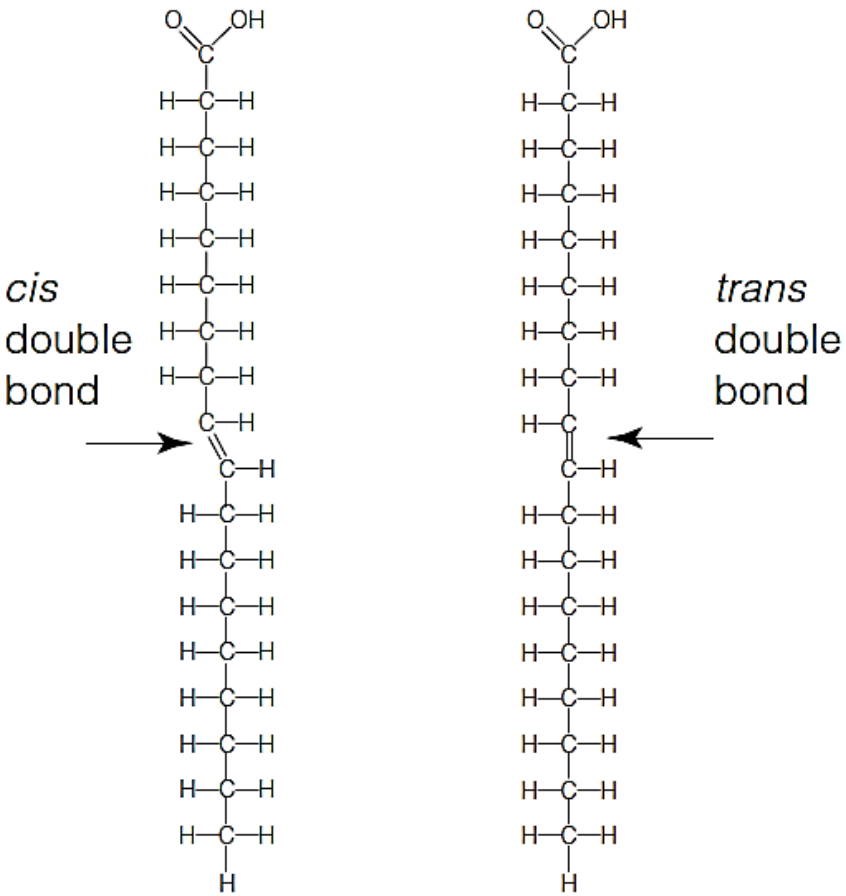
Biochemistry

Introduction to Macromolecules

Small differences in molecules can have big effects in a living organism



C oleic acid **D** elaidic acid

Partially hydrogenated vegetable oils are trans-fats

Main elements of life

Living organisms are made of only a small selection of the 92 naturally occurring elements, four of which—carbon (C), hydrogen (H), nitrogen (N), and oxygen (O)—make up 96.5% of an organism's weight.

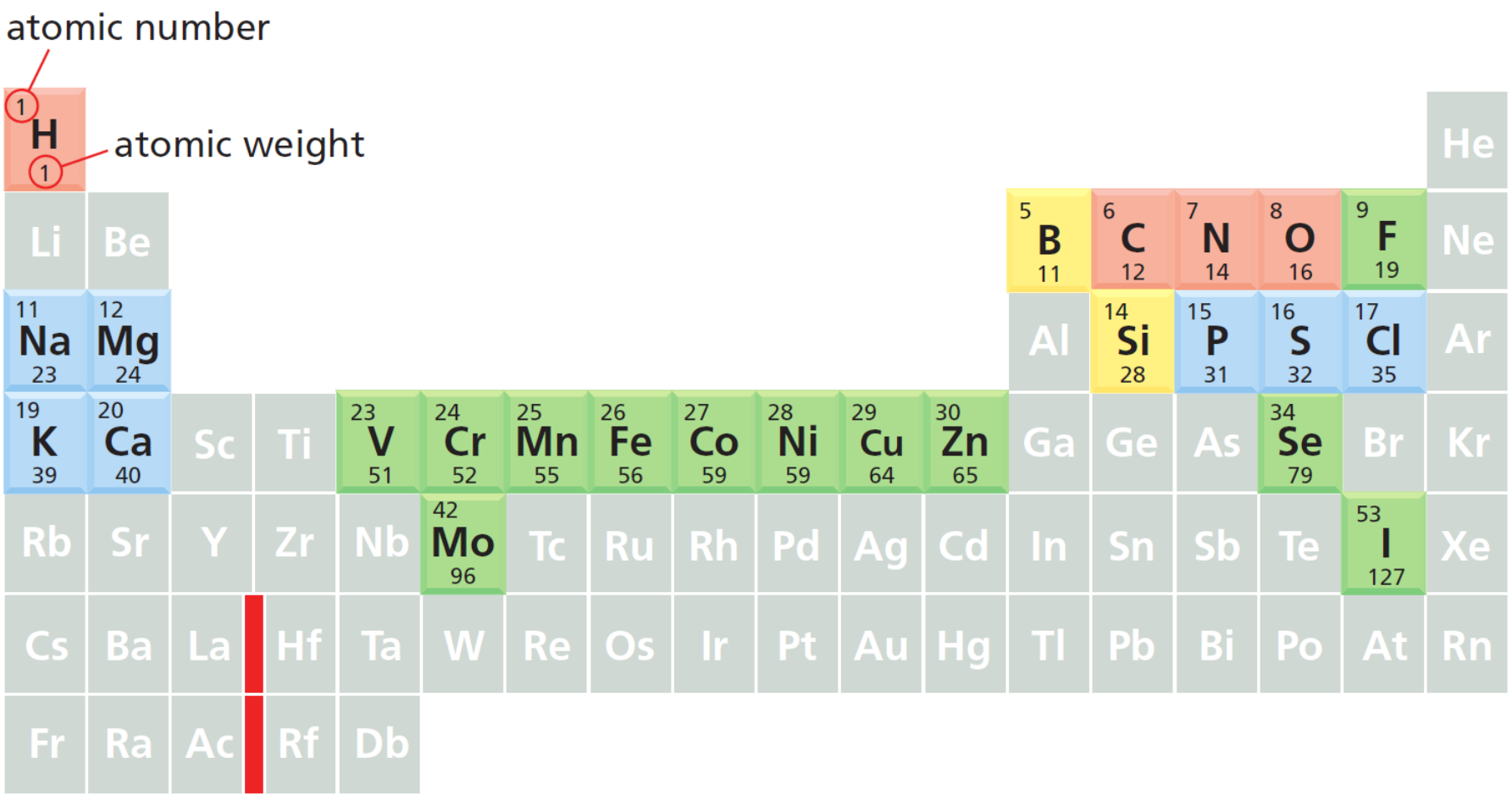


Figure 2–1 The main elements in cells, highlighted in the periodic table. When ordered by their atomic number and arranged in this manner, elements fall into vertical columns that show similar properties. Atoms in the same vertical column must gain (or lose) the same number of electrons to attain a filled outer shell, and they thus behave similarly in bond or ion formation. Thus, for example, Mg and Ca tend to give away the two electrons in their outer shells. C, N, and O occur in the same horizontal row, and tend to complete their second shells by sharing electrons.

The four elements highlighted in *red* constitute 99% of the total number of atoms present in the human body. An additional seven elements, highlighted in *blue*, together represent about 0.9% of the total. The elements shown in *green* are required in trace amounts by humans. It remains unclear whether those elements shown in *yellow* are essential in humans. The chemistry of life, it seems, is therefore predominantly the chemistry of lighter elements. The atomic weights shown here are those of the most common isotope of each element.

The distribution of elements in the Earth's crust and oceans differs radically from that in a living organism.

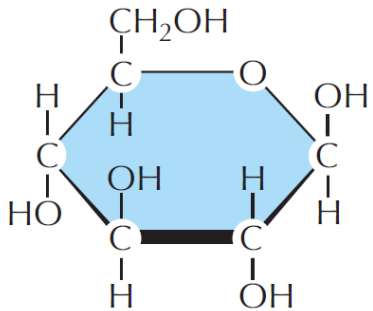
Table 2.2 Some Elemental Abundances*

Element	Human	Earth	Seawater
Hydrogen	62.0%	3.1%	66.0%
Oxygen	24.0	60.0	33.0
Carbon	12.0	0.3	<0.1
Nitrogen	1.2	<0.1	<0.1
Phosphorus	0.2	<0.1	<0.1
Calcium	<0.1	<0.1	<0.1
Sodium	<0.1	<0.1	0.3
Potassium	<0.1	0.8	<0.1
Chlorine	<0.1	<0.1	0.3

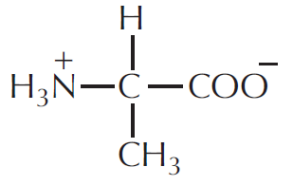
* As a percentage of the total number of atoms in each source

Carbon constitutes more than 50% of the mass of an organism what is left after water because it is backbone of every macromolecule

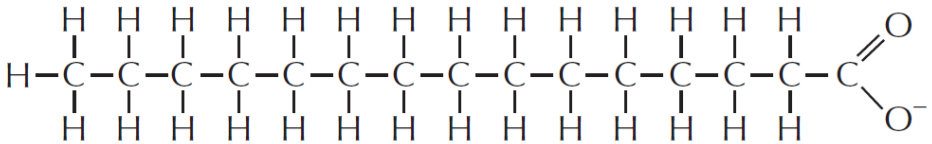
The four main families of small organic molecules in cells



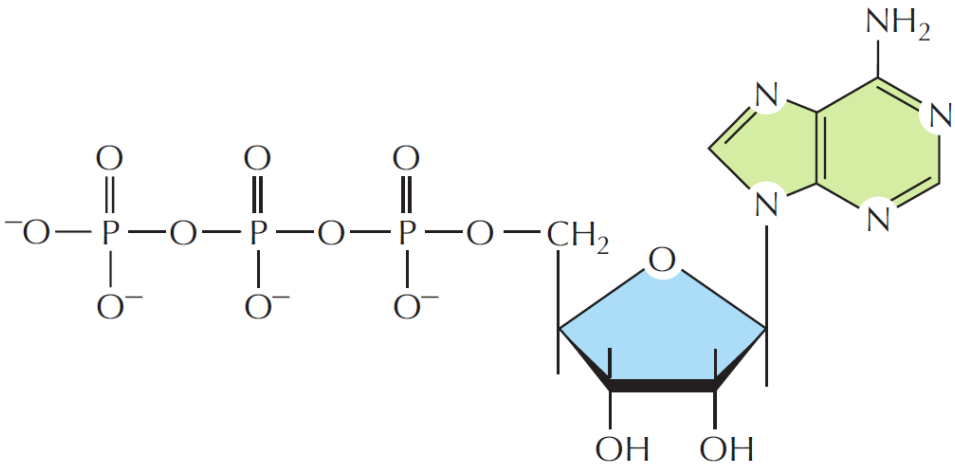
A SUGAR



AN AMINO ACID



A FATTY ACID

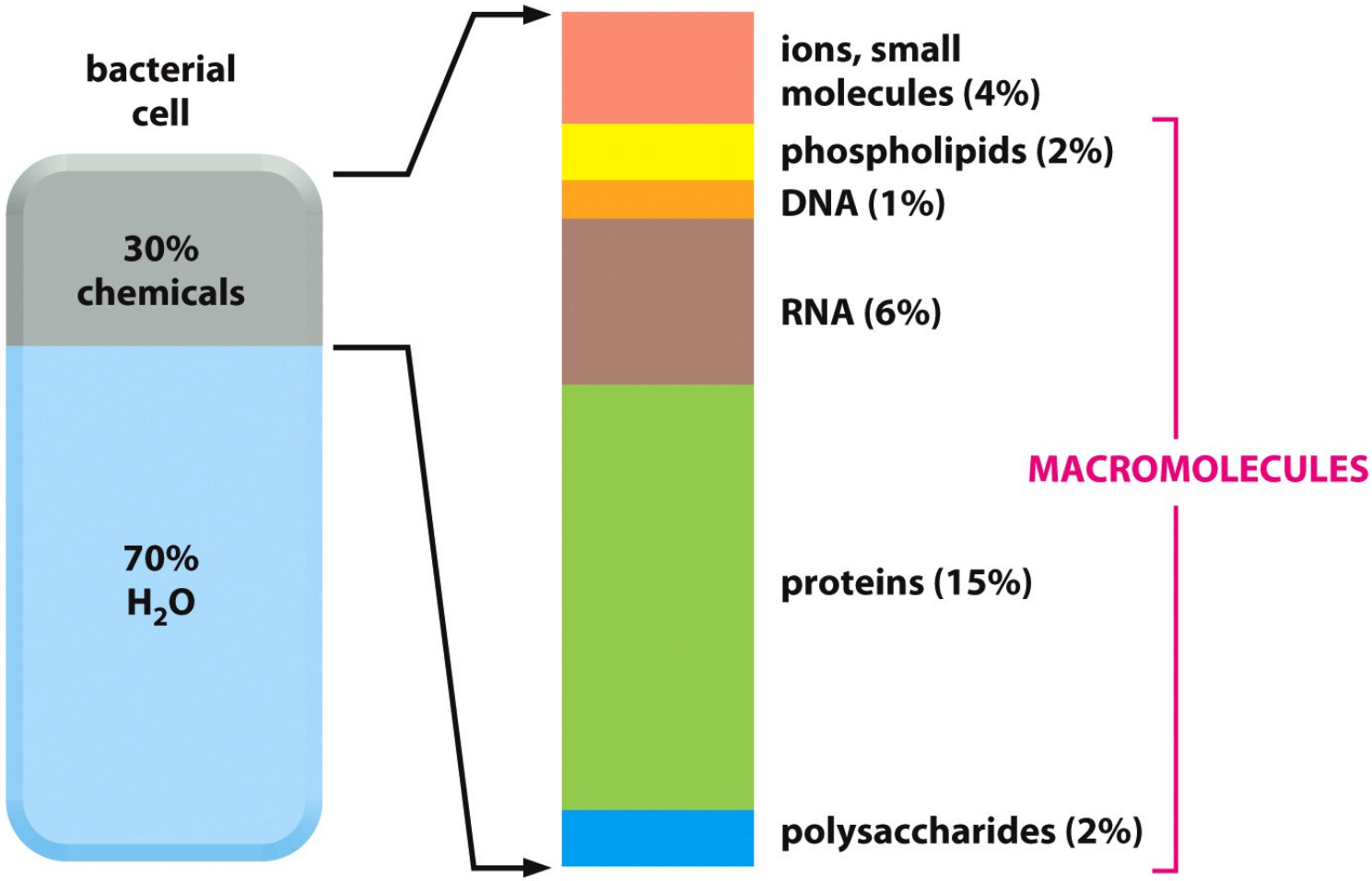


A NUCLEOTIDE

Certain combinations of atoms, such as the methyl ($–CH_3$), hydroxyl (–OH), carboxyl (–COOH), carbonyl (–C=O), phosphate ($–PO_3^{2–}$), sulfhydryl (–SH), and amino (–NH2) groups, occur repeatedly in the molecules made by cells. Each such chemical group has distinct chemical and physical properties that influence the behavior of the molecule in which the group occurs.

Figure 2–6 The four main families of small organic molecules in cells. These small molecules form the monomeric building blocks, or subunits, for most of the macromolecules and other assemblies of the cell. Some, such as the sugars and the fatty acids, are also energy sources. Their structures are outlined here and shown in more detail in the Panels at the end of this chapter and in Chapter 3.

Majority of the organic mass is contributed by macromolecules



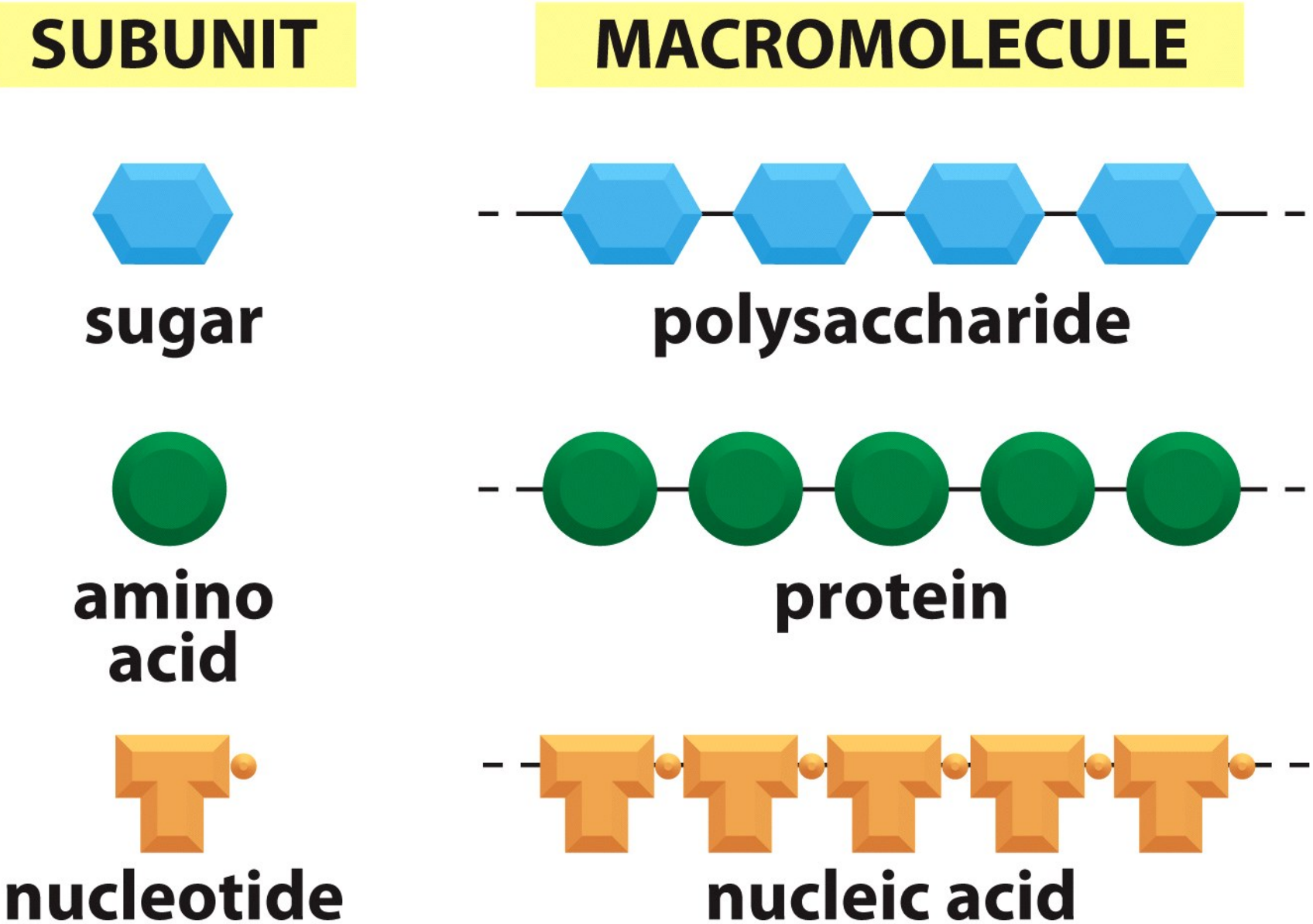
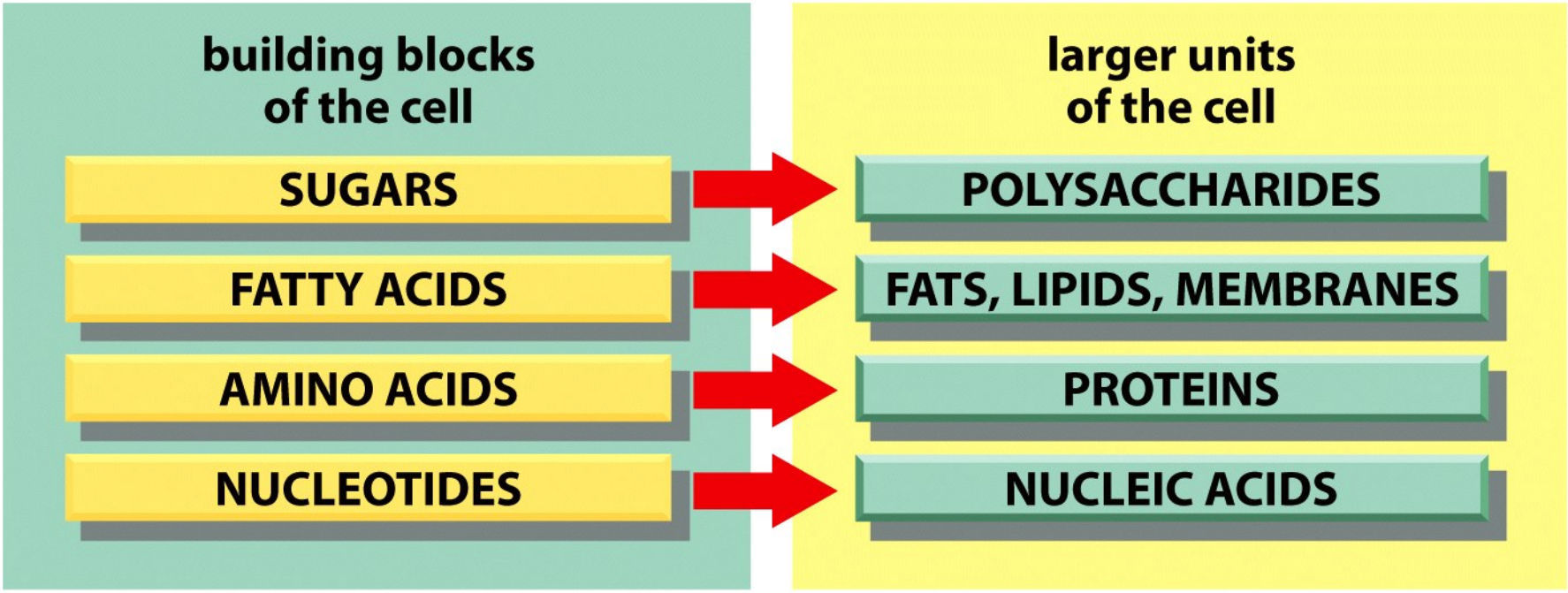
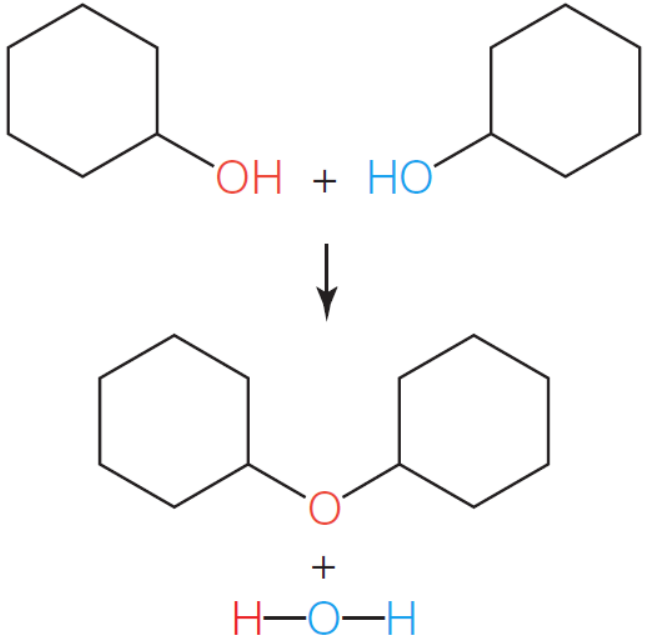


Figure 2-27 *Essential Cell Biology* (© Garland Science 2010)

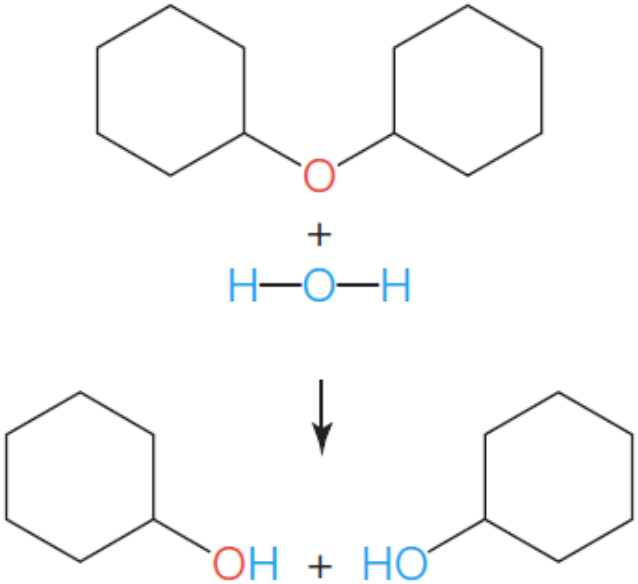
Macromolecules and their building blocks



Condensation and hydrolysis are two key reactions in metabolism



A Condensation. Cells build large molecules from smaller ones by this reaction. An enzyme removes a hydroxyl group from one molecule and a hydrogen atom from another. Water forms as a covalent bond forms between the two molecules.

