

# 5 The Structure and Function of Large Biological Molecules

## KEY CONCEPTS

- 5.1** Macromolecules are polymers, built from monomers *p. 67*
- 5.2** Carbohydrates serve as fuel and building material *p. 68*
- 5.3** Lipids are a diverse group of hydrophobic molecules *p. 72*
- 5.4** Proteins include a diversity of structures, resulting in a wide range of functions *p. 75*
- 5.5** Nucleic acids store, transmit, and help express hereditary information *p. 84*
- 5.6** Genomics and proteomics have transformed biological inquiry and applications *p. 86*

## Study Tip

**Make a visual study guide:** For each class of biological molecules, draw two examples and list their structural similarities and their functions.

Important Biological Molecules	
Carbohydrates	Proteins
Nucleic acids	Lipids

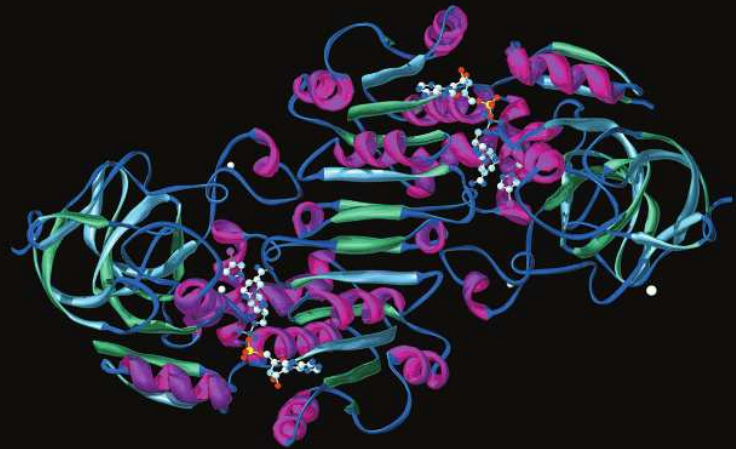
## → Go to Mastering Biology

**For Students** (in eText and Study Area)

- Animation: Making and Breaking Polymers
- Figure 5.11 Walkthrough: The Structure of a Phospholipid
- BioFlix® Animation: Gene Expression

**For Instructors to Assign** (in Item Library)

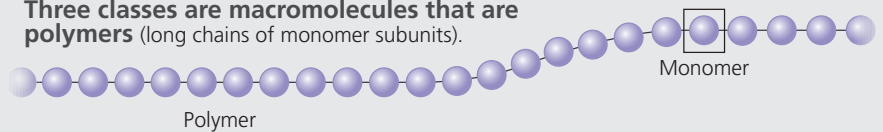
- Molecular Model: Lysozyme
- Tutorial: Nucleic Acid Structure



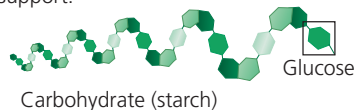
**Figure 5.1** Alcohol dehydrogenase, a protein that breaks down alcohol in the body, is shown here as a molecular model. The form of this protein that an individual possesses affects how well that person tolerates drinking alcohol. Proteins are one class of large molecules, or macromolecules.

## What are the structures and functions of the four important classes of biological molecules?

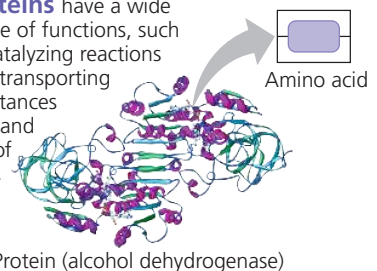
Three classes are macromolecules that are **polymers** (long chains of monomer subunits).



**Carbohydrates** are a source of energy and provide structural support.

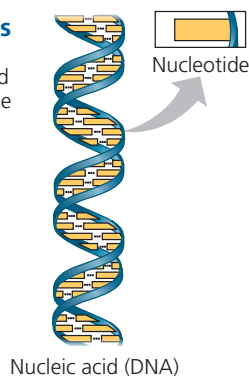


**Proteins** have a wide range of functions, such as catalyzing reactions and transporting substances into and out of cells.



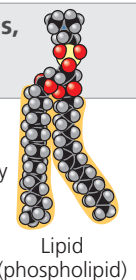
**Nucleic acids**

store genetic information and function in gene expression.



The fourth class, **lipids**, are not polymers or macromolecules.

**Lipids** are a group of diverse molecules that do not mix well with water. Key functions include providing energy, making up cell membranes, and acting as hormones.



## CONCEPT 5.1

# Macromolecules are polymers, built from monomers

Large carbohydrates, proteins, and nucleic acids, also known as **macromolecules** for their **huge size**, are **chain-like molecules** called **polymers** from the Greek *polys* (many) and *meros* (part). A **polymer** is a long molecule consisting of many similar or identical building blocks linked by covalent bonds, much as a train consists of a chain of boxcars. **The repeating units that serve as the building blocks of a polymer are smaller molecules called monomers** from the Greek *monos* (single). In addition to forming polymers, some monomers have functions of their own.

## The Synthesis and Breakdown of Polymers

Although each class of polymer is made up of a different type of monomer, the **chemical mechanisms** by which cells make **polymers (polymerization)** and break them down are similar for all classes of large biological molecules. In cells, these processes are facilitated by **enzymes**, specialized macromolecules (usually proteins) that speed up chemical reactions. The reaction that connects a monomer to another monomer or a polymer is a

**condensation reaction**, a reaction in which two molecules are covalently bonded to each other with the loss of a small molecule. If a water molecule is lost, it is known as a **dehydration reaction**.

For example, carbohydrate and protein polymers are synthesized by dehydration reactions. Each reactant contributes part of the water molecule that is released during the reaction: One provides a hydroxyl group ( $\text{—OH}$ ), while the other provides a hydrogen ( $\text{—H}$ ) (Figure 5.2a). This reaction is repeated as monomers are added to the chain one by one, lengthening the polymer.

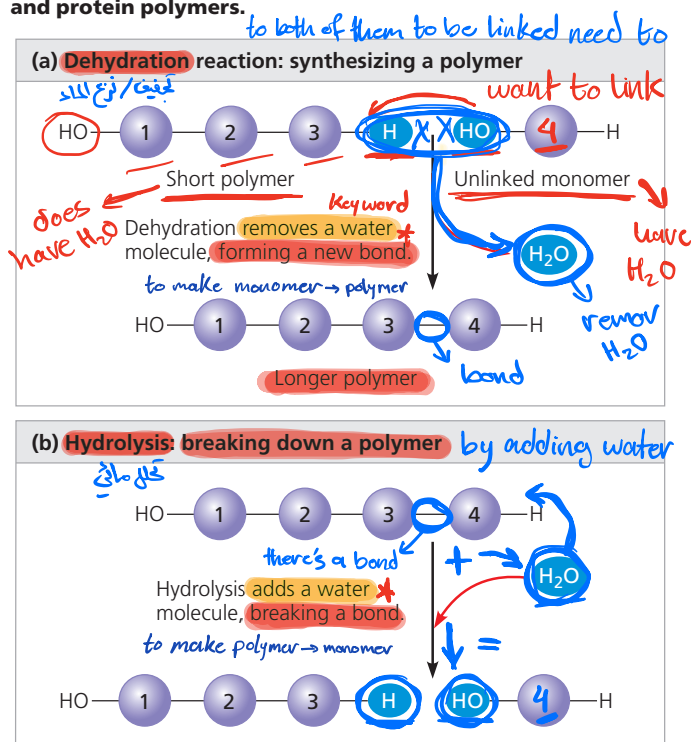
Polymers are disassembled to monomers by **hydrolysis**, a process that is essentially the reverse of the dehydration reaction

(Figure 5.2b). Hydrolysis means water breakage (from the Greek *hydro*, water, and *lysis*, break). The bond between monomers is broken by the addition of a water molecule, with a hydrogen from water attaching to one monomer and the hydroxyl group attaching to the other. An example of hydrolysis within our bodies is the process of digestion. The bulk of the organic material in our food is in the form of polymers that are much too large to enter our cells. Within the digestive tract, various enzymes attack the polymers, speeding up hydrolysis. Released monomers are then absorbed into the bloodstream for distribution to all body cells. Those cells can then use dehydration reactions to assemble the monomers into new, different polymers that can perform specific functions required by the cell. (Dehydration reactions and hydrolysis can also be involved in the formation and breakdown of molecules that are not polymers, such as some lipids.)

## The Diversity of Polymers

A cell has thousands of different macromolecules; the collection varies from one type of cell to another. The inherited

▼ Figure 5.2 The synthesis and breakdown of carbohydrate and protein polymers.

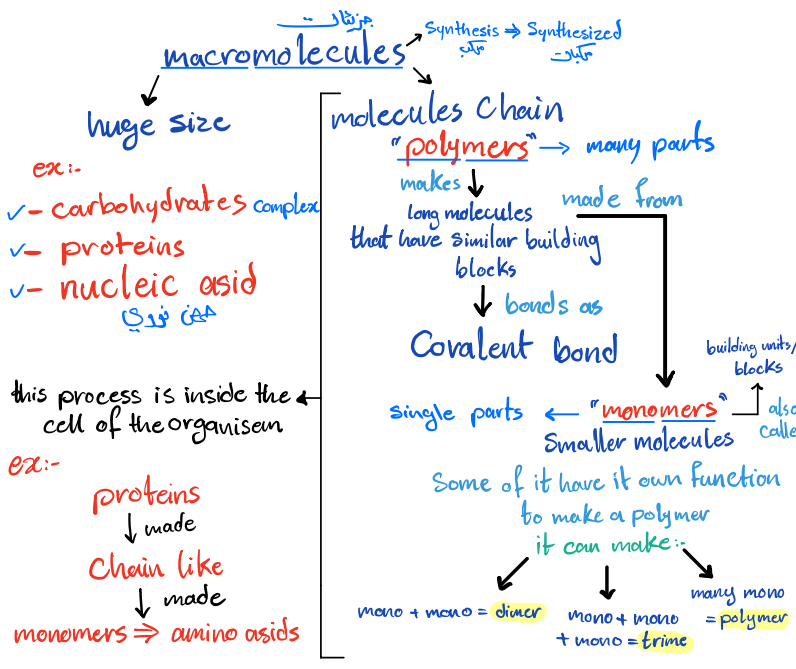


### Mastering Biology Animation: Making and Breaking Polymers

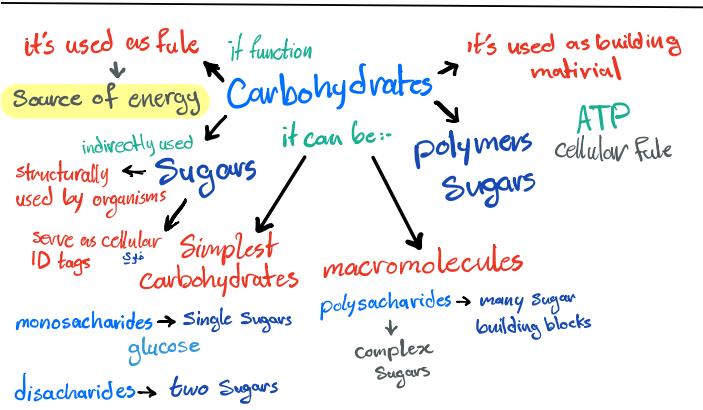
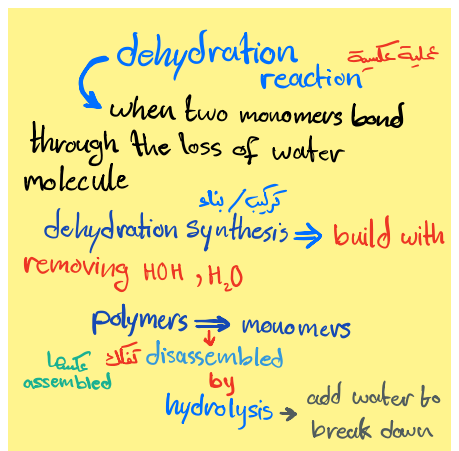
differences between close relatives, such as human siblings, reflect small variations in polymers, particularly DNA and proteins. Molecular differences between unrelated individuals are more extensive, and those between species greater still. The diversity of macromolecules in the living world is vast, and the possible variety is effectively limitless.

What is the basis for such diversity in life's polymers? These molecules are constructed from only 40 to 50 common monomers and some others that occur rarely. Building a huge variety of polymers from such a limited number of monomers is analogous to constructing hundreds of thousands of words from only 26 letters of the alphabet. The key is arrangement—the particular linear sequence that the units follow. However, this analogy falls far short of describing the great diversity of macromolecules because most biological polymers have many more monomers than the number of letters in even the longest word. Proteins, for example, are built from 20 kinds of amino acids arranged in chains that are typically hundreds of amino acids long. The molecular logic of life is simple but elegant: Small molecules common to all organisms act as building blocks that are ordered into unique macromolecules.

Despite this immense diversity, molecular structure and function can still be grouped roughly by class. Let's examine each of the four major classes of large biological molecules. For each class, the large molecules have emergent properties not found in their individual components.



