3

The Chemical Building Blocks of Life

Concept Outline

3.1 Molecules are the building blocks of life.

The Chemistry of Carbon. Because individual carbon atoms can form multiple covalent bonds, organic molecules can be quite complex.

3.2 Proteins perform the chemistry of the cell.

The Many Functions of Proteins. Proteins can be catalysts, transporters, supporters, and regulators.
Amino Acids Are the Building Blocks of Proteins. Proteins are long chains of various combinations of amino acids.
A Protein's Function Depends on the Shape of the Molecule. A protein's shape is determined by its amino acid sequence.
How Proteins Fold Into Their Functional Shape. The distribution of nonpolar amino acids along a protein chain largely determines how the protein folds.
How Proteins Unfold. When conditions such as pH or temperature fluctuate, proteins may denature or unfold.

3.3 Nucleic acids store and transfer genetic information.

Information Molecules. Nucleic acids store information in cells. RNA is a single-chain polymer of nucleotides, while DNA possesses two chains twisted around each other.

3.4 Lipids make membranes and store energy.

Phospholipids Form Membranes. The spontaneous aggregation of phospholipids in water is responsible for the formation of biological membranes.
Fats and Other Kinds of Lipids. Organisms utilize a wide variety of water-insoluble molecules.
Fats as Food. Fats are very efficient energy storage molecules because of their high proportion of C—H bonds.

3.5 Carbohydrates store energy and provide building materials.

Simple Carbohydrates. Sugars are simple carbohydrates, often consisting of six-carbon rings.
Linking Sugars Together. Sugars can be linked together to form long polymers, or polysaccharides.
Structural Carbohydrates. Structural carbohydrates like cellulose are chains of sugars linked in a way that enzymes cannot easily attack.

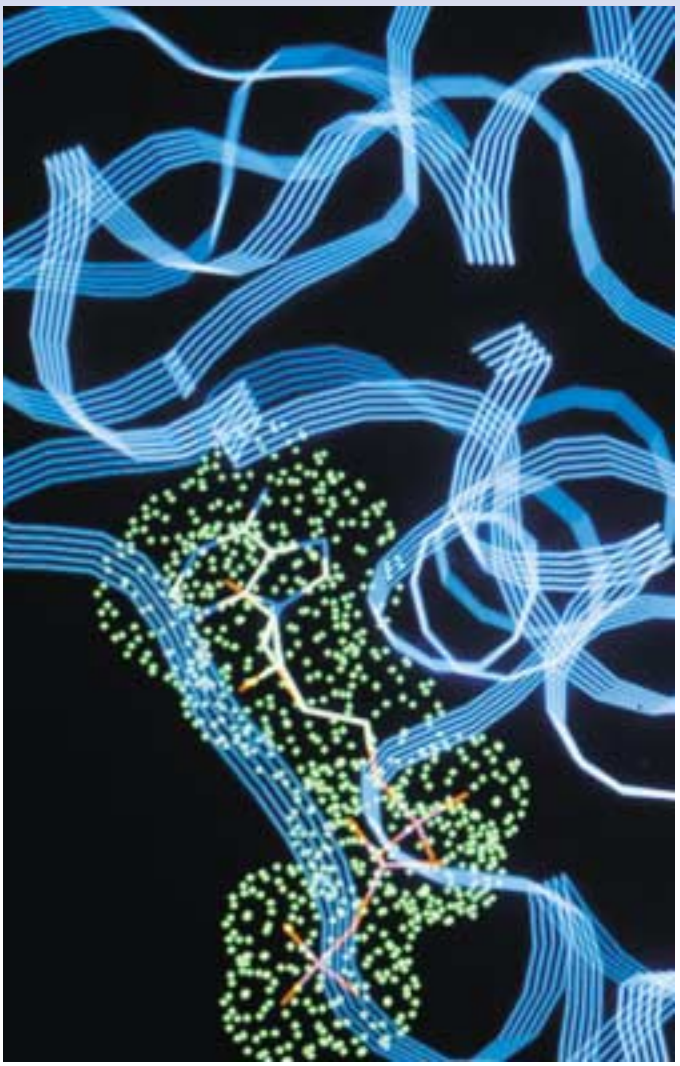


FIGURE 3.1
Computer-generated model of a macromolecule. Pictured is an enzyme responsible for releasing energy from sugar. This complex molecule consists of hundreds of different amino acids linked into chains that form the characteristic coils and folds seen here.

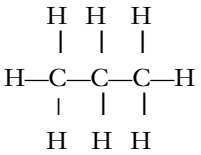
Molecules are extremely small compared with the familiar world we see about us. Imagine: there are more water molecules in a cup than there are stars in the sky. Many other molecules are gigantic, compared with water, consisting of thousands of atoms. These atoms are organized into hundreds of smaller molecules that are linked together into long chains (figure 3.1). These enormous molecules, almost always synthesized by living things, are called macromolecules. As we shall see, there are four general types of macromolecules, the basic chemical building blocks from which all organisms are assembled.

3.1 Molecules are the building blocks of life.

The Chemistry of Carbon

In chapter 2 we discussed how atoms combine to form molecules. In this chapter, we will focus on **organic molecules,** those chemical compounds that contain carbon. The frameworks of biological molecules consist predominantly of carbon atoms bonded to other carbon atoms or to atoms of oxygen, nitrogen, sulfur or hydrogen. Because carbon atoms possess four valence electrons and so can form four covalent bonds, molecules containing carbon can form straight chains, branches, or even rings. As you can imagine, all of these possibilities generate an immense range of molecular structures and shapes.

Organic molecules consisting only of carbon and hydrogen are called **hydrocarbons.** Covalent bonds between carbon and hydrogen are energy-rich. We use hydrocarbons from fossil fuels as a primary source of energy today. Propane gas, for example, is a hydrocarbon consisting of a chain of three carbon atoms, with eight hydrogen atoms bound to it:



Because carbon-hydrogen covalent bonds store considerable energy, hydrocarbons make good fuels. Gasoline, for example, is rich in hydrocarbons.

Functional Groups

Carbon and hydrogen atoms both have very similar electronegativities, so electrons in C—C and C—H bonds are evenly distributed, and there are no significant differences in charge over the molecular surface. For this reason, hydrocarbons are nonpolar. Most organic molecules that are produced by cells, however, also contain other atoms. Because these other atoms often have different electronegativities, molecules containing them exhibit regions of positive or negative charge, and so are polar. These molecules can be thought of as a C—H core to which specific groups of atoms called **functional groups** are attached. For example, a hydrogen atom bonded to an oxygen atom (—OH) is a functional group called a *hydroxyl group.*

Functional groups have definite chemical properties that they retain no matter where they occur. The hydroxyl group, for example, is polar, because its oxygen atom, being very electronegative, draws electrons toward itself (as we saw in chapter 2). Figure 3.2 illustrates the hydroxyl group and other biologically important functional groups. Most chemical reactions that occur within organisms involve the transfer of a functional group as an intact unit from one molecule to another.

Biological Macromolecules

Some organic molecules in organisms are small and simple, containing only one or a few functional groups. Others are large complex assemblies called **macromolecules.** In many cases, these macromolecules are polymers, molecules built by linking together a large number of small, similar chemical subunits, like railroad cars coupled to form a train. For example, complex carbohydrates like starch are polymers of simple ring-shaped sugars, proteins are polymers of amino acids, and nucleic acids (DNA and RNA) are polymers of nucleotides. Biological macromolecules are traditionally grouped into four major categories: proteins, nucleic acids, lipids, and carbohydrates (table 3.1).

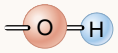
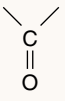
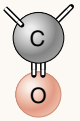
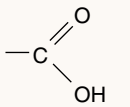
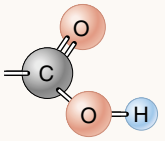
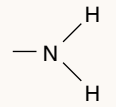
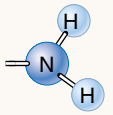
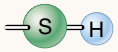
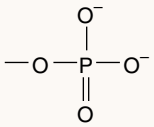
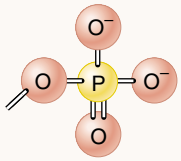
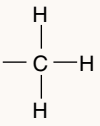
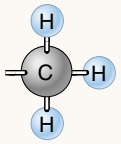
Group	Structural Formula	Ball-and-Stick Model	Found In:
Hydroxyl	—OH		Carbohydrates, alcohols
Carbonyl			Formaldehyde
Carboxyl			Amino acids, vinegar
Amino			Ammonia
Sulfhydryl	—S—H		Proteins, rubber
Phosphate			Phospholipids, nucleic acids, ATP
Methyl			Methane gas

FIGURE 3.2
The primary functional chemical groups. These groups tend to act as units during chemical reactions and confer specific chemical properties on the molecules that possess them. Amino groups, for example, make a molecule more basic, while carboxyl groups make a molecule more acidic.

Table 3.1 Macromolecules

Macromolecule	Subunit	Function	Example
PROTEINS			
Globular	Amino acids	Modified glucose	Hemoglobin
Structural	Amino acids	Catalysis; transport Support	Hair; silk
NUCLEIC ACIDS			
DNA	Nucleotides	Encodes genes	Chromosomes
RNA	Nucleotides	Needed for gene expression	Messenger RNA
LIPIDS			
Fats	Glycerol and three fatty acids	Energy storage	Butter; corn oil; soap
Phospholipids	Glycerol, two fatty acids, phosphate, and polar R groups	Cell membranes	Lecithin
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	Carotene; rubber
CARBOHYDRATES			
Starch, glycogen	Glucose	Energy storage	Potatoes
Cellulose	Glucose	Cell walls	Paper; strings of celery
Chitin		Structural support	Crab shells

Building Macromolecules

Although the four categories of macromolecules contain different kinds of subunits, they are all assembled in the same fundamental way: to form a covalent bond between two subunit molecules, an —OH group is removed from one subunit and a hydrogen atom (H) is removed from the other (figure 3.3*a*). This condensation reaction is called a **dehydration synthesis,** because the removal of the —OH group and H during the synthesis of a new molecule in effect constitutes the removal of a molecule of water (H_2O). For every subunit that is added to a macromolecule, one water molecule is removed. Energy is required to break the chemical bonds when water is extracted from the subunits, so cells must supply energy to assemble macromolecules. These and other biochemical reactions require that the reacting substances be held close together and that the correct chemical bonds be stressed and broken. This process of positioning and stressing, termed catalysis, is carried out in cells by a special class of proteins known as enzymes.

Cells disassemble macromolecules into their constituent subunits by performing reactions that are essentially the reverse of dehydration—a molecule of water is added instead of removed (figure 3.3*b*). In this process, which is called **hydrolysis** (Greek *hydro*, "water" + *lyse*, "break"), a hydrogen atom is attached to one subunit and a hydroxyl group to the other, breaking a specific covalent bond in the macromolecule. Hydrolytic reactions release the energy that was stored in the bonds that were broken.

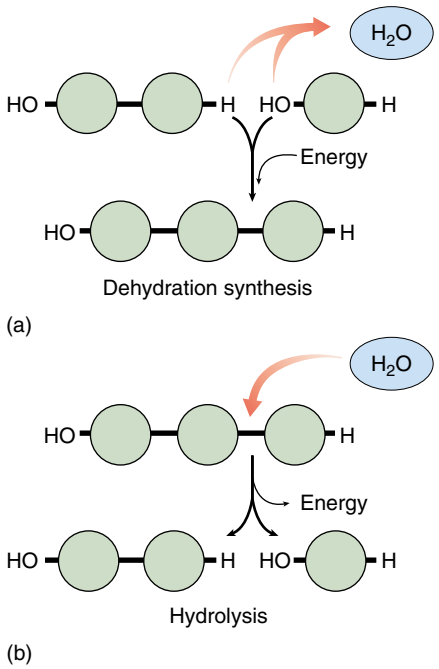


FIGURE 3.3
Making and breaking macromolecules. (*a*) Biological macromolecules are polymers formed by linking subunits together. The covalent bond between the subunits is formed by dehydration synthesis, an energy-requiring process that creates a water molecule for every bond formed. (*b*) Breaking the bond between subunits requires the returning of a water molecule with a subsequent release of energy, a process called hydrolysis.

Polymers are large molecules consisting of long chains of similar subunits joined by dehydration reactions. In a dehydration reaction, a hydroxyl (—OH) group is removed from one subunit and a hydrogen atom (H) is removed from the other.

3.2 Proteins perform the chemistry of the cell.

The Many Functions of Proteins

We will begin our discussion of macromolecules that make up the bodies of organisms with proteins (see table 3.1). The proteins within living organisms are immensely diverse in structure and function (table 3.2 and figure 3.4).

1. **Enzyme catalysis.** We have already encountered one class of proteins, enzymes, which 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 globular proteins, with a three-dimensional shape that fits snugly around the chemicals they work on, facilitating 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 hormone and immune systems.
3. **Transport.** A variety of globular proteins transport specific small molecules and ions. The transport protein hemoglobin, for example, transports oxygen in the blood, and myoglobin, a similar protein, transports oxygen in muscle. Iron is transported in blood by the protein transferrin.

