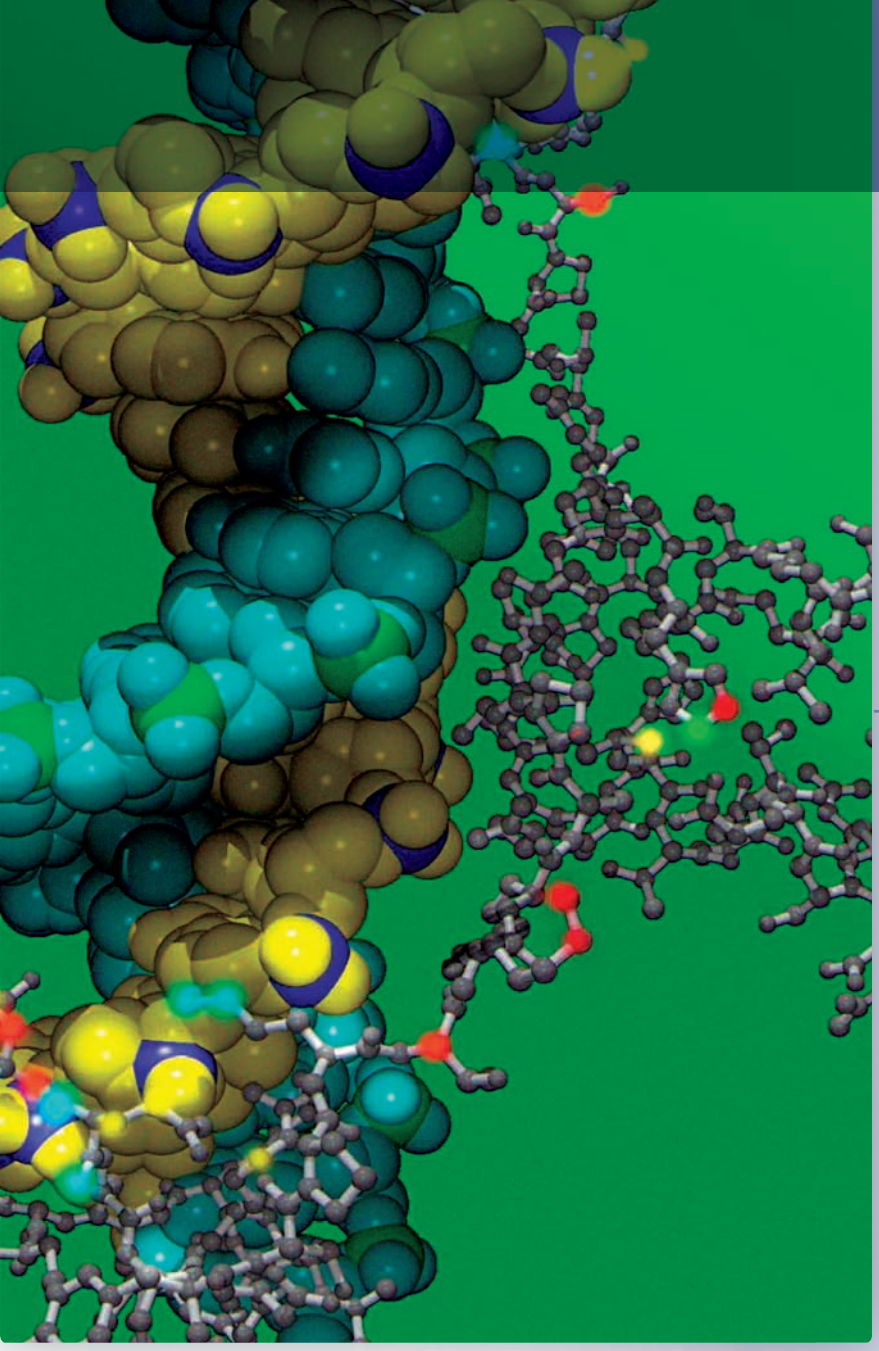


CHAPTER 3

The Chemical Building Blocks of Life

Chapter Contents

Introduction

A cup of water contains more molecules than there are stars in the sky. But many molecules are much larger than water molecules. Many thousands of distinct biological molecules are long chains made of thousands or even billions of atoms. These enormous assemblages, which are almost always synthesized by living things, are *macromolecules*. As you may know, biological macromolecules can be divided into four categories: *carbohydrates, nucleic acids, proteins,* and *lipids,* and they are the basic chemical building blocks from which all organisms are composed.

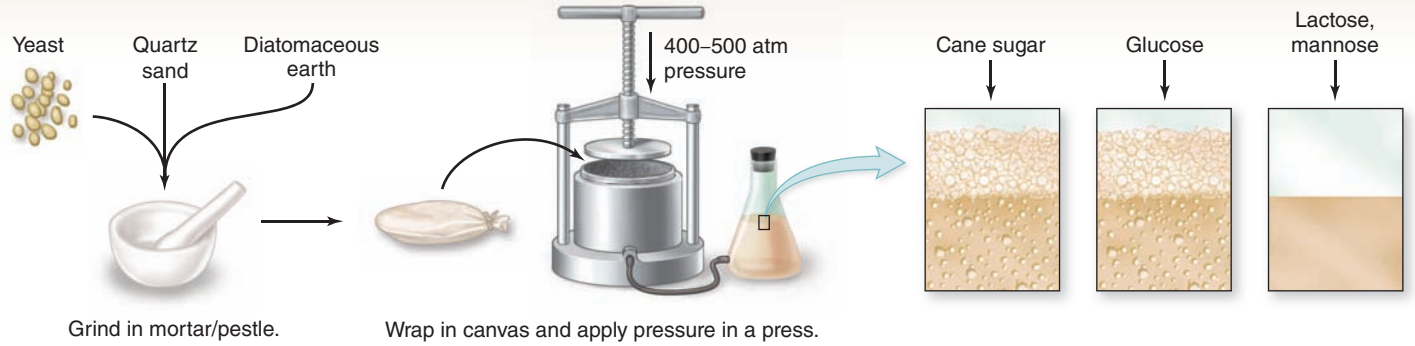
We take the existence of these classes of macromolecules for granted now, but as late as the 19th century many theories of "vital forces" were associated with living systems. One such theory held that cells contained a substance, protoplasm, that was responsible for the chemical reactions in living systems. Any disruption of cells was thought to disturb the protoplasm. Such a view makes studying the chemical reactions of cells in the lab (in vitro) impossible. The demonstration of fermentation in a cell-free system marked the beginning of modern biochemistry (figure 3.1). This approach involves studying biological molecules outside of cells to infer their role inside cells. Because these biological macromolecules all involve carbon-containing compounds, we begin with a brief summary of carbon and its chemistry.

SCIENTIFIC THINKING

Hypothesis: *Chemical reactions, such as the fermentation reaction in yeast, are controlled by enzymes and do not require living cells.*

Prediction: *If yeast cells are broken open, these enzymes should function outside of the cell.*

Test: *Yeast is mixed with quartz sand and diatomaceous earth and then ground in a mortar and pestle. The resulting paste is wrapped in canvas and subjected to 400–500 atm pressure in a press. Fermentable and nonfermentable substrates are added to the resulting fluid, with fermentation being measured by the production of CO_2.*



Result: *When a fermentable substrate (cane sugar, glucose) is used, CO_2 is produced; when a nonfermentable substrate (lactose, mannose) is used, no CO_2 is produced. In addition, visual inspection of the fluid shows no visible yeast cells.*

Conclusion: *The hypothesis is supported. The fermentation reaction can occur in the absence of live yeast.*

Historical Significance: *Although this is not precisely the intent of the original experiment, it represents the first use of a cell-free system. Such systems allow for the study of biochemical reactions in vitro and the purification of proteins involved. We now know that the "fermentation reaction" is actually a complex series of reactions. Would such a series of reactions be your first choice for this kind of demonstration?*

Figure 3.1 The demonstration of cell-free fermentation. The German chemist Eduard Buchner's (1860–1917) demonstration of fermentation by fluid produced from yeast, but not containing any live cells, both argued against the protoplasm theory and provided a method for future biochemists to examine the chemistry of life outside of cells.

3.1 Carbon: The Framework of Biological Molecules

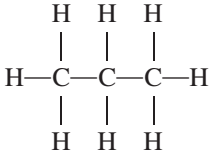
Learning Outcomes

1. *Describe the relationship between functional groups and macromolecules.*
2. *Recognize the different kinds of isomers.*
3. *List the different kinds of biological macromolecules.*

In chapter 2, we reviewed the basics of atomic structure and chemical bonding. Biological systems obey all the laws of chemistry. Thus, chemistry forms the basis of living systems.

The framework of biological molecules consists predominantly of carbon atoms bonded to other carbon atoms or to atoms of oxygen, nitrogen, sulfur, phosphorus, or hydrogen. Because carbon atoms can form up to four covalent bonds, molecules containing carbon can form straight chains, branches, or even rings, balls, tubes, and coils.

Molecules consisting only of carbon and hydrogen are called *hydrocarbons*. Because carbon–hydrogen covalent bonds store considerable energy, hydrocarbons make good fuels. Gasoline, for example, is rich in hydrocarbons, and propane gas, another hydrocarbon, consists of a chain of three carbon atoms, with eight hydrogen atoms bound to it. The chemical formula for propane is C_3H_8. Its structural formula is



Propane structural formula

Theoretically speaking, the length of a chain of carbon atoms is unlimited. As described in the rest of this chapter, the four main types of biological molecules often consist of huge chains of carbon-containing compounds.

Functional groups account for differences in molecular properties

Carbon and hydrogen atoms both have very similar electronegativities. Electrons in C—C and C—H bonds are therefore evenly distributed, with no significant differences in charge over the molecular surface. For this reason, hydrocarbons are nonpolar. Most biological molecules produced by cells, however, also contain other atoms. Because these other atoms frequently have different electronegativities (see table 2.2), molecules containing them exhibit regions of partial positive or negative charge. They are polar.

These molecules can be thought of as a C—H core to which specific molecular groups, called **functional groups,** are attached. One such common functional group is —OH, called a *hydroxyl group.*

Functional groups have definite chemical properties that they retain no matter where they occur. Both the hydroxyl and carbonyl (C═O) groups, for example, are polar because of the electronegativity of the oxygen atoms (see chapter 2). Other common functional groups are the acidic carboxyl (COOH), phosphate (PO_4^-), and the basic amino (NH_2) group. Many of these functional groups can also participate in hydrogen bonding. Hydrogen bond donors and acceptors can be predicted based on their electronegativities shown in table 2.2. Figure 3.2 illustrates these biologically important functional groups and lists the macromolecules in which they are found.

Functional Group	Structural Formula	Example	Found In
Hydroxyl	—OH	Ethanol	carbohydrates, proteins, nucleic acids, lipids
Carbonyl	—C(=O)—	Acetaldehyde	carbohydrates, nucleic acids
Carboxyl	—C(=O)OH	Acetic acid	proteins, lipids
Amino	—N(H)H	Alanine	proteins, nucleic acids
Sulfhydryl	—S—H	Cysteine	proteins
Phosphate	—O—P(=O)(O⁻)—O⁻	Glycerol phosphate	nucleic acids
Methyl	—C(H)(H)H	Alanine	proteins

Figure 3.2 The primary functional chemical groups. These groups tend to act as units during chemical reactions and give specific chemical properties to the molecules that possess them. Amino groups, for example, make a molecule more basic, and carboxyl groups make a molecule more acidic. These functional groups are also not limited to the examples in the "Found In" column but are widely distributed in biological molecules.

Isomers have the same molecular formulas but different structures

Organic molecules having the same molecular or empirical formula can exist in different forms called **isomers.** If there are differences in the actual structure of their carbon skeleton, we call them *structural isomers.* In section 3.2, you will see that glucose and fructose are structural isomers of $C_6H_{12}O_6$. Another form of isomers, called *stereoisomers,* have the same carbon skeleton but differ in how the groups attached to this skeleton are arranged in space.

Enzymes in biological systems usually recognize only a single, specific stereoisomer. A subcategory of stereoisomers, called *enantiomers,* are actually mirror images of each other. A molecule that has mirror-image versions is called a *chiral* molecule. When carbon is bound to four different molecules, this inherent asymmetry exists (figure 3.3).

Chiral compounds are characterized by their effect on polarized light. Polarized light has a single plane, and chiral molecules rotate this plane either to the right (Latin, *dextro*) or left (Latin, *levo*). We therefore call the two chiral forms *D* for *dextrorotatory* and *L* for *levorotatory.* Living systems tend to produce only a single enantiomer of the two possible forms; for example, in most organisms we find primarily D-sugars and L-amino acids.

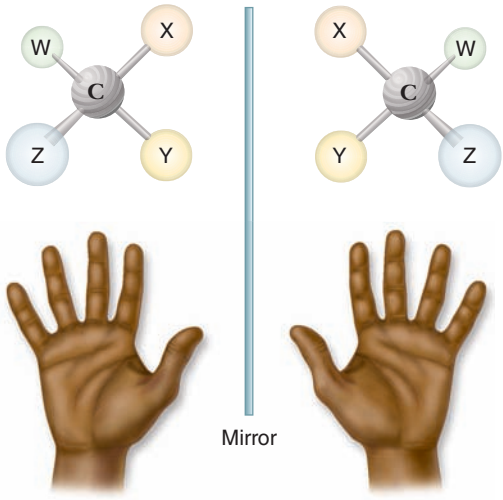


Figure 3.3 Chiral molecules. When carbon is bound to four different groups, the resulting molecule is said to be chiral (from Greek *cheir,* meaning "hand"). A chiral molecule will have stereoisomers that are mirror images. The two molecules shown have the same four groups but cannot be superimposed, much like your two hands cannot be superimposed but must be flipped to match. These types of stereoisomers are called *enantiomers.*

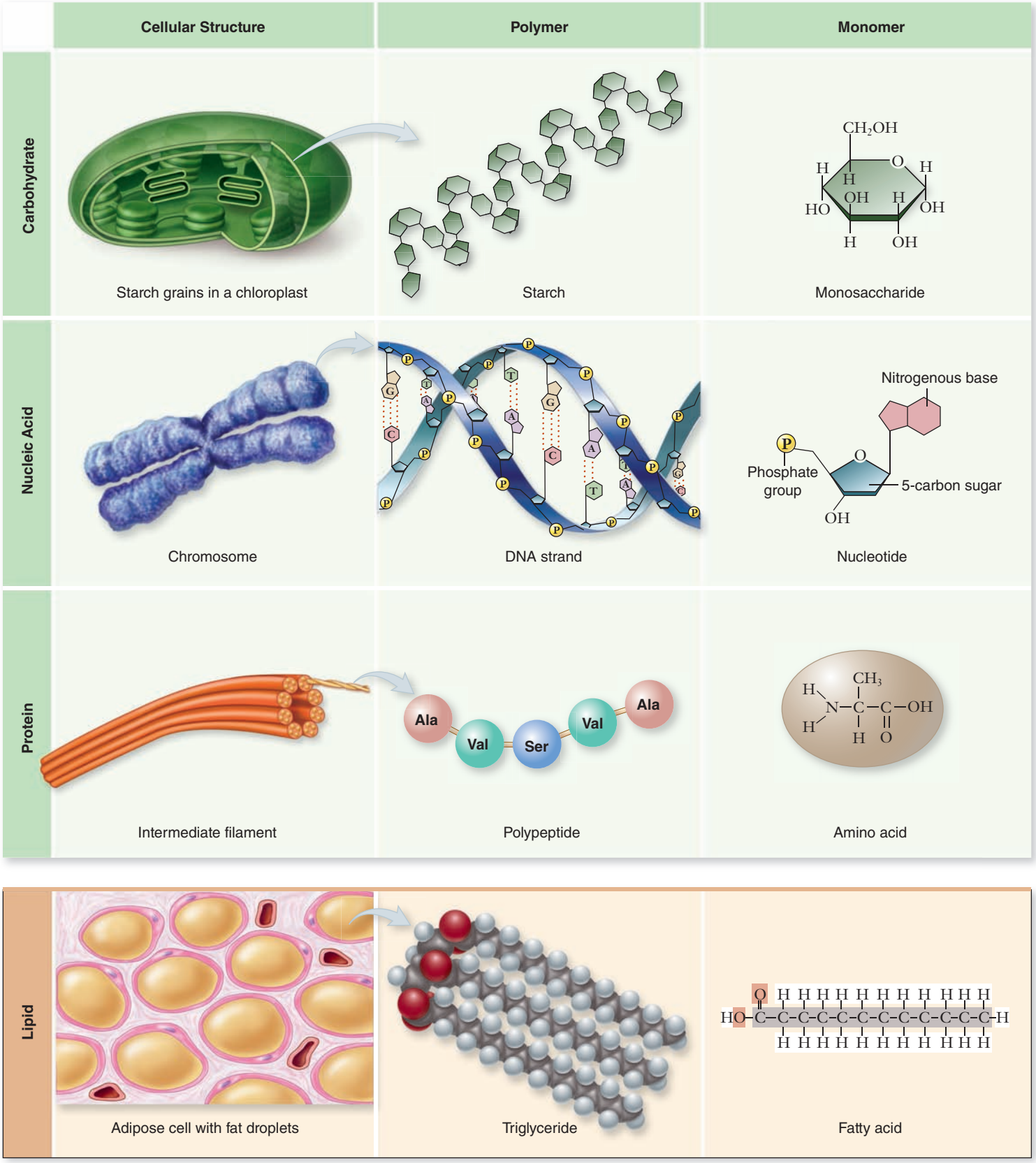


Figure 3.4 Polymer macromolecules. The four major biological macromolecules are shown. Carbohydrates, nucleic acids, and proteins all form polymers and are shown with the monomers used to make them. Lipids do not fit this simple monomer–polymer relationship. The triglyceride shown is constructed from glycerol and fatty acids. All four types of macromolecules are also shown in their cellular context.

