linked in molecules (**Table 2.4**). Two commonly encountered groups of atoms that undergo ionization in molecules are the **carboxyl group** ($-\text{COOH}$) and the **amino group** ($-\text{NH}_2$). The shorthand formula for only a portion of a molecule can be written as $\text{R}-\text{COOH}$ or $\text{R}-\text{NH}_2$, with R being the remainder of the molecule. The carboxyl group ionizes when the oxygen linked to the hydrogen captures the hydrogen's only electron to form a carboxyl ion ($\text{R}-\text{COO}^-$), releasing a hydrogen ion (H^+):



The amino group can bind a hydrogen ion to form an ionized amino group ($\text{R}-\text{NH}_3^+$):



The ionization of each of these groups can be reversed, as indicated by the double arrows; the ionized carboxyl group can combine with a hydrogen ion to form a nonionized carboxyl group, and the ionized amino group can lose a hydrogen ion and become a nonionized amino group.

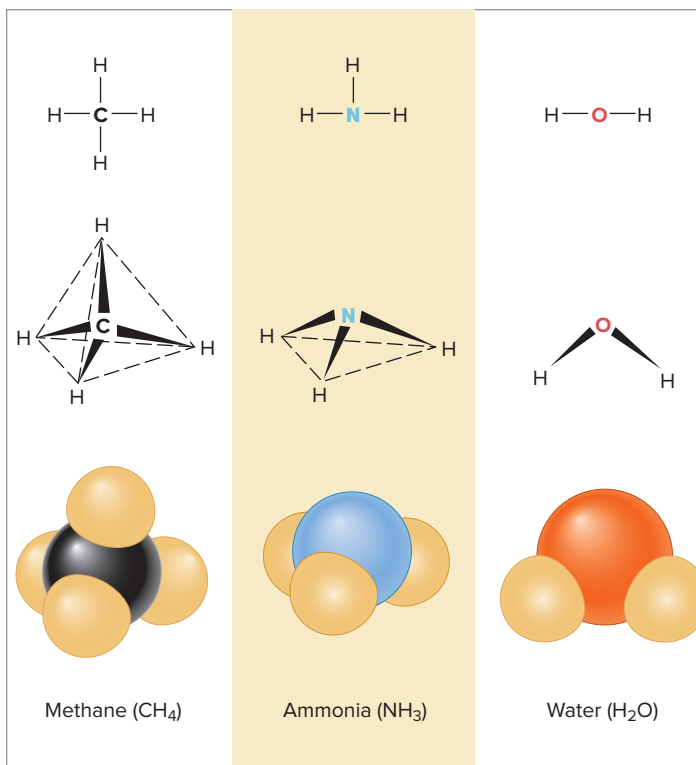


Figure 2.6 Three different ways of representing the geometric configuration of covalent bonds around the carbon, nitrogen, and oxygen atoms bonded to hydrogen atoms.

Free Radicals

As described earlier, the electrons that revolve around the nucleus of an atom occupy electron shells, each of which can be occupied by one or more orbitals containing up to two electrons each. An atom is most stable when each orbital in the outer shell is occupied by its full complement of electrons. An atom containing a single (unpaired) electron in an orbital of its outer shell is known as a **free radical**, as are molecules containing such atoms. Free radicals are unstable molecules that can react with other atoms, through the process known as oxidation. When a free radical oxidizes another atom, the free radical gains an electron and the other atom usually becomes a new free radical.

Free radicals are formed by the actions of certain enzymes in some cells, such as types of white blood cells that destroy pathogens. The free radicals are highly reactive, removing electrons from the outer shells of atoms within molecules present in the pathogen cell wall or membrane, for example. This mechanism begins the process whereby the pathogen is destroyed.

In addition, however, free radicals can be produced in the body following exposure to radiation or toxin ingestion. These free radicals can do considerable harm to the cells of the body. For example, oxidation due to long-term buildup of free radicals has been proposed as one cause of several different human diseases, notably eye, cardiovascular, and neural diseases associated with aging. Thus, it is important that free radicals be inactivated by molecules that can donate electrons to free radicals without becoming dangerous free radicals themselves. Examples of such protective molecules are the antioxidant vitamins C and E.

Free radicals are diagrammed with a dot next to the atomic symbol. Examples of biologically important free radicals are

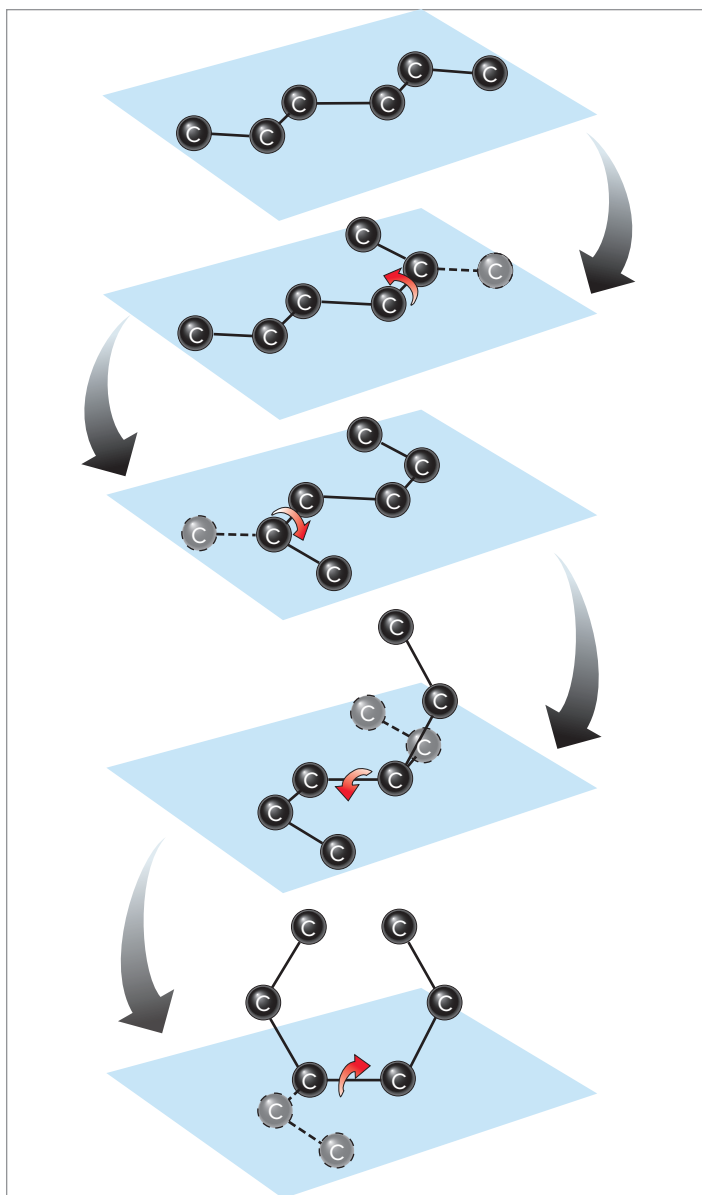


Figure 2.7 Changes in molecular shape occur as portions of a molecule rotate around different carbon-to-carbon bonds, transforming this molecule's shape, for example, from a relatively straight chain (top) into a ring (bottom).

superoxide anion, $\text{O}_2 \cdot^-$; hydroxyl radical, $\text{OH} \cdot$; and nitric oxide, $\text{NO} \cdot$. Note that a free radical configuration can occur in either an ionized (charged) or a nonionized molecule.

We turn now to a discussion of solutions and molecular solubility in water. We begin with a review of some of the properties of water that make it so suitable for life.

2.3 Solutions

Substances dissolved in a liquid are known as **solutes**, and the liquid in which they are dissolved is the **solvent**. Solutes dissolve in a solvent to form a **solution**. Water is the most abundant solvent in the body, accounting for approximately 60% of total body weight. Most of the chemical reactions that occur in the body involve molecules that are dissolved in water, either in the intracellular or extracellular fluid. However, not all molecules dissolve in water.

TABLE 2.4

Examples of Ionized Groups in Molecules

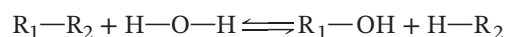
Ionized Groups	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{O}^- \end{array}$	Carboxyl group ($\text{R}-\text{COO}^-$)
	$\begin{array}{c} \text{H} \\ \\ \text{R}-\text{N}^+-\text{H} \\ \\ \text{H} \end{array}$	Amino group ($\text{R}-\text{NH}_3^+$)
	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{O}-\text{P}-\text{O}^- \\ \\ \text{O}^- \end{array}$	Phosphate group ($\text{R}-\text{PO}_4^{2-}$)

Water

Out of every 100 molecules in the human body, about 99 are water. The covalent bonds linking the two hydrogen atoms to the oxygen atom in a water molecule are polar. Therefore, as noted earlier, the oxygen in water has a partial negative charge, and each hydrogen has a partial positive charge. The positively charged regions near the hydrogen atoms of one water molecule are electrically attracted to the negatively charged regions of the oxygen atoms in adjacent water molecules by hydrogen bonds (see Figure 2.5).

At temperatures between 0°C and 100°C , water exists as a liquid; in this state, the weak hydrogen bonds between water molecules are continuously forming and breaking, and occasionally some water molecules escape the liquid phase and become a gas. If the temperature is increased, the hydrogen bonds break more readily and more molecules of water escape into the gaseous state. However, if the temperature is reduced, hydrogen bonds break less frequently, so larger and larger clusters of water molecules form until at 0°C , water freezes into a solid crystalline matrix—ice. Body temperature in humans is normally close to 37°C , and therefore water exists in liquid form in the body. Nonetheless, even at this temperature, some water leaves the body as a gas (water vapor) each time we exhale during breathing. This water loss in the form of water vapor has considerable importance for total-body-water homeostasis and must be replaced with water obtained from food or drink.

Water molecules take part in many chemical reactions of the general type:



In this reaction, the covalent bond between R_1 and R_2 and the one between a hydrogen atom and oxygen in water are broken, and the hydroxyl group and hydrogen atom are transferred to R_1 and R_2 , respectively. Reactions of this type are known as hydrolytic reactions, or **hydrolysis**. Many large molecules in the body are broken down into smaller molecular units by hydrolysis, usually with the assistance of a class of molecules called enzymes. These reactions are usually reversible, a process known as **condensation** or **dehydration**. In dehydration, one net water molecule is removed to combine two small molecules into one larger one. Dehydration reactions are responsible for, among other things, building proteins and other large molecules required by the body.

Other properties of water that are of importance in physiology include the colligative properties—those that depend on the *number* of dissolved substances, or solutes, in water. For example, water moves between fluid compartments by the process of osmosis, which you will learn about in detail in Chapter 4. In osmosis, water moves from regions of low solute concentrations to regions of high solute concentrations, regardless of the specific type of solute. Osmosis is the mechanism by which water is absorbed from the intestinal tract (Chapter 15) and from the kidney tubules into the blood (Chapter 14).

Having presented this brief survey of some of the physiologically relevant properties of water, we turn now to a discussion of how molecules dissolve in water. Keep in mind as you read on that most of the chemical reactions in the body take place between molecules that are in watery solution. Therefore, the relative solubilities of different molecules influence their abilities to participate in chemical reactions.

Molecular Solubility

Molecules having a number of polar bonds and/or ionized groups will dissolve in water. Such molecules are said to be **hydrophilic**, or “water-loving.” Therefore, the presence of ionized groups such as carboxyl and amino groups or of polar groups such as hydroxyl groups in a molecule promotes solubility in water. In contrast, molecules composed predominantly of carbon and hydrogen are poorly or almost completely insoluble in water because their electrically neutral covalent bonds are not attracted to water molecules. These molecules are **hydrophobic**, or “water-fearing.”