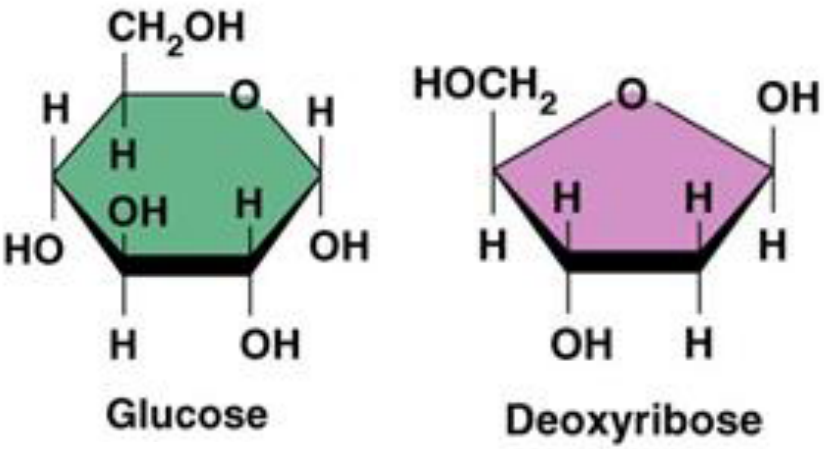


B Hydrolysis. Cells split molecules into smaller ones by this water-requiring reaction. An enzyme splits a molecule by attaching a hydroxyl group and a hydrogen atom (both from water) to each half.

Carbohydrates

Carbohydrates or sugar

- Constitutes of C, H and O in 1:2:1 ratio. General formula $(CH_2O)_n$, where *n* is usually 3, 4, 5, or 6.
- Simple sugars are water soluble, but complex are not.
- Most common types of monosaccharide have 6 or 5 carbon back bone.



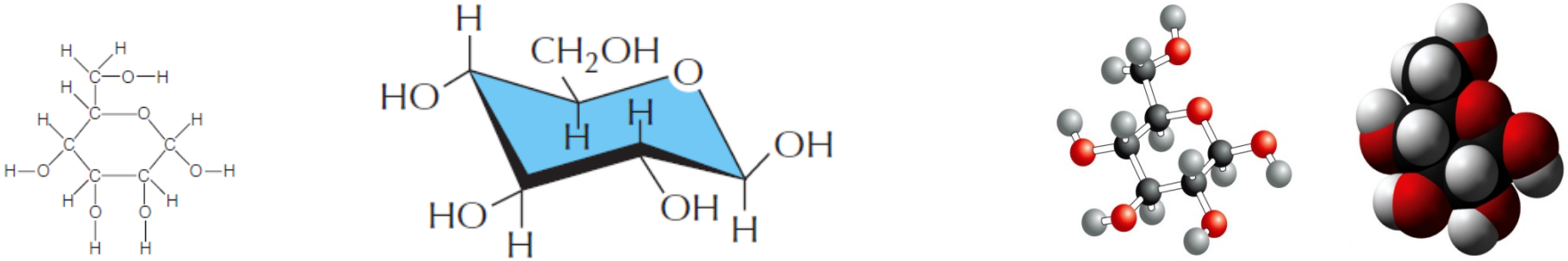
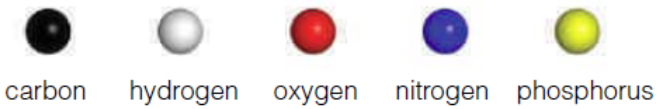
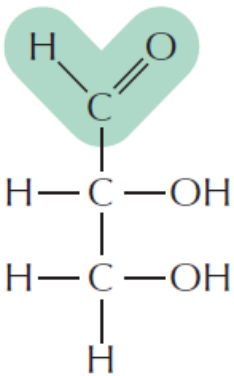


FIGURE 2.11 Modeling an organic molecule. **A** A structural formula shows atoms and bonds. **B** Another kind of structural formula that shows the 3D structure of glucose in the so-called "chair configuration." . **D** A ball-and-stick model shows the arrangement of atoms in three dimensions. **E** A space-filling model shows a molecule's overall shape. *Right*, typical color code for elements in molecular models.

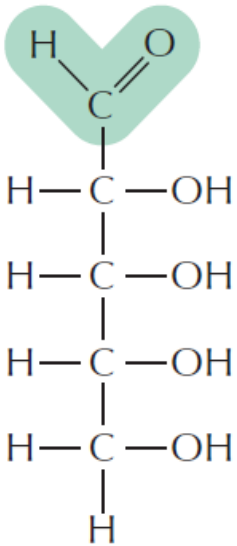


Triose pentose and hexose

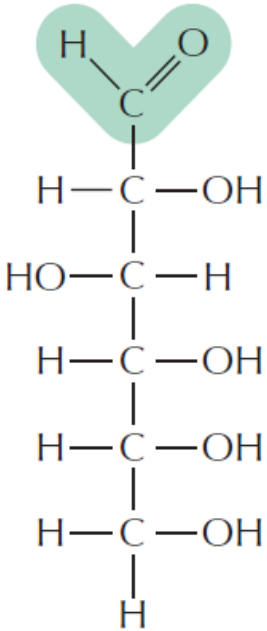
3-carbon (TRIOSES)	5-carbon (PENTOSES)	6-carbon (HEXOSES)



glyceraldehyde



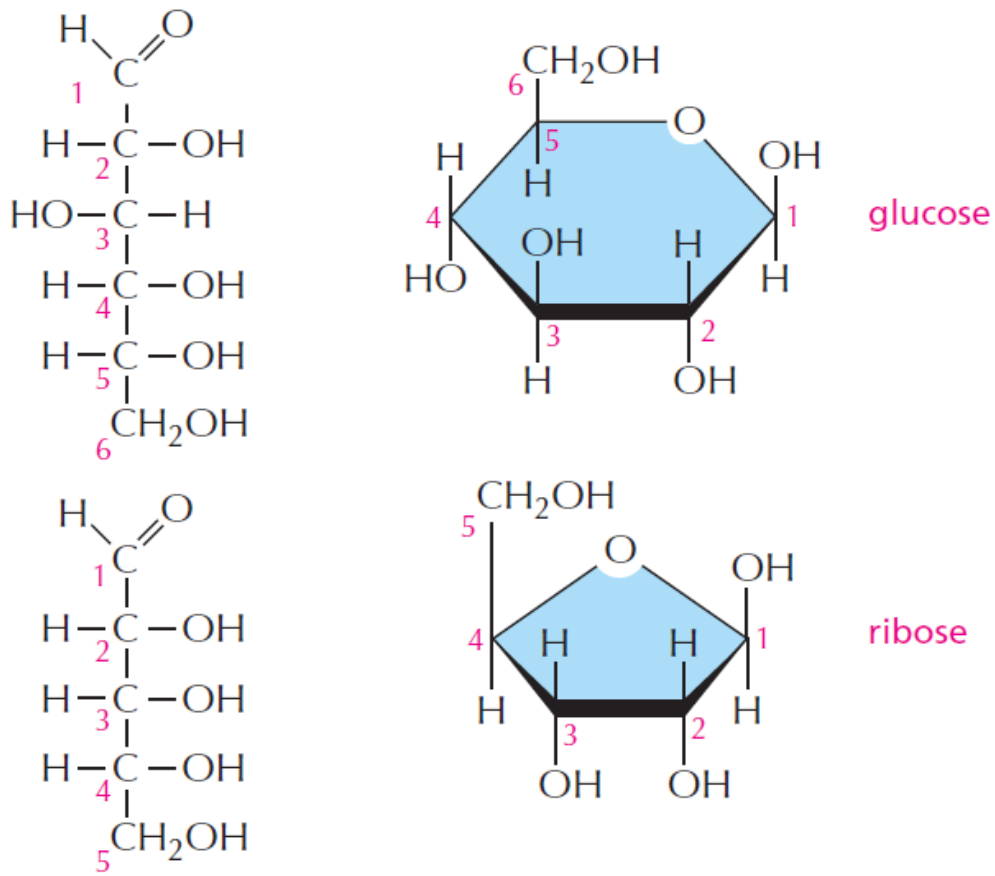
ribose



glucose

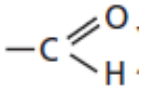
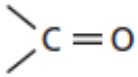
Sugar molecules tend to make a ring structure in water

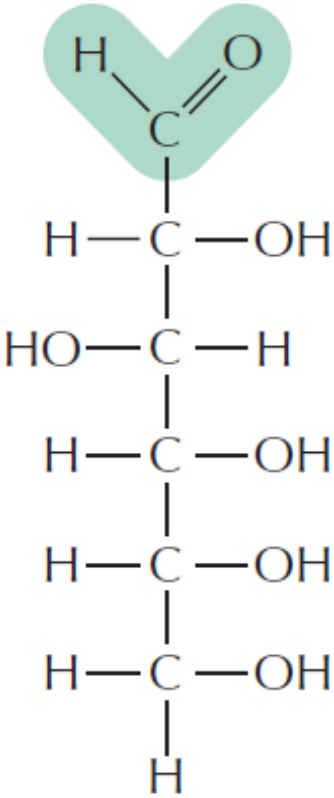
In aqueous solution, the aldehyde or ketone group of a sugar molecule tends to react with a hydroxyl group of the same molecule, thereby closing the molecule into a ring.



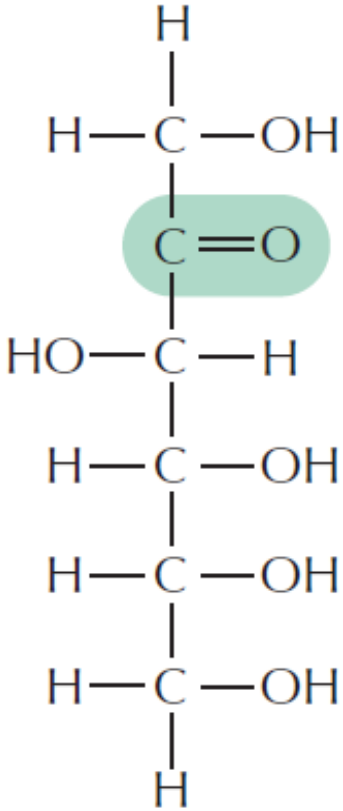
Note that each carbon atom has a number.

Aldose and ketose

Monosaccharides either contain an aldehyde group () and are called aldoses, or a ketone group () and are called ketoses.



glucose

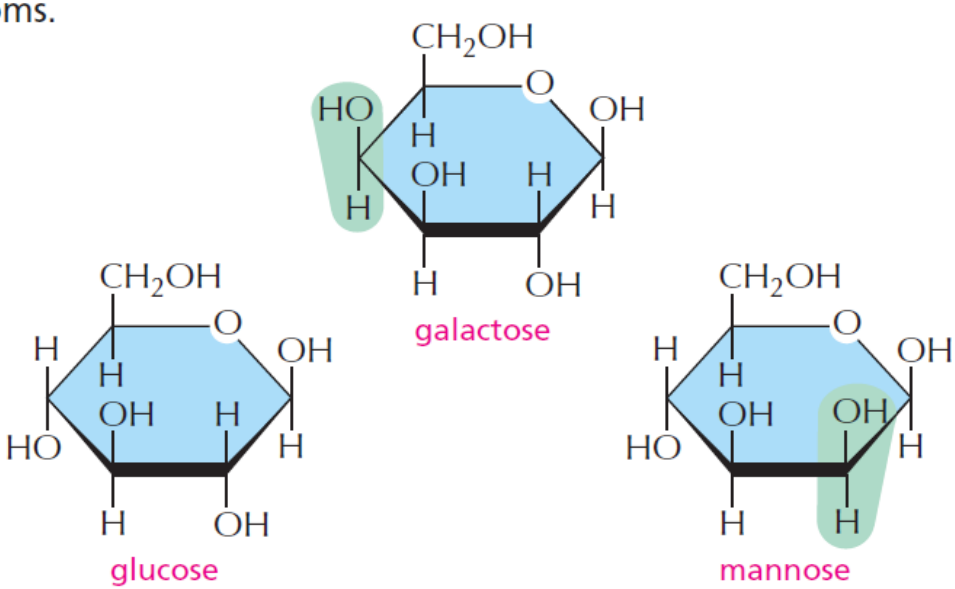


fructose

Isomers and stereoisomers

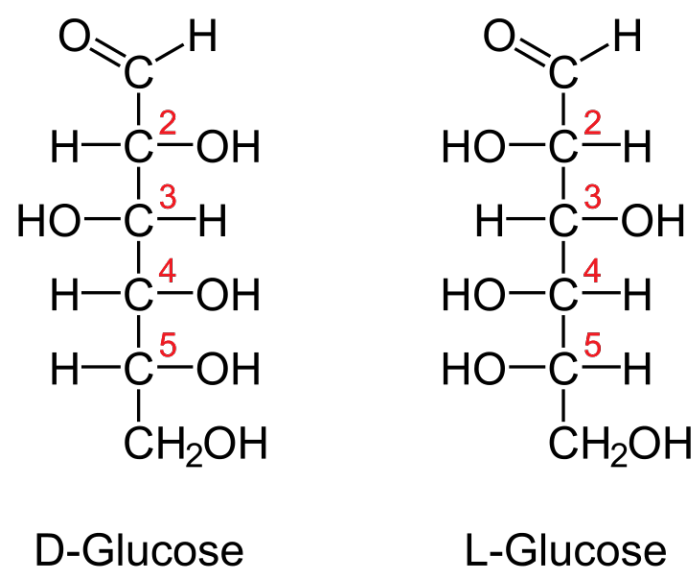
Sets of molecules with the same chemical formula but different structures are called isomers, and mirror-image pairs of such molecules are called optical isomers or stereoisomers. Isomers are widespread among organic molecules in general, and they play a major part in generating the enormous variety of sugars.

Many monosaccharides differ only in the spatial arrangement of atoms—that is, they are isomers. For example, glucose, galactose, and mannose have the same formula ($C_6H_{12}O_6$) but differ in the arrangement of groups around one or two carbon atoms.



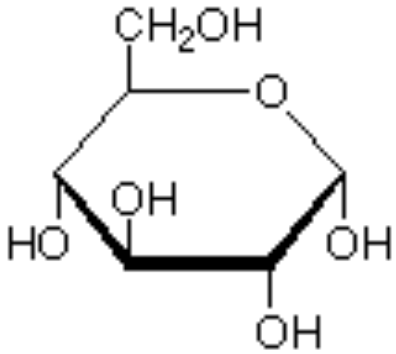
These small differences make only minor changes in the chemical properties of the sugars. But the differences are recognized by enzymes and other proteins and therefore can have major biological effects.

Stereoisomers of glucose

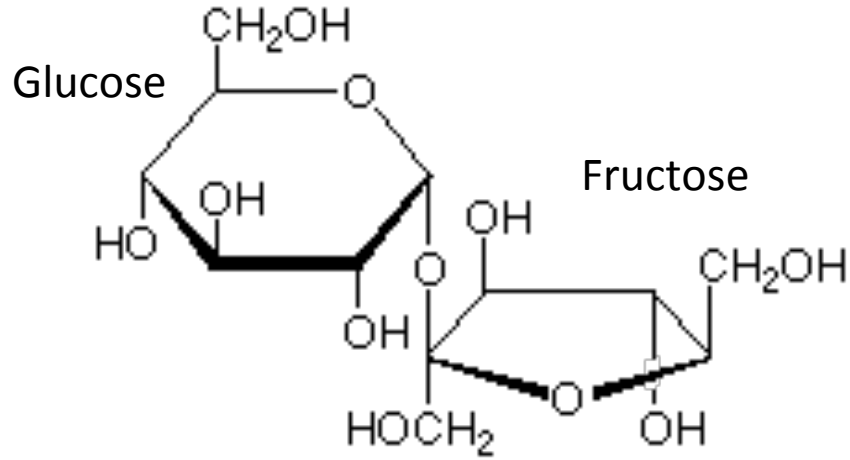


Monosaccharide, disaccharide and polysaccharide

Simple sugar

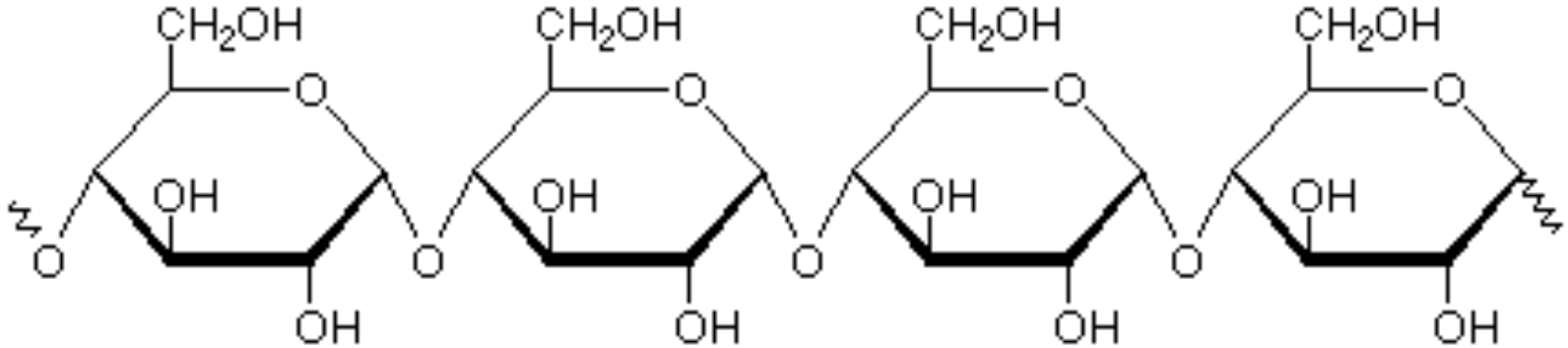


monosaccharide (glucose)



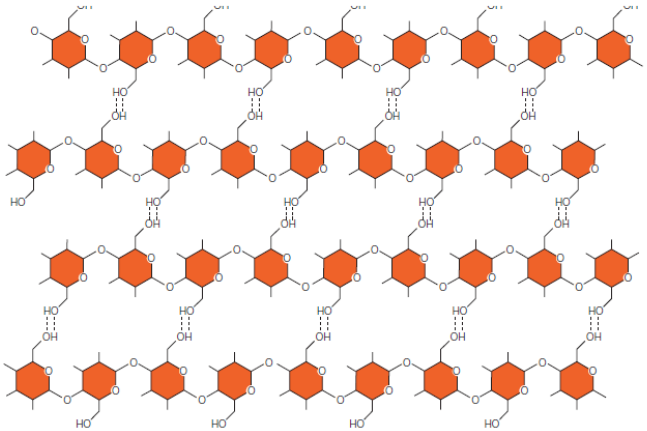
disaccharide (sucrose)