\* macromolecule can be identical  
 ex:- glucose + glucose = identical  
 or  
 ex :- amino acid + amino acid = similar  
 \* Lipids are large molecules but it's not polymers



**monosaccharides**  $\rightarrow$  it's classified by carbonyl location as **aldose or ketose**

it molecular form usually come from multiples  $\text{CH}_2\text{O}$  and by carbons numbers in carbon skeleton

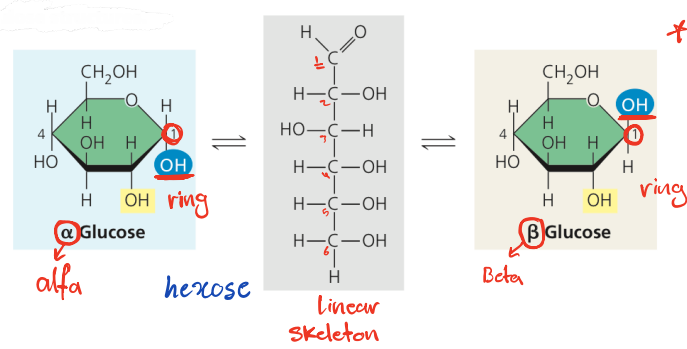
the most common monosaccharides  $\rightarrow$  **glucose**

it form  $\text{C}_6\text{H}_{12}\text{O}_6$

\* we should know that when we say sugars it should ends with **ose**

the formula of  $\text{CH}_2\text{O}$  is  $(\text{CH}_2\text{O})^n$  ex the  $n=3$

$\therefore \text{C}_3\text{H}_6\text{O}_3$



\* although sometimes sugars it's drawn as a skeleton linear but in aqueous solution it may form as a rings.

**disaccharide**

formed when dehydration reaction join two monosaccharide that will remove  $\text{HOH}, \text{H}_2\text{O}$  to form a covalent bond

it's called **glycosidic linkage**

$\therefore \text{C}_6\text{H}_{12}\text{O}_6 + \text{C}_6\text{H}_{12}\text{O}_6 = \text{C}_{12}\text{H}_{22}\text{O}_{11}$

$\rightarrow$  a  $\text{H}_2\text{O}$  molecule was removed

important thing to know:-

the processes that happens in the cell are facilitated by **enzymes** (الإنزيمات)

the reaction that connect two monomer or a monomer & polymer is **Condensation reaction** (عملية التكثيف)



**CONCEPT CHECK 5.1**

1. What are the four main classes of large biological molecules? Which class does not consist of polymers?
2. How many molecules of water are needed to completely hydrolyze a polymer that is ten monomers long?
3. **WHAT IF?** If you eat a piece of fish, what reactions must occur for the amino acid monomers in the protein of the fish to be converted to new proteins in your body?

For suggested answers, see Appendix A.

**CONCEPT 5.2**

General/basic formula



**Carbohydrates serve as fuel and building material**

**Carbohydrates** include sugars and polymers of sugars. The simplest carbohydrates are the **monosaccharides**, or **simple sugars**; these are the monomers from which more complex carbohydrates are built. **Disaccharides** are double sugars, consisting of two monosaccharides joined by a covalent bond. Carbohydrate macromolecules are polymers called **polysaccharides**, composed of many sugar building blocks.

➔ **Mastering Biology Animation: Carbohydrates**

**Sugars**

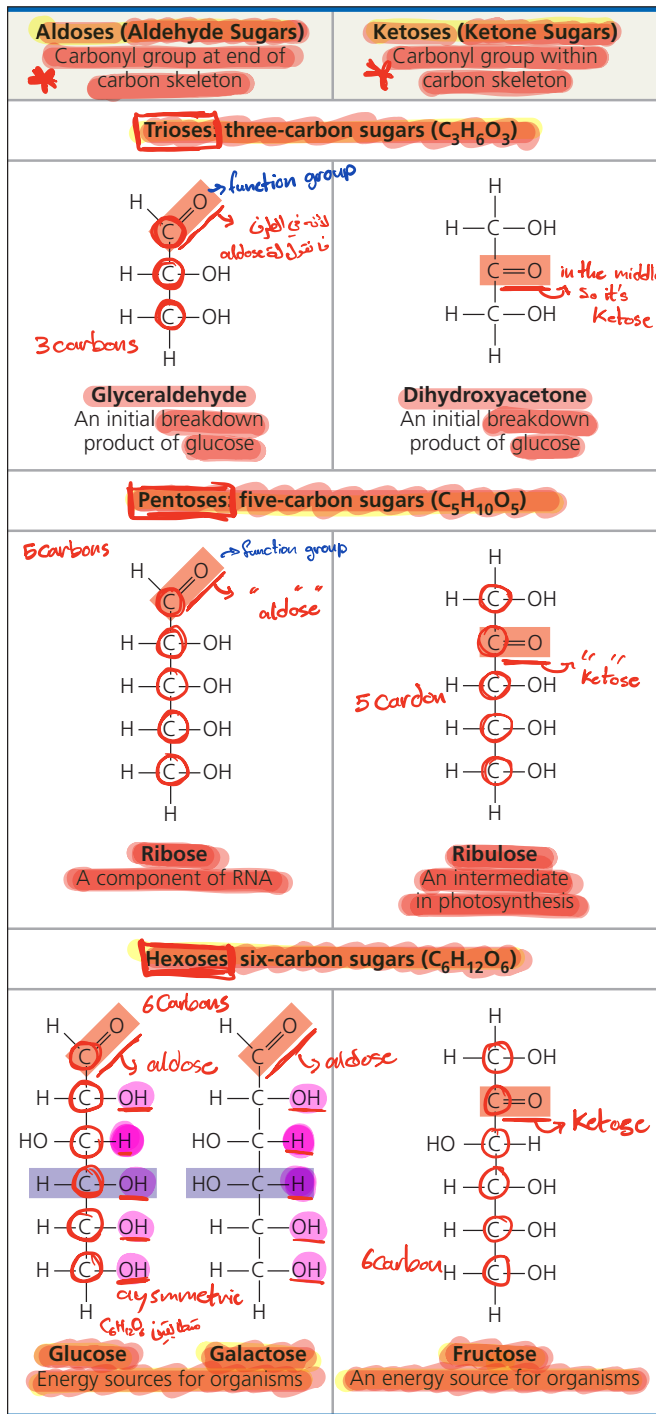
**Monosaccharides** (from the Greek *monos*, single, and *sacchar*, sugar) generally have molecular formulas that are some multiple of the unit  $CH_2O$ . Glucose ( $C_6H_{12}O_6$ ), the most common monosaccharide, is of central importance in the chemistry of life. In the structure of glucose, we can see the trademarks of a monosaccharide: The molecule has a carbonyl group,  $C=O$ , and multiple hydroxyl groups,  $-OH$  (Figure 5.3).

Depending on the location of the carbonyl group, a monosaccharide is either an **aldose** (aldehyde sugar) or a **ketose** (ketone sugar). Glucose, for example, is an aldose; fructose, an isomer of glucose, is a ketose. (Most names for sugars end in *-ose*.) Another criterion for classifying monosaccharides is the size of the carbon skeleton, which ranges from three to seven carbons long. Glucose, fructose, and other sugars that have six carbons are called **hexoses**. **Trioses** (three-carbon sugars) and **pentoses** (five-carbon sugars) are also common.

Still another source of diversity for simple sugars is in the way their parts are arranged spatially around **asymmetric carbons**. (Recall that an **asymmetric carbon** is a carbon attached to four different atoms or groups of atoms.) Glucose and galactose, for example, differ only in the placement of parts around one asymmetric carbon (see the purple boxes in Figure 5.3). What seems like a small difference is significant enough to give the two sugars distinctive shapes and binding activities, thus different behaviors.

Although it is convenient to draw glucose with a linear carbon skeleton, this representation is not completely accurate. In aqueous solutions, glucose molecules, as well as most other

**Figure 5.3 The structure and classification of some monosaccharides.** Sugars vary in the location of their carbonyl groups (orange), the length of their carbon skeletons, and the way their parts are arranged spatially around asymmetric carbons (compare, for example, the purple portions of glucose and galactose).

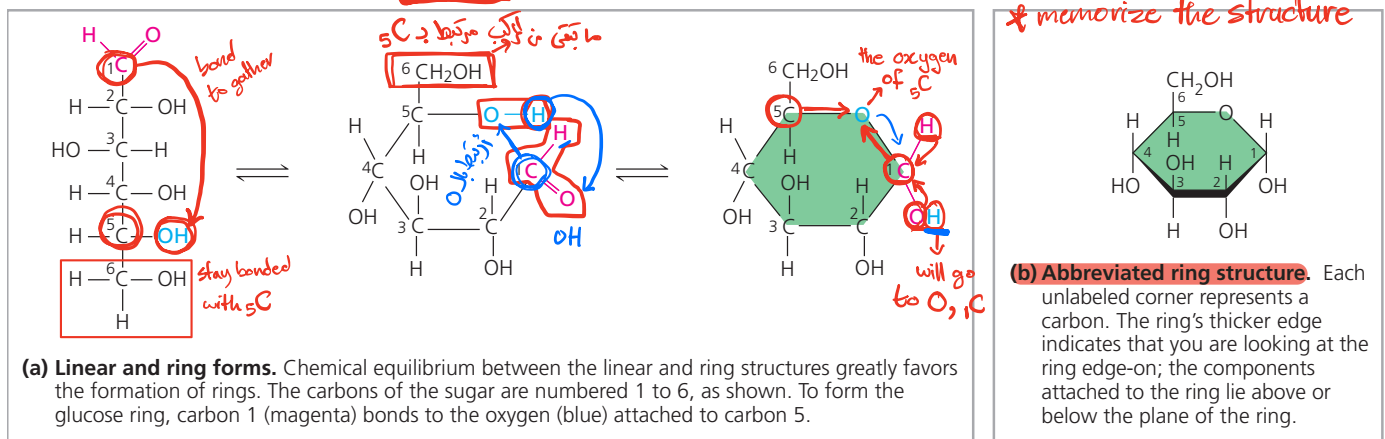


**MAKE CONNECTIONS** In the 1970s, a process was developed that converts the glucose in corn syrup to its sweeter-tasting isomer, fructose. High-fructose corn syrup, a common ingredient in soft drinks and processed food, is a mixture of glucose and fructose. What type of isomers are glucose and fructose? (See Figure 4.7.)

➔ **Mastering Biology Animation: Monosaccharides**



▼ **Figure 5.4 Linear and ring forms of glucose.**



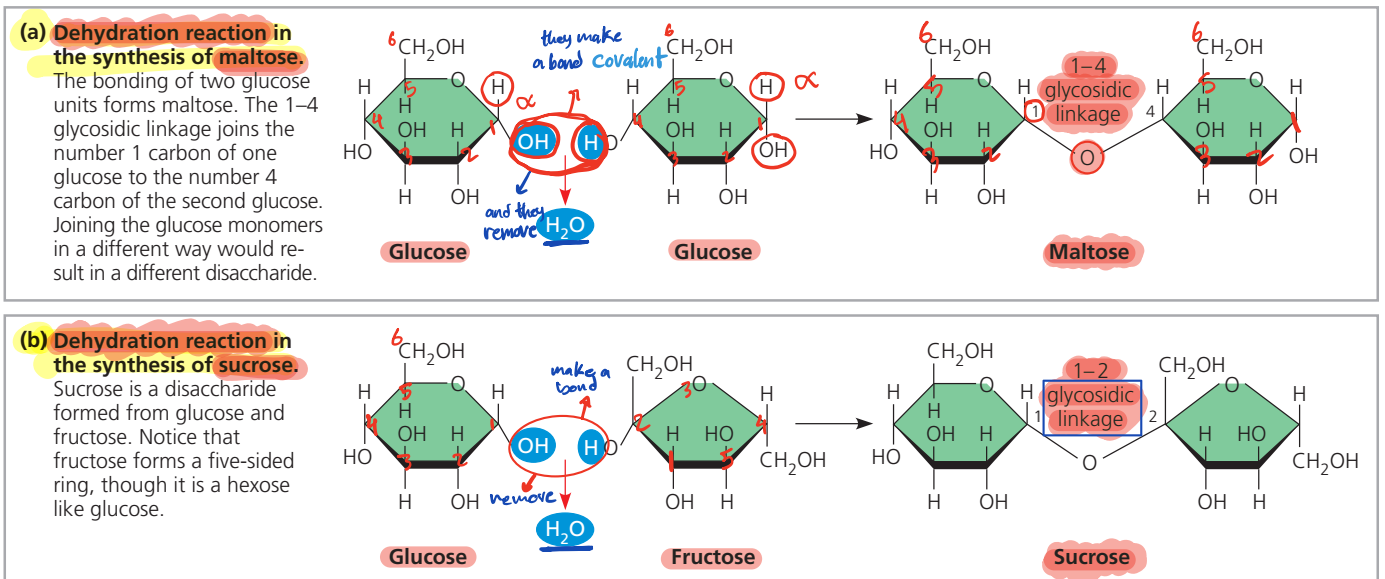
**DRAW IT** Start with the linear form of fructose (see Figure 5.3) and draw the formation of the fructose ring in two steps, as shown in (a). First, number the carbons starting at the top of the linear structure. Then draw the molecule in a ringlike orientation, attaching carbon 5 via its oxygen to carbon 2. Compare the number of carbons in the ring portions of fructose and glucose.

five- and six-carbon sugars, form rings, because they are the most stable form of these sugars under physiological conditions (Figure 5.4).