When hydrophobic molecules are mixed with water, two phases form, as occurs when oil is mixed with water. The strong attraction between polar molecules “squeezes” the nonpolar molecules out of the water phase. Such a separation is rarely if ever 100% complete, however, so very small amounts of nonpolar solutes remain dissolved in the water phase.

A special class of molecules has a polar or ionized region at one site and a nonpolar region at another site. Such molecules are called **amphipathic**, derived from Greek terms meaning “dislike both.” When mixed with water, amphipathic molecules form clusters, with their polar (hydrophilic) regions at the surface of the cluster where they are attracted to the surrounding water molecules. The nonpolar (hydrophobic) ends are oriented toward the interior of the cluster (Figure 2.8). This arrangement provides the maximal interaction between water molecules and the polar ends of the amphipathic molecules. Nonpolar molecules can dissolve in the central nonpolar regions of these clusters and thus exist in aqueous solutions in far greater amounts than would otherwise be possible based on their decreased solubility in water. As we will see, the orientation of amphipathic molecules has an important function in plasma membrane structure (Chapter 3) and in both the absorption of nonpolar molecules such as fats from the intestines and their transport in the blood (Chapter 15).

Concentration

Solute **concentration** is defined as the amount of the solute present in a unit volume of solution. The concentrations of solutes in a solution are key to their ability to produce physiological actions. For example, the extracellular signaling molecules described in Chapter 1, including neurotransmitters and hormones, cannot alter

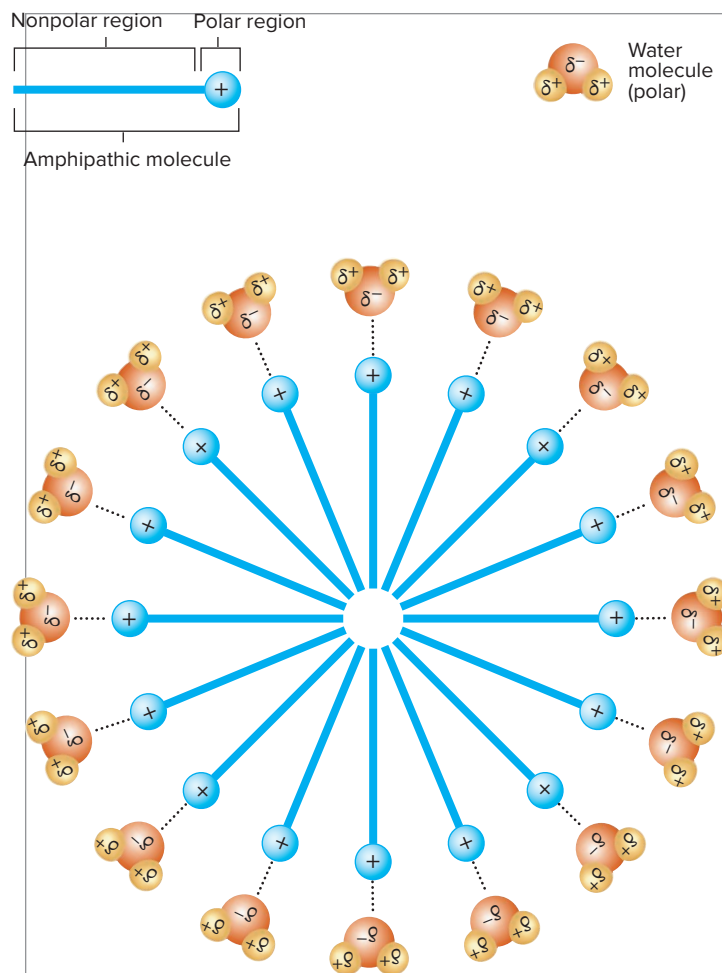


Figure 2.8 In water, amphipathic molecules aggregate into spherical clusters. Their polar regions form hydrogen bonds with water molecules at the surface of the cluster, whereas the nonpolar regions cluster together and exclude water.

cellular activity unless they are present in appropriate concentrations in the extracellular fluid.

One measure of the amount of a substance is its mass expressed in grams. The unit of volume in the metric system is a liter (L). (One liter equals 1.06 quarts; see the conversion table at the back of the book for metric and English units.) The concentration of a solute in a solution can then be expressed as the number of grams of the substance present in one liter of solution (g/L). Smaller units commonly used in physiology are the deciliter (dL, or 0.1 liter), the milliliter (mL, or 0.001 liter), and the microliter (μL, or 0.001 mL).

A comparison of the concentrations of two different substances on the basis of the number of grams per liter of solution does not directly indicate how many molecules of each substance are present. For example, if the molecules of compound X are heavier than those of compound Y, 10 g of compound X will contain fewer molecules than 10 g of compound Y. Thus, concentrations are expressed based upon the number of solute molecules in solution, using a measure of mass called the molecular weight. The **molecular weight** of a molecule is equal to the sum of the atomic masses of all the atoms in the molecule. For example, glucose ($C_6H_{12}O_6$) has a molecular weight of 180 because $[(6 \times 12) + (12 \times 1) + (6 \times 16)] = 180$. One **mole** (mol) of a compound is the amount of the compound in

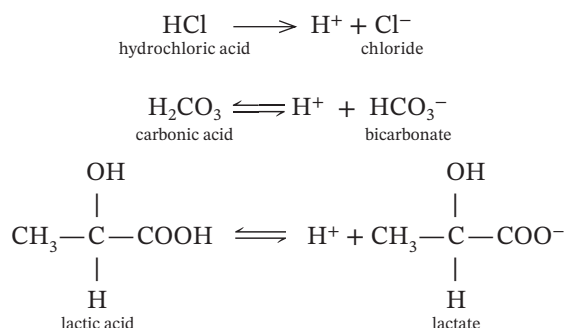
grams equal to its molecular weight. A solution containing 180 g glucose (1 mol) in 1 L of solution is a 1 molar solution of glucose (1 mol/L). If 90 g of glucose were dissolved in 1 L of water, the solution would have a concentration of 0.5 mol/L. Just as 1 g atomic mass of any element contains the same number of atoms, 1 mol of any molecule will contain the same number of molecules— 6×10^{23} (Avogadro's number). Thus, a 1 mol/L solution of glucose contains the same number of solute molecules per liter as a 1 mol/L solution of any other substance.

The concentrations of solutes dissolved in the body fluids are much less than 1 mol/L. Many have concentrations in the range of millimoles per liter (1 mmol/L = 0.001 mol/L), whereas others are present in even smaller concentrations—micromoles per liter (1 μ mol/L = 0.000001 mol/L) or nanomoles per liter (1 nmol/L = 0.000000001 mol/L). By convention, the liter (L) term is sometimes dropped when referring to concentrations. Thus, a 1 mmol/L solution is often written as 1 mM (the capital “M” stands for “molar” and is defined as mol/L).

An example of the importance of solute concentrations is related to a key homeostatic variable, that of the pH of the body fluids, as described next. Maintenance of a narrow range of pH (that is, hydrogen ion concentration) in the body fluids is absolutely critical to most physiological processes, in part because enzymes and other proteins depend on pH for their normal shape and activity.

Hydrogen Ions and Acidity

As mentioned earlier, a hydrogen atom consists of a single proton in its nucleus orbited by a single electron. The most common type of hydrogen ion (H^+) is formed by the loss of the electron and is, therefore, a single free proton. A molecule that releases protons (hydrogen ions) in solution is called an **acid**, as in these examples:



Conversely, any substance that can accept a hydrogen ion is termed a **base**. In the reactions shown, bicarbonate and lactate are bases because they can combine with hydrogen ions (note the two-way arrows in the two reactions). Also, note that by convention, separate terms are used for the acid forms—*lactic acid* and *carbonic acid*—and the bases derived from the acids—*lactate* and *bicarbonate*. By combining with hydrogen ions, bases decrease the hydrogen ion concentration of a solution.

When hydrochloric acid is dissolved in water, 100% of its atoms separate to form hydrogen and chloride ions, and these ions do not recombine in solution (note the one-way arrow in the preceding reaction). In the case of lactic acid, however, only a fraction of the lactic acid molecules in solution release hydrogen ions at any instant. Therefore, if a 1 mol/L solution of lactic acid is compared with a 1 mol/L solution of hydrochloric acid, the hydrogen ion concentration will be lower in the lactic acid solution than in the hydrochloric acid solution. Hydrochloric acid and other

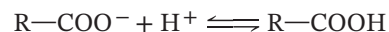
acids that are completely or nearly completely ionized in solution are known as **strong acids**, whereas carbonic and lactic acids and other acids that do not completely ionize in solution are **weak acids**. The same principles apply to bases.

It is important to understand that the hydrogen ion concentration of a solution refers only to the hydrogen ions that are free in solution and not to those that may be bound, for example, to amino groups ($R-NH_3^+$). The **acidity** of a solution thus refers to the *free* (unbound) hydrogen ion concentration in the solution; the greater the hydrogen ion concentration, the greater the acidity. The hydrogen ion concentration is often expressed as the solution's **pH**, which is defined as the negative logarithm to the base 10 of the hydrogen ion concentration. The brackets around the symbol for the hydrogen ion in the following formula indicate concentration:

$$\text{pH} = -\log [H^+]$$

As an example, a solution with a hydrogen ion concentration of 10^{-7} mol/L has a pH of 7. Pure water, due to the ionization of some of the molecules into H^+ and OH^- , has hydrogen ion and hydroxyl ion concentrations of 10^{-7} mol/L (pH = 7.0) at 25°C. The product of the concentrations of H^+ and OH^- in pure water is always 10^{-14} M. A solution of pH 7.0 is termed a neutral solution. **Alkaline solutions** have a lower hydrogen ion concentration (a pH greater than 7.0), whereas those with a greater hydrogen ion concentration (a pH lower than 7.0) are **acidic solutions**. Note that as the acidity *increases*, the pH *decreases*; a change in pH from 7 to 6 represents a 10-fold increase in the hydrogen ion concentration. The extracellular fluid of the body has a hydrogen ion concentration of about 4×10^{-8} mol/L (pH = 7.4), with a homeostatic range of about pH 7.35 to 7.45, and is thus slightly alkaline. Most intracellular fluids have a slightly greater hydrogen ion concentration (pH 7.0 to 7.2) than extracellular fluids.

As we saw earlier, the ionization of carboxyl and amino groups involves the release and uptake, respectively, of hydrogen ions. These groups behave as weak acids and bases. Changes in the acidity of solutions containing molecules with carboxyl and amino groups alter the net electrical charge on these molecules by shifting the ionization reaction in one or the other direction according to the general form:



For example, if the acidity of a solution containing lactate is increased by adding hydrochloric acid, the concentration of lactic acid will increase and that of lactate will decrease.

In the extracellular fluid, *hydrogen ion concentrations beyond the 10-fold pH range of 7.8 to 6.8 are incompatible with life if maintained for more than a brief period of time*. Even small changes in the hydrogen ion concentration can produce large changes in molecular interaction. For example, many enzymes in the body operate efficiently within very narrow ranges of pH. Should pH vary from the normal homeostatic range due to disease, these enzymes work at reduced rates, creating an even worse pathological situation.

This concludes our overview of atomic and molecular structure, water, and pH. We turn now to a description of the organic molecules essential for life in all living organisms, including humans. These are the carbon-based molecules required for forming the building blocks of cells, tissues, and

organs; providing energy; and forming the genetic blueprints of all life.