TABLE 3.1 Macromolecules

Macromolecule	Subunit	Function	Example
CARBOHYDRATES			
Starch, glycogen	Glucose	Energy storage	Potatoes
Cellulose	Glucose	Structural support in plant cell walls	Paper; strings of celery
Chitin	Modified glucose	Structural support	Crab shells
NUCLEIC ACIDS			
DNA	Nucleotides	Encodes genes	Chromosomes
RNA	Nucleotides	Needed for gene expression	Messenger RNA
PROTEINS			
Functional	Amino acids	Catalysis; transport	Hemoglobin
Structural	Amino acids	Support	Hair; silk
LIPIDS			
Triglycerides (animal fat, oils)	Glycerol and three fatty acids	Energy storage	Butter; corn oil; soap
Phospholipids	Glycerol, two fatty acids, phosphate, and polar R groups	Cell membranes	Phosphatidylcholine
Prostaglandins	Five-carbon rings with two nonpolar tails	Chemical messengers	Prostaglandin E (PGE)
Steroids	Four fused carbon rings	Membranes; hormones	Cholesterol; estrogen
Terpenes	Long carbon chains	Pigments; structural support	Carotene; rubber

Biological macromolecules include carbohydrates, nucleic acids, proteins, and lipids

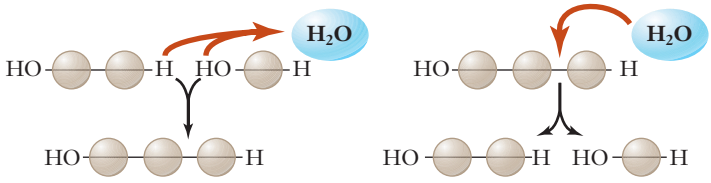
Remember that biological macromolecules are traditionally grouped into carbohydrates, nucleic acids, proteins, and lipids (table 3.1). In many cases, these macromolecules are polymers. A **polymer** is a long molecule built by linking together a large number of small, similar chemical subunits called **monomers.** They are like railroad cars coupled to form a train. The nature of a polymer is determined by the monomers used to build the polymer. Here are some examples. Complex carbohydrates such as starch are polymers composed of simple ring-shaped sugars. Nucleic acids (DNA and RNA) are polymers of nucleotides, and proteins are polymers of amino acids (figure 3.4). These long chains are built via chemical reactions termed *dehydration reactions* and are broken down by *hydrolysis reactions.* Lipids are macromolecules, but they really don't follow the monomer–polymer relationship. However, lipids are formed through dehydration reactions, which link the fatty acids to glycerol.

The dehydration reaction

Despite the differences between monomers of these major polymers, the basic chemistry of their synthesis is similar: To form a covalent bond between two monomers, an —OH group is removed from one monomer, and a hydrogen atom (H) is removed from the other (figure 3.5*a*). This reaction is the same for joining nucleotides when synthesizing DNA or joining glucose units together to make starch. This reaction is also used to link fatty acids to glycerol in lipids. This chemical reaction is called condensation, or a **dehydration reaction,** because the removal of —OH and —H is the same as the removal of a molecule of water (H_2O). For every subunit added to a macromolecule, one water molecule is removed. These and other biochemical reactions require that the reacting substances are held close together and that the correct chemical bonds are stressed and broken. This process of positioning and stressing, termed *catalysis,* is carried out within cells by enzymes.

The hydrolysis reaction

Cells disassemble polymers into their constituent monomers by reversing the dehydration reaction—a molecule of water is added instead of removed (figure 3.5*b*). In this reaction, called hydrolysis, a hydrogen atom is attached to one subunit and a hydroxyl group to the other, breaking the covalent bond joining the subunits. When you eat a potato, which contains starch (see section 3.2), your body breaks the starch down into glucose units by hydrolysis. The potato plant built the starch molecules originally by dehydration reactions.



a. Dehydration reaction ***b.*** Hydrolysis reaction

Figure 3.5 Making and breaking macromolecules.
a. Biological macromolecules are polymers formed by linking monomers together through dehydration reactions. This process releases a water molecule for every bond formed. ***b.*** Breaking the bond between subunits involves hydrolysis, which reverses the loss of a water molecule by dehydration.

Learning Outcomes Review 3.1

Functional groups account for differences in chemical properties in organic molecules. Isomers are compounds with the same empirical formula but different structures. This difference may affect biological function. Macromolecules are polymers consisting of long chains of similar subunits that are joined by dehydration reactions and are broken down by hydrolysis reactions.

- *What is the relationship between dehydration and hydrolysis?*

3.2 Carbohydrates: Energy Storage and Structural Molecules

Learning Outcomes

1. *Describe the structure of simple sugars with three to six carbons.*
2. *Relate the structure of polysaccharides to their functions.*

Monosaccharides are simple sugars

Carbohydrates are a loosely defined group of molecules that all contain carbon, hydrogen, and oxygen in the molar ratio 1:2:1. Their empirical formula (which lists the number of atoms in the molecule with subscripts) is $(CH_2O)_n$, where n is the number of carbon atoms. Because they contain many carbon–hydrogen (C—H) bonds, which release energy when oxidation occurs, carbohydrates are well suited for energy storage. Sugars are among the most important energy-storage molecules, and they exist in several different forms.

The simplest of the carbohydrates are the **monosaccharides** (Greek *mono,* "single," and Latin *saccharum,* "sugar"). Simple sugars contain as few as three carbon atoms, but those that play the central role in energy storage have six (figure 3.6). The empirical formula of 6-carbon sugars is:

$C_6H_{12}O_6$ or $(CH_2O)_6$

Six-carbon sugars can exist in a straight-chain form, but dissolved in water (an aqueous environment) they almost always form rings.

The most important of the 6-carbon monosaccharides for energy storage is glucose, which you first encountered in the examples of chemical reactions in chapter 2. Glucose has seven energy-storing C—H bonds (figure 3.7). Depending on the orientation of the carbonyl group (C═O) when the ring is closed, glucose can exist in two different forms: alpha (α) or beta (β).

Sugar isomers have structural differences

Glucose is not the only sugar with the formula $C_6H_{12}O_6$. Both structural isomers and stereoisomers of this simple 6-carbon skeleton exist in nature. Fructose is a structural isomer that differs in the position of the carbonyl carbon (C═O); galactose is a stereoisomer that differs in the position of —OH and —H groups relative to the ring (figure 3.8). These differences often account for substantial functional differences between the isomers. Your taste buds can discern them: Fructose tastes much sweeter than glucose, despite the fact that both sugars have identical chemical composition. Enzymes that act on different sugars can distinguish both the structural and stereoisomers of this basic 6-carbon skeleton. The different stereoisomers of glucose are also important in the polymers that can be made using glucose as a monomer, as you will see later in this section.

Disaccharides serve as transport molecules in plants and provide nutrition in animals

Most organisms transport sugars within their bodies. In humans, the glucose that circulates in the blood does so as a simple monosaccharide. In plants and many other organisms, however, glucose is converted into a transport form before it is moved from place to place within the organism. In such a form, it is less readily metabolized during transport.

Transport forms of sugars are commonly made by linking two monosaccharides together to form a **disaccharide** (Greek *di,* "two"). Disaccharides serve as effective reservoirs of glucose because the enzymes that normally use glucose in the organism cannot break the bond linking the two monosaccharide subunits. Enzymes that can do so are typically present only in the tissue that uses glucose.

Transport forms differ depending on which monosaccharides are linked to form the disaccharide. Glucose forms transport disaccharides with itself and with many other monosaccharides,

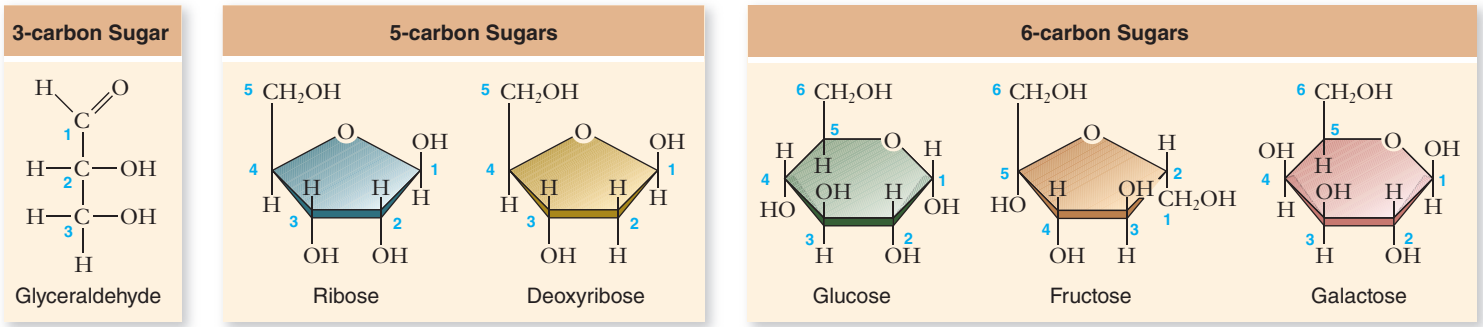


Figure 3.6 Monosaccharides. Monosaccharides, or simple sugars, can contain as few as three carbon atoms and are often used as building blocks to form larger molecules. The 5-carbon sugars ribose and deoxyribose are components of nucleic acids (see figure 3.15). The carbons are conventionally numbered (in *blue*) from the more oxidized end.

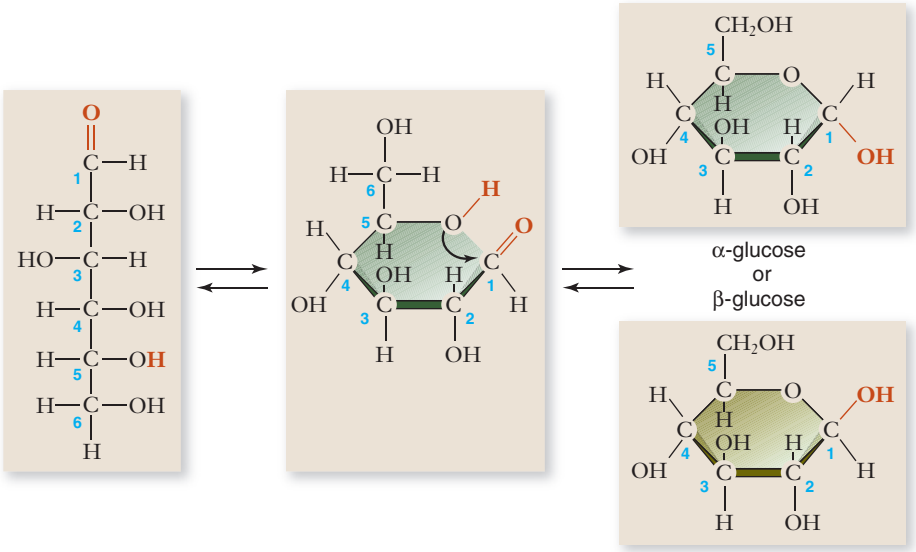


Figure 3.7 Structure of the glucose molecule. Glucose is a linear, 6-carbon molecule that forms a six-membered ring in solution. Ring closure occurs such that two forms can result: α-glucose and β-glucose. These structures differ only in the position of the —OH bound to carbon 1. The structure of the ring can be represented in many ways; shown here are the most common, with the carbons conventionally numbered so that the forms can be compared easily. The heavy lines in the ring structures represent portions of the molecule that are projecting out of the page toward you.

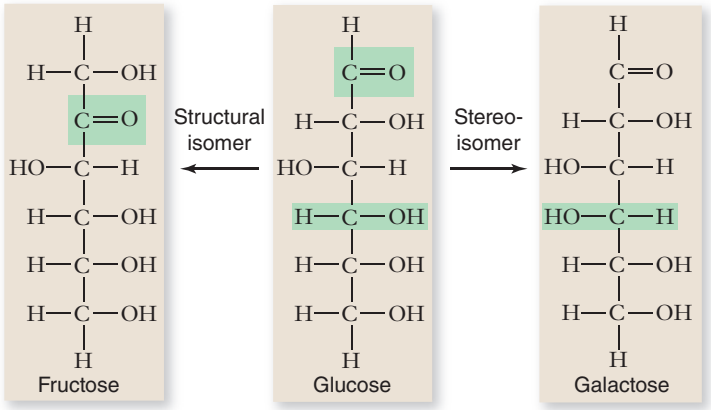


Figure 3.8 Isomers and stereoisomers. Glucose, fructose, and galactose are isomers with the empirical formula $C_6H_{12}O_6$. A structural isomer of glucose, such as fructose, has identical chemical groups bonded to different carbon atoms. Notice that this results in a five-membered ring in solution (see figure 3.6). A stereoisomer of glucose, such as galactose, has identical chemical groups bonded to the same carbon atoms but in different orientations (the —OH at carbon 4).

including fructose and galactose. When glucose forms a disaccharide with the structural isomer fructose, the resulting disaccharide is *sucrose,* or table sugar (figure 3.9*a*). Sucrose is the form most plants use to transport glucose and is the sugar that most humans and other animals eat. Sugarcane and sugar beets are rich in sucrose.

When glucose is linked to the stereoisomer galactose, the resulting disaccharide is *lactose,* or milk sugar. Many mammals supply energy to their young in the form of lactose. Adults often have greatly reduced levels of lactase, the enzyme required to cleave lactose into its two monosaccharide components, and thus they cannot metabolize lactose efficiently. This can result in lactose intolerance in humans. Most of the energy that is channeled into lactose production is therefore reserved for offspring. For this reason, lactose as an energy source is primarily for offspring in mammals.

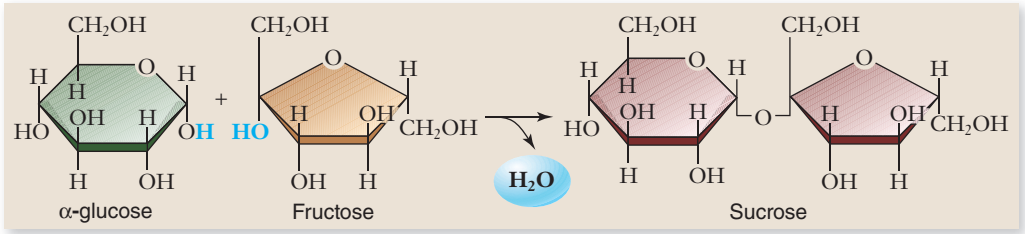
Polysaccharides provide energy storage and structural components

Polysaccharides are longer polymers made up of monosaccharides that have been joined through dehydration reactions. **Starch,** a storage polysaccharide, consists entirely of α-glucose molecules linked in long chains. **Cellulose,** a structural polysaccharide, also consists of glucose molecules linked in chains, but these molecules are β-glucose. Because starch is built from α-glucose we call the linkages α linkages; cellulose has β linkages.

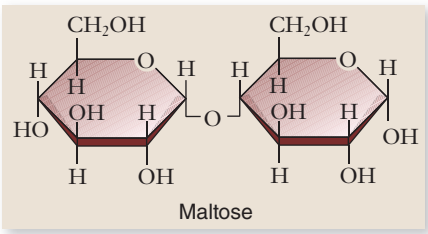
Starches and glycogen

Organisms store the metabolic energy contained in monosaccharides by converting them into disaccharides, such as *maltose* (figure 3.9*b*). These are then linked together into the insoluble polysaccharides called *starches.* These polysaccharides differ mainly in how the polymers branch.

The starch with the simplest structure is *amylose.* It is composed of many hundreds of α-glucose molecules linked together in long, unbranched chains. Each linkage occurs between the carbon 1 (C-1) of one glucose molecule and the C-4 of another, making them α-(1⟶4) linkages (figure 3.10*a*). The long chains of amylose tend to coil up in water, a property that renders amylose insoluble. Potato starch is about 20% amylose (figure 3.10*b*).



a.



b.