Table 3.2 The Many Functions of Proteins

Function	Class of Protein	Examples	Use
Metabolism (Catalysis)	Enzymes	Hydrolytic enzymes	Cleave polysaccharides
		Proteases	Break down proteins
		Polymerases	Produce nucleic acids
		Kinases	Phosphorylate sugars and proteins
Defense	Immunoglobulins	Antibodies	Mark foreign proteins for elimination
Cell recognition	Toxins	Snake venom	Block nerve function
Transport throughout body	Cell surface antigens	MHC proteins	"Self" recognition
	Globins	Hemoglobin	Carries O_2 and CO_2 in blood
		Myoglobin	Carries O_2 and CO_2 in muscle
		Cytochromes	Electron transport
Membrane transport	Transporters	Sodium-potassium pump	Excitable membranes
		Proton pump	Chemiosmosis
		Anion channels	Transport Cl^- ions
Structure/Support	Fibers	Collagen	Cartilage
		Keratin	Hair, nails
		Fibrin	Blood clot
Motion	Muscle	Actin	Contraction of muscle fibers
		Myosin	Contraction of muscle fibers
Osmotic regulation	Albumin	Serum albumin	Maintains osmotic concentration of blood
Regulation of gene action	Repressors	lac repressor	Regulates transcription
Regulation of body functions	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

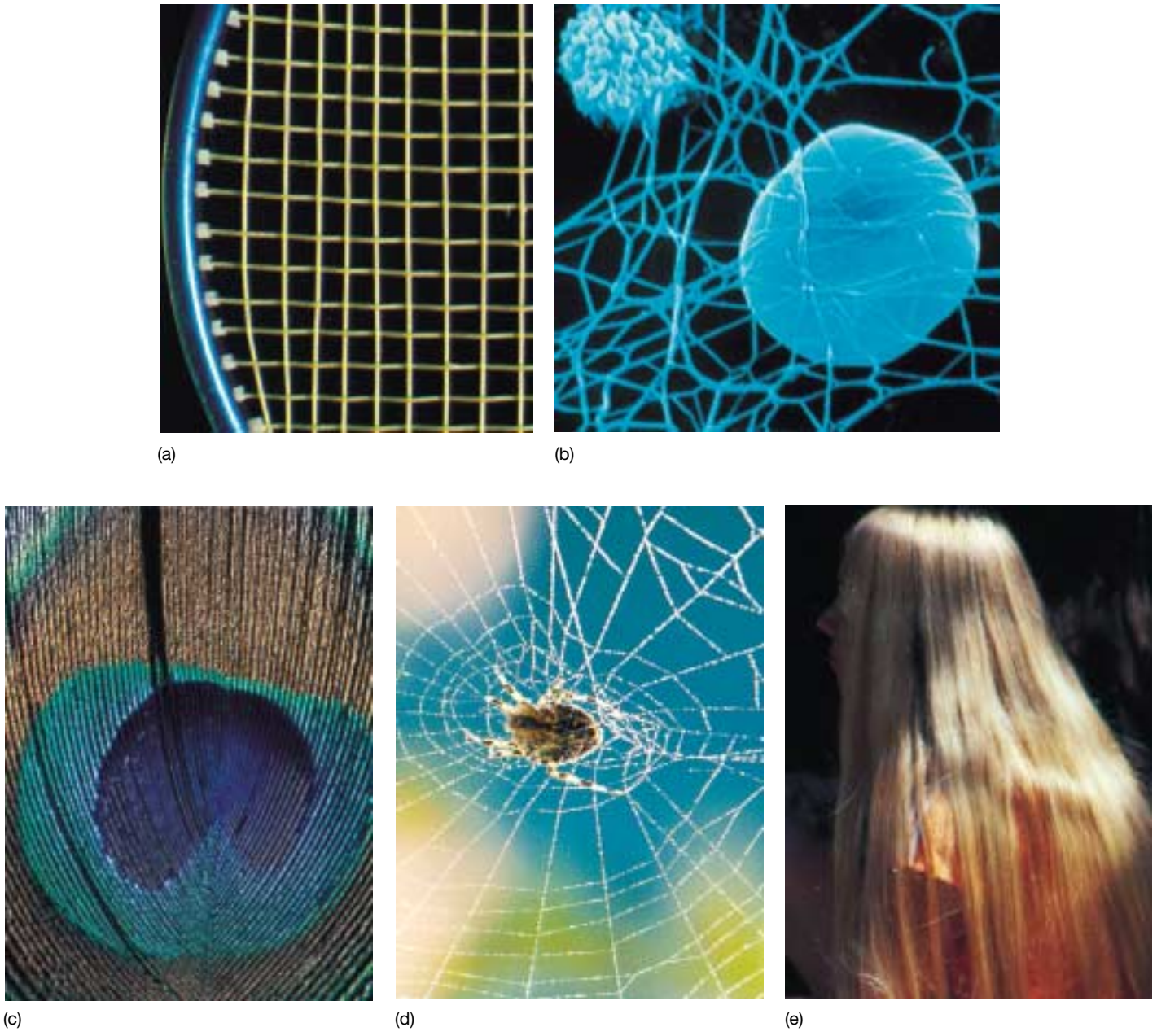


FIGURE 3.4
Some of the more common structural proteins. (*a*) Collagen: strings of a tennis racket from gut tissue; (*b*) fibrin: scanning electron micrograph of a blood clot (3000×); (*c*) keratin: a peacock feather; (*d*) silk: a spider's web; (*e*) keratin: human hair.

4. **Support.** Fibrous, or threadlike, proteins play structural roles; these structural proteins (see figure 3.4) include keratin in hair, fibrin in blood clots, and collagen, which 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 filament: 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 also receive information, acting as cell surface receptors.

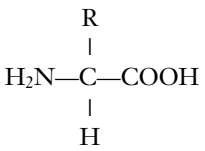
Proteins carry out a diverse array of functions, including catalysis, defense, transport of substances, motion, and regulation of cell and body functions.

Amino Acids Are the Building Blocks of Proteins

Although proteins are complex and versatile molecules, they are all polymers of only 20 amino acids, in a specific order. Many scientists believe amino acids were among the first molecules formed in 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

An **amino acid** is a molecule containing an amino group ($—NH_2$), a carboxyl group (—COOH), and a hydrogen atom, all bonded to a central carbon atom:



Each amino acid has unique chemical properties determined by the nature of the side group (indicated by R) covalently bonded to the central carbon atom. For example, when the side group is $—CH_2OH$, the amino acid (serine) is polar, but when the side group is $—CH_3$, the amino acid (alanine) is nonpolar. The 20 common amino acids are grouped into five chemical classes, based on their side groups:

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 only —H).
3. Ionizable amino acids, such as glutamic acid, have R groups that contain acids or bases.
4. Aromatic amino acids, such as phenylalanine, have R groups that contain an organic (carbon) ring with alternating single and double bonds.
5. Special-function amino acids have unique individual properties; methionine often is the first amino acid in a chain of amino acids, proline causes kinks in chains, and cysteine links chains together.

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

Proteins Are Polymers of Amino Acids

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 end. The amino and carboxyl groups on a pair of amino acids can undergo a condensation reaction, losing a molecule of water and forming a covalent bond. A covalent bond that links two amino acids is called a **peptide bond** (figure 3.5). 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, unlike the N—C and C—C bonds to the central carbon of the amino acid. The stiffness of the peptide bond is one factor that makes it possible for chains of amino acids to form coils and other regular shapes.

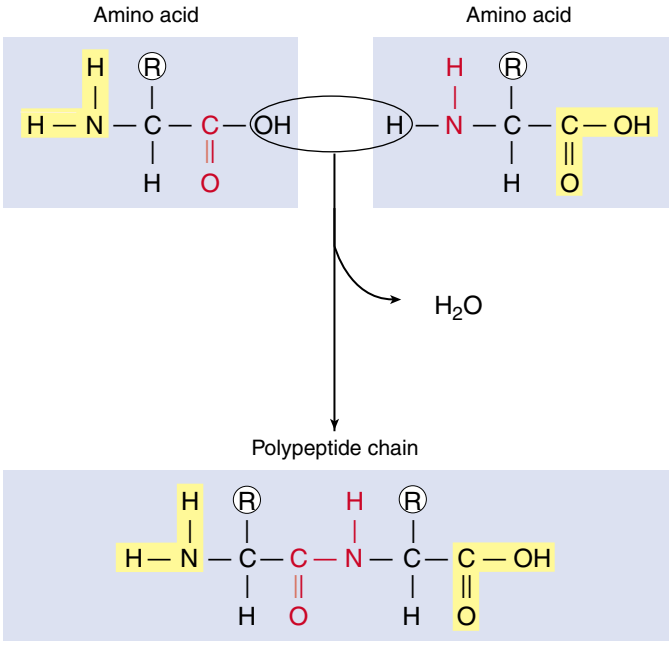


FIGURE 3.5
The peptide bond. A peptide bond forms when the $—NH_2$ end of one amino acid joins to the —COOH end of another. Because of the partial double-bond nature of peptide bonds, the resulting peptide chain cannot rotate freely around these bonds.

A **protein** is composed of one or more long chains, or **polypeptides,** composed of amino acids linked by peptide bonds. It was not until the pioneering work of Frederick Sanger in the early 1950s that it became clear that each kind of protein had a specific amino acid sequence. Sanger succeeded in determining the amino acid sequence of insulin and in so doing demonstrated clearly that this protein had a defined sequence, the same for all insulin molecules in the solution. Although many different amino acids occur in nature, only 20 commonly occur in proteins. Figure 3.6 illustrates these 20 "common" amino acids and their side groups.

A protein is a polymer containing a combination of up to 20 different kinds of amino acids. The amino acids fall into five chemical classes, each with different properties. These properties determine the nature of the resulting protein.

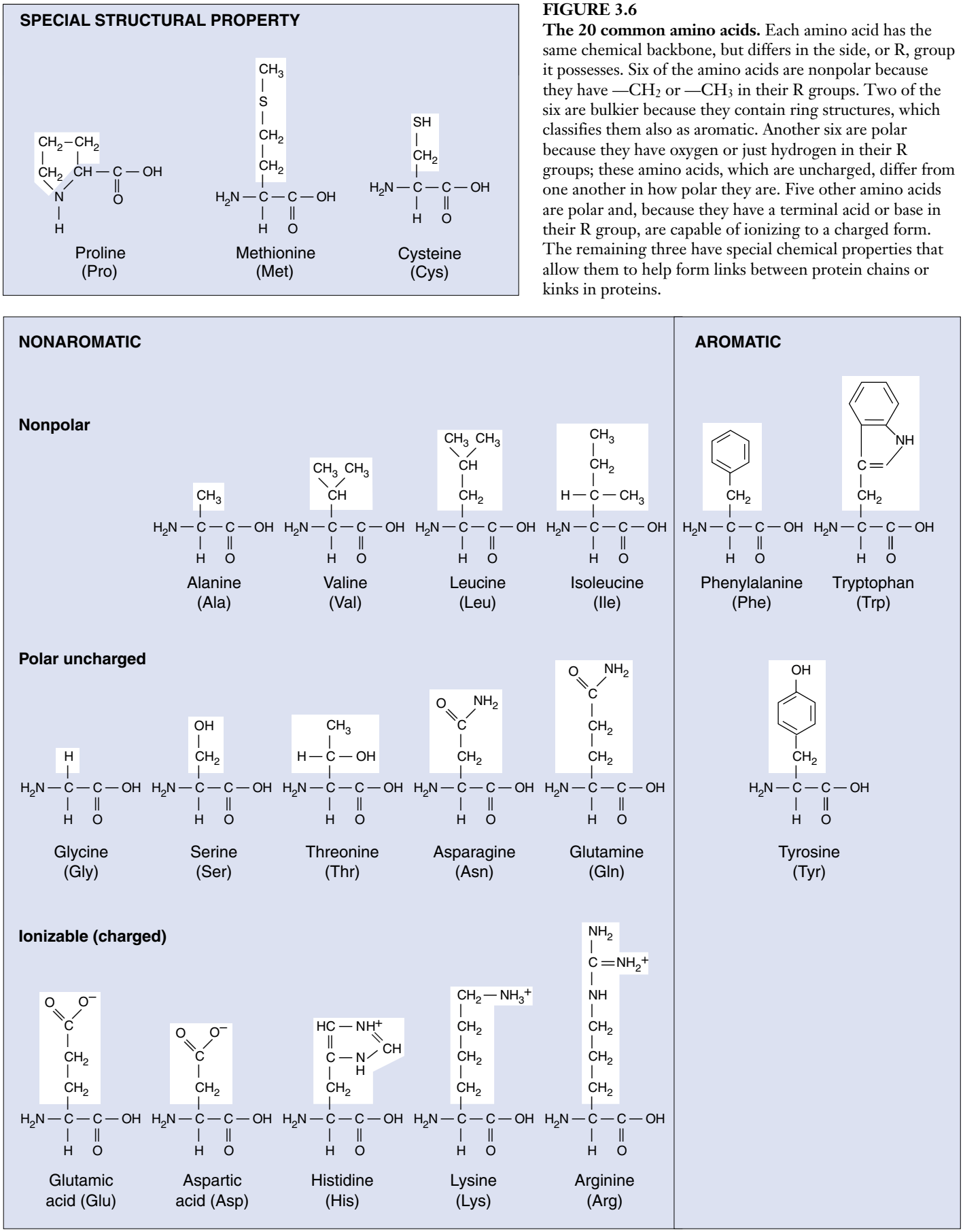


FIGURE 3.6
The 20 common amino acids. Each amino acid has the same chemical backbone, but differs in the side, or R, group it possesses. Six of the amino acids are nonpolar because they have —CH_2 or —CH_3 in their R groups. Two of the six are bulkier because they contain ring structures, which classifies them also as aromatic. Another six are polar because they have oxygen or just hydrogen in their R groups; these amino acids, which are uncharged, differ from one another in how polar they are. Five other amino acids are polar and, because they have a terminal acid or base in their R group, are capable of ionizing to a charged form. The remaining three have special chemical properties that allow them to help form links between protein chains or kinks in proteins.