2.4 Classes of Organic Molecules

Because most naturally occurring carbon-containing molecules are found in living organisms, the study of these compounds is known as organic chemistry. (Inorganic chemistry refers to the study of non-carbon-containing molecules.) However, the chemistry of living organisms, or biochemistry, now forms only a portion of the broad field of organic chemistry.

One of the properties of the carbon atom that makes life possible is its ability to form four covalent bonds with other atoms, including with other carbon atoms. Because carbon atoms can also combine with hydrogen, oxygen, nitrogen, and sulfur atoms, a vast number of compounds can form from relatively few chemical elements. Some of these molecules are extremely large (**macromolecules**), composed of thousands of atoms. In some cases, such large molecules form when many identical smaller molecules, called subunits or monomers (literally, “one part”), link together. These large molecules are known as **polymers** (“many parts”). The structure of any polymer depends upon the structure of the subunits, the number of subunits bonded together, and the three-dimensional way in which the subunits are linked.

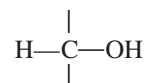
Most of the organic molecules in the body can be classified into one of four groups: carbohydrates, lipids, proteins, and nucleic acids (**Table 2.5**). We will consider each of these groups separately, but it is worth mentioning here that many molecules in the body are made up of two or more of these groups. For example, glycoproteins are composed of a protein covalently bonded to one or more carbohydrates.

Carbohydrates

Although carbohydrates account for only about 1% of body weight, they have a central contribution in the chemical reactions that provide cells with energy. As you will learn in greater detail in Chapter 3, energy is stored in the chemical bonds of sugar

molecules; this energy can be released within cells when required and stored in the bonds of another molecule called adenosine triphosphate (ATP). The energy stored in the bonds in ATP is used to power many different reactions in the body, including those necessary for cell survival, muscle contraction, protein synthesis, and many others.

Carbohydrates are composed of carbon, hydrogen, and oxygen atoms. Linked to most of the carbon atoms in a carbohydrate are a hydrogen atom and a hydroxyl group:



The presence of numerous polar hydroxyl groups makes most carbohydrates readily soluble in water.

Many carbohydrates taste sweet, particularly the carbohydrates known as sugars. The simplest sugars are the monomers called **monosaccharides** (from the Greek for “single sugars”), the most abundant of which is **glucose**, a six-carbon molecule ($\text{C}_6\text{H}_{12}\text{O}_6$). Glucose is often called “blood sugar” because it is the major monosaccharide found in the blood.

Glucose may exist in an open chain form, or, more commonly, a cyclic structure as shown in **Figure 2.9**. Five carbon

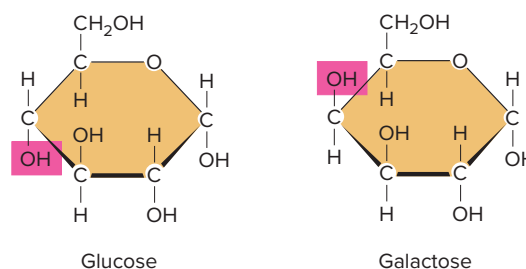


Figure 2.9 The structural difference between the monosaccharides glucose and galactose is based on whether the hydroxyl group at the position indicated lies below or above the plane of the ring.

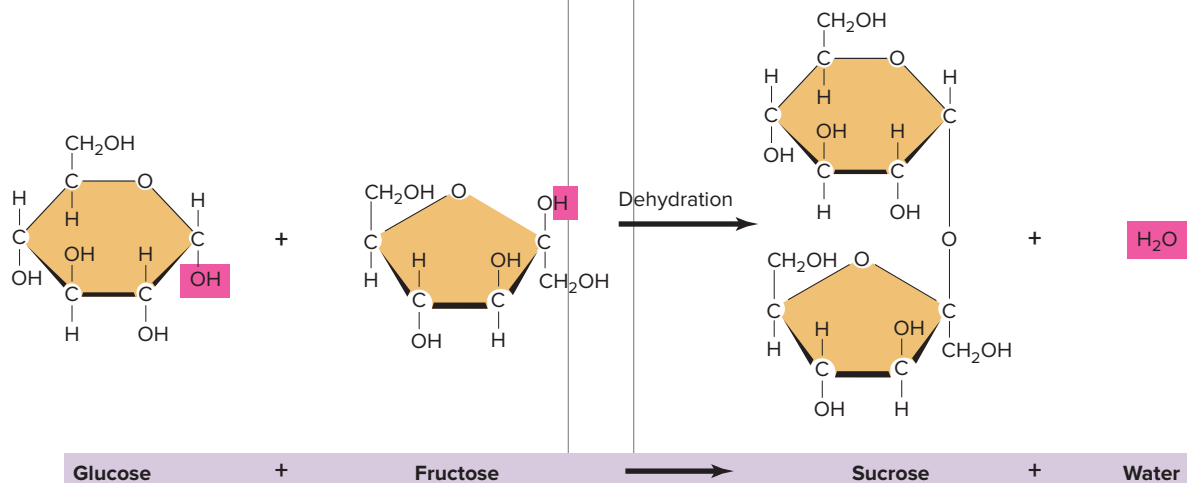
TABLE 2.5 Major Categories of Organic Molecules in the Body

Category	Percentage of Body Weight	Predominant Atoms	Subclass	Subunits
Carbohydrates	1	C, H, O	Polysaccharides (and disaccharides)	Monosaccharides
Lipids	15	C, H	Triglycerides	3 fatty acids + glycerol
			Phospholipids	2 fatty acids + glycerol + phosphate + small charged nitrogen-containing group
			Steroids	None
Proteins	17	C, H, O, N	None	Amino acids
Nucleic acids	2	C, H, O, N	DNA	Nucleotides containing the bases adenine, cytosine, guanine, thymine; the sugar deoxyribose; and phosphate
			RNA	Nucleotides containing the bases adenine, cytosine, guanine, uracil; the sugar ribose; and phosphate

atoms and an oxygen atom form a ring that lies in an essentially flat plane. The hydrogen and hydroxyl groups on each carbon lie above and below the plane of this ring. If one of the hydroxyl groups below the ring is shifted to a position above the ring, a different monosaccharide is produced.

Most monosaccharides in the body contain five or six carbon atoms and are called **pentoses** and **hexoses**, respectively. Larger carbohydrates can be formed by joining a number of monosaccharides together. Carbohydrates composed of two monosaccharides are known as **disaccharides**. **Sucrose**, or table sugar, is composed of two monosaccharides, glucose and fructose (**Figure 2.10**). The linking together of most monosaccharides involves a dehydration reaction in which a hydroxyl group is removed from one monosaccharide and a hydrogen atom is removed from the other, giving rise to a molecule of water and covalently bonding the two sugars together through an oxygen atom. Conversely, hydrolysis of the disaccharide breaks this linkage by adding back the water and thus uncoupling the two monosaccharides. Other disaccharides frequently encountered are maltose (glucose–glucose), formed during the digestion of large carbohydrates in the intestinal tract, and lactose (glucose–galactose), present in milk.

When many monosaccharides are linked together to form polymers, the molecules are known as **polysaccharides**. Starch, found in plant cells, and **glycogen**, present in animal cells, are examples of polysaccharides (**Figure 2.11**). Both of these polysaccharides are composed of thousands of glucose molecules linked together in long chains, differing only in the degree of branching along the chain. Glycogen exists in the body as a reservoir of available energy that is stored in the chemical bonds within individual glucose monomers. Hydrolysis of glycogen, as occurs during periods of fasting, leads to release of the glucose monomers into the blood, thereby preventing blood glucose from decreasing to dangerously low concentrations.



APIR **Figure 2.10** Sucrose (table sugar) is a disaccharide formed when two monosaccharides, glucose and fructose, bond together through a dehydration reaction.

PHYSIOLOGICAL INQUIRY

- What is the reverse reaction of a dehydration reaction called?

Answer can be found at end of chapter.

Lipids

Lipids are molecules composed predominantly (but not exclusively) of hydrogen and carbon atoms. These atoms are linked by nonpolar covalent bonds; therefore, lipids are nonpolar and have a very low solubility in water. Lipids, which account for about 40% of the organic matter in the average body (15% of the body weight), can be divided into four subclasses: fatty acids, triglycerides, phospholipids, and steroids. Like carbohydrates, lipids are important in physiology partly because some of them provide a valuable source of energy. Other lipids are a major component of all cellular membranes, and still others are important signaling molecules.

Fatty Acids A **fatty acid** consists of a chain of carbon and hydrogen atoms with an acidic carboxyl group at one end (**Figure 2.12a**). Therefore, fatty acids contain two oxygen atoms in addition to their complement of carbon and hydrogen. Fatty acids are synthesized in cells by the covalent bonding together of two-carbon fragments, resulting most commonly in fatty acids of 16 to 20 carbon atoms. When all the carbons in a fatty acid are linked by single covalent bonds, the fatty acid is said to be a **saturated fatty acid**, because both of the remaining available bonds in each carbon atom are occupied—or saturated—with covalently bound hydrogen. Some fatty acids contain one or more double bonds between carbon atoms, and these are known as **unsaturated fatty acids**. If one double bond is present, a **monounsaturated fatty acid** is formed, and if there is more than one double bond, a **polyunsaturated fatty acid** is formed (see **Figure 2.12a**).

Most naturally occurring unsaturated fatty acids exist in the *cis* position, with both hydrogens on the same side of the double-bonded carbons (see **Figure 2.12a**). It is possible, however, to modify fatty acids during the processing of certain fatty foods,

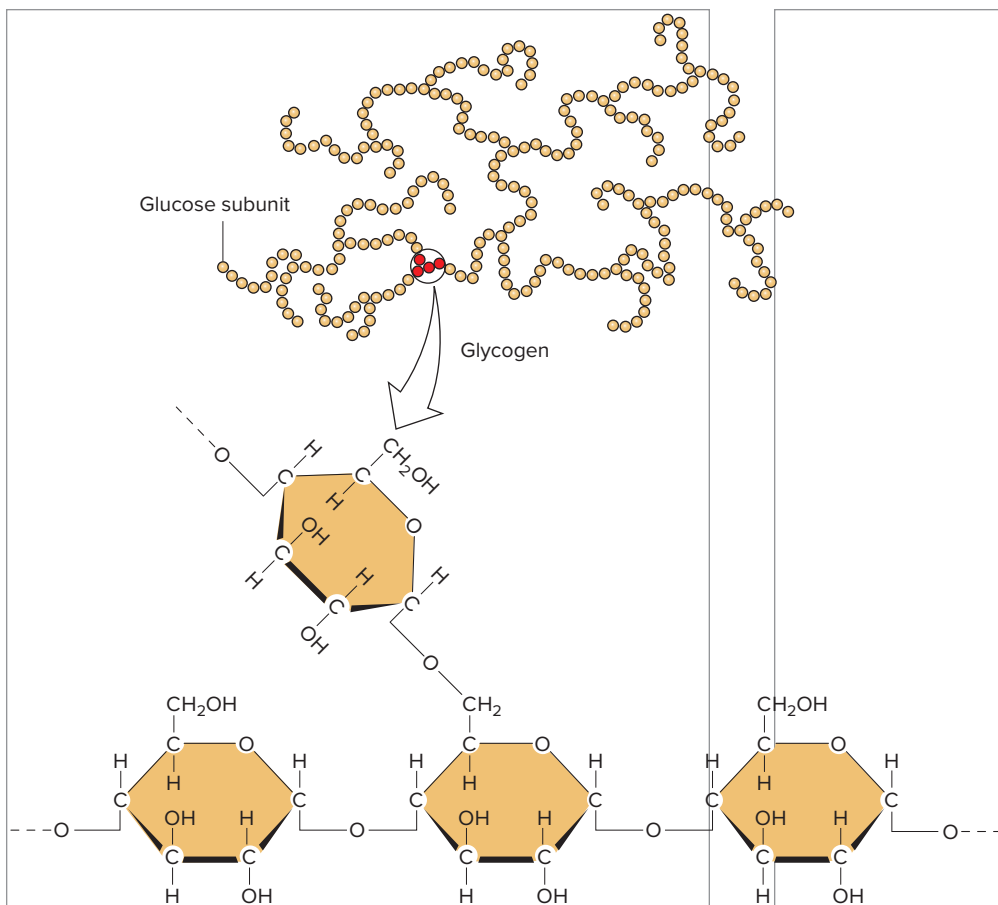


Figure 2.11 Many molecules of glucose joined end to end and at branch points form the branched-chain polysaccharide glycogen, shown here in diagrammatic form. The four red subunits in the glycogen molecule correspond to the four glucose subunits shown at the bottom.