Figure 3.9 How disaccharides form. Some disaccharides are used to transport glucose from one part of an organism's body to another; one example is sucrose ***(a)***, which is found in sugarcane. Other disaccharides, such as maltose ***(b)***, are used in grain for storage.

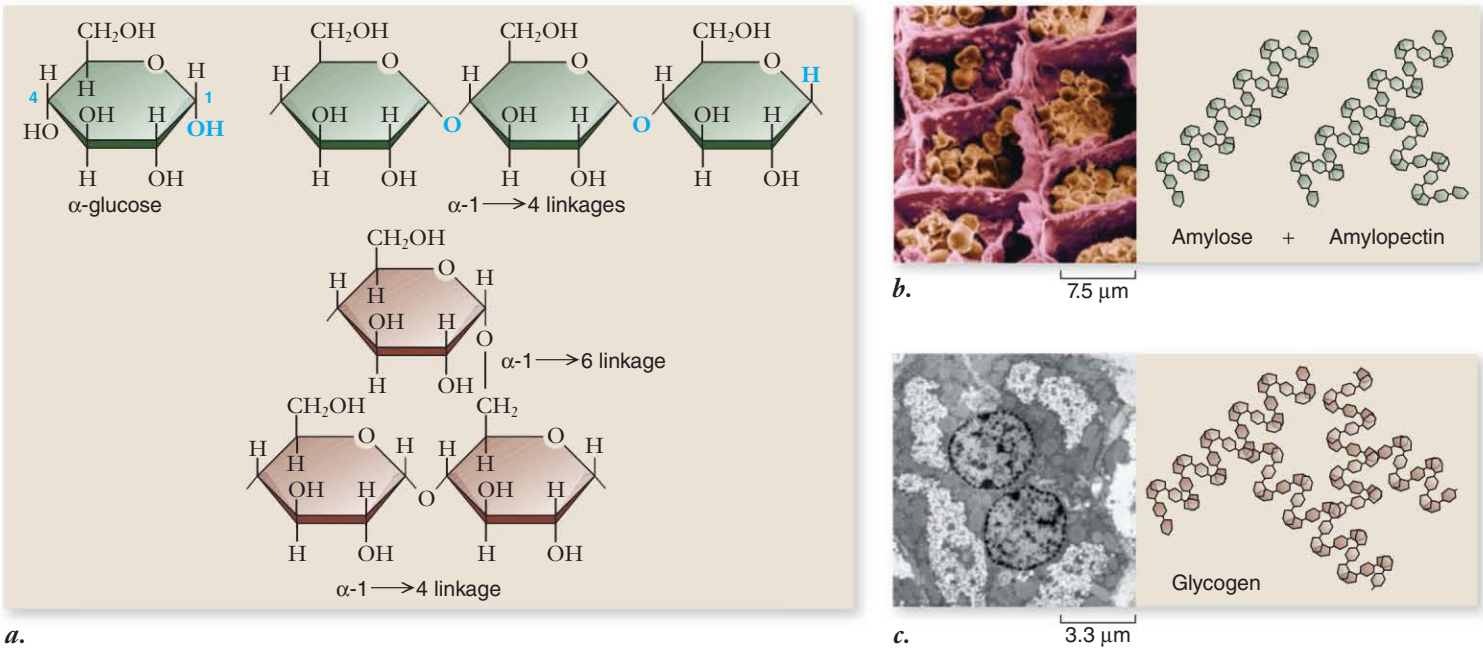


Figure 3.10 Polymers of glucose: Starch and glycogen. ***a.*** Starch chains consist of polymers of α-glucose subunits joined by α-(1⟶4) glycosidic linkages. These chains can be branched by forming similar α-(1⟶6) glycosidic bonds. These storage polymers then differ primarily in their degree of branching. ***b.*** Starch is found in plants and is composed of amylose and amylopectin, which are unbranched and branched, respectively. The branched form is insoluble and forms starch granules in plant cells. ***c.*** Glycogen is found in animal cells and is highly branched and also insoluble, forming glycogen granules.

Most plant starch, including the remaining 80% of potato starch, is a somewhat more complicated variant of amylose called *amylopectin.* Pectins are branched polysaccharides with the branches occurring due to bonds between the C-1 of one molecule and the C-6 of another [α-(1⟶6) linkages]. These short amylose branches consist of 20 to 30 glucose subunits (figure 3.10*b*).

The comparable molecule to starch in animals is **glycogen.** Like amylopectin, glycogen is an insoluble polysaccharide containing branched amylose chains. Glycogen has a much longer average chain length and more branches than plant starch (figure 3.10*c*).

Cellulose

Although some chains of sugars store energy, others serve as structural material for cells. For two glucose molecules to link together, the glucose subunits must be of the same form. *Cellulose* is a polymer of β-glucose (figure 3.11). The bonds between adjacent

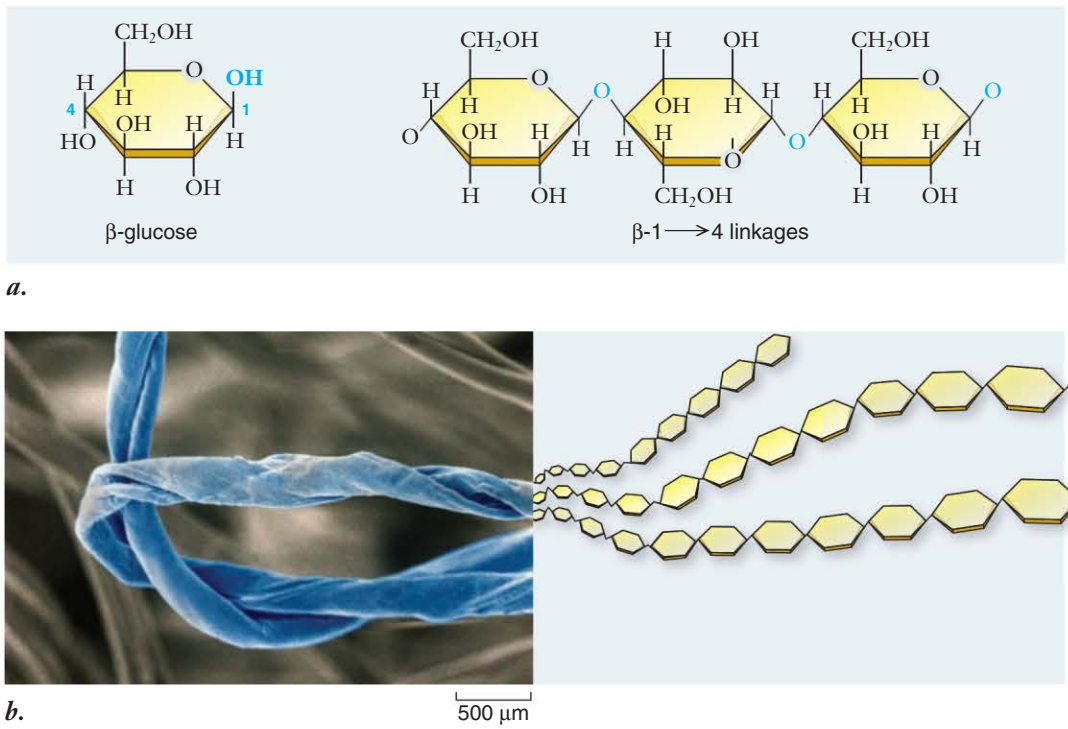


Figure 3.11 Polymers of glucose: Cellulose. Starch chains consist of α-glucose subunits, and cellulose chains consist of β-glucose subunits. ***a.*** Thus the bonds between adjacent glucose molecules in cellulose are β-(1⟶4) glycosidic linkages. ***b.*** Cellulose is unbranched and forms long fibers. Cellulose fibers can be very strong and are quite resistant to metabolic breakdown, which is one reason wood is such a good building material.

glucose molecules still exist between the C-1 of the first glucose and the C-4 of the next glucose, but these are β-(1⟶4) linkages.

The properties of a chain of glucose molecules consisting of all β-glucose are very different from those of starch. These long, unbranched β-linked chains make tough fibers. Cellulose is the chief component of plant cell walls (see figure 3.11*b*). It is chemically similar to amylose, with one important difference: The starch-hydrolyzing enzymes that occur in most organisms cannot break the bond between two β-glucose units because they only recognize α linkages.

Because cellulose cannot be broken down readily by most animals, it works well as a biological structural material. But some animals, such as cows, are able to utilize cellulose aided by symbiotic bacteria and protists in their digestive tracts. These organisms provide the necessary enzymes for cleaving the β-(1⟶4) linkages, thus providing access to a rich source of energy.

Chitin

Chitin, the structural material found in arthropods and many fungi, is a polymer of *N*-acetylglucosamine, a substituted version of glucose. When cross-linked by proteins, it forms a tough, resistant surface material that serves as the hard exoskeleton of insects and crustaceans (figure 3.12; see chapter 34). Few organisms are able to digest chitin, but most possess a chitinase enzyme, probably to protect against fungi.

Learning Outcomes Review 3.2

Monosaccharides have three to six or more carbon atoms typically arranged in a ring form. Disaccharides consist of two linked monosaccharides; polysaccharides are long chains of monosaccharides. Structural differences between sugar isomers can lead to functional differences. Starches are branched polymers of α-glucose used for energy storage. Cellulose in plants consists of unbranched chains of β-glucose that are not easily digested.

- *How do the structures of starch, glycogen, and cellulose affect their function?*

Figure 3.12 Chitin. Chitin is the principal structural element in the external skeletons of many invertebrates, such as this lobster.

3.3 Nucleic Acids: Information Molecules

Learning Outcomes

1. *Describe the structure of nucleotides.*
2. *Contrast the structures of DNA and RNA.*
3. *Discuss the functions of DNA and RNA.*
4. *Recognize other nucleotides involved in energy metabolism.*

The biochemical activity of a cell depends on production of a large number of proteins, each with a specific sequence. The information necessary to produce the correct proteins is passed through generations of organisms, even though the proteins themselves are not inherited.

Nucleic acids carry information inside cells, just as disks contain the information in a computer or road maps display information needed by travelers. Two main varieties of nucleic acids are **deoxyribonucleic acid** (**DNA;** figure 3.13) and **ribonucleic acid (RNA).**

Genetic information is stored in DNA, and short-lived copies of this are made in the form of RNA, which is then used to direct the synthesis of proteins during the process of gene expression (as discussed in detail in chapter 15). Unique among macromolecules, nucleic acids are able to serve as templates for producing precise copies of themselves. This characteristic allows genetic information to be preserved during cell division and during the reproduction of organisms.

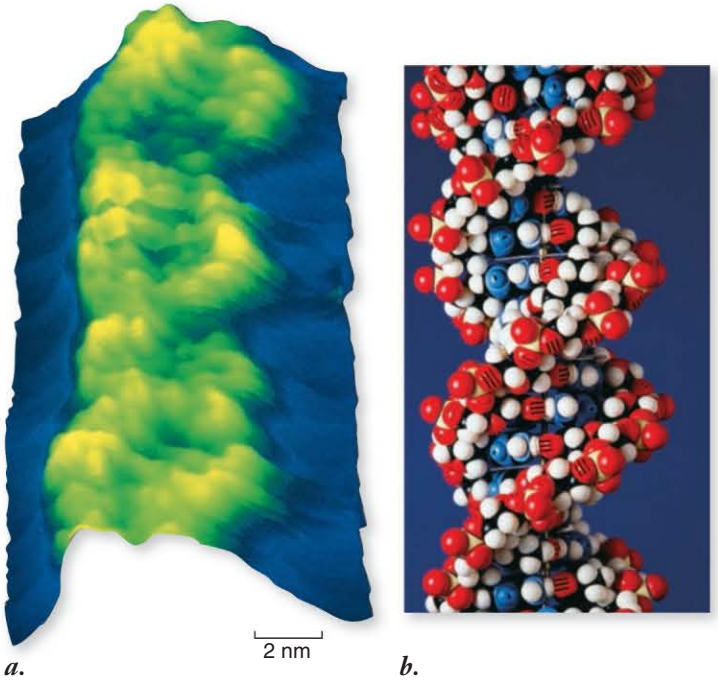


Figure 3.13 Images of DNA. ***a.*** A scanning-tunneling micrograph of DNA (false color; 2,000,000×) showing approximately three turns of the DNA double helix. ***b.*** A space-filling model for comparison to the image of actual DNA in ***(a)***.

The role of RNA in cells is much more complicated: RNA carries information, is part of the organelle responsible for protein synthesis, and recent work indicates it is also involved in the control of gene expression. As a carrier of information, the form of RNA called **messenger RNA (mRNA)** consists of transcribed single-stranded copies of portions of the DNA. These transcripts serve as blueprints specifying the amino acid sequences of proteins. This process will be described in detail in chapter 15.

Nucleic acids are nucleotide polymers

Nucleic acids are long polymers of repeating subunits called **nucleotides.** Each nucleotide consists of three components: a pentose, or 5-carbon sugar (ribose in RNA and deoxyribose in DNA); a phosphate ($—PO_4^-$) group; and an organic nitrogenous (nitrogen-containing) base (figure 3.14). Nucleotides can form polymers by joining the phosphate of one nucleotide to a hydroxyl group on the sugar of another nucleotide by a dehydration reaction. This forms a *phosphodiester bond* linking the two sugars through a phosphate. A **nucleic acid,** then, is simply a chain of 5-carbon sugars linked together by phosphodiester bonds with a nitrogenous base protruding from each sugar (see figure 3.15*a*). These chains of nucleotides, *polynucleotides,* have polarity, or different ends: a phosphate on one end and an —OH from a sugar on the other end. We conventionally refer to these ends as 5′ ("five-prime," $—PO_4^-$) and 3′ ("three-prime," —OH) taken from the carbon numbering of the sugar (figure 3.15*a*).

Nucleotides have five types of nitrogenous bases (figure 3.15*b*). Two of these are large, double-ring molecules called *purines* that are each found in both DNA and RNA; the two purines are adenine (A) and guanine (G). The other three bases are single-ring molecules

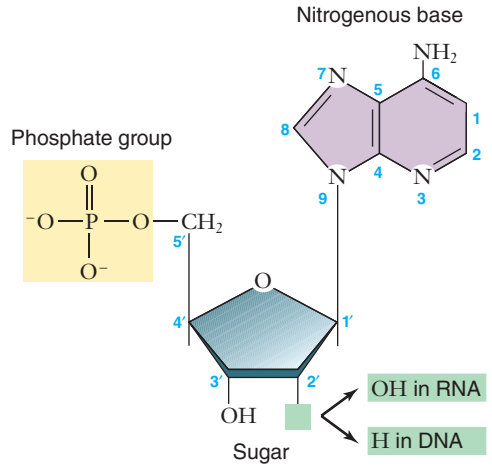
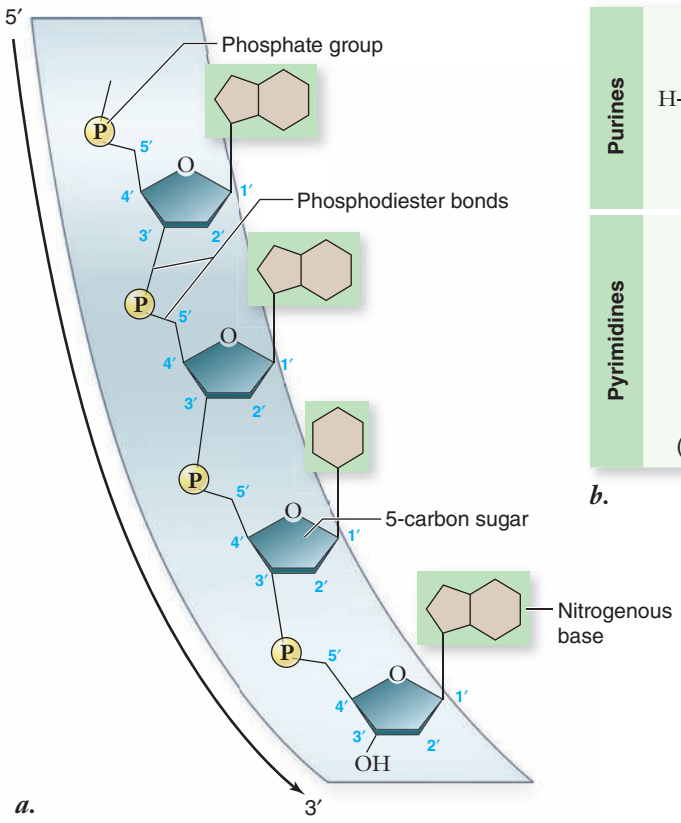


Figure 3.14 Structure of a nucleotide. The nucleotide subunits of DNA and RNA are made up of three elements: a 5-carbon sugar (ribose or deoxyribose), an organic nitrogenous base (adenine is shown here), and a phosphate group. Notice that all the numbers on the sugar are given as "primes" (1′, 2′, etc.) to distinguish them from the numbering on the rings of the bases.

called *pyrimidines* that include cytosine (C, in both DNA and RNA), thymine (T, in DNA only), and uracil (U, in RNA only).