Monosaccharides, particularly glucose, are major nutrients for cells. In the process known as cellular respiration, cells extract energy from glucose molecules by breaking them down in a series of reactions. Not only are monosaccharides a major fuel for cellular work, but their carbon skeletons also serve as raw material for the synthesis of other types of small organic molecules, such as amino acids and fatty acids. Monosaccharides that are not immediately used in these ways are generally incorporated as monomers into disaccharides or polysaccharides, discussed next.

A **disaccharide** consists of two monosaccharides joined by a **glycosidic linkage**, a covalent bond formed between two monosaccharides by a dehydration reaction (glyco refers to carbohydrate). For example, maltose is a disaccharide formed by the linking of two molecules of glucose (Figure 5.5a). Also known as malt sugar, maltose is an ingredient used in brewing beer. The most prevalent disaccharide is sucrose, or table sugar. Its two monomers are glucose and fructose (Figure 5.5b). Plants generally transport carbohydrates from leaves to roots and other nonphotosynthetic organs in the form of sucrose. Lactose, the sugar present in milk, is another disaccharide, in this case a glucose molecule joined

▼ **Figure 5.5 Examples of disaccharide synthesis.**



**DRAW IT** Referring to Figures 5.3 and 5.4, number the carbons in each sugar in this figure. How does the name of each linkage relate to the numbers?

➔ **Mastering Biology Animation: Synthesis of Sucrose**

to a galactose molecule. Disaccharides must be broken down into monosaccharides to be used for energy by organisms. Lactose intolerance is a common condition in humans who lack lactase, the enzyme that breaks down lactose. The sugar is instead broken down by intestinal bacteria, causing formation of gas and subsequent cramping. The problem may be avoided by taking the enzyme lactase when eating or drinking dairy products or consuming dairy products that have already been treated with lactase to break down the lactose.

## Polysaccharides

**Polysaccharides** are macromolecules, polymers with a few hundred to a few thousand monosaccharides joined by glycosidic linkages. Some polysaccharides serve as **storage material**, hydrolyzed as needed to provide monosaccharides for cells.

Starch  
glycogen

Other polysaccharides serve as building material for structures that protect the cell or the whole organism. The architecture and function of a polysaccharide are determined by its monosaccharides and by the positions of its glycosidic linkages.

Cellulose  
Chitin

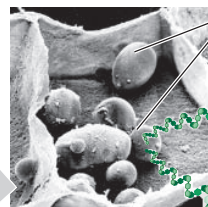
### Storage Polysaccharides

Both plants and animals store sugars for later use in the form of storage polysaccharides (Figure 5.6). Plants store **starch**, a polymer of glucose monomers, as granules within cellular structures known as **plastids**. (Plastids include chloroplasts. Synthesizing starch enables the plant to stockpile surplus glucose. Because glucose is a major cellular fuel, starch represents stored energy. The sugar can later be withdrawn by the plant from this carbohydrate "bank" by hydrolysis, which breaks the bonds between the glucose monomers. Most animals, including humans, also have enzymes that can hydrolyze plant starch, making glucose

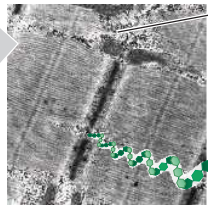
**Figure 5.6 Polysaccharides of plants and animals.** (a) Starch stored in plant cells, (b) glycogen stored in muscle cells, and (c) structural cellulose fibers in plant cell walls are all polysaccharides composed entirely of glucose monomers (green hexagons). In starch and glycogen, the polymer chains tend to form helices in unbranched regions because of the angle of the 1-4 linkages between glucose molecules. There are two kinds of starch: amylose and amylopectin. Cellulose, with a different kind of glucose linkage, is always unbranched.



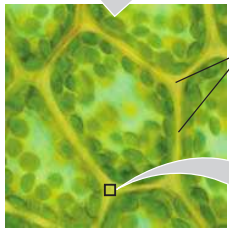
Muscle tissue



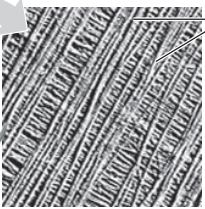
(a) Starch



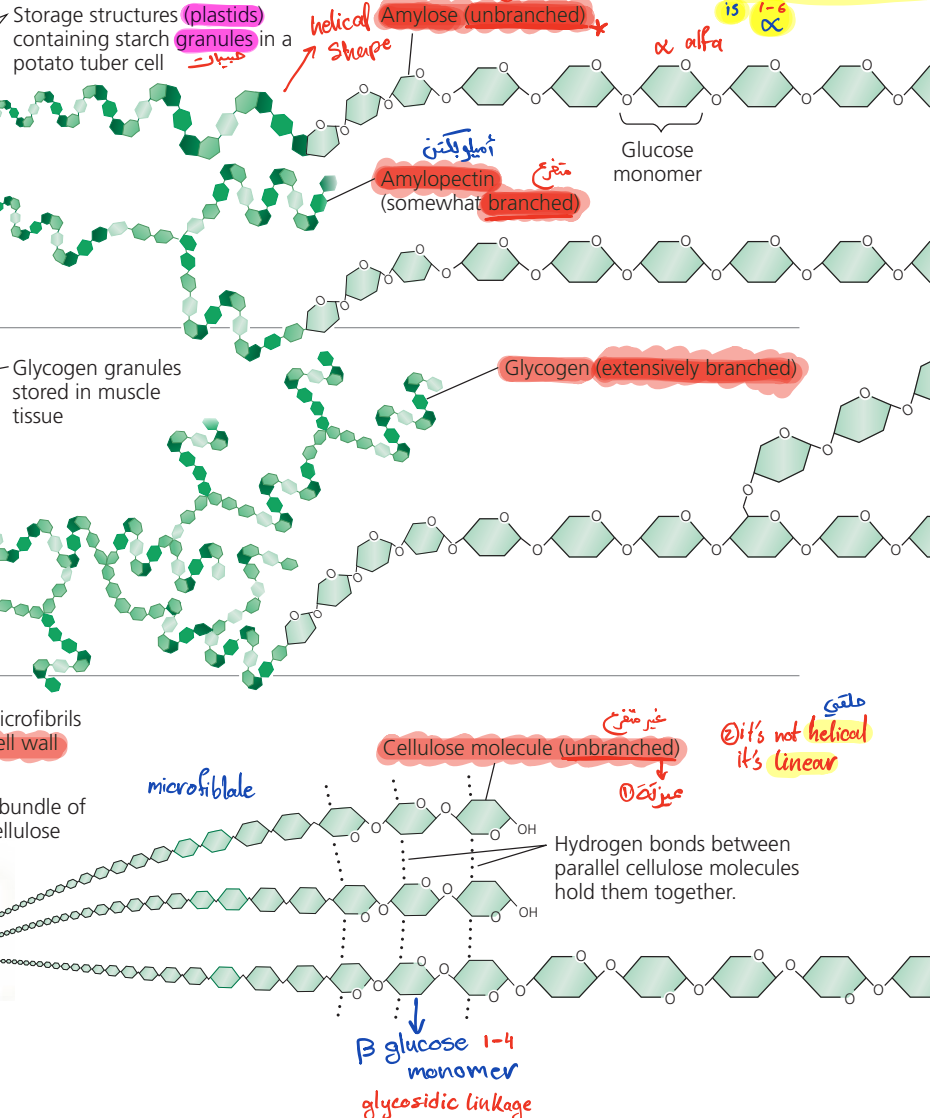
(b) Glycogen



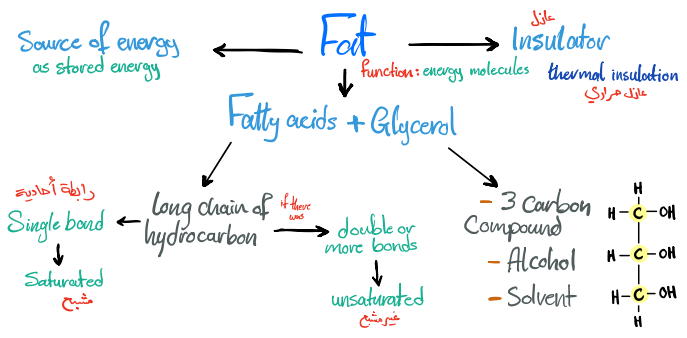
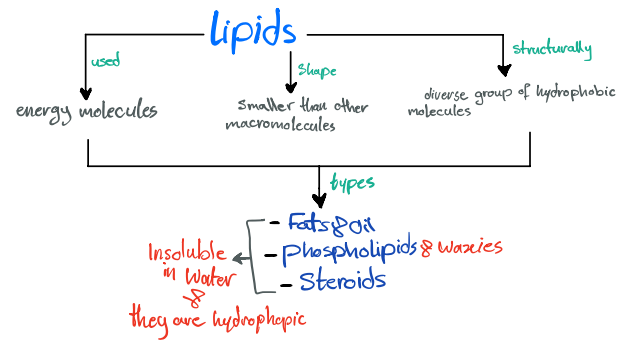
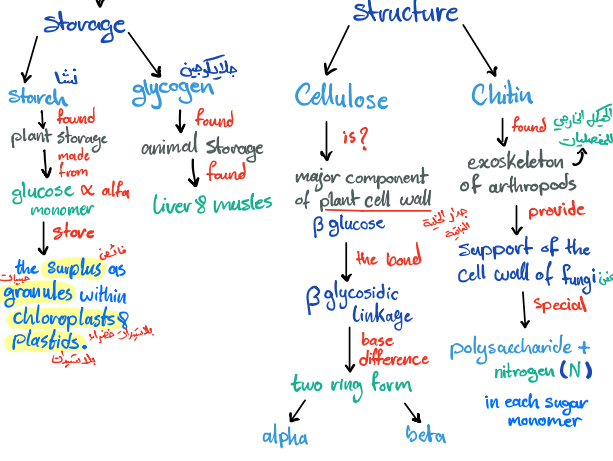
Plant cell, surrounded by cell wall



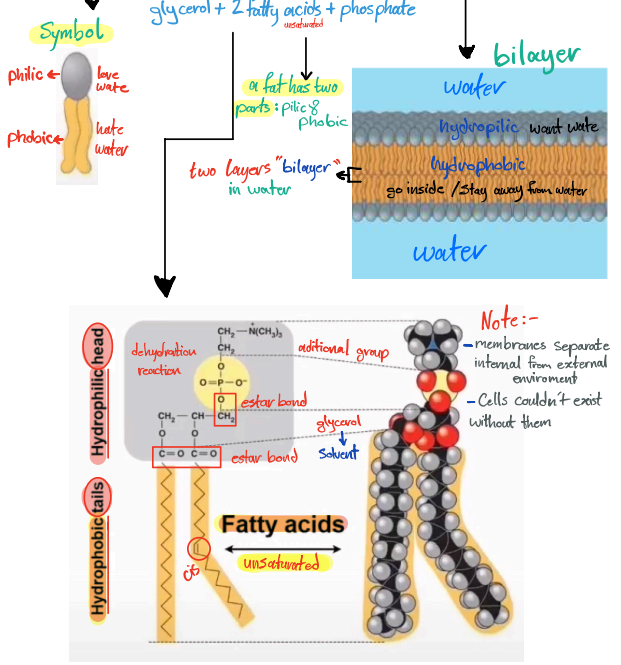
(c) Cellulose



**polysaccharide** → the function get determined by the monosaccharides & the position of the glycosidic linkage  
**polymers of Sugar**



**phospholipids** → remember membranes it marks important component of cell membranes



**hydrogenated oils** aka...trans-fats

**GOOD!** cis (unprocessed EFA) Fatty-acid molecule

This is the structure your body is designed to get to maintain healthy cell structure. Healthy cells are the first defense against disease and illness!

**BAD!** Trans-fatty acid (damaged EFA) molecule

This damaged structure is NOT what your body needs and is harmful to cell structure. Trans-fatty acids are now linked to cancer, heart disease and other terrible diseases and health conditions!

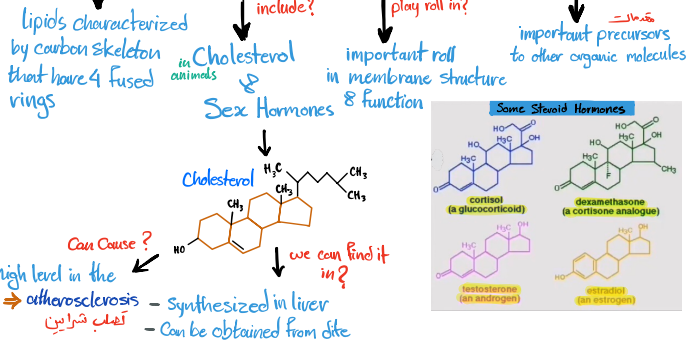
they're isomers/geometric isomers

**linoleic acid: (trans configuration (trans isomer))**

**linoleic acid: (cis configuration (cis isomer))**

unsaturated → just applied on unsaturated → dangerous → atherosclerosis

**Steroids** → precursors: things that comes before another of the same kind





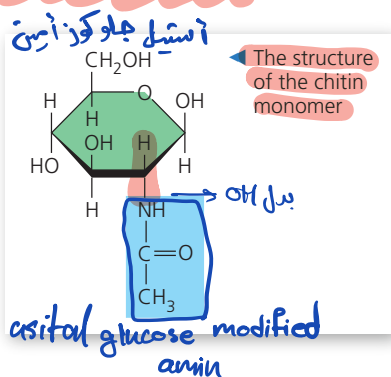
few organisms possess enzymes that can digest cellulose. Almost all animals, including humans, do not; the cellulose in our food passes through the digestive tract and is eliminated with the feces. Along the way, the cellulose abrades the wall of the digestive tract and stimulates the lining to secrete mucus, which aids in the smooth passage of food through the tract. Thus, although cellulose is not a nutrient for humans, it is an important part of a healthy diet. Most fruits, vegetables, and whole grains are rich in cellulose. On food packages, “insoluble fiber” refers mainly to cellulose (see Figure 5.7).

