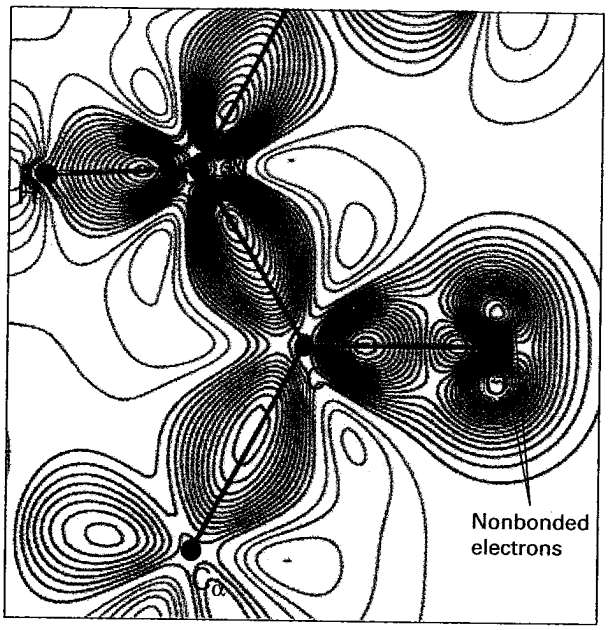


▲ **FIGURE 2-9 Distribution of bonding and outer nonbonding electrons in the peptide group.** Shown here is a peptide bond linking two amino acids within a protein called crambin. The black lines represent the covalent bonds between atoms. The red (negative) and blue (positive) lines represent contours of charge determined using x-ray crystallography and computational methods. The greater the number of contour lines, the higher the charge. The high density of red contour lines between atoms represents the covalent bonds (shared electron pairs). The two sets of red contour lines emanating from the oxygen (O) and not falling on a covalent bond (black line) represent the two pairs of nonbonded electrons on the oxygen that are available to participate in hydrogen bonding. The high density of blue contour lines near the hydrogen (H) bonded to nitrogen (N) represents a partial positive charge, indicating that this H can act as a donor in hydrogen bonding. [From C. Jelsch et al., 2000, *Proc. Nat'l. Acad. Sci.* USA **97**:3171. Courtesy of M. M. Teeter.]

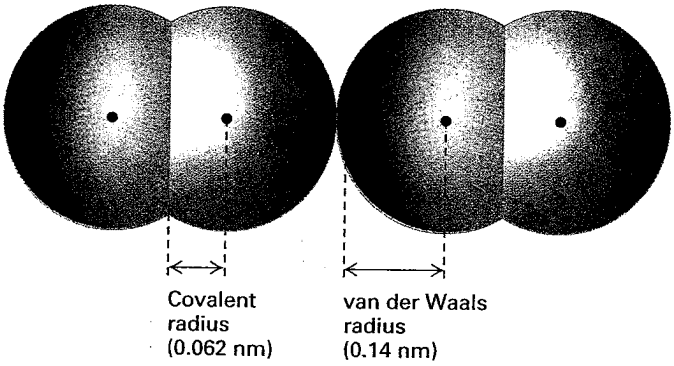
unequal distribution of electrons. If two noncovalently bonded atoms are close enough together, electrons of one atom will perturb the electrons of the other. This perturbation generates a transient dipole in the second atom, and the two dipoles will attract each other weakly (Figure 2-10). Similarly, a polar covalent bond in one molecule will attract an oppositely oriented dipole in another.

Van der Waals interactions, involving either transiently induced or permanent electric dipoles, occur in all types of molecules, both polar and nonpolar. In particular, van der Waals interactions are responsible for the cohesion between nonpolar molecules such as heptane, $CH_3—(CH_2)_5—CH_3$, that cannot form hydrogen bonds or ionic interactions with other molecules. The strength of van der Waals interactions decreases rapidly with increasing distance; thus these noncovalent bonds can form only when atoms are quite close to one another. However, if atoms get too close together, they become repelled by the negative charges of their electrons. When the van der Waals attraction between two atoms exactly balances the repulsion between their two electron clouds, the atoms are said to be in van der Waals contact. The strength of the van der Waals interaction is about 1 kcal/mol, weaker than typical hydrogen bonds and only slightly higher than the average thermal energy of molecules at 25 °C. Thus multiple van der Waals interactions, a van der Waals interaction in conjunction with other noncovalent interactions, or both are required to significantly influence the stability of inter- and intramolecular contacts.

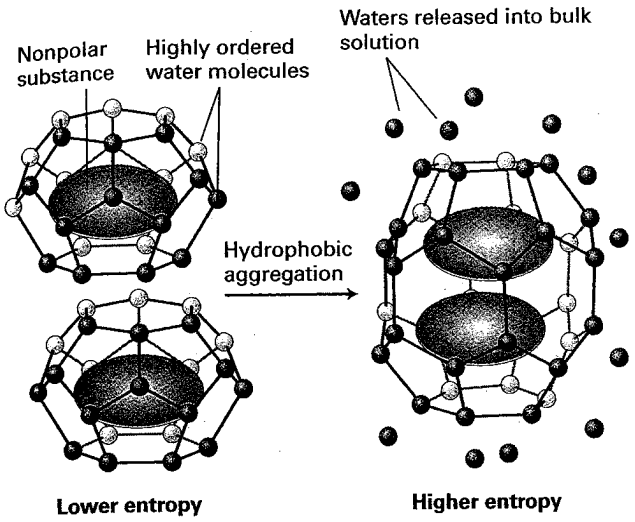
The Hydrophobic Effect Causes Nonpolar Molecules to Adhere to One Another

Because nonpolar molecules do not contain charged groups, possess a dipole moment, or become hydrated, they are insoluble or almost insoluble in water; that is, they are hydrophobic (water fearing). The covalent bonds between two carbon atoms and between carbon and hydrogen atoms are the most common nonpolar bonds in biological systems. **Hydrocarbons**—molecules made up only of carbon and hydrogen—are virtually insoluble in water. Large triacylglycerols (or triglycerides), which make up animal fats and vegetable oils, also are insoluble in water. As we will see later, the major portion of these molecules consists of long hydrocarbon chains. After being shaken in water, triacylglycerols form a separate phase. A familiar example is the separation of oil from the water-based vinegar in an oil-and-vinegar salad dressing.

Nonpolar molecules or nonpolar portions of molecules tend to aggregate in water owing to a phenomenon called the **hydrophobic effect.** Because water molecules cannot form hydrogen bonds with nonpolar substances, they tend to form "cages" of *relatively* rigid hydrogen-bonded pentagons and hexagons around nonpolar molecules



▲ **FIGURE 2-10 Two oxygen molecules in van der Waals contact.** In this model, red indicates negative charge and blue indicates positive charge. Transient dipoles in the electron clouds of all atoms give rise to weak attractive forces, called *van der Waals interactions.* Each type of atom has a characteristic van der Waals radius at which van der Waals interactions with other atoms are optimal. Because atoms repel one another if they are close enough together for their outer electrons to overlap without being shared in a covalent bond, the van der Waals radius is a measure of the size of the electron cloud surrounding an atom. The covalent radius indicated here is for the double bond of O=O; the single-bond covalent radius of oxygen is slightly longer.



