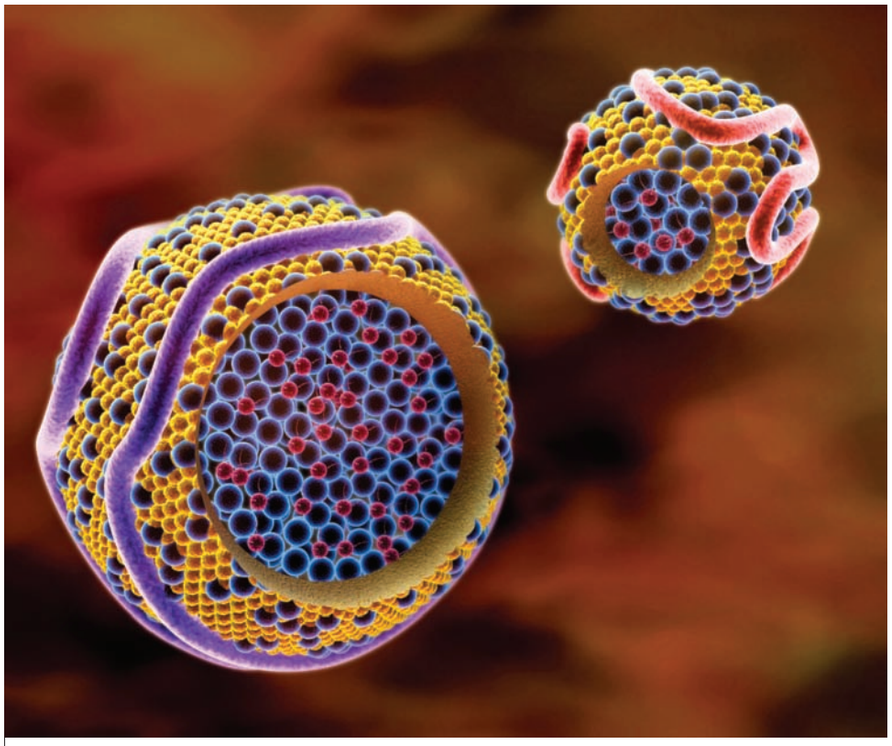


Hybrid Medical Animation/Science Photo Library/Photo Researchers, Inc.

The lipoproteins HDL and LDL, cholesterol-transporting molecules composed of protein and lipid units, which are found in the bloodstream (computer illustration).

Study Plan

3 Biological Molecules: The Carbon Compounds of Life

Why It Matters

High in the mountains of the Pacific Northwest, vast forests of coniferous trees have survived another cold winter **(Figure 3.1).** With the arrival of spring, rising temperatures and water from melting snow stimulate renewed growth. Carbon dioxide (CO_2) from the air enters the needle-like leaves of the trees through microscopic pores. Using energy from sunlight, the trees combine the water and carbon dioxide into sugars and other carbon-based compounds through the process known as photosynthesis. The lives of plants, and almost all other organisms, depend directly or indirectly on the products of photosynthesis.

The amount of CO_2 in the atmosphere is critical to photosynthesis. Researchers have been studying the atmospheric concentration of CO_2 since the early 1950s. Among other things, they found that the concentration shifts with the seasons. It declines during spring and summer, when plants and other photosynthetic organisms withdraw large amounts of the gas from the air and convert it into sugars and other complex carbon compounds. It increases during autumn and winter, when global photosynthesis decreases and decomposers that release the gas as a metabolic by-product increase. Great quantities of CO_2 are also added to the atmosphere by forest fires and by the

David Schiefelbein

Figure 3.1
Conifers in winter on Silver Star Mountain in Washington State. As is true of all other organisms, the structure, activities, and survival of these trees start with the carbon atom and its diverse molecular partners in organic compounds.

burning of coal, oil, gasoline, and other fossil fuels in automobiles, aircraft, trains, power plants, and other industries. The resulting increase in atmospheric CO_2 contributes to global warming, which may have profound effects on life in years to come.

The importance of atmospheric CO_2 to food production and world climate are just two examples of how carbon and its compounds are fundamental to the entire living world, from the structures and activities of single cells to physical effects on a global scale. Carbon compounds form the structures of living organisms and take part in all biological reactions. They also serve as sources of energy for living organisms and as an energy resource for much of the world's industry—for example, coal and oil are the fossil remains of long-dead organisms. This chapter outlines the structures and functions of biological carbon compounds.

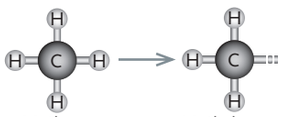
3.1 Carbon Bonding

Carbon Chains and Rings Form the Backbones of All Biological Molecules

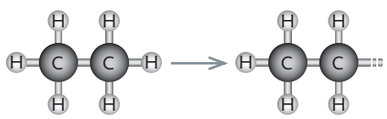
Carbon's central role in life arises from its bonding properties: it can assemble into an astounding variety of chain and ring structures that form the backbones of all biological molecules. Collectively, molecules based on carbon are known as **organic molecules.** All other substances, that is, those without carbon atoms in their structures, are **inorganic molecules.** A few of the smallest carbon-containing molecules that occur in the environment as minerals or atmospheric gases, such as CO_2, are also considered inorganic molecules.

In organic molecules, carbon atoms bond covalently to each other and to other atoms, chiefly hydrogen, oxygen, nitrogen, and sulfur, in molecular structures that range in size from a few to thousands or even millions of atoms. Molecules consisting of carbon linked only to hydrogen atoms are called **hydrocarbons** (*hydro-* refers to hydrogen, not to water).

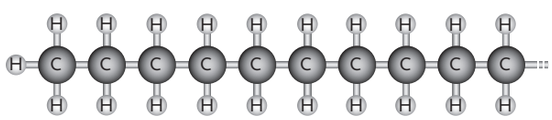
As discussed in Section 2.3, carbon has four unpaired outer electrons that it readily shares to complete its outermost energy level, forming four covalent bonds. The simplest hydrocarbon, CH_4 (methane), consists of a single carbon atom bonded to four hydrogen atoms (see Figure 2.8a). Removing one hydrogen from methane leaves a methyl group, which occurs in many biological molecules:



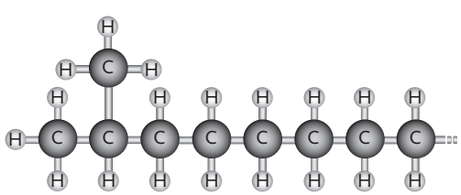
Now imagine bonding two methyl groups together. Removing a hydrogen atom from the resulting structure, ethane, produces an ethyl group:



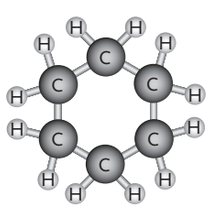
Repeating the process builds a linear hydrocarbon chain:



Branches can be added to produce a branched hydrocarbon chain:

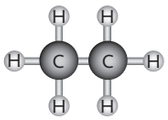


A chain can loop back on itself to form a ring. For example, cyclohexane is C_6H_{12}, with single covalent bonds between each pair of carbon atoms and two hydrogen atoms attached to each carbon atom:

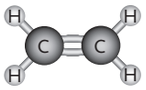


C_6H_{12}, cyclohexane

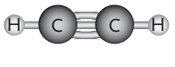
Hydrocarbons gain added complexity when neighboring carbon atoms form double or triple bonds. Because each carbon atom can form a maximum of four bonds, the number of hydrogen atoms in a molecule decreases as the number of bonds between any two carbon atoms increases:



Single bonding: C_2H_6, ethane

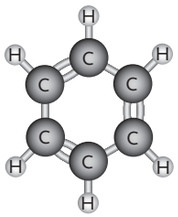


Double bonding: C_2H_4, ethene (ethylene)

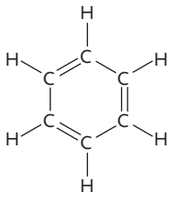


Triple bonding: C_2H_2, ethyne (acetylene)

Double bonds between carbon atoms are also found in carbon rings:



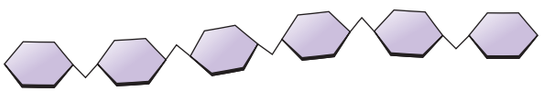
or



C_6H_6, benzene

We will also use this depiction of a carbon ring in figures:

Many carbon rings can join together to produce larger molecules, as in the string of sugar molecules that makes up a polysaccharide chain:



There is almost no limit to the number of different hydrocarbon structures that carbon and hydrogen can form. As you will learn in the next section, the molecules of living systems typically contain other elements in addition to carbon and hydrogen. These other elements confer functional properties on organic molecules. Subsequent sections detail the four major classes of organic molecules—*carbohydrates, lipids, proteins,* and *nucleic acids*—that form almost the entire substance of living organisms.

Study Break

1. Distinguish between hydrocarbons and other organic molecules.
2. What is the maximum number of bonds that a carbon atom can form?

3.2 Functional Groups in Biological Molecules

Carbohydrates, lipids, proteins, and nucleic acids are synthesized and degraded in living organisms through interactions between small, reactive groups of atoms attached to the organic molecules. The atoms in these reactive groups, called **functional groups**, occur in positions in which their covalent bonds are more readily broken or rearranged than the bonds in other parts of the molecules.

The functional groups that enter most frequently into biological reactions are the *hydroxyl, carbonyl, carboxyl, amino, phosphate,* and *sulfhydryl* groups **(Table 3.1).** The unconnected covalent bonds written to the left of each structure link these functional groups to other atoms in biological molecules, usually carbon atoms. A double bond, such as that in the carbonyl group, indicates that two pairs of electrons are shared between the carbon and oxygen atoms.

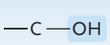
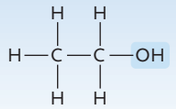
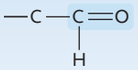
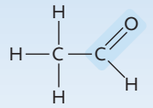
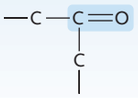
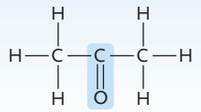
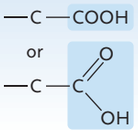
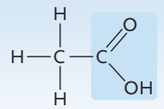
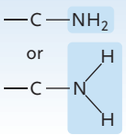
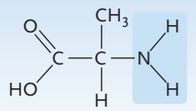
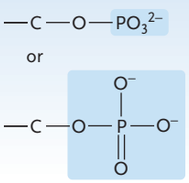
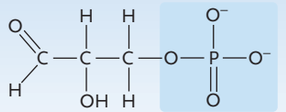
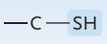
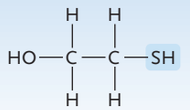
In many of the reactions that involve functional groups, the components of a water molecule, —H and —OH, are removed from or added to the groups as they interact. When the components of a water molecule are *removed* during a reaction, usually as part of the assembly of a larger molecule from smaller subunits, the reaction is called a **dehydration synthesis reaction** or **condensation reaction (Figure 3.2a).** For example, this type of reaction occurs when individual sugar molecules combine to form a starch molecule. In **hydrolysis**, the reverse reaction, the components of a water molecule are *added* to functional groups as molecules are broken into smaller subunits **(Figure 3.2b).** For example, the breakdown of a protein molecule into individual amino acids occurs by hydrolysis in the digestive processes of animals.

The Hydroxyl Group Is a Key Component of Alcohols

A **hydroxyl group** (—OH) consists of an oxygen atom linked to a hydrogen atom on one side and to a carbon chain on the other side. Hydroxyl groups readily enter dehydration synthesis reactions, and they are formed as part of hydrolysis reactions. Hydroxyl groups are polar, and they give a polar nature to parts of the molecules that contain them (see Section 2.3 for a discussion of polarity).

The hydroxyl group is a key component of **alcohols.** Alcohols take the form R—OH, in which *R* indicates a chain of one or more carbon atoms. In the R chain of an alcohol, the carbon atoms are all linked to hydrogen atoms, as in ethyl alcohol (see Table 3.1). Ethyl alcohol (ethanol) is the alcohol found in beer, wine, and spirits, and it is used to precipitate DNA from solutions in molecular biology experiments. The hydroxyl group enables an alcohol to form linkages to other organic molecules through dehydration synthesis reactions (see Figure 3.2a).

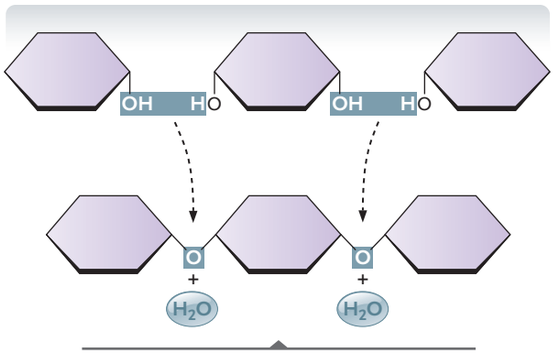
Table 3.1 **Common Functional Groups of Organic Molecules**

Functional Group	Major Classes of Molecules	Example
Hydroxyl 	Alcohols	 Ethyl alcohol (in alcoholic beverages)
Carbonyl 	Aldehydes	 Acetaldehyde
	Ketones	 Acetone (a solvent)
Carboxyl 	Organic acids	 Acetic acid (in vinegar)
Amino 	Amino acids	 Alanine (an amino acid)
Phosphate 	Nucleotides, nucleic acids, many other cellular molecules	 Glyceraldehyde-3-phosphate (product of photosynthesis)
Sulfhydryl 	Many cellular molecules	 Mercaptoethanol

The Carbonyl Group Is the Reactive Part of Aldehydes and Ketones

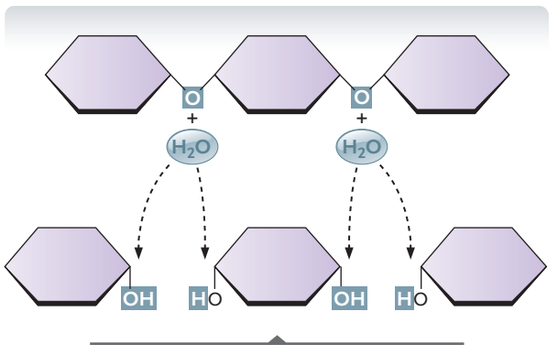
A **carbonyl group**  consists of an oxygen atom linked to a carbon atom by a double bond. The oxygen atom of a carbonyl group is highly reactive, especially with substances that act as bases (see Section 2.5 for a discussion of acids and bases).

a. Dehydration synthesis reactions



The components of a water molecule are removed as subunits join into a larger molecule.

b. Hydrolysis



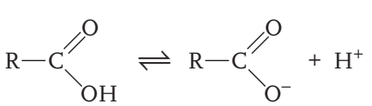
The components of a water molecule are added as molecules are split into smaller subunits.

Figure 3.2
Dehydration synthesis and hydrolysis reactions.

Carbonyl groups are the reactive parts of aldehydes and ketones, molecules that are important building blocks of carbohydrates and that also take part in the reactions supplying energy for cellular activities. In an **aldehyde**, the carbonyl group is linked to a carbon atom at the end of a carbon chain, along with a hydrogen atom, as in acetaldehyde (see Table 3.1). In a **ketone**, the carbonyl group is linked to a carbon atom in the interior of a carbon chain, as in acetone (see Table 3.1).

The Carboxyl Group Forms Organic Acids

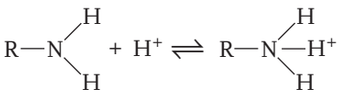
Carbonyl and hydroxyl groups combine to form a **carboxyl group** (—COOH), the characteristic functional group of **organic acids** (also called *carboxylic acids*); an example is acetic acid (see Table 3.1). The carboxyl group gives organic molecules acidic properties because the —OH group readily releases its hydrogen as a proton (H^+) in water solutions (see Section 2.5):



The carboxyl group readily enters into dehydration synthesis reactions, giving up its hydroxyl group as organic molecules combine into larger assemblies (see Figure 3.17). Many organic acids, such as citric acid and acetic acid, are central components of energy-generating reactions in living organisms.

The Amino Group Acts as an Organic Base

The **amino group** (—NH_2) consists of a nitrogen atom bonded on one side to two hydrogen atoms and on the other side to a carbon chain, as in the amino acid alanine (see Table 3.1) and all other amino acids. It readily acts as a base by accepting H^+ (a proton) in water solutions:

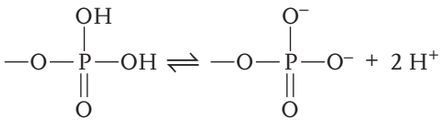


The amino group also readily enters dehydration synthesis reactions, releasing a hydrogen ion as it links subunits into larger molecules (see Figure 3.17).

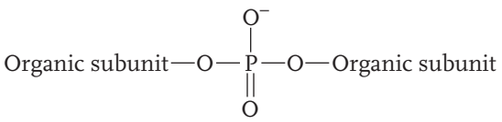
The Phosphate Group Is a Reactive Jack-of-All-Trades

The **phosphate group** (—OPO_3^{2-}) consists of a central phosphorus atom held in four linkages. Two of the linkages bind —OH groups to the central phosphorus atom; a third linkage, formed by a double bond, binds an oxygen atom to the central phosphorus atom. The remaining bond links the phosphate group to an oxygen atom, which, in turn, binds to a carbon chain. An example is glyceraldehyde-3-phosphate, a product of photosynthesis (see Table 3.1).

Phosphate groups give molecules that contain them the ability to react as weak acids because one or both —OH groups readily release their hydrogens as H^+:



A phosphate group can also form a chemical bridge that links two organic building blocks into a larger structure:



Among the large biological molecules linked together by phosphate groups is the nucleic acid DNA, the genetic material of all living organisms. When acting as a linking bridge, a phosphate group still has one —OH group that can dissociate to release a hydrogen ion (shown in dissociated form above as O^-).

Phosphate groups are also added to or removed from biological molecules as part of reactions that conserve or release energy. In addition, they control biological activity—the activity of many proteins is turned on or off by the addition or removal of phosphate groups.