A Protein's Function Depends on the Shape of the Molecule

The shape of a protein is very important because it determines the protein's function. If we picture a polypeptide as a long strand similar to a reed, a protein might be the basket woven from it.

Overview of Protein Structure

Proteins consist of long amino acid chains folded into complex shapes. What do we know about the shape of these proteins? One way to study the shape of something as small as a protein is to look at it with very short wavelength energy—with X rays. X-ray diffraction is 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, soon followed by the related protein hemoglobin. As more and more proteins were added to the list, 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. This positions the nonpolar amino acids in 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.

Levels of Protein Structure

The structure of proteins is traditionally discussed in terms of four levels of structure, as *primary*, *secondary*, *tertiary*, and *quaternary* (figure 3.7). Because of progress in our knowledge of protein structure, two additional levels of structure are increasingly distinguished by molecular biologists: *motifs* and *domains*. Because these latter two elements play important roles in coming chapters, we introduce them here.

Primary Structure. The specific amino acid sequence of a protein is its primary structure. This sequence is determined by the nucleotide sequence of the gene that encodes the protein. Because the R groups that distinguish the various amino acids play no role in the peptide backbone of proteins, a protein can consist of any sequence of amino acids. Thus, 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

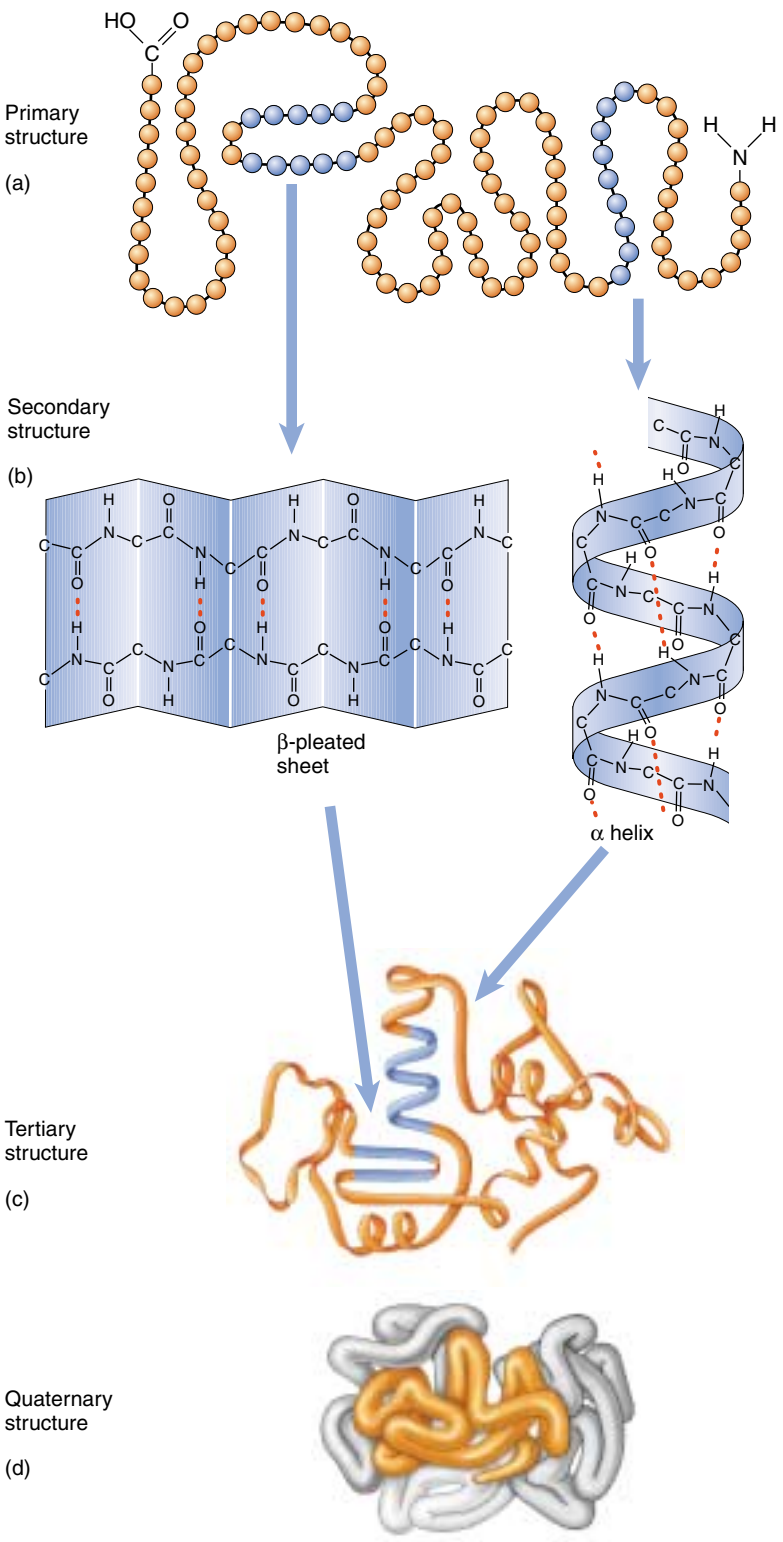


FIGURE 3.7
Levels of protein structure. The amino acid sequence of a protein is called its (*a*) primary structure. Hydrogen bonds form between nearby amino acids, producing (*b*) fold-backs called beta-pleated sheets and coils called alpha helices. These fold-backs and coils constitute the protein's secondary structure. A globular protein folds up on itself further to assume a three-dimensional (*c*) tertiary structure. Many proteins aggregate with other polypeptide chains in clusters; this clustering is called the (*d*) quaternary structure of the protein.

followed by 130 zeros—more than the number of atoms known in the universe). This is an important property of proteins because it permits such great diversity.

Secondary Structure. The amino acid side groups are not the only portions of proteins that form hydrogen bonds. The —COOH and —NH_2 groups of the main chain also form quite good hydrogen bonds—so good that their interactions with water might be expected to offset the tendency of nonpolar sidegroups to be forced into the protein interior. Inspection of the protein structures determined by X-ray diffraction reveals why they don't—the polar groups of the main chain form hydrogen bonds with each other! Two patterns of H bonding occur. In one, hydrogen bonds form along a single chain, linking one amino acid to another farther down the chain. This tends to pull the chain into a coil called an alpha (α) helix. In the other pattern, hydrogen bonds occur across two chains, linking the amino acids in one chain to those in the other. Often, many parallel chains are linked, forming a pleated, sheet-like structure called a β-pleated sheet. The folding of the amino acid chain by hydrogen bonding into these characteristic coils and pleats is called a protein's secondary structure.

Motifs. The elements of secondary structure can combine in proteins in characteristic ways called motifs, or sometimes "supersecondary structure." One very common 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 is a β α β α β motif. A second motif that occurs in many proteins is the β barrel, a β sheet folded around to form a tube. A third type of motif, the α turn α motif, is important because many proteins use it to bind the DNA double helix.

Tertiary Structure. The final folded shape of a globular protein, which positions the various motifs and folds nonpolar side groups into the interior, is called a protein's tertiary structure. A protein is driven into its tertiary structure by hydrophobic interactions with water. The final folding of a protein is determined by its primary structure—by the chemical nature of its side groups. Many proteins can be fully unfolded ("denatured") and will spontaneously refold back into their characteristic shape.

The stability of a protein, once it has folded into its 3-D shape, is strongly influenced by how well its interior fits together. When two nonpolar chains in the interior are in very close proximity, they experience a form of molecular attraction called van der Waal's 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. They are effective forces only over short distances, however; there are no "holes" or cavities in the interior of proteins. That is why there are so many different nonpolar amino acids (alanine, valine, leucine, isoleucine). Each has a different-sized R group, allowing very precise fitting of nonpolar chains within the protein interior. Now you can understand why a mutation that converts one nonpolar amino acid within the protein interior (alanine) into another (leucine) very often disrupts the protein's stability; leucine is a lot bigger than alanine and disrupts the precise way the chains fit together within the protein interior. A change in even a single amino acid can have profound effects on protein shape and can result in loss or altered function of the protein.

Domains. Many proteins in your body are encoded within your genes in functional sections called exons (exons will be discussed in detail in chapter 15). Each exon-encoded section of a protein, typically 100 to 200 amino acids long, folds into a structurally independent functional unit called a **domain.** As the polypeptide chain folds, the domains fold into their proper shape, each more-or-less independent of the others. This can be demonstrated experimentally by artificially producing the fragment of polypeptide that forms the domain in the intact protein, and showing that the fragment folds to form the same structure as it does in the intact protein.

A single polypeptide chain connects the domains of a protein, like a rope tied into several adjacent knots. Often the domains of a protein have quite separate functions—one domain of an enzyme might bind a cofactor, for example, and another the enzyme's substrate.

Quaternary Structure. When two or more polypeptide chains associate to form a functional protein, the individual chains are referred to as subunits of the protein. The subunits need not be the same. Hemoglobin, for example, is a protein composed of two α-chain subunits and two β-chain subunits. A protein's subunit arrangement is called its quaternary structure. In proteins composed of subunits, the interfaces where the subunits contact one another are often nonpolar, and play a key role in transmitting information between the subunits about individual subunit activities.

A change in the identity of one of these amino acids can have profound effects. Sickle cell hemoglobin is a mutation that alters the identity of a single amino acid at the corner of the β subunit from polar glutamate to nonpolar valine. Putting a nonpolar amino acid on the surface creates a "sticky patch" that causes one hemoglobin molecule to stick to another, forming long nonfunctional chains and leading to the cell sickling characteristic of this hereditary disorder.

Protein structure can be viewed at six levels: 1. the amino acid sequence, or primary structure; 2. coils and sheets, called secondary structure; 3. folds or creases, called motifs; 4. the three-dimensional shape, called tertiary structure; 5. functional units, called domains; and 6. individual polypeptide subunits associated in a quaternary structure.

How Proteins Fold Into Their Functional Shape

How does a protein fold into a specific shape? Nonpolar amino acids play a key role. Until recently, investigators thought that newly made proteins fold spontaneously as hydrophobic interactions with water shove nonpolar amino acids into the protein interior. We now know this is too simple a view. 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 the same protein environment that occurs in a cell, they stick to other unwanted protein partners, forming a gluey mess.

Chaperonins

How do cells avoid this? A vital clue came in studies of unusual mutations that prevented viruses from replicating in *E. coli* bacterial cells—it turned out the virus proteins could not fold properly! Further study revealed that normal cells contain special proteins called **chaperonins** that help new proteins fold correctly (figure 3.8). When the *E. coli* gene encoding its chaperone protein is disabled by mutation, the bacteria die, clogged with lumps of incorrectly folded proteins. Fully 30% of the bacteria's proteins fail to fold to the right shape.

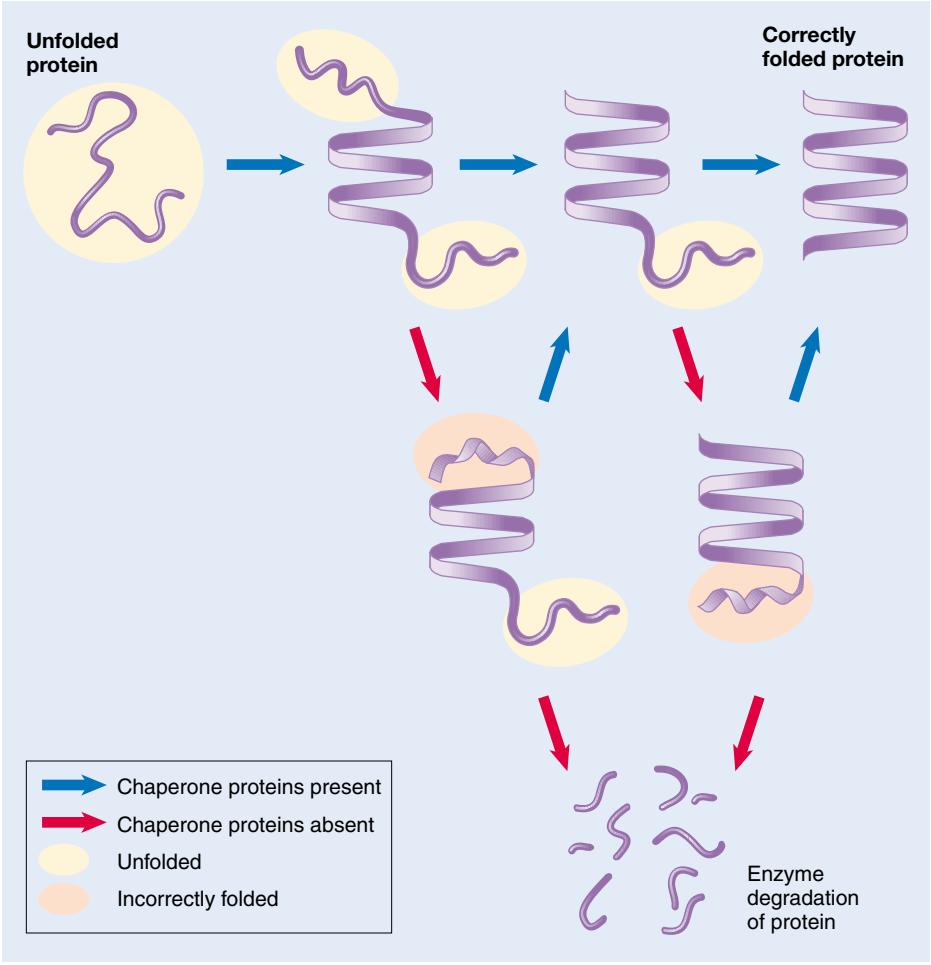


FIGURE 3.8
A current model of protein folding. A newly synthesized protein rapidly folds into characteristic motifs composed of α helices and β sheets, but these elements of structure are only roughly aligned in an open conformation. Subsequent folding occurs more slowly, by trial and error. This process is aided by chaperone proteins, which appear to recognize improperly folded proteins and unfold them, giving them another chance to fold properly. Eventually, if proper folding is not achieved, the misfolded protein is degraded by proteolytic enzymes.