Some microorganisms can digest cellulose, breaking it down into glucose monomers. A cow harbors cellulose-digesting prokaryotes and protists in its gut. These microbes hydrolyze the cellulose of hay and grass and convert the glucose to other compounds that nourish the cow. Similarly, a termite, which is unable to digest cellulose by itself, has prokaryotes or protists living in its gut that can make a meal of wood. Some fungi can also digest cellulose in soil and elsewhere, thereby helping recycle chemical elements within Earth’s ecosystems.

Another important structural polysaccharide is **chitin**, the carbohydrate used by arthropods (insects, spiders, crustaceans, and related animals) to build their exoskeletons—hard cases that surround the soft parts of an animal (Figure 5.8). Made up of chitin embedded in a layer of proteins, the case is leathery and flexible at first, but becomes hardened when the proteins are chemically linked to each other (as in insects) or encrusted with calcium carbonate (as in crabs). Chitin is also found in fungi, which use this polysaccharide rather than cellulose as the building material for their cell walls. Chitin is similar to cellulose, with  $\beta$  linkages, except that the glucose monomer of chitin has a nitrogen-containing attachment (see Figure 5.8).

Chitin بولي سكر اير جتوي حل فائورجين امين

▼ Figure 5.8 Chitin, a structural polysaccharide.



◀ Chitin, embedded in proteins, forms the exoskeleton of arthropods. This emperor dragonfly (*Anax imperator*) is molting—shedding its old exoskeleton (brown) and emerging upside down in adult form.

### CONCEPT CHECK 5.2

1. Write the formula for a monosaccharide that has three carbons.
2. A dehydration reaction joins two glucose molecules to form maltose. The formula for glucose is  $C_6H_{12}O_6$ . What is the formula for maltose?
3. **WHAT IF?** After a cow is given antibiotics to treat an infection, a vet gives the animal a drink of “gut culture” containing various prokaryotes. Why is this necessary?

For suggested answers, see Appendix A.

### CONCEPT 5.3

## Lipids are a diverse group of hydrophobic molecules

Insoluble + hydrophobic

Lipids are the one class of large biological molecules that does not include true polymers, and they are generally not big enough to be considered macromolecules. The compounds called **lipids** are grouped with each other because they share one important trait: They are hydrophobic: They mix poorly, if at all, with water. This behavior of lipids is based on their molecular structure. Although they may have some polar bonds associated with oxygen, lipids consist mostly of hydrocarbon regions with relatively non-polar C—H bonds. Lipids are varied in form and function. They include waxes and certain pigments, but we will focus on the types of lipids that are most important biologically: fats, phospholipids, and steroids.

➔ Mastering Biology Animation: Lipids

Fats = Fatty acids + Glycerol

Although fats are not polymers, they are large molecules assembled from smaller molecules by dehydration reactions, like the dehydration reaction described in Figure 5.2a. A **fat** consists of a glycerol molecule joined to three fatty acids (Figure 5.9). Glycerol is an alcohol; each of its three carbons bears a hydroxyl group. A **fatty acid** has a long carbon skeleton, usually 16 or 18 carbon atoms in length. The carbon at one end of the skeleton is part of a carboxyl group, the functional group that gives these molecules the name *fatty acid*. The rest of the skeleton consists of a hydrocarbon chain. The relatively nonpolar C—H bonds in the hydrocarbon chains of fatty acids are the reason fats are hydrophobic. Fats separate from water because the water molecules hydrogen-bond to one another and exclude the fats. This is why vegetable oil (a liquid fat) separates from the aqueous vinegar solution in a bottle of salad dressing.

In making a fat, each fatty acid molecule is joined to glycerol by a dehydration reaction (Figure 5.9a). This results in an ester linkage, a bond between a hydroxyl group and a carboxyl group. The completed fat consists of three fatty acids linked to one glycerol molecule. (Other names for a fat are *triacylglycerol* and *triglyceride*; levels of triglycerides are

available as a nutrient for cells. Potato tubers and grains—the fruits of wheat, maize (corn), rice, and other grasses—are the major sources of starch in the human diet.

Most of the glucose monomers in starch are joined by 1–4 linkages (number 1 carbon to number 4 carbon), like the glucose units in maltose (see Figure 5.5a). The simplest form of starch, amylose, is unbranched. Amylopectin, a more complex starch, is a branched polymer with 1–6 linkages at the branch points. Both of these starches are shown in Figure 5.6a.

Animals store a polysaccharide called **glycogen**, a polymer of glucose that is like amylopectin but more extensively branched (Figure 5.6b). Vertebrates store glycogen mainly in liver and muscle cells. Breakdown of glycogen in these cells releases glucose when the demand for energy increases. (The extensively branched structure of glycogen fits its function: More free ends are available for breakdown.) This stored fuel cannot sustain an animal for long, however. In humans, for example, glycogen stores are depleted in about a day unless they are replenished by eating. This is an issue of concern in low-carbohydrate diets, which can result in weakness and fatigue.

### Structural Polysaccharides

Organisms build strong materials from structural polysaccharides. For example, the polysaccharide called **cellulose** is a major component of the tough walls that enclose plant cells (Figure 5.6c). Globally, plants produce almost  $10^{14}$  kg (100 billion tons) of cellulose per year; it is the most abundant organic compound on Earth.

Like starch, cellulose is a polymer of glucose with 1–4 glycosidic linkages, but the linkages in these two polymers differ. The

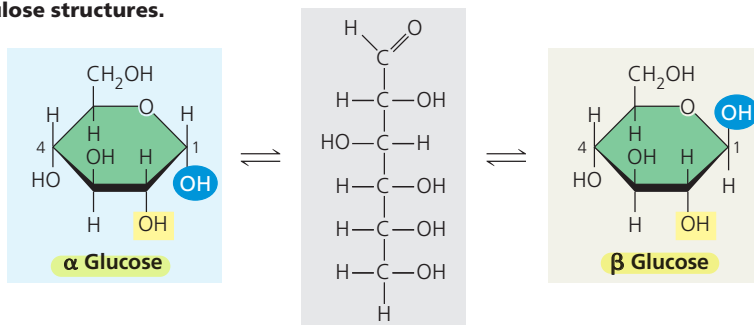
difference is based on the fact that there are actually two slightly different ring structures for glucose (Figure 5.7a). When glucose forms a ring, the hydroxyl group attached to the number 1 carbon is positioned either below or above the plane of the ring. These two ring forms for glucose are called alpha ( $\alpha$ ) and beta ( $\beta$ ), respectively. (Greek letters are often used as a “numbering” system for different versions of biological structures, much as we use the letters a, b, c, and so on for the parts of a question or a figure.) In starch, all the glucose monomers are in the  $\alpha$  configuration (Figure 5.7b), the arrangement we saw in Figures 5.4 and 5.5. In contrast, the glucose monomers of cellulose are all in the  $\beta$  configuration, making every glucose monomer “upside down” with respect to its neighbors (Figure 5.7c; see also Figure 5.6c).

The differing glycosidic linkages in starch and cellulose give the two molecules distinct three-dimensional shapes. Certain starch molecules are largely helical, fitting their function of efficiently storing glucose units. Conversely, a cellulose molecule is straight. Cellulose is never branched, and some hydroxyl groups on its glucose monomers are free to hydrogen-bond with the hydroxyls of other cellulose molecules lying parallel to it. In plant cell walls, parallel cellulose molecules held together in this way are grouped into units called microfibrils (see Figure 5.6c). These cable-like microfibrils are a strong building material for plants and an important substance for humans because cellulose is the major constituent of paper and the only component of cotton. The unbranched structure of cellulose thus fits its function: imparting strength to parts of the plant.

Enzymes that digest starch by hydrolyzing its  $\alpha$  linkages are unable to hydrolyze the  $\beta$  linkages of cellulose due to the different shapes of these two molecules. In fact,

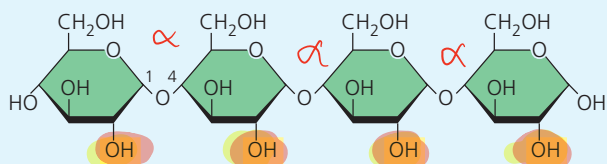
▼ Figure 5.7 Starch and cellulose structures.

(a)  $\alpha$  and  $\beta$  glucose ring structures. These two interconvertible forms of glucose differ in the placement of the hydroxyl group (highlighted in blue) attached to the number 1 carbon.

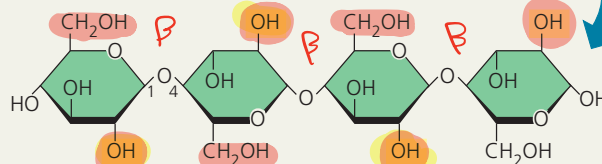


إليمان غير مذابة  
“Insoluble Fiber”  
listed on food labels  
is mainly cellulose,  
shown below.

Nutrition Facts	
Dietary Fiber 4g	16%
Soluble Fiber 2g	
Insoluble Fiber 2g	



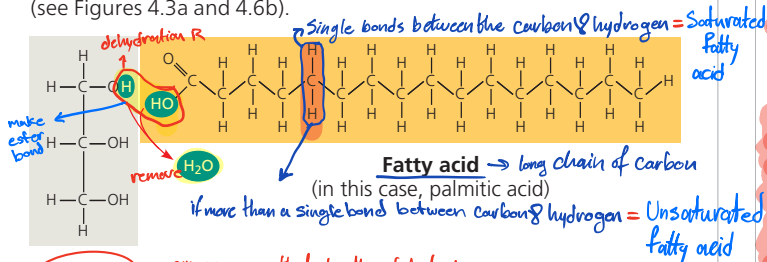
(b) Starch: 1–4 linkage of  $\alpha$  glucose monomers. All monomers are in the same orientation. Compare the positions of the  $-OH$  groups highlighted in yellow with those in cellulose (c).



(c) Cellulose: 1–4 linkage of  $\beta$  glucose monomers. In cellulose, every  $\beta$  glucose monomer is upside down with respect to its neighbors. (See the highlighted  $-OH$  groups.)

➔ Mastering Biology Animation: Starch, Cellulose, and Glycogen Structures

**Figure 5.9 The synthesis and structure of a fat, or triacylglycerol.** The molecular building blocks of a fat are one molecule of glycerol and three molecules of fatty acids. The carbons of the fatty acids are arranged zigzag to suggest the actual orientations of the four single bonds extending from each carbon (see Figures 4.3a and 4.6b).

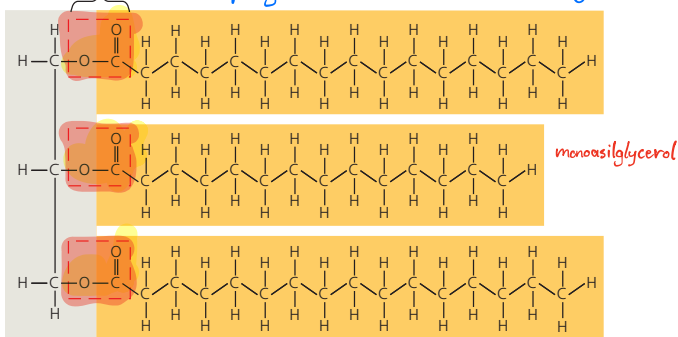


**Glycerol** on enzyme that do the dehydration

**(a) One of three dehydration reactions in the synthesis of a fat.**

One water molecule is removed for each fatty acid joined to the glycerol.

all saturated ← Ester linkage polysaturated → Solid object



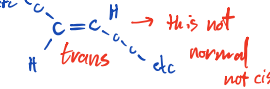
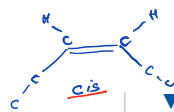
**(b) A fat molecule (triacylglycerol) with three fatty acid units.**

In this example, two of the fatty acid units are identical.

reported when blood is tested for lipids.) The fatty acids in a fat can all be the same, or they can be of two or three different kinds, as in Figure 5.9b.

The terms *saturated* fats and *unsaturated* fats are commonly used in the context of nutrition (Figure 5.10). These terms refer to the structure of the hydrocarbon chains of the fatty acids. If there are no double bonds between carbon atoms composing a chain, then as many hydrogen atoms as possible are bonded to the carbon skeleton. Such a structure is said to be *saturated* with hydrogen, and the resulting fatty acid is therefore called a **saturated fatty acid** (Figure 5.10a). An **unsaturated fatty acid** has one or more double bonds, with one fewer hydrogen atom on each double-bonded carbon. Nearly every double bond in naturally occurring fatty acids is a *cis* double bond, which creates a kink in the hydrocarbon chain wherever it occurs (Figure 5.10b). (See Figure 4.7b to remind yourself about *cis* and *trans* double bonds.)