The Sulfhydryl Group Works as a Molecular Fastener

In the **sulfhydryl group** (—SH), a sulfur atom is linked on one side to a hydrogen atom and on the other side to a carbon chain, as in mercaptoethanol (see Table 3.1). The sulfhydryl group is easily converted into a covalent linkage, in which it loses its hydrogen atom as it binds. In many of these linking reactions, two sulfhydryl groups interact to form a **disulfide linkage** (—S—S—):

In many proteins, the disulfide linkage forms a sort of molecular fastener that holds proteins in their folded form or links protein subunits into larger structures (see Figure 3.16).

The hydroxyl, carbonyl, carboxyl, amino, phosphate, and sulfhydryl functional groups provide most of the reactive sites on biological molecules. We now turn to the arrangement of these groups and carbon chains in the four classes of organic molecules—carbohydrates, lipids, proteins, and nucleic acids.

Study Break

1. Distinguish between a dehydration synthesis reaction (condensation reaction) and hydrolysis.
2. Explain whether carboxyl groups, amino groups, and phosphate groups act as acids or bases.

3.3 Carbohydrates

Carbohydrates, the most abundant organic molecules in the world, serve many functions. Together with fats, they act as the major fuel substances providing chemical energy for cellular activities. Table sugar is an example of a carbohydrate consumed in large quantities as an energy source in the human diet. For example, athletic activity is partly fueled by carbohydrates. Energy-providing carbohydrates are stored in plant cells as **starch** and in animal cells as **glycogen**, both consisting of long chains of repeating carbohydrate subunits linked end to end. Chains of carbohydrate subunits also form many structural molecules, such as **cellulose**, one of the primary constituents of plant cell walls.

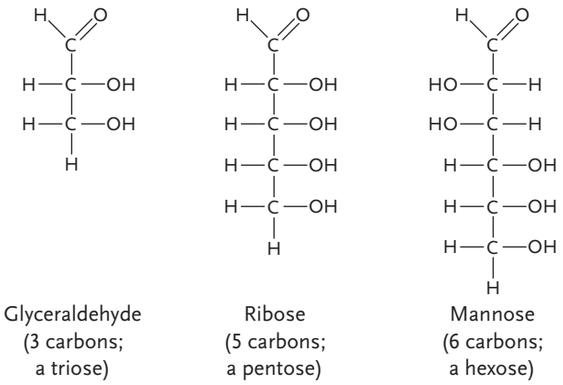


Figure 3.3
Some representative monosaccharides. The triose, glyceraldehyde, takes part in energy-yielding reactions and photosynthesis. The pentose, ribose, is a component of RNA and of molecules that carry energy. The hexose, mannose, is a fuel substance and a component of glycolipids and glycoproteins.

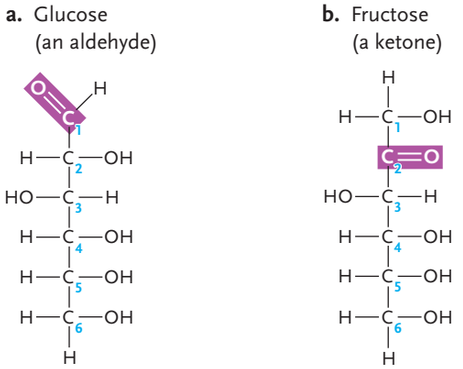


Figure 3.4
The aldehyde and ketone positions for the carbonyl group (shaded regions) in monosaccharides. **(a)** In the aldehyde position, the carbonyl group is located at the end of the carbon chain. **(b)** In the ketone position, the carbonyl group is located inside the carbon chain. For convenience, the carbons of monosaccharides are numbered, with 1 being the carbon at the end nearest the carbonyl group.

Carbohydrates contain only carbon, hydrogen, and oxygen atoms, in an approximate ratio of 1 carbon: 2 hydrogens: 1 oxygen (CH_2O). The names of many carbohydrates end in *-ose*. The smallest carbohydrates, the **monosaccharides** (*mono* = one; *saccharum* = sugar), contain three to seven carbon atoms. For example, the monosaccharide glucose consists of a chain of six carbons and has the molecular formula $C_6H_{12}O_6$. Two monosaccharides combine to form a *disaccharide* such as sucrose, common table sugar. Chains with more than 10 linked monosaccharide subunits are called **polysaccharides** (*poly* = many). Starch, glycogen, and cellulose are common polysaccharides.

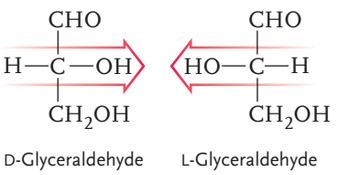
Monosaccharides Are the Structural Units of Carbohydrates

Carbohydrates occur either as monosaccharides or as chains of monosaccharide units linked together. Monosaccharides are soluble in water, and most have a distinctly sweet taste. Of the monosaccharides, those that contain three carbons *(trioses)*, five carbons *(pentoses)*, and six carbons *(hexoses)* are most common in living organisms **(Figure 3.3).**

Linear and Ring Forms of the Monosaccharides. All monosaccharides can occur in the linear form shown in Figure 3.3. In this form, each carbon atom in the chain except one has both an —H and an —OH group attached to it. The remaining carbon is part of a carbonyl group, which may be located at the end of the carbon chain in the aldehyde position (as in glucose in **Figure 3.4a**) or inside the chain in the ketone position (as in fructose in **Figure 3.4b**).

Monosaccharides with five or more carbons can fold back on themselves to assume a ring form. Folding into a ring occurs through a reaction between two functional groups in the same monosaccharide, as occurs in glucose **(Figure 3.5).** The ring form of most five- and six-carbon sugars is much more common in cells than the linear form.

Isomers of the Monosaccharides. Typically, one or more of the carbon atoms in a monosaccharide links to four different atoms or chemical groups. Carbons linked in this way are called *asymmetric* carbons; they have important effects on the structure of a monosaccharide because they can take either of two fixed positions with respect to other carbons in a carbon chain. For example, the middle carbon of the three-carbon sugar glyceraldehyde is asymmetric because it shares electrons in covalent bonds with four different atoms or groups: —H, —OH, —CHO, and —CH_2OH. The —H and —OH groups can take either of two positions, with the —OH extending to either the left or right of the carbon chain relative to the —CHO and —CH_2OH groups:



Note that the two forms of glyceraldehyde have the same chemical formula, $C_3H_6O_3$. The difference between the two forms is similar to the difference between your two hands. Although both hands have four fingers and a thumb, they are not identical; rather, they are mirror images of each other. That is, when you hold your right hand in front of a mirror, the reflection looks like your left hand and vice versa.

Two or more molecules with the same chemical formula but different molecular structures are called **isomers.** Isomers that are mirror images of each other, like the two forms of glyceraldehyde, are called **enantiomers**, or **optical isomers.** One of the enantiomers—the one in which the hydroxyl group extends

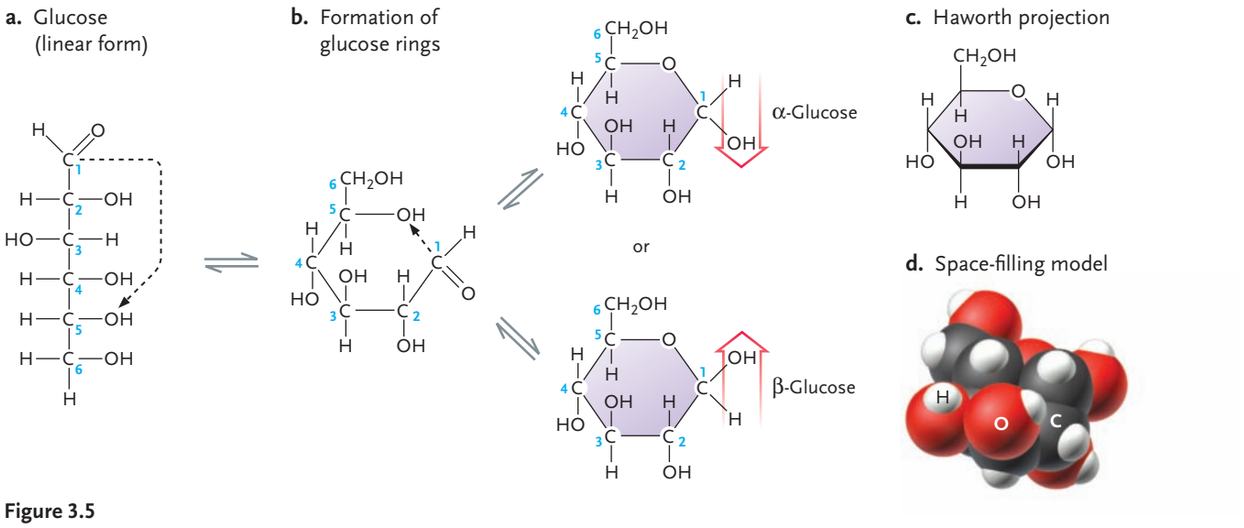


Figure 3.5
Ring formation by glucose. **(a)** Glucose in linear form. **(b)** The ring form of glucose is produced by a reaction between the aldehyde group at the 1 carbon and the hydroxyl group at the 5 carbon. The reaction produces two alternate glucose enantiomers, α- and β-glucose. If the ring is considered to lie in the plane of the page, the —OH group points below the page in α-glucose and upward from the page in β-glucose. For simplicity, the group at the 6 carbon is shown as CH_2OH in this and later diagrams. **(c)** A commonly used, simplified representation of the glucose ring, in which the C's designating carbons of the ring are omitted. The thicker lines along one side indicate that the ring lies in a flat plane with the thickest edge closest to the viewer. **(d)** A space-filling model of glucose, showing the volumes occupied by the atoms. Carbon atoms are shown in black, oxygen in red, and hydrogen in white.

to the left in the view just shown—is called the L-form (*laevus* = left). The other enantiomer, in which the —OH extends to the right, is called the D-form (*dexter* = right). The difference between L- and D-enantiomers is critical to biological function. Typically, one of the two forms enters much more readily into cellular reactions; just as your left hand does not fit readily into a right-hand glove, enzymes (proteins that accelerate chemical reactions in living organisms) fit best to one of the two forms of an enantiomer. For example, most of the enzymes that catalyze the biochemical reactions of monosaccharides react more rapidly with the D-form, making this form much more common among cellular carbohydrates than L-forms. Many other kinds of biological molecules besides carbohydrates form enantiomers; an example is the amino acids.

In the ring form of many five- or six-carbon monosaccharides, including glucose, the carbon at the 1 position of the ring is asymmetric because its four bonds link to different groups of atoms. This asymmetry allows monosaccharides such as glucose to exist as two different enantiomers. The glucose enantiomer with an —OH group pointing below the plane of the ring is known as *alpha-glucose,* or *α-glucose;* the enantiomer with an —OH group pointing above the plane of the ring is known as *beta-glucose,* or *β-glucose* (see Figure 3.5b). Other five- and six-carbon monosaccharide rings have similar α- and β-configurations.

The α- and β-rings of monosaccharides can give the polysaccharides assembled from them vastly different chemical properties. For example, starches, which are assembled from α-glucose units, are biologically reactive polysaccharides easily digested by animals; cellulose, which is assembled from β-glucose units, is relatively unreactive and, for most animals, completely indigestible.

Another form of isomerism is found in monosaccharides, as well as in other molecules. Two molecules with the same chemical formula but atoms that are arranged in different ways are called **structural isomers**. The sugars glucose and fructose are examples of structural isomers (see Figure 3.4).

Two Monosaccharides Link to Form a Disaccharide

Disaccharides typically are assembled from two monosaccharides linked together by a dehydration synthesis reaction. For example, the disaccharide maltose is formed by the linkage of two α-glucose molecules **(Figure 3.6a)** with oxygen as a bridge between the number 1 carbon of the first glucose unit and the 4 carbon of the second glucose unit. Bonds of this type, which commonly link monosaccharides into chains, are known as **glycosidic bonds.** A glycosidic bond between a 1 carbon and a 4 carbon is written in chemical shorthand as a 1→4 linkage; 1→2, 1→3, and 1→6 linkages are also common in carbohydrate chains. The linkages are designated as α or β depending on the orientation of the —OH group at the 1 carbon that forms the bond.

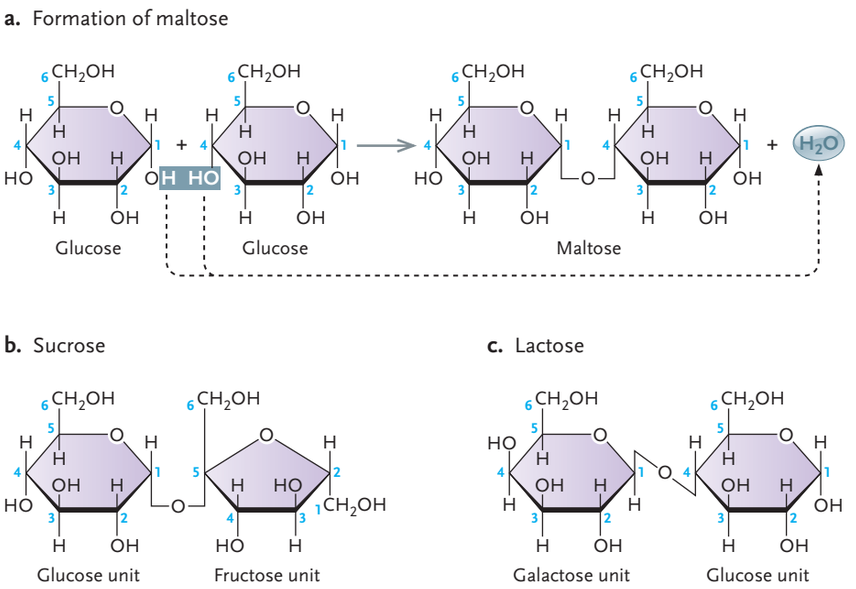


Figure 3.6
Disaccharides. **(a)** Combination of two glucose molecules by a dehydration synthesis reaction to form the disaccharide maltose. The components of a water molecule (in blue) are removed from the monosaccharides as they join. **(b)** Sucrose, assembled from glucose and fructose. **(c)** Lactose, assembled from galactose and glucose.

In maltose, the —OH group is in the α position. Therefore, the link between the two glucose subunits of maltose is written as an α(1→4) linkage.

Maltose, sucrose, and lactose are common disaccharides. Maltose is present in germinating seeds and is a major sugar used in the brewing industry. Sucrose, which contains a glucose and a fructose unit **(Figure 3.6b),** is transported to and from different parts of leafy plants. It is probably the most plentiful sugar in nature. Table sugar is made by extracting and crystallizing sucrose from plants, such as sugar cane and sugar beets. Lactose, assembled from a glucose and a galactose unit **(Figure 3.6c),** is the primary sugar of milk.

Monosaccharides Link in Longer Chains to Form Polysaccharides

Polysaccharides are longer chains formed by end-to-end linkage of monosaccharides through dehydration synthesis reactions. A polysaccharide is a type of **macromolecule**, meaning a very large molecule assembled by the covalent linkage of smaller subunit molecules. The subunit for a polysaccharide is the monosaccharide.

The dehydration synthesis reactions that assemble polysaccharides from monosaccharides are examples of **polymerization**, in which identical or nearly identical subunits, called the **monomers** of the reaction, join like links in a chain to form a larger molecule called a **polymer.** Linkage of a relatively small number of nonidentical subunits can create highly diverse and varied biological molecules. Many kinds of polymers are found in cells, not just polysaccharides. DNA is a primary example of a highly diverse polymer assembled from various combinations of only four different types of monomers.

The most common polysaccharides—the plant starches, glycogen, and cellulose—are all assembled from hundreds or thousands of glucose units. Other polysaccharides are built up from a variety of different sugar units. Polysaccharides may be linear, unbranched molecules, or they may contain one or more branches in which side chains of sugar units attach to a main chain.

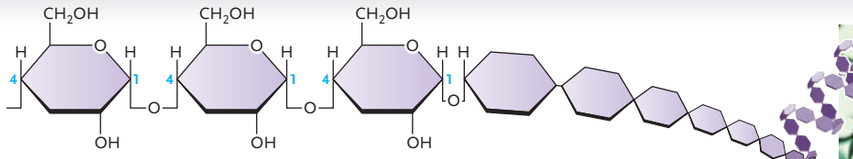
Figure 3.7 shows four common polysaccharides. Plant starches include both linear, unbranched forms such as amylose (Figure 3.7a) and branched forms such as amylopectin. Glycogen (Figure 3.7b), a more highly branched polysaccharide than amylopectin, can be assembled or disassembled readily to take up or release glucose; it is stored in large quantities in the liver and muscle tissues of many animals.

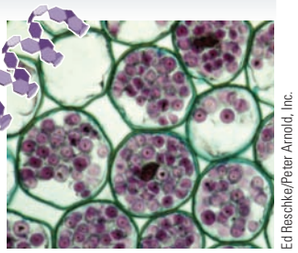
Cellulose (Figure 3.7c), probably the most abundant carbohydrate on Earth, is an unbranched polysaccharide assembled from glucose units bound together by β-linkages. It is the primary structural fiber of plant cell walls; in this role, cellulose has been likened to the steel rods in reinforced concrete. Its tough fibers enable the cell walls of plants to withstand enormous weight and stress. Fabrics such as cotton and linen are made from cellulose fibers extracted from plant cell walls. Animals such as mollusks, crustaceans, and insects synthesize an enzyme that digests the cellulose they eat. In ruminant mammals, such as cows, microorganisms in the digestive tract break down cellulose. Cellulose passes unchanged through the human digestive tract as indigestible fibrous matter. Many nutritionists maintain that the bulk provided by cellulose fibers helps maintain healthy digestive function.

Chitin (Figure 3.7d), another tough and resilient polysaccharide, is assembled from glucose units modified by the addition of nitrogen-containing groups. Similar to the subunits of cellulose, the modified glucose units of chitin are held together by β-linkages. Chitin is the main structural fiber in the external skeletons and other hard body parts of arthropods such as insects, crabs, and spiders. It is also a structural

a.

Amylose, formed from α-glucose units joined end to end in α(1→4) linkages. The coiled structures are induced by the bond angles in the α-linkages.