PHYSIOLOGICAL INQUIRY

- How is the ability to store glucose as glycogen related to the general principle of physiology that physiological processes require the transfer and balance of matter and energy?

Answer can be found at end of chapter.

such that the hydrogens are on opposite sides of the double bond. These structurally altered fatty acids are known as **trans fatty acids**. The trans configuration imparts stability to the food for longer storage and alters the food's flavor and consistency. However, trans fatty acids have recently been linked with a number of serious health conditions, including an elevated blood concentration of cholesterol; current health guidelines recommend against the consumption of foods containing trans fatty acids.

Fatty acids have many important functions in the body, including but not limited to providing energy for cellular metabolism. The bonds between carbon and hydrogen atoms in a fatty acid can be broken to release chemical energy that can be stored in the chemical bonds of ATP. Like glucose, therefore, fatty acids are an extremely important source of energy. In addition, some fatty acids can be altered to produce a special class of molecules that regulate a number of cell functions by acting as cell signaling molecules. These modified fatty acids—collectively termed *eicosanoids*—are derived from the 20-carbon, polyunsaturated fatty acid arachidonic acid. They have been implicated in the control of blood pressure

(Chapter 12), inflammation (Chapters 12 and 18), and smooth muscle contraction (Chapter 9), among other things. Finally, fatty acids form part of the structure of triglycerides, described next.

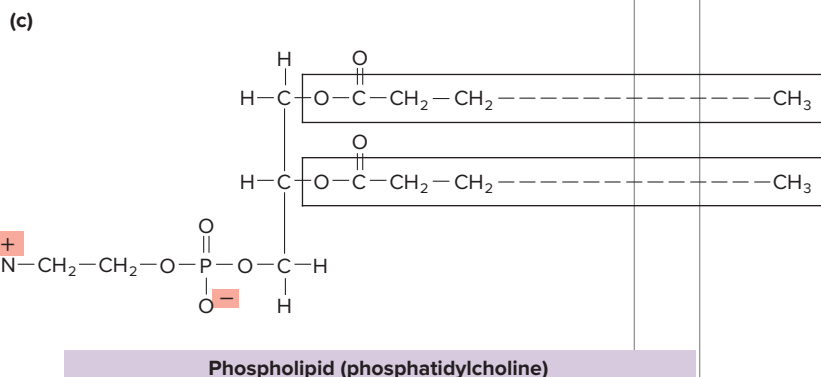
Triglycerides Triglycerides (also known as *triacylglycerols*) constitute the majority of the lipids in the body; these molecules are generally referred to simply as “fats.” Triglycerides form when **glycerol**, a three-carbon sugar-alcohol, bonds to three fatty acids (**Figure 2.12b**). Each of the three hydroxyl groups in glycerol is bonded to the carboxyl group of a fatty acid by a dehydration reaction.

The three fatty acids in a molecule of triglyceride are usually not identical. Therefore, a variety of triglycerides can be formed with fatty acids of different chain lengths and degrees of saturation. Animal triglycerides generally contain a high proportion of saturated fatty acids, whereas plant triglycerides contain more unsaturated fatty acids. Saturated fats tend to be solid at low temperatures. In a familiar example, heating a hamburger on the stove melts the saturated animal fats, leaving grease in the frying pan. When allowed to cool, however, the oily grease returns to its solid form. Unsaturated fats, on the other hand, have a very low melting point, and thus they are liquids (oil) even at low temperatures.

Triglycerides are present in the blood and can be synthesized in the liver. They are stored in great quantities in adipose tissue, where they serve as an energy reserve for the body, particularly

during times when a person is fasting or requires additional energy (exercise, for example). This occurs by hydrolysis, which releases the fatty acids from triglycerides in adipose tissue; the fatty acids enter the blood and are carried to the tissues and organs where they can be metabolized to provide energy for cell functions. Therefore, as with polysaccharides, storing energy in the form of triglycerides requires dehydration reactions, and both polysaccharides and triglycerides can be broken down by hydrolysis reactions to usable forms of energy. Throughout this text, you will see how these reactions are a key mechanism underlying the general principle of physiology that physiological processes require the transfer and balance of matter and energy.

Phospholipids Phospholipids are similar in overall structure to triglycerides, with one important difference. The third hydroxyl group of glycerol, rather than being attached to a fatty acid, is linked to phosphate. In addition, a small polar or ionized nitrogen-containing molecule is usually attached to this phosphate (**Figure 2.12c**). These groups constitute a polar



(hydrophilic) region at one end of the phospholipid, whereas the two fatty acid chains provide a nonpolar (hydrophobic) region at the opposite end. Therefore, phospholipids are amphipathic. In aqueous solution, they become organized into clusters, with their polar ends attracted to the water molecules. This property of phospholipids permits them to form the lipid bilayers of cellular membranes (Chapter 3).

Steroids Steroids have a distinctly different structure from those of the other subclasses of lipid molecules. Four interconnected rings of carbon atoms form the skeleton of every steroid (Figure 2.13). A few hydroxyl groups, which are polar, may be attached to this ring structure, but they are not numerous enough to make a steroid water-soluble. Examples of steroids are cholesterol, cortisol from the adrenal glands, and female and male sex hormones (estrogen and testosterone, respectively) secreted by the gonads.

Proteins

The term **protein** comes from the Greek *proteios* (“of the first rank”), which aptly describes their importance. Proteins account for about 50% of the organic material in the body (17% of the body weight), and they have critical functions in almost every physiological and homeostatic process (summarized in Table 2.6). Proteins are composed of carbon, hydrogen, oxygen, nitrogen, and small amounts of other elements, notably sulfur. They are macromolecules, often containing thousands of atoms; they are formed when a large number of small subunits (monomers) bond together via dehydration reactions to create a polymer.

Amino Acids The subunit monomers of proteins are **amino acids**; therefore, proteins are polymers of amino acids. Every amino

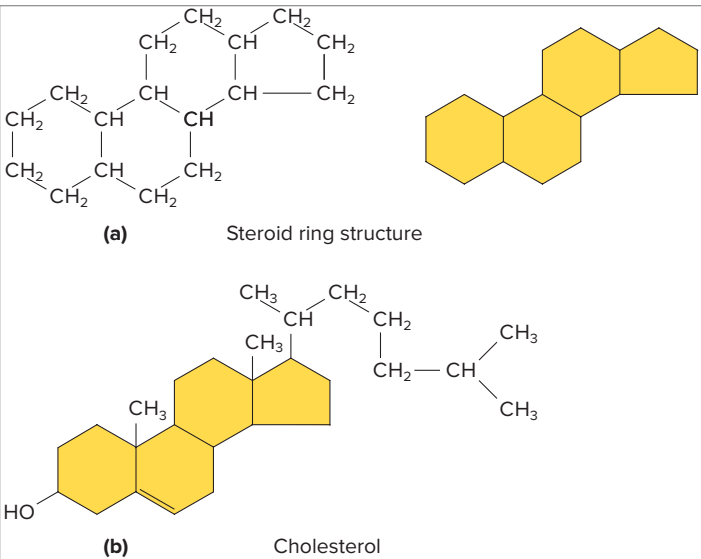


Figure 2.13 (a) Steroid ring structure, shown with all the carbon and hydrogen atoms in the rings and again without these atoms to emphasize the overall ring structure of this class of lipids. (b) Different steroids have different types and numbers of chemical groups attached at various locations on the steroid ring, as shown by the structure of cholesterol.

acid except one (proline) has an amino (–NH₂) and a carboxyl (–COOH) group bound to the terminal carbon atom in the molecule:

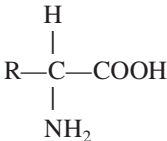


TABLE 2.6 Major Categories and Functions of Proteins		
Category	Functions	Examples
Proteins that regulate gene expression	Make RNA from DNA; synthesize polypeptides from RNA	Transcription factors activate genes; RNA polymerase transcribes genes; ribosomal proteins are required for translation of mRNA into protein.
Transporter proteins	Mediate the movement of solutes such as ions and organic molecules across plasma membranes	Ion channels in plasma membranes allow movement across the membrane of ions such as Na ⁺ and K ⁺ .
Enzymes	Accelerate the rate of specific chemical reactions, such as those required for cellular metabolism	Pancreatic lipase, amylase, and proteases released into the small intestine break down macromolecules into smaller molecules that can be absorbed by the intestinal cells; protein kinases modify other proteins by the addition of phosphate groups, which changes the function of the protein.
Cell signaling proteins	Enable cells to communicate with each other, themselves, and with the external environment	Plasma membrane receptors bind to hormones or neurotransmitters in extracellular fluid.
Motor proteins	Initiate movement	Myosin, found in muscle cells, provides the contractile force that shortens a muscle.
Structural proteins	Support, connect, and strengthen cells, tissues, and organs	Collagen and elastin provide support for ligaments, tendons, and certain large blood vessels; actin makes up much of the cytoskeleton of cells.
Defense proteins	Protect against infection and disease due to pathogens	Cytokines and antibodies attack foreign cells and proteins, such as those from bacteria and viruses.

Chemical nature of side chain	Side chain	Amino acid
	$\begin{array}{c} \text{R} - \text{C} - \text{C} - \text{OH} \\ \quad \quad \\ \text{H} \quad \quad \text{O} \\ \quad \quad \\ \text{NH}_2 \quad \text{Carboxyl (acid) group} \end{array}$	
Nonpolar	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH} - \text{CH}_2 - \text{C} - \text{COOH} \\ \quad \quad \\ \text{CH}_3 \quad \quad \text{H} \\ \quad \quad \quad \\ \quad \quad \quad \text{NH}_2 \end{array}$	Leucine
Polar (not ionized)	$\begin{array}{c} (\delta^+) (\delta^-) \\ \quad \\ \text{H} - \text{O} - \text{CH}_2 - \text{C} - \text{COOH} \\ \quad \quad \\ \quad \quad \quad \text{H} \\ \quad \quad \quad \\ \quad \quad \quad \text{NH}_2 \end{array}$	Serine
Polar (ionized)	$\begin{array}{c} + \\ \\ \text{NH}_3 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{C} - \text{COOH} \\ \quad \quad \\ \quad \quad \quad \text{H} \\ \quad \quad \quad \\ \quad \quad \quad \text{NH}_2 \end{array}$	Lysine

Figure 2.14 Representative structures of each class of amino acids found in proteins.