▲ **FIGURE 2-11 Schematic depiction of the hydrophobic effect.** Cages of water molecules that form around nonpolar molecules in solution are more ordered than water molecules in the surrounding bulk liquid. Aggregation of nonpolar molecules reduces the number of water molecules involved in highly ordered cages, resulting in a higher-entropy, more energetically favorable state (*right*) compared with the unaggregated state (*left*).

(Figure 2-11, *left*). This state is energetically unfavorable because it decreases the randomness (entropy) of the population of water molecules. (The role of entropy in chemical systems is discussed in a later section.) If nonpolar molecules in an aqueous environment aggregate with their hydrophobic surfaces facing each other, the hydrophobic surface area exposed to water is reduced (Figure 2-11, *right*). As a consequence, less water is needed to form the cages surrounding the nonpolar molecules, and entropy increases (an energetically more favorable state) relative to the unaggregated state. In a sense, then, water squeezes the nonpolar molecules into spontaneously forming aggregates. Rather than constituting an attractive force such as in hydrogen bonds, the hydrophobic effect results from an avoidance of an unstable state (extensive water cages around individual nonpolar molecules).

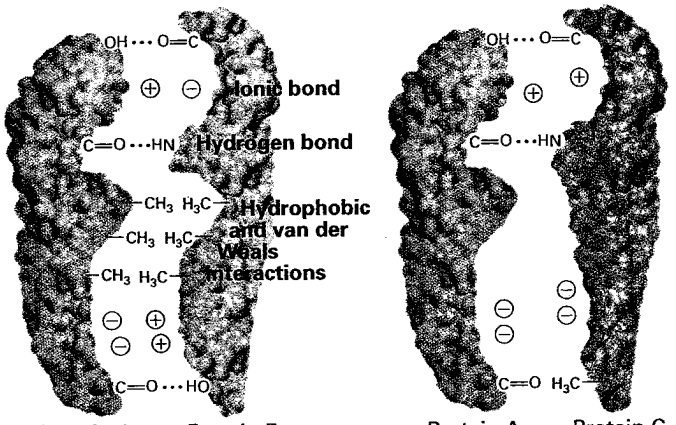
Nonpolar molecules can also associate, albeit weakly, through van der Waals interactions. The net result of the hydrophobic and van der Waals interactions is a very powerful tendency for hydrophobic molecules to interact with one another, not with water. Simply put, *like dissolves like*. Polar molecules dissolve in polar solvents such as water; nonpolar molecules dissolve in nonpolar solvents such as hexane.

Molecular Complementarity Mediated via Noncovalent Interactions Permits Tight, Highly Specific Binding of Biomolecules

Both inside and outside cells, ions and molecules are constantly bumping into one another. The greater the number of copies of any two types of molecules per unit volume (i.e., the higher their concentration), the more likely they are to encounter one another. When two molecules encounter each other, they most likely will simply bounce apart because the noncovalent interactions that would bind them together are weak and have a transient existence at physiological temperatures. However, molecules that exhibit **molecular complementarity**, a lock-and-key kind of fit between their shapes, charges, or other physical properties, can form multiple noncovalent interactions at close range. When two such structurally complementary molecules bump into each other, they can bind (stick) together.

Figure 2-12 illustrates how multiple, different weak bonds can bind two proteins together. Almost any other arrangement of the same groups on the two surfaces would not allow the molecules to bind so tightly. Such multiple, specific interactions between complementary regions within a protein molecule allow it to fold into a unique three-dimensional shape (Chapter 3) and hold the two chains of DNA together in a double helix (Chapter 4). Similar interactions underlie the association of groups of more than two molecules into multimolecular complexes, leading to formation of muscle fibers, to the gluelike associations between cells in solid tissues, and to numerous other cellular structures.

Depending on the number and strength of the noncovalent interactions between the two molecules and on their environment, their binding may be tight (strong) or loose (weak) and, as a consequence, either long lasting or transient. The higher the *affinity* of two molecules for each other, the better the molecular "fit" between them, the more noncovalent interactions can form, and the tighter they can bind



▲ **FIGURE 2-12 Molecular complementarity and the binding of proteins via multiple noncovalent interactions.** The complementary shapes, charges, polarity, and hydrophobicity of two protein surfaces permit multiple weak interactions, which in combination produce a strong interaction and tight binding. Because deviations from molecular complementarity substantially weaken binding, a particular surface region of any given biomolecule usually can bind tightly to only one or a very limited number of other molecules. The complementarity of the two protein molecules on the left permits them to bind much more tightly than the two noncomplementary proteins on the right.

together. An important quantitative measure of affinity is the binding dissociation constant K_d, described later.

As we discuss in Chapter 3, nearly all the chemical reactions that occur in cells also depend on the binding properties of enzymes. These proteins not only speed up, or catalyze, reactions but also do so with a high degree of *specificity*, a reflection of their ability to bind tightly to only one or a few related molecules. The specificity of intermolecular interactions and reactions, which depends on molecular complementarity, is essential for many processes critical to life.