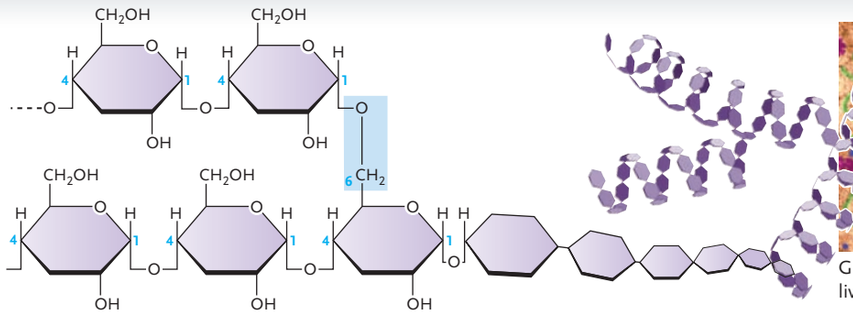


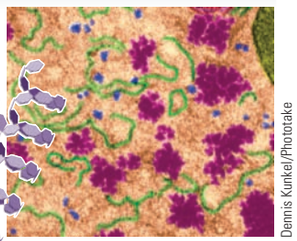
Amylose grains (purple) in plant root tissue

Ed Reschke/Peter Arnold, Inc.

b.

Glycogen, formed from glucose units joined in chains by α(1→4) linkages; side branches are linked to the chains by α(1→6) linkages (boxed in blue).



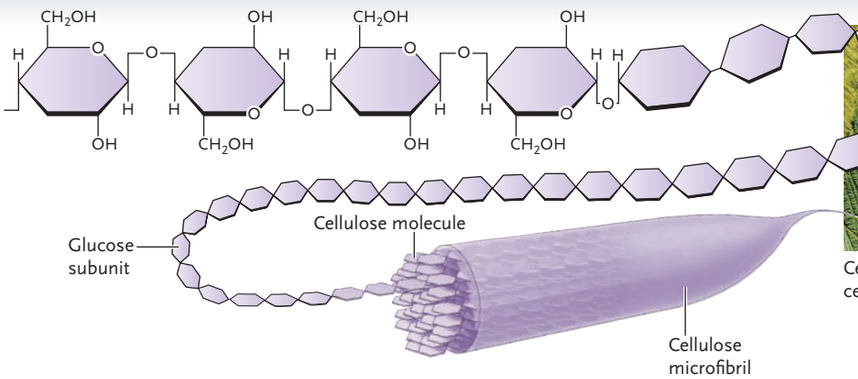


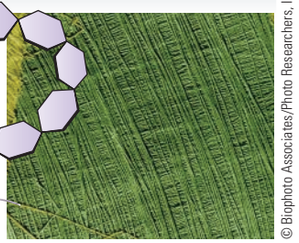
Glycogen particles (magenta) in liver cell

Dennis Kunkel/Phototake

c.

Cellulose, formed from glucose units joined end to end by β(1→4) linkages. Hundreds to thousands of cellulose chains line up side by side, in an arrangement reinforced by hydrogen bonds between the chains, to form cellulose microfibrils in plant cells.





Cellulose microfibrils in plant cell wall

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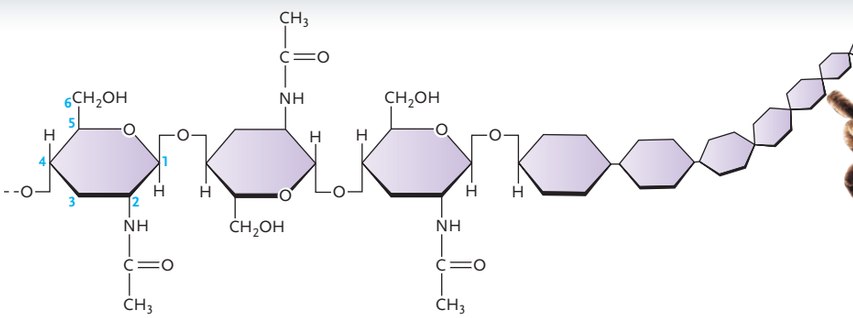
d.

Chitin, formed from β-linkages joining glucose units modified by the addition of nitrogen-containing groups. The external body armor of the tick is reinforced by chitin fibers.



David Scharf/Peter Arnold, Inc.

Figure 3.7
Four common polysaccharides: **(a)** amylose, a plant starch; **(b)** glycogen; **(c)** cellulose, the primary fiber in plant cell walls; and **(d)** chitin, a reinforcing fiber in the external skeleton of arthropods and the cell walls of some fungi.

material in the cell walls of fungi such as mushrooms and yeasts. Unlike cellulose, chitin is digested by enzymes that are widespread among microorganisms, plants, and many animals. In plants and animals, including humans and other mammals, chitin-digesting enzymes occur primarily as part of defenses against fungal infections. However, humans cannot digest chitin as a food source.

Polysaccharides also occur on the surfaces of cells, particularly in animals. These surface polysaccharides are attached to both the protein and lipid molecules in membranes. They help hold the cells of animals together and serve as recognition sites between cells.

Study Break

Distinguish among a monosaccharide, a disaccharide, and a polysaccharide. Give examples of each.

3.4 Lipids

Lipids are a diverse group of water-insoluble, primarily nonpolar biological molecules composed mostly of hydrocarbons. Some are large molecules, but they are not large enough to be considered macromolecules. As a result of their nonpolar character, lipids typically dissolve much more readily in nonpolar solvents, such as acetone and chloroform, than in water, the polar solvent of living organisms. Their insolubility in water underlies their ability to form cell membranes, the thin molecular films that create boundaries between and within cells.

In addition to forming membranes, some lipids are stored and used in cells as an energy source. Other lipids serve as hormones that regulate cellular activities. Three types of lipid molecules—*neutral lipids, phospholipids,* and *steroids*—occur most commonly in living organisms.

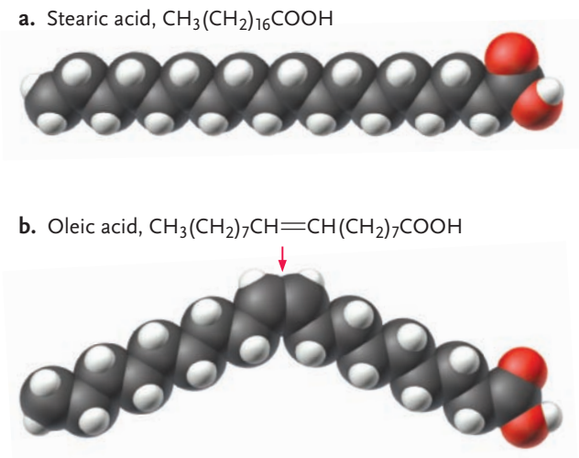


Figure 3.8
Fatty acids, one of two components of a neutral lipid. **(a)** Stearic acid, a saturated fatty acid. **(b)** Oleic acid, an unsaturated fatty acid. An arrow marks the "kink" introduced by the double bond.

Neutral Lipids Are Familiar as Fats and Oils

Neutral lipids, commonly found in cells as energy-storage molecules, are called "neutral" because at cellular pH they have no charged groups; they are therefore nonpolar. There are two types of neutral lipids: **oils** and **fats.** Oils are liquid at biological temperatures, and fats are semisolid. Generally, neutral lipids are insoluble in water. Almost all neutral lipids consist of a three-carbon backbone chain formed from glycerol, an alcohol, with each carbon of the glycerol backbone linked to a side chain consisting of a *fatty acid*.

Fatty Acids. A **fatty acid** contains a single hydrocarbon chain with a carboxyl group (—COOH) linked at one end **(Figure 3.8).** The carboxyl group gives the fatty acid its acidic properties. The fatty acids in living organisms contain 4 or more carbons in their hydrocarbon chain, with the most common forms having even-numbered chains of 14 to 22 carbons. Only the shortest fatty acid chains are water-soluble. As chain length increases, fatty acids become progressively less water-soluble and become oily.

If the hydrocarbon chain of a fatty acid binds the maximum possible number of hydrogen atoms, so that only single bonds link the carbon atoms, the fatty acid is said to be **saturated** with hydrogen atoms (as in stearic acid in Figure 3.8a). If one or more double bonds link the carbons (see Figure 3.8b, arrow), reducing the number of hydrogen atoms bound, the fatty acid is **unsaturated.** Fatty acids with one double bond are **monounsaturated;** those with more than one double bond are **polyunsaturated.**

Unsaturated fatty acid chains tend to bend or "kink" at a double bond (see Figures 3.8b and 3.12c). The kink makes the chains more disordered and thus more fluid at biological temperatures. Consequently, unsaturated fatty acids—and lipids that contain them—melt at lower temperatures than saturated fatty acids of the same length, and they generally have oily rather than fatty characteristics.

In foods, saturated fatty acids are usually found in solid animal fat, such as butter, whereas unsaturated fatty acids are usually found in vegetable oils, such as liquid canola oil. Nonetheless, both solid animal fat and liquid vegetable oils contain some saturated and some unsaturated fatty acids.

Glycerol and Triglyceride Formation. The glycerol unit that forms the backbone of neutral lipids has three —OH groups at which fatty acids may link **(Figure 3.9a).** In its free state, glycerol is a polar, water-soluble, sweet-tasting substance with the properties of an alcohol. If a fatty acid binds by a dehydration synthesis reaction at each of glycerol's three —OH-bearing sites, the polar groups are eliminated, producing a nonpolar compound known as a **triglyceride** (see Figure 3.9). Most

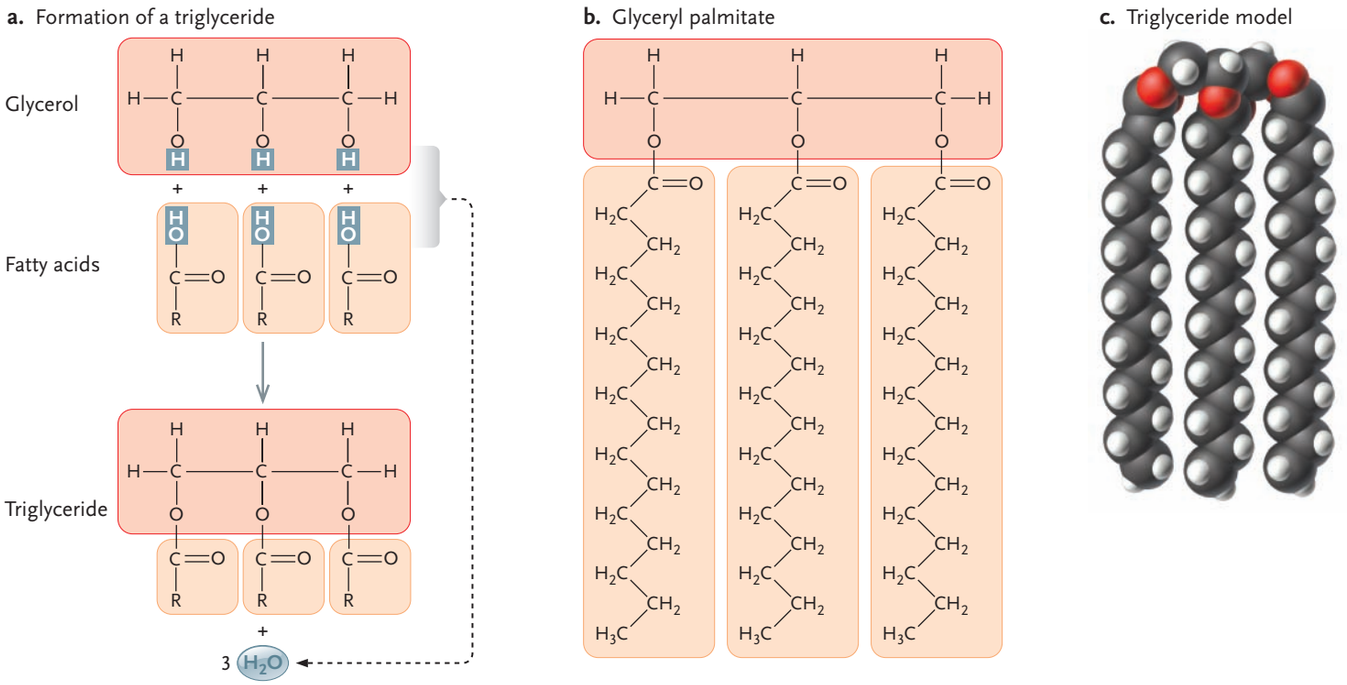


Figure 3.9
Triglycerides. **(a)** Formation of a triglyceride by dehydration synthesis of glycerol with three fatty acids. The R groups represent the hydrocarbon chains of the fatty acids. The components of a water molecule (in blue) are removed from the glycerol and fatty acids in each of the three bonds formed. **(b)** Chemical structure and **(c)** space-filling model of glyceryl palmitate, a triglyceride.

lipids stored as an energy reserve in living systems are triglycerides.

The fatty acids linked to glycerol may be different or the same. Different organisms usually have distinctive combinations of fatty acids in their triglycerides. As with individual fatty acids, triglycerides generally become less fluid as the length of their fatty acid chains increases; those with shorter chains remain liquid as oils at biological temperatures, and those with longer chains solidify as fats. The degree of saturation of the fatty acid chains also affects the fluidity of triglycerides—the more saturated, the less fluid the triglyceride. Plant oils are converted commercially to fats by *hydrogenation*—that is, adding hydrogen atoms to increase the degree of saturation, as in the conversion of vegetable oils to margarines and shortening.

Triglycerides are used widely as stored energy in animals. Gram for gram, they yield more than twice as much energy as carbohydrates by weight. Therefore, fats are an excellent source of energy in the diet. Storing the equivalent amount of energy as carbohydrates rather than fats would add more than 100 pounds to the weight of an average man or woman. A layer of fatty tissue just under the skin also serves as an insulating blanket in humans, other mammals, and birds. Triglycerides secreted from special glands in waterfowl and other birds help make feathers water repellent (as in the penguins shown in **Figure 3.10**).

Unsaturated fats are considered healthier than saturated fats in the human diet. Saturated fats have been implicated in the development of atherosclerosis (see the *Focus on Research*), a disease in which arteries, particularly those serving the heart, become clogged with fatty deposits.

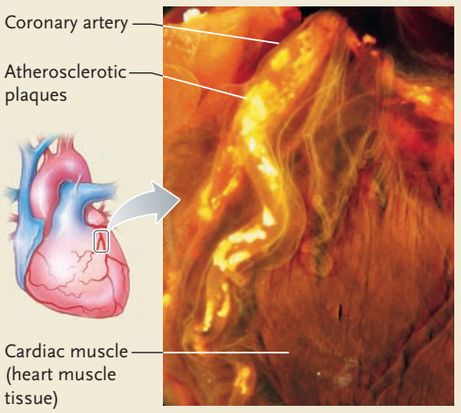
Figure 3.10
Penguins of the Antarctic, one of several animals that have a thick, insulating layer of fatty tissue that contains triglycerides under the skin. Penguins also use their face and bill to spread oil, secreted by a gland near their tail, over their feathers. The oily coating keeps their feathers watertight and dry.

Focus on Research

Applied Research: Fats, Cholesterol, and Coronary Artery Disease

Butter! Bacon and eggs! Ice cream! Cheesecake! Possibly you think of such foods as irresistible, off limits, or both. After all, who doesn't know about animal fats, cholesterol, and hardening of the arteries? Hardening of the arteries, or *atherosclerosis,* is a condition in which deposits of lipid and fibrous material called plaque build up in the walls of arteries, the vessels that supply oxygenated blood to body tissues. Plaque reduces the internal diameter of the arteries, restricting or even completely blocking the flow of blood. One of the most serious consequences occurs when atherosclerosis narrows or blocks the coronary arteries that supply oxygenated blood to the heart muscle (see figure). This condition can severely impair heart function, as in coronary heart disease, and, in extreme cases, can lead to destruction of heart muscle tissue, as occurs in a heart attack.

Your body requires a certain amount of cholesterol, but the liver normally makes enough to meet this demand. Additional cholesterol is made from fats taken in as food.

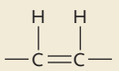


Atherosclerotic plaques (bright areas) in the coronary arteries of a patient with heart disease.

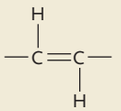
Cholesterol is found in the blood bound to low-density lipoprotein (LDL) and high-density lipoprotein (HDL). LDL cholesterol is considered "bad" because clinical studies have shown a positive correlation between its level in the blood and the risk for coronary heart disease. LDL cholesterol contributes to plaque formation as atherosclerosis proceeds. In contrast, HDL cholesterol is "good" because clinical studies have shown that high levels of this form appear to provide some protection against coronary heart disease. Simplifying, HDL cholesterol removes excess cholesterol from plaques in arteries, thereby reducing plaque buildup. The cholesterol that has been removed is transported by the HDL cholesterol to the liver where it is broken down.

Fats in food affect cholesterol levels in the blood. Diets high in saturated fats raise LDL cholesterol levels, but levels of HDL cholesterol appear not to be affected by such a diet. Foods of animal origin typically contain saturated fats, and foods of plant origin typically contain unsaturated fats.

In the food industry, unsaturated vegetable oils are often processed to solidify the fats. The process, partial hydrogenation, adds hydrogen atoms to unsaturated sites, eliminating many double bonds and generating substances known as trans fatty acids (or trans fats). Usually the hydrogen atoms at a double bond are positioned on the same side of the carbon chain, producing a cis (Latin, "on the same side") fatty acid:



but in a trans (Latin, "across") fatty acid, the hydrogen atoms are on different sides of the chain at some double bonds:



Trans fatty acids are found in many vegetable shortenings, some margarines, cookies, cakes, doughnuts, and other foods made with or fried in partially hydrogenated fats.

Research from human feeding studies has shown that trans fatty acids raise LDL cholesterol levels nearly as much as saturated fatty acids do. More seriously, intake of trans fatty acids at levels found in a typical U.S. diet also appears to reduce HDL cholesterol levels. In addition, clinical studies have demonstrated a positive correlation between the intake of trans fatty acids and the occurrence of coronary heart disease. A regulation to add the trans fatty acid content to nutritional labels went into effect in the United States in January 2006. A number of federal and state agencies are considering legislation to ban trans fatty acids in food.