The third bond of this terminal carbon is to a hydrogen atom and the fourth to the remainder of the molecule, which is known as the **amino acid side chain** (R in the formula). These side chains are of varied sizes, ranging from a single hydrogen atom to nine carbon atoms with their associated hydrogen atoms.

The proteins of all living organisms are composed of the same set of 20 different amino acids, corresponding to 20 different side

chains. The side chains may be nonpolar (eight amino acids), polar but not ionized (seven amino acids), or polar and ionized (five amino acids) (**Figure 2.14**). The human body can synthesize many amino acids, but several must be obtained in the diet; the latter are known as essential amino acids. This term does not imply that these amino acids are somehow more important than others, only that they must be obtained in the diet.

Polypeptides Amino acids are joined together by linking the carboxyl group of one amino acid to the amino group of another. As in the formation of glycogen and triglycerides, a molecule of water is formed by dehydration (**Figure 2.15**). The bond formed between the amino and carboxyl group is called a **peptide bond**. Although peptide bonds are covalent, they can be enzymatically broken by hydrolysis to yield individual amino acids, as happens in the stomach and intestines, for example, when we digest protein in the food we eat.

Notice in **Figure 2.15** that when two amino acids are linked together, one end of the resulting molecule has a free amino group and the other has a free carboxyl group.

Additional amino acids can be linked by peptide bonds to these free ends. A sequence of amino acids linked by peptide bonds is known as a **polypeptide**. The peptide bonds form the backbone of the polypeptide, and the side chain of each amino acid sticks out from the chain. Strictly speaking, the term *polypeptide* refers to a structural unit and does not necessarily suggest that the molecule is functional. When one or more polypeptides are folded into a

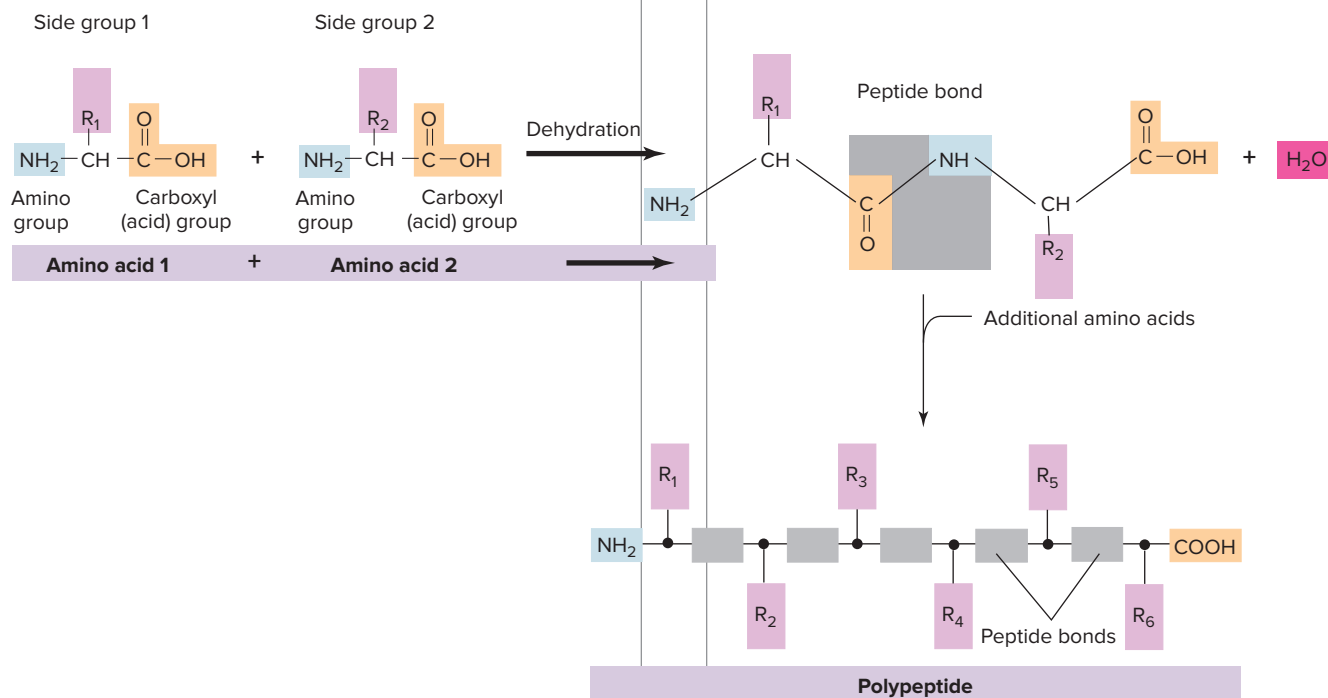


Figure 2.15 Linkage of amino acids by peptide bonds to form a polypeptide.

characteristic shape forming a functional molecule, that molecule is called a protein. (By convention, if the number of amino acids in a functional polypeptide is about 50 or fewer, the molecule is often referred to simply as a peptide, a term we will use throughout the text where relevant.)

As mentioned earlier, one or more monosaccharides may become covalently attached to the side chains of specific amino acids in a protein; such proteins are known as **glycoproteins**. These proteins are present in plasma membranes; are major components of connective tissue; and are also abundant in fluids like mucus, where they exert a protective or lubricating function.

All proteins have multiple levels of structure that give each protein a unique shape; these are called the primary, secondary, tertiary, and—in some proteins—quaternary structure. A general principle of physiology is that structure and function are linked. This is true even at the molecular level. The shape of a protein determines its physiological activity. In all cases, a protein's shape depends on its amino acid sequence, known as the *primary structure* of the protein.

Primary Structure Two variables determine the **primary structure** of a protein: (1) the number of amino acids in the chain, and (2) the specific sequence of different amino acids (**Figure 2.16**). Each position along the chain can be occupied by any one of the 20 different amino acids. Every protein is defined by its own unique primary structure.

Secondary Structure A polypeptide can be envisioned as analogous to a string of beads, each bead representing one amino acid (see **Figure 2.16**). Moreover, because amino acids can rotate

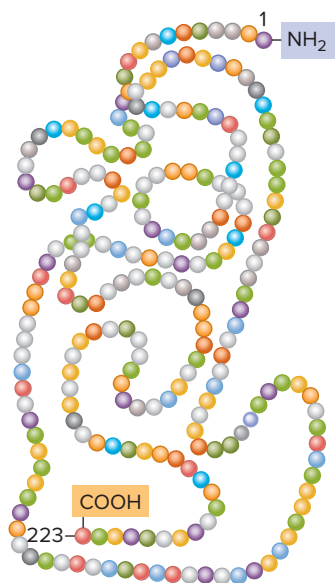


Figure 2.16 The primary structure of a polypeptide chain is the sequence of amino acids in that chain. The polypeptide illustrated contains 223 amino acids. Different amino acids are represented by different-colored circles. The numbering system begins with the amino terminal (NH_2).

PHYSIOLOGICAL INQUIRY

- What is the difference between the terms *polypeptide* and *protein*?

Answer can be found at end of chapter.

around bonds within a polypeptide chain, the chain is flexible and can bend into a number of shapes, just as a string of beads can be twisted into many configurations. Proteins do not appear in nature like a linear string of beads on a chain; interactions between side groups of each amino acid lead to bending, twisting, and folding of the chain into a more compact structure. The final shape of a protein is known as its **conformation**.

The attractions between various regions along a polypeptide chain create **secondary structure**. For example, hydrogen bonds can occur between a hydrogen linked to the nitrogen atom in one peptide bond and the double-bonded oxygen atom in another peptide bond (**Figure 2.17**). Because peptide bonds occur at regular intervals along a polypeptide chain, the hydrogen bonds between them tend to force the chain into a coiled conformation known as an **alpha helix**. Hydrogen bonds can also form between peptide bonds when extended regions of a polypeptide chain run approximately parallel to each other, forming a relatively straight, extended region known as a **beta pleated sheet** (see **Figure 2.17**). However, for several reasons, a given region of a polypeptide chain may assume neither a helical nor beta pleated sheet conformation. For example, the sizes of the side chains and the presence of ionic bonds between side chains with opposite charges can interfere with the repetitive hydrogen bonding required to produce these shapes. These irregular regions, known as random coil conformations, occur in regions linking the more regular helical and beta pleated sheet patterns (see **Figure 2.17**).

Beta pleated sheets and alpha helices tend to impart upon a protein the ability to anchor itself into a lipid bilayer, like that of a plasma membrane, because these regions of the protein usually contain amino acids with hydrophobic side chains. The hydrophobicity of the side chains makes them more likely to remain in the lipid environment of the plasma membrane.

Tertiary Structure Once secondary structure has been formed, associations between additional amino acid side chains become possible. For example, two amino acids that may have been too far apart in the linear sequence of a polypeptide to interact with each other may become very near each other once secondary structure has changed the shape of the molecule. These interactions fold the polypeptide into a new three-dimensional conformation called its **tertiary structure**, making it a functional protein (see **Figure 2.17**). Five major factors determine the tertiary structure of a protein (**Figure 2.18**): (1) hydrogen bonds between side groups of amino acids or with surrounding water molecules; (2) ionic interactions (attractive or repulsive) between ionized regions along the chain; (3) interactions between nonpolar (hydrophobic) regions; (4) covalent disulfide bonds linking the sulfur-containing side chains of two cysteine amino acids; and (5) van der Waals forces, which are very weak and transient electrical interactions between the electrons in the outer shells of two atoms that are in close proximity to each other.

Quaternary Structure As shown in **Figure 2.19**, some proteins are composed of more than one polypeptide chain bonded together; such proteins are said to have **quaternary structure** and are known as multimeric (“many parts”) proteins. Each polypeptide chain in a multimeric protein is called a subunit. The same factors that influence the conformation of a single polypeptide also determine the interactions between the