Molecular biologists have now identified more than 17 kinds of proteins that act as molecular chaperones. Many are heat shock proteins, produced in greatly elevated amounts if a cell is exposed to elevated temperature; high temperatures cause proteins to unfold, and heat shock chaperonins help the cell's proteins refold.

There is considerable controversy about how chaperonins work. It was first thought that they provided a protected environment within which folding could take place unhindered by other proteins, but it now seems more likely that chaperonins rescue proteins that are caught in a wrongly folded state, giving them another chance to fold correctly. When investigators "fed" a deliberately misfolded protein called malate dehydrogenase to chaperonins, the protein was rescued, refolding to its active shape.

Protein Folding and Disease

There are tantalizing suggestions that chaperone protein deficiencies may play a role in certain diseases by failing to facilitate the intricate folding of key proteins. Cystic fibrosis is a hereditary disorder in which a mutation disables a protein that plays a vital part in moving ions across cell membranes. In at least some cases, the vital membrane protein appears to have the correct amino acid sequence, but fails to fold to its final form. It has also been speculated that chaperone deficiency may be a cause of the protein clumping in brain cells that produces the amyloid plaques characteristic of Alzheimer's disease.

Proteins called chaperones aid newly produced proteins to fold properly.

How Proteins Unfold

If a protein's environment is altered, the protein may change its shape or even unfold. This process is called **denaturation.** Proteins can be denatured when the pH, temperature, or ionic concentration of the surrounding solution is changed. When proteins are denatured, they are usually rendered biologically inactive. This 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 remain functional. That is the rationale behind traditional methods of salt-curing and pickling: prior to the ready availability of refrigerators and freezers, the only practical way to keep microorganisms from growing in food was to keep the food in a solution containing high salt or vinegar concentrations, which denatured the enzymes of microorganisms and kept them from growing on the food.

Most enzymes function within a very narrow range of physical parameters. 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. On the other hand, the protein-degrading enzymes that function at a pH of 2 or less in the stomach would be denatured in the basic pH of the blood. Similarly, organisms that live near oceanic hydrothermal vents have enzymes that work well at the temperature of this extreme environment (over 100°C). They cannot survive in cooler waters, because their enzymes would denature 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 3.9). Larger proteins can rarely refold spontaneously because of the complex nature of their final shape. It is important to distinguish denaturation from **dissociation.** The four subunits of hemoglobin (figure 3.10) may dissociate into four individual molecules (two α-globin and two β-globin) without denaturation of the folded globin proteins, and will readily reassume their four-subunit quaternary structure.

Every globular protein has a narrow range of conditions in which it folds properly; outside that range, proteins tend to unfold.

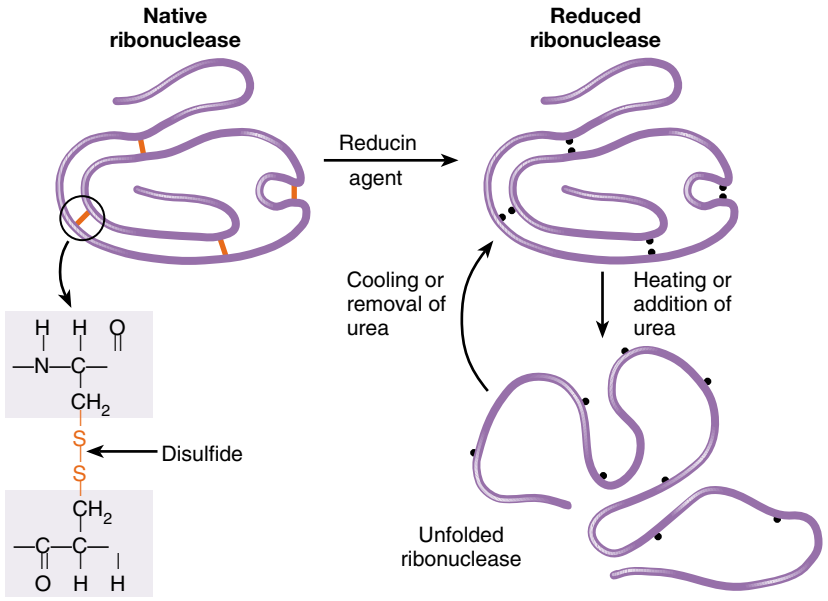


FIGURE 3.9
Primary structure determines tertiary structure. When the protein ribonuclease is treated with reducing agents to break the covalent disulfide bonds that cross-link its chains, and then placed in urea or heated, the protein denatures (unfolds) and loses its enzymatic activity. Upon cooling or removal of urea, it refolds and regains its enzymatic activity. This demonstrates that no information but the amino acid sequence of the protein is required for proper folding: the primary structure of the protein determines its tertiary structure.

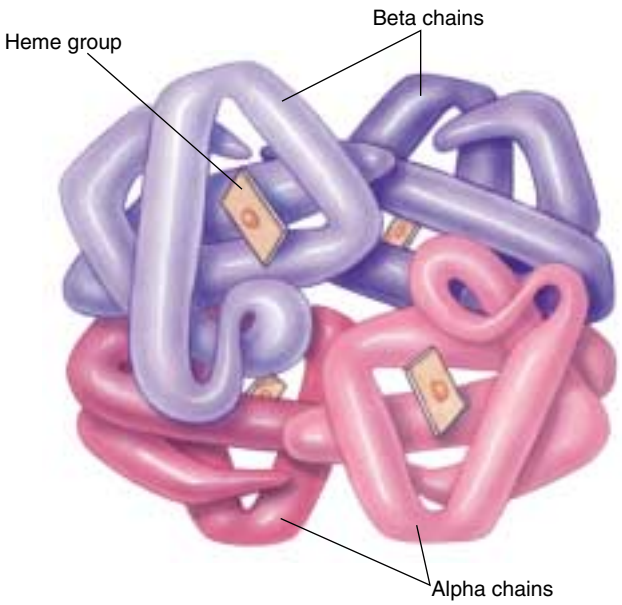


FIGURE 3.10
The four subunits of hemoglobin. The hemoglobin molecule is made of four globin protein subunits, informally referred to as polypeptide chains. The two lower α chains, identical α-globin proteins, are shaded pink; the two upper β chains, identical β-globin proteins, are shaded blue.

3.3 Nucleic acids store and transfer genetic information.

Information Molecules

The biochemical activity of a cell depends on production of a large number of proteins, each with a specific sequence. The ability to produce the correct proteins is passed between generations of organisms, even though the protein molecules themselves are not.

Nucleic acids are the information storage devices of cells, just as disks or tapes store the information that computers use, blueprints store the information that builders use, and road maps store the information that tourists use. There are two varieties of nucleic acids: *deoxyribonucleic acid* (**DNA;** figure 3.11) and *ribonucleic acid* (**RNA**). The way in which DNA encodes the information used to assemble proteins is similar to the way in which the letters on a page encode information (see chapter 14). Unique among macromolecules, nucleic acids are able to serve as templates to produce precise copies of themselves, so that the information that specifies what an organism is can be copied and passed down to its descendants. For this reason, DNA is often referred to as the hereditary material. Cells use the alternative form of nucleic acid, RNA, to read the cell's DNA-encoded information and direct the synthesis of proteins. RNA is similar to DNA in structure and is made as a transcripted copy of portions of the DNA. This transcript passes out into the rest of the cell, where it serves as a blueprint specifying a protein's amino acid sequence. This process will be described in detail in chapter 15.

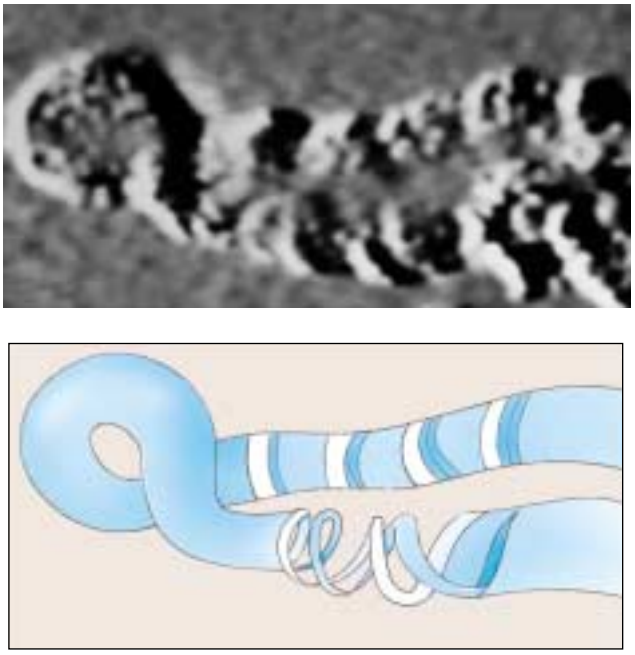


FIGURE 3.11
The first photograph of a DNA molecule. This micrograph, with sketch below, shows a section of DNA magnified a million times! The molecule is so slender that it would take 50,000 of them to equal the diameter of a human hair.

"Seeing" DNA

DNA molecules cannot be seen with an optical microscope, which is incapable of resolving anything smaller than 1000 atoms across. An electron microscope can image structures as small as a few dozen atoms across, but still cannot resolve the individual atoms of a DNA strand. This limitation was finally overcome in the last decade with the introduction of the scanning-tunneling microscope (figure 3.12).

How do these microscopes work? Imagine you are in a dark room with a chair. To determine the shape of the chair, you could shine a flashlight on it, so that the light bounces off the chair and forms an image on your eye. That's what optical and electron microscopes do; in the latter, the "flashlight" emits a beam of electrons instead of light. You could, however, also reach out and feel the chair's surface with your hand. In effect, you would be putting a probe (your hand) near the chair and measuring how far away the surface is. In a scanning-tunneling microscope, computers advance a probe over the surface of a molecule in steps smaller than the diameter of an atom.

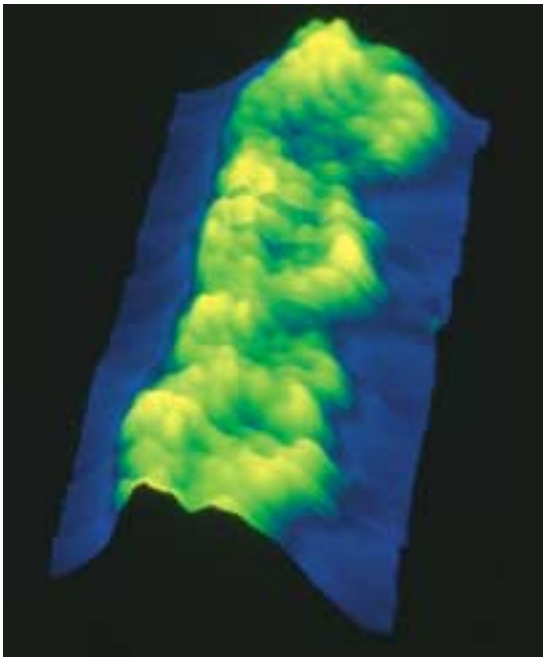


FIGURE 3.12
A scanning tunneling micrograph of DNA (false color; 2,000,000×). The micrograph shows approximately three turns of the DNA double helix (see figure 3.15).

The Structure of Nucleic Acids

Nucleic acids are long polymers of repeating subunits called **nucleotides.** Each nucleotide consists of three components: a five-carbon sugar (ribose in RNA and deoxyribose in DNA); a phosphate ($—PO_4$) group; and an organic nitrogen-containing base (figure 3.13). When a nucleic acid polymer forms, the phosphate group of one nucleotide binds to the hydroxyl group of another, releasing water and forming a phosphodiester bond. A **nucleic acid,** then, is simply a chain of five-carbon sugars linked together by phosphodiester bonds with an organic base protruding from each sugar (figure 3.14).

Two types of organic bases occur in nucleotides. The first type, *purines*, are large, double-ring molecules found in both DNA and RNA; they are adenine (A) and guanine (G). The second type, *pyrimidines*, are smaller, single-ring molecules; they include cytosine (C, in both DNA and RNA), thymine (T, in DNA only), and uracil (U, in RNA only).

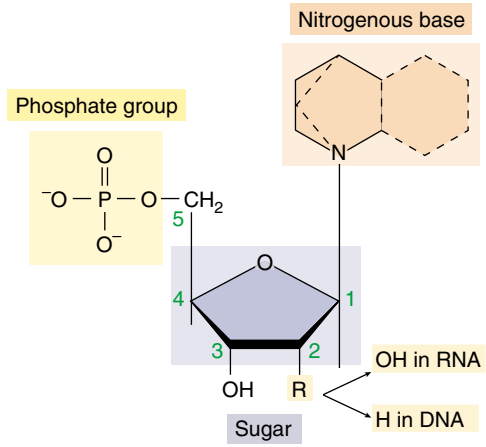


FIGURE 3.13
Structure of a nucleotide. The nucleotide subunits of DNA and RNA are made up of three elements: a five-carbon sugar, an organic nitrogenous base, and a phosphate group.