Many questions about dietary cholesterol still remain. For example, people in some cultures consume large quantities of fatty foods of the "wrong" kind yet rarely develop atherosclerosis. For example, atherosclerosis was once virtually nonexistent in Inuits, whose diet in their native culture contained more than 90% animal fat; however, atherosclerosis developed in that same population when they adopted a "civilized" diet and lifestyle. In France, the incidence of atherosclerosis is relatively low even though cheese and other dairy products are diet staples. Of course, the French say that wine keeps them healthy!

Waxes. Fatty acids may also combine with long-chain alcohols or hydrocarbon structures to form **waxes**, which are harder and less greasy than fats. Insoluble in water, waxy coatings help keep skin, hair, or feathers of animals protected, lubricated, and pliable. In humans, earwax lubricates the outer ear canal and protects the eardrum. Honeybees use a wax secreted by glands in their abdomen to construct the comb in which larvae are raised and honey is stored **(Figure 3.11a).**

Many plants secrete waxes that form a protective exterior layer, which greatly reduces water loss from

plants and resists invasion by infective agents such as bacteria and viruses. This waxy covering gives cherries, apples, and many other fruits their shiny appearance **(Figure 3.11b).**

Figure 3.11
Waxy structures in nature. **(a)** The comb constructed by honeybees is made from a wax secreted by abdominal glands. **(b)** Beads of water on the waxy cuticle of cherries.

Phospholipids Provide the Framework of Biological Membranes

Phosphate-containing lipids called **phospholipids** are the primary lipids of cell membranes. In the most common phospholipids, glycerol forms the backbone of the molecule as in triglycerides, but only two of its binding sites are linked to fatty acids **(Figure 3.12).** The third site is linked to a polar phosphate group, which binds to yet another polar unit. The end of the molecule containing the fatty acids is nonpolar and hydrophobic, and the end with the phosphate group is polar and hydrophilic.

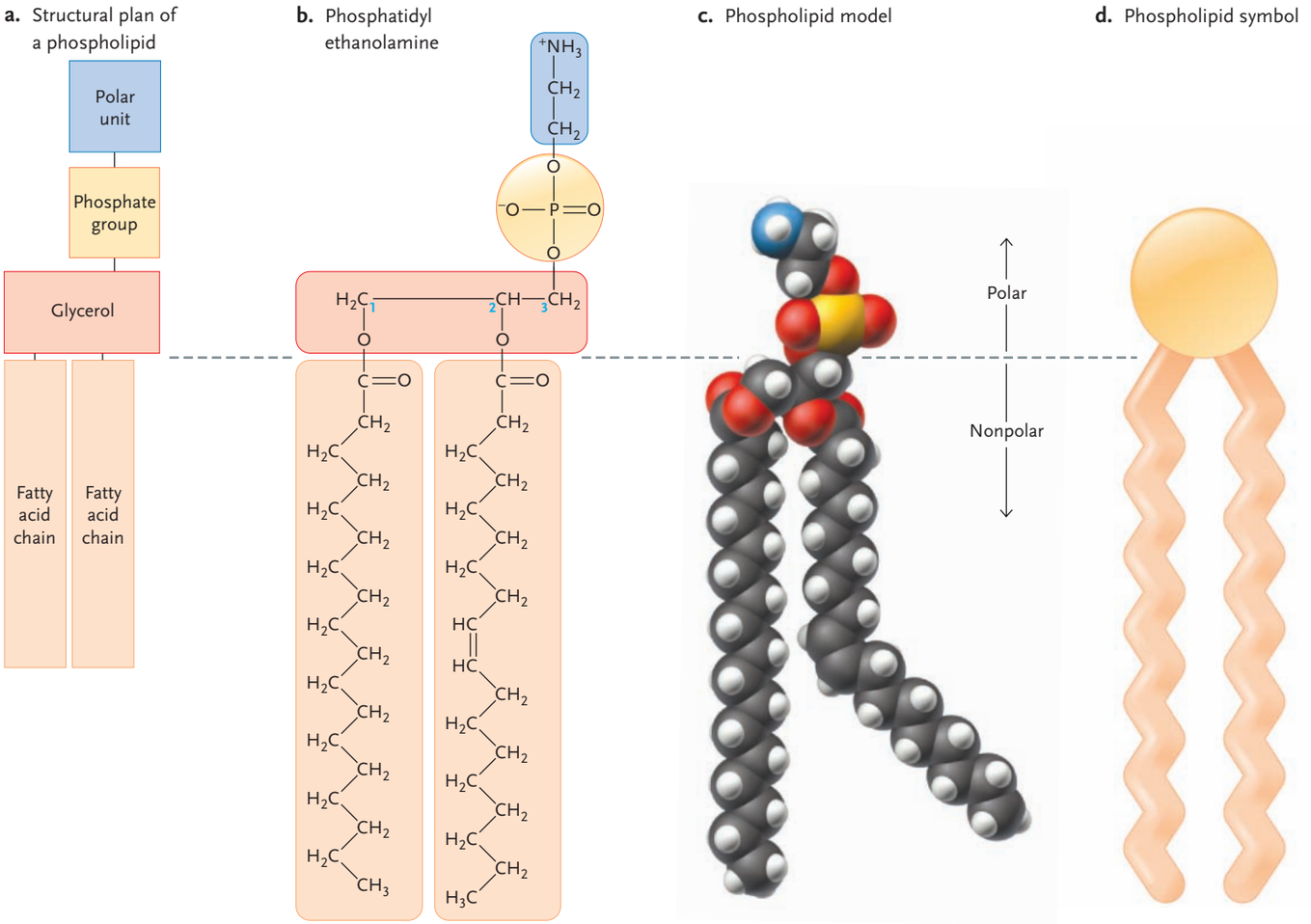


Figure 3.12
Phospholipid structure. **(a)** The arrangement of components in phospholipids. **(b)** Phosphatidyl ethanolamine, a common membrane phospholipid. **(c)** Space-filling model of phosphatidyl ethanolamine. The kink in the fatty acid chain on the right reflects a double bond at this position. **(d)** Diagram widely used to depict a phospholipid molecule in cell membrane diagrams. The sphere represents the polar end of the molecule, and the zigzag lines represent the nonpolar fatty acid chains.

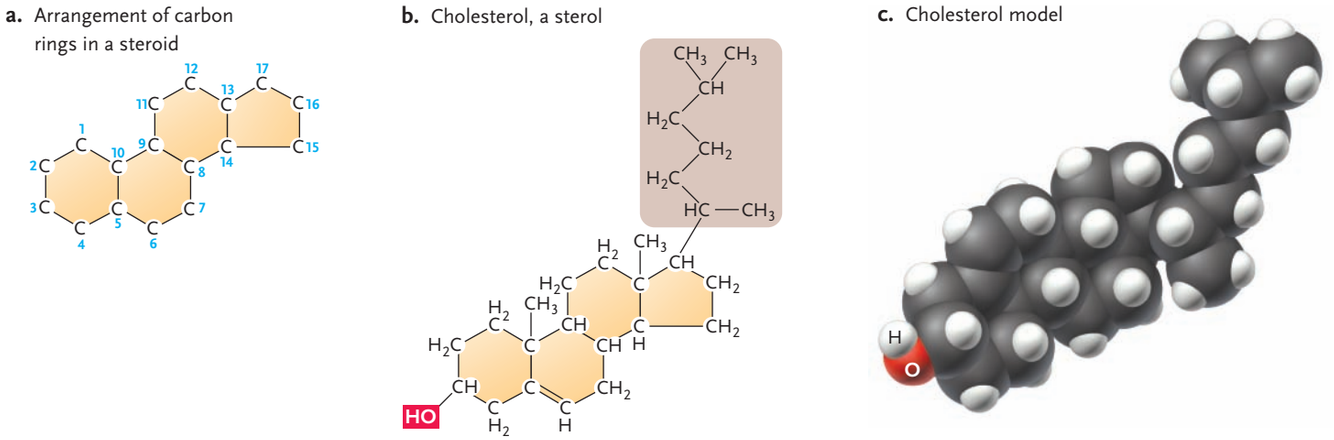


Figure 3.13
Steroids. **(a)** Typical arrangement of four carbon rings in a steroid molecule. **(b)** A sterol, cholesterol. Sterols have a hydrocarbon side chain linked to the ring structure at one end and a single —OH group at the other end (boxed in red). The —OH group makes its end of a sterol slightly polar. The rest of the molecule is nonpolar. **(c)** A space-filling model of cholesterol.

In polar environments, such as a water solution, phospholipids assume arrangements in which only their polar ends are exposed to the water; their nonpolar ends collect together in a region that excludes water. One of these arrangements, the *bilayer,* is the structural basis of membranes, the organizing boundaries of all living cells (see Figure 2.13). In a bilayer, formed by a film of phospholipids just two molecules thick, the phospholipid molecules are aligned so that the polar groups face the surrounding water molecules at the surfaces of the bilayer. The hydrocarbon chains of the phospholipids are packed together in the interior of the bilayer, where they form a nonpolar, hydrophobic region that excludes water. The bilayer remains stable because, if disturbed, the hydrophobic, nonpolar hydrocarbon chains of the phospholipids become exposed to the surrounding watery solution, and the molecule returns to its normal arrangement.

Steroids Contribute to Membrane Structure and Work as Hormones

Steroids are a group of lipids with structures based on a framework of four carbon rings **(Figure 3.13a).** Small differences in the side groups attached to the rings distinguish one steroid from another. The most abundant steroids, the **sterols,** have a single polar —OH group linked to one end of the ring framework and a complex, nonpolar hydrocarbon chain at the other end **(Figure 3.13b).** Although sterols are almost completely hydrophobic, the single hydroxyl group gives one end of the molecules a slightly polar, hydrophilic character. As a result, sterols also have dual solubility properties and, like phospholipids, tend to assume positions that satisfy these properties. In biological membranes, they line up beside the phospholipid molecules with their polar —OH group facing the membrane surface and their nonpolar ends buried in the nonpolar membrane interior.

Cholesterol (see **Figure 3.13b, c**) is an important component of the boundary membrane surrounding animal cells; similar sterols, called **phytosterols,** occur in plant cell membranes. Deposits derived from cholesterol also collect inside arteries in atherosclerosis (see the *Focus on Research*).

Other steroids, the *steroid hormones,* are important regulatory molecules in animals; they control development, behavior, and many internal biochemical pro-

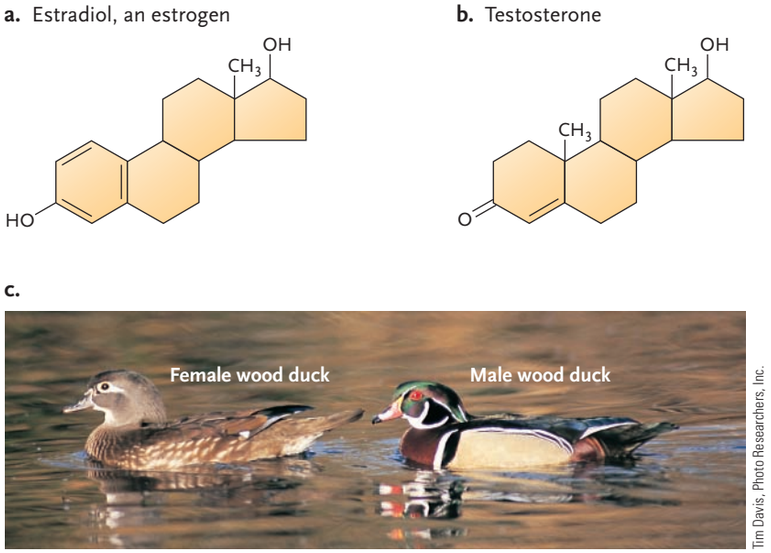


Figure 3.14
Steroid sex hormones and their effects. The female sex hormone, estradiol **(a),** and the male sex hormone, testosterone **(b),** differ only in substitution of an —OH group for an oxygen and the absence of one methyl group (—CH_3) in the estrogen. Although small, these differences greatly alter sexual structures and behavior in animals, such as humans, and the wood ducks *(Aix sponsa)* shown in **(c).**

cesses. The sex hormones that control differentiation of the sexes and sexual behavior are primary examples of steroid hormones **(Figure 3.14).** Small differences in the functional groups of steroid hormones have vastly different effects in animals. For instance, the male and female sex hormones are almost identical, except that the female sex hormone contains a single hydrogen atom that is absent from the male sex hormone, and the male sex hormone contains a single methyl group ($—CH_3$) that is absent from the female sex hormone.

Bodybuilders and other athletes sometimes use hormonelike steroids (anabolic-androgenic steroids) to increase their muscle mass (see the *Focus on Research* in Chapter 40). Unfortunately, these substances also produce numerous side effects, including elevated cholesterol, elevated blood pressure, and acne. Other steroids occur as poisons in the venoms of toads and other animals.

Several other lipid types have structures unrelated to triglycerides, phospholipids, or steroids. Among these are *chlorophylls* and *carotenoids,* pigments that absorb light and participate in its conversion to chemical energy in plants (see Chapter 9). Lipid groups also combine with carbohydrates to form *glycolipids* and with proteins to form *lipoproteins*. Both glycolipids and lipoproteins form parts of cell membranes, where they perform vital structural and functional roles.

Study Break

What are the three most common lipids in living organisms? Distinguish between their structures.

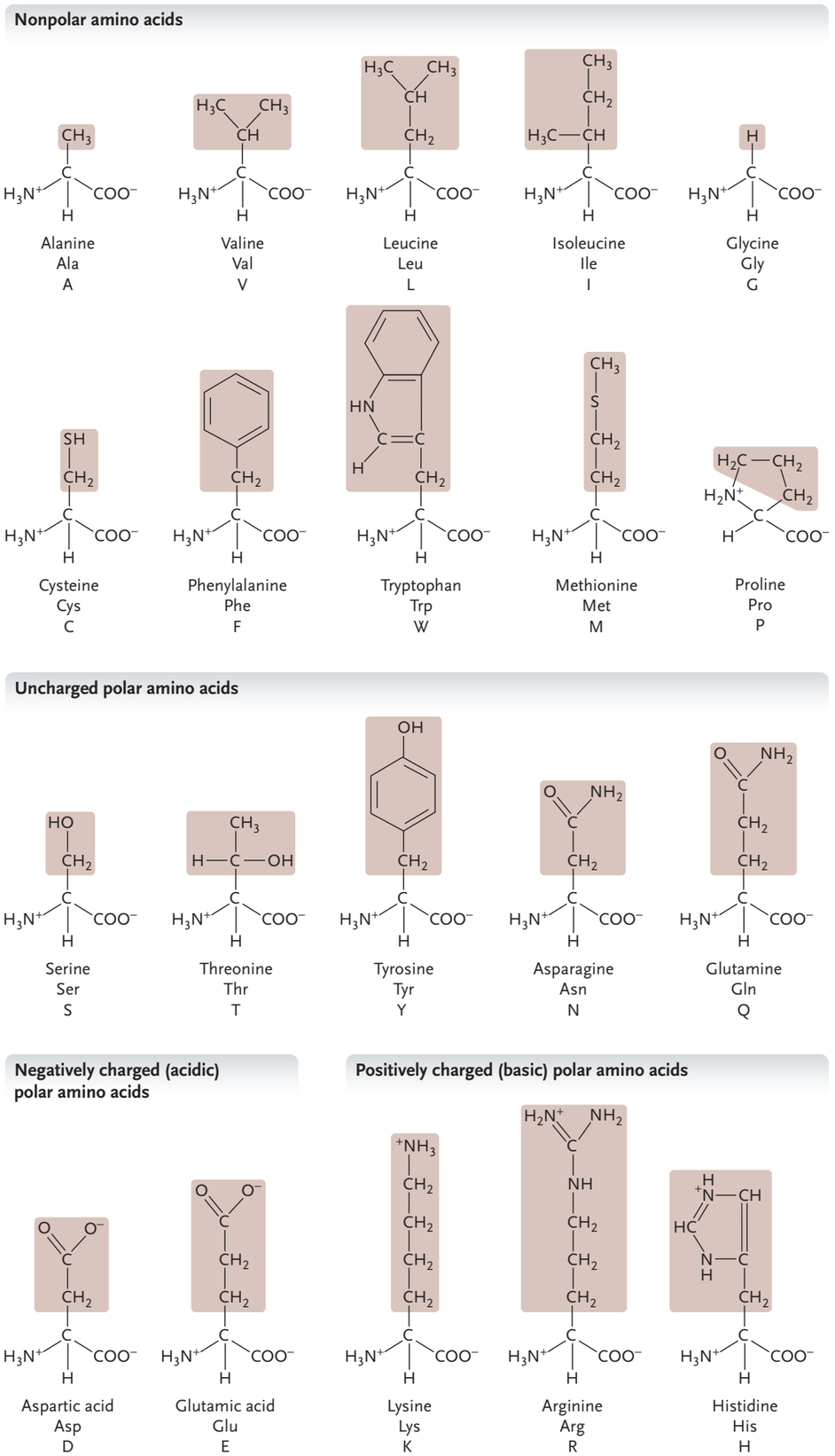
3.5 Proteins

Proteins perform many vital functions in living organisms **(Table 3.2):** as structural molecules, they provide much of the supporting framework of cells; as **enzymes,** perhaps the most important type of protein, they accelerate the rate of cellular reactions; and as motile molecules, they impart movement to cells and cellular structures. Proteins also transport substances across biological membranes, serve as recognition and recep-

Table 3.2 **Major Protein Functions**

Protein Type	Function	Examples
Structural	Support	Microtubule and microfilament proteins, which form supporting fibers inside cells; collagen and other proteins that surround and support animal cells; cell wall proteins of plant cells
Enzymatic	Speed biological reactions	Among thousands of examples, DNA polymerase, the enzyme that speeds the duplication of DNA molecules; RuBP (ribulose 1,5-bisphosphate) carboxylase, which speeds the first synthetic reactions of photosynthesis; digestive enzymes such as lipases and proteases, which speed the breakdown of fats and proteins, respectively
Membrane transport	Speed movement of substances across biological membranes	Ion transporters, which move ions such as Na^+, K^+, and Ca^{2+} across membranes; glucose transporters, which move glucose into cells; aquaporins, which allow water molecules to move across membranes
Motile	Produce cellular movements	Myosin, which acts on microfilaments (called thin filaments in muscle) to produce muscle movements; dynein, which acts on microtubules to produce the whipping movements of sperm tails, flagella, and cilia (the last two are whiplike appendages on the surfaces of many eukaryotic cells); kinesin, which acts on microtubules of the cytoskeleton, a three-dimensional structure in the cytoplasm of eukaryotic cells responsible for cellular movement, cell division, and the organization of organelles
Regulatory	Promote or inhibit the activity of other cellular molecules	Nuclear regulatory proteins, which turn genes on or off to control the activity of DNA; protein kinases, which add phosphate groups to other proteins to modify their activity
Receptor	Bind molecules at cell surface or within cell; some trigger internal cellular responses	Hormone receptors, which bind hormones at the cell surface or within cells and trigger cellular responses; cellular adhesion molecules, which help hold cells together by binding molecules on other cells; LDL receptors, which bind cholesterol-containing particles to cell surfaces
Hormones	Carry regulatory signals between cells	Insulin, which regulates sugar levels in the bloodstream; growth hormone, which regulates cellular growth and division
Antibodies	Defend against invading molecules and organisms	Recognize, bind, and help eliminate essentially any protein of infecting bacteria and viruses, and many other types of molecules, both natural and artificial
Storage	Hold amino acids and other substances in stored form	Ovalbumin, a storage protein of eggs; apolipoproteins, which hold cholesterol in stored form for transport through the bloodstream
Venoms and toxins	Interfere with competing organisms	Ricin, a castor-bean protein that stops protein synthesis; bungarotoxin, a snake venom that causes muscle paralysis

Figure 3.15
The 20 amino acids used by cells to make proteins. The side group of each amino acid is boxed in brown. The amino acids are shown in the ionic forms in which they are found at the pH within the cell; the amino group becomes —NH_3^+, and the carboxyl group becomes —COO^-. Three-letter and one-letter abbreviations commonly used for the amino acids appear below each diagram. All amino acids assembled into proteins are in the L-form, one of two possible enantiomers.