KEY CONCEPTS OF SECTION 2.1

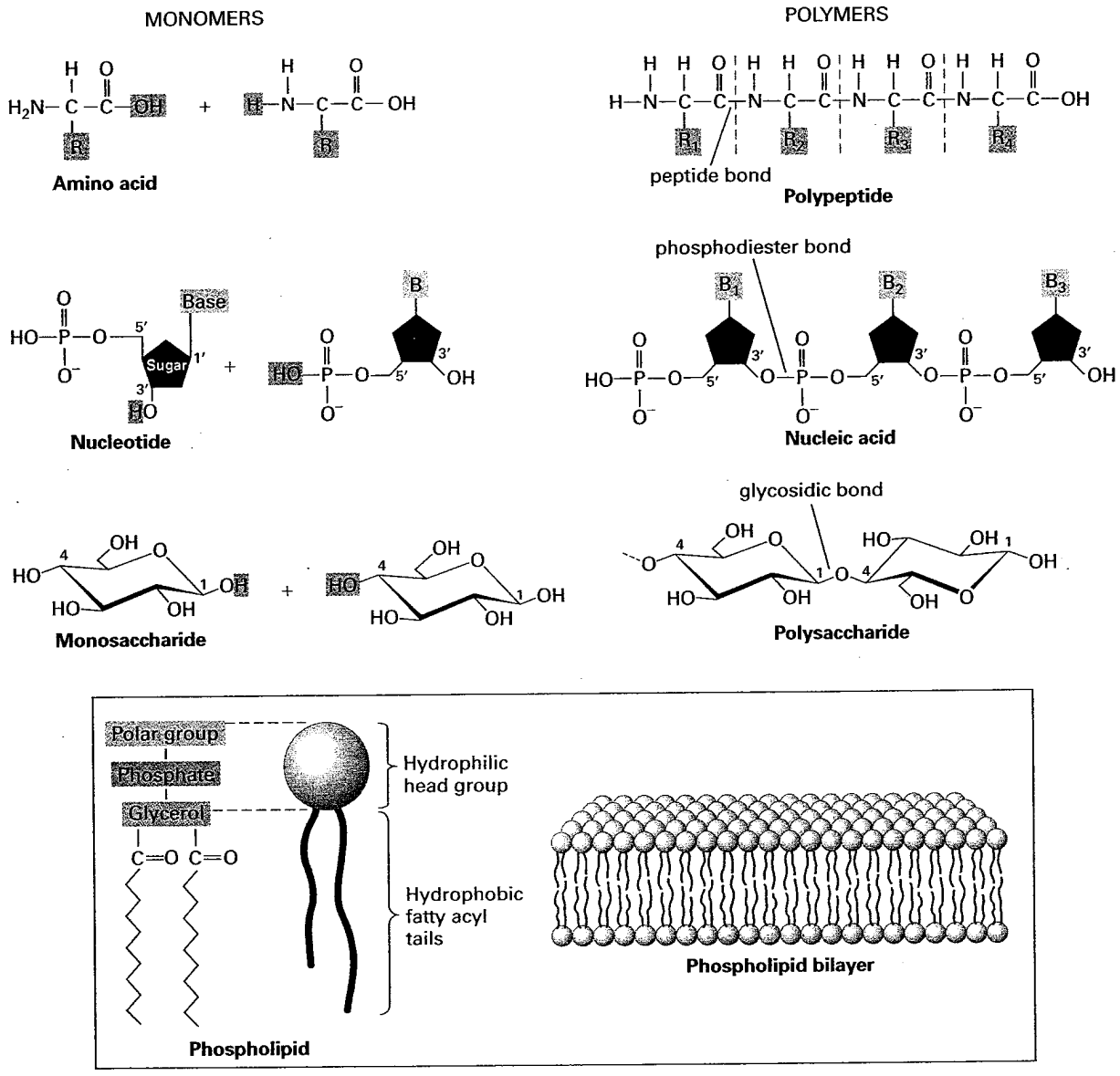
Covalent Bonds and Noncovalent Interactions

- Covalent bonds, which bind the atoms composing a molecule in a fixed orientation, consist of pairs of electrons shared by two atoms. They are stable in biological systems because the relatively high energies required to break them (50–200 kcal/mol) are much larger than the thermal kinetic energy available at room (25 °C) or body (37 °C) temperatures.
- Many molecules in cells contain at least one asymmetric carbon atom, which is bonded to four dissimilar atoms. Such molecules can exist as optical isomers (mirror images), designated D and L (see Figure 2-4), which have different biological activities. In biological systems, nearly all sugars are D isomers, whereas nearly all amino acids are L isomers.
- Electrons may be shared equally or unequally in covalent bonds. Atoms that differ in electronegativity form polar covalent bonds in which the bonding electrons are distributed unequally. One end of a polar bond has a partial positive charge and the other end has a partial negative charge (see Figure 2-5).
- Noncovalent interactions between atoms are considerably weaker than covalent bonds, with bond energies ranging from about 1–5 kcal/mol (see Figure 2-6).
- Four main types of noncovalent interactions occur in biological systems: ionic bonds, hydrogen bonds, van der Waals interactions, and interactions due to the hydrophobic effect.
- Ionic bonds result from the electrostatic attraction between the positive and negative charges of ions. In aqueous solutions, all cations and anions are surrounded by a shell of bound water molecules (see Figure 2-7c). Increasing the salt (e.g., NaCl) concentration of a solution can weaken the relative strength of and even break the ionic bonds between biomolecules.
- In a hydrogen bond, a hydrogen atom covalently bonded to an electronegative atom associates with an acceptor atom whose nonbonding electrons attract the hydrogen (see Figure 2-8).
- Weak and relatively nonspecific van der Waals interactions are created whenever any two atoms approach each other closely. They result from the attraction between transient dipoles associated with all molecules (see Figure 2-10).
- In an aqueous environment, nonpolar molecules or nonpolar portions of larger molecules are driven together by the hydrophobic effect, thereby reducing the extent of their direct contact with water molecules (see Figure 2-11).
- Molecular complementarity is the lock-and-key fit between molecules whose shapes, charges, and other physical properties are complementary. Multiple noncovalent interactions can form between complementary molecules, causing them to bind tightly (see Figure 2-12), but not between molecules that are not complementary.
- The high degree of binding specificity that results from molecular complementarity is one of the features that underlies intermolecular interactions and thus is essential for many processes critical to life.

2.2 Chemical Building Blocks of Cells

A common theme in biology is the construction of large molecules (**macromolecules**) and structures by the covalent or noncovalent association of many similar or identical smaller molecules. The three most abundant classes of the critically important biological macromolecules—**proteins, nucleic acids,** and **polysaccharides**—are all **polymers** composed of multiple covalently linked building block small molecules, or **monomers** (Figure 2-13). Proteins are linear polymers containing 10 to several thousand amino acids linked by **peptide bonds.** Nucleic acids are linear polymers containing hundreds to millions of nucleotides linked by **phosphodiester bonds.** Polysaccharides are linear or branched polymers of monosaccharides (sugars) such as glucose linked by **glycosidic bonds.** Although the actual mechanisms by which covalent bonds between monomers form are complex and will be discussed later, the formation of a covalent bond between two monomer molecules usually involves the net loss of a hydrogen (H) from one monomer and a hydroxyl (OH) from the other monomer—or the net loss of one water—and can therefore be thought of as a *dehydration reaction.* These bonds are stable under normal biological conditions (e.g., 37°C, neutral pH), and so these *biopolymers* are stable and can perform a wide variety of jobs in cells (store information, catalyze chemical reactions, serve as structural elements in defining cell shape and movement, etc.).