Complex sugar



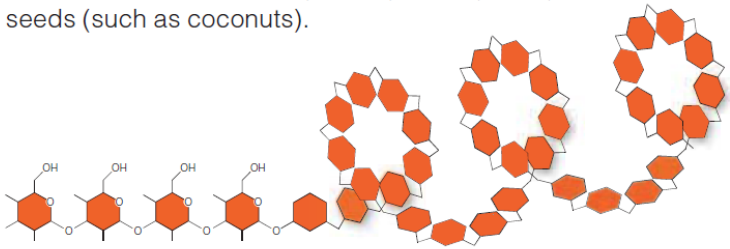
Oligo and polysaccharide (amylose starch)

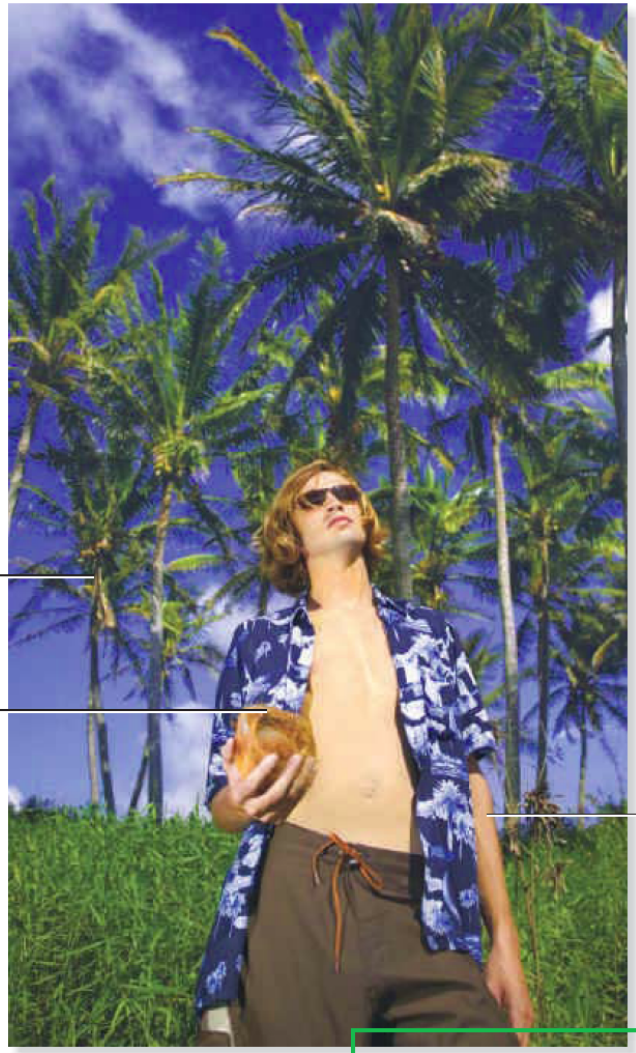
Complex carbohydrates are water insoluble

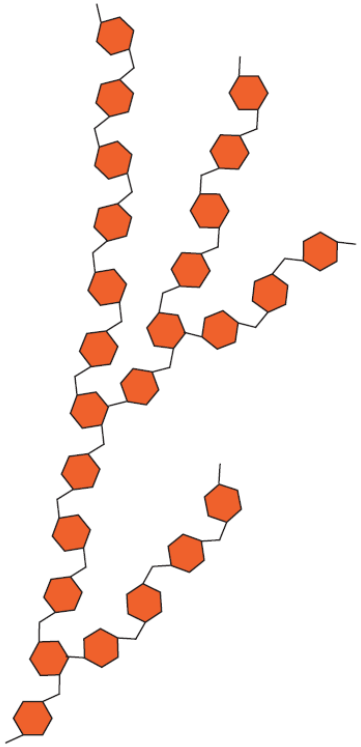


A Cellulose, a structural component of plants. Chains of glucose units stretch side by side and hydrogen-bond at many —OH groups. The hydrogen bonds stabilize the chains in tight bundles that form long fibers. Very few types of organisms can digest this tough, insoluble material.

B In starch, a series of glucose units form a chain that coils. Starch is the main energy reserve in plants, which store it in their roots, stems, leaves, fruits, and seeds (such as coconuts).





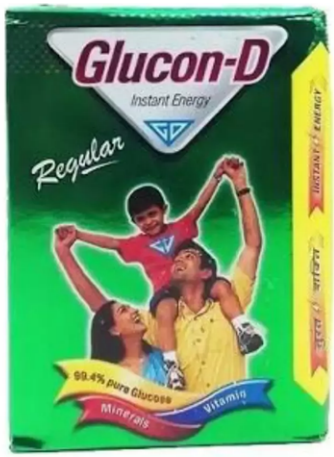


C Glycogen. In animals, this polysaccharide functions as an energy reservoir. It is especially abundant in the liver and muscles of active animals, including people.

FIGURE 2.13 Three of the most common complex carbohydrates and their locations in a few organisms.

Some functions of carbohydrates

Source of energy



D-glucose

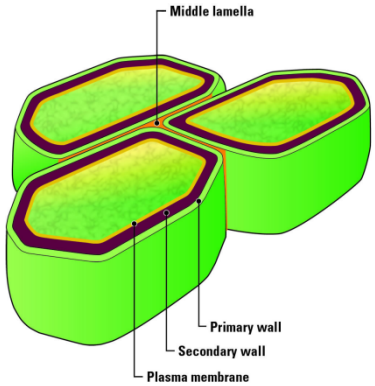
Lactose

Storage form of energy:

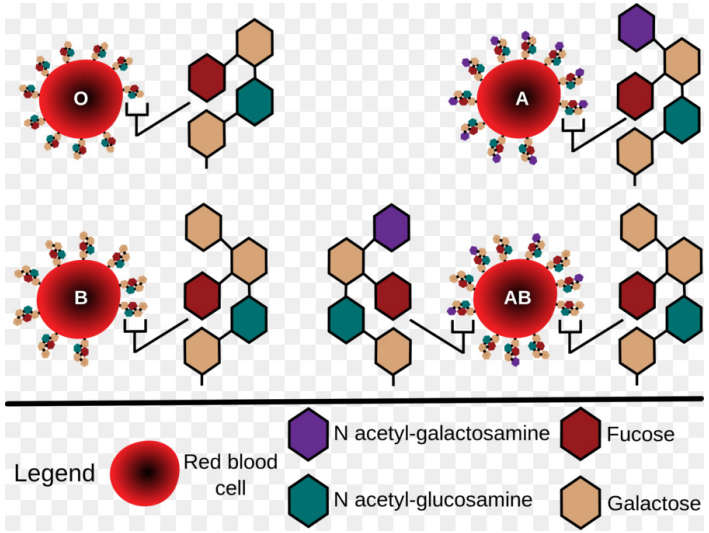
Starch

Structural component:

cellulose



Cell recognitions:



Glycolipids and glycoproteins

carbohydrate Molecule that consists primarily of carbon, hydrogen, and oxygen atoms in a 1:2:1 ratio.

condensation Process by which enzymes build large molecules from smaller subunits; water also forms.

hydrolysis Process by which an enzyme breaks a molecule into smaller subunits by attaching a hydroxyl group to one part and a hydrogen atom to the other.

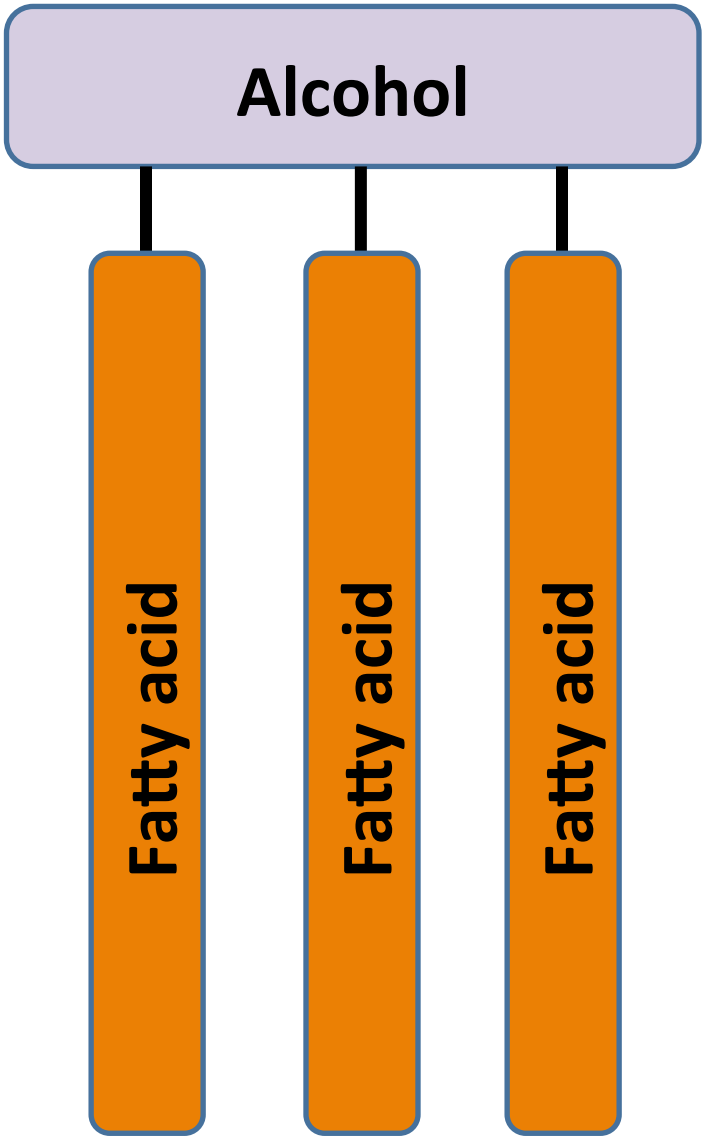
metabolism All the enzyme-mediated chemical reactions by which cells acquire and use energy as they build and break down organic molecules.

monomer Molecule that is a subunit of polymers.

polymer Molecule that consists of multiple monomers.

Lipids

Lipids

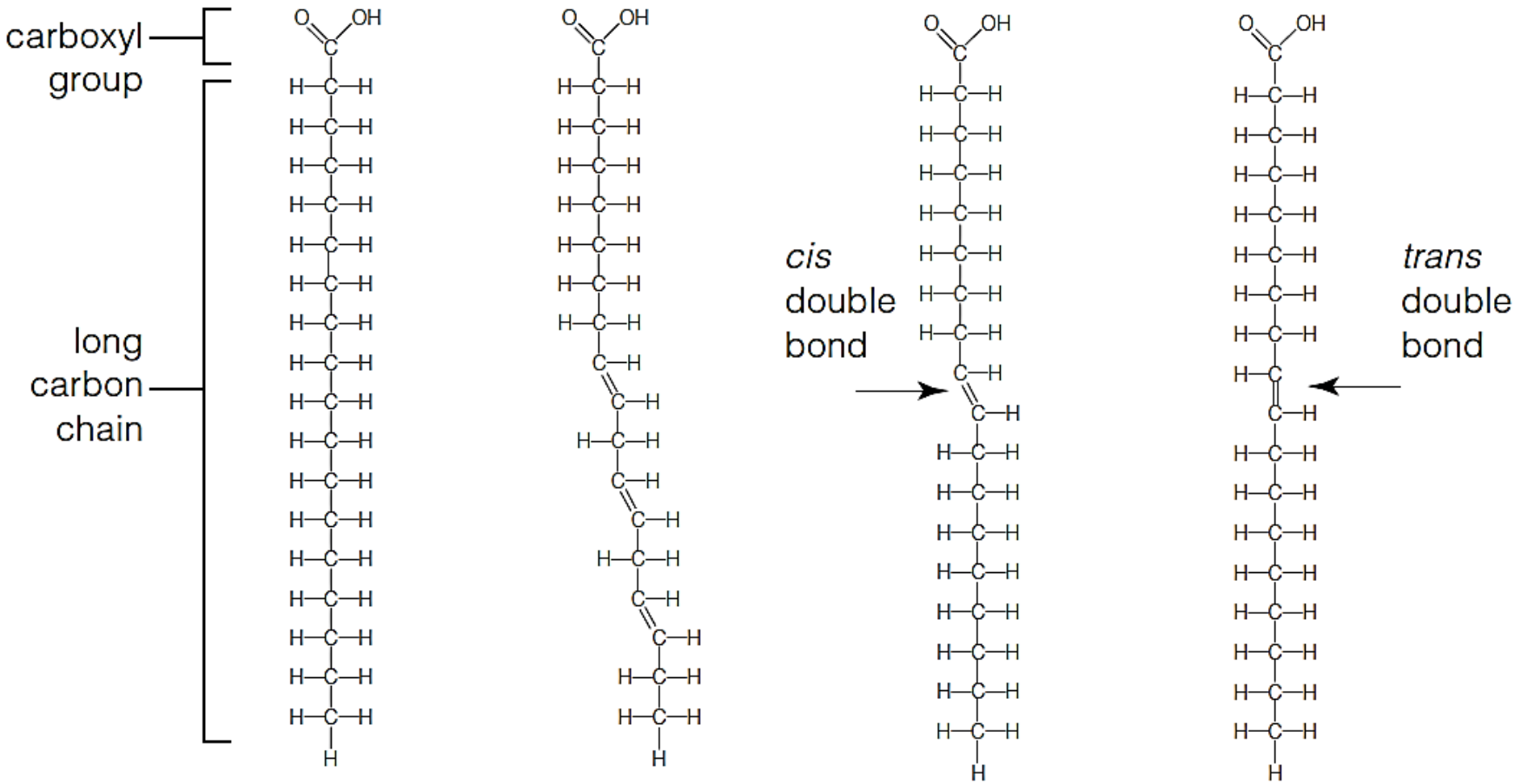


Many lipids incorporate **fatty acids**, small organic compounds that consist of a long carbon chain with an acidic carboxyl group at one end.

Fats are lipids with one, two, or three fatty acids that dangle like tails from a small alcohol called glycerol.

Lipids are fatty, oily or waxy

It depends on the fatty acid it contains



A stearic acid **B** linolenic acid **C** oleic acid **D** elaidic acid

Saturated

Unsaturated

FIGURE 2.14 Fatty acids.

A The backbone of stearic acid is fully saturated with hydrogen atoms.

B The backbone of linolenic acid, with three double bonds, is unsaturated. The first double bond occurs at the third carbon from the end, so linoleic acid is called an omega-3 fatty acid. Omega-3 and omega-6 fatty acids are "essential fatty acids." Your body does not make them, so they must come from food.

The only difference between oleic acid **C**, a *cis* fatty acid, and elaidic acid **D**, a *trans* fatty acid, is the arrangement of hydrogens around the one double bond in the backbone.

Fluidity of fats depend on the length and saturation of the fatty acid chains

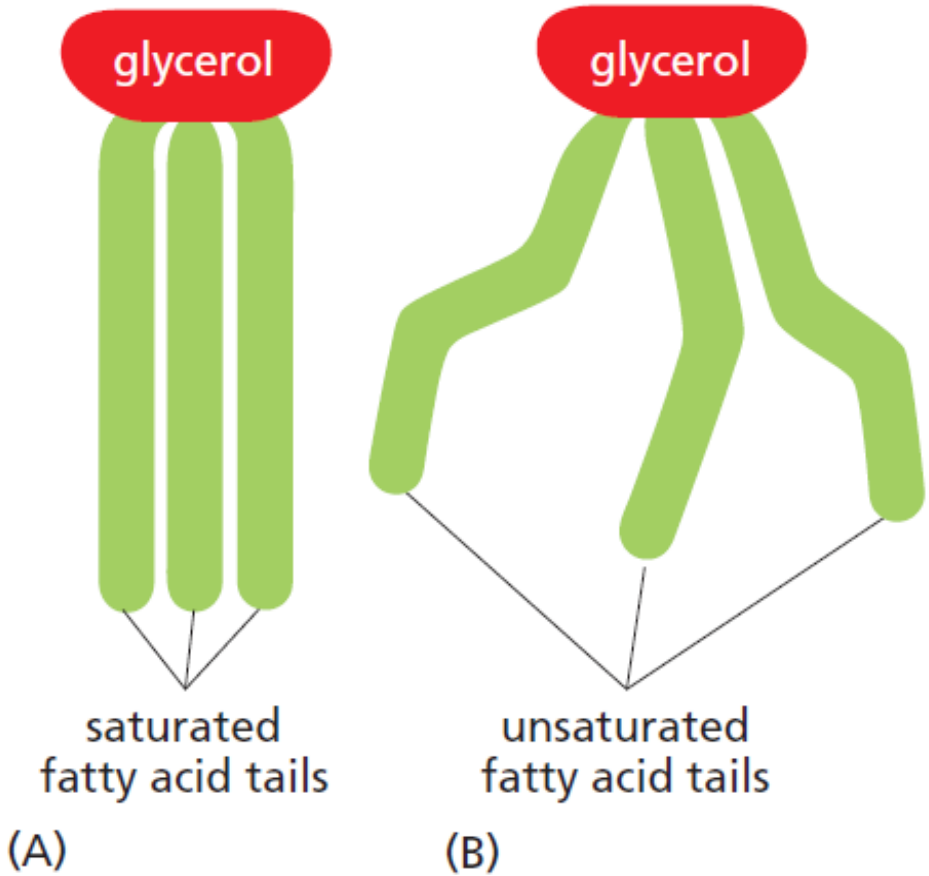
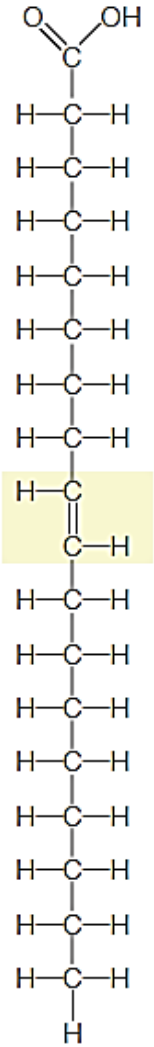


Figure 2–20 The properties of fats depend on the length and saturation of the fatty acid chains they carry. Fatty acids are stored in the cytoplasm of many cells in the form of droplets of *triacylglycerol* molecules made of three fatty acid chains joined to a glycerol molecule. (A) Saturated fats are found in meat and dairy products. (B) Plant oils, such as corn oil, contain unsaturated fatty acids, which may be monounsaturated (containing one double bond) or polyunsaturated (containing multiple double bonds); this is why plant oils are liquid at room temperature. Although fats are essential in the diet, saturated fats are not: they raise the concentration of cholesterol in the blood, which tends to clog the arteries, increasing the risk of heart attacks and strokes.

Partially hydrogenated vegetable oils

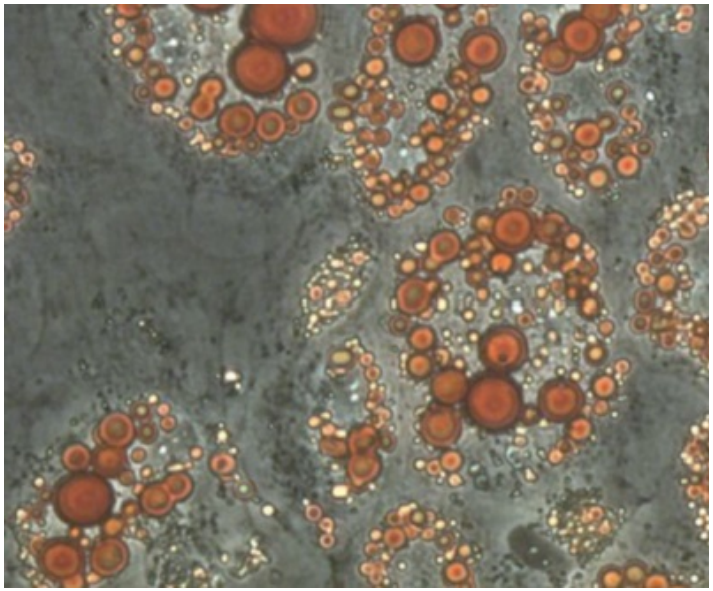


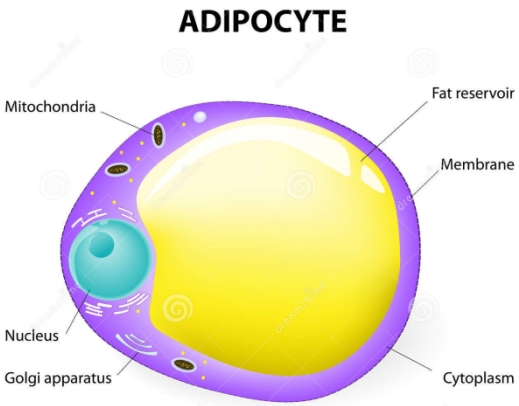
trans fatty acid

Triglycerides

Most **neutral** fats, including butter and vegetable oils, have three fatty acid tails, so they are called **triglycerides**.

Triglycerides are the most abundant and richest energy source in vertebrate bodies. They are concentrated in adipose tissue that insulates and cushions body parts.