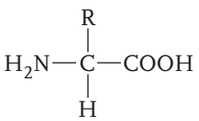
tor molecules at cell surfaces, and regulate the activity of other proteins and DNA.

Proteins are also released to the cell exterior. Some form parts of extracellular structures, such as cell walls in plants and tendons, bone, cartilage, hair, hooves, and claws in animals. Other proteins released by animals work as hormones, digestive enzymes, or antibodies. (Antibodies are protein molecules that recognize and inactivate foreign material, such as infectious microorganisms.) Many toxins and venoms are based on proteins. For example, botulinum toxin, which is produced by the bacterium *Clostridium botulinum,* is one of the most toxic substances known, with a lethal dose to humans of about 200 to 300 pg/kg (picogram [pg] = 10^{-12} gram).

All of the protein molecules that carry out these and other functions are fundamentally similar in structure. All are macromolecules—polymers consisting of one or more unbranched chains of monomers called amino acids. An **amino acid** is a chemical that contains both an amino and a carboxyl group. Although the most common proteins contain 50 to 1000 amino acids, some proteins found in nature have as few as 3 or as many as 50,000 amino acid units. Proteins range in shape from globular or spherical forms to elongated fibers, and they vary from soluble to completely insoluble in water solutions. Some proteins have single functions, whereas others have multiple functions.

Cells Assemble 20 Kinds of Amino Acids into Proteins by Forming Peptide Bonds

The cells of all organisms use 20 different amino acids as the initial building blocks of proteins. Of these 20 amino acids, 19 have the same structural plan **(Figure 3.15).** In this plan, a central carbon atom is attached to an amino group (—NH_2), a carboxyl group (—COOH), and a hydrogen atom:



The remaining bond of the central carbon is linked to 1 of 19 different side groups represented by the *R* (see shaded regions in Figure 3.15), ranging from a single hydrogen atom to complex carbon chains or rings. The remaining amino acid, proline, differs slightly in that it has a ring structure that includes the central carbon atom; the central carbon bonds to a —COOH group on one side and to an *imino* (═NH) group that forms part of the ring at the other side (see Figure 3.15). Although they are called acids, all 20 of the amino acids can act as either acids or bases—depending on cellular conditions, the amino (or imino) group can produce a basic reaction by accepting H^+, or the carboxyl group can produce an acidic reaction by releasing H^+.

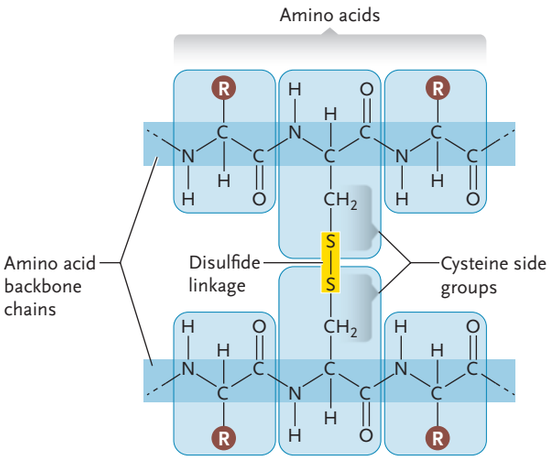


Figure 3.16
A disulfide linkage between two amino acid chains or two regions of the same chain. The linkage is formed by a reaction between the sulfhydryl groups (—SH) of cysteines. The circled *R*'s indicate the side groups of other amino acids in the chains. Figure 3.19 shows disulfide linkages in a real protein.

Differences in the side groups give the amino acids their individual properties. Some side groups are polar, and some are nonpolar; among the polar side groups, some carry a positive or negative charge and some act as acids or bases (see Figure 3.15). Many of the side groups contain reactive functional groups, such as —NH_2, —OH, —COOH, or —SH, which may interact with atoms located elsewhere in the same protein or with molecules and ions outside the protein.

The sulfhydryl group (—SH) in the amino acid cysteine is particularly important in protein structure. The sulfhydryl groups of cysteines located in different regions of the same protein, or in different proteins, can interact to produce disulfide linkages (—S—S—). The linkages fasten amino acid chains together **(Figure 3.16)** and help hold proteins in their three-dimensional shape.

Overall, the varied properties and functions of proteins depend on the types and locations of the different amino acid side groups in their structures. The variations in the number and types of amino acids mean that the total number of possible proteins is extremely large.

Covalent bonds link amino acids into the chains of subunits that make proteins. The link, a **peptide bond,** is formed by a dehydration synthesis reaction between the —NH_2 group of one amino acid and the —COOH group of a second **(Figure 3.17).** An amino acid chain always has an —NH_2 group at one end, called the **N-terminal end,** and a —COOH group at the other end, called the **C-terminal end.** In cells, amino acids are added only to the —COOH end of another amino acid.

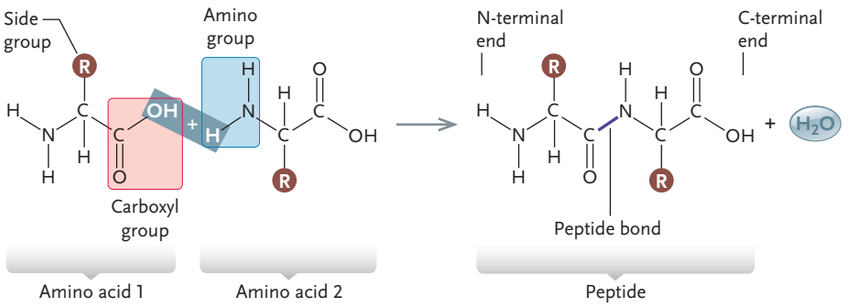


Figure 3.17
A peptide bond formed by reaction of the carboxyl group of one amino acid with the amino group of a second amino acid. The reaction is a typical dehydration synthesis reaction.

The chain of amino acids formed by sequential peptide bonds, that is, a **polypeptide**, is only part of the complex structure of proteins. Once assembled, an amino acid chain may fold in various patterns, and more than one chain may combine to form a finished protein, adding to the structural and functional variability of proteins.

Proteins Have as Many as Four Levels of Structure

Proteins potentially have four levels of structure, with each level imparting different characteristics and degrees of structural complexity to the molecule **(Figure 3.18). Primary structure** is the particular and unique sequence of amino acids forming a polypeptide; **secondary structure** is produced by the twists and turns of the amino acid chain. **Tertiary structure** is the folding of the amino acid chain, with its secondary structures, into the overall three-dimensional shape of a protein. All proteins have primary, secondary, and tertiary structures. **Quaternary structure**, when present, refers to the arrangement of amino acid chains in a protein that is formed from more than one chain.

Primary Structure Is the Fundamental Determinant of Protein Form and Function

The primary structure of a protein—that is, the sequence in which amino acids are linked—underlies the other, higher levels of structure. Changing even a single amino acid of the primary structure alters the secondary, tertiary, and quaternary structures to at least some degree and, by so doing, can alter or even destroy the biological functions of a protein. For example, substitution of a single amino acid in the blood protein hemoglobin produces an altered form responsible for sickle-cell disease (see Chapter 12); many other blood disorders are caused by single amino acid substitutions in other parts of the protein.

Because primary structure is so fundamentally important, many years of intensive research have been devoted to determining the amino acid sequence of proteins. Initial success came in 1953, when the English biochemist Frederick Sanger deduced the amino acid sequence of insulin, a protein-based hormone, from samples obtained from cows **(Figure 3.19).** Now, the amino acid sequences of literally thousands of proteins have been determined, and more are constantly being added to the list. Knowledge of the primary structure of proteins often allows their three-dimensional structure and functions to be predicted and reveals relationships among proteins.

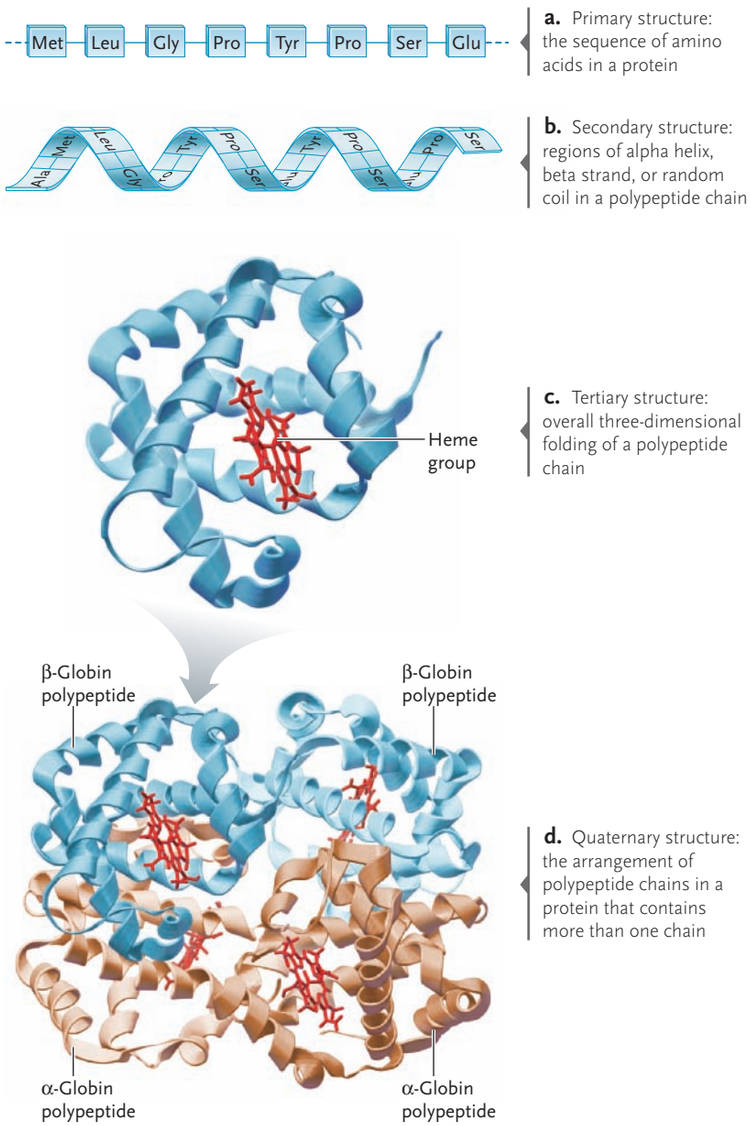


Figure 3.18
The four levels of protein structure. The protein shown in **(c)** is one of the subunits of a hemoglobin molecule; the heme group (in red) is an iron-containing group that binds oxygen. **(d)** A complete hemoglobin molecule.

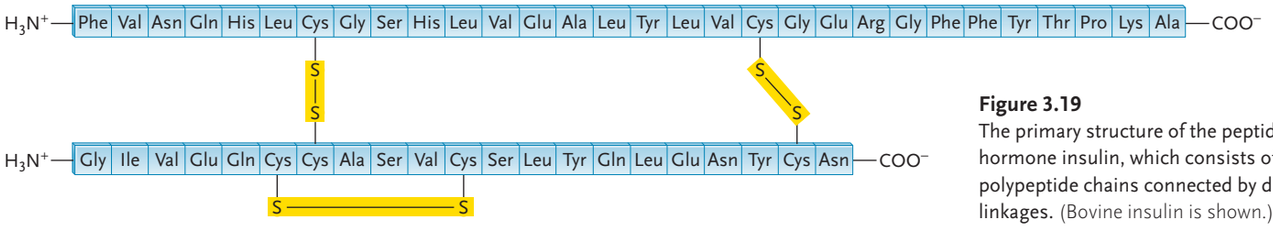


Figure 3.19
The primary structure of the peptide hormone insulin, which consists of two polypeptide chains connected by disulfide linkages. (Bovine insulin is shown.)

Twists and Other Arrangements of the Amino Acid Chain Form the Secondary Structure of a Protein

The amino acid chain of a protein, rather than being stretched out in linear form, is folded into arrangements that form the protein's secondary structure. Two highly regular secondary structures, the *alpha helix* and the *beta strand,* are particularly stable and make an amino acid chain resistant to bending. A third, less regular arrangement, the *random coil* or *loop,* provides flexible regions that allow sections of amino acid chains containing them to bend. Most proteins have segments of all three arrangements.

The Alpha Helix. In the alpha (α) helix, first identified by Linus Pauling and Robert Corey at the California Institute of Technology in 1951, the backbone of the amino acid chain is twisted into a regular, right-hand spiral **(Figure 3.20).** The amino acid side groups extend outward from the twisted backbone. The structure is stabilized by regularly spaced hydrogen bonds (see dotted lines in Figure 3.20) between atoms in the backbone.

Most proteins contain segments of α helix, which are rigid and rodlike, in at least some regions. Globular proteins usually contain several short α-helical segments that run in different directions, connected by segments of random coil. Fibrous proteins, such as the collagens, a major component of tendons, bone, and other extracellular structures in animals, typically contain one or more α-helical segments that run the length of the molecule, with few or no bendable regions of random coil.

The Beta Strand. Pauling and Corey were also the first to identify the beta strand as a major secondary protein structure **(Figure 3.21a).** In a beta (β) strand, the amino acid chain zigzags in a flat plane rather than twisting into a coil.

In many proteins, β strands are aligned side by side in the same or opposite directions to form a structure known as a **beta (β) sheet (Figure 3.21b).** Hydrogen bonds between adjacent β strands stabilize the sheet, making it a highly rigid structure. Beta sheets may lie in a flat plane or may twist into propeller- or barrel-like structures.

Beta strands and sheets occur in many proteins, usually in combination with α-helical segments. One notable exception is in the silk protein secreted by silkworms, which contains only β sheets. This exceptionally stable structure, reinforced by an extensive network of hydrogen bonds, underlies the unusually high tensile strength of silk fibers.

The Random Coil. In a **random coil** the amino acid chain has an irregularly folded arrangement. The amino acid proline is often present in random-coil structures. Its ring form does not fit into an α helix or β sheet, and it has no sites available for formation of stabilizing hydrogen bonds.

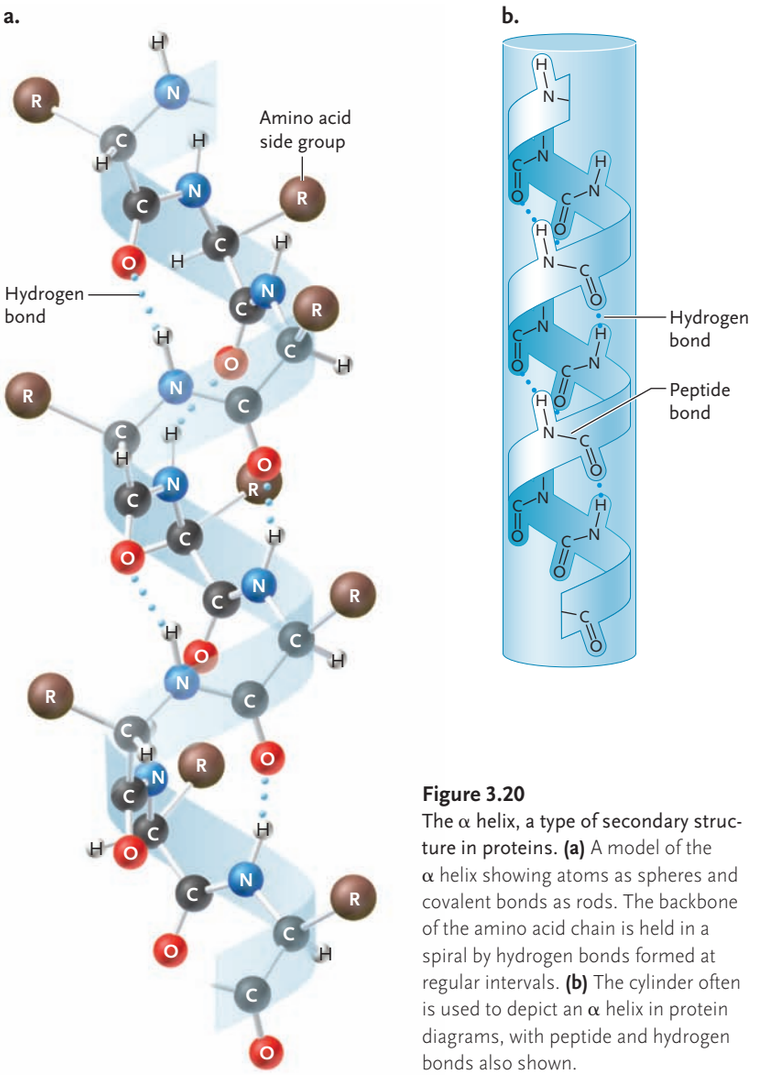


Figure 3.20
The α helix, a type of secondary structure in proteins. **(a)** A model of the α helix showing atoms as spheres and covalent bonds as rods. The backbone of the amino acid chain is held in a spiral by hydrogen bonds formed at regular intervals. **(b)** The cylinder often is used to depict an α helix in protein diagrams, with peptide and hydrogen bonds also shown.