A fat made from saturated fatty acids is called a **saturated fat**. Most animal fats are saturated: The hydrocarbon chains of their fatty acids—the “tails” of the fat molecules—lack double bonds (see Figure 5.10a), and their flexibility allows the fat molecules to pack together tightly. Saturated animal



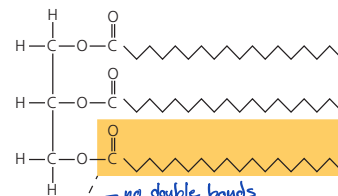
**Figure 5.10 Saturated and unsaturated fats and fatty acids.**

**(a) Saturated fat**

At room temperature, the molecules of a saturated fat, such as the fat in **butter**, are packed closely together, forming a solid.



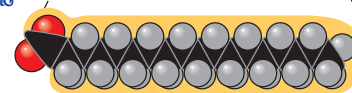
Structural formula of a saturated fat molecule (Each hydrocarbon chain is represented as a zigzag line, where each bend represents a carbon atom; hydrogens are not shown.)



it have OH in all the C and it's single bond

- no double bonds
- packed slightly together
- Solid at room temperature

Space-filling model of stearic acid, a saturated fatty acid (red = oxygen, black = carbon, gray = hydrogen)



Contributes → Cardiovascular disease

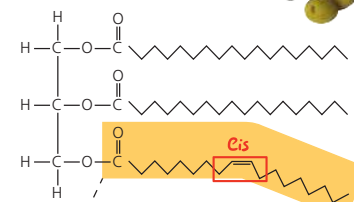
**(b) Unsaturated fat → much better**

At room temperature, the molecules of an **unsaturated fat** such as **olive oil** cannot pack together closely enough to solidify because of the kinks in some of their fatty acid hydrocarbon chains.

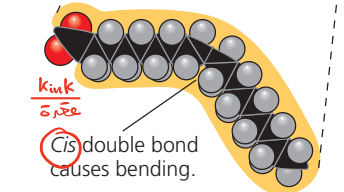


- double bond
- pack less tightly together
- liquid at room temperature

Structural formula of an unsaturated fat molecule



Space-filling model of oleic acid, an unsaturated fatty acid



moves atoms ← bend away from each other

kink space Cis double bond causes bending.

fats, such as lard and butter, are solid at room temperature. In contrast, the fats of plants and fishes are generally unsaturated, meaning that they are composed of one or more types of unsaturated fatty acids. Usually liquid at room temperature, plant and fish fats are referred to as oils—olive oil and cod liver oil are examples. The kinks where the *cis* double bonds are located (see Figure 5.10b) prevent the molecules from packing together closely enough to solidify at room temperature. The phrase **hydrogenated vegetable oils** on food labels means that



unsaturated fats have been synthetically converted to saturated fats by adding hydrogen, allowing them to solidify. Peanut butter, margarine, and many other products are hydrogenated to prevent lipids from separating out in liquid (oil) form.

A diet rich in saturated fats is one of several factors that may contribute to the cardiovascular disease known as atherosclerosis. In this condition, deposits called plaques develop within the walls of blood vessels, causing inward bulges that impede blood flow and reduce the resilience of the vessels. The process of hydrogenating vegetable oils produces not only saturated fats but also unsaturated fats with *trans* double bonds. It appears that *trans* fats can contribute to coronary heart disease (see Concept 42.4). Because *trans* fats are especially common in baked goods and processed foods, the U.S. Food and Drug Administration (FDA) requires nutritional labels to include information on *trans* fat content. In addition, the FDA has ordered U.S. food manufacturers to stop producing *trans* fats in foods by 2021. Some countries, such as Denmark and Switzerland, have already banned artificially produced *trans* fats in foods.

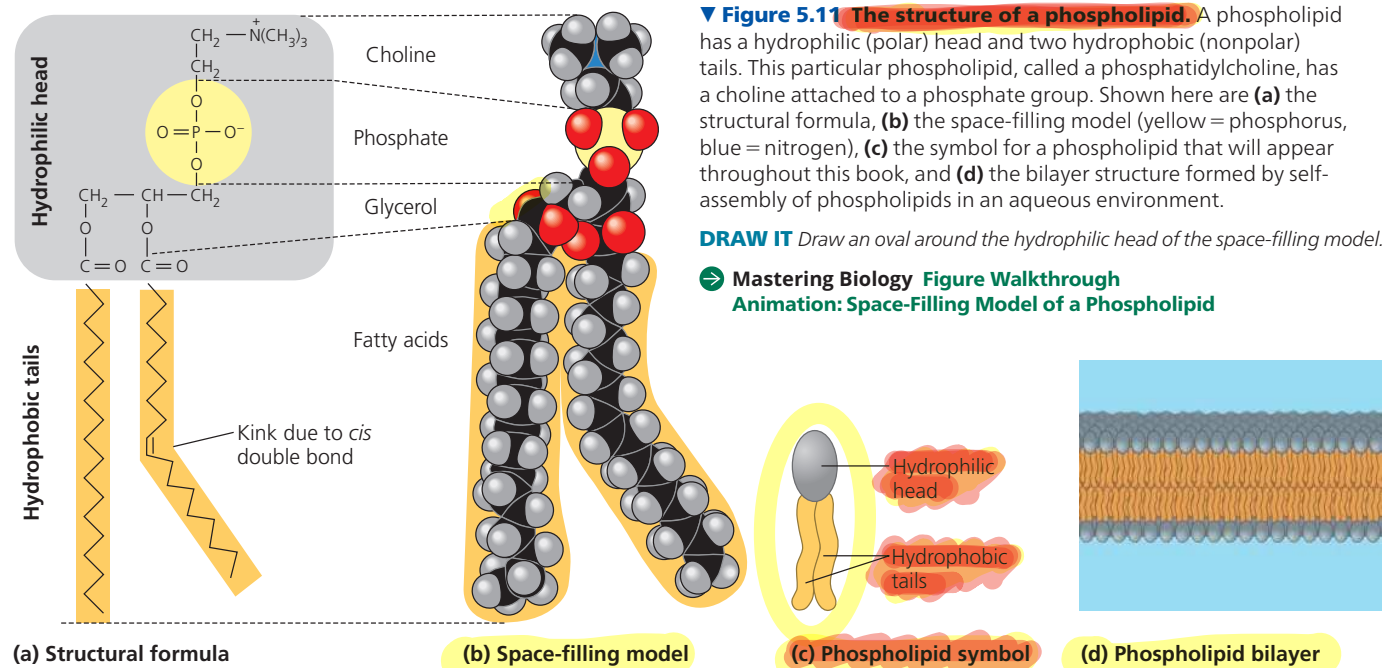
The major function of fats is energy storage. The hydrocarbon chains of fats are similar to gasoline molecules and just as rich in energy. A gram of fat stores more than twice as much energy as a gram of a polysaccharide, such as starch. Because plants are relatively immobile, they can function with bulky energy storage in the form of starch. (Vegetable oils are generally obtained from seeds, where more compact storage is an asset to the plant.) Animals, however, must carry their energy stores with them, so there is an advantage to having a more compact reservoir of fuel—fat. Humans and other mammals stock their long-term food reserves in adipose cells (see Figure 4.6a), which swell and shrink as fat is deposited

and withdrawn from storage. In addition to storing energy, adipose tissue also cushions such vital organs as the kidneys, and a layer of fat beneath the skin insulates the body. This subcutaneous layer is especially thick in whales, seals, and most other marine mammals, insulating their bodies in cold ocean water.

## Phospholipids

Cells as we know them could not exist without another type of lipid, called phospholipids. Phospholipids are essential for cells because they are major constituents of cell membranes. Their structure provides a classic example of how form fits function at the molecular level. As shown in Figure 5.11, a phospholipid is similar to a fat molecule but has only two fatty acids attached to glycerol rather than three. The third hydroxyl group of glycerol is joined to a phosphate group, which has a negative electrical charge in the cell. Typically, an additional small charged or polar molecule is also linked to the phosphate group. Choline is one such molecule (see Figure 5.11), but there are many others as well, allowing formation of a variety of phospholipids that differ from each other.

The two ends of phospholipids show different behaviors with respect to water. The hydrocarbon tails are hydrophobic and are excluded from water. However, the phosphate group and its attachments form a hydrophilic head that has an affinity for water. When phospholipids are added to water, they self-assemble into a double-layered sheet called a “bilayer” that shields their hydrophobic fatty acid tails from water (Figure 5.11d).

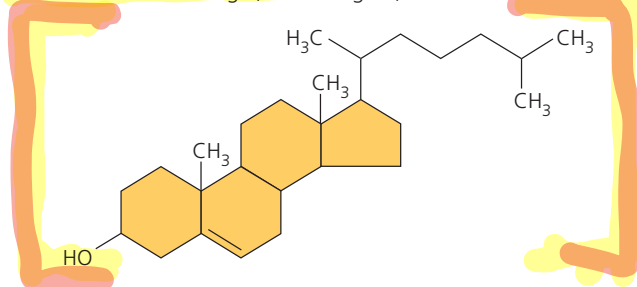


At the surface of a cell, phospholipids are arranged in a similar bilayer. The hydrophilic heads of the molecules are on the outside of the bilayer, in contact with the aqueous solutions inside and outside of the cell. The hydrophobic tails point toward the interior of the bilayer, away from the water. The phospholipid bilayer forms a boundary between the cell and its external environment and establishes separate compartments within eukaryotic cells; in fact, the existence of cells depends on the properties of phospholipids.

## Steroids

**Steroids** are lipids characterized by a carbon skeleton consisting of four fused rings. Different steroids are distinguished by the particular chemical groups attached to this ensemble of rings. **Cholesterol**, a type of steroid, is a crucial molecule in animals (Figure 5.12). It is a common component of animal cell membranes and is also the precursor from which other steroids, such as the vertebrate sex hormones, are synthesized. In vertebrates, cholesterol is synthesized in the liver and is also obtained from the diet. A high level of cholesterol in the blood may contribute to atherosclerosis, although some researchers are questioning the roles of cholesterol and saturated fats in the development of this condition.

▼ **Figure 5.12 Cholesterol, a steroid.** Cholesterol is the molecule from which other steroids, including the sex hormones, are synthesized. Steroids vary in the chemical groups attached to their four interconnected rings (shown in gold).



**MAKE CONNECTIONS** Compare cholesterol with the sex hormones shown in the figure at the beginning of Concept 4.3. Circle the chemical groups that cholesterol has in common with estradiol; put a square around the chemical groups that cholesterol has in common with testosterone.

➔ **Mastering Biology**  
Interview with Lovell Jones: Investigating the effects of sex hormones on cancer



### CONCEPT CHECK 5.3

1. Compare the structure of a fat (triglyceride) with that of a phospholipid.
2. Why are human sex hormones considered lipids?
3. **WHAT IF?** Suppose a membrane surrounded an oil droplet, as it does in the cells of plant seeds and in some animal cells. Describe and explain the form it might take.

For suggested answers, see Appendix A.

### CONCEPT 5.4

## Proteins include a diversity of structures, resulting in a wide range of functions

Viteals

Nearly every dynamic function of a living being depends on proteins. In fact, the importance of proteins is underscored by their name, which comes from the Greek word *proteios*, meaning “first,” or “primary.” Proteins account for more than 50% of the dry mass of most cells, and they are instrumental in almost everything organisms do. Some proteins speed up chemical reactions, while others play a role in defense, storage, transport, cellular communication, movement, or structural support. Figure 5.13 shows examples of proteins with these functions, which you’ll learn more about in later chapters.

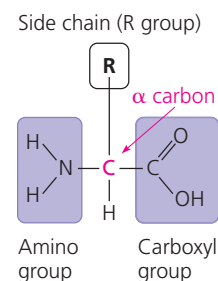
Life would not be possible without enzymes, most of which are proteins. Enzymatic proteins regulate metabolism by acting as **catalysts**, chemical agents that selectively speed up chemical reactions without being consumed in the reaction. Because an enzyme can perform its function over and over again, these molecules can be thought of as workhorses that keep cells running by carrying out the processes of life.

A human has tens of thousands of different proteins, each with a specific structure and function; proteins, in fact, are the most structurally sophisticated molecules known. Consistent with their diverse functions, they vary extensively in structure, each type of protein having a unique three-dimensional shape.

Proteins are all constructed from the same set of 20 amino acids, linked in unbranched polymers. The bond between amino acids is called a *peptide bond*, so a polymer of amino acids is called a **polypeptide**. A **protein** is a biologically functional molecule made up of one or more polypeptides, each folded and coiled into a specific three-dimensional structure.