Macromolecular structures can also be assembled using noncovalent interactions. The macromolecular two-layered (bilayer) structure of cellular membranes is built up by the noncovalent assembly of many thousands of small molecules called phospholipids (see Figure 2-13). In this chapter, we will focus on the characteristics of the monomeric chemical



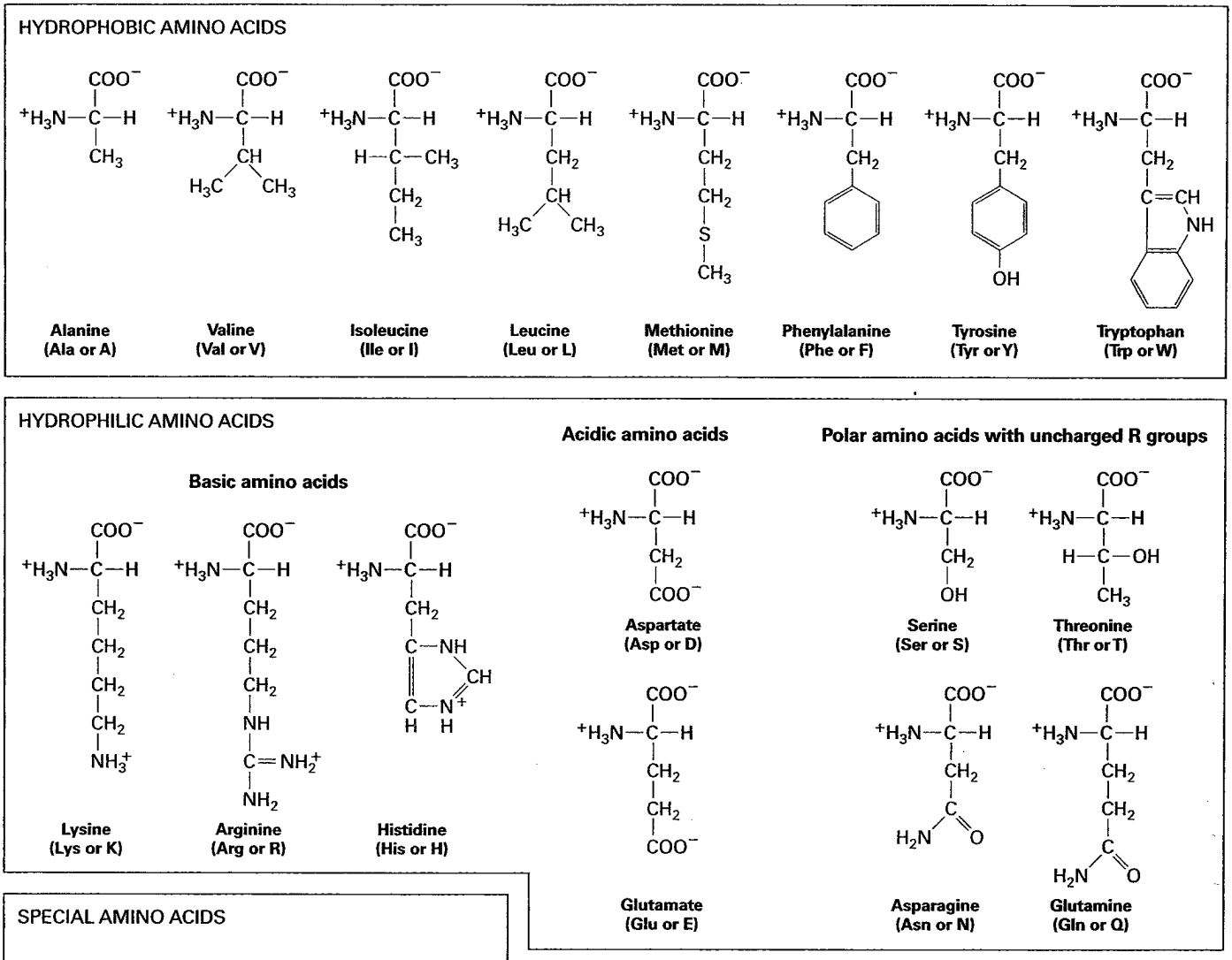
▲ **FIGURE 2-13 Overview of the cell's principal chemical building blocks.** *(Top)* The three major types of biological macromolecules are each assembled by the polymerization of multiple small molecules (monomers) of a particular type: proteins from amino acids (Chapter 3), nucleic acids from nucleotides (Chapter 4), and polysaccharides from monosaccharides (sugars). Each monomer is covalently linked into the polymer by a reaction whose net result is loss of a water molecule (dehydration). *(Bottom)* In contrast, phospholipid monomers noncovalently assemble into a bilayer structure, which forms the basis of all cellular membranes (Chapter 10).

building blocks—amino acids, nucleotides, sugars, and phospholipids. The structure, function, and assembly of proteins, nucleic acids, polysaccharides, and biomembranes are discussed in subsequent chapters.

Amino Acids Differing Only in Their Side Chains Compose Proteins

The monomeric building blocks of proteins are 20 **amino acids**, which when incorporated into a protein polymer are sometimes called **residues.** All amino acids have a characteristic structure consisting of a central **alpha (α) carbon atom** (C_α) bonded to four different chemical groups: an amino (NH_2) group, a carboxylic acid or carboxyl (COOH) group (hence the name *amino acid*), a hydrogen (H) atom, and one variable group, called a **side chain** or R group. Because the α carbon in all amino acids except glycine is asymmetric, these molecules can exist in two mirror-image forms called by convention the D (dextro) and the L (levo) isomers (see Figure 2-4). The two isomers cannot be interconverted (one made identical with the other) without breaking and then re-forming a chemical bond in one of them. With rare exceptions, only the L forms of amino acids are found in proteins.

To understand the three-dimensional structures and functions of proteins, discussed in detail in Chapter 3, you must be familiar with some of the distinctive properties of



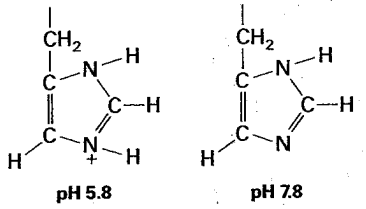
▲ **FIGURE 2-14 The 20 common amino acids used to build proteins.** The side chain (R group; red) determines the characteristic properties of each amino acid and is the basis for grouping amino acids into three main categories: hydrophobic, hydrophilic, and special. Shown are the ionized forms that exist at the pH (≈7) of the cytosol. In parentheses are the three-letter and one-letter abbreviations for each amino acid.

amino acids, which are determined in part by their side chains. You need not memorize the detailed structure of each type of side chain to understand how proteins work because amino acids can be classified into several broad categories based on the size, shape, charge, hydrophobicity (a measure of water solubility), and chemical reactivity of the side chains (Figure 2-14). However, you should be familiar with the general properties of each category.

Amino acids with nonpolar side chains are hydrophobic and so poorly soluble in water. The larger the nonpolar side chain, the more hydrophobic—less water soluble—the amino acid. The noncyclic side chains of *alanine, valine, leucine,* and *isoleucine* (called aliphatic), as well as *methionine,* consist entirely of hydrocarbons, except for the one sulfur atom in methionine, and all are nonpolar. *Phenylalanine, tyrosine,* and *tryptophan* have large, bulky aromatic side chains. In later chapters, we will see in detail how these hydrophobic side chains under the influence of the hydrophobic effect often pack in the interior of proteins or line the surfaces of proteins that are embedded within hydrophobic regions of biomembranes.