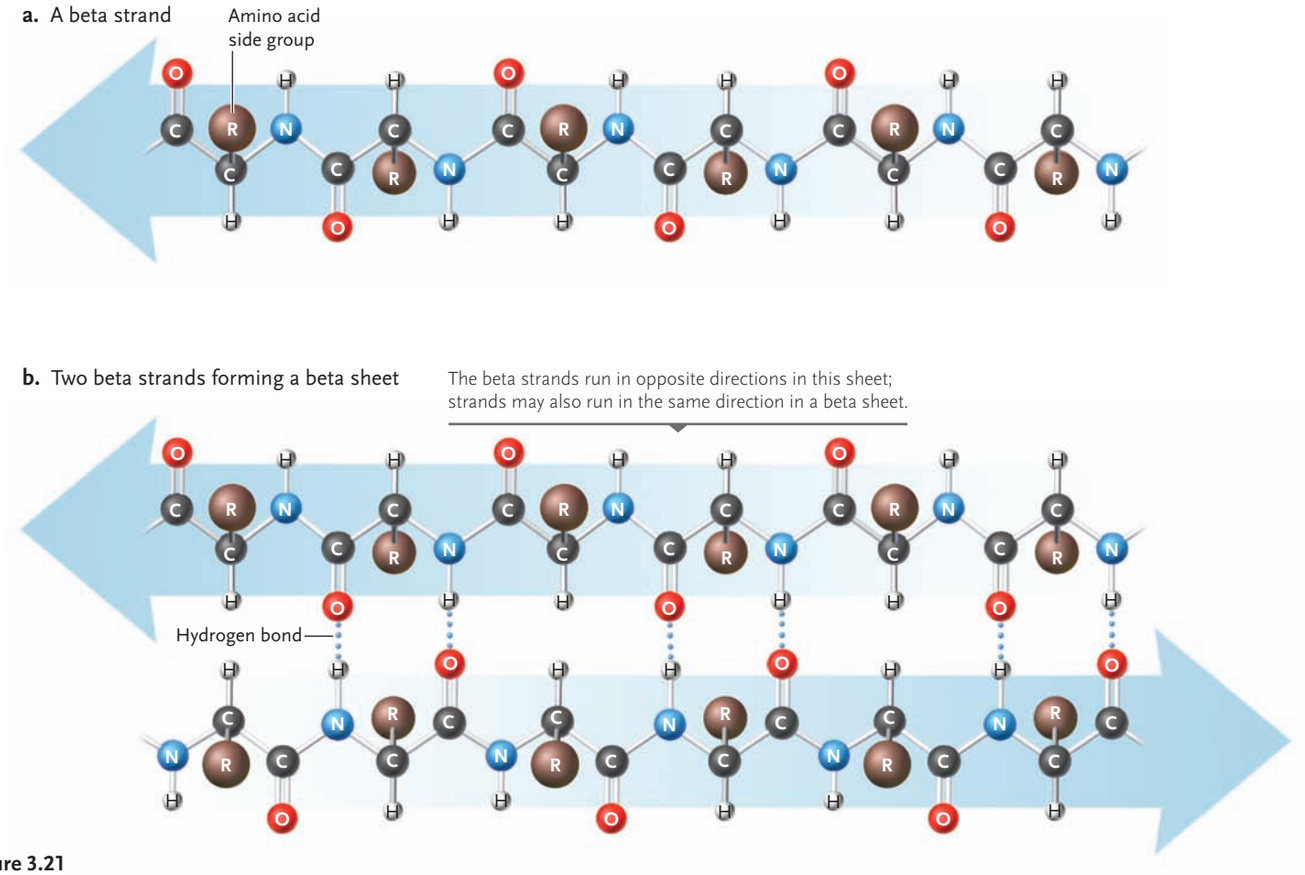
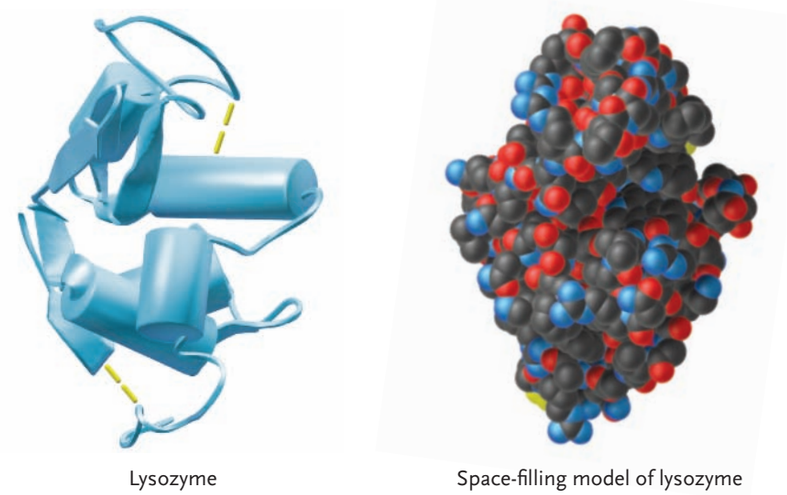


Figure 3.21
The β strand, a type of secondary structure in proteins. (a) A single β strand; the arrow points in the direction of the C-terminal end of the amino acid chain. Arrows alone often are used to represent β strands in protein diagrams. **(b)** A β sheet formed by side-by-side alignment of two β strands, held together stably by hydrogen bonds.



Lysozyme

Space-filling model of lysozyme

Figure 3.22
Tertiary structure of the protein lysozyme, with α helices shown as cylinders, β strands as arrows, and random coils as lines. Lysozyme is an enzyme found in nasal mucus, tears, and other body secretions; it destroys the cell walls of bacteria by breaking down molecules in the wall. Disulfide bonds are shown in yellow. A space-filling model of lysozyme is shown for comparison.

Segments of random coil provide flexible sites that allow α-helical or β-strand segments to bend or fold back on themselves. The fold-back loops of random coils often occur at the surfaces of proteins, at points where they link segments of α helix or β strand located deeper in the protein. Segments of random coil also commonly act as "hinges" that allow major parts of proteins to move with respect to one another.

The Tertiary Structure of a Protein Is Its Overall Three-Dimensional Conformation

The content of α-helical, β-strand, and random-coil segments, together with the number and position of disulfide linkages and hydrogen bonds, folds each protein into its tertiary structure—that is, its overall three-dimensional shape, or **conformation (Figure 3.22).** Attractions between positively and negatively charged side groups and polar or nonpolar associations also contribute to the tertiary structure.

A protein's tertiary structure buries some amino acid side groups in its interior and exposes others at the surface. The distribution and three-dimensional arrangement of the side groups, in combination with their chemical properties, determine the overall chemical activity of a protein. For example, the tertiary structure of the antibacterial enzyme lysozyme (see Figure

Insights from the Molecular Revolution

Getting Good Vibrations from Proteins

Many functions of proteins—their ability to speed biochemical reactions, obtain energy from sugars, transport molecules in and out of cells, move the limbs of animals, and even produce your thoughts as you read this page—depend on their ability to undergo changes in conformation (shape).

While conformational changes can produce major effects, the molecular movements that underlie these actions are often so minute that they are extremely difficult for scientists to detect. The information is well worth the quest, however, because detecting the exact instant that a protein's shape changes can lead to answers about the part of the protein that produces an effect. Through these answers, researchers can unearth the molecular processes responsible for activities such as muscle contraction or cellular transport.

A number of methods exist for detecting conformational changes in proteins. Atomic force sensing, developed by investigators at the Jerusalem Hebrew University and the Weizmann Institute in Israel, is a technique that can detect protein motion directly, by watching the "wiggles" of a microscopic glass fiber touching the surface of a protein. As a test object, the researchers chose bacteriorhodopsin, a protein found in some members of the prokaryotic domain Archaea (introduced in Chapter 1). They knew that, when bacteriorhodopsin absorbs light at a certain wavelength, it undergoes a conformational change that pumps H^+ from one side of a membrane to the other, initiating a primitive form of photosynthesis. A related animal protein, rhodopsin, undergoes similar changes when it absorbs light as part of the visual process.

The investigators isolated bacteriorhodopsin from the archaean *Halobacterium*, together with lipid molecules from the surface membrane of the organism. They created a film only a few molecules thick on the surface of a glass slide and positioned a curved, microscopic glass probe so that its tip just touched the surface of the film. By shining a microscopic laser beam at the glass fiber, the investigators could detect minute changes in its position by noting changes in the direction of the light reflected from the fiber.

When the researchers directed a brief pulse of light toward the protein film at the wavelength absorbed by bacteriorhodopsin (532 nm), the glass fiber wiggled directionally for a few thousandths of a second, indicating that the protein's conformation changed. Then, they directed a second pulse at a different wavelength known to reverse the pumping action of bacteriorhodopsin (410 nm), and the fiber wiggles also reversed their direction. These results provided further evidence that light causes a conformational change in the protein.

This experiment also produced some novel results. The wiggles showed some motions of bacteriorhodopsin that had never before been detected by measurement of changes in light absorption. These newly detected motions, as the investigators pointed out, may lead to new hypotheses and novel findings about how bacteriorhodopsin, as well as its rhodopsin cousin in animals, functions in living cells.

3.22) has a cleft that binds a polysaccharide found in bacterial cell walls; hydrolysis of the polysaccharide is accelerated by the enzyme.

Tertiary structure also determines the solubility of a protein. Water-soluble proteins have mostly polar or charged amino acid side groups exposed at their surfaces, whereas nonpolar side groups are clustered in the interior. Proteins embedded in nonpolar membranes are arranged in patterns similar to phospholipids, with their polar segments facing the surrounding watery solution and their nonpolar surfaces embedded in the nonpolar membrane interior. These dual-solubility proteins perform many important functions in membranes, such as transporting ions and molecules into and out of cells.

The tertiary structure of most proteins is flexible, allowing them to undergo limited alterations in three-dimensional shape known as **conformational changes.** These changes contribute to the function of many proteins, particularly those working as enzymes, in cellular movements or in the transport of substances across cell membranes. *Insights from the Molecular Revolution* describes a method that allows researchers to detect directly movements produced by the conformational changes of proteins.

Extreme conditions can unfold a protein from its conformation, causing **denaturation**, a loss of both the structure and function of the protein **(Figure 3.23).** For example, excessive heat can break the hydrogen bonds holding a protein in its natural conformation, causing it to unfold and lose its biological activity. Denaturation is one of the major reasons few living organisms can tolerate temperatures greater than 45°C. Extreme changes in pH, which alter the charge of amino acid side groups and weaken or destroy ionic bonds, can also cause protein denaturation.

For some proteins, denaturation is permanent. A familiar example of a permanently denatured protein is a cooked egg white. In its natural form, the egg white protein albumin dissolves in water to form a clear solution. The heat of cooking denatures it permanently into an insoluble, whitish mass.

For other proteins (for example, the enzyme in Figure 3.23), denaturation is reversible: the proteins can re-

turn to their natural, functional form if the temperature or pH returns to normal values. Disulfide linkages in an enzyme help limit protein denaturation by preventing amino acid chains from unfolding completely.

One of the active research areas of biology concerns the process by which proteins fold into their tertiary structure as they are made inside cells. Results indicate that proteins fold gradually as they are made—as successive amino acids are linked into the primary structure, the chain folds into increasingly complex structures. As the final amino acids are added to the sequence, the protein completes its folding to the final three-dimensional form. One nagging question about this process is how proteins assume their correct tertiary structure among the different possibilities that may exist for a given amino acid sequence. For many proteins, "guide" proteins called **chaperone proteins** or **chaperonins** solve this problem; they bind temporarily with newly synthesized proteins, directing their conformation toward the correct tertiary structure and inhibiting incorrect arrangements as the new proteins fold **(Figure 3.24).**

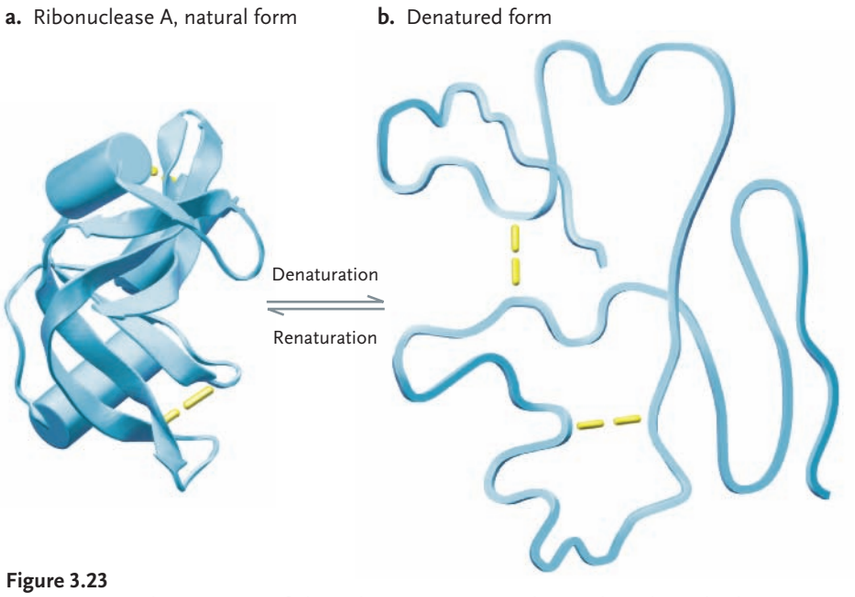


Figure 3.23
Denaturation and renaturation of ribonuclease A, an enzyme that is released into the digestive tract. Note that all segments of the α helix and β strand are lost when the protein is denatured. Disulfide bonds (in yellow) help the protein return to its natural form during renaturation. (Not all of the disulfide bonds are shown.)

Multiple Amino Acid Chains Form Quaternary Structure

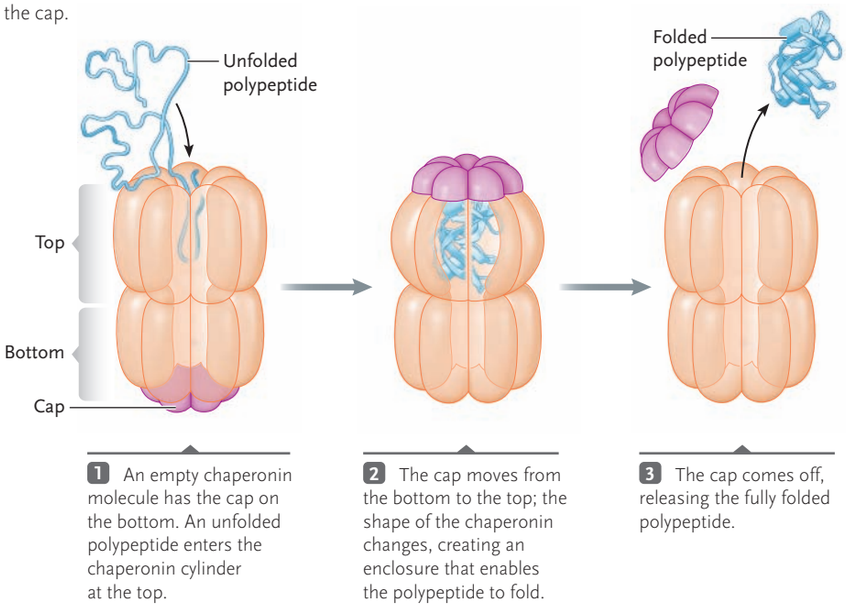
Some complex proteins, such as hemoglobin and antibody molecules, have quaternary structure—that is, the presence and arrangement of two or more amino acid chains (see Figure 3.18d). The same bonds and forces that fold single amino acid chains into tertiary structures, including hydrogen bonds, polar and nonpolar attractions, and disulfide linkages, also hold the multiple polypeptide chains together. During the assembly of multichain proteins, chaperonins also promote correct association of the individual amino acid chains and inhibit incorrect formations.

Combinations of Secondary, Tertiary, and Quaternary Structure Form Functional Domains in Many Proteins

In many proteins, folding of the amino acid chain produces distinct, large structural subdivisions called **domains (Figure 3.25a, b).** Often, one domain of a protein is connected to another by a segment of random coil. The hinge formed by the flexible random coil allows domains to move with respect to one another. Hinged domains of this type are typical of proteins that produce motion and also occur in many enzymes.

Many proteins have multiple functions. For instance, the sperm surface protein SPAM1 (sperm adhesion molecule 1) plays

Figure 3.24
Role of a chaperonin in folding a polypeptide. The three parts of the chaperonin are the top and bottom, which form a cylinder, and the cap.



multiple roles in mammalian fertilization. In proteins with multiple functions, individual functions are often located in different domains (see Figure 3.25), meaning domains are functional as well as structural subdivisions. Different proteins often share one or more domains with particular functions. For example, a type of domain that releases energy to power biological reactions appears in similar form in many enzymes and motile proteins. The appearance of similar domains in different proteins suggests that the proteins may have evolved through a mechanism that mixes existing domains into new combinations.