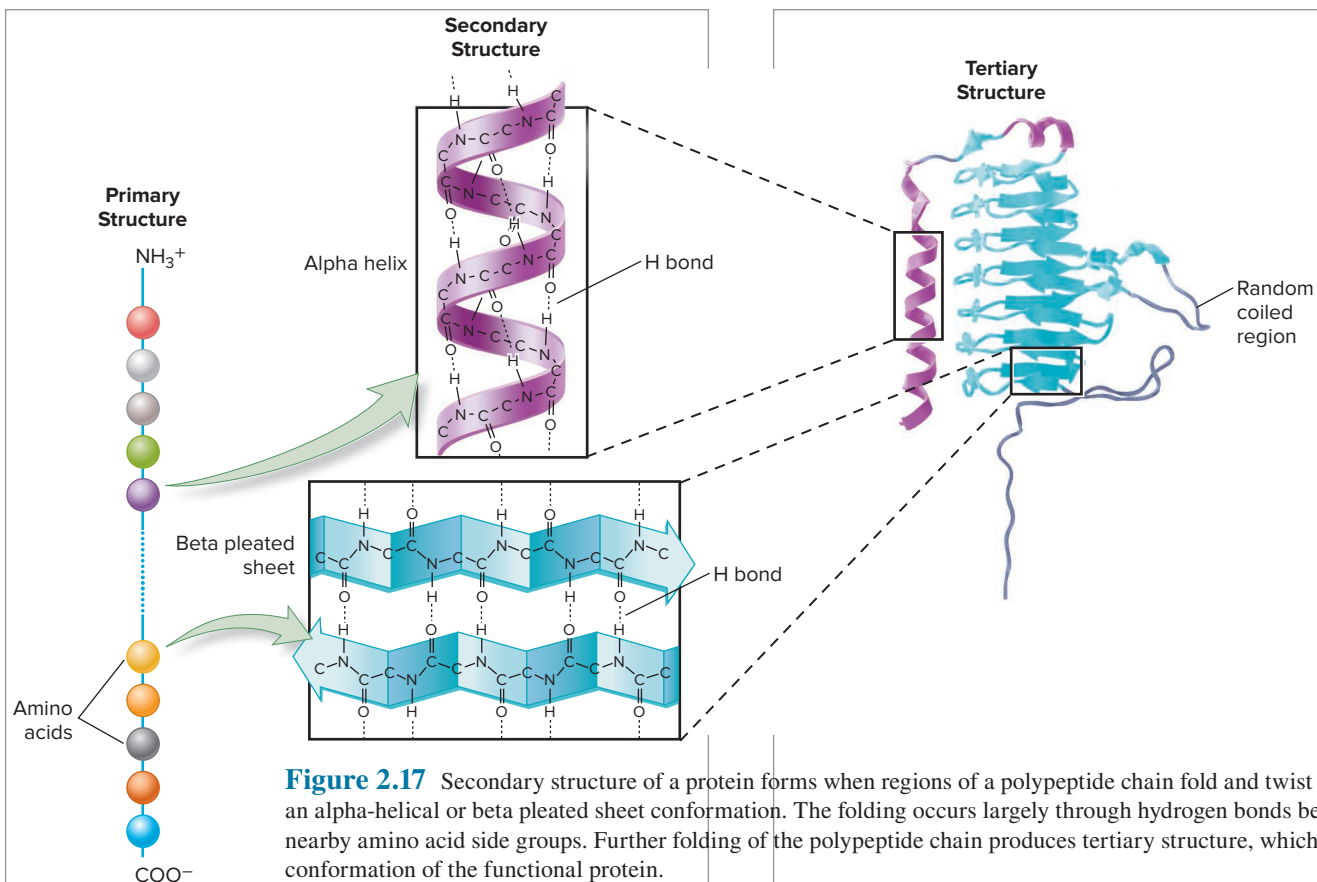


Figure 2.17 Secondary structure of a protein forms when regions of a polypeptide chain fold and twist into either an alpha-helical or beta pleated sheet conformation. The folding occurs largely through hydrogen bonds between nearby amino acid side groups. Further folding of the polypeptide chain produces tertiary structure, which is the final conformation of the functional protein.

subunits in a multimeric protein. Therefore, the subunits can be held together by interactions between various ionized, polar, and nonpolar side chains, as well as by disulfide covalent bonds between the subunits.

Multimeric proteins have many diverse functions. The subunits in a multimeric protein may be identical or different. For example, hemoglobin, the protein that transports oxygen in the blood, is a multimeric protein with four subunits, two of one kind and two of another (see Figure 2.19). Each subunit

can bind one oxygen molecule. Other multimeric proteins that you will learn of in this textbook create pores, or channels, in plasma membranes to allow movement of small solutes in and out of cells.

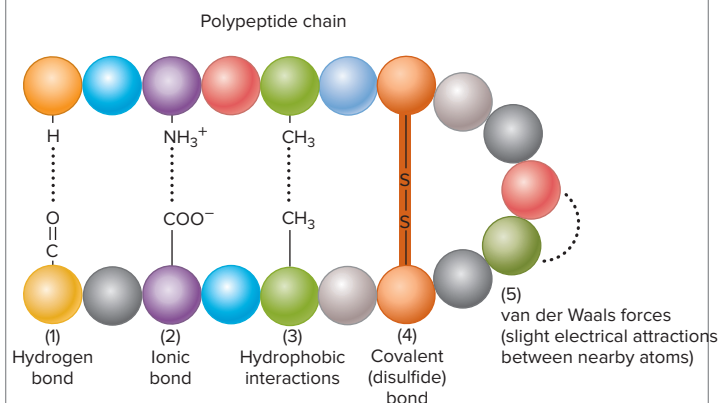


Figure 2.18 Factors that contribute to the folding of polypeptide chains and thus to their conformation are (1) hydrogen bonds between side chains or with surrounding water molecules, (2) ionic interactions between ionized side chains, (3) hydrophobic attractive forces between nonpolar side chains, (4) disulfide bonds between side chains, and (5) van der Waals forces between atoms in the side chains of nearby amino acids.

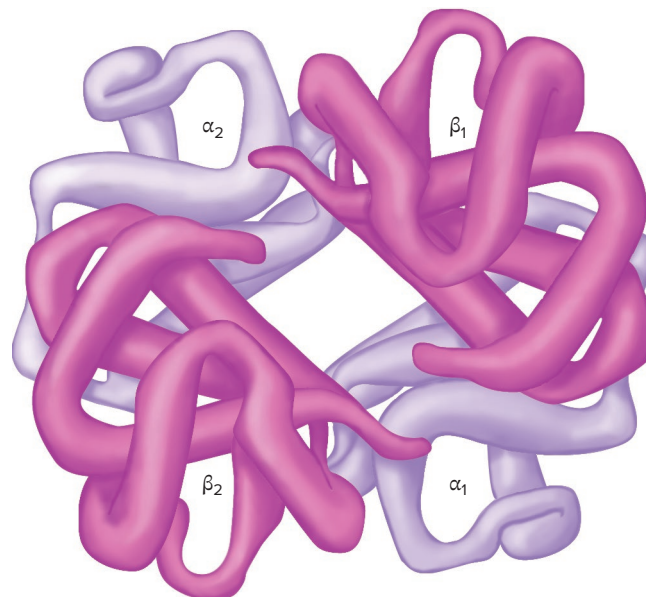


Figure 2.19 Hemoglobin, a multimeric protein composed of two identical alpha (a) subunits and two identical beta (b) subunits. (The iron-containing heme groups attached to each subunit are not shown.) In this simplified view, the tertiary structure of subunits and their arrangement into quaternary structure are shown without details of primary or secondary structure.

The primary structures (amino acid sequences) of a large number of proteins are known, but three-dimensional conformations have been determined for only a small number. Because of the multiple factors that can influence the folding of a polypeptide chain, it is not yet possible to accurately predict the conformation of a protein from its primary amino acid sequence. However, it should be clear that a change in the primary structure of a protein may alter its secondary, tertiary, and quaternary structures. Such an alteration in primary structure is called a **mutation**. Even a single amino acid change resulting from a mutation may have devastating consequences, as occurs when a molecule of valine replaces a molecule of glutamic acid in the beta chains of hemoglobin. The result of this change is a serious disease called **sickle-cell disease** (also called *sickle-cell anemia*; see the Case Study at the end of this chapter).

Nucleic Acids

Nucleic acids account for only 2% of body weight, yet these molecules are extremely important because they are responsible for the storage, expression, and transmission of genetic information. The expression of genetic information in the form of specific proteins determines whether one is a human or a mouse, or whether a cell is a muscle cell or an epithelial cell.

There are two classes of nucleic acids, **deoxyribonucleic acid (DNA)** and **ribonucleic acid (RNA)**. DNA molecules store genetic information coded in the sequence of their genes, whereas RNA molecules are involved in decoding this information into instructions for linking together a specific sequence of amino acids to form a specific polypeptide chain.

Both types of nucleic acids are polymers and are therefore composed of linear sequences of repeating subunits. Each subunit, known as a **nucleotide**, has three components: a phosphate group, a sugar, and a ring of carbon and nitrogen atoms known as a base because it can accept hydrogen ions (**Figure 2.20**). The phosphate group of one nucleotide is linked to the sugar of the adjacent nucleotide to form a chain, with the bases sticking out from the side of the phosphate–sugar backbone (**Figure 2.21**).

DNA The nucleotides in DNA contain the five-carbon sugar **deoxyribose** (hence the name “deoxyribonucleic acid”). Four different nucleotides are present in DNA, corresponding to the four

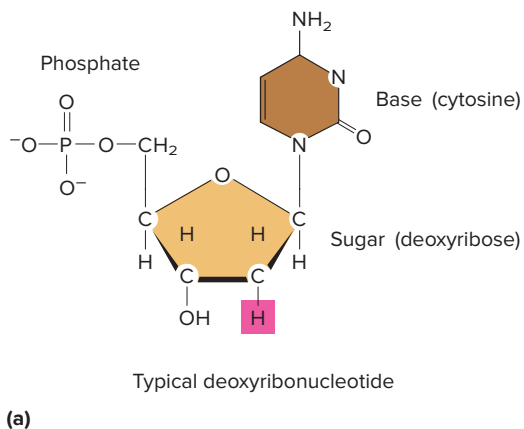
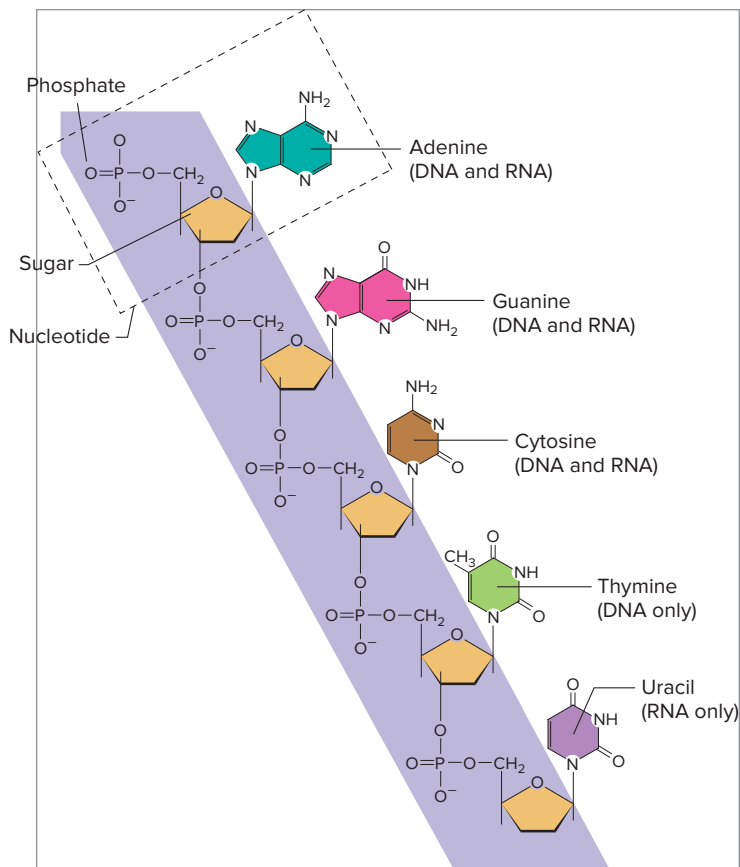


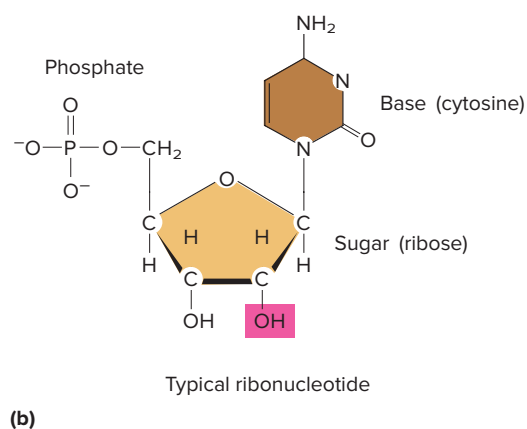
Figure 2.20 Nucleotide subunits of DNA and RNA. Nucleotides are composed of a sugar, a base, and a phosphate group. (a) Deoxyribonucleotides present in DNA contain the sugar deoxyribose. (b) The sugar in ribonucleotides, present in RNA, is ribose, which has an OH at a position in which deoxyribose has only a hydrogen atom.