DNA stores genetic information

Organisms use sequences of nucleotides in DNA to encode the information specifying the amino acid sequences of their proteins. This method of encoding information is very similar to the way in which sequences of letters encode information in a sentence.



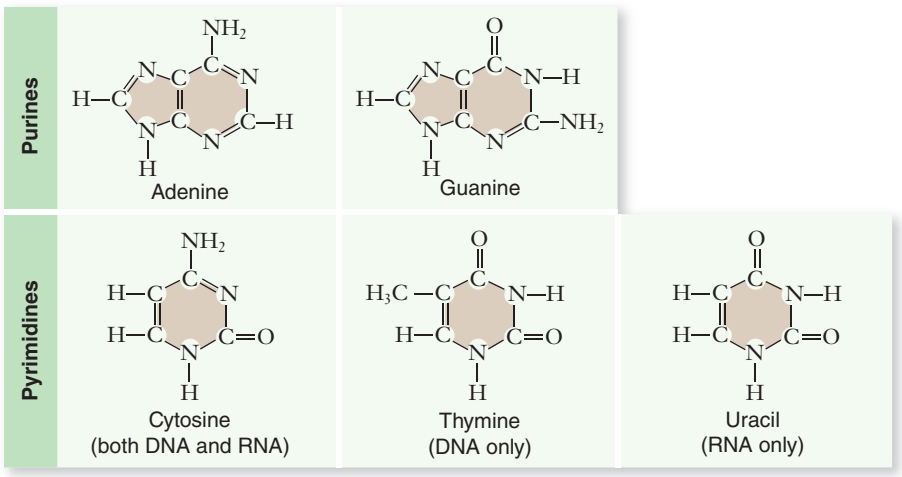


Figure 3.15 The structure of a nucleic acid and the organic nitrogenous bases. ***a.*** In a nucleic acid, nucleotides are linked to one another via phosphodiester bonds formed between the phosphate of one nucleotide and the sugar of the next nucleotide. We call this the sugar-phosphate backbone, with the organic bases protrude from this chain. The backbone also has different ends: a 5′ phosphate end and a 3′ hydroxyl end (the blue numbers come from the numbers in the sugars). ***b.*** The organic nitrogenous bases can be either purines or pyrimidines. The base thymine is found in DNA. The base uracil is found in RNA.

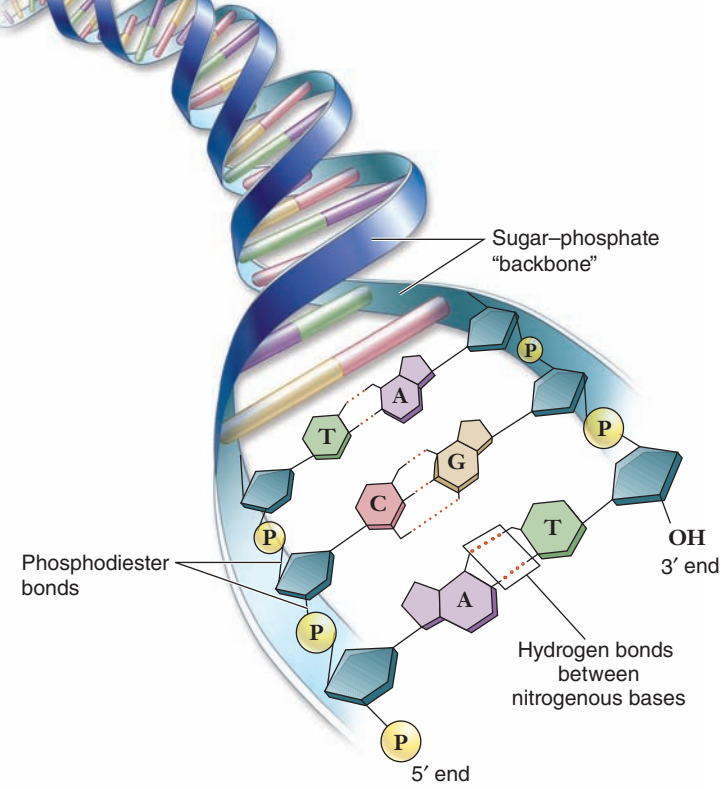


Figure 3.16 The structure of DNA. DNA consists of two polynucleotide chains running in opposite directions wrapped about a single helical axis. Hydrogen bond formation (dashed lines) between the nitrogenous bases, called base-pairing, causes the two chains of DNA to bind to each other and form a double helix.

A sentence written in English consists of a combination of the 26 different letters of the alphabet in a certain order; the code of a DNA molecule consists of different combinations of the four types of nucleotides in specific sequences, such as CGCTTACG.

DNA molecules in organisms exist as two chains wrapped about each other in a long linear molecule in eukaryotes, and a circular molecule in most prokaryotes. The two strands of a DNA polymer wind around each other like the outside and inside rails of a spiral staircase. Such a spiral shape is called a helix, and a helix composed of two chains is called a **double helix.** Each step of DNA's helical staircase is composed of a base-pair. The pair consists of a base in one chain attracted by hydrogen bonds to a base opposite it on the other chain (figure 3.16).

The base-pairing rules arise from the most stable hydrogen bonding configurations between the bases: Adenine pairs with thymine (in DNA) or with uracil (in RNA), and cytosine pairs with guanine. The bases that participate in base-pairing are said to be **complementary** to each other. Additional details of the structure of DNA and how it interacts with RNA in the production of proteins are presented in chapters 14 and 15.

In eukaryotic organisms, the DNA is further complexed with protein to form structures we call chromosomes. This actually forms a higher order structure that affects the function of DNA as it is involved in the control of gene expression (see chapter 16).

RNA has many roles in a cell

RNA is similar to DNA, but with two major chemical differences. First, RNA molecules contain ribose sugars, in which the C-2 is bonded to a hydroxyl group. (In DNA, a hydrogen atom replaces this hydroxyl group.) Second, RNA molecules use uracil in place of thymine. Uracil has a similar structure to thymine, except that one of its carbons lacks a methyl (—CH_3) group.

RNA is produced by transcription (copying) from DNA, and is usually single-stranded (figure 3.17). The role of RNA in cells is quite varied: it carries information in the form of **mRNA,** it is part of the ribosome, in the form of **ribosomal RNA (rRNA),** and it carries amino acids in the form of **transfer RNA (tRNA).** There has been a revolution of late in how we view RNA since it has been found to function as an enzyme, and other forms of RNA are involved in regulating gene expression (explored in more detail in chapter 16).

Other nucleotides are vital components of energy reactions

In addition to serving as subunits of DNA and RNA, nucleotide bases play other critical roles in the life of a cell. For example, adenine is a key component of the molecule **adenosine triphosphate**

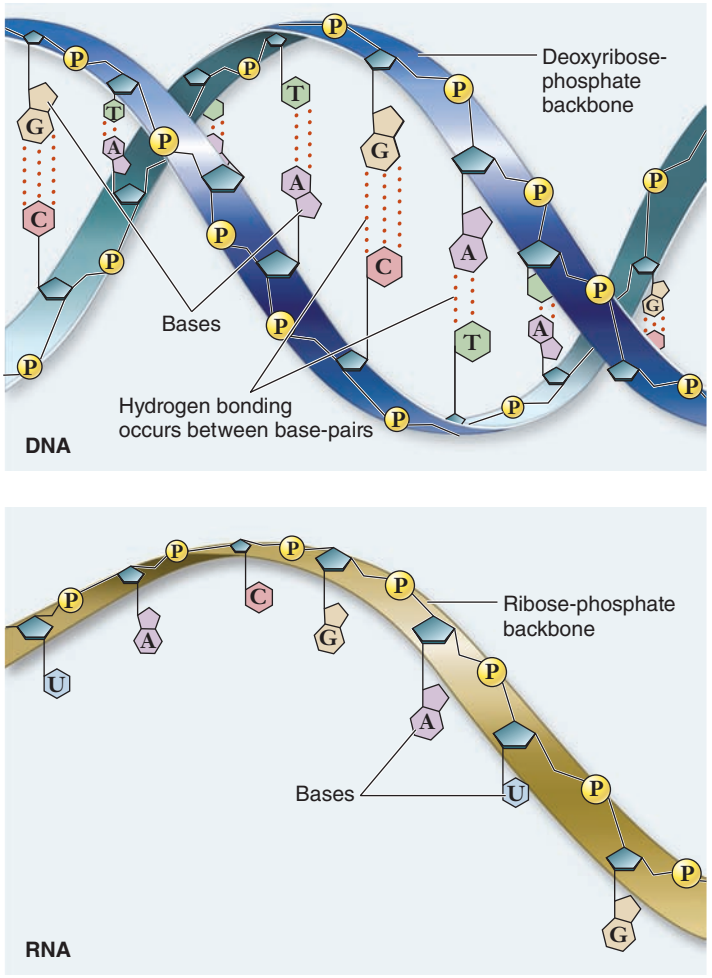


Figure 3.17 DNA versus RNA. DNA forms a double helix, uses deoxyribose as the sugar in its sugar–phosphate backbone, and uses thymine among its nitrogenous bases. RNA is usually single-stranded, uses ribose as the sugar in its sugar–phosphate backbone, and uses uracil in place of thymine.

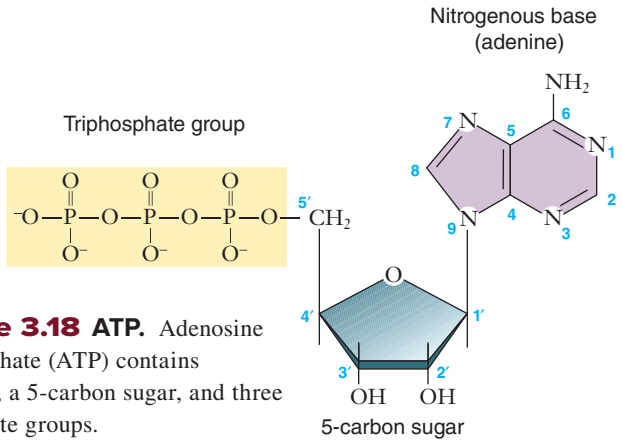


Figure 3.18 ATP. Adenosine triphosphate (ATP) contains adenine, a 5-carbon sugar, and three phosphate groups.

(**ATP;** figure 3.18)—the energy currency of the cell. Cells use ATP as energy in a variety of transactions, the way we use money in society. ATP is used to drive energetically unfavorable chemical reactions, to power transport across membranes, and to power the movement of cells.

Two other important nucleotide-containing molecules are **nicotinamide adenine dinucleotide (NAD^+)** and **flavin adenine dinucleotide (FAD).** These molecules function as electron carriers in a variety of cellular processes. You will see the action of these molecules in detail when we discuss photosynthesis and respiration (see chapters 7 and 8).

Learning Outcomes Review 3.3

A nucleic acid is a polymer composed of alternating phosphate and 5-carbon sugar groups with a nitrogenous base protruding from each sugar. In DNA, this sugar is deoxyribose. In RNA, the sugar is ribose. RNA also contains the base uracil instead of thymine. DNA is a double-stranded helix that stores hereditary information as a specific sequence of nucleotide bases. RNA has multiple roles in a cell, including carrying information from DNA and forming part of the ribosome.

- ***If an RNA molecule is copied from a DNA strand, what is the relationship between the sequence of bases in RNA and each DNA strand?***

3.4 Proteins: Molecules with Diverse Structures and Functions

Learning Outcomes

1. *Describe the possible levels of protein structure.*
2. *Explain how motifs and domains contribute to protein structure.*
3. *Understand the relationship between amino acid sequence and their three-dimensional structure.*

Proteins are the most diverse group of biological macromolecules, both chemically and functionally. Because proteins have so many different functions in cells we could not begin to list them all. We can, however, group these functions into the following seven categories. This list is a summary only, however; the function of proteins is relevant to most topics in biology:

1. **Enzyme catalysis.** Enzymes are biological catalysts that facilitate specific chemical reactions. Because of this property, the appearance of enzymes was one of the most important events in the evolution of life. Enzymes are three-dimensional globular proteins that fit snugly around the molecules they act on. This fit facilitates chemical reactions by stressing particular chemical bonds.
2. **Defense.** Other globular proteins use their shapes to "recognize" foreign microbes and cancer cells. These cell-surface receptors form the core of the body's endocrine and immune systems.
3. **Transport.** A variety of globular proteins transport small molecules and ions. The transport protein hemoglobin, for example, transports oxygen in the blood. Membrane transport proteins help move ions and molecules across the membrane.
4. **Support.** Protein fibers play structural roles. These fibers include keratin in hair, fibrin in blood clots, and collagen. The last one, collagen, forms the matrix of skin, ligaments, tendons, and bones and is the most abundant protein in a vertebrate body.
5. **Motion.** Muscles contract through the sliding motion of two kinds of protein filaments: actin and myosin. Contractile proteins also play key roles in the cell's cytoskeleton and in moving materials within cells.
6. **Regulation.** Small proteins called hormones serve as intercellular messengers in animals. Proteins also play many regulatory roles within the cell—turning on and shutting off genes during development, for example. In addition, proteins receive information, acting as cell-surface receptors.
7. **Storage.** Calcium and iron are stored in the body by binding as ions to storage proteins.

Table 3.2 summarizes these functions and includes examples of the proteins that carry them out in the human body.

Proteins are polymers of amino acids

Proteins are linear polymers made with 20 different amino acids. **Amino acids,** as their name suggests, contain an amino group (—NH_2) and an acidic carboxyl group (—COOH). The specific order of amino acids determines the protein's structure and function. Many scientists believe amino acids were among the first molecules formed on the early Earth. It seems highly likely that the oceans that existed early in the history of the Earth contained a wide variety of amino acids.

Amino acid structure

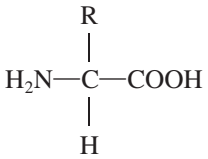
The generalized structure of an amino acid is shown as amino and carboxyl groups bonded to a central carbon atom, with an additional hydrogen and a functional side group indicated

TABLE 3.2 The Many Functions of Protein

Function	Class of Protein	Examples	Examples of Use
Enzyme catalysis	Enzymes	Glycosidases	Cleave polysaccharides
		Proteases	Break down proteins
		Polymerases	Synthesize nucleic acids
		Kinases	Phosphorylate sugars and proteins
Defense	Immunoglobulins	Antibodies	Mark foreign proteins for elimination
	Toxins	Snake venom	Blocks nerve function
	Cell-surface antigens	MHC* proteins	"Self"-recognition
Transport	Circulating transporters	Hemoglobin	Carries O_2 and CO_2 in blood
		Myoglobin	Carries O_2 and CO_2 in muscle
		Cytochromes	Electron transport
	Membrane transporters	Sodium–potassium pump	Excitable membranes
		Proton pump	Chemiosmosis
		Glucose transporter	Transports glucose into cells
Support	Fibers	Collagen	Forms cartilage
		Keratin	Forms hair, nails
		Fibrin	Forms blood clots
Motion	Muscle	Actin	Contraction of muscle fibers
		Myosin	Contraction of muscle fibers
Regulation	Osmotic proteins	Serum albumin	Maintains osmotic concentration of blood
	Gene regulators	*lac* Repressor	Regulates transcription
	Hormones	Insulin	Controls blood glucose levels
		Vasopressin	Increases water retention by kidneys
		Oxytocin	Regulates uterine contractions and milk production
Storage	Ion-binding	Ferritin	Stores iron, especially in spleen
		Casein	Stores ions in milk
		Calmodulin	Binds calcium ions

*MHC, major histocompatibility complex.

by R. These components completely fill the bonds of the central carbon:



The unique character of each amino acid is determined by the nature of the R group. Notice that unless the R group is an H atom, as in glycine, amino acids are chiral and can exist as two enantiomeric forms: D or L. In living systems, only the L-amino acids are found in proteins, and D-amino acids are rare.

The R group also determines the chemistry of amino acids. Serine, in which the R group is —CH_2OH, is a polar molecule. Alanine, which has —CH_3 as its R group, is nonpolar. The 20 common amino acids are grouped into five chemical classes, based on their R group:

1. Nonpolar amino acids, such as leucine, often have R groups that contain —CH_2 or —CH_3.
2. Polar uncharged amino acids, such as threonine, have R groups that contain oxygen (or —OH).
3. Charged amino acids, such as glutamic acid, have R groups that contain acids or bases that can ionize.
4. Aromatic amino acids, such as phenylalanine, have R groups that contain an organic (carbon) ring with alternating single and double bonds. These are also nonpolar.
5. Amino acids that have special functions have unique properties. Some examples are methionine, which is often the first amino acid in a chain of amino acids; proline, which causes kinks in chains; and cysteine, which links chains together.

Each amino acid affects the shape of a protein differently, depending on the chemical nature of its side group. For example, portions of a protein chain with numerous nonpolar amino acids tend to fold into the interior of the protein by hydrophobic exclusion.