The three-dimensional arrangement of amino acid chains within and between domains also produces highly specialized regions called **motifs.** Several types of motifs, each with a specialized function, occur in proteins. For example, a structural motif called the *leucine zipper* **(Figure 3.25c, d)** holds together proteins that become functional when they join into pairs. The amino acid sequence of the α helix forming each half of the zipper has leucine at every seventh position. The rows of leucine side groups, which project from the α helices, are the "teeth" of the zipper. When two zipper halves come together, as on proteins that join into a pair, they line up by hydrophobic associations (see Section 2.3) into a stable, closed zipper that links the proteins. Many other types of motifs occur in proteins, including some that fit perfectly to a segment of a DNA molecule; for example, the *helix-turn-helix motif* **(Figure 3.25e)** is found in many proteins that regulate DNA activity.

Proteins Combine with Units Derived from Other Classes of Biological Molecules

We have already mentioned the linkage of proteins to lipids to form lipoproteins. Proteins also link with carbohydrates to form *glycoproteins,* which function as

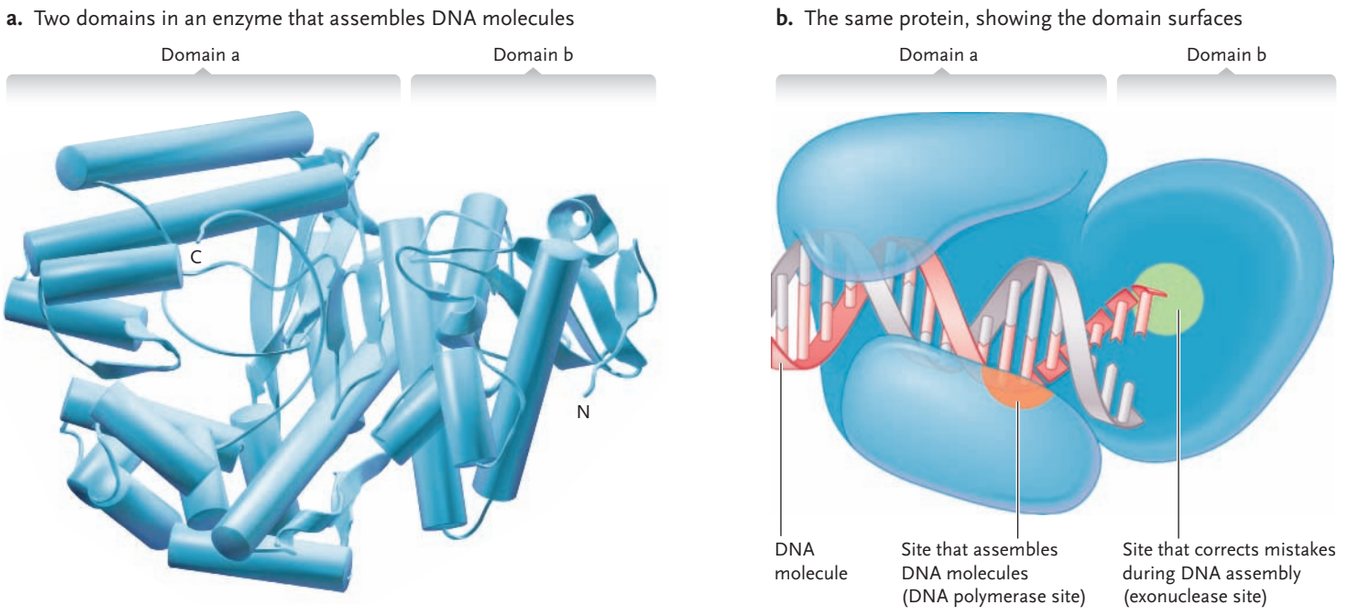


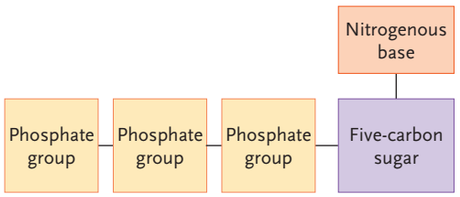
Figure 3.25
Domains and motifs in proteins. **(a)** Two domains in part of an enzyme that assembles DNA molecules in the bacterium *Escherichia coli,* showing α helices as cylinders and β strands as arrows. **(b)** The same view of the protein as in **(a),** showing only the domain surfaces. **(c, d)** The leucine zipper motif, which holds proteins together in active pairs. **(e)** The helix-turn-helix motif, found in regulatory proteins, which fits precisely into the side of a DNA molecule.

enzymes, antibodies, recognition and receptor molecules at the cell surface, and parts of extracellular supports such as collagen. In fact, most of the known proteins located at the cell surface or in the spaces between cells are glycoproteins. Linkage of proteins to nucleic acids produces *nucleoproteins,* which form such vital structures as *chromosomes,* the structures that organize DNA inside cells.

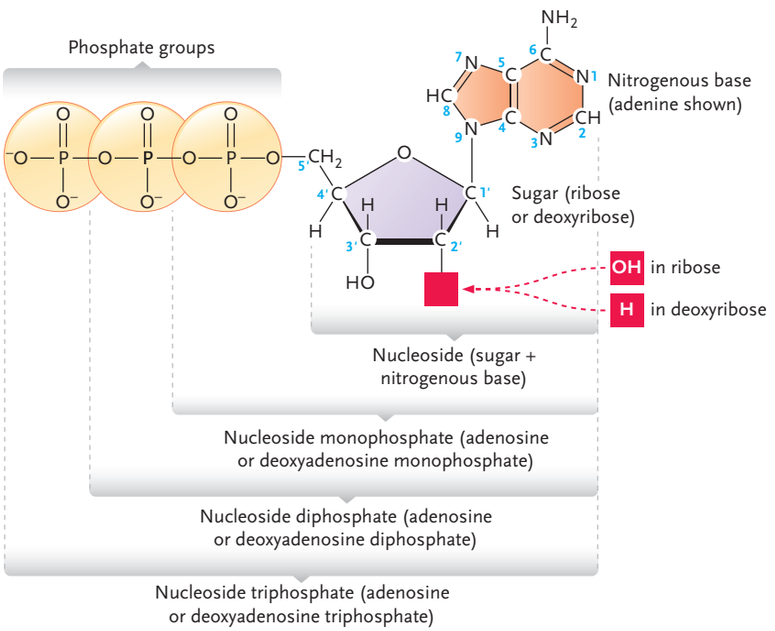
This section has demonstrated the importance of the amino acid sequence to the structure and function of proteins and highlighted the great variability in proteins produced by differences in their amino acid sequence. The next section considers the nucleic acids, which store and transmit the information required to arrange amino acids into particular sequences in proteins.

Figure 3.26
Nucleotide structure.

a. Overall structural plan of a nucleotide



b. Chemical structures of nucleotides



Other nucleotides:

Containing guanine:	Guanosine or deoxyguanosine monophosphate, diphosphate, or triphosphate
Containing cytosine:	Cytidine or deoxycytidine monophosphate, diphosphate, or triphosphate
Containing thymine:	Thymidine monophosphate, diphosphate, or triphosphate
Containing uracil:	Uridine monophosphate, diphosphate, or triphosphate

Study Break

1. What gives amino acids their individual properties?
2. What is a peptide bond, and what type of reaction forms it?
3. What are functional domains of proteins, and how are they formed?

3.6 Nucleotides and Nucleic Acids

Nucleic acids are another class of macromolecules, in this case, long polymers assembled from repeating monomers called *nucleotides*. Two types of nucleic acids exist: DNA and RNA. **DNA (deoxyribonucleic acid)** stores the hereditary information responsible for inherited traits in all eukaryotes and prokaryotes and in many viruses. **RNA (ribonucleic acid)** is the hereditary molecule of some viruses; in all organisms, one type of RNA carries the instructions for assembling proteins from DNA to the sites where the proteins are made inside cells. Another type of RNA forms part of ribosomes, the structural units that assemble proteins, and a third type of RNA functions to bring amino acids to the ribosome for their assembly into proteins (see Chapter 15).

Nucleotides Consist of a Nitrogenous Base, a Five-Carbon Sugar, and One or More Phosphate Groups

A **nucleotide**, the monomer of nucleic acids, consists of three parts linked together by covalent bonds: (1) a **nitrogenous base** (a nitrogen-containing molecule with the property of a base), formed from rings of carbon and nitrogen atoms; (2) a five-carbon, ring-shaped sugar; and (3) one to three phosphate groups **(Figure 3.26).** The two types of nitrogenous bases are **pyrimidines**, with one carbon-nitrogen ring, and **purines**, with two rings **(Figure 3.27).** Three pyrimidine bases—uracil (U), thymine (T), and cytosine (C)—and two purine bases—adenine (A) and guanine (G)—form parts of nucleic acids in cells.

In nucleotides, the nitrogenous bases link covalently to a five-carbon sugar, either **deoxyribose** or **ribose.** The carbons of the two sugars are numbered with a prime symbol—1′, 2′, 3′, 4′, and 5′ (see Figure 3.26). The prime symbols are added to distinguish the carbons in the sugars from those in the nitrogenous bases, which are written without primes. The two sugars differ only in the chemical group bound to the 2′ carbon (boxed in red in Figure 3.26b): deoxyribose has

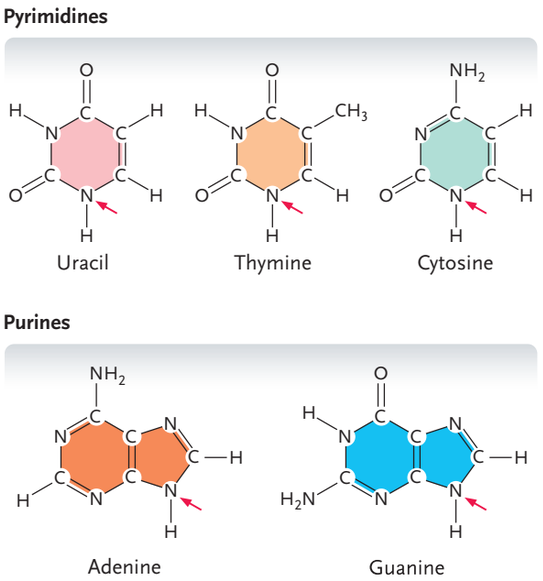


Figure 3.27
Pyrimidine and purine bases of nucleotides and nucleic acids. Red arrows indicate where the bases link to ribose or deoxyribose sugars in the formation of nucleotides.

an —H at this position and ribose has an —OH group. The prefix *deoxy-* in deoxyribose reflects the oxygen that is absent at this position in the DNA sugar. In nucleotides in the free, unlinked form, a chain of one, two, or three phosphate groups links to the ribose or deoxyribose sugar at the 5′ carbon; nucleotides are called monophosphates, diphosphates, or triphosphates according to the length of this phosphate chain.

A structure that contains only a nitrogenous base and a five-carbon sugar is called a *nucleoside* (see Figure 3.26b). Thus, nucleotides are *nucleoside phosphates*. For example, the nucleoside containing adenine and ribose is called *adenosine*. Adding one phosphate group to this structure produces *adenosine monophosphate (AMP)*, adding two phosphate groups produces *adenosine diphosphate (ADP)*, and adding three produces *adenosine triphosphate (ATP)*. The corresponding adenine–deoxyribose complexes are named *deoxyadenosine monophosphate (dAMP)*, *deoxyadenosine diphosphate (dADP)*, and *deoxyadenosine triphosphate (dATP)*. The lowercase *d* in the abbreviations indicates that the nucleoside contains the deoxyribose form of the sugar. Equivalent names and abbreviations are used for the other nucleotides (see Figure 3.26b). Whether a nucleotide is a monophosphate, diphosphate, or triphosphate has fundamentally important effects on its activities.

Nucleotides perform many functions in cells in addition to serving as the building blocks of nucleic acids. Two nucleotides in particular, ATP and guanosine triphosphate (GTP), are the primary molecules that transport chemical energy from one reaction system to another; the same nucleotides function to regulate and adjust cellular activity. Molecules derived from nucleotides play important roles in biochemical reactions by delivering reactants or electrons from one system to another.

Nucleic Acids DNA and RNA Are the Informational Molecules of All Organisms

DNA and RNA consist of chains of nucleotides, *polynucleotide chains*, with one nucleotide linked to the next by a bridging phosphate group between the 5′ carbon of one sugar and the 3′ carbon of the next sugar in line; this linkage is called a **phosphodiester bond (Figure 3.28).** This arrangement of alternating sugar and phosphate groups forms the backbone of a nucleic acid chain. The nitrogenous bases of the nucleotides project from this backbone.

Each nucleotide of a DNA chain contains deoxyribose and one of the four bases A, T, G, or C. Each nucleotide of an RNA chain contains ribose and one of the four bases A, U, G, or C. Thymine and uracil differ only in a single methyl (—CH_3) group linked to the ring in T but replaced by a hydrogen in U (see Figure 3.27). The differences in sugar and pyrimidine bases

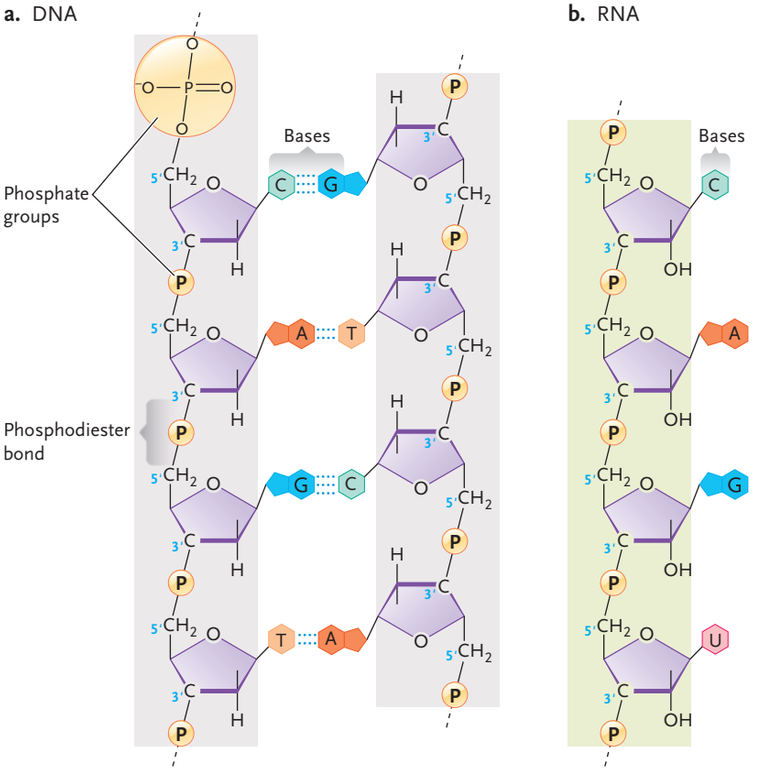


Figure 3.28
Linkage of nucleotides to form the nucleic acids DNA and RNA. P is a phosphate group (see Figure 3.26). **(a)** In DNA, the bases adenine (A), thymine (T), cytosine (C), or guanine (G) are bound at the positions marked "base." **(b)** In RNA, A, G, C, or uracil (U) may occur at these sites.

between DNA and RNA account for important differences in the structure and functions of these nucleic acids inside cells.

DNA Molecules Consist of Two Nucleotide Chains Wound Together

In cells, DNA takes the form of a **double helix**, first discovered by James D. Watson and Francis H. C. Crick in 1953, in collaboration with Maurice Wilkins and Rosalind Franklin (see Chapter 14 for details of their discovery). The double helix they described consists of two nucleotide chains wrapped around each other in a spiral that resembles a twisted ladder **(Figure 3.29).** The sides of the ladder are the sugar–phosphate backbones of the two chains, which twist around each other in a right-handed direction to form the double spiral. The rungs of the ladder are the nitrogenous bases, which extend inward from the sugars toward the center of the helix. Each rung consists of a pair of nitrogenous bases held in a flat plane roughly perpendicular to the long axis of the helix. The two nucleotide chains of a DNA double helix are held together primarily by hydrogen bonds between the base pairs. Slightly more than 10 base pairs are packed into each turn of the double helix. A DNA double-helix molecule is also referred to as double-stranded DNA.

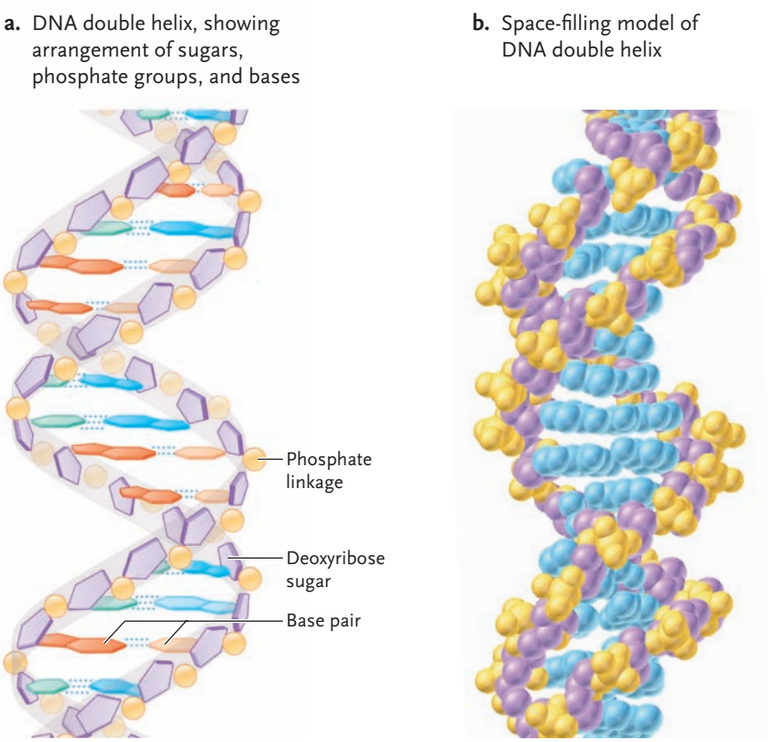


Figure 3.29
The DNA double helix. **(a)** Arrangement of sugars, phosphate groups, and bases in the DNA double helix. **(b)** Space-filling model of the DNA double helix. The paired bases, which lie in flat planes, are seen on the edge in this view.