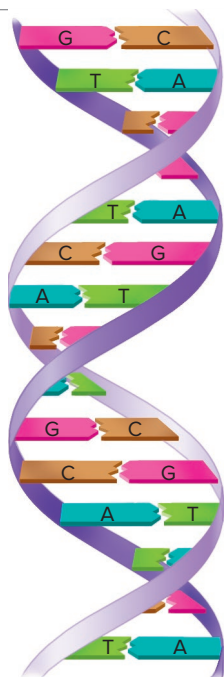


AP|R Figure 2.21 Phosphate–sugar bonds link nucleotides in sequence to form nucleic acids. Note that the pyrimidine base thymine is only found in DNA, and uracil is only present in RNA.

different bases that can be bound to deoxyribose. These bases are divided into two classes: (1) the **purine** bases, **adenine (A)** and **guanine (G)**, which have double rings of nitrogen and carbon atoms; and (2) the **pyrimidine** bases, **cytosine (C)** and **thymine (T)**, which have only a single ring (see **Figure 2.21**).

A DNA molecule consists of not one but two chains of nucleotides coiled around each other in the form of a double helix (**Figure 2.22**). The two chains are held together by hydrogen bonds between a purine base on one chain and a pyrimidine base





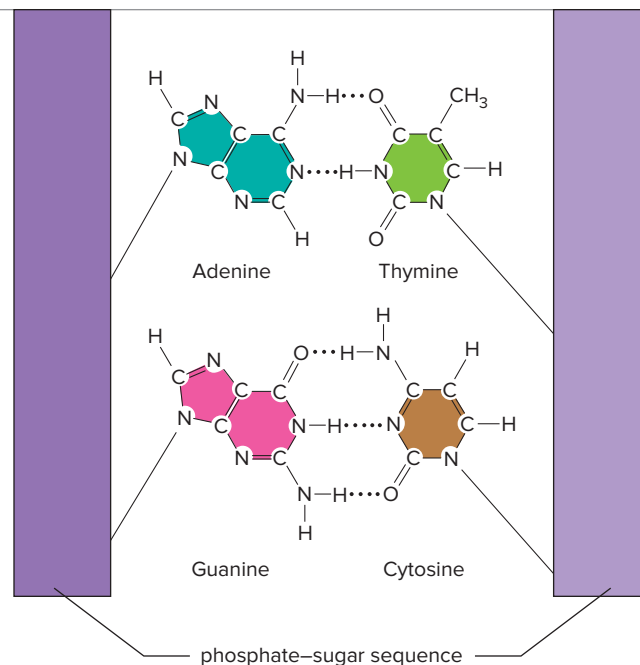
AP|R Figure 2.22 Base pairings between a purine and pyrimidine base link the two polynucleotide strands of the DNA double helix.

on the opposite chain. The ring structure of each base lies in a flat plane perpendicular to the phosphate–sugar backbone, like steps on a spiral staircase. This base pairing maintains a constant distance between the sugar–phosphate backbones of the two chains as they coil around each other.

Specificity is imposed on the base pairings by the location of the hydrogen-bonding groups in the four bases (**Figure 2.23**). Three hydrogen bonds form between the purine guanine and the pyrimidine cytosine (G–C pairing), whereas only two hydrogen bonds can form between the purine adenine and the pyrimidine thymine (A–T pairing). As a result, G is always paired with C, and A with T. This specificity provides the mechanism for duplicating and transferring genetic information.

The hydrogen bonds between the bases can be broken by enzymes. This separates the double helix into two strands; such DNA is said to be denatured. Each single strand can be replicated to form two new molecules of DNA. This occurs during cell division such that each daughter cell has a full complement of DNA. The bonds can also be broken by heating DNA in a test tube, which provides a convenient way for researchers to examine such processes as DNA replication.

RNA RNA molecules differ in only a few respects from DNA: (1) RNA consists of a single (rather than a double) chain of nucleotides; (2) in RNA, the sugar in each nucleotide is **ribose** rather than deoxyribose; and (3) the pyrimidine base thymine in DNA is replaced in RNA by the pyrimidine base **uracil** (U) (see **Figure 2.21**), which can base-pair with the purine adenine (A–U pairing). The other three bases—adenine, guanine, and cytosine—are the same in both DNA and RNA. Because RNA contains only a single chain of nucleotides, portions of this chain can bend back upon themselves and undergo base pairing with nucleotides in the same chain or in other molecules of DNA or RNA. ■



AP|R Figure 2.23 Hydrogen bonds between the nucleotide bases in DNA determine the specificity of base pairings: adenine with thymine, and guanine with cytosine.

PHYSIOLOGICAL INQUIRY

- When a DNA molecule is heated to an extreme temperature in a test tube, the two chains break apart. Which type of DNA molecule would you expect to require less heat to break apart, one with more G–C bonds, or one with more A–T bonds?

Answer can be found at end of chapter.

SUMMARY

Atoms

- I. Atoms are composed of three subatomic particles: positive protons and neutral neutrons, both located in the nucleus, and negative electrons revolving around the nucleus in orbitals contained within electron shells.
- II. The atomic number is the number of protons in an atom, and because atoms (except ions) are electrically neutral, it is also the number of electrons.
- III. The atomic mass of an atom is the ratio of the atom's mass relative to that of a ^{12}C atom.
- IV. One gram atomic mass is the number of grams of an element equal to its atomic mass. One gram atomic mass of any element contains the same number of atoms: 6×10^{23} .
- V. When an atom gains or loses one or more electrons, it acquires a net electrical charge and becomes an ion.

Molecules

- I. Molecules are formed by linking atoms together.
- II. A covalent bond forms when two atoms share a pair of electrons. Each type of atom can form a characteristic number of covalent bonds: Hydrogen forms one; oxygen, two; nitrogen, three; and carbon, four. In polar covalent bonds, one atom attracts the bonding electrons more than the other atom of the pair. Nonpolar covalent bonds are between two atoms of similar electronegativities.

- III. Molecules have characteristic shapes that can be altered within limits by the rotation of their atoms around covalent bonds.
- IV. The electrical attraction between hydrogen and an oxygen or nitrogen atom in a separate molecule, or between different regions of the same molecule, forms a hydrogen bond.
- V. Molecules may have ionic regions within their structure.
- VI. Free radicals are atoms or molecules that contain atoms having an unpaired electron in their outer electron orbital.

Solutions

- I. Water, a polar molecule, is attracted to other water molecules by hydrogen bonds. Water is the solvent in which most of the chemical reactions in the body take place.
- II. Substances dissolved in a liquid are solutes, and the liquid in which they are dissolved is the solvent.
- III. Substances that have polar or ionized groups dissolve in water by being electrically attracted to the polar water molecules.
- IV. In water, amphipathic molecules form clusters with the polar regions at the surface and the nonpolar regions in the interior of the cluster.
- V. The molecular weight of a molecule is the sum of the atomic weights of all its atoms. One mole of any substance is its molecular weight in grams and contains 6×10^{23} molecules.
- VI. Substances that release a hydrogen ion in solution are called acids. Those that accept a hydrogen ion are bases.
 - a. The acidity of a solution is determined by its free hydrogen ion concentration; the greater the hydrogen ion concentration, the greater the acidity.
 - b. The pH of a solution is the negative logarithm of the hydrogen ion concentration. As the acidity of a solution increases, the pH decreases. Acid solutions have a pH less than 7.0, whereas alkaline solutions have a pH greater than 7.0.

Classes of Organic Molecules

- I. Carbohydrates are composed of carbon, hydrogen, and oxygen atoms.
 - a. The presence of the polar hydroxyl groups makes carbohydrates soluble in water.
 - b. The most abundant monosaccharide in the body is glucose ($C_6H_{12}O_6$), which is stored in cells in the form of the polysaccharide glycogen.
- II. Most lipids have many fewer polar and ionized groups than carbohydrates, a characteristic that makes them nearly or completely insoluble in water.
 - a. Triglycerides (fats) form when fatty acids are bound to each of the three hydroxyl groups in glycerol.
 - b. Phospholipids contain two fatty acids bound to two of the hydroxyl groups in glycerol, with the third hydroxyl bound to phosphate, which in turn is linked to a small charged or polar compound. The polar and ionized groups at one end of phospholipids make these molecules amphipathic.
 - c. Steroids are composed of four interconnected rings, often containing a few hydroxyl and other groups.
 - d. One fatty acid (arachidonic acid) can be converted to a class of signaling substances called eicosanoids.
- III. Proteins, macromolecules composed primarily of carbon, hydrogen, oxygen, and nitrogen, are polymers of 20 different amino acids.
 - a. Amino acids have an amino ($-NH_2$) and a carboxyl ($-COOH$) group bound to their terminal carbon atom.
 - b. Amino acids are bound together by peptide bonds between the carboxyl group of one amino acid and the amino group of the next.
 - c. The primary structure of a polypeptide chain is determined by (1) the number of amino acids in sequence and (2) the type of amino acid at each position.

- d. Hydrogen bonds between peptide bonds along a polypeptide force much of the chain into an alpha helix or beta pleated sheet (secondary structure).
- e. Covalent disulfide bonds can form between the sulfhydryl groups of cysteine side chains to hold regions of a polypeptide chain close to each other; together with hydrogen bonds, ionic bonds, hydrophobic interactions, and van der Waals forces, this creates the final conformation of the protein (tertiary structure).
- f. Multimeric proteins have multiple polypeptide chains (quaternary structure).
- IV. Nucleic acids are responsible for the storage, expression, and transmission of genetic information.
 - a. Deoxyribonucleic acid (DNA) stores genetic information.
 - b. Ribonucleic acid (RNA) is involved in decoding the information in DNA into instructions for linking amino acids together to form proteins.
 - c. Both types of nucleic acids are polymers of nucleotides, each containing a phosphate group; a sugar; and a base of carbon, hydrogen, oxygen, and nitrogen atoms.
 - d. DNA contains the sugar deoxyribose and consists of two chains of nucleotides coiled around each other in a double helix. The chains are held together by hydrogen bonds between purine and pyrimidine bases in the two chains.
 - e. Base pairings in DNA always occur between guanine and cytosine and between adenine and thymine.
 - f. RNA consists of a single chain of nucleotides, containing the sugar ribose and three of the four bases found in DNA. The fourth base in RNA is the pyrimidine uracil rather than thymine. Uracil base-pairs with adenine.

REVIEW QUESTIONS

1. Describe the electrical charge, mass, and location of the three major subatomic particles in an atom.
2. Which four kinds of atoms are most abundant in the body?
3. Describe the distinguishing characteristics of the three classes of essential chemical elements found in the body.
4. How many covalent bonds can be formed by atoms of carbon, nitrogen, oxygen, and hydrogen?
5. What property of molecules allows them to change their three-dimensional shape?
6. Define *ion* and *ionic bond*.
7. Draw the structures of an ionized carboxyl group and an ionized amino group.
8. Define *free radical*.
9. Describe the polar characteristics of a water molecule.
10. What determines a molecule's solubility or lack of solubility in water?
11. Describe the organization of amphipathic molecules in water.
12. What is the molar concentration of 80 g of glucose dissolved in sufficient water to make 2 L of solution?
13. What distinguishes a weak acid from a strong acid?
14. What effect does increasing the pH of a solution have upon the ionization of a carboxyl group? An amino group?
15. Name the four classes of organic molecules in the body.
16. Describe the three subclasses of carbohydrate molecules.
17. What properties are characteristic of lipids?
18. Describe the subclasses of lipids.
19. Describe the linkages between amino acids that form polypeptide chains.
20. What distinguishes the terms *polypeptide* and *protein*?
21. What two factors determine the primary structure of a polypeptide chain?