## Amino Acids (Monomers)

All amino acids share a common structure. An **amino acid** is an organic molecule with both an amino group and a carboxyl group (see Figure 4.9); the small figure shows the general formula for an amino acid. At the center of the amino acid is an asymmetric carbon atom called the **alpha ( $\alpha$ ) carbon**. Its four different partners are an amino group, a carboxyl group, a hydrogen atom, and a variable group symbolized by R. The R group, also called the side chain, differs with each amino acid. The R group may be as simple as a



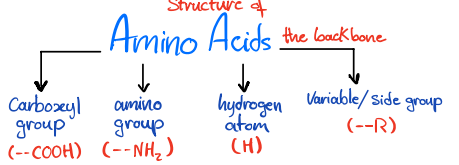
\* you can't find any cell without proteins

no proteins = no life

# are? proteins

macromolecules that's formed from amino acids  
 joined by? peptide bond it's a covalent bond  
 "polymers of amino acids"

poly peptide amino acid polymers  
 Linker with a covalent bonds peptide bonds  
 polymer of amino acid  
 range length from few to more than 1,000 monomers  
 each polypeptide has unique linear sequence of amino acid  
 Carboxyl end (C-terminus)  
 amino end (N-terminus)

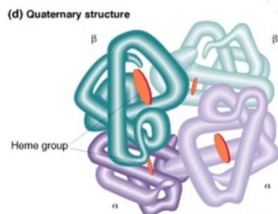
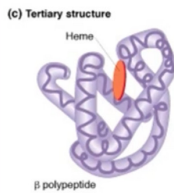
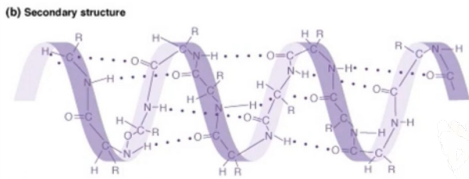
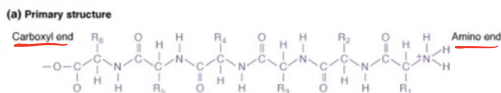
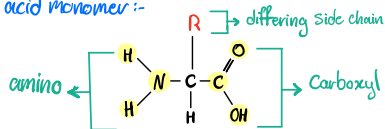


\* 20 amino acids commonly found in proteins is in their R group

\* لا يوجد حامض أميني لا يتبع على المجموعة المذكورة

Because it's the backbone ليكن الأساسي

amino acid monomer :-

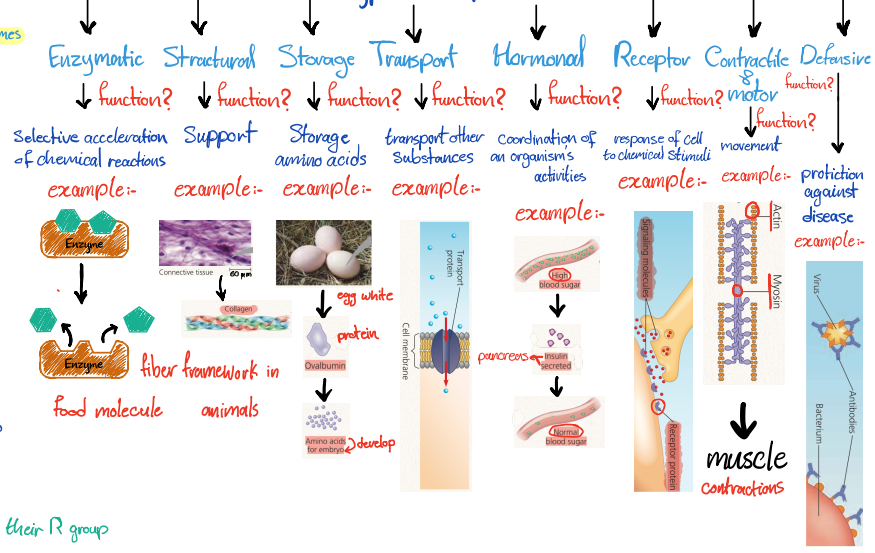


A functional protein is not just a polypeptide chain, but one or more polypeptides precisely twisted, folded, and coiled into a molecule of unique shape. It is the amino-acid sequence of a polypeptide that determines what three-dimensional conformation the protein will take

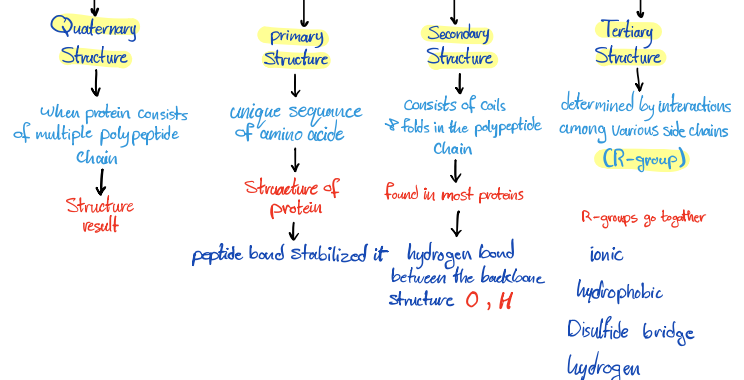
Contain? Carbon hydrogen Oxygen Nitrogen Sulfur Sometimes

function? have many different functions :-

## types of protein



## Four levels of protein structure



\* the sequence of amino acid makes the base structure for any protein and that's why it's called primary structure of protein



**Figure 5.13 An overview of protein functions.**

**Enzymatic proteins**

**Function:** Selective acceleration of chemical reactions

**Example:** Digestive enzymes catalyze the hydrolysis of bonds in food molecules.

**Defensive proteins**

**Function:** Protection against disease

**Example:** Antibodies inactivate and help destroy viruses and bacteria.

**Storage proteins**

**Function:** Storage of amino acids

**Examples:** Casein, the protein of milk, is the major source of amino acids for baby mammals. Plants have storage proteins in their seeds. Ovalbumin is the protein of egg white used as an amino acid source for the developing embryo.

**Transport proteins**

**Function:** Transport of substances

**Examples:** Hemoglobin, the iron-containing protein of vertebrate blood, transports oxygen from the lungs to other parts of the body. Other proteins transport molecules across membranes, as shown here.

**Hormonal proteins**

**Function:** Coordination of an organism's activities

**Example:** Insulin, a hormone secreted by the pancreas, causes other tissues to take up glucose, thus regulating blood sugar concentration.

**Receptor proteins**

**Function:** Response of cell to chemical stimuli

**Example:** Receptors built into the membrane of a nerve cell detect signaling molecules released by other nerve cells.

**Contractile and motor proteins**

**Function:** Movement

**Examples:** Motor proteins are responsible for the undulations of cilia and flagella. Actin and myosin proteins are responsible for the contraction of muscles.

**Structural proteins**

**Function:** Support

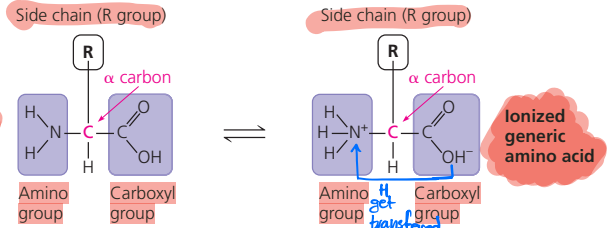
**Examples:** Keratin is the protein of hair, horns, feathers, and other skin appendages. Insects and spiders use silk fibers to make their cocoons and webs, respectively. Collagen and elastin proteins provide a fibrous framework in animal connective tissues.

hydrogen atom, or it may be a carbon skeleton with various functional groups attached. The physical and chemical properties of the side chain determine the unique characteristics of a particular amino acid, thus affecting its functional role in a polypeptide.

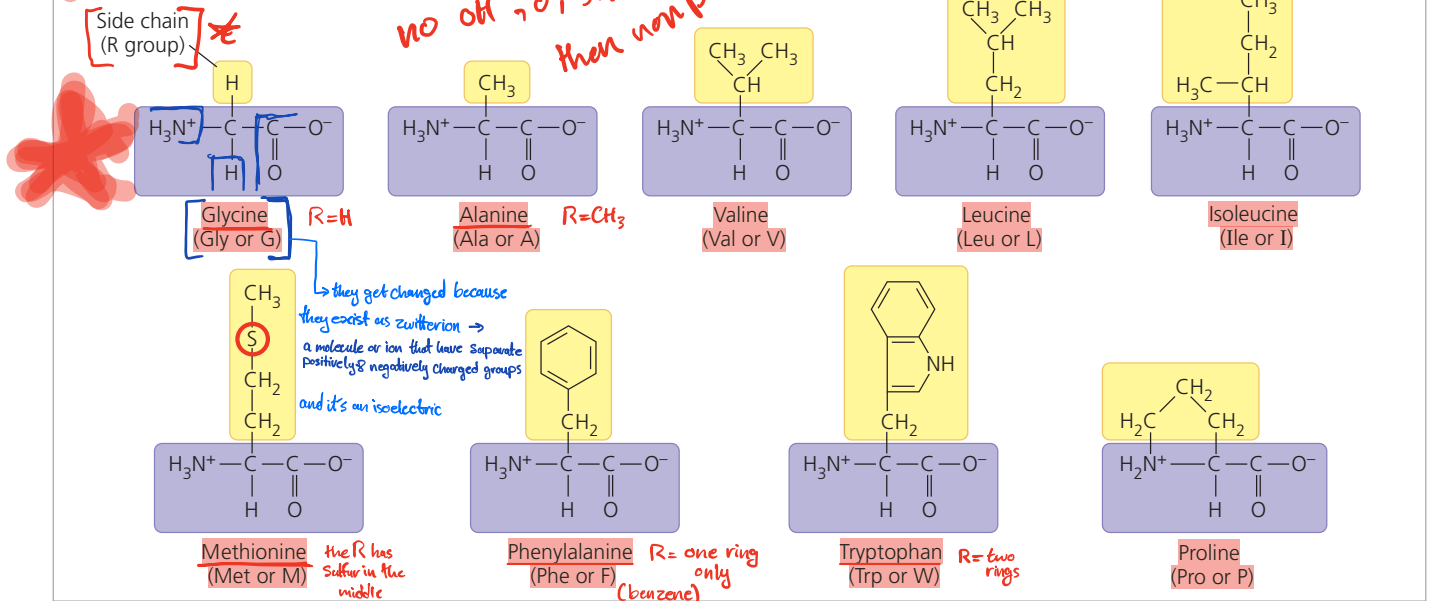
Figure 5.14 shows the 20 amino acids that cells use to build their thousands of proteins. Here the amino groups and carboxyl groups are all depicted in ionized form, the way they usually exist at the pH found in a cell. The amino acids are grouped according to the properties of their side chains. One group consists of amino acids with nonpolar side chains,

which are hydrophobic. Another group consists of amino acids with polar side chains, which are hydrophilic. Acidic amino acids have side chains that are generally negative in charge due to the presence of a carboxyl group, which is usually dissociated (ionized) at cellular pH. Basic amino acids have amino groups in their side chains that are generally positive in charge. (The terms *acidic* and *basic* in this context refer only to groups in the side chains because all amino acids—as monomers—have carboxyl groups and amino groups.) Because they are charged, acidic and basic side chains are also hydrophilic.

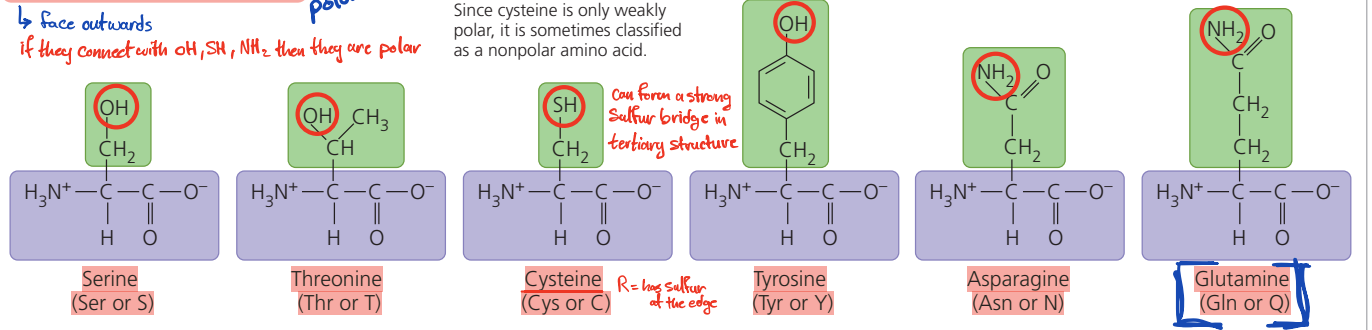
**Figure 5.14 The 20 amino acids of proteins.** At the top right are the non-ionized and ionized forms of a generic amino acid. The specific amino acids are shown below in their ionized form, prevalent at the pH within a cell (pH 7.2). The amino acids are grouped by properties of their side chains. The three-letter and one-letter abbreviations for the amino acids are in parentheses. All of the amino acids used in proteins are L enantiomers (see Figure 4.7c).