Peptide bonds

In addition to its R group, each amino acid, when ionized, has a positive amino (NH_3^+) group at one end and a negative carboxyl (COO^-) group at the other. The amino and carboxyl groups on a pair of amino acids can undergo a dehydration reaction to form a covalent bond. The covalent bond that links two amino acids is called a **peptide bond** (figure 3.19). The two amino acids linked by such a bond are not free to rotate around the N—C linkage because the peptide bond has a partial double-bond character. This is different from the N—C and C—C bonds to the central carbon of the amino acid. This lack of rotation about the peptide bond is one factor that determines the structural character of the coils and other regular shapes formed by chains of amino acids.

A protein is composed of one or more long unbranched chains. Each chain is called a **polypeptide** and is composed of amino acids linked by peptide bonds. The terms *protein* and *polypeptide* tend to be used loosely and may be confusing. For proteins that include only a single polypeptide chain, the two terms are synonymous.

The pioneering work of Frederick Sanger in the early 1950s provided the evidence that each kind of protein has a specific amino acid sequence. Using chemical methods to remove successive amino acids and then identify them, Sanger succeeded in determining the amino acid sequence of insulin. In so doing he demonstrated clearly that this protein had a defined sequence, which was the same for all insulin molecules in the solution. Although many different amino acids occur in nature, only 20 commonly occur in proteins. Of these 20, 8 are called essential amino acids because humans cannot synthesize them and thus must get them from their diets. Figure 3.20 illustrates these 20 amino acids and their side groups.

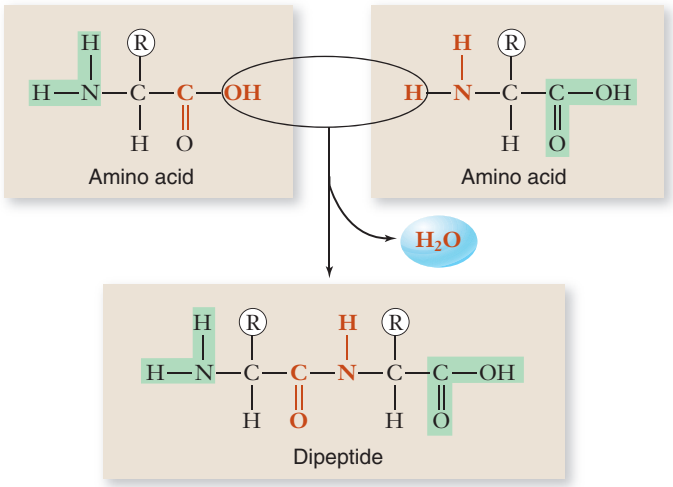


Figure 3.19 The peptide bond. A peptide bond forms when the amino end of one amino acid joins to the carboxyl end of another. Reacting amino and carboxyl groups are shown in red and nonreacting groups are highlighted in green. Notice that the resulting dipeptide still has an amino end and a carboxyl end. Because of the partial double-bond nature of peptide bonds, the resulting peptide chain cannot rotate freely around these bonds.

Proteins have levels of structure

The shape of a protein determines its function. One way to study the shape of something as small as a protein is to look at it with very short wavelength energy—in other words, with X-rays. X-rays can be passed through a crystal of protein to produce a diffraction pattern. This pattern can then be analyzed by a painstaking procedure that allows the investigator to build up a three-dimensional picture of the position of each atom. The first protein to be analyzed in this way was myoglobin, and the related protein hemoglobin was analyzed soon thereafter.

As more and more proteins were studied, a general principle became evident: In every protein studied, essentially all the internal amino acids are nonpolar ones—amino acids such as leucine, valine, and phenylalanine. Water's tendency to hydrophobically exclude nonpolar molecules literally shoves the nonpolar portions of the amino acid chain into the protein's interior (figure 3.21). This tendency forces the nonpolar amino acids into close contact with one another, leaving little empty space inside. Polar and charged amino acids are restricted to the surface of the protein, except for the few that play key functional roles.

The structure of proteins is usually discussed in terms of a hierarchy of four levels: *primary, secondary, tertiary,* and *quaternary* (figure 3.22). We will examine this view and then integrate it with a more modern approach arising from our increasing knowledge of protein structure.

Primary structure: Amino acid sequence

The **primary structure** of a protein is its amino acid sequence. Because the R groups that distinguish the amino acids play no role in the peptide backbone of proteins, a protein can consist of any sequence of amino acids. Thus, because any of 20 different amino acids might appear at any position, a protein containing 100 amino acids could form any of 20^{100} different amino acid sequences (that's the same as 10^{130}, or 1 followed by 130 zeros—more than the number of atoms known in the universe). This important property of proteins permits great diversity.

Consider the protein hemoglobin, the protein your blood uses to transport oxygen. Hemoglobin is composed of two α-globin peptide chains and two β-globin peptide chains. The α-globin chains differ from the β-globin ones in the sequence of amino acids. Furthermore, any alteration in the normal sequence of either of the types of globin proteins, even by a single amino acid, can have drastic effects on how the protein functions.

Secondary structure: Hydrogen bonding patterns

The amino acid side groups are not the only portions of proteins that form hydrogen bonds. The peptide groups of the main chain can also do so. These hydrogen bonds can be with water or with other peptide groups. If the peptide groups formed too many hydrogen bonds with water, the proteins would tend to behave like a random coil and wouldn't produce the kinds of globular

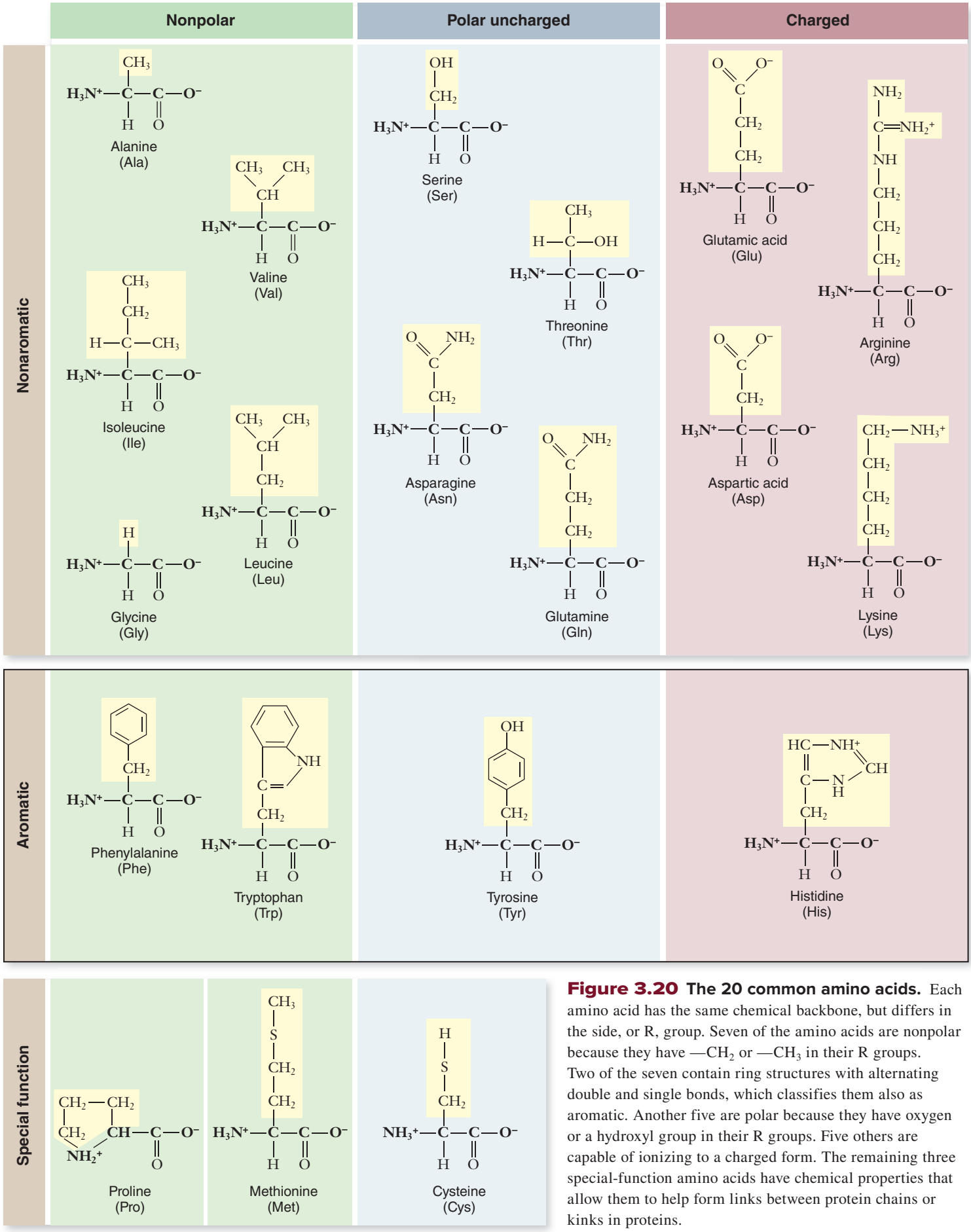
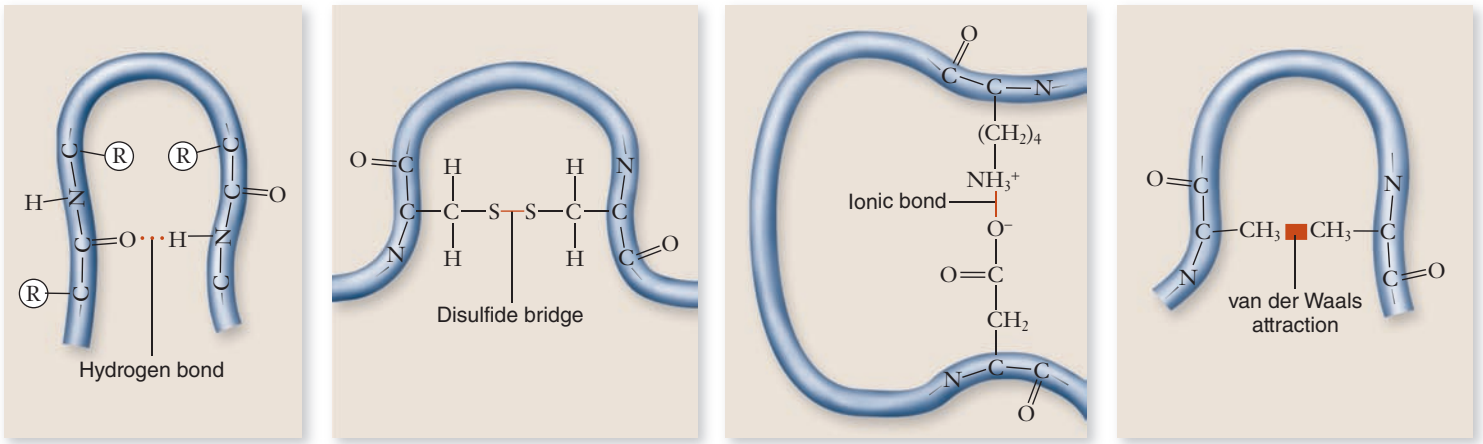


Figure 3.20 The 20 common amino acids. Each amino acid has the same chemical backbone, but differs in the side, or R, group. Seven of the amino acids are nonpolar because they have $—CH_2$ or $—CH_3$ in their R groups. Two of the seven contain ring structures with alternating double and single bonds, which classifies them also as aromatic. Another five are polar because they have oxygen or a hydroxyl group in their R groups. Five others are capable of ionizing to a charged form. The remaining three special-function amino acids have chemical properties that allow them to help form links between protein chains or kinks in proteins.



a. *b.* *c.* *d.* *e.*

Figure 3.21 Interactions that contribute to a protein's shape. Aside from the bonds that link together the amino acids in a protein, several other weaker forces and interactions stabilize protein structure. ***a.*** Hydrogen bonds can form between the different amino acids. ***b.*** Covalent disulfide bridges can form between two cysteine side chains. ***c.*** Ionic bonds can form between groups with opposite charge. ***d.*** van der Waals attractions, which are weak attractions between atoms due to oppositely polarized electron clouds, can occur. ***e.*** Polar portions of the protein tend to gather on the outside of the protein and interact with water, whereas the hydrophobic portions of the protein, including nonpolar amino acid chains, are shoved toward the interior of the protein.

structures that are common in proteins. Linus Pauling suggested that the peptide groups could interact with one another if the peptide was coiled into a spiral that he called the **α helix.** We now call this sort of regular interaction of groups in the peptide backbone **secondary structure.** Another form of secondary structure can occur between regions of peptide aligned next to each other to form a planar structure called a **β sheet.** These can be either parallel or antiparallel depending on whether the adjacent sections of peptide are oriented in the same direction, or opposite direction.

These two kinds of secondary structure create regions of the protein that are cylindrical (α helices) and planar (β sheets). A protein's final structure can include regions of each type of secondary structure. For example, DNA-binding proteins usually have regions of α helix that can lay across DNA and interact directly with the bases of DNA. Porin proteins that form holes in membranes are composed of β sheets arranged to form a pore in the membrane. Finally in hemoglobin, the α- and β-globin peptide chains that make up the final molecule each have characteristic regions of secondary structure.

Tertiary structure: Folds and links

The final folded shape of a globular protein is called its **tertiary structure.** This tertiary structure contains regions that have secondary structure and determines how these are further arranged in space to produce the overall structure. A protein is initially driven into its tertiary structure by hydrophobic exclusion from water. Ionic bonds between oppositely charged R groups bring regions into close proximity, and disulfide bonds (covalent links between two cysteine R groups) lock particular regions together. The final folding of a protein is determined by its primary structure—the chemical nature of its side groups (see figures 3.21 and 3.22). Many small proteins can be fully unfolded ("denatured") and will spontaneously refold into their characteristic shape. Other larger proteins tend to associate together and form insoluble clumps when denatured, such as the film that can form when you heat milk for hot chocolate.

The tertiary structure is stabilized by a number of forces including hydrogen bonding between R groups of different amino acids, electrostatic attraction between R groups with opposite charge (also called salt bridges), hydrophobic exclusion of nonpolar R groups, and covalent bonds in the form of disulfides. The stability of a protein, once it has folded into its tertiary shape, is strongly influenced by how well its interior fits together. When two nonpolar chains in the interior are very close together, they experience a form of molecular attraction called van der Waals forces. Individually quite weak, these forces can add up to a strong attraction when many of them come into play, like the combined strength of hundreds of hooks and loops on a strip of Velcro. These forces are effective only over short distances, however. No "holes" or cavities exist in the interior of proteins. The variety of different nonpolar amino acids, with a different-sized R group with its own distinctive shape, allows nonpolar chains to fit very precisely within the protein interior.