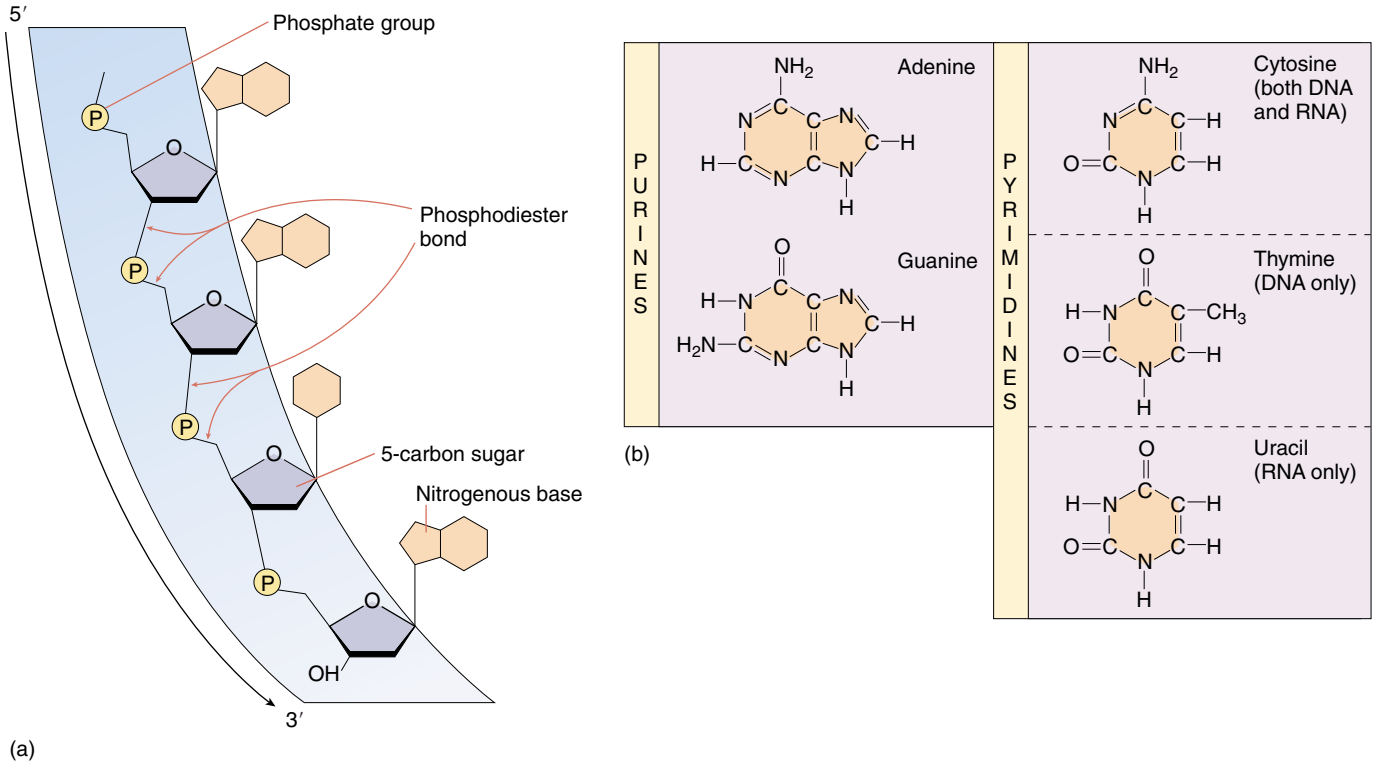


FIGURE 3.14
The structure of a nucleic acid and the organic nitrogen-containing bases. (*a*) In a nucleic acid, nucleotides are linked to one another via phosphodiester bonds, with organic bases protruding from the chain. (*b*) The organic nitrogenous bases can be either purines or pyrimidines. In DNA, thymine replaces the uracil found in RNA.

DNA

Organisms encode the information specifying the amino acid sequences of their proteins as sequences of nucleotides in the DNA. This method of encoding information is very similar to that by which the sequences of letters encode information in a sentence. While a sentence written in English consists of a combination of the 26 different letters of the alphabet in a specific order, the code of a DNA molecule consists of different combinations of the four types of nucleotides in specific sequences such as CGCTTACG. The information encoded in DNA is used in the everyday metabolism of the organism and is passed on to the organism's descendants.

DNA molecules in organisms exist not as single chains folded into complex shapes, like proteins, but rather as double chains. Two DNA polymers wind around each other like the outside and inside rails of a circular staircase. Such a winding shape is called a helix, and a helix composed of two chains winding about one another, as in DNA, is called a **double helix.** Each step of DNA's helical staircase is a base-pair, consisting of a base in one chain attracted by hydrogen bonds to a base opposite it on the other chain. These hydrogen bonds hold the two chains together as a duplex (figure 3.15). The base-pairing rules are rigid: adenine can pair only with thymine (in DNA) or with uracil (in RNA), and cytosine can pair only 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.

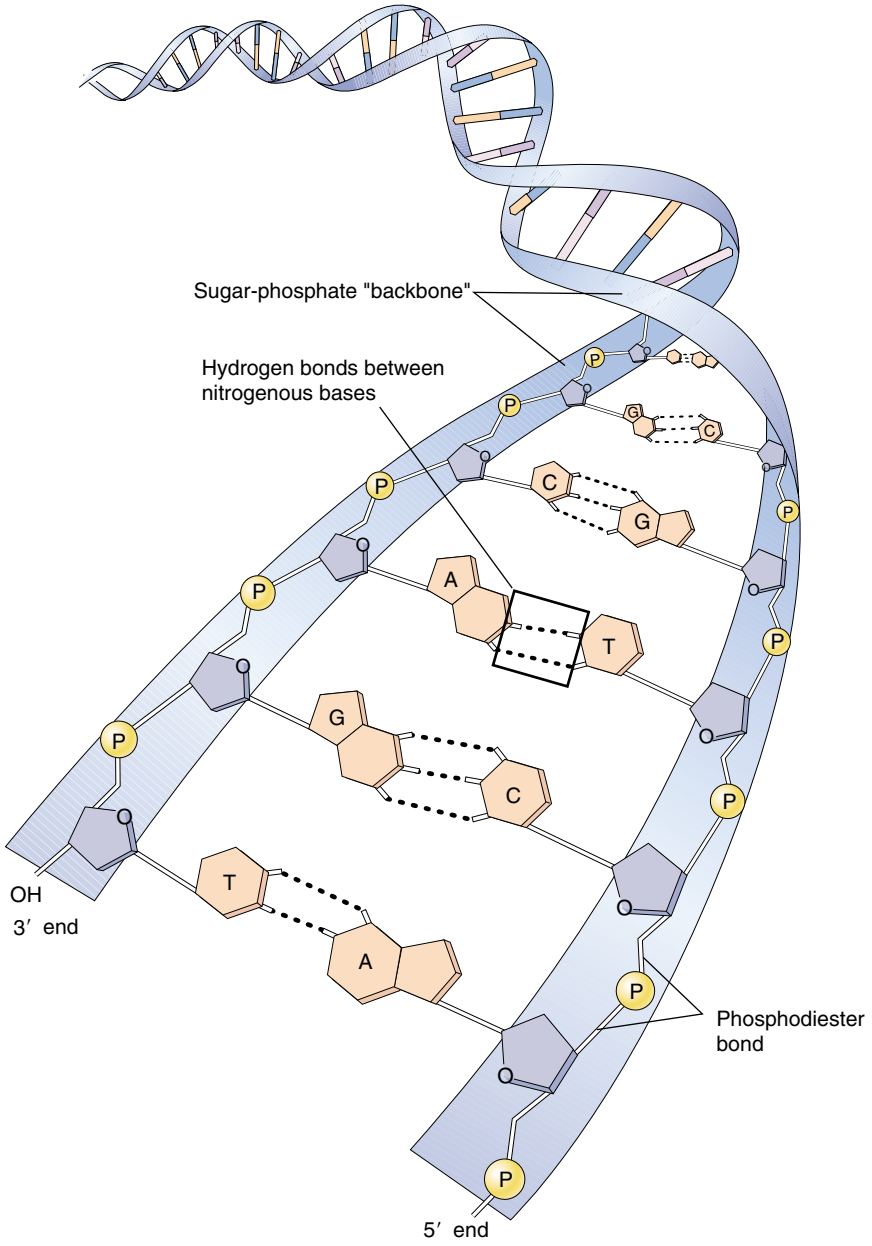
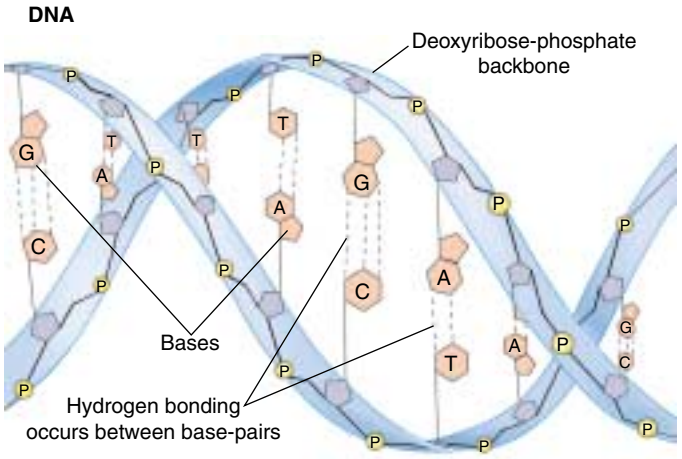


FIGURE 3.15
The structure of DNA. Hydrogen bond formation (dashed lines) between the organic bases, called base-pairing, causes the two chains of a DNA duplex to bind to each other and form a double helix.

RNA

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

Transcribing the DNA message into a chemically different molecule such as RNA allows the cell to tell which is the original information storage molecule and which is the transcript. DNA molecules are always double-stranded (except for a few single-stranded DNA viruses that will be discussed in chapter 33), while the RNA molecules transcribed from DNA are typically single-stranded (figure



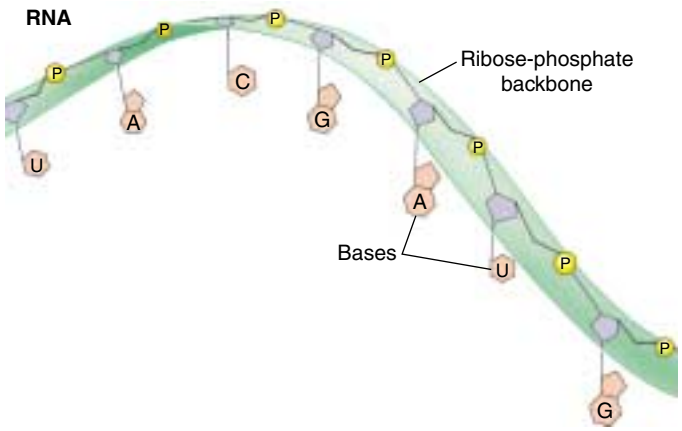


FIGURE 3.16
DNA versus RNA. DNA forms a double helix, uses deoxyribose as the sugar in its sugar-phosphate backbone, and utilizes thymine among its nitrogenous bases. RNA, on the other hand, is usually single-stranded, uses ribose as the sugar in its sugar-phosphate backbone, and utilizes uracil in place of thymine.

3.16). Although there is no chemical reason why RNA cannot form double helices as DNA does, cells do not possess the enzymes necessary to assemble double strands of RNA, as they do for DNA. Using two different molecules, one single-stranded and the other double-stranded, separates the role of DNA in storing hereditary information from the role of RNA in using this information to specify protein structure.

Which Came First, DNA or RNA?

The information necessary for the synthesis of proteins is stored in the cell's double-stranded DNA base sequences. The cell uses this information by first making an RNA transcript of it: RNA nucleotides pair with complementary

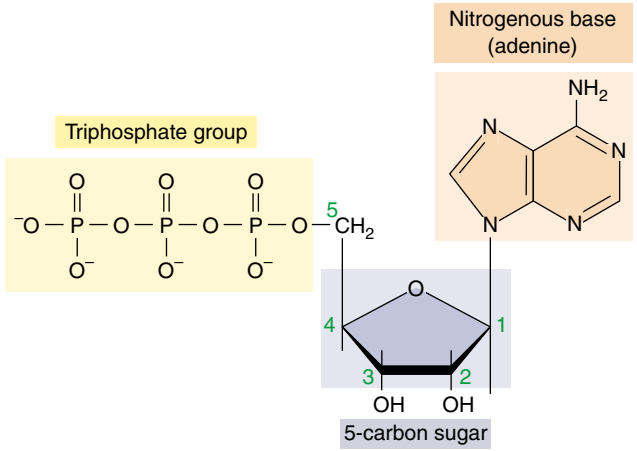


FIGURE 3.17
ATP. Adenosine triphosphate (ATP) contains adenine, a five-carbon sugar, and three phosphate groups. This molecule serves to transfer energy rather than store genetic information.

DNA nucleotides. By storing the information in DNA while using a complementary RNA sequence to actually direct protein synthesis, the cell does not expose the information-encoding DNA chain to the dangers of single-strand cleavage every time the information is used. Therefore, DNA is thought to have evolved from RNA as a means of preserving the genetic information, protecting it from the ongoing wear and tear associated with cellular activity. This genetic system has come down to us from the very beginnings of life.

The cell uses the single-stranded, short-lived RNA transcript to direct the synthesis of a protein with a specific sequence of amino acids. Thus, the information flows from DNA to RNA to protein, a process that has been termed the "central dogma" of molecular biology.