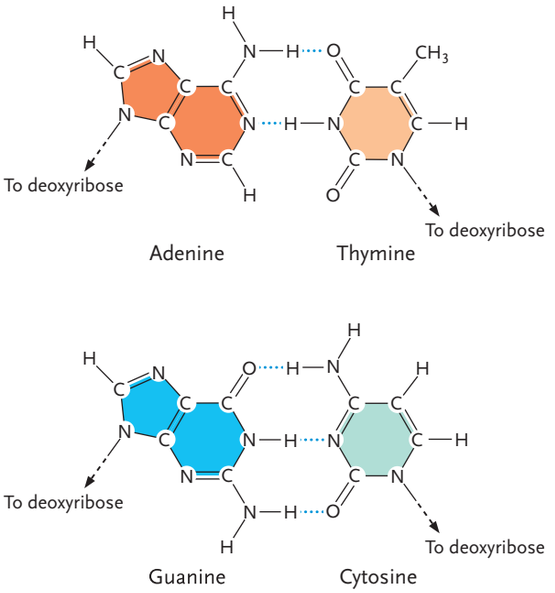


Figure 3.30
The DNA base pairs A–T (adenine–thymine) and G–C (guanine–cytosine), as seen from one end of a DNA molecule. Dotted lines designate hydrogen bonds.

The space separating the sugar–phosphate backbones of a DNA double helix is just wide enough to accommodate a base pair that consists of one purine and one pyrimidine. Purine–purine base pairs are too wide and pyrimidine–pyrimidine pairs are too narrow to fit this space exactly. More specifically, of the possible purine–pyrimidine pairs, only two combinations, adenine with thymine, and guanine with cytosine, can form stable hydrogen bonds so that the base pair fits precisely within the double helix **(Figure 3.30).** An adenine–thymine (A–T) pair forms two stabilizing hydrogen bonds; a guanine–cytosine (G–C) pair forms three.

As Watson and Crick pointed out in the initial report of their discovery, the formation of A–T and G–C pairs allows the sequence of one nucleotide chain to determine the sequence of its partner in the double helix. Thus, wherever a T occurs on one chain of a DNA double helix, an A occurs opposite it on the other chain; wherever a C occurs on one chain, a G occurs on the other side (see Figure 3.28). That is, the nucleotide sequence of one chain is said to be *complementary* to the nucleotide sequence of the other chain. The complementary nature of the two chains underlies the processes when DNA molecules are copied—replicated—to pass hereditary information from parents to offspring and when RNA copies are made of DNA molecules to transmit information within cells. In DNA replication, one nucleotide chain is used as a **template** for the assembly of a complementary chain according to the A–T and G–C base-pairing rules **(Figure 3.31).**

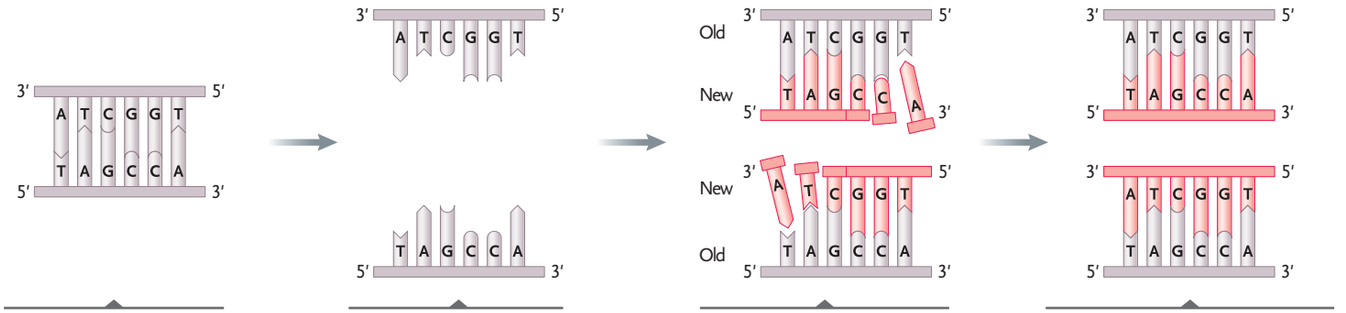


Figure 3.31
How complementary base pairing allows DNA molecules to be replicated precisely.

RNA Molecules Are Usually Single Nucleotide Chains

In contrast to DNA, RNA molecules exist largely as single, rather than double, nucleotide chains in living cells. That is, RNA is typically single-stranded. However, RNA molecules can fold and twist back on themselves to form double-helical regions. The patterns of these fold-back double helices are as vital to RNA function as the folding of amino acid chains is to protein function. "Hybrid" double helices, which consist of an RNA chain paired with a DNA chain, are formed temporarily when RNA copies are made of DNA chains. In the RNA–RNA or hybrid RNA–DNA helices, U in RNA takes over the pairing functions of T, forming A–U rather than A–T base pairs.

Unanswered Questions

Much of biological investigation has become molecular in nature. Here are a few highlights of the extensive research to answer questions about biological molecules.

How is the synthesis of cholesterol and fatty acids regulated?

The regulation of cholesterol and fatty acid synthesis is important because of the link between LDL cholesterol levels and the formation of plaques in arteries. Nobel Prize winners Michael Brown and Joseph Goldstein (University of Texas, Southwestern) recently identified sterol regulatory element-binding proteins (SREBPs), regulatory proteins that control the expression of genes involved in cholesterol and fatty acid synthesis. If lipid is at a low concentration in the cell, the cell needs to make more lipids. To do so, SREBPs enter the nucleus of the cell and activate genes required for the synthesis of cholesterol and fatty acids. In the initial steps of the pathway, SREBPs are escorted by SCAP, another protein. If cholesterol levels in cells are high, the genes must be turned off to prevent cholesterol overproduction. In this case, the accumulation of cholesterol in the cell causes SCAP to change its conformation. As a result, SREBPs cannot follow the pathway for activating the cholesterol and fatty acid genes, and those genes remain inactive.

Brown and Goldstein's lab has been characterizing the SREBPs and the genes that encode them. Current research focuses on understanding how the steps in the pathway for activating the cholesterol and fatty acid genes are regulated, particularly how physiological changes affect the pathway. Their research approaches include molecular analysis of the genes involved, biochemical analysis of the steps in the pathway, protein crystallography to characterize the structures and functions of the proteins involved, cell biology studies to examine the process in living cells, and animal physiology studies to investigate the system at the whole organism level.

What is the role of chaperonins in protein folding?

Chaperonins are crucial in the folding of proteins into their final and functional forms, and properly folded proteins are key to the life of a cell.

Many research groups are studying how chaperonins do their job. One group, headed by Martin Carden at the University of Kent (UK), is studying the structure and function of the human chaperonin CCT. CCT is a barrel-shaped, multiprotein ring that folds actin and tubulin proteins into their final shapes. Actins and tubulins help give eukaryotic cells their shape and provide mechanical strength, among other key properties.

The mechanism, roles, and cellular interactions of CCT are poorly understood. For example, what functions does each of the eight different proteins in the CCT molecule have? Carden's group is studying to what extent CCT separates into individual proteins in the living cell, whether the individual proteins have specialized roles in the cell, and whether they interact in other ways from those already characterized for the folding of actin and tubulin. Using structural information about the individual proteins in the chaperonin, they are building possible models of CCT that can be tested to determine the form of the chaperonin in the living cell. Understanding CCT's structure and function more completely may contribute to research investigating a variety of human diseases caused by protein misfolding. Examples of such diseases are Alzheimer disease, Parkinson disease, and non–insulin-dependent (type 2) diabetes.

Peter J. Russell

The description of nucleic acid molecules in this section, with the discussions of carbohydrates, lipids, and proteins in earlier sections, completes our survey of the major classes of organic molecules found in living organisms. The next chapter discusses the functions of molecules in one of these classes, the enzymatic proteins, and the relationships of energy changes to the biological reactions speeded by enzymes.

Study Break

1. What is the monomer of a nucleic acid macromolecule?
2. What are the chemical differences between DNA and RNA?

Review

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3.1 Carbon Bonding

- Carbon atoms readily share electrons, allowing each carbon atom to form four covalent bonds with other carbon atoms or atoms of other elements. The resulting extensive chain and ring structures form the backbones of diverse organic compounds.

3.2 Functional Groups in Biological Molecules

- The structure and behavior of organic molecules, as well as their linkage into larger units, depend on the chemical properties of functional groups (Table 3.1).
- Particular combinations of functional groups determine whether an organic molecule is an alcohol, aldehyde, ketone, or acid (Table 3.1).
- In a dehydration synthesis reaction, the components of a water molecule are removed as subunits assemble. In hydrolysis, the components of a water molecule are added as subunits are broken apart (Figure 3.2).

Animation: Functional groups

Animation: Dehydration synthesis and hydrolysis

3.3 Carbohydrates

- Carbohydrates are molecules in which carbon, hydrogen, and oxygen occur in the approximate ratio 1:2:1.
- Monosaccharides are carbohydrate subunits that contain three to seven carbons (Figures 3.3–3.5).
- Monosaccharides have D and L enantiomers. Typically, one of the two forms is used in cellular reactions because it has a molecular shape that can be recognized by the enzyme accelerating the reaction, whereas the other form does not.
- Two monosaccharides join to form a disaccharide; greater numbers form polysaccharides (Figures 3.6 and 3.7).
- In polymerization reactions, monomers link to form the polymer. Polysaccharides, proteins, and nucleic acids are assembled by polymerization reactions.

Animation: Structure of starch and cellulose

3.4 Lipids

- Lipids are hydrocarbon-based, water-insoluble, nonpolar molecules. Biological lipids include neutral lipids, phospholipids, and steroids.
- Neutral lipids, which are primarily energy-storing molecules, have a glycerol backbone and three fatty acid chains (Figures 3.8 and 3.9).
- Phospholipids are similar to neutral lipids except that a phosphate group and a polar organic unit substitute for one of the fatty acids (Figure 3.12).
- In polar environments (such as a water solution), phospholipids orient with their polar end facing the water and their nonpolar ends clustered in a region that excludes water. This orientation underlies the formation of bilayers, the structural framework of biological membranes.
- Steroids, which consist of four carbon rings carrying primarily nonpolar groups, function chiefly as components of membranes and as hormones in animals (Figures 3.13 and 3.14).
- Lipids link with carbohydrates to form glycolipids and with proteins to form lipoproteins, both of which play important roles in cell membranes.

Animation: Structure of a phospholipid

3.5 Proteins

- Proteins are assembled from 20 different amino acids. Amino acids have a central carbon to which is attached an amino group, a carboxyl group, a hydrogen atom, and a side group that differs in each amino acid (Figure 3.15).
- Peptide bonds between the amino group of one amino acid and the carboxyl group of another amino acid link amino acids into chains (Figure 3.17).
- A protein may have four levels of structure. Its primary structure is the linear sequence of amino acids in a polypeptide chain; secondary structure is the arrangement of the amino acid chain into α helices, β strands and sheets, or random coils; tertiary structure is the protein's overall conformation. Quaternary structure is the number and arrangement of polypeptide chains in a protein (Figures 3.18–3.22).
- In many proteins, combinations of secondary, tertiary, and quaternary structure form functional domains.
- Proteins combine with lipids to produce lipoproteins, with carbohydrates to produce glycoproteins, and with nucleic acids to form nucleoproteins.

Animation: Structure of an amino acid

Animation: Peptide bond formation

Animation: The primary and secondary structure of proteins

Animation: Secondary and tertiary structure

Animation: Globin and hemoglobin structure

3.6 Nucleotides and Nucleic Acids

- A nucleotide consists of a nitrogenous base, a five-carbon sugar, and one to three phosphate groups (Figures 3.26 and 3.27).
- Nucleotides are linked into nucleic acid chains by covalent bonds between their sugar and phosphate groups. The alternat-

ing sugar and phosphate groups form the backbone of a nucleic acid chain (Figure 3.28).

- There are two nucleic acids: DNA and RNA. DNA contains nucleotides with the nitrogenous bases adenine (A), thymine (T), guanine (G), or cytosine (C) linked to the sugar deoxyribose; RNA contains nucleotides with the nitrogenous bases adenine, uracil (U), guanine, or cytosine linked to the sugar ribose (Figures 3.26–3.28).
- In a DNA double helix, two nucleotide chains wind around each other like a twisted ladder, with the sugar–phosphate backbones of the two chains forming the sides of the ladder and the nitrogenous bases forming the rungs of the ladder (Figure 3.29).
- A-T and G-C base pairs mean that the sequences of the two nucleotide chains of a DNA double helix are complements of each other. The complementary pairing underlies the processes that replicate DNA and copy RNA from DNA (Figures 3.30 and 3.31).

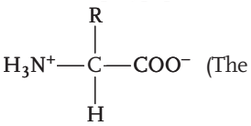
Questions

Self-Test Questions

1. Which functional group has a double bond?
   a. carboxyl
   b. amino
   c. hydroxyl
   d. methyl
   e. sulfhydryl
2. Which of the following characteristics is *not* common to carbohydrates, lipids, and proteins?
   a. They are composed of a carbon backbone with functional groups attached.
   b. Monomers of these molecules undergo dehydration synthesis to form polymers.
   c. Their polymers are broken apart by hydrolysis.
   d. The backbones of the polymers are primarily polar molecules.
   e. The molecules are held together by covalent bonding.
3. Cellulose is to carbohydrate as:
   a. amino acid is to protein.
   b. lipid is to fat.
   c. keratin is to protein.
   d. nucleic acid is to DNA.
   e. nucleic acid is to RNA.
4. Maltose, sucrose, and lactose differ from one another:
   a. because not all contain glucose.
   b. because not all of them exist in ring form.
   c. in the number of carbons in the sugar.
   d. in the number of hexose monomers involved.
   e. by the linkage of the monomers.
5. Lipids that are liquid at room temperature:
   a. are fats.
   b. contain more hydrogen atoms than lipids that are solids at room temperature.
   c. if polyunsaturated, contain several double bonds in their fatty acid chains.
   d. lack glycerol.
   e. are not stored in cells as triglycerides.
6. Which of the following statements about steroids is *false*?
   a. They are classified as lipids because, like lipids, they are nonpolar.
   b. They can act as regulatory molecules in animals.
   c. They are composed of four interlocking rings.
   d. They are highly soluble in water.
   e. Their most abundant form is as sterols.
7. The term *secondary structure* refers to a protein's:
   a. sequence of amino acids.
   b. structure that results from local interactions between different amino acids in the chain.
   c. interactions with a second protein chain.
   d. interaction with a chaperonin.
   e. interactions with carbohydrates.
8. The first and major effect in denaturation of proteins is that:
   a. peptide bonds break.
   b. α helices unwind.
   c. β sheet structures unfold.
   d. tertiary structure is changed.
   e. quaternary structures disassemble.
9. In living systems:
   a. proteins rarely combine with other macromolecules.
   b. enzymes are always proteins.
   c. proteins are composed of 24 amino acids.
   d. chaperonins inhibit protein movement.
   e. a protein domain refers to the place in the cell where proteins are synthesized and function.
10. RNA differs from DNA because:
    a. RNA may contain the pyrimidine uracil, and DNA does not.
    b. RNA is always single-stranded when functioning, and DNA is always double-stranded.
    c. the pentose sugar in RNA has one less O atom than the pentose sugar in DNA.
    d. RNA is more stable and is broken down by enzymes less easily than DNA.
    e. RNA is much a much larger molecule than DNA.

Questions for Discussion

1. Identify the following structures as a carbohydrate, fatty acid, amino acid, or polypeptide:

   a.  (The *R* indicates an organic group.)

   b. $C_6H_{12}O_6$

   c. $(glycine)_{20}$

   d. $CH_3(CH_2)_{16}COOH$

2. Cholesterol from food or synthesized in the liver is too hydrophobic to circulate in the blood; complexes of proteins and lipids ferry it around. Low-density lipoprotein (LDL) transports cholesterol out of the liver and into cells. High-density lipoprotein (HDL) ferries the cholesterol that is released from dead cells back into the liver.

   High LDL levels are implicated in atherosclerosis, heart problems, and strokes. The main protein in LDL is called ApoA1 (apolipoprotein A1). A mutant form of ApoA1 has the wrong amino acid (cysteine instead of arginine) at one place in its primary sequence. Carriers of this LDL mutation have very low levels of HDL, which is typically predictive of heart disease. Yet, the carriers have no heart problems. When medical investigators gave some heart patients injections of the mutant LDL, it acted like a drain cleaner, quickly reducing the size of cholesterol deposits in the patients' arteries.

   Soon, such a treatment may reverse years of damage. However, many researchers caution that a low-fat, low-cholesterol diet is still the best assurance of long-term health. Would you choose artery-cleansing treatments over a healthy diet? Explain your choice.

3. The shapes of a protein's domains often give clues to its functions. For example, protein HLA (human leukocyte antigen) is a type of recognition protein on the outer surface of all vertebrate body cells. Certain cells of the immune system use HLAs to distinguish self (the body's own cells) from nonself (invading cells). Each HLA protein has a jawlike region that can bind to molecular parts of an invader. It thus alerts the immune system that the body has been invaded. Speculate on what might happen if a mutation makes the jawlike region misfold.
4. Explain how polar and nonpolar groups are important in the structure and functions of lipids, proteins, and nucleic acids.

Experimental Analysis

A clerk in a health food store tells you that natural vitamin C extracted from rose hips is better for you than synthetic vitamin C. Given your understanding of the structure of organic molecules, how would you respond? Design an experiment to test whether the rose hips and synthetic vitamin C preparations differ in their effects.

Evolution Link

How do you think the primary structure (amino acid) sequence of proteins could inform us about the evolutionary relationships of proteins?

How Would You Vote?

Scientists have discovered vast reservoirs of methane (natural gas, an important fossil fuel) under sediments covering the seafloor. It occurs in a highly unstable form that can cause immense explosions if the temperature rises or the pressure falls slightly. Should we work toward developing these vast undersea methane deposits as an energy source, given that the environmental costs and risks to life are unknown? Go to www.thomsonedu.com/login to investigate both sides of the issue and then vote.