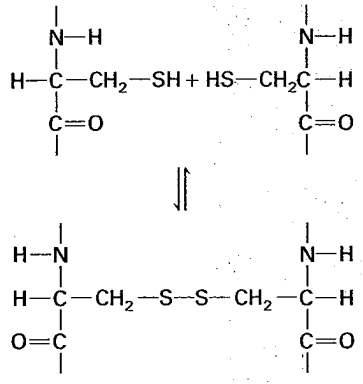
Amino acids with polar side chains are hydrophilic; the most hydrophilic of these amino acids is the subset with side chains that are charged (ionized) at the pH typical of biological fluids (≈7)—both inside and outside the cell (see Section 2.3). *Arginine* and *lysine* have positively charged side chains and are called basic amino acids; *aspartic acid* and *glutamic acid* have negatively charged side chains due to the carboxylic acid groups in their side chains (their charged forms are called *aspartate* and *glutamate*) and are called acidic. A fifth amino acid, *histidine,* has a side chain containing a ring

with two nitrogens, called imidazole, which can shift from being positively charged to uncharged depending on small changes in the acidity of its environment:



The activities of many proteins are modulated by shifts in environmental acidity through protonation or deprotonation of histidine side chains. *Asparagine* and *glutamine* are uncharged but have polar side chains containing amide groups with extensive hydrogen-bonding capacities. Similarly, *serine* and *threonine* are uncharged but have polar hydroxyl groups, which also participate in hydrogen bonds with other polar molecules.

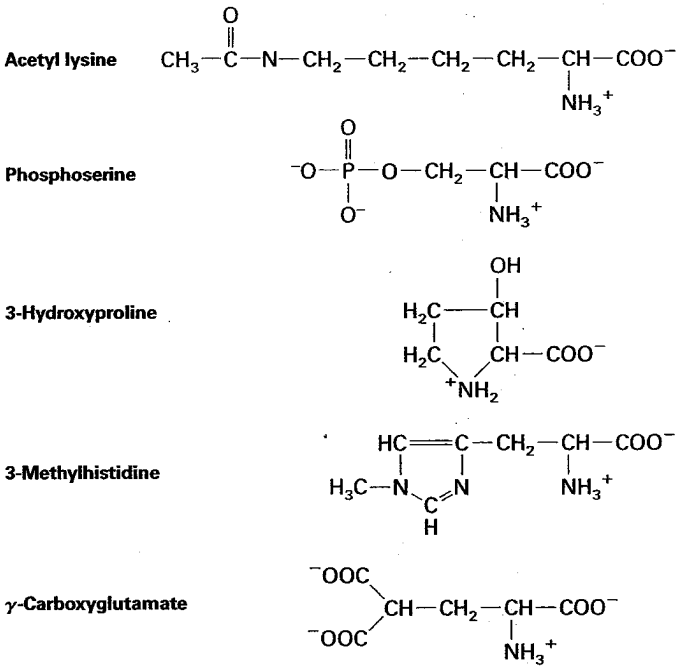
Lastly, cysteine, glycine, and proline exhibit special roles in proteins because of the unique properties of their side chains. The side chain of *cysteine* contains a reactive *sulfhydryl group (—SH),* which can oxidize to form a covalent *disulfide bond (—S—S—)* to a second cysteine:



Regions within a single protein chain (intramolecular) or in separate chains (intermolecular) sometimes are cross-linked through disulfide bonds. Disulfide bonds stabilize the folded structure of some proteins. The smallest amino acid, *glycine,* has a single hydrogen atom as its R group. Its small size allows it to fit into tight spaces. Unlike the other common amino acids, the side chain of *proline* bends around to form a ring by covalently bonding to the nitrogen atom (amino group) attached to the C_α. As a result, proline is very rigid and creates a fixed kink in a protein chain, limiting how a protein can fold in the region of proline residues.

Some amino acids are more abundant in proteins than others. Cysteine, tryptophan, and methionine are rare amino acids: together they constitute approximately 5 percent of the amino acids in a protein. Four amino acids—leucine, serine, lysine, and glutamic acid—are the most abundant amino acids, totaling 32 percent of all the amino acid residues in a typical protein. However, the amino acid composition of proteins can vary widely from these values.

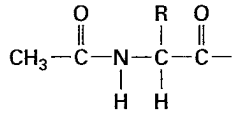
Although cells use the 20 amino acids shown in Figure 2-14 in the *initial* synthesis of proteins, analysis of cellular proteins



▲ **FIGURE 2-15 Common modifications of amino acid side chains in proteins.** These modified residues and numerous others are formed by addition of various chemical groups (red) to the amino acid side chains during or after synthesis of a polypeptide chain.

reveals that they contain upward of 100 different amino acids. Chemical modifications of the amino acids account for this difference. Acetyl groups (CH_3CO) and a variety of other chemical groups can be added to specific internal amino acids after they are incorporated into proteins (Figure 2-15). An important modification is the addition of a phosphate (PO_4, phosphorylation) to hydroxyl groups in serine, threonine, and tyrosine residues. We will encounter numerous examples of proteins whose activity is regulated by reversible phosphorylation and dephosphorylation. Phosphorylation of nitrogen in the side chain of histidine is well known in bacteria, fungi, and plants but less studied—perhaps because of the relative instability of phosphorylated histidine—and apparently rare in mammals. The side chains of asparagine, serine, and threonine are sites for glycosylation, the attachment of linear and branched carbohydrate chains. Many secreted proteins and membrane proteins contain glycosylated residues. Other amino acid modifications found in selected proteins include the hydroxylation of proline and lysine residues in collagen (Chapter 19), the methylation of histidine residues in membrane receptors, and the γ carboxylation of glutamate in blood-clotting factors such as prothrombin.

Acetylation, addition of an acetyl group, to the amino group of the N-terminal residue, is the most common form of amino acid chemical modification, affecting an estimated 80 percent of all proteins:

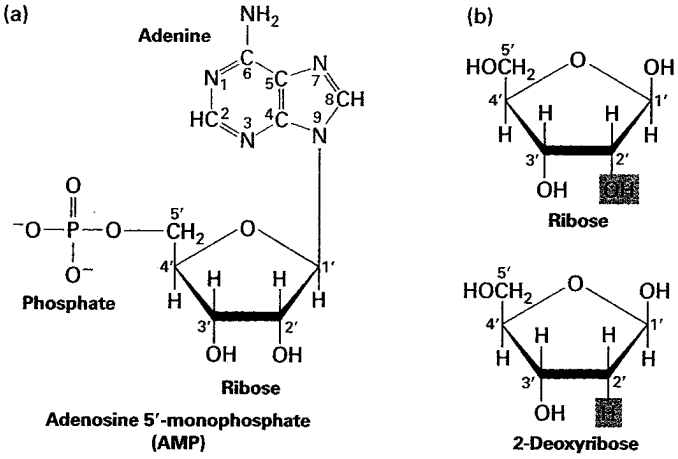


This modification may play an important role in controlling the life span of proteins within cells because nonacetylated proteins are rapidly degraded.