ATP

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* (ATP; figure 3.17), the energy currency of the cell. It also occurs in the molecules *nicotinamide adenine dinucleotide* (NAD^+) and *flavin adenine dinucleotide* (FAD^+), which carry electrons whose energy is used to make ATP.

A nucleic acid is a long chain of five-carbon sugars with an organic base protruding from each sugar. DNA is a double-stranded helix that stores hereditary information as a specific sequence of nucleotide bases. RNA is a single-stranded molecule that transcribes this information to direct protein synthesis.

3.4 Lipids make membranes and store energy.

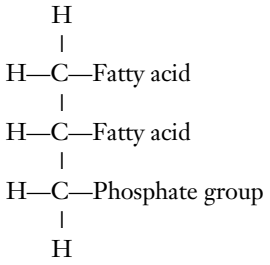
Lipids are a loosely defined group of molecules with one main characteristic: they are insoluble in water. The most familiar lipids are fats and oils. Lipids have a very high proportion of nonpolar carbon-hydrogen (C—H) bonds, and so long-chain lipids cannot fold up like a protein to sequester their nonpolar portions away from the surrounding aqueous environment. Instead, when placed in water many lipid molecules will spontaneously cluster together and expose what polar groups they have to the surrounding water while sequestering the nonpolar parts of the molecules together within the cluster. This spontaneous assembly of lipids is of paramount importance to cells, as it underlies the structure of cellular membranes.

Phospholipids Form Membranes

Phospholipids are among the most important molecules of the cell, as they form the core of all biological membranes. An individual phospholipid is a composite molecule, made up of three kinds of subunits:

1. Glycerol, a three-carbon alcohol, with each carbon bearing a hydroxyl group. Glycerol forms the backbone of the phospholipid molecule.
2. *Fatty acids*, long chains of C—H bonds (hydrocarbon chains) ending in a carboxyl (—COOH) group. Two fatty acids are attached to the glycerol backbone in a phospholipid molecule.
3. Phosphate group, 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. In water, the nonpolar tails of nearby phospholipids aggregate away from the water, forming two layers of tails pointed toward each other—a lipid bilayer (figure 3.18). Lipid bilayers are the basic framework of biological membranes, discussed in detail in chapter 6.



Because the C—H bonds in lipids are very nonpolar, they are not water-soluble, and aggregate together in water. This kind of aggregation by phospholipids forms biological membranes.

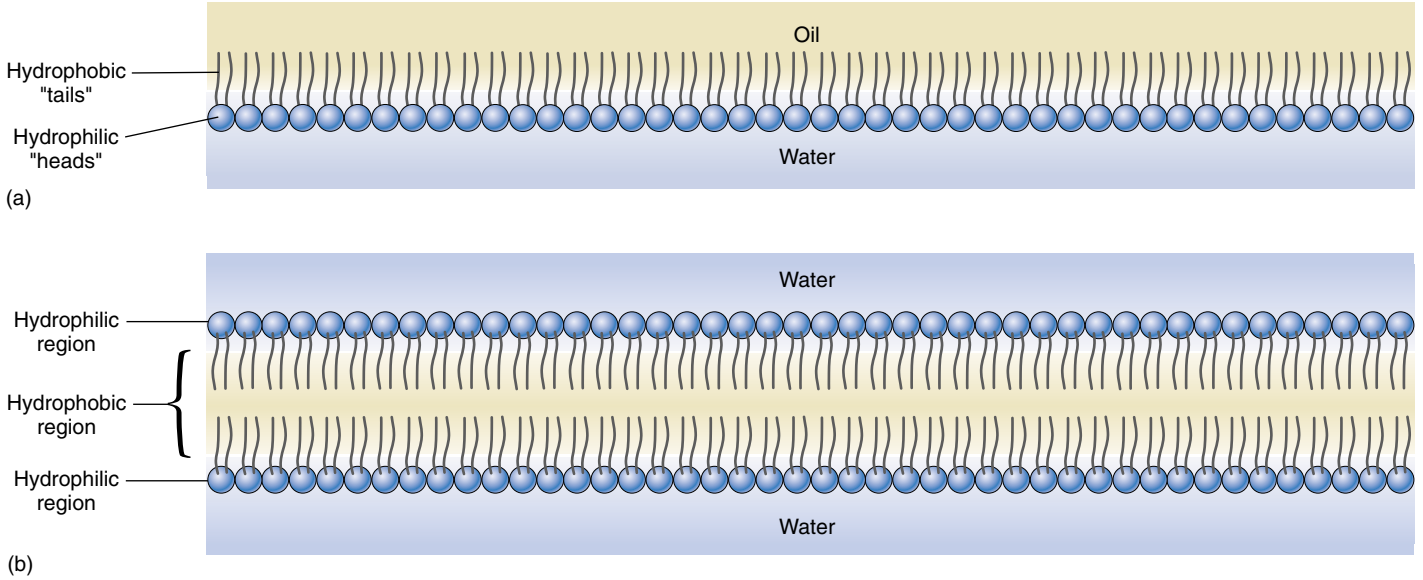


FIGURE 3.18
Phospholipids. (*a*) At an oil-water interface, phospholipid molecules will orient so that their polar (hydrophilic) heads are in the polar medium, water, and their nonpolar (hydrophobic) tails are in the nonpolar medium, oil. (*b*) When surrounded by water, phospholipid molecules arrange themselves into two layers with their heads extending outward and their tails inward.

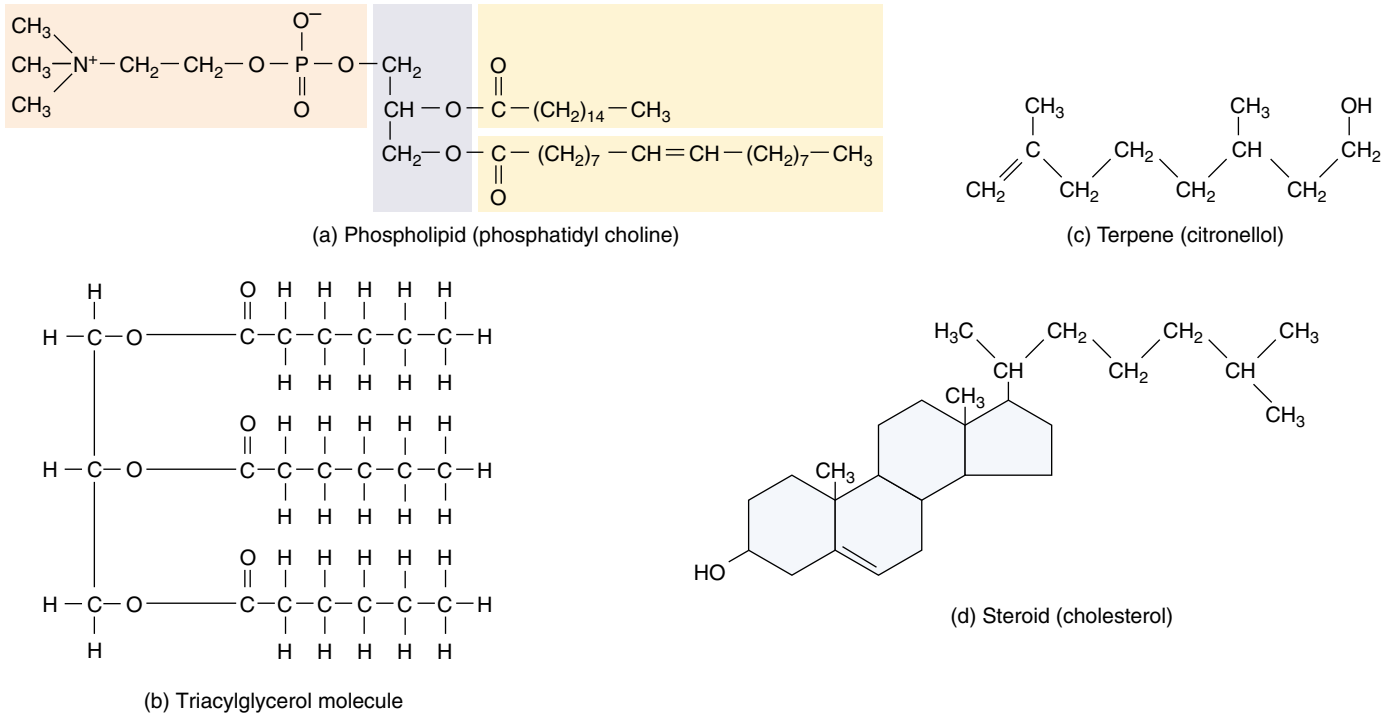


FIGURE 3.19
Lipids. These structures represent four major classes of biologically important lipids: (*a*) phospholipids, (*b*) triacylglycerols (triglycerides), (*c*) terpenes, and (*d*) steroids.

Fats and Other Kinds of Lipids

Fats are another kind of lipid, but unlike phospholipids, fat molecules do not have a polar end. **Fats** consist of a glycerol molecule to which is attached three fatty acids, one to each carbon of the glycerol backbone. Because it contains three fatty acids, a fat molecule is called a **triglyceride**, or, more properly, a triacylglycerol (figure 3.19). The three fatty acids of a triglyceride need not be identical, and often they differ markedly from one another. Organisms store the energy of certain molecules for long periods in the many C—H bonds of fats.

Because triglyceride molecules lack a polar end, they are not soluble in water. Placed in water, they spontaneously clump together, forming fat globules that are very large relative to the size of the individual molecules. Because fats are insoluble, they can be deposited at specific locations within an organism.

Storage fats are one kind of lipid. Oils such as olive oil, corn oil, and coconut oil are also lipids, as are waxes such as beeswax and earwax (see table 3.1). The hydrocarbon chains of fatty acids vary in length; the most common are even-numbered chains of 14 to 20 carbons. If all of the internal carbon atoms in the fatty acid chains are bonded to at least two hydrogen atoms, the fatty acid is said to be **saturated,** because it contains the maximum possible number of hydrogen atoms (figure 3.20). If a fatty acid has double bonds between one or more pairs of successive carbon atoms, the fatty acid is said to be **unsaturated.** If a given fatty acid has more than one double bond, it is said to be **polyunsaturated.** Fats made from 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. Consequently, a polyunsaturated fat such as corn oil is usually liquid at room temperature and is called an oil. In contrast, most saturated fats such as those in butter are solid at room temperature.

Organisms contain many other kinds of lipids besides fats (see figure 3.19). *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 type of lipid found in membranes, are composed of four carbon rings. Most animal cell membranes contain the steroid cholesterol. Other steroids, such as testosterone and estrogen, function in multicellular organisms as hormones. *Prostaglandins* are a group of about 20 lipids that are modified fatty acids, with two nonpolar "tails" attached to a five-carbon ring. Prostaglandins act as local chemical messengers in many vertebrate tissues.

Cells contain many kinds of molecules in addition to membrane phospholipids that are not soluble in water.

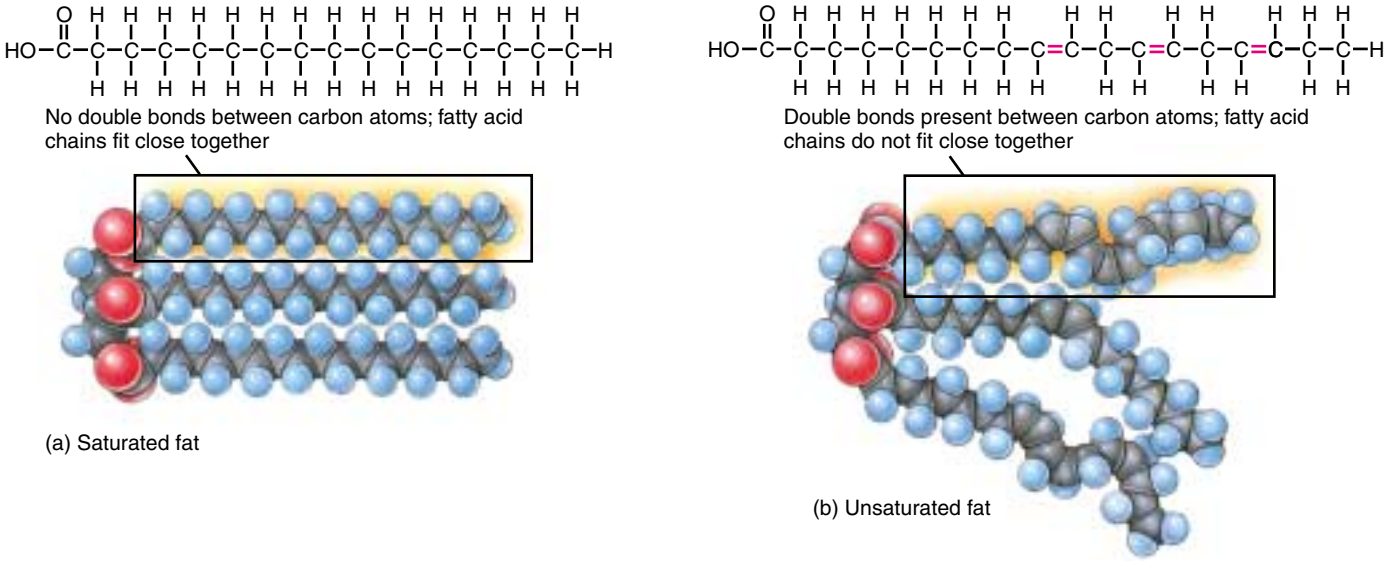


FIGURE 3.20
Saturated and unsaturated fats. (*a*) Palmitic acid, with no double bonds and, thus, a maximum number of hydrogen atoms bonded to the carbon chain, is a saturated fatty acid. Many animal triacylglycerols (fats) are saturated. Because their fatty acid chains can fit closely together, these triacylglycerols form immobile arrays called hard fat. (*b*) Linoleic acid, with three double bonds and, thus, fewer than the maximum number of hydrogen atoms bonded to the carbon chain, is an unsaturated fatty acid. Plant fats are typically unsaturated. The many kinks the double bonds introduce into the fatty acid chains prevent the triacylglycerols from closely aligning and produce oils, which are liquid at room temperature.