Phospholipids are major constituents of cell membrane (amphipathic)

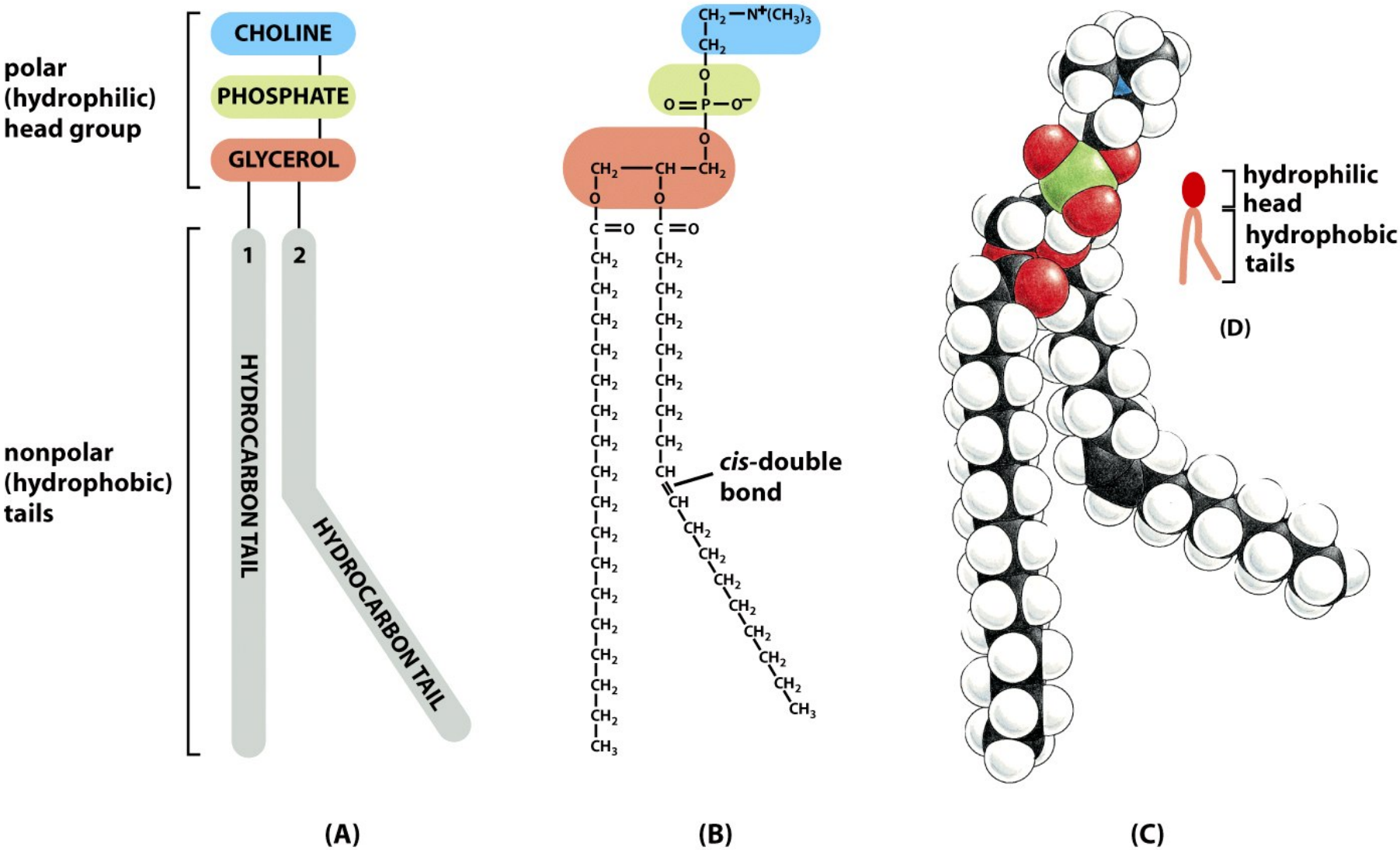


Figure 10-2 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Cell Membranes

A Phospholipids are the most abundant component of eukaryotic cell membranes. Each phospholipid molecule has a hydrophilic head and two hydrophobic tails.

B In a watery fluid, phospholipids spontaneously line up into two layers: hydrophobic tails cluster together, and hydrophilic heads face outward, toward the fluid. This lipid bilayer forms the framework of all cell membranes.

C A lipid bilayer spontaneously shapes itself into a sheet or bubble. A plasma membrane is basically a lipid bilayer balloon filled with fluid. Many types of proteins intermingle among the lipids in a cell membrane—a few that are typical of plasma membranes are shown *opposite*.

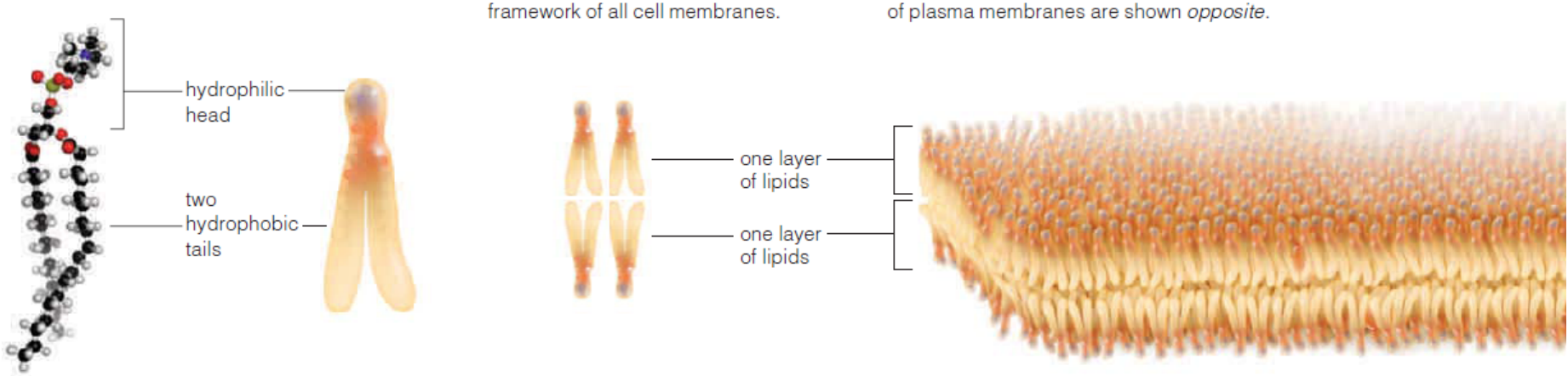
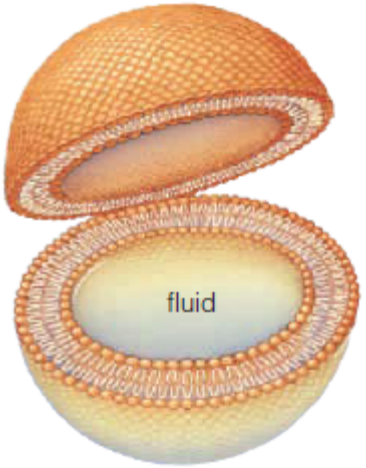


FIGURE 3.6 **Animated!** Cell membrane structure. **A–C** Organization of lipids in cell membranes. **D–G** Examples of membrane proteins.

A plasma membrane is basically a lipid bilayer balloon filled with fluid.



Cholesterol

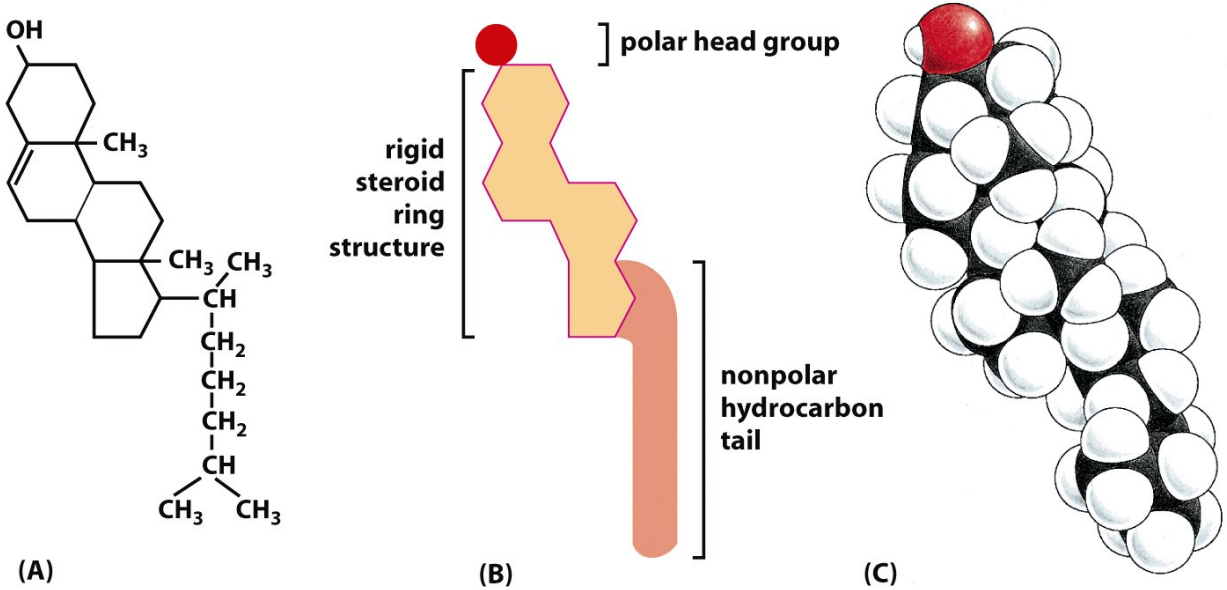


Figure 10-4 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Some plasma membrane has all most 50% of cholesterol. Needed to give proper rigidity to plasma membrane.

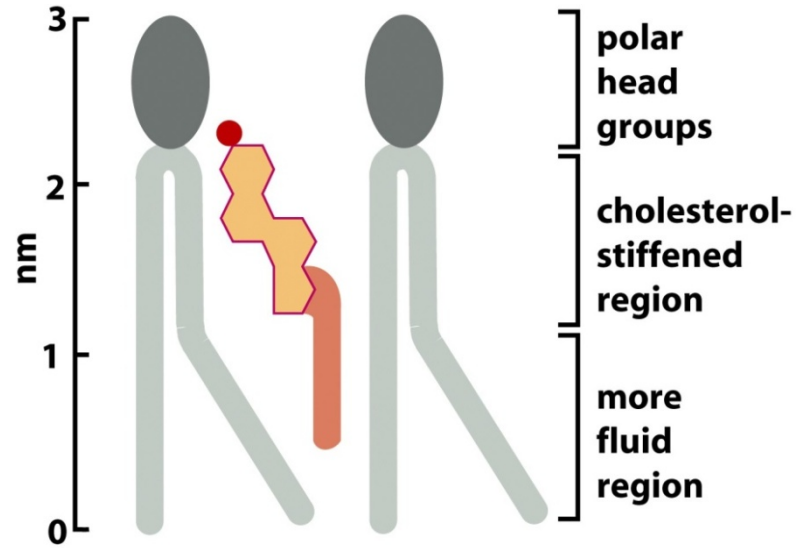
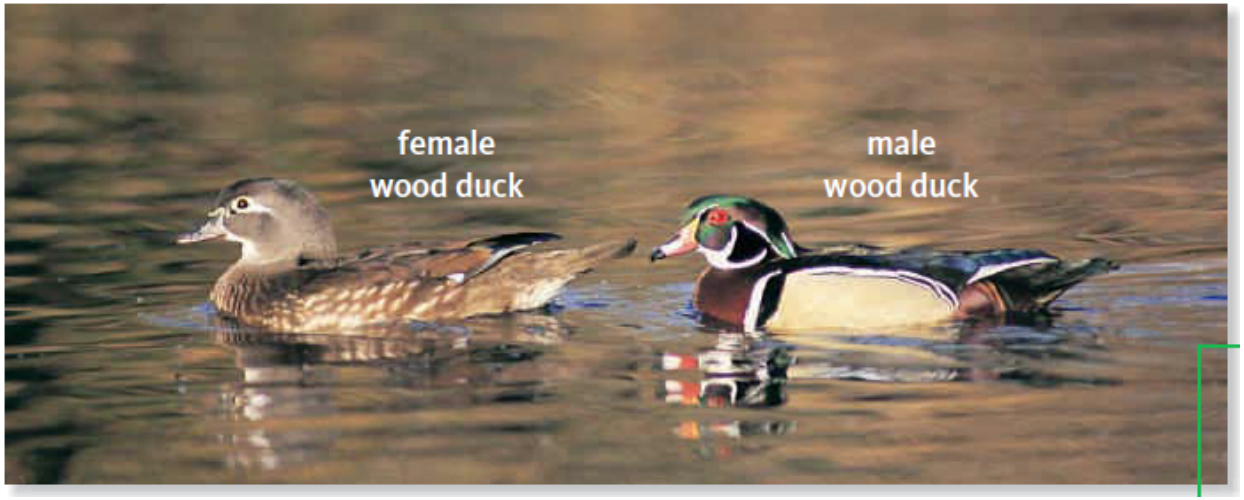


Figure 10-5 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Cholesterol is starting material for synthesis of bile salt, vitamin D and hormones



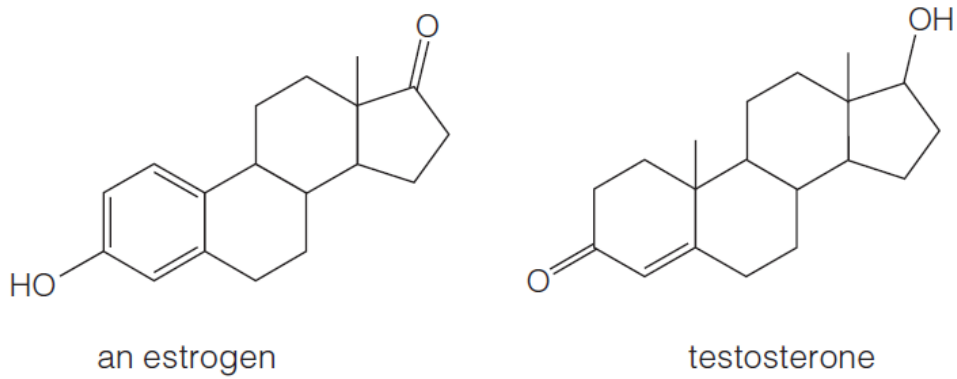


FIGURE 2.16 Estrogen and testosterone, steroid hormones that cause different traits to arise in males and females of many species such as wood ducks (*Aix sponsa*).

Waxes

Waxes are complex, varying mixtures of lipids with long fatty acid tails bonded to long-chain alcohols or carbon rings. The molecules pack tightly, so the resulting substance is firm and water-repellent.

Plant cuticle, a layer of secreted waxes, that covers the exposed surfaces of plants helps restrict water loss and keep out parasites and other pests.

Bees store honey and raise new generations of bees inside honeycomb, which they make from beeswax.

Other types of waxes protect, lubricate, and soften skin and hair. Waxes, together with fats and fatty acids, make feathers waterproof.

amino acid Small organic compound with a carboxyl group, an amine group, and a characteristic side group (R).

fat Lipid with one, two, or three fatty acid tails.

fatty acid Organic compound that consists of a long chain of carbon atoms with an acidic carboxyl group at one end.

lipid Fatty, oily, or waxy organic compound.

phospholipid A lipid with a phosphate group in its hydrophilic head, and two nonpolar fatty acid tails.

protein Organic compound that consists of one or more chains of amino acids.

saturated fat Fatty acid with no double bonds in its carbon tail.

steroid A type of lipid with four carbon rings and no fatty acid tails.

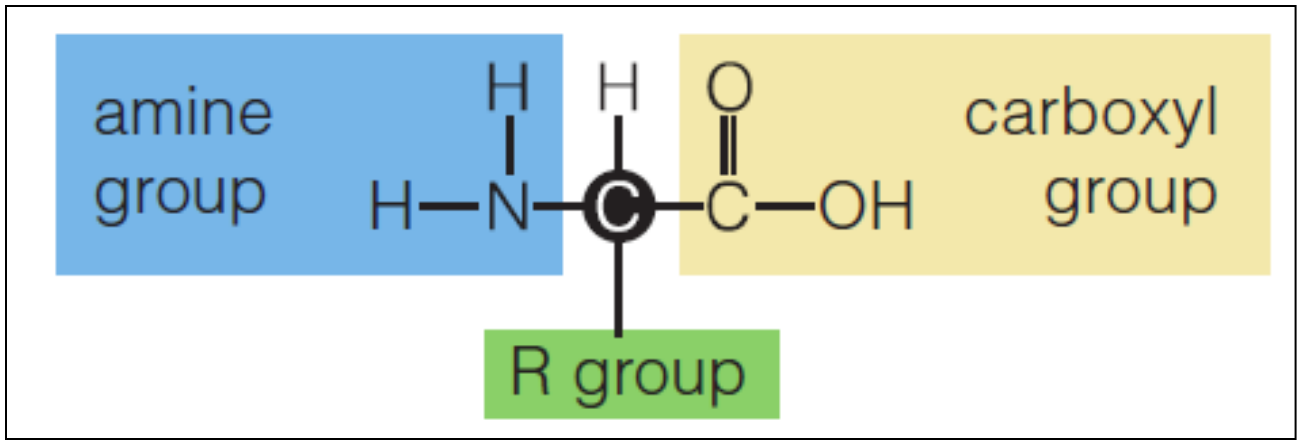
triglyceride A lipid with three fatty acid tails attached to a glycerol backbone.

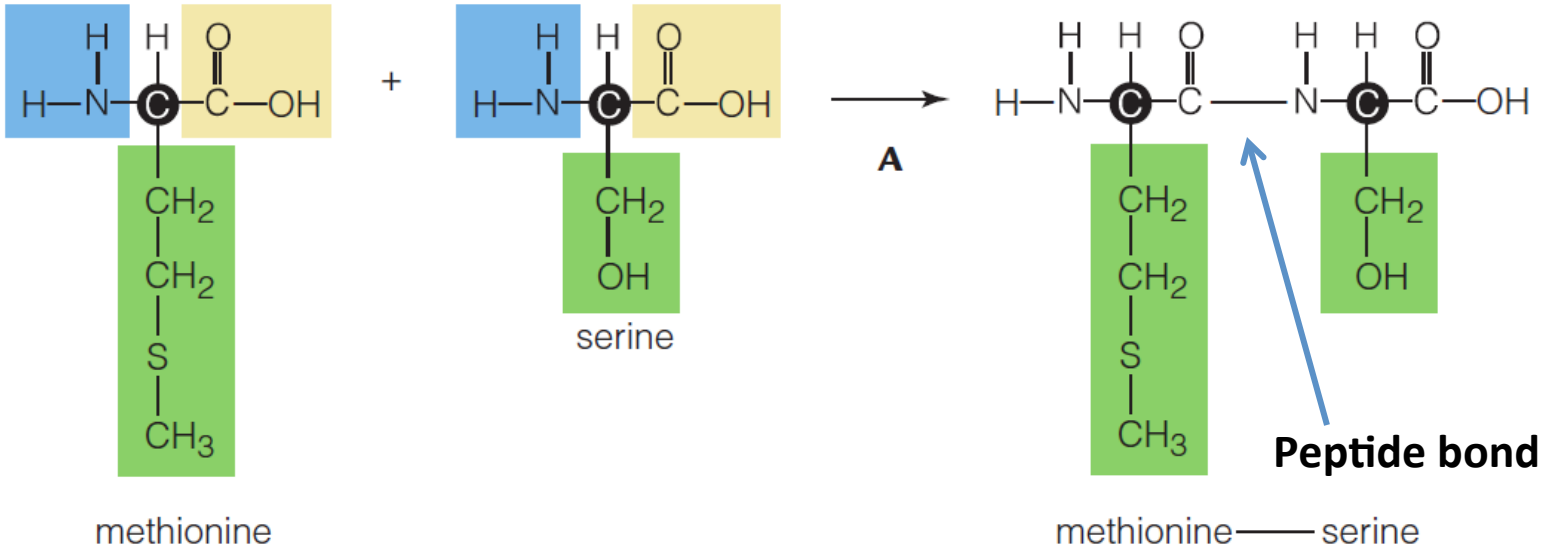
unsaturated fat Lipid with at least one double bond in a fatty acid tail.

wax Water-repellent lipid with long fatty acid tails bonded to long-chain alcohols or carbon rings.