It is therefore not surprising that changing a single amino acid can drastically alter the structure, and thus the function of a

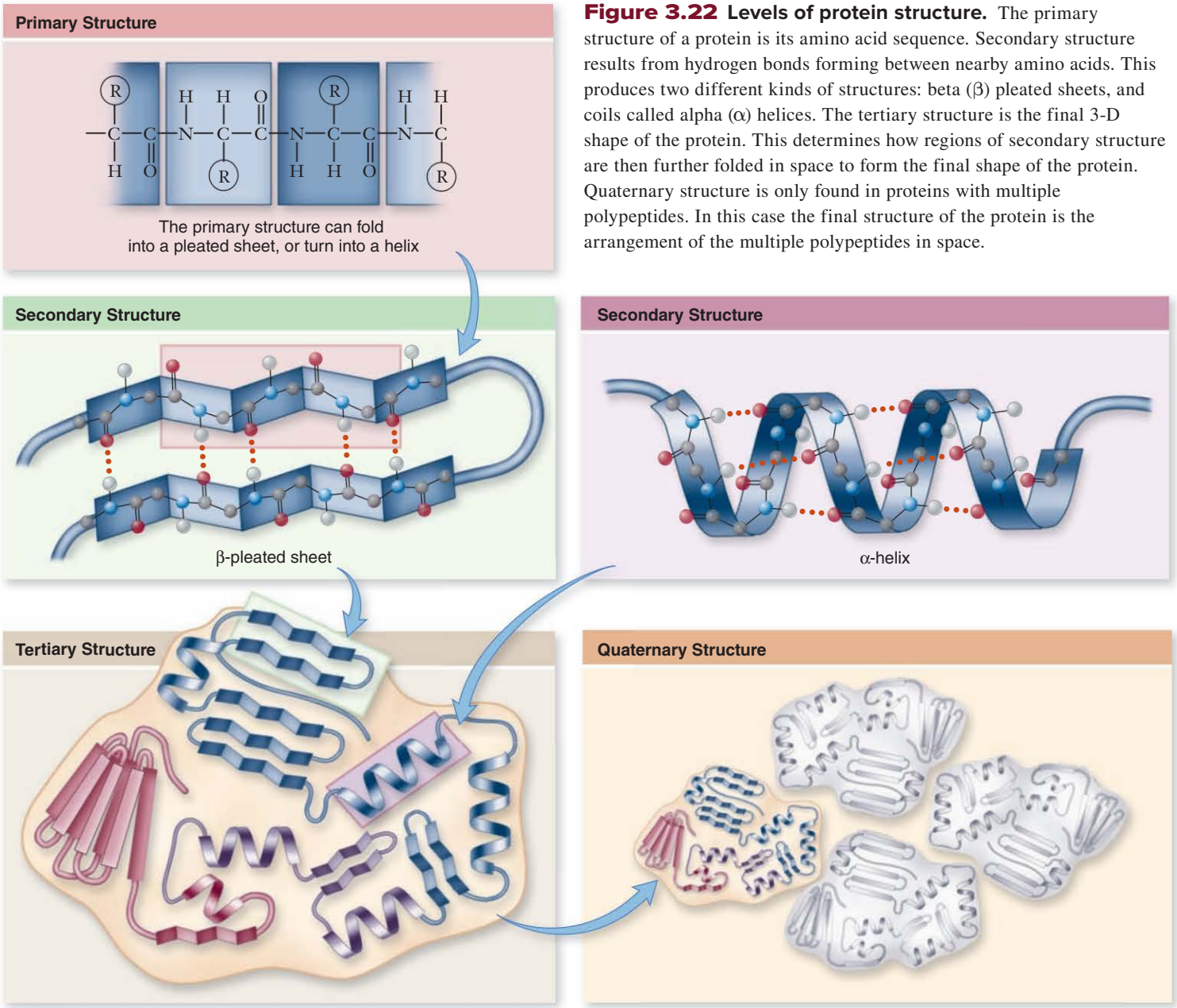


Figure 3.22 Levels of protein structure. The primary structure of a protein is its amino acid sequence. Secondary structure results from hydrogen bonds forming between nearby amino acids. This produces two different kinds of structures: beta (β) pleated sheets, and coils called alpha (α) helices. The tertiary structure is the final 3-D shape of the protein. This determines how regions of secondary structure are then further folded in space to form the final shape of the protein. Quaternary structure is only found in proteins with multiple polypeptides. In this case the final structure of the protein is the arrangement of the multiple polypeptides in space.

protein. The sickle cell version of hemoglobin (HbS), for example, is a change of a single glutamic acid for a valine in the β-globin chain. This change substitutes a charged amino acid for a nonpolar one on the surface of the protein, leading the protein to become sticky and form clumps. Another variant of hemoglobin called HbE, actually the most common in human populations, causes a change from glutamic acid to lysine at a different site in the β-globin chain. In this case the structural change is not as dramatic, but it still impairs function, resulting in blood disorders called anemia and thalassemia. More than 700 structural variants of hemoglobin are known, with up to 7% of the world's population being carriers of forms that are medically important.

Quaternary structure: Subunit arrangements

When two or more polypeptide chains associate to form a functional protein, the individual chains are referred to as subunits of the protein. The arrangement of these subunits is termed its **quaternary structure.** In proteins composed of subunits, the interfaces where the subunits touch one another are often nonpolar, and they play a key role in transmitting information between the subunits about individual subunit activities.

Remember that the protein hemoglobin is composed of two α-chain subunits and two β-chain subunits. Each α- and β-globin chain has a primary structure consisting of a specific sequence of amino acids. This then assumes a characteristic secondary structure consisting of α helices and β sheets that are then arranged into a specific tertiary structure for each α- and β-globin subunit. Lastly, these subunits are then arranged into their final quaternary structure. This is the final structure of the protein. For proteins that consist of only a single peptide chain, the enzyme lysozyme for example, the tertiary structure is the final structure of the protein.

Motifs and domains are structural elements of proteins

To directly determine the sequence of amino acids in a protein is a laborious task. Although the process has been automated, it remains slow and difficult.

The ability to sequence DNA changed this situation rather suddenly. Originally done manually, the Human Genome Project drove the development of automated sequencing. This increased throughput significantly, but the advent of next-generation sequencing technologies resulted in quantum increases in sequence data. Today, over 40,000 bacterial genomes have been sequenced, and almost 8000 eukaryotic genomes, including more than 80 mammalian genomes. Because the DNA sequence is directly related to amino acid sequence in proteins, biologists now have an enormous database of protein sequences to compare and analyze. This new information has also stimulated thought about the logic of the genetic code and whether underlying patterns exist in protein structure. Our view of protein structure has evolved with these data. Researchers still view the four-part hierarchical structure as important, but two additional terms have entered the biologist's vocabulary: motif and domain.

Motifs

As biologists discovered the three-dimensional structure of proteins (an even more laborious task than determining the sequence), they noticed similarities between otherwise dissimilar proteins. These similar structures are called **motifs,** or sometimes "supersecondary structure." The term *motif* is borrowed from the arts and refers to a recurring thematic element in music or design.

One very common protein motif is the β-α-β motif, which creates a fold or crease; the so-called "Rossmann fold" at the core of nucleotide-binding sites in a wide variety of proteins. A second motif that occurs in many proteins is the β barrel, which is a β sheet folded around to form a tube. A third type of motif, the helix-turn-helix, consists of two α helices separated by a bend. This motif is important because many proteins use it to bind to the DNA double helix (figure 3.23; see also chapter 16).

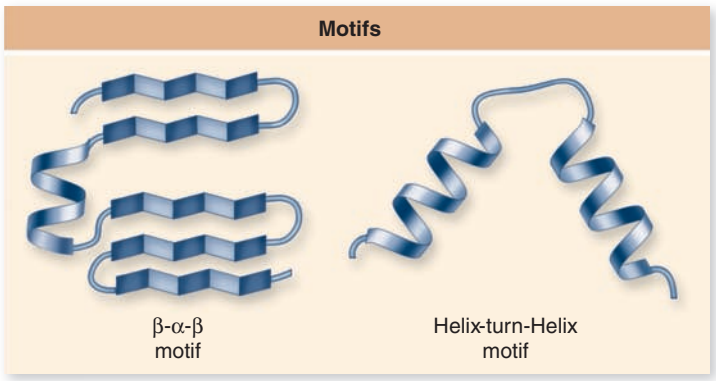
Motifs indicate a logic to structure that investigators still do not understand. Do they simply represent a reuse by evolution of something that already works, or are they an optimal solution to a problem, such as how to bind a nucleotide? One way to think about it is that if amino acids are letters in the language of proteins, then motifs represent repeated words or phrases. Motifs have been useful in determining the function of unknown proteins. Databases of protein motifs are used to search new unknown proteins. Finding motifs with known functions may allow an investigator to infer the function of a new protein.

Domains

Domains of proteins are functional units within a larger structure. They can be thought of as substructure within the tertiary structure of a protein (figure 3.23). To continue the metaphor: Amino acids are letters in the protein language, motifs are words or phrases, and domains are paragraphs.

Most proteins are made up of multiple domains that perform different parts of the protein's function. In many cases, these domains can be physically separated. For example, transcription factors (discussed in chapter 16) are proteins that bind to DNA and initiate its transcription. If the DNA-binding region is exchanged with a different transcription factor, then the specificity of the factor for DNA can be changed without changing its ability to stimulate transcription. Such "domain-swapping" experiments have been performed with many transcription factors, and they indicate, among other things, that the DNA-binding and activation domains are functionally separate.

These functional domains of proteins may also help the protein to fold into its proper shape. As a polypeptide chain folds, the



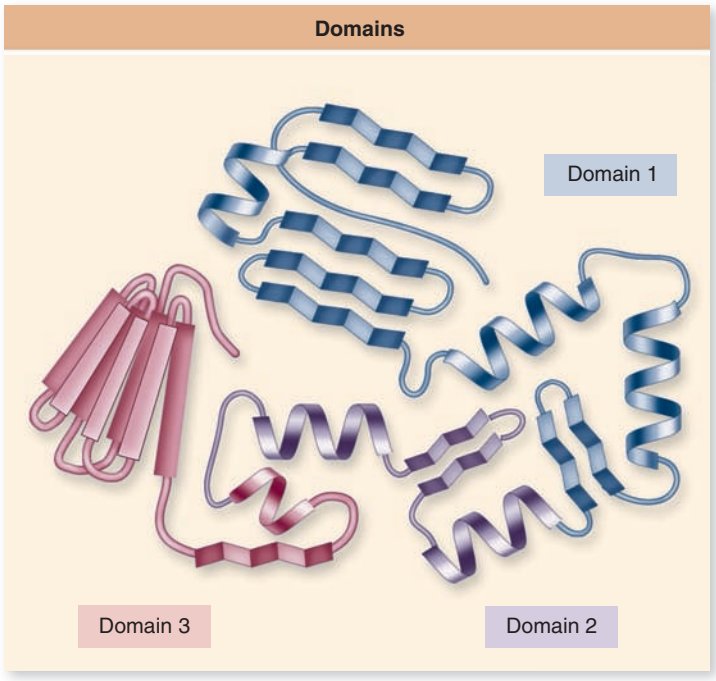


Figure 3.23 Motifs and domains. The elements of secondary structure can combine, fold, or crease to form motifs. These motifs are found in different proteins and can be used to predict function. Proteins also are made of larger domains, which are functionally distinct parts of a protein. The arrangement of these domains in space is the tertiary structure of a protein.

domains take their proper shape, each more or less independently of the others. This action can be demonstrated experimentally by artificially producing the fragment of a polypeptide that forms the domain in the intact protein, and showing that the fragment folds to form the same structure as it exhibits in the intact protein. A single polypeptide chain connects the domains of a protein, like a rope tied into several adjacent knots.

Domains can also correspond to the structure of the genes that encode them. Later, in chapter 15, you will see that genes in eukaryotes are often in pieces within the genome, and these pieces, called *exons,* sometimes encode the functional domains of a protein. This finding led to the idea of evolution acting by shuffling protein-encoding domains.

The process of folding relies on chaperone proteins

Originally, biochemists thought that newly made proteins fold spontaneously, randomly trying out different configurations as hydrophobic interactions with water shoved nonpolar amino acids into the protein's interior until the final structure was arrived at. We now know this view is too simple. Protein chains can fold in so many different ways that trial and error would simply take too long. In addition, as the open chain folds its way toward its final form, nonpolar "sticky" interior portions are exposed during intermediate stages. If these intermediate forms are placed in a test tube in an environment identical to that inside a cell, they stick to other, unwanted protein partners, forming a gluey mess.

How do cells avoid having their proteins clump into a mass? A vital clue came in studies of unusual mutations that prevent viruses from replicating in bacterial cells. It turns out that the virus proteins produced inside the cells could not fold properly. Further study revealed that normal cells contain **chaperone proteins,** which help other proteins to fold correctly.

Molecular biologists have now identified many proteins that act as molecular chaperones. This large class of proteins can be divided into subclasses, and representatives have been found in essentially every organism that has been examined. At least some of these proteins have been shown to be necessary for viability, illustrating their fundamental importance. Many are so-called heat shock proteins, produced in large amounts in response to elevated temperature. High temperatures cause proteins to unfold, and heat shock chaperone proteins help the cell's proteins to refold properly.

One class of these proteins, called chaperonins, has been extensively studied. In the bacterium *Escherichia coli (E. coli),* one example is the essential protein GroE chaperonin. In mutants in which the GroE chaperonin is inactivated, fully 30% of the bacterial proteins fail to fold properly. Chaperonins associate to form a large macromolecular complex that resembles a cylindrical container. Proteins can move into the container, and the container itself can change its shape considerably (figure 3.24). Experiments have shown that an improperly folded protein can enter the chaperonin and be refolded. Although we don't know exactly how this happens, it seems to involve changes in the hydrophobicity of the interior of the chamber.

The flexibility of the structure of chaperonins is amazing. We tend to think of proteins as being fixed structures, but this is clearly not the case for chaperonins and this flexibility is necessary for their function. It also illustrates that even domains that may be very widely separated in a very large protein are still functionally connected. The folding process within a chaperonin harnesses the hydrolysis of ATP to power these changes in structure necessary for function. This entire process can occur in a cyclic manner until the appropriate structure is achieved. Cells use these chaperonins both to accomplish the original folding of some proteins and to restore the structure of incorrectly folded ones.

Improper folding of proteins can result in disease

Chaperone protein deficiencies may be implicated in certain diseases in which key proteins are improperly folded. Cystic fibrosis is a hereditary disorder in which a mutation disables a vital protein

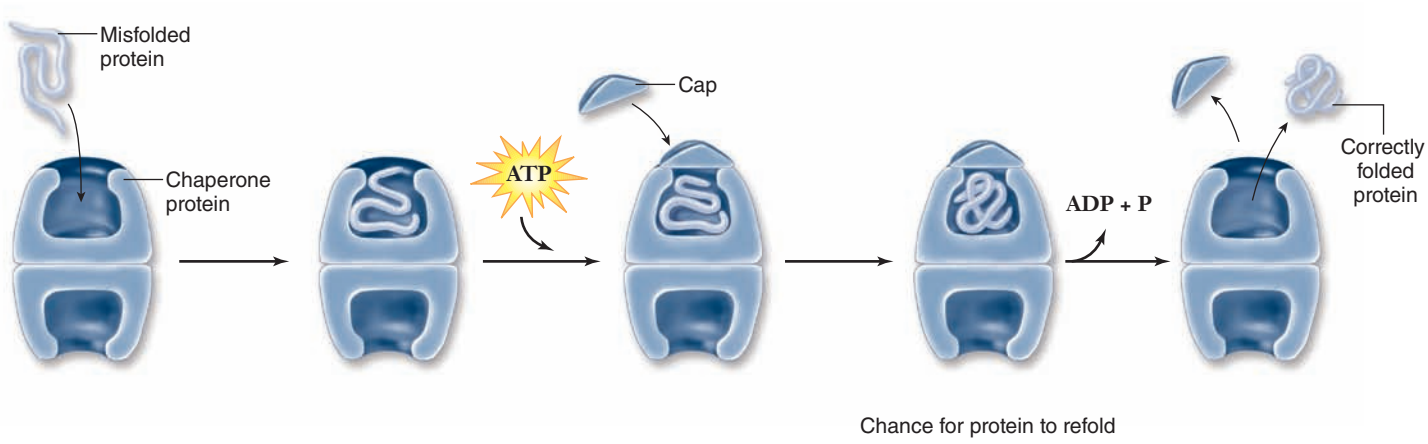


Figure 3.24 How one type of chaperone protein works. This barrel-shaped chaperonin is from the GroE family of chaperone proteins. It is composed of two identical rings each with seven identical subunits, each of which has three distinct domains. An incorrectly folded protein enters one chamber of the barrel, and a cap seals the chamber. Energy from the hydrolysis of ATP fuels structural alterations to the chamber, changing it from hydrophobic to hydrophilic. This change allows the protein to refold. After a short time, the protein is ejected, either folded or unfolded, and the cycle can repeat itself.

that moves ions across cell membranes. As a result, people with cystic fibrosis have thicker than normal mucus. This results in breathing problems, lung disease, and digestive difficulties, among other things. One interesting feature of the molecular analysis of this disease has been the number of different mutations found in human populations. One diverse class of mutations all result in problems with protein folding. The number of different mutations that can result in improperly folded proteins may be related to the fact that the native protein often fails to fold properly.

Denaturation inactivates proteins

If a protein's environment is altered, the protein may change its shape or even unfold completely. This process is called **denaturation** (figure 3.25). Proteins can be denatured when the pH, temperature, or ionic concentration of the surrounding solution changes.

Denatured proteins are usually biologically inactive. This action is particularly significant in the case of enzymes. Because practically every chemical reaction in a living organism is catalyzed by a specific enzyme, it is vital that a cell's enzymes work properly.