22. Describe the types of interactions that determine the conformation of a polypeptide chain.
23. Describe the structure of DNA and RNA.
24. Describe the characteristics of base pairings between nucleotide bases.

KEY TERMS

2.1 Atoms

anions	gram atomic mass
atomic mass	ion
atomic nucleus	isotopes
atomic number	mineral elements
atoms	neutrons
cations	protons
chemical element	radioisotopes
electrolytes	trace elements
electrons	

2.2 Molecules

amino group	ionic bond
carboxyl group	molecule
covalent bond	nonpolar covalent bonds
electronegativity	nonpolar molecules
free radical	polar covalent bonds
hydrogen bond	polar molecules
hydroxyl group	

2.3 Solutions

acid	hydrophobic
acidic solutions	mole
acidity	molecular weight
alkaline solutions	pH
amphipathic	solutes
base	solution
concentration	solvent
dehydration	strong acids
hydrolysis	weak acids
hydrophilic	

2.4 Classes of Organic Molecules

adenine	pentoses
alpha helix	peptide bond
amino acids	phospholipids
amino acid side chain	polymers
beta pleated sheet	polypeptide
carbohydrates	polysaccharides
conformation	polyunsaturated fatty acid
cytosine	primary structure
deoxyribonucleic acid (DNA)	protein
deoxyribose	purine
disaccharides	pyrimidine
fatty acid	quaternary structure
glucose	ribonucleic acid (RNA)
glycerol	ribose
glycogen	saturated fatty acid
glycoproteins	secondary structure
guanine	steroids
hexoses	sucrose
lipids	tertiary structure
macromolecules	thymine
monosaccharides	trans fatty acids
monounsaturated fatty acid	triglyceride
mutation	unsaturated fatty acids
nucleic acids	uracil
nucleotide	

CLINICAL TERMS

2.1 Atoms

PET (positron emission tomography) scans

2.4 Classes of Organic Molecules

sickle-cell disease

CHAPTER 2

Clinical Case Study: A Young Man with Severe Abdominal Pain While Mountain Climbing



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An athletic, 21-year-old African-American male in good health spent part of the summer before his senior year in college traveling with friends in the western United States. Although not an experienced mountain climber, he joined his friends in a professionally guided climb partway up Mt. Rainier in Washington. Despite his overall fitness, the rigors of the climb were far greater than he expected, and he found himself breathing heavily. At an elevation

of around 6000 feet, he began to feel twinges of pain on the left side of his upper abdomen. By the time he reached 9000 feet, the pain worsened to the point that he stopped climbing and descended the mountain. However, the pain did not go away and in fact

became very severe during the days after his climb. At that point, he went to a local emergency room, where he was subjected to a number of tests that revealed a disorder in his red blood cells due to an abnormal form of the protein hemoglobin.

Recall from Figure 2.19 that hemoglobin is a protein with quaternary structure. Each subunit in hemoglobin is noncovalently bound to the other subunits by the forces described in Figure 2.18. The three-dimensional (tertiary) structure of each subunit spatially aligns the individual amino acids in such a way that the bonding forces exert themselves between specific amino acid side groups. Therefore, anything that disrupts the tertiary structure of hemoglobin also disrupts the way in which subunits bond with one another. The patient described here had a condition called **sickle-cell trait** (SCT). Such individuals are carriers of the gene that causes

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sickle-cell disease (SCD), also called sickle-cell anemia. Individuals with SCT have one normal gene inherited from one parent and one gene with a mutation inherited from the other parent.

Reflect and Review #1

- Which level or levels of protein structure may be altered by a mutation in a gene?

The SCT/SCD gene is prevalent in several regions of the world, particularly in sub-Saharan Africa. In SCD, a mutation in the gene for the beta subunits of hemoglobin results in the replacement of a single glutamic acid residue with one of valine resulting in a change in primary structure of the protein. Glutamic acid has a charged, polar side group, whereas valine has a nonpolar side group. Thus, in hemoglobin containing the mutation, one type of intermolecular bonding force is replaced with a completely different one, and this can lead to abnormal bonding of hemoglobin subunits with each other. In fact, the hydrophobic interactions created by the valine side groups cause multiple hemoglobin molecules to bond with each other, forming huge polymer-like structures that precipitate out of solution within the cytoplasm of the red blood cell resulting in a deformation of the entire cell (**Figure 2.24**). This happens most noticeably when the amount of oxygen in the red blood cell is decreased. Such a situation can occur at high altitude, where the atmospheric pressure is low and consequently the amount of oxygen that diffuses into the lung circulation is also low. (You will learn about the relationship between altitude, oxygen, and atmospheric pressure in Chapter 13.)

When red blood cells become deformed into the sicklelike shape characteristic of this disease, they are removed from the circulation by the spleen, an organ that lies in the upper left quadrant of the abdomen and has an important function in eliminating dead or damaged red blood cells from the circulation. However, in the event of a sudden, large increase in the number of sickled cells, the spleen can become overfilled with damaged cells and painfully enlarged. Moreover, some of the



Figure 2.24 Light micrograph of blood sample from a person with sickle-cell disease. ©Southern Illinois University/Science Source

sickled cells can block some of the small blood vessels in the spleen, which also causes pain and damage to the organ. This may begin quickly but may also continue for several days, which is why our subject's pain did not become very severe until a day or two after his climb.

Why would our subject attempt to climb a mountain to high altitude, knowing that the available amount of oxygen in the air is decreased at such altitudes? Recall that we said that the man had sickle-cell *trait*, not sickle-cell disease. Individuals with sickle-cell trait produce enough normal hemoglobin to be symptom-free their entire lives and may never know that they are carriers of a mutated gene. However, when pushed to the limits of oxygen deprivation by high altitude and exercise, as our subject was, the result is sickling of some of the red blood cells. Once the young man's condition was confirmed, he was given analgesics (painkillers) and advised to rest for the next 2 to 3 weeks until his spleen returned to normal. His spleen was carefully monitored during this time, and he recovered fully. Our subject was lucky; numerous deaths due to unrecognized SCT have occurred throughout the world as a result of situations just like the one described here. It is a striking example of how a protein's overall conformation and function depend upon its primary structure, and how polypeptide interactions are critically dependent on the bonding forces described in this chapter.

Clinical term: sickle-cell trait

See Chapter 19 for complete, integrative case studies.

CHAPTER 2 TEST QUESTIONS *Recall and Comprehend*

Answers appear in Appendix A.

These questions test your recall of important details covered in this chapter. They also help prepare you for the type of questions encountered in standardized exams. Many additional questions of this type are available on Connect and LearnSmart.

1. A molecule that loses an electron to a free radical
 - a. becomes more stable.
 - b. becomes electrically neutral.
 - c. becomes less reactive.
 - d. is permanently destroyed.
 - e. becomes a free radical itself.
2. Of the bonding forces between atoms and molecules, which are strongest?
 - a. hydrogen bonds
 - b. bonds between oppositely charged ionized groups
 - c. bonds between nearby nonpolar groups
 - d. covalent bonds
 - e. bonds between polar groups
3. The process by which monomers of organic molecules are made into larger units
 - a. requires hydrolysis.
 - b. results in the generation of water molecules.
 - c. is irreversible.
 - d. occurs only with carbohydrates.
 - e. results in the production of ATP.

4. Which of the following is/are not found in DNA?
 - a. adenine
 - b. uracil
 - c. cytosine
 - d. deoxyribose
 - e. both b and d
5. Which of the following statements is incorrect about disulfide bonds?
 - a. They form between two cysteine amino acids.
 - b. They are noncovalent.
 - c. They contribute to the tertiary structure of some proteins.
 - d. They contribute to the quaternary structure of some proteins.
 - e. They involve the loss of two hydrogen atoms.
6. Match the following compounds with choices (a) monosaccharide, (b) disaccharide, or (c) polysaccharide:
 - Sucrose
 - Glucose
 - Glycogen
 - Fructose
 - Starch

7. Which of the following reactions involve/involves hydrolysis?

- a. formation of triglycerides
- b. formation of proteins
- c. breakdown of proteins
- d. formation of polysaccharides
- e. a, b, and d

8. A solution of pH greater than 7.0 is an (*acidic/alkaline*) solution, and has an H^+ concentration that is (*greater/less than*) 10^{-7} M.

9. Molecules containing both polar and nonpolar regions are known as _____ molecules.
10. Mutations arise from changes to the _____ structure of a protein.

CHAPTER 2 TEST QUESTIONS *Apply, Analyze, and Evaluate*

Answers appear in Appendix A.

These questions, which are designed to be challenging, require you to integrate concepts covered in the chapter to draw your own conclusions. See if you can first answer the questions without using the hints that are provided; then, if you are having difficulty, refer back to the figures or sections indicated in the hints.

1. What is the molarity of a solution with 100 g fructose dissolved in 0.7 L water? *Hint:* See Figure 2.10 for the chemical structure of fructose.
2. The pH of the fluid in the human stomach following a meal is generally around 1.5. What is the hydrogen ion concentration in such a fluid? *Hint:* See Section 2.3 and recall that pH is logarithmic.

3. Potassium has an atomic number of 19 and an atomic mass of 39 (ignore the possibility of isotopes for this question). How many neutrons and electrons are present in potassium in its nonionized (K) and ionized (K^+) forms? *Hint:* See Section 2.1 and Table 2.2 for help.

CHAPTER 2 TEST QUESTIONS *General Principles Assessment*

Answers appear in Appendix A.

These questions reinforce the key theme first introduced in Chapter 1, that general principles of physiology can be applied across all levels of organization and across all organ systems.

1. Proteins have important functions in many physiological processes. Using Figures 2.17 through 2.19 as your guide, explain how protein structure is an

example of the general principle of physiology that *physiological processes are dictated by the laws of chemistry and physics*.

CHAPTER 2 ANSWERS TO PHYSIOLOGICAL INQUIRY QUESTIONS

Figure 2.5 The presence of hydrogen bonds helps stabilize water in its liquid form such that less water escapes into the gaseous phase.

Figure 2.10 The reverse of a dehydration reaction is called hydrolysis, which is derived from Greek words for “water” and “break apart.” In hydrolysis, a molecule of water is added to a complex molecule that is broken down into two smaller molecules.

Figure 2.11 Glucose is transferred from the blood to liver cells, which can polymerize glucose into glycogen. At other times, hepatic glycogen can be broken down into many glucose molecules, which are released back into the blood and from there are transported to all cells. The breakdown of glucose within cells supplies the energy required for most cellular activities. Therefore, the storage of glucose as glycogen is an efficient means of storing energy, which can be tapped when the body’s energy

requirements increase. Many molecules of glucose can be stored as one molecule of glycogen.

Figure 2.12 The portion of the phospholipid containing the charged phosphate and nitrogen groups would face the water, and the two fatty acid tails would exclude water.

Figure 2.16 *Polypeptide* refers to a structural unit of two or more amino acids bonded together by peptide bonds and does not imply anything about function. A *protein* is a functional molecule formed by the folding of a polypeptide into a characteristic shape, or conformation.

Figure 2.23 Because adenine and thymine are bonded by two hydrogen bonds, whereas guanine and cytosine are held together by three hydrogen bonds, A–T bonds would be more easily broken by heat.

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