Proteins

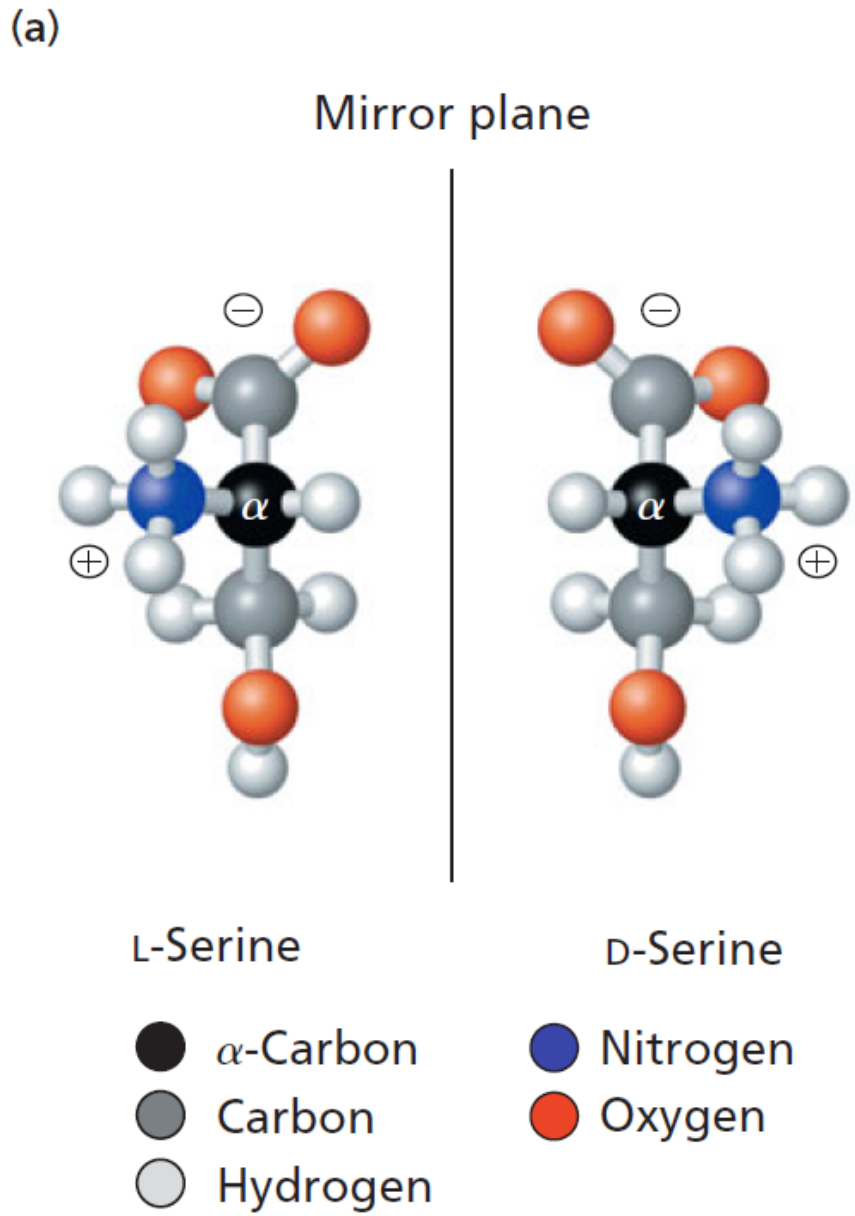
Amino acid

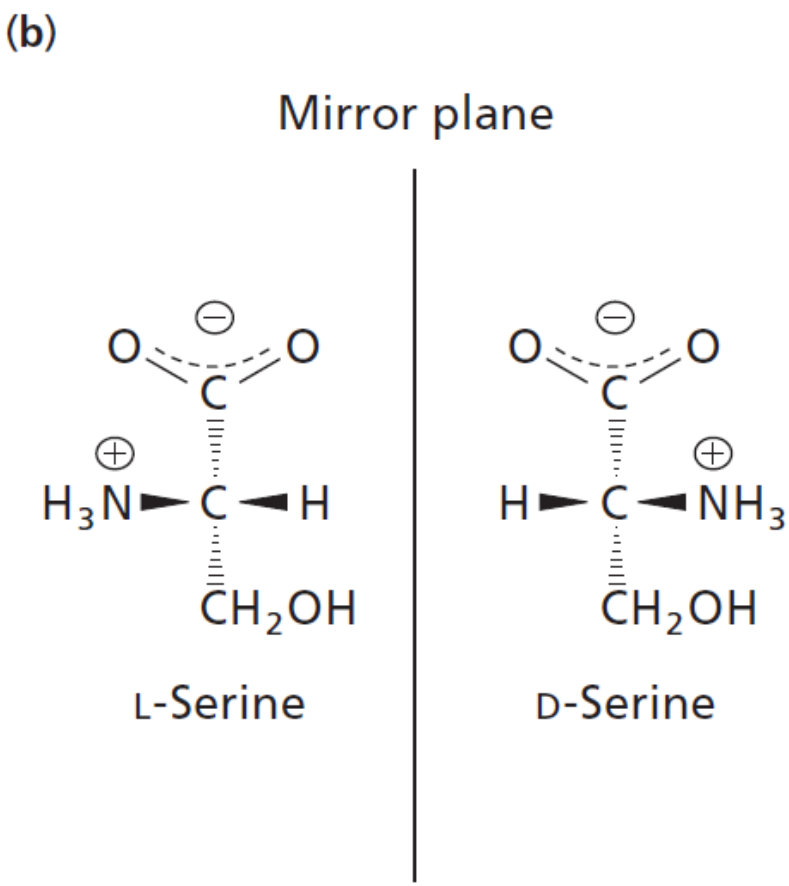




Cells can make thousands of different kinds of proteins from only 20 kinds of amino acids

Proteins are made up of L-aa





◄ **Figure 3.2**
Mirror-image pairs of amino acids. (a) Ball-and-stick models of L-serine and D-serine. Note that the two molecules are not identical; they cannot be superimposed. **(b)** L-Serine and D-serine. The common amino acids all have the L configuration.

Polar/ hydrophilic nature of peptide bond

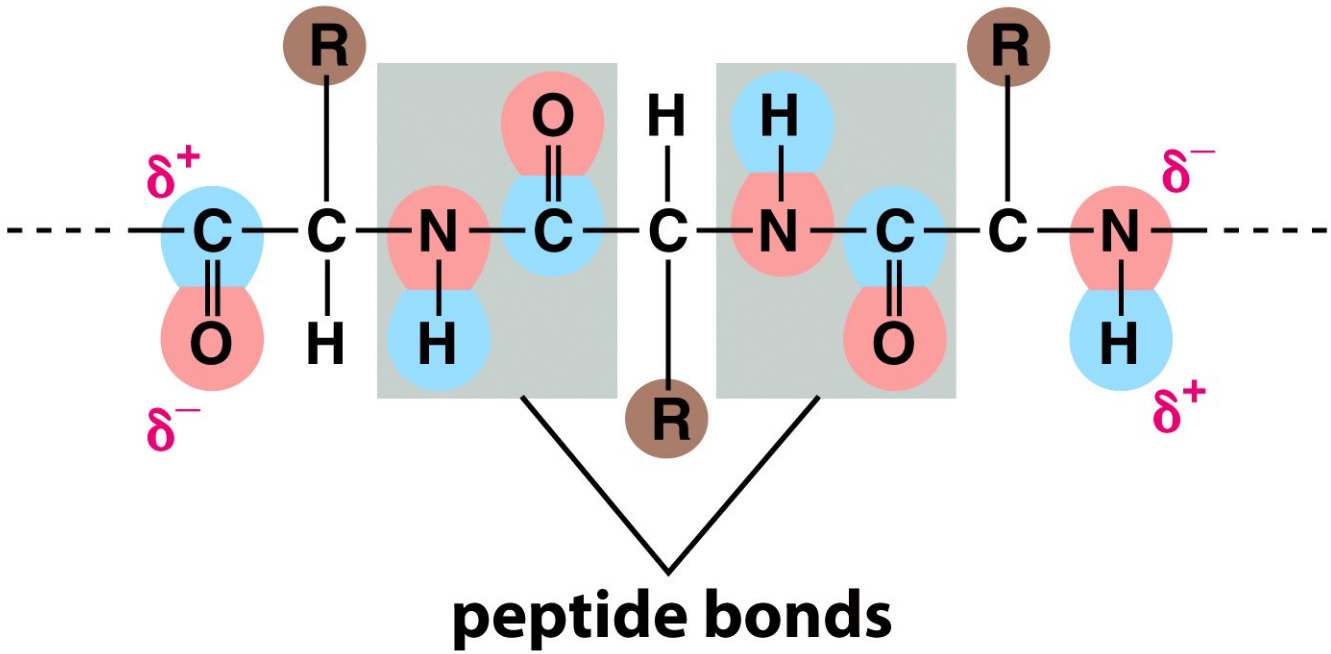
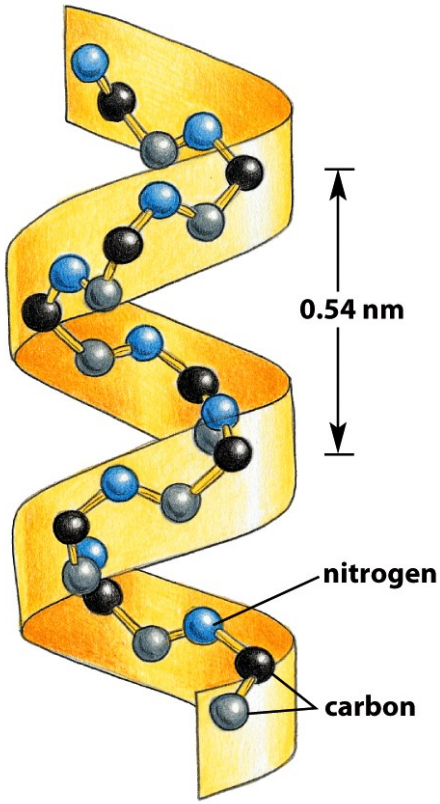


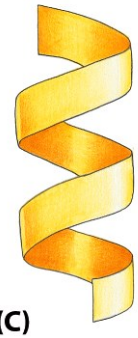
Figure 11–22 **The peptide bonds (shaded in *gray*) that join adjacent amino acids together in a polypeptide chain are polar and therefore hydrophilic.** The partial charges (δ^- indicates a partial negative charge and δ^+ indicates a partial positive charge) allow these atoms to hydrogen bond with one another when the polypeptide folds into an α helix that spans the membrane (see Figure 11–23).

Regions of polypeptide chain can take a helical or sheet like structures



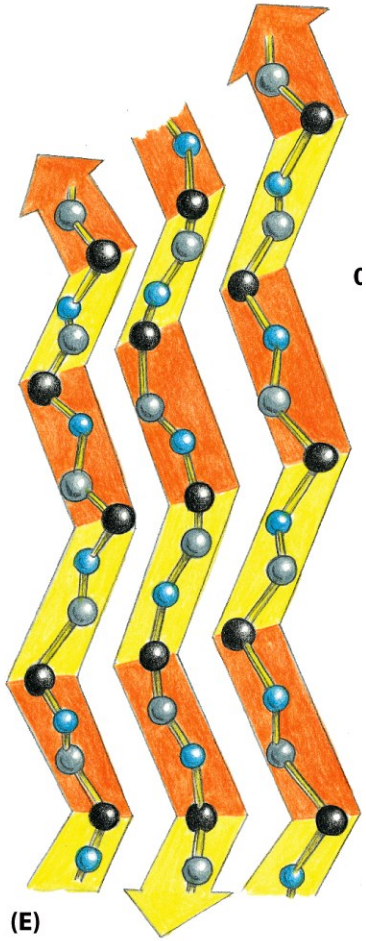
(B)

α helix



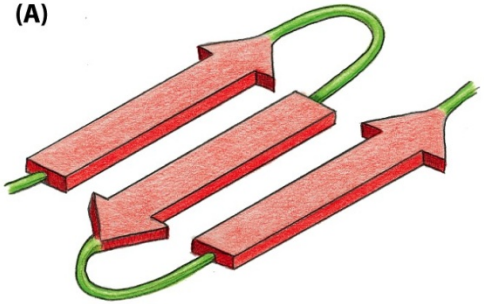
(C)

β-sheet



(E)

(A)



H-bonds between atoms of peptide backbone plays important role in protein folding

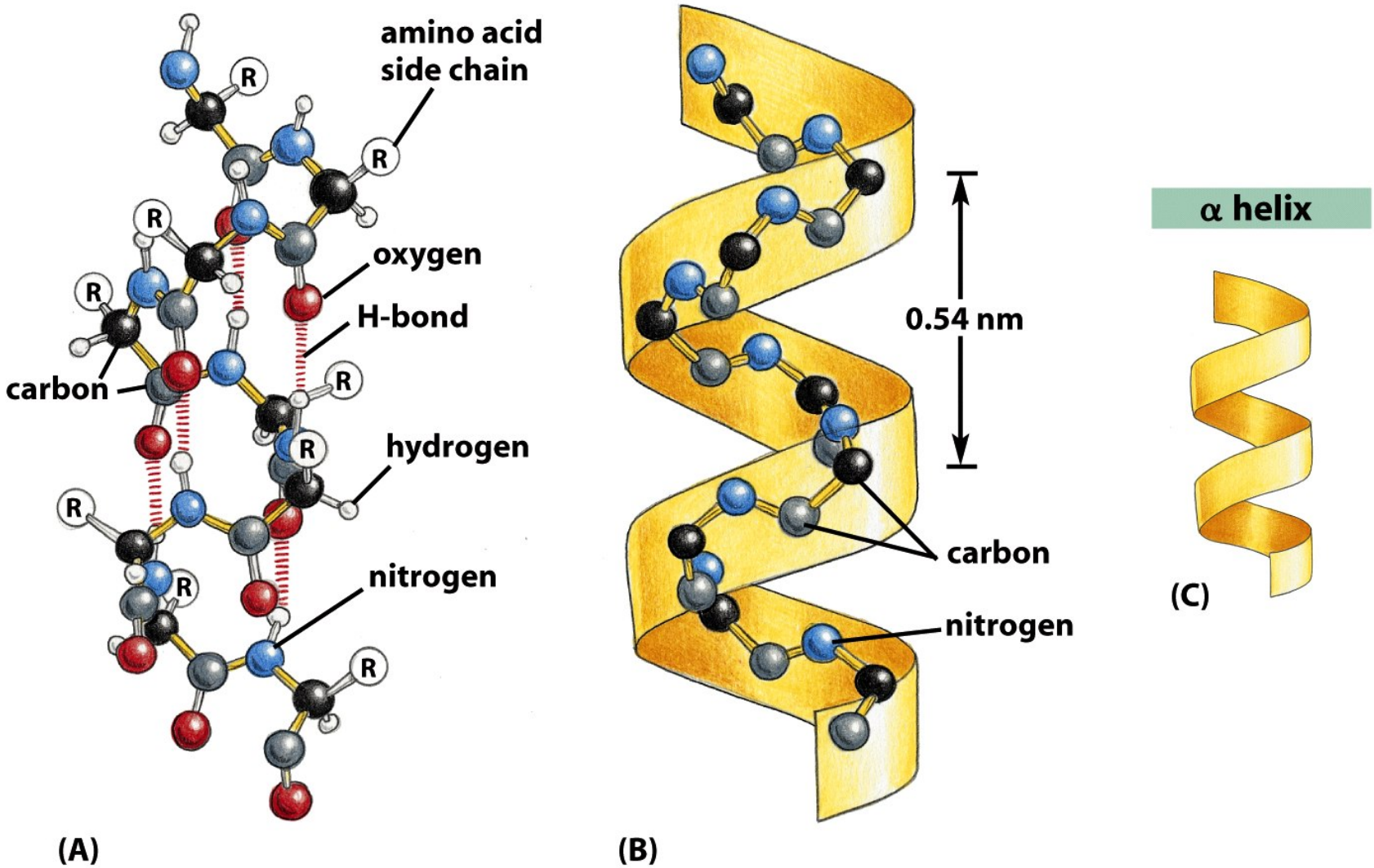


Figure 3-7a-c Molecular Biology of the Cell 5/e (© Garland Science 2008)

Four noncovalent interaction helps protein to fold

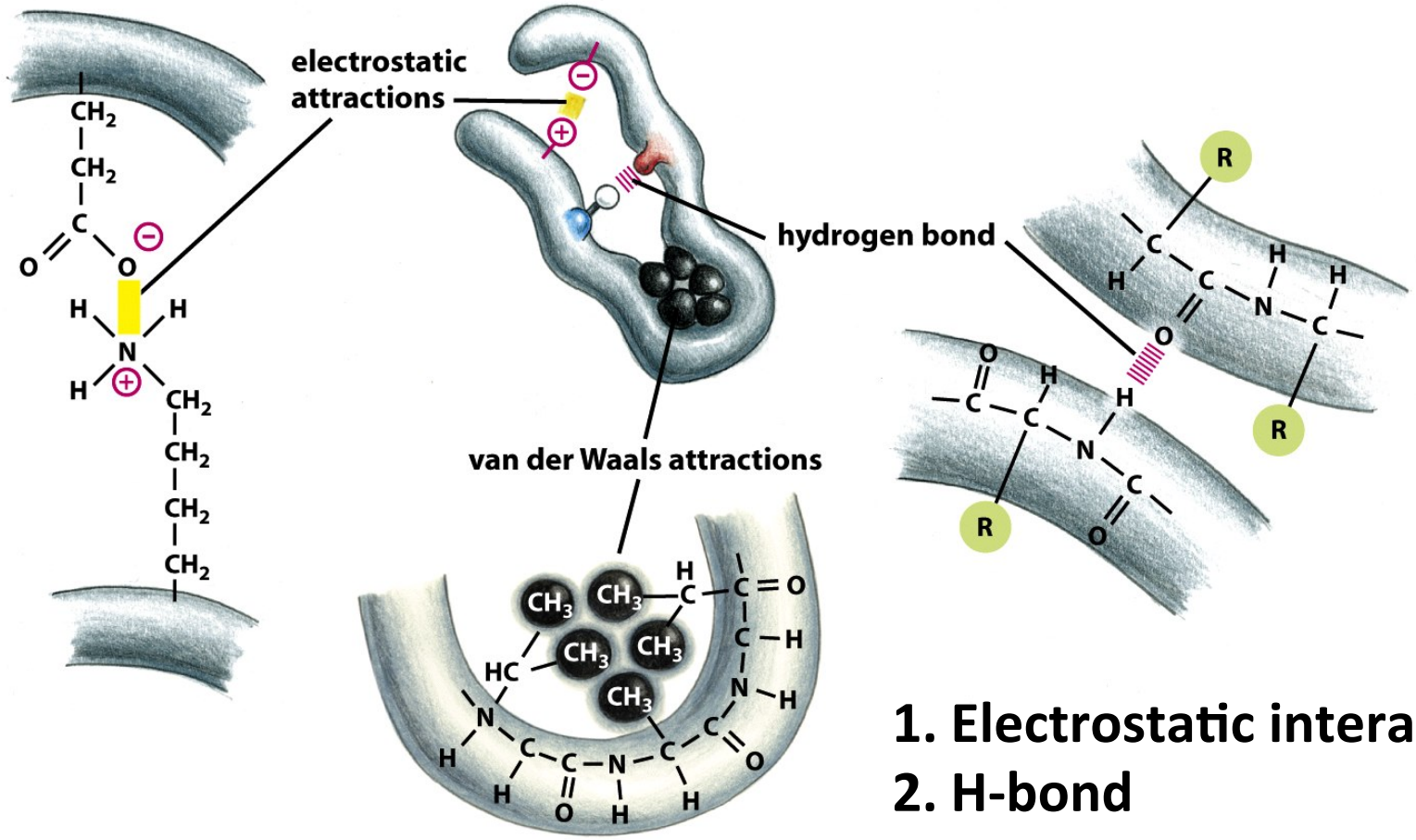
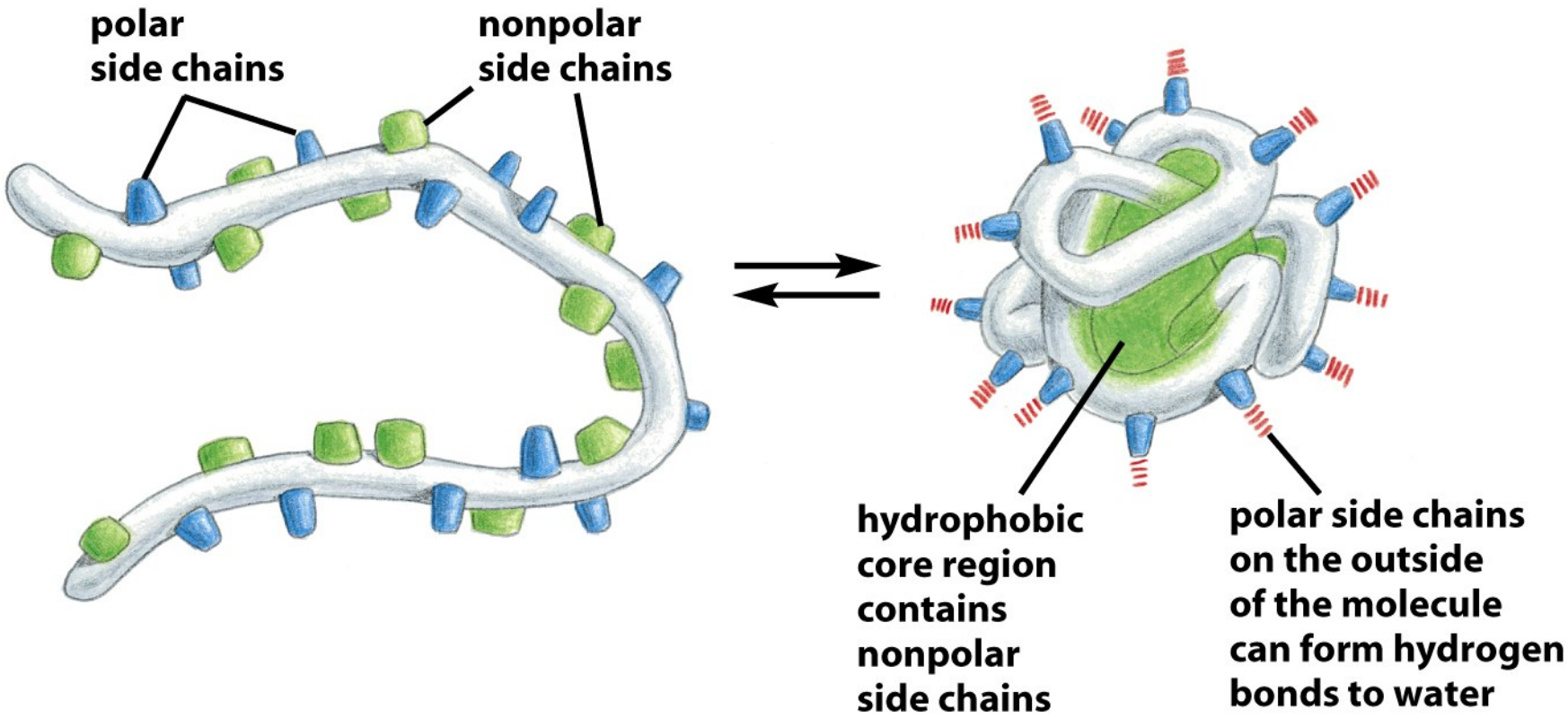


Figure 3-4 Molecular Biology of the Cell 5/e (© Garland Science 2008)

1. **Electrostatic interaction**
2. **H-bond**
3. **Van der Waals attraction**
4. **Hydrophobic interaction**

Hydrophobic interactions



unfolded polypeptide

folded conformation in aqueous environment

Figure 3-5 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Disulfide bond have a major stabilizinge ffect on protein