Fats as Food

Most fats contain over 40 carbon atoms. The ratio of energy-storing C—H bonds to carbon atoms in fats is more than twice that of carbohydrates (see next section), making fats much more efficient molecules for storing chemical energy. On the average, fats yield about 9 kilocalories (kcal) of chemical energy per gram, as compared with somewhat less than 4 kcal per gram for carbohydrates.

All fats produced by animals are saturated (except some fish oils), while most plant fats are unsaturated. The exceptions are the tropical oils (palm oil and coconut oil), which are saturated despite their fluidity at room temperature. It is possible to convert an oil into a solid fat by adding hydrogen. Peanut butter sold in stores is usually artificially hydrogenated to make the peanut fats solidify, preventing them from separating out as oils while the jar sits on the store shelf. However, artificially hydrogenating unsaturated fats seems to eliminate the health advantage they have over saturated fats, as it makes both equally rich in C—H bonds. Therefore, it now appears that margarine made from hydrogenated corn oil is no better for your health than butter.

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

A diet rich in fats is one of several factors that are thought to contribute to heart disease, particularly to atherosclerosis, a condition in which deposits of fatty tissue called plaque adhere to the lining of blood vessels, blocking the flow of blood. Fragments of plaque, breaking off from a deposit, are a major cause of strokes.

Fats are efficient energy-storage molecules because of their high concentration of C—H bonds.

3.5 Carbohydrates store energy and provide building materials.

Simple Carbohydrates

Carbohydrates function as energy-storage molecules as well as structural elements. Some are small, simple molecules, while others form long polymers.

Sugars Are Simple Carbohydrates

The **carbohydrates** are a loosely defined group of molecules that contain carbon, hydrogen, and oxygen in the molar ratio 1:2:1. Their empirical formula (which lists the atoms in the molecule with subscripts to indicate how many there are of each) 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 they are broken, carbohydrates are well suited for energy storage.

Monosaccharides. The simplest of the carbohydrates are the simple sugars, or **monosaccharides** (Greek *mono*, "single" + Latin *saccharum*, "sugar"). Simple sugars may contain as few as three carbon atoms, but those that play the central role in energy storage have six (figure 3.21). The empirical formula of six-carbon sugars is:

$$C_6H_{12}O_6, \text{ or } (CH_2O)_6$$

Six-carbon sugars can exist in a straight-chain form, but in an aqueous environment they almost always form rings. The most important of these for energy storage is *glucose* (figure 3.22), a six-carbon sugar which has seven energy-storing C—H bonds.

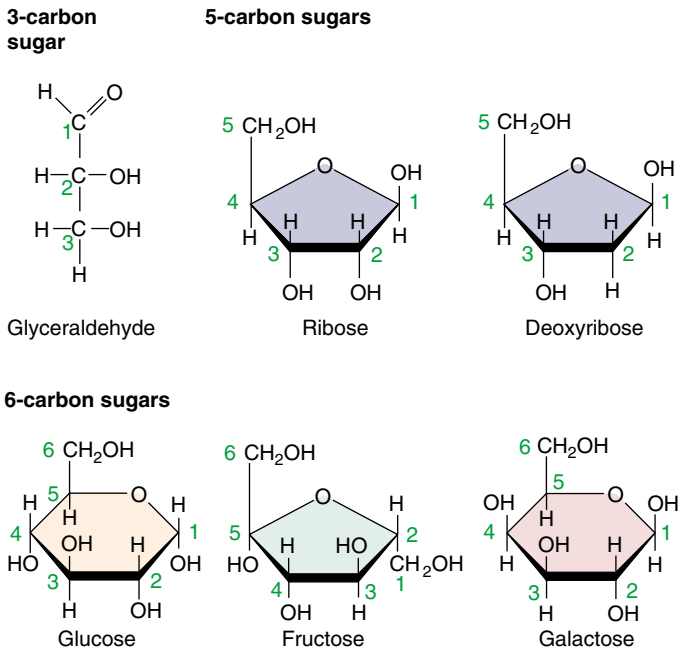


FIGURE 3.21
Monosaccharides. Monosaccharides, or simple sugars, can contain as few as three carbon atoms and are often used as building blocks to form larger molecules. The five-carbon sugars ribose and deoxyribose are components of nucleic acids (see figure 3.15). The six-carbon sugar glucose is a component of large energy-storage molecules.

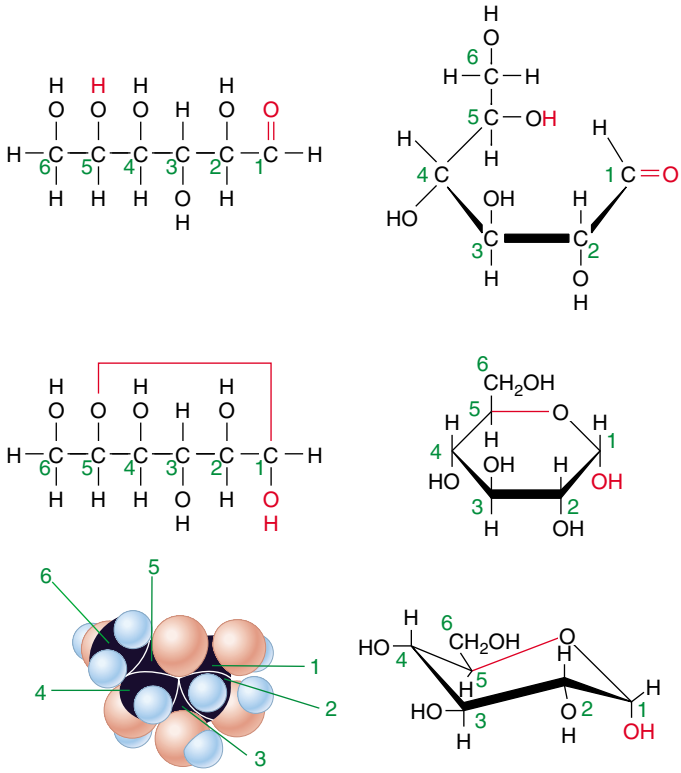


FIGURE 3.22
Structure of the glucose molecule. Glucose is a linear six-carbon molecule that forms a ring shape in solution. The structure of the ring can be represented in many ways; the ones shown here are the most common, with the carbons conventionally numbered (in green) so that the forms can be compared easily. The bold, darker lines represent portions of the molecule that are projecting out of the page toward you—remember, these are three-dimensional molecules!

Disaccharides. Many familiar sugars like sucrose are "double sugars," two monosaccharides joined by a covalent bond (figure 3.23). Called **disaccharides,** they often play a role in the transport of sugars, as we will discuss shortly.

Polysaccharides. **Polysaccharides** are macromolecules made up of monosaccharide subunits. Starch is a polysaccharide used by plants to store energy. It consists entirely of glucose molecules, linked one after another in long chains. Cellulose is a polysaccharide that serves as a structural building material in plants. It too consists entirely of glucose molecules linked together into chains, and special enzymes are required to break the links.

Sugar Isomers

Glucose is not the only sugar with the formula $C_6H_{12}O_6$. Other common six-carbon sugars such as fructose and galactose also have this same empirical formula (figure 3.24). These sugars are **isomers,** or alternative forms, of glucose. Even though isomers have the same empirical formula, their atoms are arranged in different ways; that is, their three-dimensional structures are different. These structural differences often account for substantial functional differences between the isomers. Glucose and fructose, for example, are *structural isomers.* In fructose, the double-bonded oxygen is attached to an internal carbon rather than to a terminal one. Your taste buds can tell the difference, as fructose tastes much sweeter than glucose, despite the fact that both sugars have the same chemical composition. This structural difference also has an important chemical consequence: the two sugars form different polymers.

Unlike fructose, galactose has the same bond structure as glucose; the only difference between galactose and glucose is the orientation of one hydroxyl group. Because the hydroxyl group positions are mirror images of each other, galactose and glucose are called *stereoisomers.* Again, this seemingly slight difference has important consequences, as this hydroxyl group is often involved in creating polymers with distinct functions, such as starch (energy storage) and cellulose (structural support).

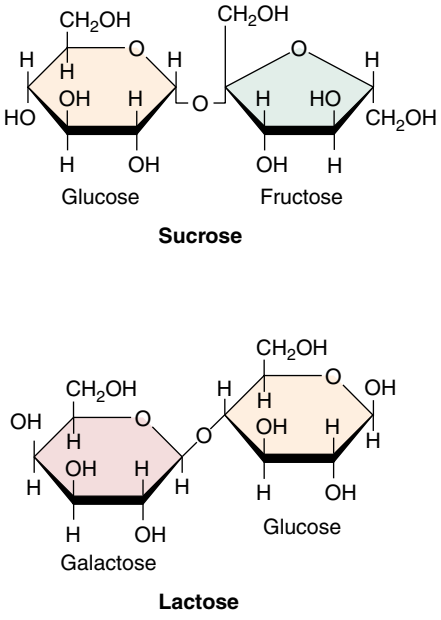


FIGURE 3.23
Disaccharides. Sugars like sucrose and lactose are disaccharides, composed of two monosaccharides linked by a covalent bond.

Sugars are among the most important energy-storage molecules in organisms, containing many energy-storing C—H bonds. The structural differences among sugar isomers can confer substantial functional differences upon the molecules.

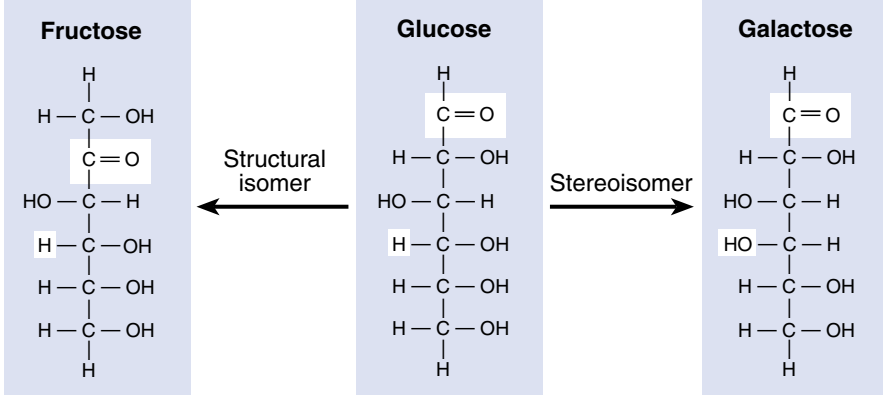


FIGURE 3.24
Isomers and stereoisomers. Glucose, fructose, and galactose are isomers with the empirical formula $C_6H_{12}O_6$. A structural isomer of glucose, such as fructose, has identical chemical groups bonded to different carbon atoms, while a stereoisomer of glucose, such as galactose, has identical chemical groups bonded to the same carbon atoms but in different orientations.

Linking Sugars Together

Transport Disaccharides

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 (used for energy) 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 normal glucose-utilizing enzymes of the organism cannot break the bond linking the two monosaccharide subunits. Enzymes that can do so are typically present only in the tissue where the glucose is to be used.

Transport forms differ depending on which monosaccharides link to form the disaccharide. Glucose forms transport disaccharides with itself and many other monosaccharides, including fructose and galactose. When glucose forms a disaccharide with its structural isomer, fructose, the resulting disaccharide is *sucrose*, or table sugar (figure 3.25*a*). Sucrose is the form in which most plants transport glucose and the sugar that most humans (and other animals) eat. Sugarcane is rich in sucrose, and so are sugar beets.

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

Storage Polysaccharides

Organisms store the metabolic energy contained in monosaccharides by converting them into disaccharides, such as *maltose* (figure 3.25*b*), which are then linked together into insoluble forms that are deposited in specific storage areas in their bodies. These insoluble polysaccharides are long polymers of monosaccharides formed by dehydration synthesis. Plant polysaccharides formed from glucose are called **starches.** Plants store starch as granules within chloroplasts and other organelles. Because glucose is a key metabolic fuel, the stored starch provides a reservoir of energy available for future needs. Energy for cellular work can be retrieved by hydrolyzing the links that bind the glucose subunits together.

The starch with the simplest structure is *amylose*, which is composed of many hundreds of glucose molecules linked together in long, unbranched chains. Each linkage occurs between the number 1 carbon of one glucose molecule and the number 4 carbon of another, so that amylose is, in effect, a longer form of maltose. The long chains of amylose tend to coil up in water (figure 3.26*a*), a property that renders amylose insoluble. Potato starch is about 20% amylose. When amylose is digested by a sprouting potato plant (or by an animal that eats a potato), enzymes first break it into fragments of random length, which are more soluble because they are shorter. Baking or boiling potatoes has the same effect, breaking the chains into fragments. Another enzyme then cuts these fragments into molecules of maltose. Finally, the maltose is cleaved into two glucose molecules, which cells are able to metabolize.

Most plant starch, including the remaining 80% of potato starch, is a somewhat more complicated variant of amylose called *amylopectin* (figure 3.26*b*). Pectins are branched polysaccharides. Amylopectin has short, linear amylose branches consisting of 20 to 30 glucose subunits.