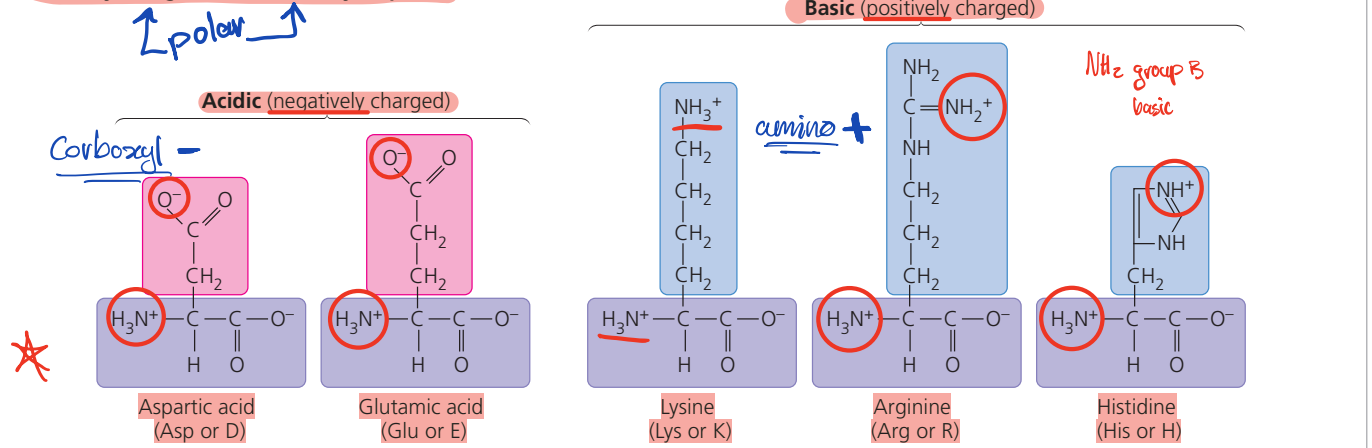
**Nonpolar side chains; hydrophobic**



**Polar side chains; hydrophilic**



**Electrically charged side chains; hydrophilic**



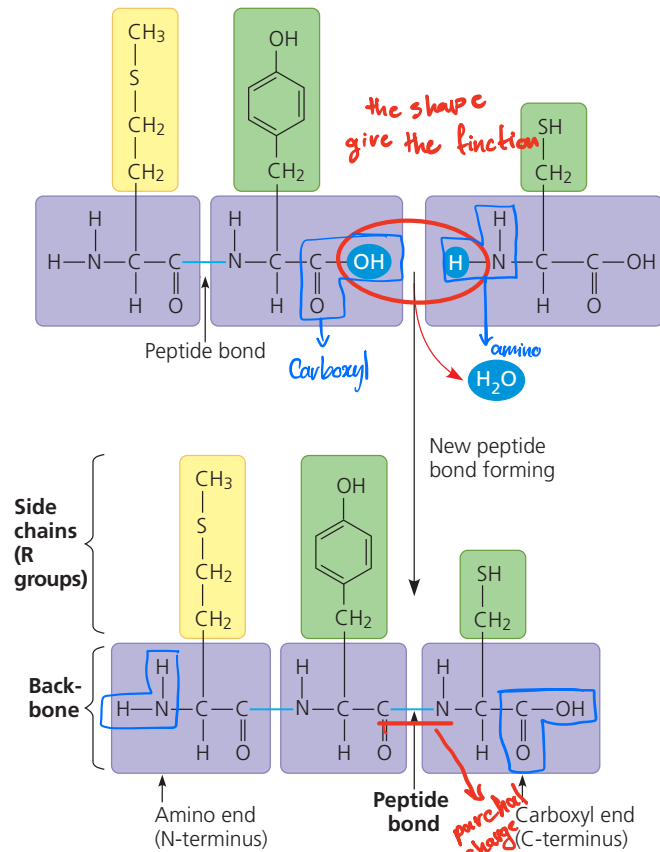
not isoelectric at pH = 7  
acidic are isoelectric at pH < 7  
basic are isoelectric at pH > 7

## Polypeptides (Amino Acid Polymers)

Now that we have examined amino acids, let's see how they are linked to form polymers (Figure 5.15). When two amino acids are positioned so that the carboxyl group of one is adjacent to the amino group of the other, they can become joined by a dehydration reaction, with the removal of a water molecule. The resulting covalent bond is called a **peptide bond**. Repeated over and over, this process yields a **polypeptide**, a polymer of many amino acids linked by peptide bonds. You'll learn more about how cells synthesize polypeptides in Concept 17.4.

The repeating sequence of atoms highlighted in purple in Figure 5.15 is called the **polypeptide backbone**. Extending from this backbone are the different **side chains** (R groups) of the amino acids. Polypeptides range in length from a few amino acids to 1,000 or more. Each specific polypeptide has a unique linear sequence of amino acids. Note that one end of the polypeptide chain has a free amino group (the **N-terminus** of the polypeptide), while the opposite end has a free carboxyl

▼ **Figure 5.15 Making a polypeptide chain.** Peptide bonds are formed by dehydration reactions, which link the carboxyl group of one amino acid to the amino group of the next. The peptide bonds are formed one at a time, starting with the amino acid at the amino end (N-terminus). The polypeptide has a repetitive backbone (purple) to which the amino acid side chains (yellow and green) are attached.



**DRAW IT** Label the three amino acids in the upper part of the figure using three-letter and one-letter codes. Circle and label the carboxyl and amino groups that will form the new peptide bond.

group (the C-terminus). The chemical nature of the molecule as a whole is determined by the kind and sequence of the side chains, which determine how a polypeptide folds and thus its final shape and chemical characteristics. The immense variety of polypeptides in nature illustrates an important concept introduced earlier—that cells can make many different polymers by linking a limited set of monomers into diverse sequences.

## Protein Structure and Function

The specific activities of proteins result from their intricate three-dimensional architecture, the simplest level of which is the sequence of their amino acids. What can the amino acid sequence of a polypeptide tell us about the three-dimensional structure (commonly referred to simply as the “structure”) of the protein and its function? The term *polypeptide* is not synonymous with the term *protein*. Even for a protein consisting of a single polypeptide, the relationship is somewhat analogous to that between a long strand of yarn and a sweater of particular size and shape that can be knitted from the yarn. A functional protein is not *just* a polypeptide chain, but one or more polypeptides precisely twisted, folded, and coiled into a molecule of unique shape, which can be shown in several different types of models (Figure 5.16). And it is the amino acid sequence of each polypeptide that determines what three-dimensional structure the protein will have under normal cellular conditions.

When a cell synthesizes a polypeptide, the chain may fold spontaneously, assuming the functional structure for that protein. This folding is driven and reinforced by the formation of various bonds between parts of the chain, which in turn depends on the sequence of amino acids. Many proteins are roughly spherical (*globular proteins*), while others are shaped like long fibers (*fibrous proteins*). Even within these broad categories, countless variations exist.

A protein's specific structure determines how it works. In almost every case, the function of a protein depends on its ability to recognize and bind to some other molecule. In an especially striking example of the marriage of form and function, Figure 5.17 shows the exact match of shape between an antibody (a protein in the body) and the particular foreign substance on a flu virus that the antibody binds to and marks for destruction. Also, you may recall another example of molecules with matching shapes from Concept 2.3: endorphin molecules (produced by the body) and morphine molecules (a manufactured drug), both of which fit into receptor proteins on the surface of brain cells in humans, producing euphoria and relieving pain. Morphine, heroin, and other opiate drugs are able to mimic endorphins because they all have a shape similar to that of endorphins and can thus fit into and bind to endorphin receptors in the brain. This fit is very specific, something like a handshake (see Figure 2.16). The endorphin receptor, like other receptor molecules, is a protein. The function of a protein—for instance, the ability of a receptor protein to bind to a particular pain-relieving signaling molecule—is an emergent property resulting from exquisite molecular order.



## ▼ Figure 5.16 VISUALIZING PROTEINS

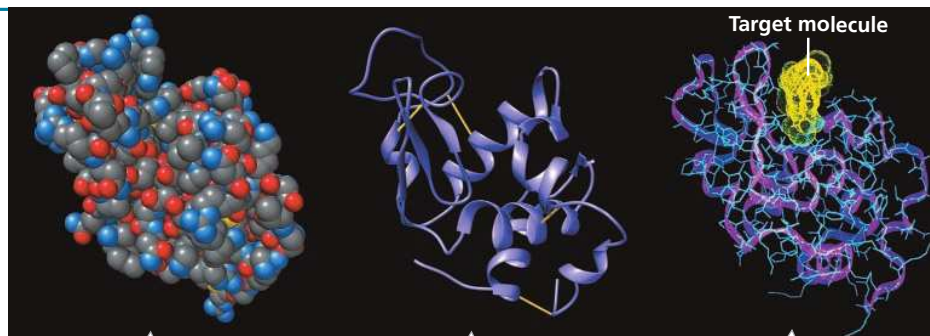
Proteins can be represented in different ways, depending on the goal of the illustration.

### Structural Models

\* ← Using data from structural studies of proteins, computers can generate various types of models. Each model emphasizes a different aspect of the protein's structure, but no model can show what a protein actually looks like. These three models depict lysozyme, a protein in tears and saliva that helps prevent infection by binding to target molecules on bacteria.

#### 1. In which model is it easiest to follow the polypeptide backbone?

➔ **Instructors:** The tutorial "Molecular Model: Lysozyme," in which students rotate 3-D models of lysozyme, can be assigned in **Mastering Biology**.



**Space-filling model:** Emphasizes the overall globular shape. Shows all the atoms of the protein (except hydrogen), which are color-coded: gray = carbon, red = oxygen, blue = nitrogen, and yellow = sulfur.

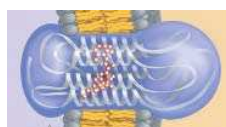
**Ribbon model:** Shows only the polypeptide backbone, emphasizing how it folds and coils to form a 3-D shape, in this case stabilized by disulfide bridges (yellow lines).

**Wireframe model (blue):** Shows the polypeptide backbone with side chains extending from it. A ribbon model (purple) is superimposed on the wireframe model. The bacterial target molecule (yellow) is bound.

### Simplified Diagrams

It isn't always necessary to use a detailed computer model; simplified diagrams are useful when the focus of the figure is on the function of the protein, not the structure.

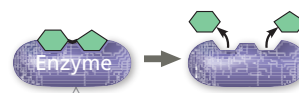
➔ **Instructors:** Additional questions related to this Visualizing Figure can be assigned in **Mastering Biology**.



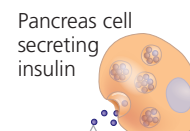
A transparent shape is drawn around the contours of a ribbon model of the protein rhodopsin, showing the shape of the molecule as well as some internal details.



When structural details are not needed, a solid shape can be used.



A simple shape is used here to represent a generic enzyme because the diagram focuses on enzyme action in general.



Sometimes a protein is represented simply as a dot, as shown here for insulin.

#### 2. Draw a simple version of lysozyme that shows its overall shape, based on the molecular models in the top section of the figure.

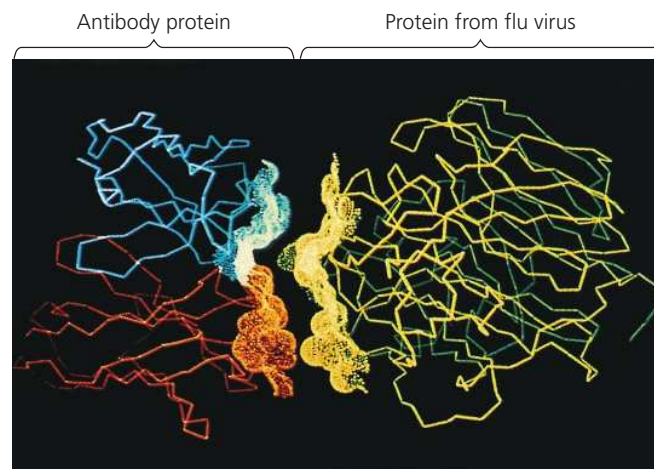
#### 3. Why is it unnecessary to show the actual shape of insulin here?

► **Figure 5.17 Complementarity of shape between two protein surfaces.** A technique called X-ray crystallography was used to generate a computer model of an antibody protein (blue and orange, left) bound to a flu virus protein (yellow and green, right). This is a wireframe model modified by adding an "electron density map" in the region where the two proteins meet. Computer software was then used to back the images away from each other slightly.

### Four Levels of Protein Structure

In spite of their great diversity, proteins share three superimposed levels of structure, known as primary, secondary, and tertiary structure. A fourth level, quaternary structure, arises when a protein consists of two or more polypeptide chains. **Figure 5.18** describes these four levels of protein structure. Be sure to study this figure thoroughly before going on to the next section.