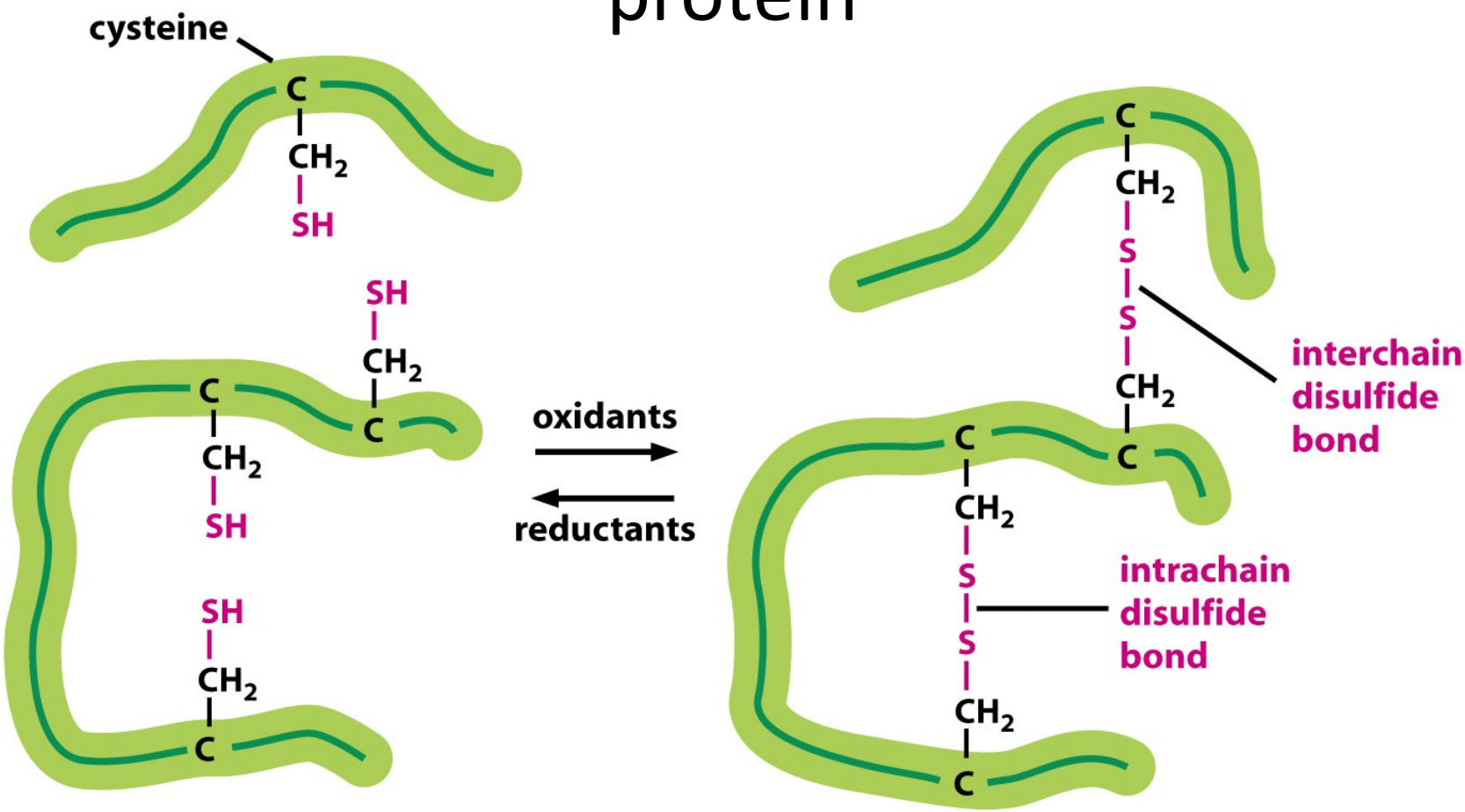


Figure 3-28 Molecular Biology of the Cell 5/e (© Garland Science 2008)

As energy required to break one covalent bond is much larger than the energy required to break even a whole set of noncovalent bonds, a disulfide bon have a major stabilizinge ffect on a protein.

Structure of a protein is important for its function

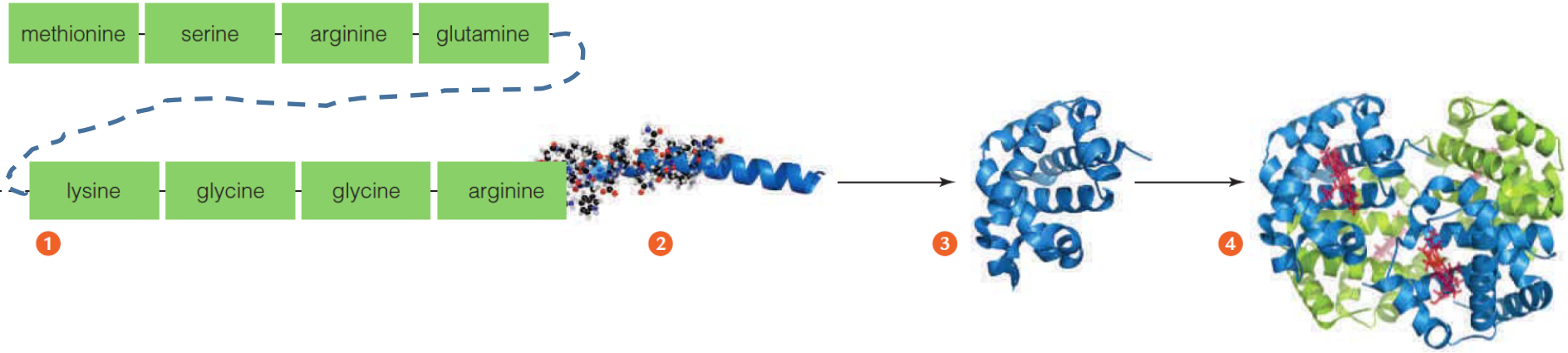


FIGURE 2.18 Animated! Protein structure.

1 A protein's primary structure consists of a linear sequence of amino acids (a polypeptide chain).

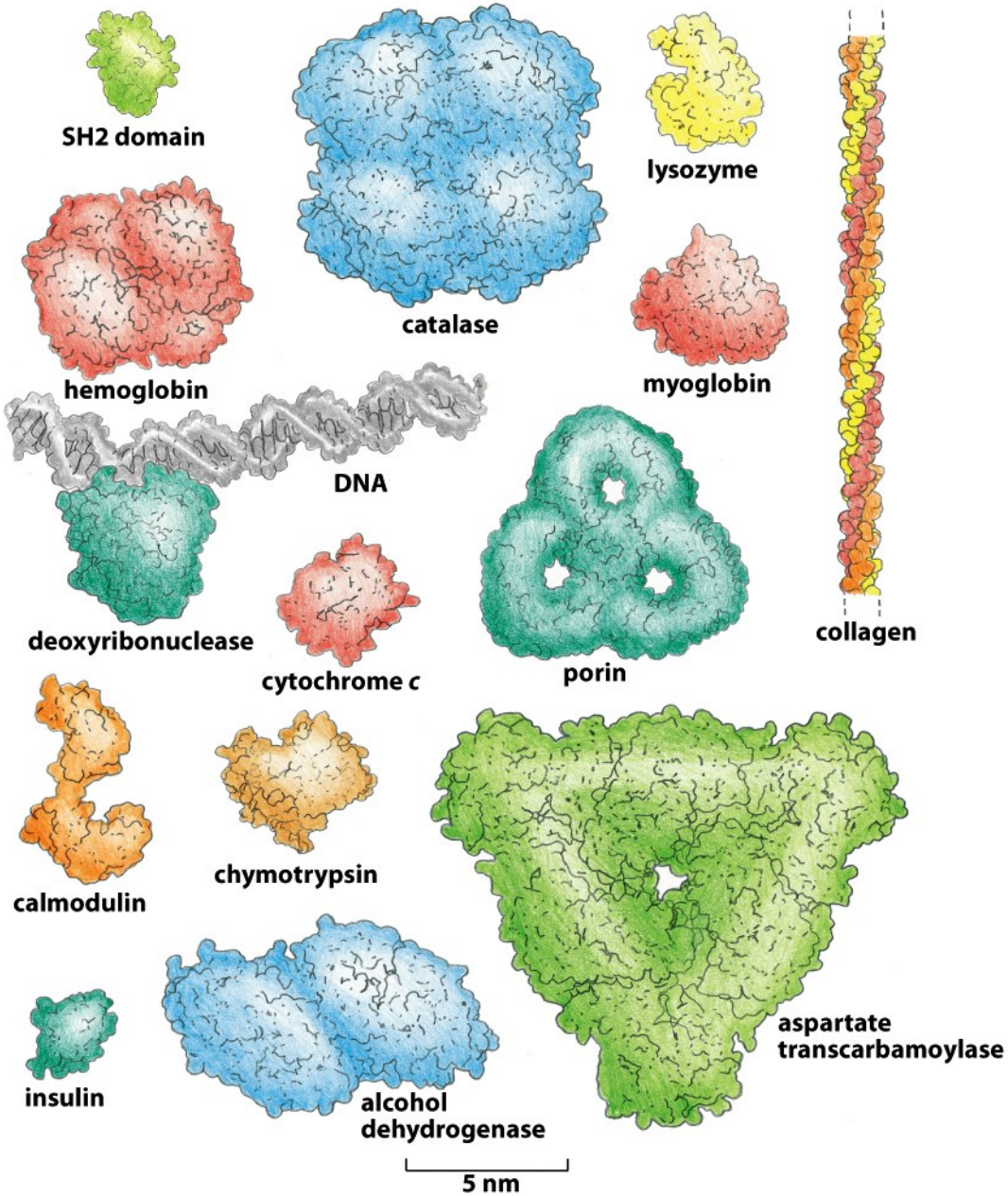
2 Secondary structure arises when a polypeptide chain twists into a coil (helix) or sheet held in place by hydrogen bonds between different parts of the molecule. The same patterns of secondary structure occur in many different proteins.

3 Tertiary structure occurs when a chain's coils and sheets fold up into a functional domain such as a barrel or pocket. In this example, the coils of a globin chain form a pocket.

4 Some proteins have quaternary structure, in which two or more polypeptide chains associate as one molecule. Hemoglobin, shown here, consists of four globin chains (*green* and *blue*). Each globin pocket now holds a heme group (*red*).

5 Many proteins aggregate by the thousands into larger structures, such as the keratin filaments that make up hair.

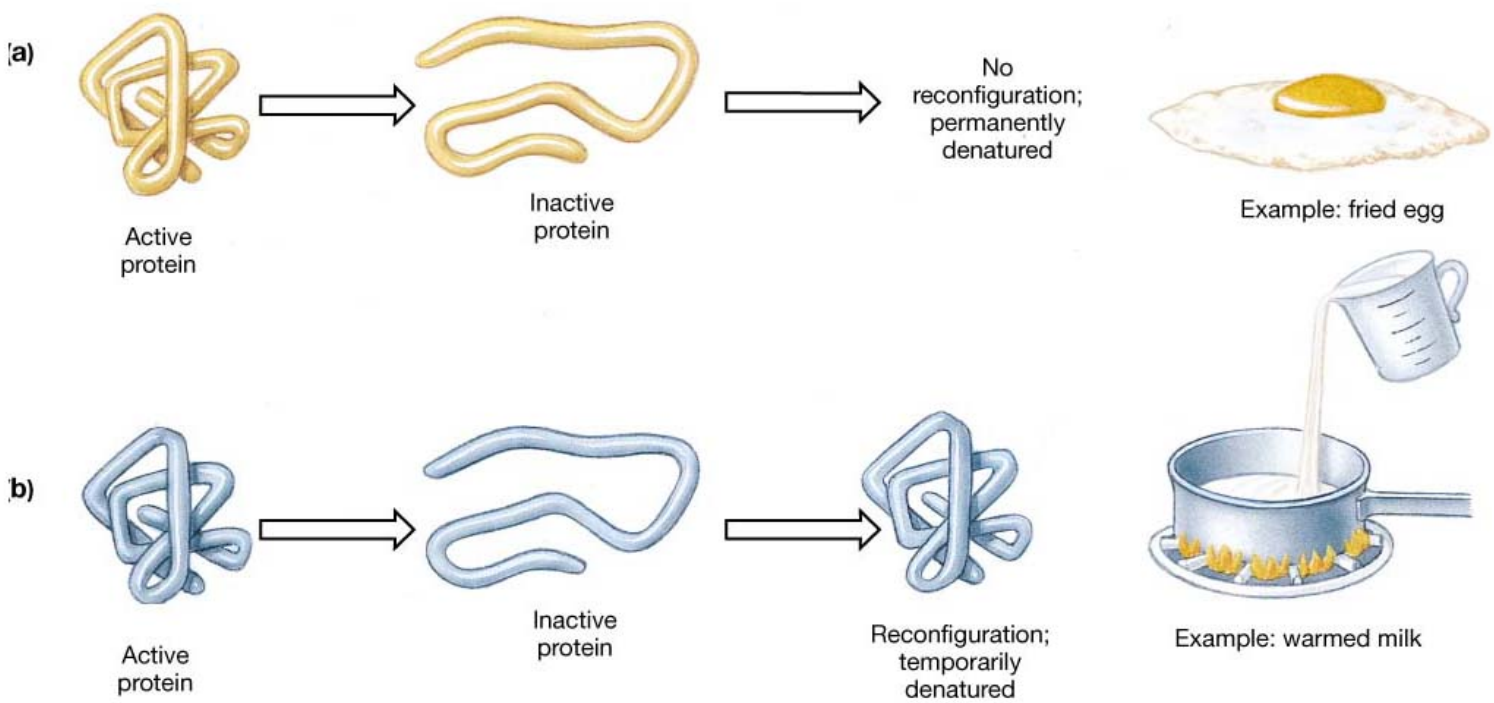
Protein can be of varied shape and size



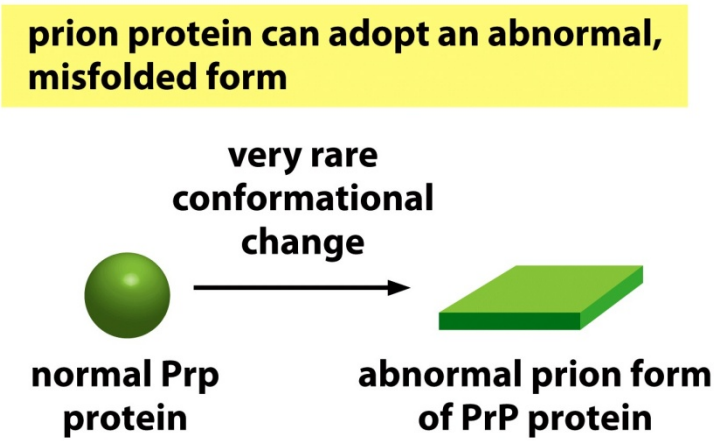
- Structural proteins support cell parts and multi celled bodies. Spider webs, feathers and hair, as well as bones and other body parts consist mainly of structural proteins.
- Foods such as seeds and eggs are nutritious in part because they are high in protein.
- Most enzymes are proteins.
- Proteins move substances, help cells communicate, and defend the body.

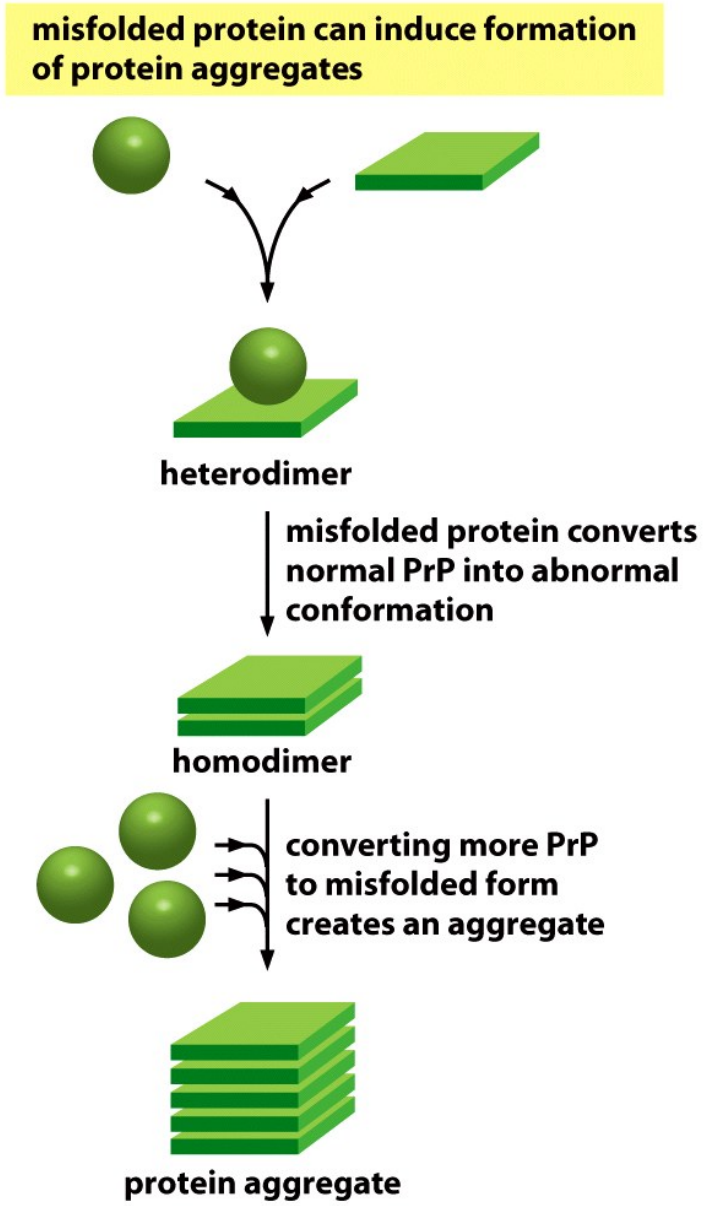
Protein denaturation

The shape depends on many hydrogen bonds and other interactions that heat, shifts in pH, or detergents can disrupt. At such times, proteins **denature**, which means they unwind and otherwise lose their three-dimensional shape. Once a protein's shape unravels, so does its function.

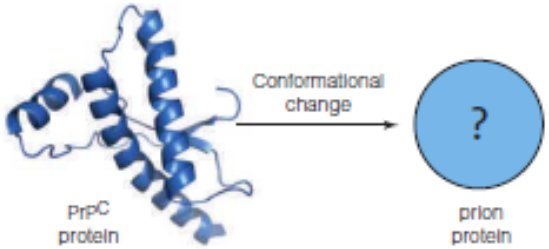


Change in protein structure can be detrimental

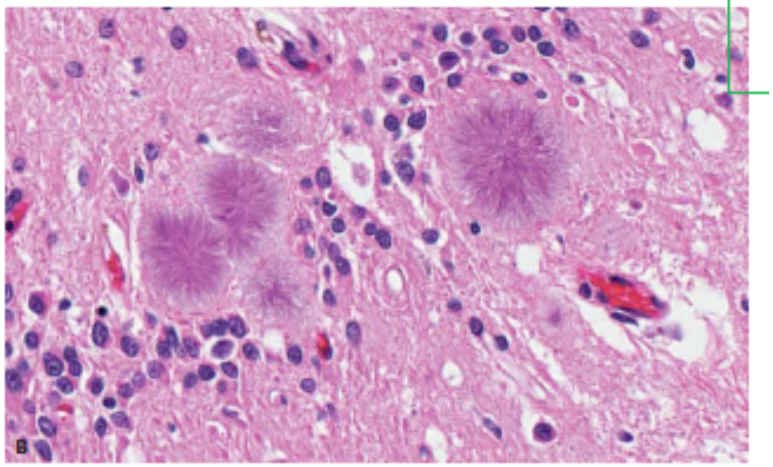




Prion disease



A



B

C

FIGURE 2.19 Variant Creutzfeldt–Jakob disease (vCJD).

A The PrP^C protein becomes a prion when it misfolds into an as-yet unknown conformation. Prions cause other PrP^C proteins to misfold, and the misfolded proteins aggregate into long fibers.

B Slice of brain tissue from a person with vCJD. Characteristic holes and prion protein fibers radiating from several deposits are visible.

C Charlene Singh, here being cared for by her mother, was one of three people who developed symptoms of the disease while living in the United States. Like the others, Singh most likely contracted the disease elsewhere; she spent her childhood in Britain. She was diagnosed in 2001, and she died in 2004.

denature To unravel the shape of a protein or other large biological molecule.

peptide bond A bond between the amine group of one amino acid and the carboxyl group of another.

polypeptide Chain of amino acids linked by peptide bonds.