The traditional methods of food preservation, salt curing and pickling, involve denaturation of proteins. Prior to the general availability of refrigerators and freezers, the only practical way to keep microorganisms from growing in food was to keep the food in

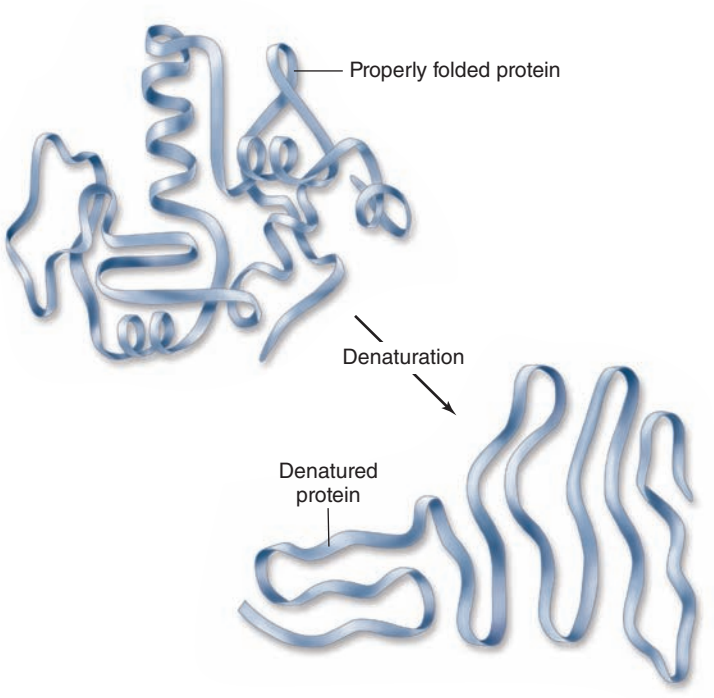


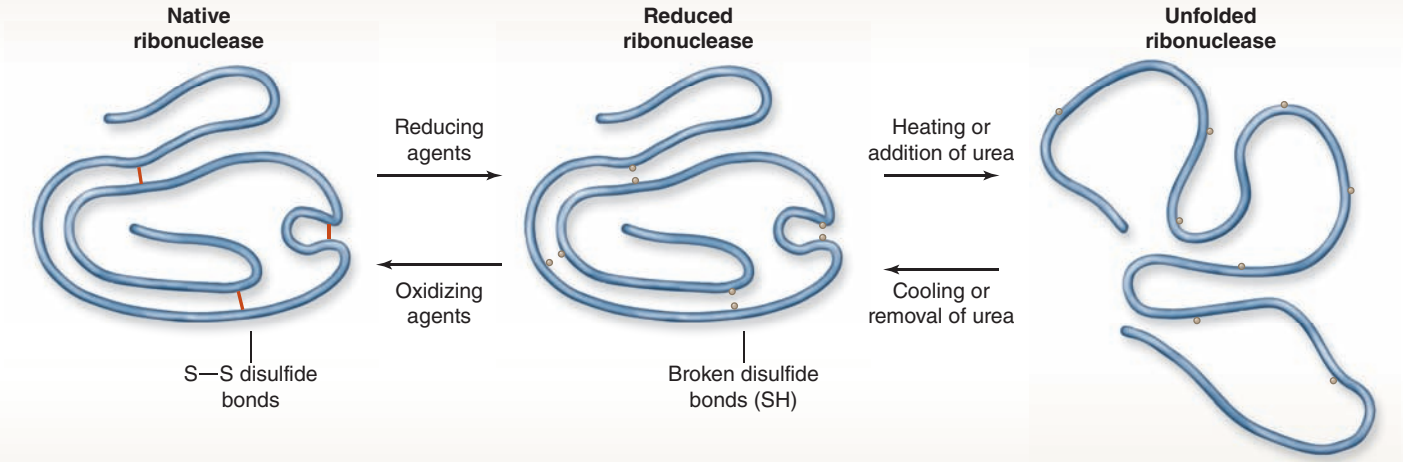
Figure 3.25 Protein denaturation. Environmental changes, such as variation in temperature or pH, can cause a protein to unfold and lose its shape. This loss of structure is called denaturation. Denatured proteins are biologically inactive.

SCIENTIFIC THINKING

Hypothesis: *The 3-D structure of a protein is the thermodynamically stable structure. It depends only on the primary structure of the protein and the solution conditions.*

Prediction: *If a protein is denatured and allowed to renature under native conditions, it will refold into the native structure.*

Test: *Ribonuclease is treated with a reducing agent to break disulfide bonds and is then treated with urea to completely unfold the protein. The disulfide bonds are re-formed under nondenaturing conditions to see if the protein refolds properly.*



Result: *Denatured ribonuclease refolds properly under nondenaturing conditions.*

Conclusion: *The hypothesis is supported. The information in the primary structure (amino acid sequence) is sufficient for refolding to occur. This implies that protein folding results in the thermodynamically stable structure.*

Further Experiments: *If the disulfide bonds were allowed to re-form under denaturing conditions, would we get the same result? How can we rule out that the protein had not been completely denatured and therefore retained some structure?*

Figure 3.26 Primary structure determines tertiary structure.

a solution containing a high concentration of salt or vinegar, which denatured the enzymes of most microorganisms and prevented them from growing on the food.

Most enzymes function within a very narrow range of environmental conditions. Blood-borne enzymes that course through a human body at a pH of about 7.4 would rapidly become denatured in the highly acidic environment of the stomach. Conversely, the protein-degrading enzymes that function at a pH of 2 or less in the stomach would be denatured in the relatively basic pH of the blood. Similarly, organisms that live near oceanic hydrothermal vents have enzymes that work well at these extremes of temperature (over 100°C). They cannot survive in cooler waters, because their enzymes do not function properly at lower temperatures. Any given organism usually has a tolerance range of pH, temperature, and salt concentration. Within that range, its enzymes maintain the proper shape to carry out their biological functions.

When a protein's normal environment is reestablished after denaturation, a small protein may spontaneously refold into its natural shape, driven by the interactions between its nonpolar amino acids and water (figure 3.26). This process is termed *renaturation,* and it was first established for the enzyme ribonuclease (RNase). The renaturation of RNase led to the doctrine that primary structure determines tertiary structure. Larger proteins can rarely refold spontaneously, however, because of the complex nature of their final shape, so this simple idea needs to be qualified.

The fact that some proteins can spontaneously renature implies that tertiary structure is strongly influenced by primary structure. In an extreme example, the *E. coli* ribosome can be taken apart and put back together experimentally. Although this process requires temperature and ion concentration shifts, it indicates an amazing degree of self-assembly. That complex structures can arise by self-assembly is a key idea in the study of modern biology.

It is important to distinguish denaturation from **dissociation.** For proteins with quaternary structure, the subunits may be dissociated (separated) without losing their individual tertiary structure. For example, the four subunits of hemoglobin may dissociate into four individual molecules (two α-globins and two β-globins) without denaturation of the folded globin proteins. They readily reassume their four-subunit quaternary structure.

Learning Outcomes Review 3.4

Proteins are molecules with diverse functions. They are constructed from 20 different kinds of amino acids. Protein structure can be viewed at four levels: (1) the amino acid sequence, or primary structure; (2) coils and sheets, called secondary structure; (3) the three-dimensional shape, called tertiary structure; and (4) individual polypeptide subunits associated in a quaternary structure. Different proteins often have similar substructures called motifs and can be broken down into functional domains. Proteins have a narrow range of conditions in which they fold properly; outside that range, proteins tend to unfold (denaturation). Under some conditions, denatured proteins can refold and become functional again (renaturation).

- ***How does our knowledge of protein structure help us to predict the function of unknown proteins?***

3.5 Lipids: Hydrophobic Molecules

Learning Outcomes

1. *Describe the structure of triglycerides.*
2. *Explain how fats function as energy-storage molecules.*
3. *Apply knowledge of the structure of phospholipids to the formation of membranes.*

Lipids are a somewhat loosely defined group of molecules with one main chemical characteristic: They are insoluble in water. Storage fats such as animal fat are one kind of lipid. Oils such as those from olives, corn, and coconut are also lipids, as are waxes such as beeswax and earwax. Even some vitamins are lipids!

Lipids have a very high proportion of nonpolar carbon–hydrogen (C—H) bonds, and so long-chain lipids cannot fold up like a protein to confine their nonpolar portions away from the surrounding aqueous environment. Instead, when they are placed in water, many lipid molecules spontaneously cluster together and expose what polar (hydrophilic) groups they have to the surrounding water, while confining the nonpolar (hydrophobic) parts of the molecules together within the cluster. You may have noticed this effect when you add oil to a pan containing water, and the oil beads up into cohesive drops on the water's surface. This spontaneous assembly of lipids is of paramount importance to cells, as it underlies the structure of cellular membranes.

Fats consist of complex polymers of fatty acids attached to glycerol

Many lipids are built from a simple skeleton made up of two main kinds of molecules: fatty acids and glycerol. Fatty acids are long-chain hydrocarbons with a carboxylic acid (COOH) at one end. Glycerol is a 3-carbon polyalcohol (three —OH groups). Many lipid molecules consist of a glycerol molecule with three fatty acids attached, one to each carbon of the glycerol backbone. Because it contains three fatty acids, a fat molecule is commonly called a **triglyceride** (the more accurate chemical name is *triacylglycerol*). This basic structure is depicted in figure 3.27. The three fatty acids of a triglyceride need not be identical, and often they are very different from one another. The hydrocarbon chains of fatty acids vary in length. The most common are even-numbered chains of 14 to 20 carbons. The many C—H bonds of fats serve as a form of long-term energy storage.

If all of the internal carbon atoms in a fatty acid chain are bonded to two hydrogen atoms, we call this **saturated,** which refers to its having the maximum hydrogen atoms possible (figure 3.27). A fatty acid with double bonds between one or more pairs of successive carbon atoms will have fewer hydrogen atoms, and thus is said to be **unsaturated.** Fatty acids with one double bond are called monounsaturated, and those with more than one double bond are termed **polyunsaturated.** Most naturally occurring unsaturated fatty acids have double bonds with a *cis* configuration, where the carbon chain is on the same side before and after the double bond

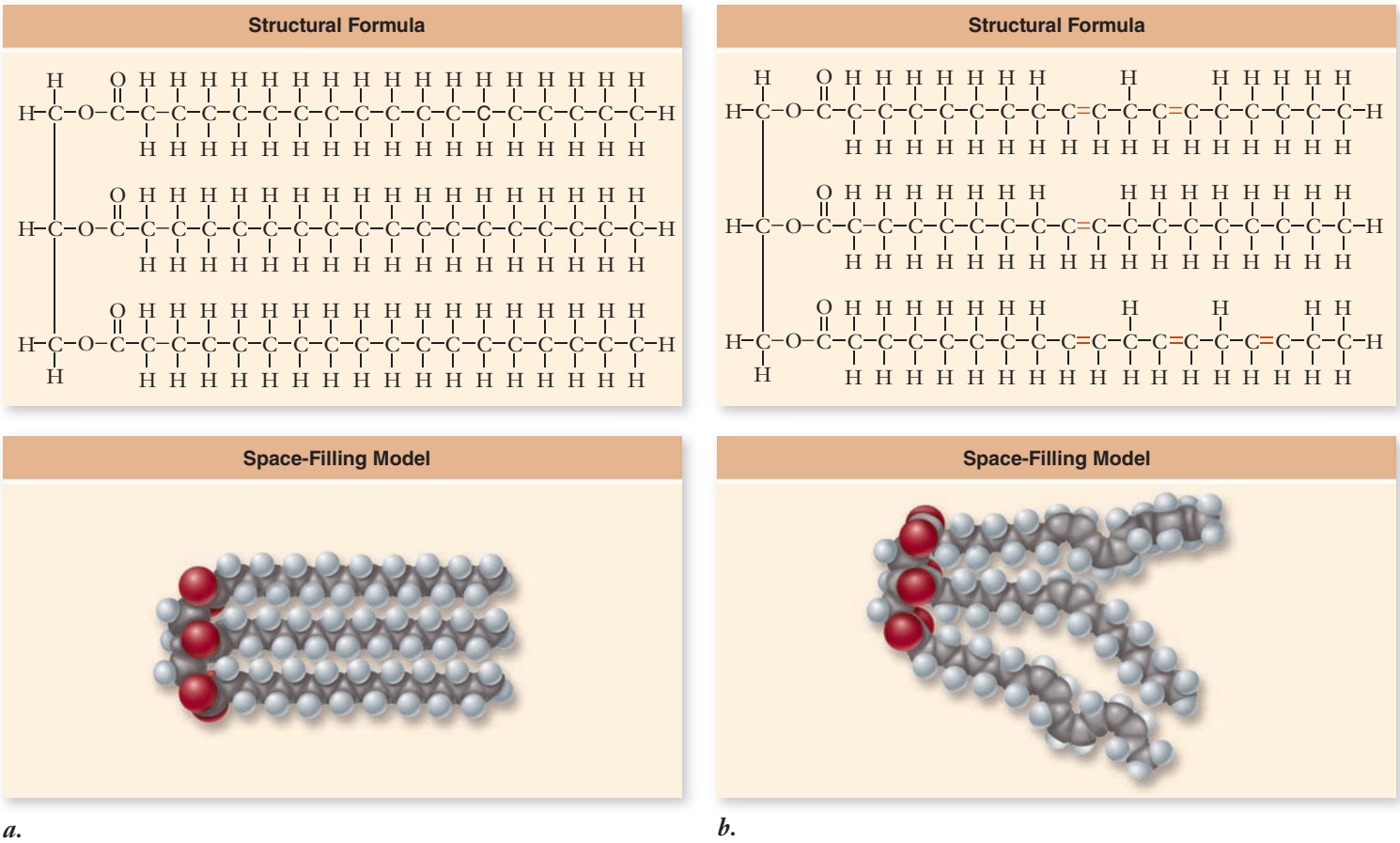


Figure 3.27 Saturated and unsaturated fats. ***a.*** A saturated fat is composed of triglycerides that contain three saturated fatty acids (the kind that have no double bonds). A saturated fat therefore has the maximum number of hydrogen atoms bonded to its carbon chain. Most animal fats are saturated. ***b.*** Unsaturated fat is composed of triglycerides that contain three unsaturated fatty acids (the kind that have one or more double bonds). These have fewer than the maximum number of hydrogen atoms bonded to the carbon chain. This example includes both a monounsaturated and two polyunsaturated fatty acids. Plant fats are typically unsaturated. The many kinks of the double bonds prevent the triglyceride from closely aligning, which makes them liquid oils at room temperature.

(double bonds in fatty acids in figure 3.27*b* are all *cis*). When fats are partially hydrogenated industrially, this can produce double bonds with a *trans* configuration where the carbon chain is on opposite sides before and after the double bond. These are the so-called trans fats. These have been linked to elevated levels of low-density lipoprotein (LDL) "bad cholesterol" and lowered levels of high-density lipoprotein (HDL) "good cholesterol." This condition is thought to be associated with an increased risk for coronary heart disease.

The correlation of dietary trans fats and coronary artery disease led the FDA in the United States to remove trans fats from the list of generally regarded as safe (GRAS) compounds. This is not the same as a ban, as they can be used as a dietary supplement, but along with product labeling, it has been effective in helping to remove trans fats from most common sources.

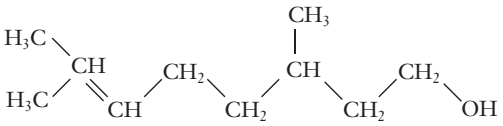
Having double bonds changes the behavior of the molecule because free rotation cannot occur about a C═C double bond as it can with a C—C single bond. This characteristic mainly affects melting point—that is, whether the fatty acid is a solid fat or a liquid oil at room temperature. Fats containing polyunsaturated fatty acids have low melting points because their fatty acid chains bend at the double bonds, preventing the fat molecules from aligning closely with one another. Most saturated fats, such as animal fat or those in butter, are solid at room temperature.

Placed in water, triglycerides spontaneously associate together, forming fat globules that can be very large relative to the size of the individual molecules. Because fats are insoluble in water, they can be deposited at specific locations within an organism, such as in vesicles of adipose tissue.

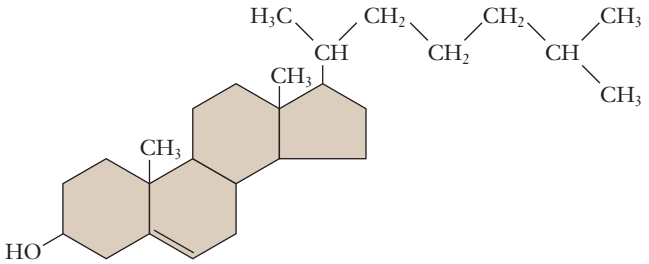
Organisms contain many other kinds of lipids besides fats (figure 3.28). *Terpenes* are long-chain lipids that are components of many biologically important pigments, such as chlorophyll and the visual pigment retinal. Rubber is also a terpene. *Steroids,* another class of lipid, are composed of four carbon rings. Most animal cell membranes contain the steroid cholesterol. Other steroids, such as testosterone and estrogen, function as hormones in multicellular animals. *Prostaglandins* are a group of about 20 lipids that are modified fatty acids, with two nonpolar "tails" attached to a 5-carbon ring. Prostaglandins act as local chemical messengers in many vertebrate tissues. Chapter 45 explores the effects of some of these complex fatty acids.

Fats are excellent energy-storage molecules

Most fats contain over 40 carbon atoms. The ratio of energy-storing C—H bonds in fats is more than twice that of carbohydrates (see section 3.2), making fats much more efficient molecules for



a. Terpene (citronellol)



b. Steroid (cholesterol)

Figure 3.28 Other kinds of lipids. ***a.*** Terpenes are found in biological pigments, such as chlorophyll and retinal, and ***(b)*** steroids play important roles in membranes and as the basis for a class of hormones involved in chemical signaling.

storing chemical energy. On average, fats yield about 9 kilocalories (kcal) of chemical energy per gram, as compared with about 4 kcal/g for carbohydrates.