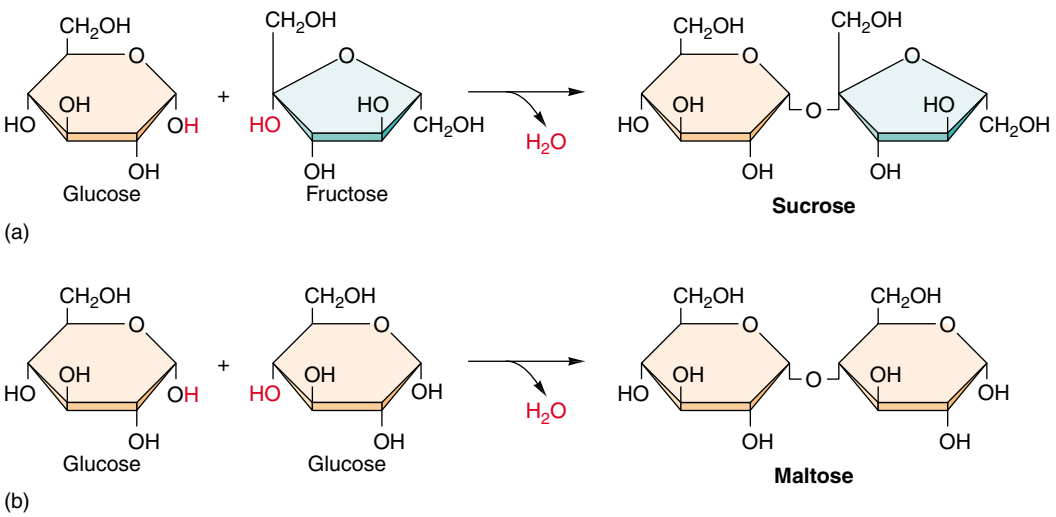


FIGURE 3.25
How disaccharides form. Some disaccharides are used to transport glucose from one part of an organism's body to another; one example is sucrose (*a*), which is found in sugarcane. Other disaccharides, such as maltose in grain (*b*), are used for storage.

In some plants these chains are cross-linked. The cross-links create an insoluble mesh of glucose, which can be degraded only by another kind of enzyme. The size of the mesh differs from plant to plant; in rice about 100 amylose chains, each with one or two cross-links, forms the mesh.

The animal version of starch is glycogen. Like amylopectin, *glycogen* is an insoluble polysaccharide containing branched amylose chains. In glycogen, the average chain length is much greater and there are more branches than in plant starch (figure 3.26*c*). Humans and other vertebrates store excess food energy as glycogen in the liver and in muscle cells; when the demand for energy in a tissue increases, glycogen is hydrolyzed to release glucose.

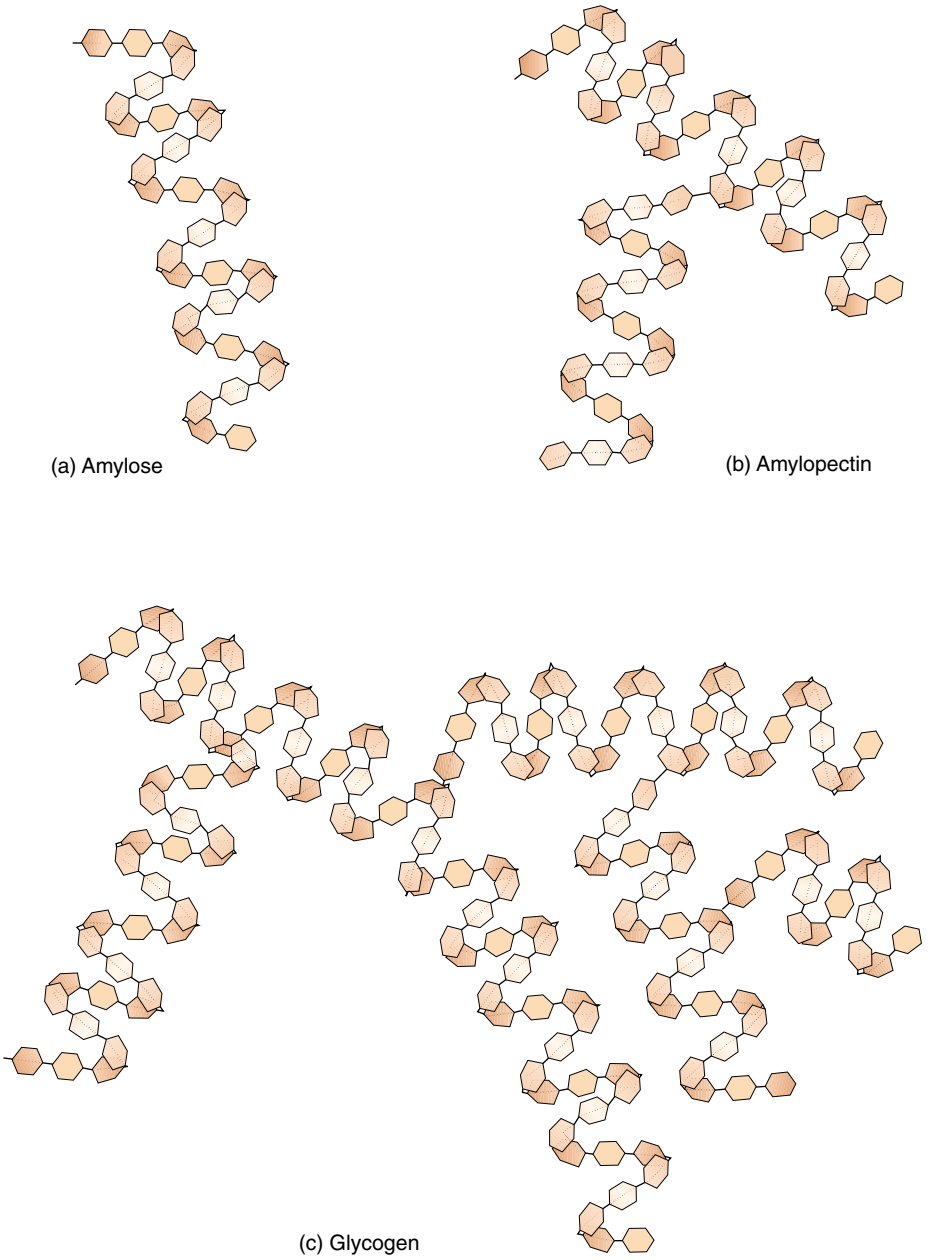


FIGURE 3.26
Storage polysaccharides. Starches are long glucose polymers that store energy in plants. (*a*) The simplest starches are long chains of maltose called amylose, which tend to coil up in water. (*b*) Most plants contain more complex starches called amylopectins, which are branched. (*c*) Animals store glucose in glycogen, which is more extensively branched than amylopectin and contains longer chains of amylose.

Nonfattening Sweets

Imagine a kind of table sugar that looks, tastes, and cooks like the real thing, but has no calories or harmful side effects. You could eat mountains of candy made from such sweeteners without gaining weight. As Louis Pasteur discovered in the late 1800s, most sugars are "right-handed" molecules, in that the hydroxyl group that binds a critical carbon atom is on the right side. However, "left-handed" sugars, in which the hydroxyl group is on the left side, can be made readily in the laboratory. These synthetic sugars are mirror-image chemical twins of the natural form, but the enzymes that break down sugars in the human digestive system can tell the difference. To digest a sugar molecule, an enzyme must first grasp it, much like a shoe fitting onto a foot, and all of the body's enzymes are right-handed! A left-handed sugar doesn't fit, any more than a shoe for the right foot fits onto a left foot.

The Latin word for "left" is *levo*, and left-handed sugars are called **levo-,** or **l-sugars.** They do not occur in nature except for trace amounts in red algae, snail eggs, and seaweed. Because they pass through the body without being used, they can let diet-conscious sweet-lovers have their cake and eat it, too. Nor will they contribute to tooth decay because bacteria cannot metabolize them, either.

Starches are glucose polymers. Most starches are branched and some are cross-linked. The branching and cross-linking render the polymer insoluble and protect it from degradation.

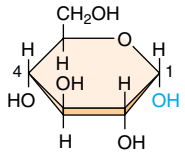
Structural Carbohydrates

While some chains of sugars store energy, others serve as structural material for cells.

Cellulose

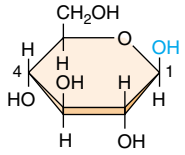
For two glucose molecules to link together, the glucose subunits must be the same form. Glucose can form a ring in two ways, with the hydroxyl group attached to the carbon where the ring closes being locked into place either below or above the plane of the ring. If below, it is called the **alpha form,** and if above, the **beta form.** All of the glucose subunits of the starch chain are alpha-glucose. When a chain of glucose molecules consists of all beta-glucose subunits, a polysaccharide with very different properties results. This **structural polysaccharide** is *cellulose*, the chief component of plant cell walls (figure 3.27). Cellulose is chemically similar to amylose, with one important difference: the starch-degrading enzymes that occur in most organisms cannot break the bond between two beta-glucose sugars. This is not because the bond is stronger, but rather because its cleavage requires an enzyme most organisms lack. Because cellulose cannot be broken down readily, it works well as a biological structural material and occurs widely in this role in plants. Those few animals able to break down cellulose find it a rich source of energy. Certain vertebrates, such as cows, can digest cellulose by means of bacteria and protists they harbor in their intestines which provide the necessary enzymes.

(a)



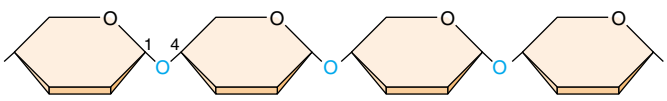
α **form of glucose**

(b)

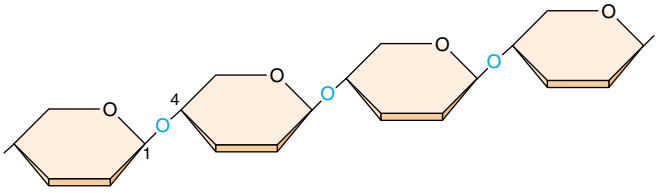


β **form of glucose**

(c)



Starch: chain of α-glucose subunits



Cellulose: chain of β-glucose subunits

FIGURE 3.27
A journey into wood. This jumble of cellulose fibers (*a*) is from a yellow pine (*Pinus ponderosa*) (20×). (*b*) While starch chains consist of alpha-glucose subunits, (*c*) cellulose chains consist of beta-glucose subunits. Cellulose fibers can be very strong and are quite resistant to metabolic breakdown, which is one reason why wood is such a good building material.

Chitin

The structural building material in insects, many fungi, and certain other organisms is called chitin (figure 3.28). *Chitin* is a modified form of cellulose with a nitrogen group added to the glucose units. When cross-linked by proteins, it forms a tough, resistant surface material that serves as the hard exoskeleton of arthropods such as insects and crustaceans (see chapter 46). Few organisms are able to digest chitin.

Structural carbohydrates are chains of sugars that are not easily digested. They include cellulose in plants and chitin in arthropods and fungi.

FIGURE 3.28
Chitin. Chitin, which might be considered to be a modified form of cellulose, is the principal structural element in the external skeletons of many invertebrates, such as this lobster.

Chapter 3

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Summary

Questions

Media Resources

3.1 Molecules are the building blocks of life.

- The chemistry of living systems is the chemistry of carbon-containing compounds.
- Carbon's unique chemical properties allow it to polymerize into chains by dehydration synthesis, forming the four key biological macromolecules: carbohydrates, lipids, proteins, and nucleic acids.

1. What types of molecules are formed by dehydration reactions? What types of molecules are formed by hydrolysis?

- Organic Chemistry

3.2 Proteins perform the chemistry of the cell.

- Proteins are polymers of amino acids.
- Because the 20 amino acids that occur in proteins have side groups with different chemical properties, the function and shape of a protein are critically affected by its particular sequence of amino acids.

2. How are amino acids linked to form proteins?

3. Explain what is meant by the primary, secondary, tertiary, and quaternary structure of a protein.

- Explorations: How Proteins Function
- Proteins
- Student Research: A new Protein in Inserts

3.3 Nucleic acids store and transfer genetic information.

- Hereditary information is stored as a sequence of nucleotides in a linear polymer called DNA, which exists in cells as a double helix.
- Cells use the information in DNA by producing a complementary single strand of RNA which directs the synthesis of a protein whose amino acid sequence corresponds to the nucleotide sequence of the DNA from which the RNA was transcribed.

4. What are the three components of a nucleotide? How are nucleotides linked to form nucleic acids?

5. Which of the purines and pyrimidines are capable of forming base-pairs with each other?

- Nucleic Acids

3.4 Lipids make membranes and store energy.

- Fats are one type of water-insoluble molecules called lipids.
- Fats are molecules that contain many energy-rich C—H bonds and, thus, provide an efficient form of long-term energy storage.
- Types of lipids include phospholipids, fats, terpenes, steroids, and prostaglandins.

6. What are the two kinds of subunits that make up a fat molecule, and how are they arranged in the molecule?

7. Describe the differences between a saturated and an unsaturated fat.

- Lipids
- Experiment: Anfinsen: Amino Acid Sequence Determines Protein Shape

3.5 Carbohydrates store energy and provide building materials.

- Carbohydrates store considerable energy in their carbon-hydrogen (C—H) bonds.
- The most metabolically important carbohydrate is glucose, a six-carbon sugar.
- Excess energy resources may be stored in complex sugar polymers called starches (in plants) and glycogen (in animals and fungi).

8. What does it mean to say that glucose, fructose, and galactose are isomers? Which two are structural isomers, and how do they differ from each other? Which two are stereoisomers, and how do they differ from each other?

- Carbohydrates