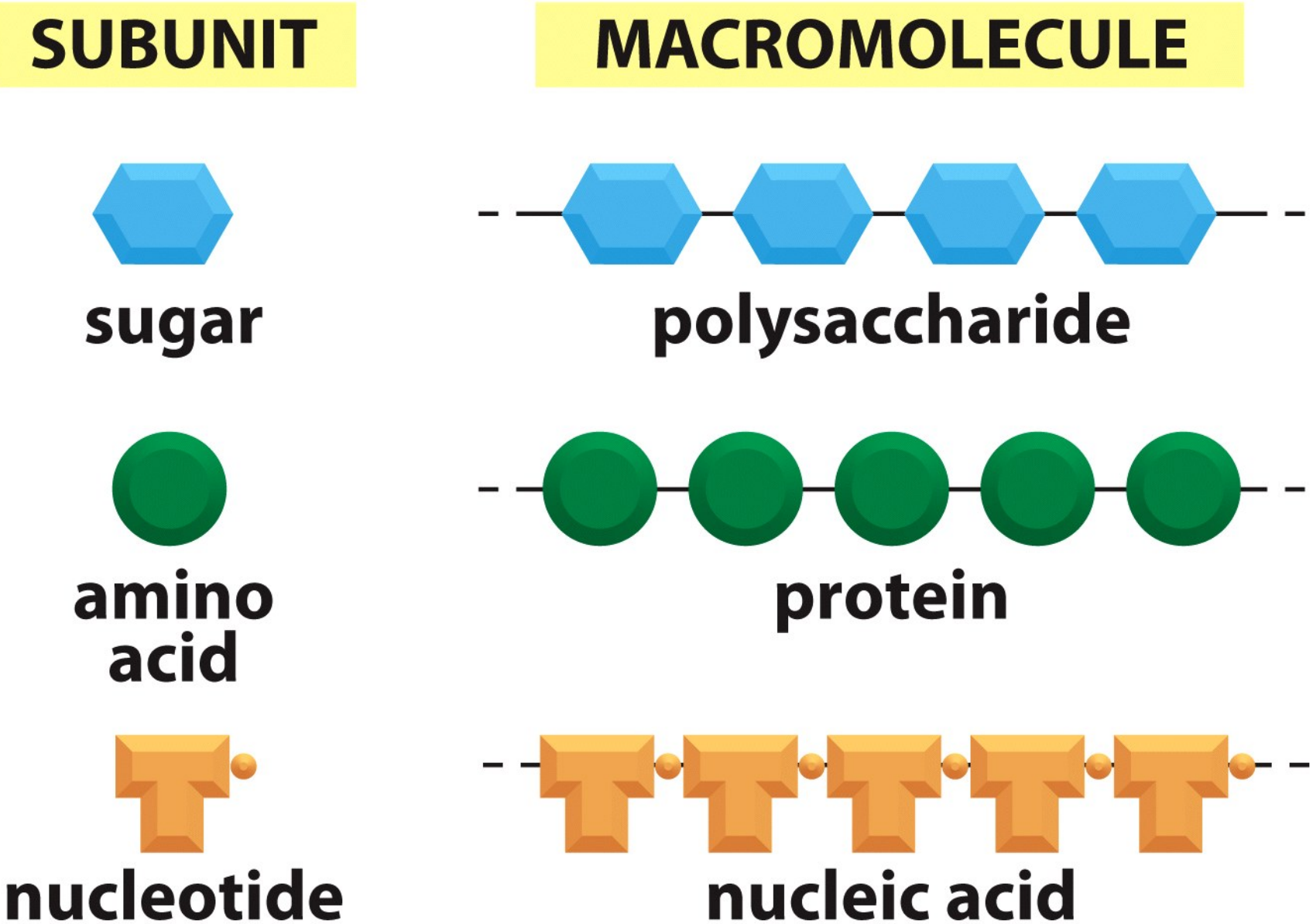


Figure 2-27 *Essential Cell Biology* (© Garland Science 2010)

Nucleotide and nucleic acids

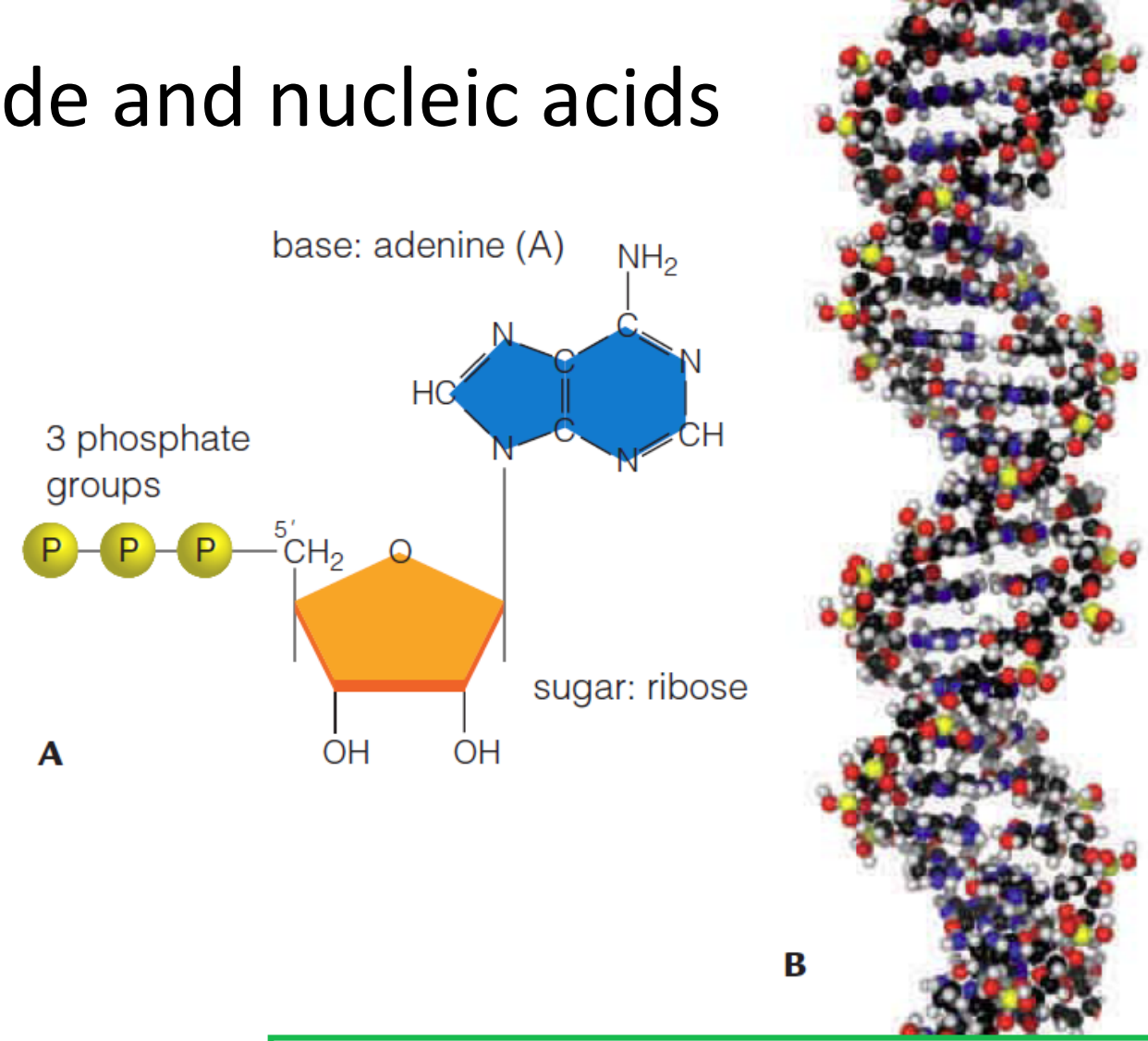
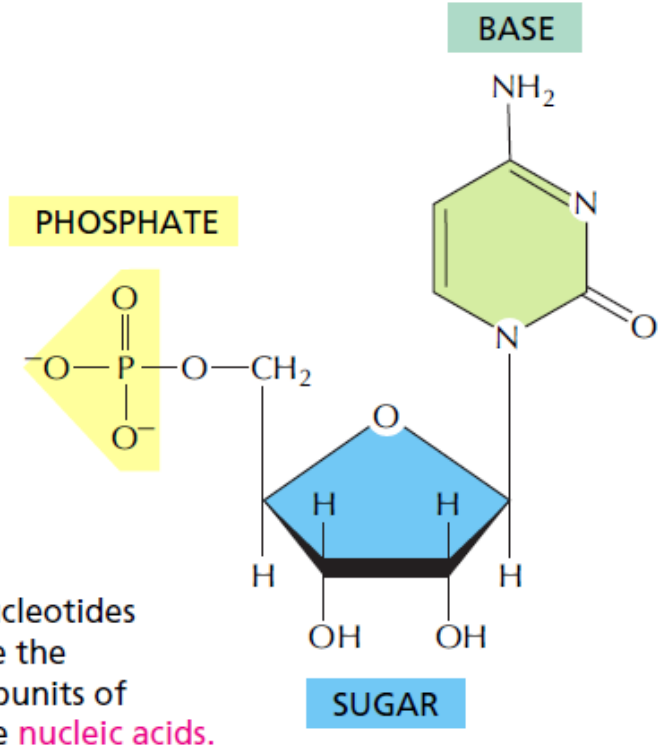


FIGURE 2.20 **Animated!** A nucleotide and a nucleic acid. **A** The nucleotide ATP. **B** DNA consists of two chains of nucleotides, twisted into a double helix held together by hydrogen bonds.

Basic structure of nucleotides

NUCLEOTIDES

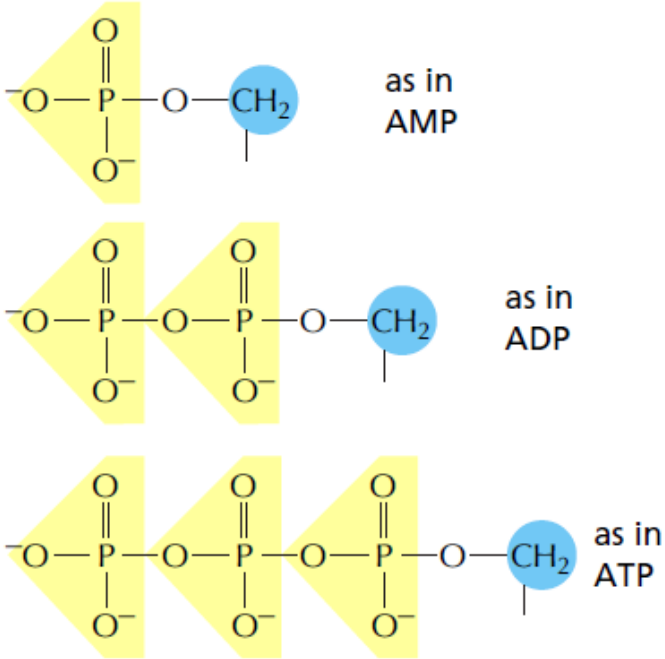
A nucleotide consists of a nitrogen-containing base, a five-carbon sugar, and one or more phosphate groups.



Nucleotides are the subunits of the nucleic acids.

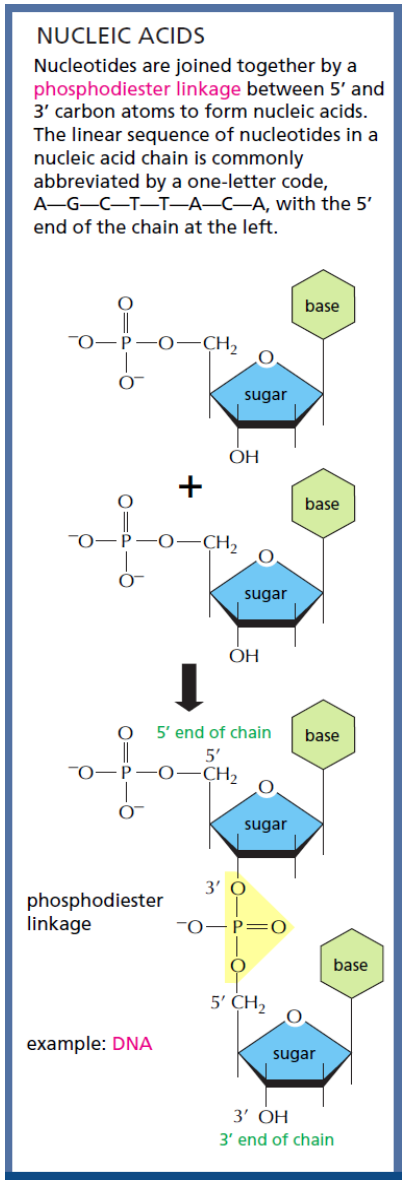
PHOSPHATES

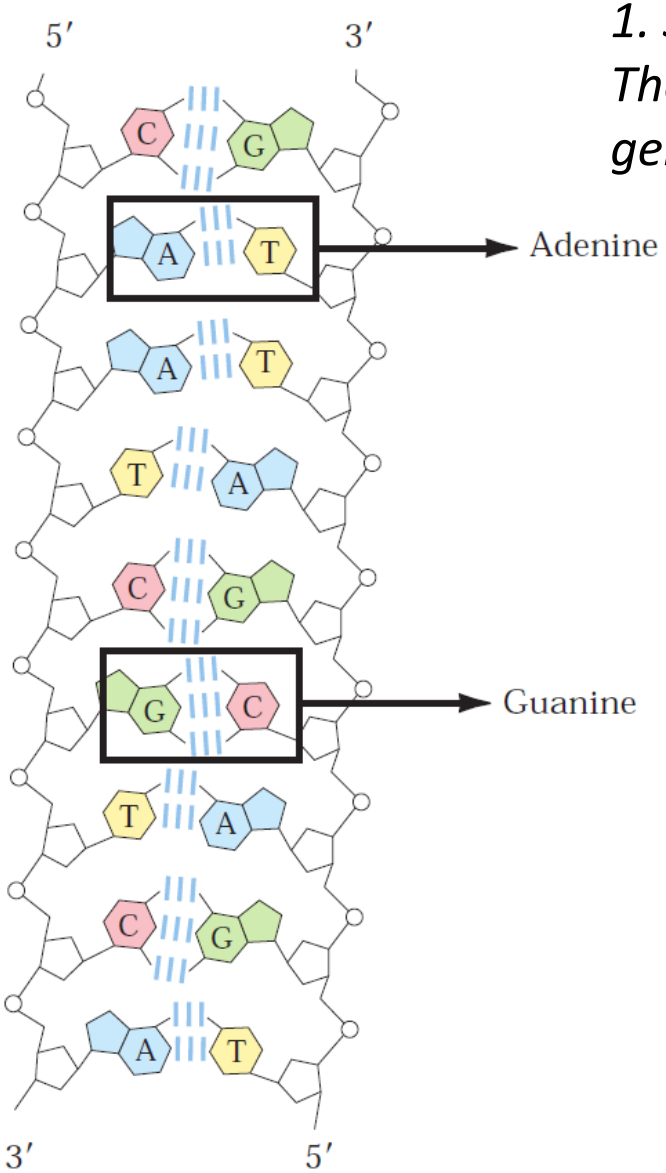
The phosphates are normally joined to the C5 hydroxyl of the ribose or deoxyribose sugar (designated 5'). Mono-, di-, and triphosphates are common.



The phosphate makes a nucleotide negatively charged.

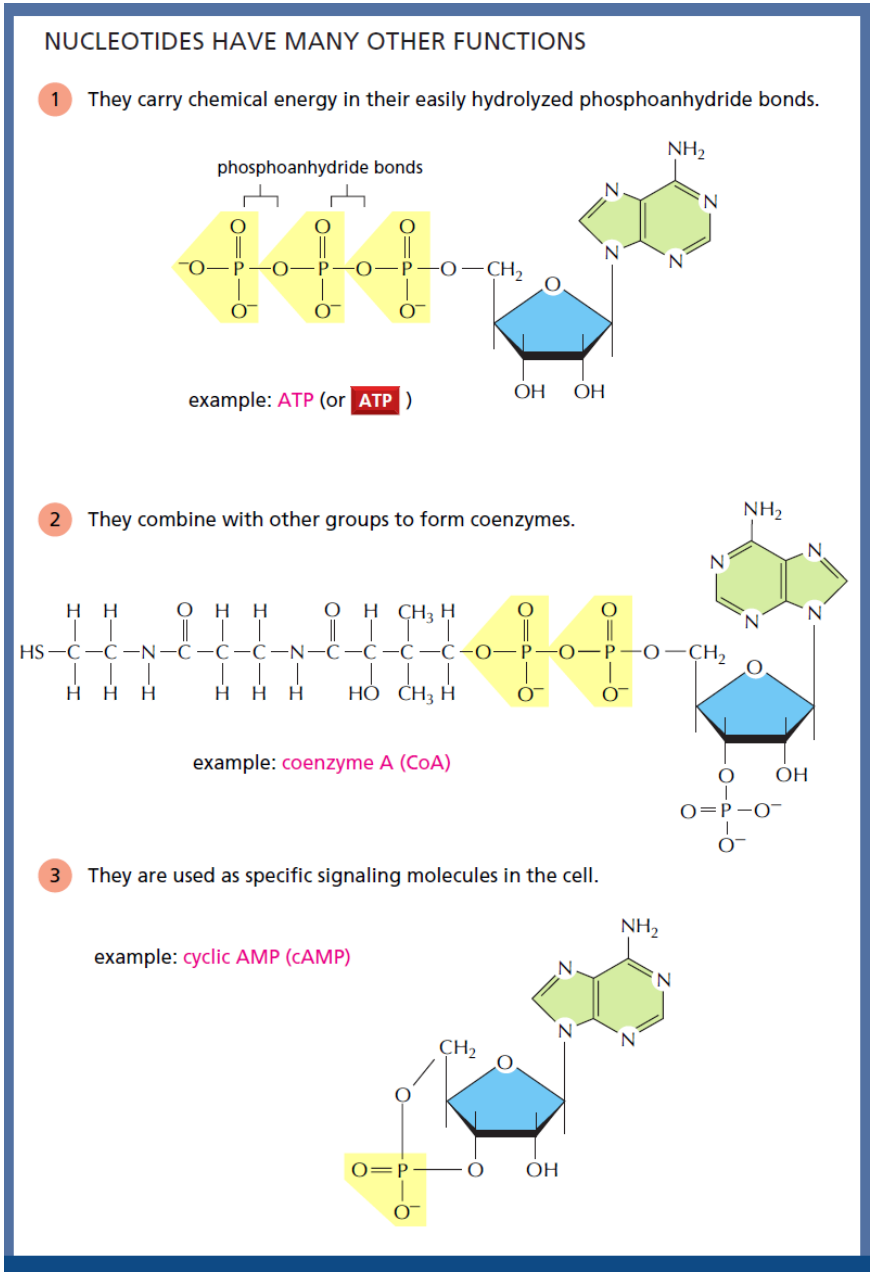
Nucleotides have diverse function





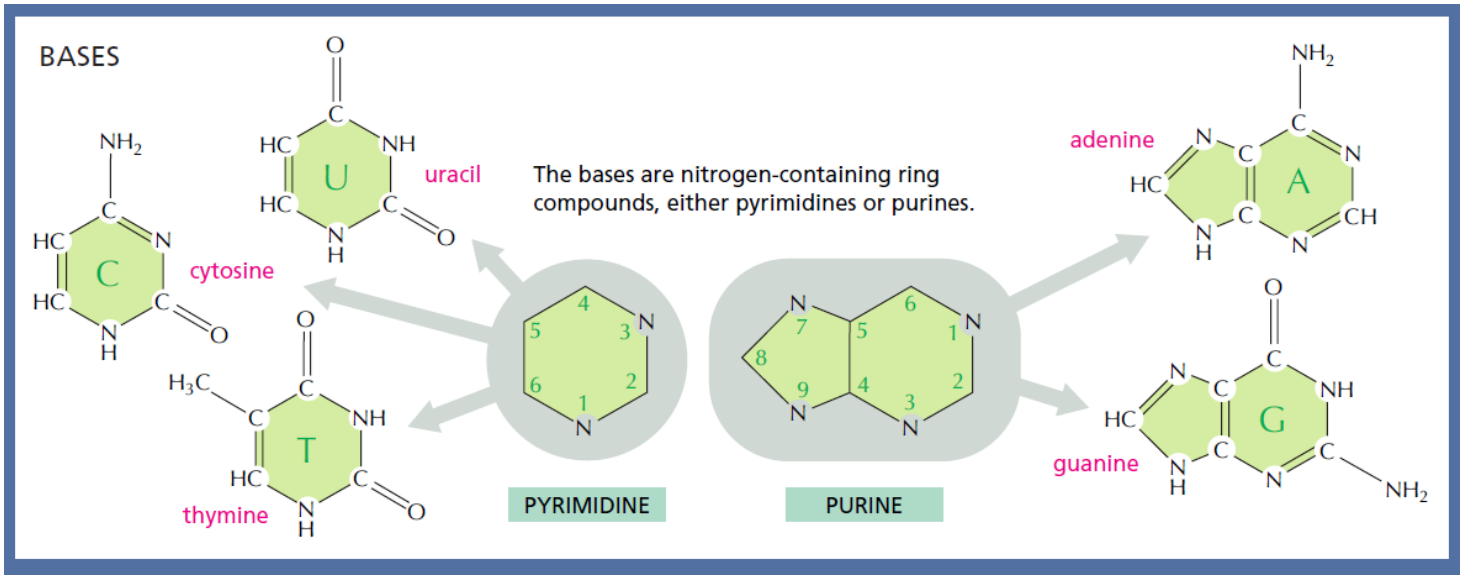
*1. Subunits of **DNA** and **RNA**. The molecular repositories of genetic information.*