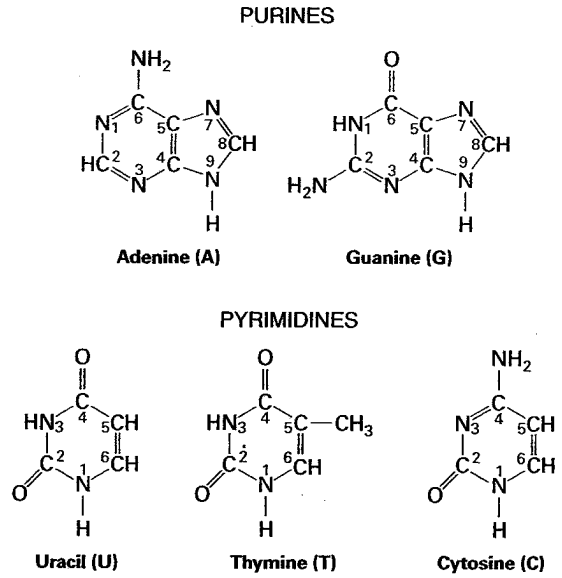
Five Different Nucleotides Are Used to Build Nucleic Acids

Two types of chemically similar nucleic acids, DNA (**deoxyribonucleic acid**) and RNA (**ribonucleic acid**), are the principal genetic-information-carrying molecules of the cell. The monomers from which DNA and RNA polymers are built, called **nucleotides**, all have a common structure: a phosphate group linked by a phosphoester bond to a pentose (a five-carbon sugar molecule) that in turn is linked to a nitrogen- and carbon-containing ring structure commonly referred to as a base (Figure 2-16a). In RNA, the pentose is ribose; in DNA, it is deoxyribose that at position 2′ has a proton rather than the hydroxyl group at that site in ribose (Figure 2-16b). The bases *adenine*, *guanine*, and *cytosine* (Figure 2-17) are found in both DNA and RNA; *thymine* is found only in DNA, and *uracil* is found only in RNA.

Adenine and guanine are **purines**, which contain a pair of fused rings; cytosine, thymine, and uracil are **pyrimidines**, which contain a single ring (see Figure 2-17). The bases are often abbreviated A, G, C, T, and U, respectively; these same single-letter abbreviations are also commonly used to denote the entire nucleotides in nucleic acid polymers. In nucleotides, the 1′ carbon atom of the sugar (ribose or deoxyribose) is attached to the nitrogen at position 9 of a purine (N_9) or at position 1 of a pyrimidine (N_1). The acidic character of nucleotides is due to the phosphate group, which under normal intracellular conditions releases hydrogen ions (H^+), leaving the phosphate negatively charged (see Figure 2-16a). Most nucleic acids in cells are associated with proteins,



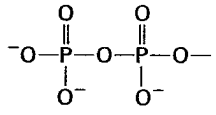
▲ **FIGURE 2-16 Common structure of nucleotides.** (a) Adenosine 5′ -monophosphate (AMP), a nucleotide present in RNA. By convention, the carbon atoms of the pentose sugar in nucleotides are numbered with primes. In natural nucleotides, the 1′ carbon is joined by a β linkage to the base (in this case adenine); both the base (blue) and the phosphate on the 5′ hydroxyl (red) extend above the plane of the sugar ring. (b) Ribose and deoxyribose, the pentoses in RNA and DNA, respectively.



▲ **FIGURE 2-17 Chemical structures of the principal bases in nucleic acids.** In nucleic acids and nucleotides, nitrogen 9 of purines and nitrogen 1 of pyrimidines (red) are bonded to the 1′ carbon of ribose or deoxyribose. U is only in RNA, and T is only in DNA. Both RNA and DNA contain A, G, and C.

which form ionic interactions with the negatively charged phosphates.

Cells and extracellular fluids in organisms contain small concentrations of **nucleosides**, combinations of a base and a sugar without a phosphate. Nucleotides are nucleosides that have one, two, or three phosphate groups esterified at the 5′ hydroxyl. Nucleoside monophosphates have a single esterified phosphate (see Figure 2-16a); nucleoside diphosphates contain a pyrophosphate group:



and nucleoside triphosphates have a third phosphate. Table 2-3 lists the names of the nucleosides and nucleotides in nucleic acids and the various forms of nucleoside phosphates. The nucleoside triphosphates are used in the synthesis of nucleic acids, which we cover in Chapter 4. Among their other functions in the cell, GTP participates in intracellular signaling and acts as an energy reservoir, particularly in protein synthesis, and ATP, discussed later in this chapter, is the most widely used biological energy carrier.

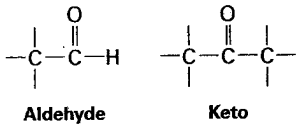
Monosaccharides Joined by Glycosidic Bonds Form Linear and Branched Polysaccharides

The building blocks of the polysaccharides are the simple sugars, or **monosaccharides**. Monosaccharides are **carbohydrates**, which are literally covalently bonded combinations of carbon and water in a one-to-one ratio $(CH_2O)_n$, where n equals 3, 4, 5, 6, or 7. **Hexoses** ($n = 6$) and **pentoses** ($n = 5$) are the most common monosaccharides. All monosaccharides