Most fats produced by animals are saturated (except some fish oils), whereas most plant fats are unsaturated (see figure 3.27). The exceptions are the tropical plant oils (palm oil and coconut oil), which are saturated even though they are liquid at room temperature.

When an organism consumes excess carbohydrate, it is converted into starch, glycogen, or fats reserved for future use. The reason that many humans in developed countries gain weight as they grow older is that the amount of energy they need decreases with age, but their intake of food does not. Thus, an increasing proportion of the carbohydrates they ingest is converted into fat.

A diet heavy in fats is one of several factors thought to contribute to heart disease, particularly atherosclerosis. In atherosclerosis, sometimes referred to as "hardening of the arteries," fatty substances called plaque adhere to the lining of blood vessels, blocking the flow of blood. Fragments of a plaque can break off from a deposit and clog arteries to the brain, causing a stroke.

Phospholipids form membranes

Complex lipid molecules called **phospholipids** are among the most important molecules of the cell because they form the core of all biological membranes. An individual phospholipid can be thought of as a substituted triglyceride—that is, a triglyceride with a phosphate replacing one of the fatty acids. The basic structure of a phospholipid includes three kinds of subunits:

1. *Glycerol,* a 3-carbon alcohol, in which each carbon bears a hydroxyl group. Glycerol forms the backbone of the phospholipid molecule.
2. *Fatty acids,* long chains of —CH_2 groups (hydrocarbon chains) ending in a carboxyl (—COOH) group. Two fatty acids are attached to the glycerol backbone in a phospholipid molecule.
3. *A phosphate group* (—PO_4^{2-}) attached to one end of the glycerol. The charged phosphate group usually has a charged organic molecule linked to it, such as choline, ethanolamine, or the amino acid serine.

The phospholipid molecule can be thought of as having a polar "head" at one end (the phosphate group) and two long, very nonpolar "tails" at the other (figure 3.29). This structure is essential for how these molecules function, although it first appears

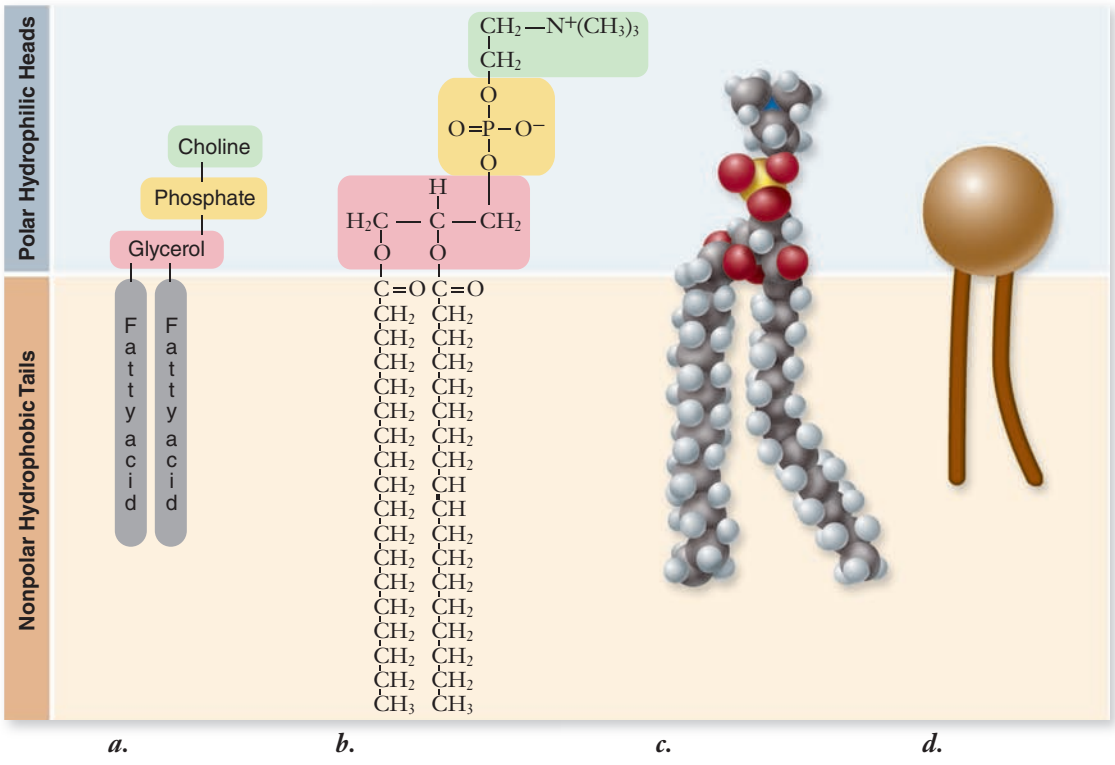


Figure 3.29 Phospholipids. The phospholipid phosphatidylcholine is shown as ***(a)*** a schematic, ***(b)*** a formula, ***(c)*** a space-filling model, and ***(d)*** an icon used in depictions of biological membranes.

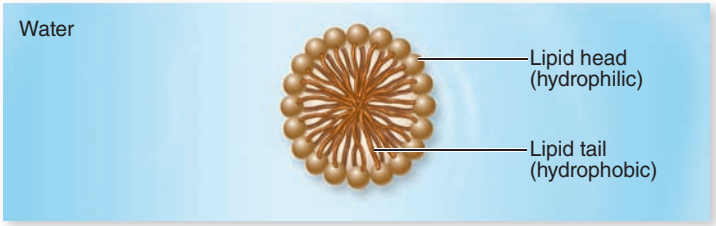
paradoxical. Why would a molecule need to be soluble in water, but also not soluble in water? The formation of a membrane shows the unique properties of such a structure.

In water, the nonpolar tails of nearby lipid molecules aggregate away from the water, forming spherical *micelles,* with the tails facing inward (figure 3.30*a*). This is actually how detergent molecules work to make grease soluble in water. The grease is soluble within the nonpolar interior of the micelle and the polar surface of the micelle is soluble in water. With phospholipids, a more complex structure forms in which two layers of molecules line up, with the hydrophobic tails of each layer pointing toward one another, or inward, leaving the hydrophilic heads oriented outward, forming a bilayer (figure 3.30*b*). Lipid bilayers are the basic framework of biological membranes, discussed in detail in chapter 5.

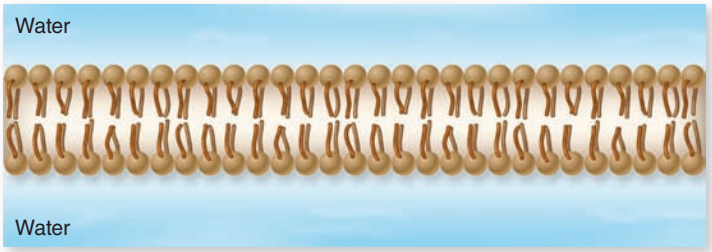
Learning Outcomes Review 3.5

Triglycerides are made of fatty acids linked to glycerol. Fats can contain twice as many C—H bonds as carbohydrates and thus they store energy efficiently. Because the C—H bonds in lipids are nonpolar, they are not water-soluble and aggregate together in water. Phospholipids replace one fatty acid with a hydrophilic phosphate group. This allows them to spontaneously form bilayers, which are the basis of biological membranes.

- ***Why do phospholipids form membranes while triglycerides form insoluble droplets?***

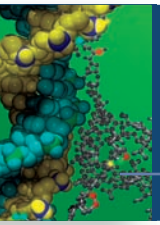


a.



b.

Figure 3.30 Lipids spontaneously form micelles or lipid bilayers in water. In an aqueous environment, lipid molecules orient so that their polar (hydrophilic) heads are in the polar medium, water, and their nonpolar (hydrophobic) tails are held away from the water. ***a.*** Droplets called micelles can form, or ***(b)*** phospholipid molecules can arrange themselves into two layers; in both structures, the hydrophilic heads extend outward and the hydrophobic tails inward. This second example is called a phospholipid bilayer.



Chapter Review

3.1 Carbon: The Framework of Biological Molecules

Carbon, the backbone of all biological molecules, can form four covalent bonds and make long chains. Hydrocarbons consist of carbon and hydrogen, and their bonds store considerable energy.

Functional groups account for differences in molecular properties.

Functional groups are small molecular entities that confer specific chemical characteristics when attached to a hydrocarbon.

Carbon and hydrogen have similar electronegativity so C—H bonds are not polar. Oxygen and nitrogen have greater electronegativity, leading to polar bonds.

Isomers have the same molecular formulas but different structures.

Structural isomers are molecules with the same formula but different structures; stereoisomers differ in how groups are attached. Enantiomers are mirror-image stereoisomers.

Biological macromolecules include carbohydrates, nucleic acids, proteins, and lipids.

Most important biological macromolecules are polymers—long chains of monomer units. Biological polymers are formed by elimination of water (H and OH) from two monomers (dehydration reaction). They are broken down by adding water (hydrolysis).

3.2 Carbohydrates: Energy Storage and Structural Molecules

The empirical formula of a carbohydrate is $(CH_2O)_n$. Carbohydrates are used for energy storage and as structural molecules.

Monosaccharides are simple sugars.

Simple sugars contain three to six or more carbon atoms. Examples are glyceraldehyde (3 carbons), deoxyribose (5 carbons), and glucose (6 carbons).

Sugar isomers have structural differences.

The general formula for 6-carbon sugars is $C_6H_{12}O_6$, and many isomeric forms are possible. Living systems often have enzymes for converting isomers from one to the other.

Disaccharides serve as transport molecules in plants and provide nutrition in animals.

Plants convert glucose into the disaccharide sucrose for transport within their bodies. Female mammals produce the disaccharide lactose to nourish their young.

Polysaccharides provide energy storage and structural components.

Glucose is used to make three important polymers: glycogen (in animals), and starch and cellulose (in plants). Chitin is a related structural material found in arthropods and many fungi.

3.3 Nucleic Acids: Information Molecules

Deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) are polymers composed of nucleotide monomers. Cells use nucleic acids for information storage and transfer.

Nucleic acids are nucleotide polymers.

Nucleic acids contain four different nucleotide bases. In DNA these are adenine, guanine, cytosine, and thymine. In RNA, thymine is replaced by uracil.

DNA stores genetic information.

DNA exists as a double helix held together by specific base pairs: adenine with thymine and guanine with cytosine. The nucleic acid sequence constitutes the genetic code.

RNA has many roles in a cell.

RNA is made by copying DNA. RNA carries information from DNA and forms part of the ribosome. RNA can also be an enzyme and affect gene expression.

Other nucleotides are vital components of energy reactions.

Adenosine triphosphate (ATP) provides energy in cells; NAD^+ and FAD transport electrons in cellular processes.

3.4 Proteins: Molecules with Diverse Structures and Functions

Most enzymes are proteins. Proteins also provide defense, transport, motion, and regulation, among many other roles.

Proteins are polymers of amino acids.

Amino acids are joined by peptide bonds to make polypeptides. The 20 common amino acids are characterized by R groups that determine their properties.

Proteins have levels of structure.

Protein structure is defined by the following hierarchy: primary (amino acid sequence), secondary (hydrogen bonding patterns), tertiary (three-dimensional folding), and quaternary (associations between two or more polypeptides).

Motifs and domains are structural elements of proteins.

Motifs are similar structural elements found in dissimilar proteins. They can create folds, creases, or barrel shapes. Domains are functional subunits or sites within a tertiary structure.

The process of folding relies on chaperone proteins.

Chaperone proteins assist in the folding of proteins. Heat shock proteins are an example of chaperone proteins.

Improper folding of proteins can result in disease.

Some forms of cystic fibrosis and Alzheimer disease are associated with misfolded proteins.

Denaturation inactivates proteins.

Denaturation refers to an unfolding of tertiary structure, which usually destroys function. Some denatured proteins may recover function when conditions are returned to normal. This implies that primary structure strongly influences tertiary structure.

Dissociation refers to separation of quaternary subunits with no changes to their tertiary structure.

3.5 Lipids: Hydrophobic Molecules

Lipids are insoluble in water because they have a high proportion of nonpolar C—H bonds.

Fats consist of complex polymers of fatty acids attached to glycerol.

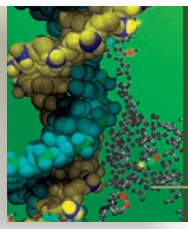
Many lipids exist as triglycerides, three fatty acids connected to a glycerol molecule. Saturated fatty acids contain the maximum number of hydrogen atoms. Unsaturated fatty acids contain one or more double bonds between carbon atoms.

Fats are excellent energy-storage molecules.

The energy stored in the C—H bonds of fats is more than twice that of carbohydrates: 9 kcal/g compared with 4 kcal/g. For this reason, excess carbohydrate is converted to fat for storage.

Phospholipids form membranes.

Phospholipids contain two fatty acids and one phosphate attached to glycerol. In phospholipid-bilayer membranes, the phosphate heads are hydrophilic and cluster on the two faces of the membrane, and the hydrophobic tails are in the center.



Review Questions

UNDERSTAND

1. How is a polymer formed from multiple monomers?
   a. From the growth of the chain of carbon atoms
   b. By the removal of an —OH group and a hydrogen atom
   c. By the addition of an —OH group and a hydrogen atom
   d. Through hydrogen bonding
2. Why are carbohydrates important molecules for energy storage?
   a. The C—H bonds found in carbohydrates store energy.
   b. The double bonds between carbon and oxygen are very strong.
   c. The electronegativity of the oxygen atoms means that a carbohydrate is made up of many polar bonds.
   d. They can form ring structures in the aqueous environment of a cell.
3. Plant cells store energy in the form of _____, and animal cells store energy in the form of _____.
   a. fructose; glucose
   b. disaccharides; monosaccharides
   c. cellulose; chitin
   d. starch; glycogen
4. Which carbohydrate would you find as part of a molecule of RNA?
   a. Galactose
   b. Deoxyribose
   c. Ribose
   d. Glucose
5. A molecule of DNA or RNA is a polymer of
   a. monosaccharides.
   b. nucleotides.
   c. amino acids.
   d. fatty acids.

6. What makes cellulose different from starch?
   a. Starch is produced by plant cells, and cellulose is produced by animal cells.
   b. Cellulose forms long filaments, and starch is highly branched.
   c. Starch is insoluble, and cellulose is soluble.
   d. All of the choices are correct.
7. What monomers make up a protein?
   a. Monosaccharides
   b. Nucleotides
   c. Amino acids
   d. Fatty acids
8. A triglyceride is a form of _____ composed of _____.
   a. lipid; fatty acids and glucose
   b. lipid; fatty acids and glycerol
   c. carbohydrate; fatty acids
   d. lipid; cholesterol

APPLY

1. You can use starch or glycogen as an energy source, but not cellulose because
   a. starch and cellulose have similar structures.
   b. cellulose and glycogen have similar structures.
   c. starch and glycogen have similar structures.
   d. your body makes starch but not cellulose.
2. Which of the following is NOT a difference between DNA and RNA?
   a. Deoxyribose sugar versus ribose sugar
   b. Thymine versus uracil
   c. Double-stranded versus single-stranded
   d. Phosphodiester versus hydrogen bonds
3. Which part of an amino acid has the greatest influence on the overall structure of a protein?
   a. The (—NH_2) amino group
   b. The R group
   c. The (—COOH) carboxyl group
   d. Both a and c are correct.
4. A mutation that alters a single amino acid within a protein can alter
   a. the primary level of protein structure.
   b. the secondary level of protein structure.
   c. the tertiary level of protein structure.
   d. All of the choices are correct.
5. Two different proteins have the same domain in their structure. From this we can infer that they have
   a. the same primary structure.
   b. similar function.
   c. very different functions.
   d. the same primary structure but different function.
6. What aspect of triglyceride structure accounts for their insolubility in water?
   a. The COOH group of fatty acids
   b. The nonpolar C—H bonds in fatty acids
   c. The OH groups in glycerol
   d. The C═C bonds found in unsaturated fatty acids
7. The spontaneous formation of a lipid bilayer in an aqueous environment occurs because
   a. the polar head groups of the phospholipids can interact with water.
   b. the long fatty acid tails of the phospholipids can interact with water.
   c. the fatty acid tails of the phospholipids are hydrophobic.
   d. Both a and c are correct.

SYNTHESIZE

1. How do the four biological macromolecules differ from one another? How does the structure of each relate to its function?
2. Hydrogen bonds and hydrophobic interactions each play an important role in stabilizing and organizing biological macromolecules. Consider the four macromolecules discussed in this chapter. Describe how these affect the form and function of each type of macromolecule. Would a disruption in the hydrogen bonds affect form and function? Hydrophobic interactions?
3. Plants make both starch and cellulose. Would you predict that the enzymes involved in starch synthesis could also be used by the plant for cellulose synthesis? Construct an argument to explain this based on the structure and function of the enzymes and the polymers synthesized.