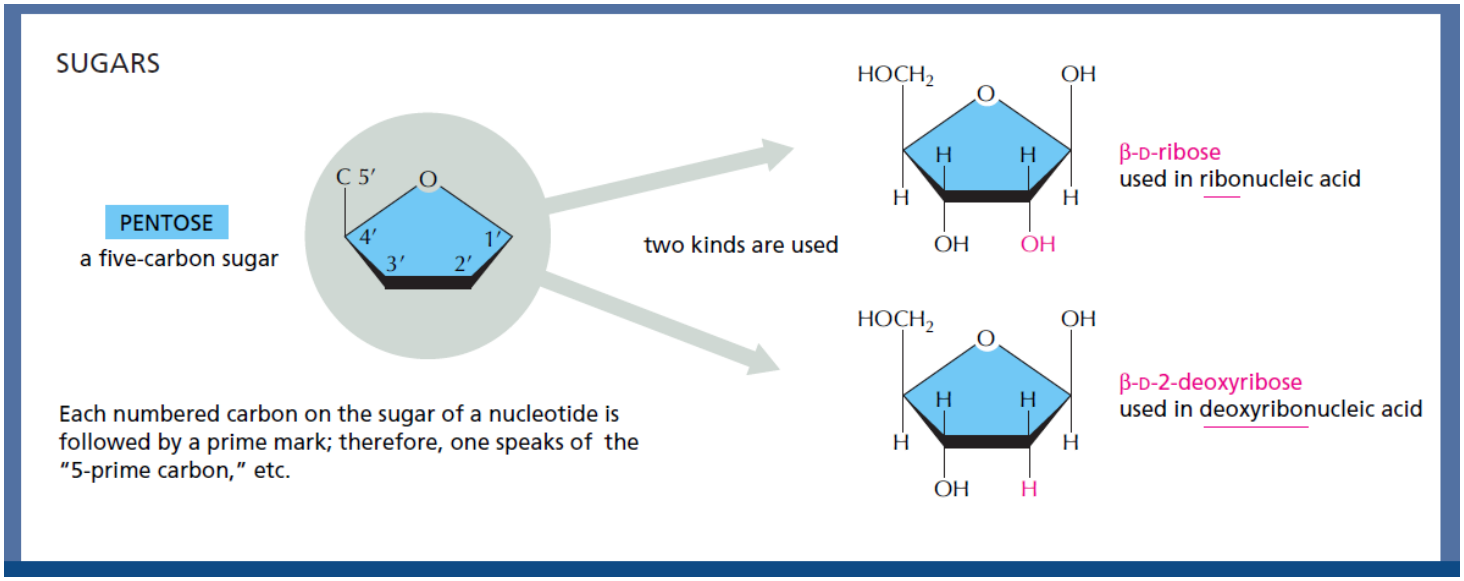
Nucleotides have diverse function



2. Energy carriers
3. Enzyme helpers
4. Chemical messengers

Types of bases and sugar in nucleotides





Nucleotide to DNA is formed by phosphodiester bond formation

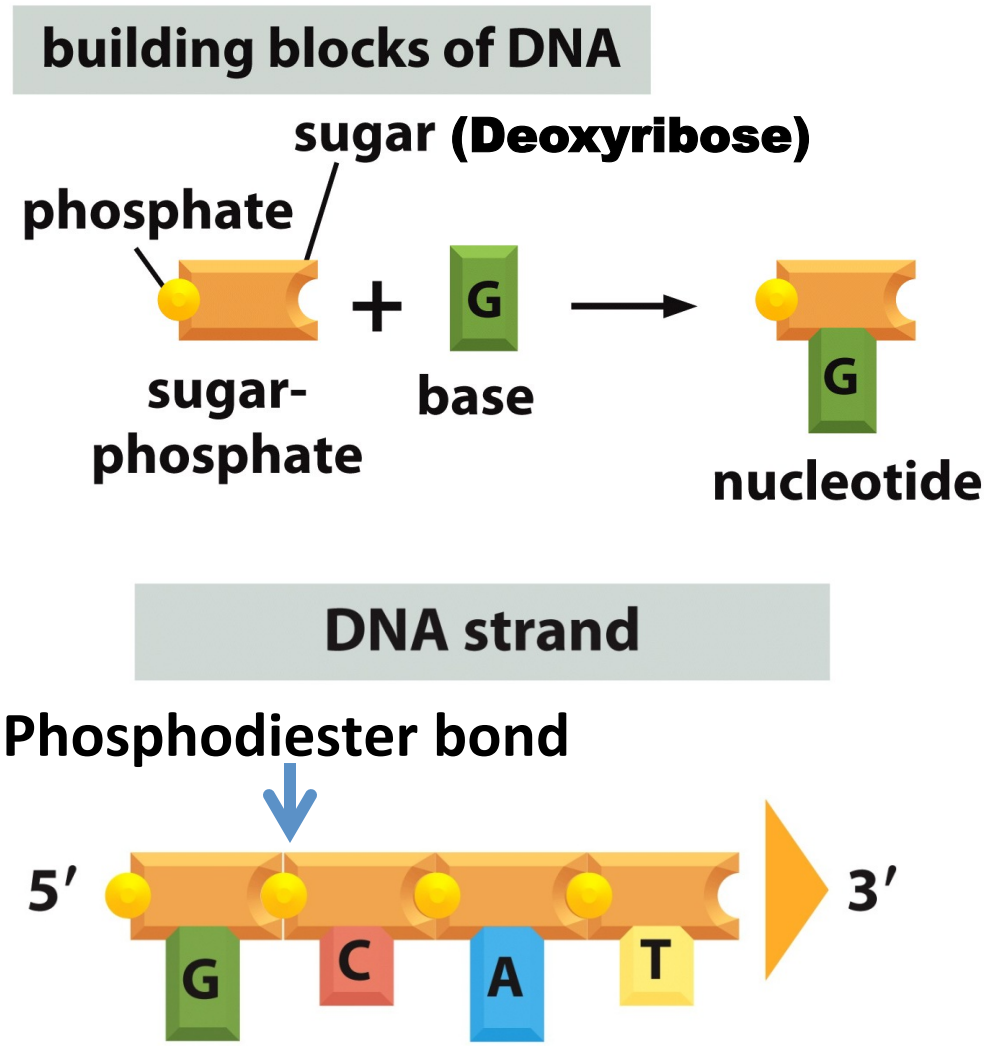


Figure 5-2a *Essential Cell Biology* (© Garland Science 2010)

Phosphodiester bond and chemical properties of nucleic acids

- The backbones of nucleic acid are hydrophilic. The hydroxyl groups of the sugar residues form hydrogen bonds with water.
- Phosphate groups are completely ionized and negatively charged at pH 7, and the negative charges are generally neutralized by ionic interactions with positive charges on proteins, metal ions, etc.

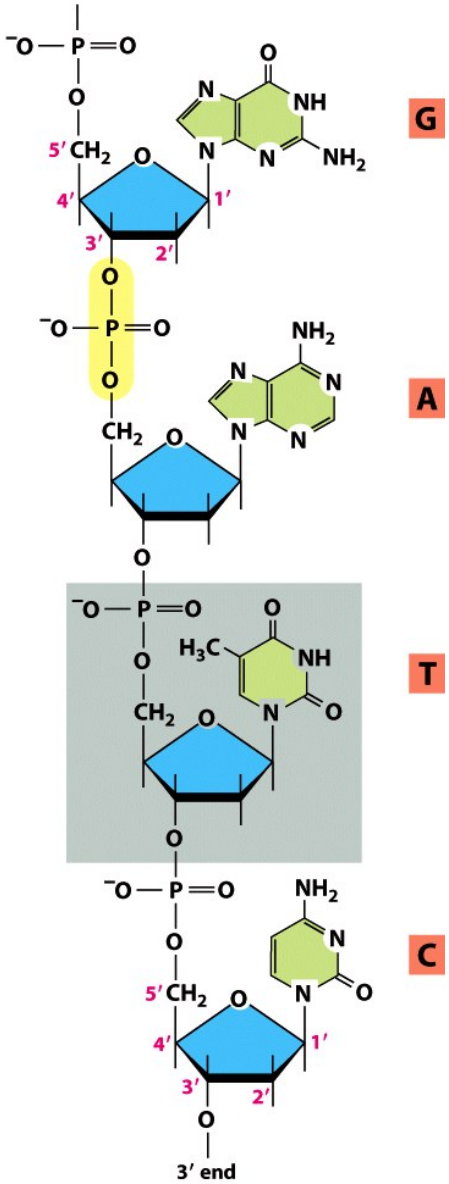
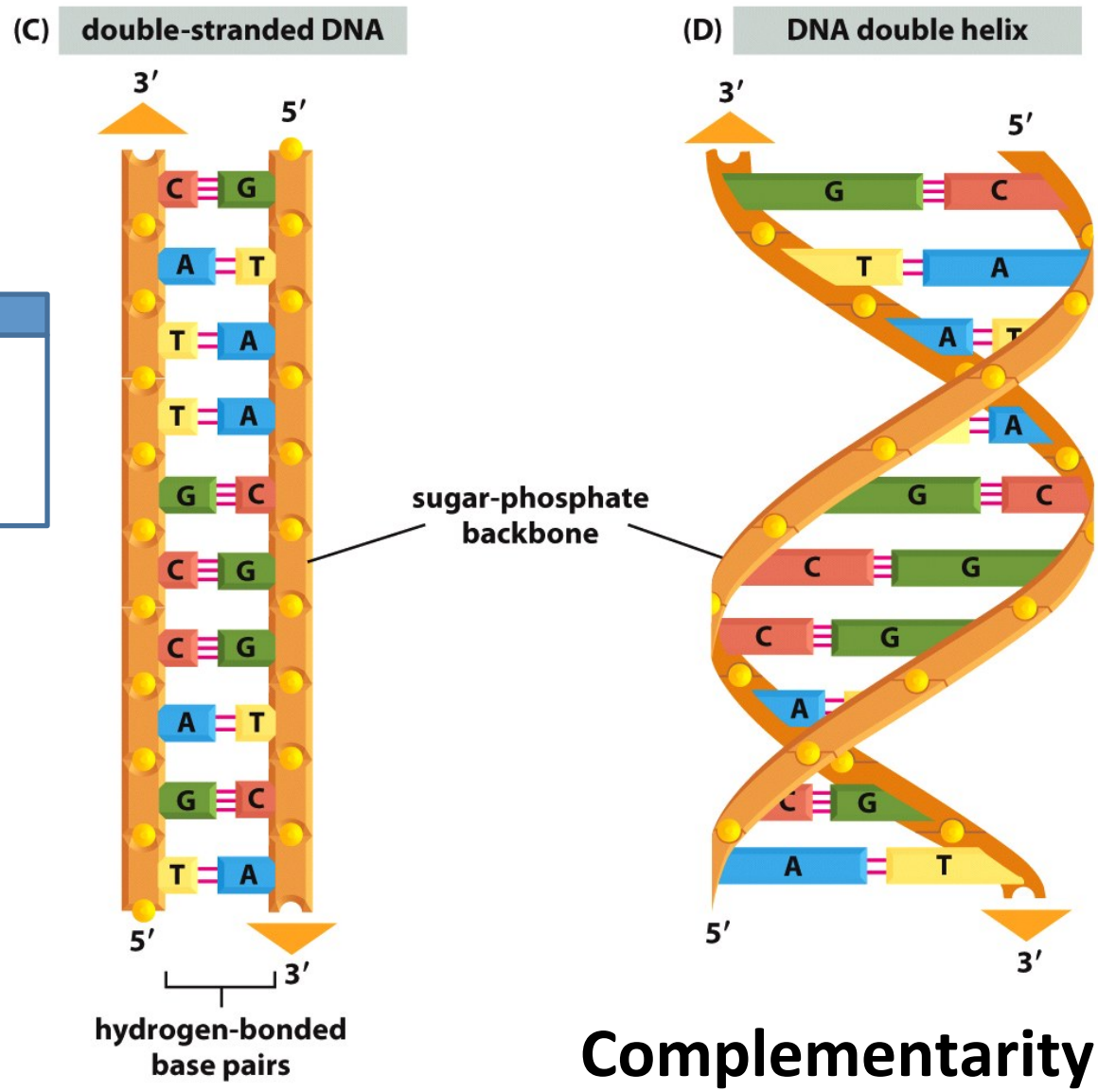


Figure 2-25 Essential Cell Biology 3/e (© Gar

Double stranded DNA and DNA double helix

4 bases in DNA

A: Adenine G: Guanine
T : Thymine C: Cytosine



Complementarity

Watson-Crick model for the structure of DNA

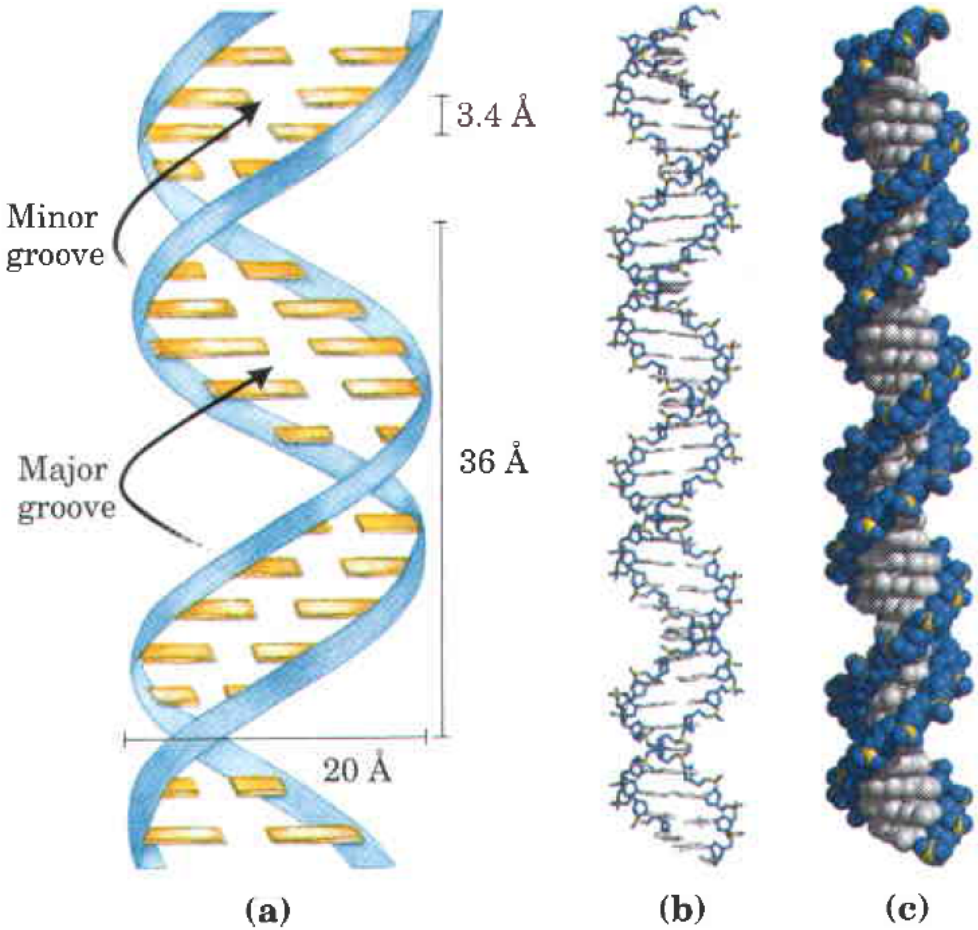


FIGURE 8–13 Watson-Crick model for the structure of DNA. The original model proposed by Watson and Crick had 10 base pairs, or 34 Å (3.4 nm), per turn of the helix; subsequent measurements revealed 10.5 base pairs, or 36 Å (3.6 nm), per turn. **(a)** Schematic representation, showing dimensions of the helix. **(b)** Stick representation showing the backbone and stacking of the bases. **(c)** Space-filling model.

James Watson

Francis Crick

Rosalind Franklin, 1920–1958

Maurice Wilkins

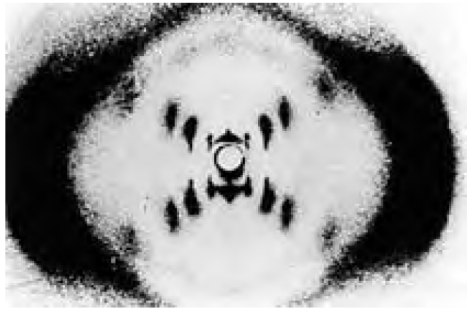
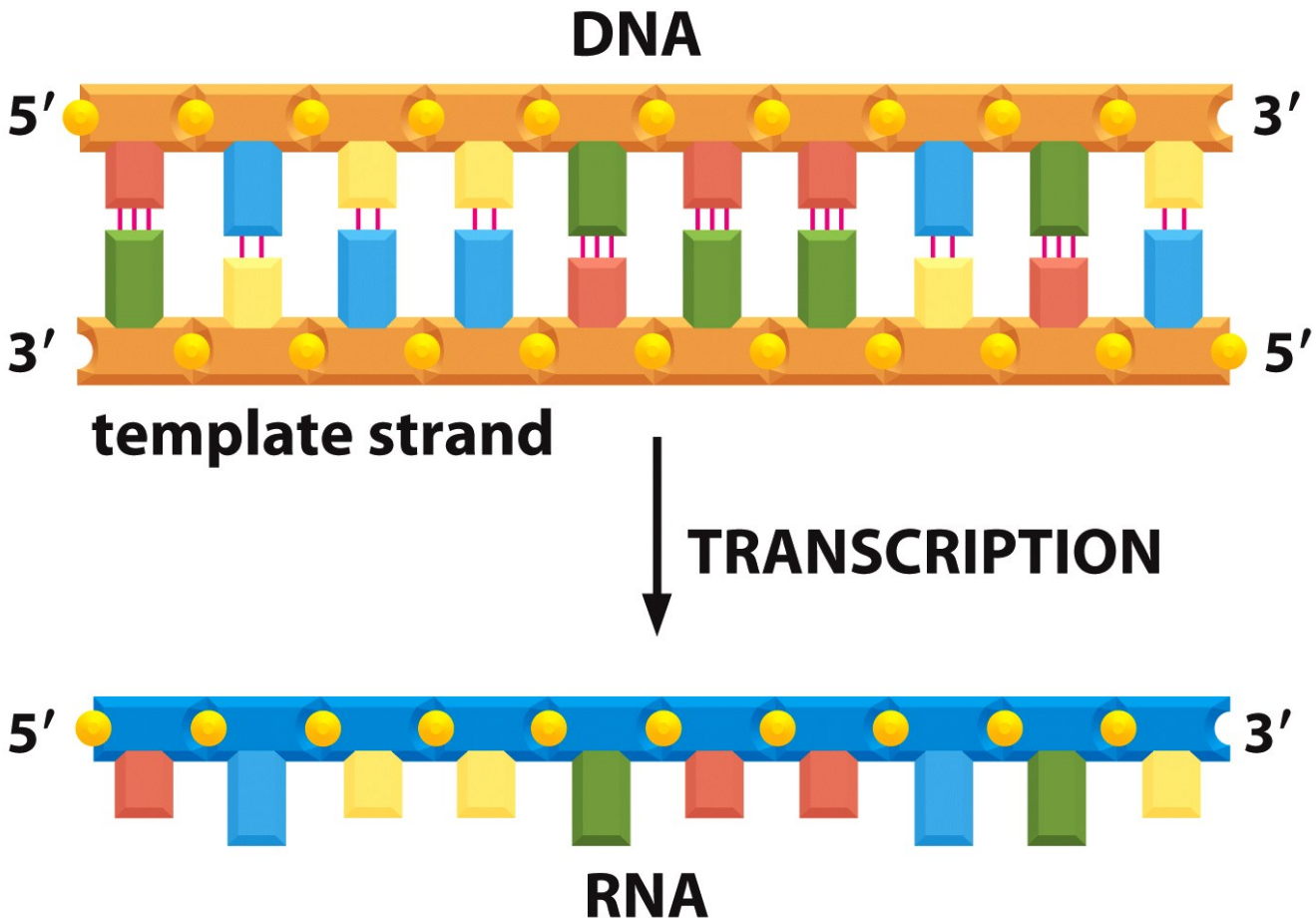


FIGURE 8–14 X-ray diffraction pattern of DNA. The spots forming a cross in the center denote a helical structure. The heavy bands at the left and right arise from the recurring bases.

Ribonucleic acid (RNA)

- Single stranded
- Ribose sugar instead of deoxyribose
- U: Uracil instead of T



ATP Nucleotide that consists of an adenine base, five-carbon ribose sugar, and three phosphate groups. Also functions as an energy carrier.

DNA Nucleic acid that carries hereditary material; consists of two nucleotide chains twisted in a double helix.

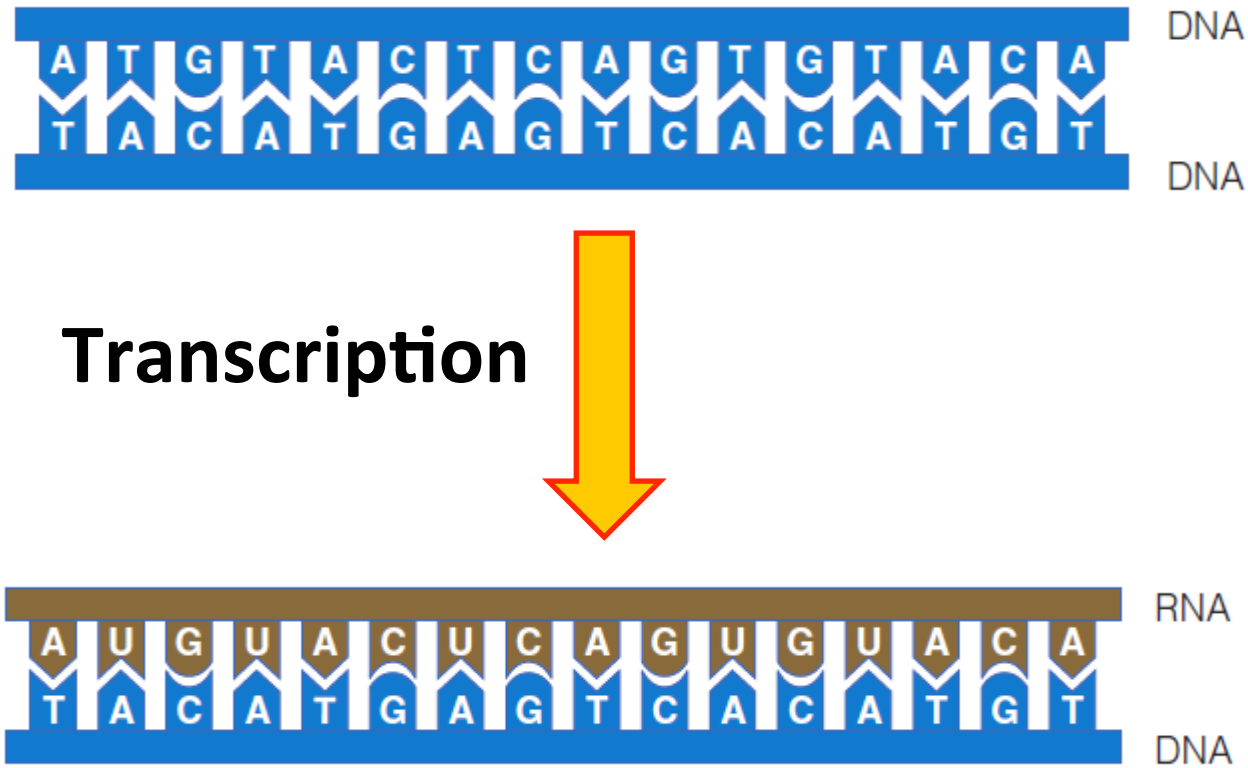
nucleic acid Chain of nucleotides joined by sugar–phosphate bonds.

nucleotide Monomer of nucleic acids; has five-carbon sugar, nitrogen-containing base, and phosphate groups.

prion Infectious protein.

RNA Typically single-stranded nucleic acid; roles in protein synthesis.

DNA to RNA: Transcription



Same base pairing complementarity is maintained except U is incorporated in place of T.