TABLE 2-3 Terminology of Nucleosides and Nucleotides

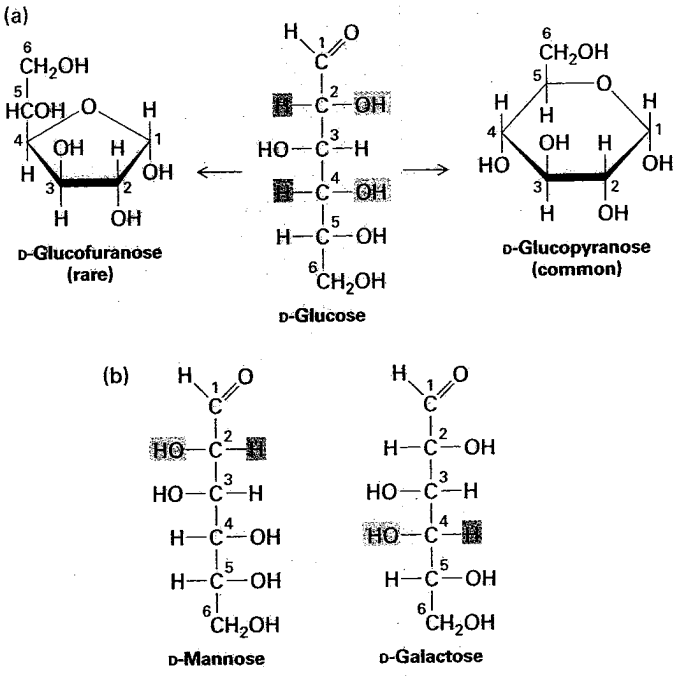
BASES	PURINES		PYRIMIDINES	
	ADENINE(A)	GUANINE(G)	CYTOSINE(C)	URACIL(U) THYMINE(T)
Nucleosides (in RNA)	Adenosine	Guanosine	Cytidine	Uridine
Nucleosides (in DNA)	Deoxyadenosine	Deoxyguanosine	Deoxycytidine	Deoxythymidine
Nucleotides (in RNA)	Adenylate	Guanylate	Cytidylate	Uridylate
Nucleotides (in DNA)	Deoxyadenylate	Deoxyguanylate	Deoxycytidylate	Deoxythymidylate
Nucleoside monophosphates	AMP	GMP	CMP	UMP
Nucleoside diphosphates	ADP	GDP	CDP	UDP
Nucleoside triphosphates	ATP	GTP	CTP	UTP
Deoxynucleoside mono-, di-, and triphosphates	dAMP, etc.	dGMP, etc.	dCMP, etc	dTMP, etc.

contain hydroxyl (—OH) groups and either an aldehyde or a keto group:



Many biologically important sugars are hexoses, including glucose, mannose, and galactose (Figure 2-18). Mannose is identical with glucose except that the orientation of the groups bonded to carbon 2 is reversed. Similarly, galactose, another hexose, differs from glucose only in the orientation of the groups attached to carbon 4. Interconversion of glucose and mannose or galactose requires the breaking and making of covalent bonds; such reactions are carried out by enzymes called *epimerases*.

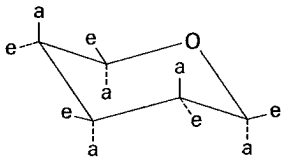
D-Glucose ($C_6H_{12}O_6$) is the principal external source of energy for most cells in higher organisms and can exist in three different forms: a linear structure and two different hemiacetal ring structures (Figure 2-18a). If the aldehyde group on carbon 1 reacts with the hydroxyl group on carbon 5, the resulting hemiacetal, D-glucopyranose, contains a six-member ring. In the α anomer of D-glucopyranose, the hydroxyl group attached to carbon 1 points "downward" from the ring as shown in Figure 2-18a; in the β anomer, this hydroxyl points "upward." In aqueous solution the α and β anomers readily interconvert spontaneously; at equilibrium there is about one-third α anomer and two-thirds β, with very little of the open-chain form. Because enzymes can distinguish between the α and β anomers of D-glucose, these forms have distinct biological roles. Condensation of the



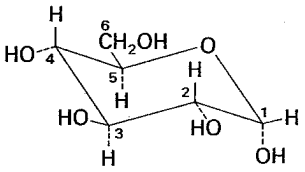
▲ **FIGURE 2-18 Chemical structures of hexoses.** All hexoses have the same chemical formula ($C_6H_{12}O_6$) and contain an aldehyde or a keto group. (a) The ring forms of D-glucose are generated from the linear molecule by reaction of the aldehyde at carbon 1 with the hydroxyl on carbon 5 or carbon 4. The three forms are readily interconvertible, although the pyranose form (*right*) predominates in biological systems. (b) In D-mannose and D-galactose, the configuration of the H (green) and OH (blue) bound to one carbon atom differs from that in glucose. These sugars, like glucose, exist primarily as pyranoses.

hydroxyl group on carbon 4 of the linear glucose with its aldehyde group results in the formation of D-glucofuranose, a hemiacetal containing a five-member ring. Although all three forms of D-glucose exist in biological systems, the pyranose form is by far the most abundant.

The pyranose ring in Figure 2-18a is depicted as planar. In fact, because of the tetrahedral geometry around carbon atoms, the most stable conformation of a pyranose ring has a nonplanar, chairlike shape. In this conformation, each bond from a ring carbon to a nonring atom (e.g., H or O) is either nearly perpendicular to the ring, referred to as axial (a), or nearly in the plane of the ring, referred to as equatorial (e):



Pyranoses

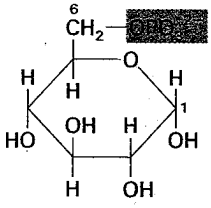


α-D-Glucopyranose

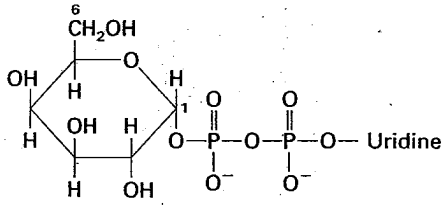
Disaccharides, formed from two monosaccharides, are the simplest polysaccharides. The disaccharide lactose, composed of galactose and glucose, is the major sugar in milk; the disaccharide sucrose, composed of glucose and fructose, is a principal product of plant photosynthesis and is refined into common table sugar (Figure 2-19).

Larger polysaccharides, containing dozens to hundreds of monosaccharide units, can function as reservoirs for glucose, as structural components, or as adhesives that help hold cells together in tissues. The most common storage carbohydrate in animal cells is **glycogen,** a very long, highly branched polymer of glucose. As much as 10 percent by weight of the liver can be glycogen. The primary storage carbohydrate in plant cells, **starch,** also is a glucose polymer. It occurs in an unbranched form (amylose) and lightly branched form (amylopectin). Both glycogen and starch are composed of the α anomer of glucose. In contrast, **cellulose,** the major constituent of plant cell walls (Chapter 19), is an unbranched polymer of the β anomer of glucose. Human digestive enzymes can hydrolyze the α glycosidic bonds in starch but not the β glycosidic bonds in cellulose. Many species of plants, bacteria, and molds produce cellulose-degrading enzymes. Cows and termites can break down cellulose because they harbor cellulose-degrading bacteria in their gut.

The enzymes that make the glycosidic bonds linking monosaccharides into polysaccharides are specific for the α or β anomer of one sugar and a particular hydroxyl group on the other. In principle, any two sugar molecules can be linked in a variety of ways because each monosaccharide has multiple hydroxyl groups that can participate in the formation of glycosidic bonds. Furthermore, any one monosaccharide has the potential of being linked to more than two other monosaccharides, thus generating a branch point and nonlinear polymers. Glycosidic bonds are usually formed between the growing polysaccharide chain and a covalently modified form of a monosaccharide. Such modifications include a phosphate (e.g., glucose 6-phosphate) or a nucleotide (e.g., UDP-galactose):



Glucose 6-phosphate



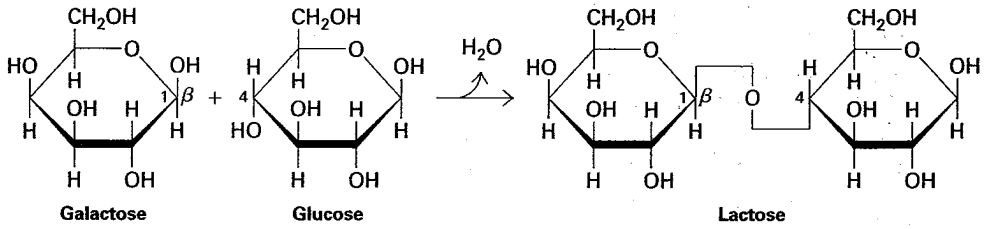
UDP-galactose

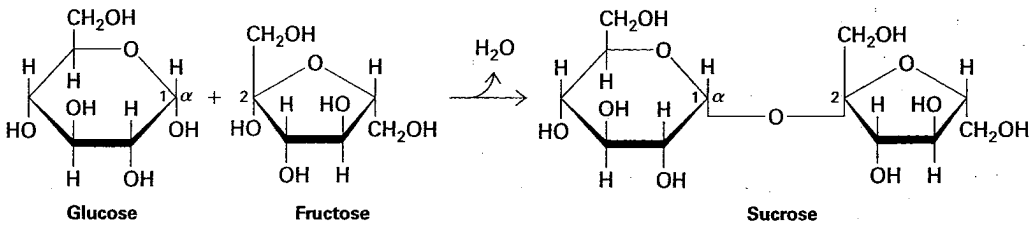
The epimerase enzymes that interconvert different monosaccharides often do so using the nucleotide sugars rather than the unsubstituted sugars.

Many complex polysaccharides contain modified sugars that are covalently linked to various small groups, particularly amino, sulfate, and acetyl groups. Such modifications are abundant in **glycosaminoglycans,** major polysaccharide components of the extracellular matrix that we describe in Chapter 19.

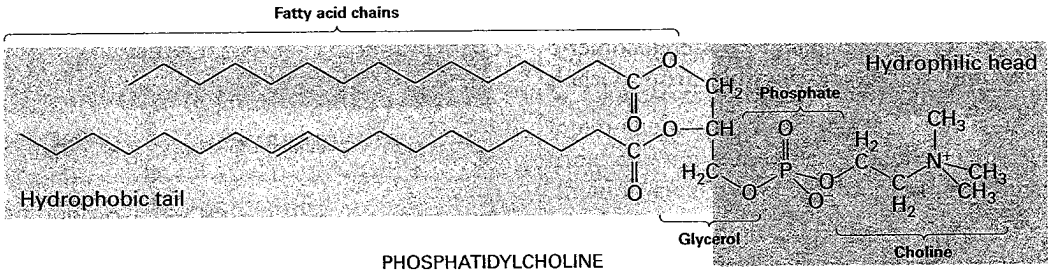
Phospholipids Associate Noncovalently to Form the Basic Bilayer Structure of Biomembranes

Biomembranes are large flexible sheets that serve as the boundaries of cells and their intracellular organelles and





► **FIGURE 2-19 Formation of the disaccharides lactose and sucrose.** In any glycosidic linkage, the anomeric carbon of one sugar molecule (in either the α or β conformation) is linked to a hydroxyl oxygen on another sugar molecule. The linkages are named accordingly; thus lactose contains a β(1 → 4) bond, and sucrose contains an α(1 → 2) bond.



▲ **FIGURE 2-20 Phosphatidylcholine, a typical phosphoglyceride.** All phosphoglycerides are amphipathic phospholipids, having a hydrophobic tail (yellow) and a hydrophilic head (blue) in which glycerol is linked via a phosphate group to an alcohol. Either or both of the fatty acyl side chains in a phosphoglyceride may be saturated or unsaturated. In phosphatidic acid (red), the simplest phospholipid, the phosphate is not linked to an alcohol.

form the outer surfaces of some viruses. Membranes literally define what is a cell (the outer membrane and the contents within the membrane) and what is not (the extracellular space outside the membrane). Unlike the proteins, nucleic acids, and polysaccharides, membranes are assembled by the *noncovalent* association of their component building blocks. The primary building blocks of all biomembranes are **phospholipids,** whose physical properties are responsible for the formation of the sheetlike structure of membranes. The structures and functions of membranes, which include in addition to phospholipids a variety of other molecules (e.g., cholesterol, glycolipids, proteins), will be described in detail in Chapter 10.

Phospholipids consist of two long-chain, nonpolar fatty acid groups linked (usually by an ester bond) to small, highly polar groups, including a phosphate and a short organic molecule, such as glycerol (trihydroxy propanol) (Figure 2-20).

Fatty acids consist of a hydrocarbon chain attached to a carboxyl group (—COOH). Like glucose, fatty acids are an important energy source for many cells (Chapter 12). They differ in length, although the predominant fatty acids in cells have an even number of carbon atoms, usually 14, 16, 18, or 20. The major fatty acids in phospholipids are listed in Table 2-4. Fatty acids often are designated by the abbreviation Cx:y, where x is the number of carbons in the chain and y is the number of double bonds. Fatty acids containing 12 or more carbon atoms are nearly insoluble in aqueous solutions because of their long hydrophobic hydrocarbon chains.

Fatty acids with no carbon-carbon double bonds are said to be **saturated;** those with at least one double bond are **unsaturated.** Unsaturated fatty acids with more than one carbon-carbon double bond are referred to as **polyunsaturated.** Two "essential" polyunsaturated fatty acids, linoleic acid (C18:2) and linolenic acid (C18:3), cannot be synthesized

TABLE 2-4 Fatty Acids That Predominate in Phospholipids

COMMON NAME OF ACID (IONIZED FORM IN PARENTHESES)	ABBREVIATION	CHEMICAL FORMULA
SATURATED FATTY ACIDS		
Myristic (myristate)	C14:0	$CH_3(CH_2)_{12}COOH$
Palmitic (palmitate)	C16:0	$CH_3(CH_2)_{14}COOH$
Stearic (stearate)	C18:0	$CH_3(CH_2)_{16}COOH$
UNSATURATED FATTY ACIDS		
Oleic (oleate)	C18:1	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$
Linoleic (linoleate)	C18:2	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$
Arachidonic (arachidonate)	C20:4	$CH_3(CH_2)_4(CH{=}CHCH_2)_3CH{=}CH(CH_2)_3COOH$