➔ **Mastering Biology Animation: Protein Structure**

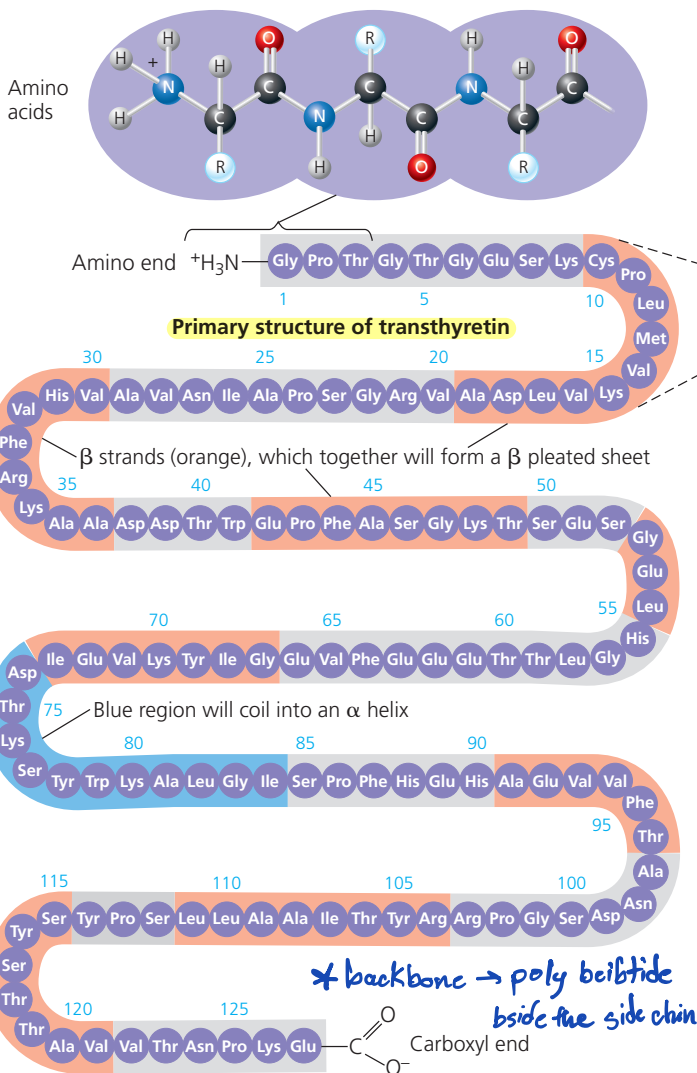


**VISUAL SKILLS** What do these computer models allow you to see about the two proteins?

## Primary Structure

### Linear chain of amino acids

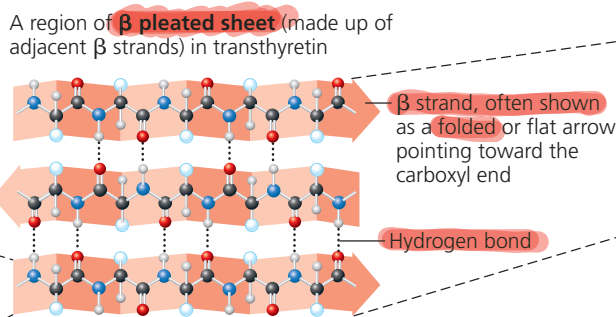
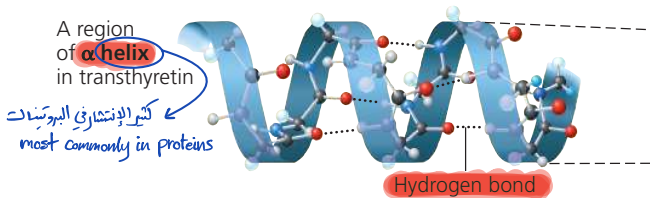
The **primary structure** of a protein is its sequence of amino acids. As an example, let's consider transthyretin, a globular blood protein that transports vitamin A and one of the thyroid hormones. Transthyretin is made up of four identical polypeptide chains, each composed of 127 amino acids. Shown here is one of these chains unraveled for a closer look at its primary structure. Each of the 127 positions along the chain is occupied by one of the 20 amino acids, indicated here by its three-letter abbreviation.



The primary structure is like the order of letters in a very long word. If left to chance, there would be  $20^{127}$  different ways of making a polypeptide chain 127 amino acids long. However, the precise primary structure of a protein is determined not by the random linking of amino acids, but by inherited genetic information. The primary structure in turn dictates secondary structure (α helices and β pleated sheets) and tertiary structure, due to the chemical nature of the backbone and the side chains (R groups) of the amino acids along the polypeptide.

## Secondary Structure

### Regions stabilized by hydrogen bonds between atoms of the polypeptide backbone



Most proteins have segments of their polypeptide chains repeatedly coiled or folded in patterns that contribute to the protein's overall shape. These coils and folds, collectively referred to as **secondary structure**, are the result of hydrogen bonds between the repeating constituents of the polypeptide backbone (not the amino acid side chains). Within the backbone, the oxygen atoms have a partial negative charge, and the hydrogen atoms attached to the nitrogens have a partial positive charge (see Figure 2.14); therefore, hydrogen bonds can form between these atoms. Individually, these hydrogen bonds are weak, but because they are repeated many times over a relatively long region of the polypeptide chain, they can support a particular shape for that part of the protein.

One such secondary structure is the **α helix**, a delicate coil held together by hydrogen bonding between every fourth amino acid, as shown above. Although each transthyretin polypeptide has only one α helix region (see the Primary and Tertiary Structure sections), other globular proteins have multiple stretches of α helix separated by nonhelical regions (see hemoglobin in the Quaternary Structure section). Some fibrous proteins, such as α-keratin, the structural protein of hair, have the α helix formation over most of their length.

The other secondary structure is the **β pleated sheet**. As shown above, two or more segments of the polypeptide chain lying side by side (called β strands) are connected by hydrogen bonds between parts of the two parallel segments. β pleated sheets make up the core of many globular proteins, as is the case for transthyretin (see Tertiary Structure), and dominate some fibrous proteins, including the silk protein of a spider's web. The teamwork of so many hydrogen bonds makes each spider silk fiber stronger than a steel strand.

► Spiders secrete silk fibers made of a structural protein containing β pleated sheets, which allow the spiderweb to stretch and recoil.

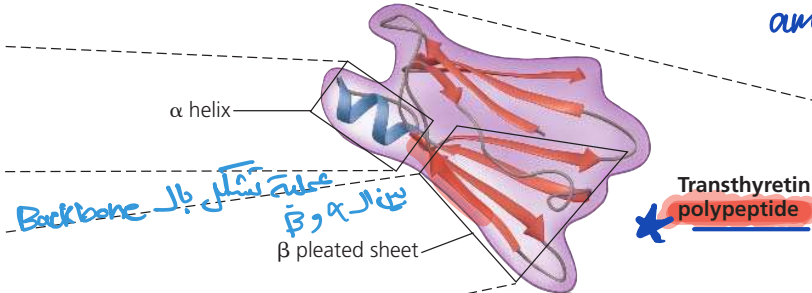




سلسلة من سلاسل ال-R-chain

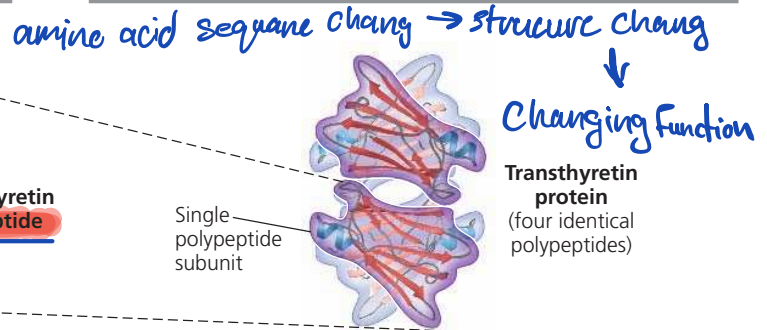
### Tertiary Structure

Three-dimensional shape stabilized by interactions between side chains



### Quaternary Structure

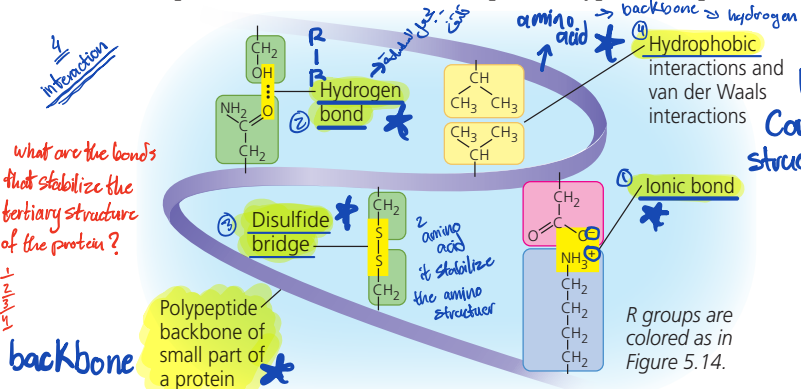
Association of two or more polypeptides (some proteins only)



\* if amino acid structure was changed everything will change and the result of that there will be a different conformation structure

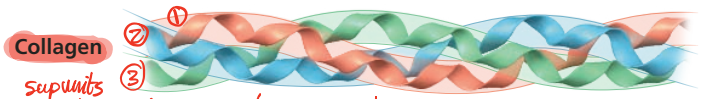
Superimposed on the patterns of secondary structure is a protein's tertiary structure, shown here in a ribbon model of the transthyretin polypeptide. While secondary structure involves interactions between backbone constituents, **tertiary structure** is the overall shape of a polypeptide resulting from interactions between the side chains (R groups) of the various amino acids. One type of interaction that contributes to tertiary structure is called—somewhat misleadingly—a **hydrophobic interaction**. As a polypeptide folds into its functional shape, amino acids with hydrophobic (nonpolar) side chains usually end up in clusters at the core of the protein, out of contact with water. Thus, a “hydrophobic interaction” is actually caused by the exclusion of nonpolar substances by water molecules. Once nonpolar amino acid side chains are close together, van der Waals interactions help hold them together. Meanwhile, hydrogen bonds between polar side chains and ionic bonds between positively and negatively charged side chains also help stabilize tertiary structure. These are all weak interactions in the aqueous cellular environment, but their cumulative effect helps give the protein a unique shape.

Covalent bonds called **disulfide bridges** may further reinforce the shape of a protein. Disulfide bridges form where two cysteine monomers, which have sulfhydryl groups (—SH) on their side chains (see Figure 4.9), are brought close together by the folding of the protein. The sulfur of one cysteine bonds to the sulfur of the second, and the disulfide bridge (—S—S—) rivets parts of the protein together (see yellow lines in Figure 5.16 ribbon model). All of these different kinds of interactions can contribute to the tertiary structure of a protein, as shown here in a small part of a hypothetical protein:

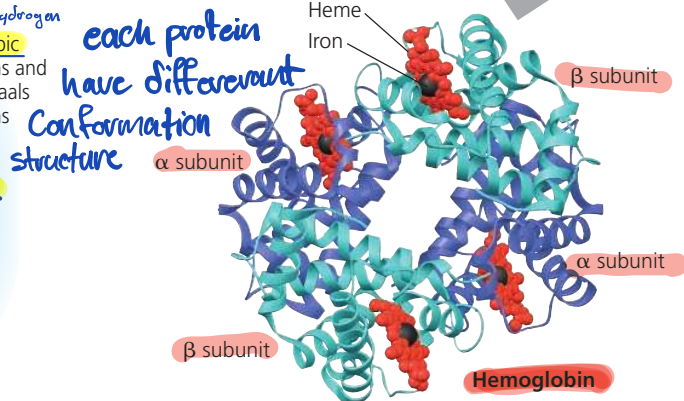


Some proteins consist of two or more polypeptide chains aggregated into one functional macromolecule. **Quaternary structure** is the overall protein structure that results from the aggregation of these polypeptide subunits. For example, shown above is the complete globular transthyretin protein, made up of its four polypeptides.

Another example is **collagen**, which is a fibrous protein that has three identical helical polypeptides intertwined into a larger triple helix, giving the long fibers great strength. This suits collagen fibers to their function as the girders of connective tissue in skin, bone, tendons, ligaments, and other body parts. (Collagen accounts for 40% of the protein in a human body.)



**Hemoglobin**, the oxygen-binding protein of red blood cells, is another example of a globular protein with quaternary structure. It consists of four polypeptide subunits, two of one kind ( $\alpha$ ) and two of another kind ( $\beta$ ). Both  $\alpha$  and  $\beta$  subunits consist primarily of  $\alpha$ -helical secondary structure. Each subunit has a nonpolypeptide component, called heme, with an iron atom that binds oxygen.




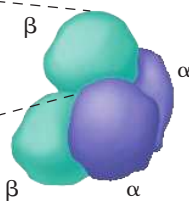
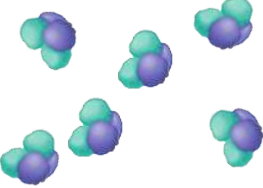

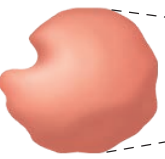
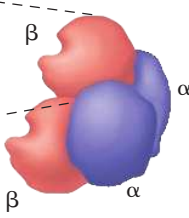
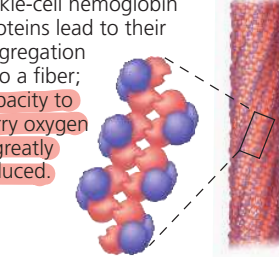

Mastering Biology Animation: Proteins  
MP3 Tutor: Protein Structure and Function

عندما تتغير فترة الارتباط بمرور الوقت، والبروتينات تكون روابطها التي تطلق عليه اسم Conformation Structure Protein

\* there are proteins that's made from more than 1 polypeptide chain 3, 4 and if these units bonded together they will make a complex protein



▼ **Figure 5.19** A single amino acid substitution in a protein causes **sickle-cell disease**.

	Primary Structure	Secondary and Tertiary Structures	Quaternary Structure	Function	Red Blood Cell Shape
Normal hemoglobin	<ol style="list-style-type: none"> <li>Val</li> <li>His</li> <li>Leu</li> <li>Thr</li> <li>Pro</li> <li><b>Glu</b></li> <li>Glu</li> </ol> <p>6 Glutamine polar</p>	Normal $\beta$ subunit  <p>the one that carries oxygen in the blood</p>	Normal hemoglobin 	Normal hemoglobin proteins do not associate with one another; each carries oxygen. 	Normal red blood cells are full of individual hemoglobin proteins.  <p>5 <math>\mu</math>m</p>
Sickle-cell hemoglobin	<ol style="list-style-type: none"> <li>Val</li> <li>His</li> <li>Leu</li> <li>Thr</li> <li>Pro</li> <li><b>Val</b></li> <li>Glu</li> </ol> <p>6 Val hydrophobic nonpolar</p>	Sickle-cell $\beta$ subunit 	Sickle-cell hemoglobin 	Hydrophobic interactions between sickle-cell hemoglobin proteins lead to their aggregation into a fiber; capacity to carry oxygen is greatly reduced. 	Fibers of abnormal hemoglobin deform red blood cell into sickle shape.  <p>5 <math>\mu</math>m</p>

this is called Denaturation Change  
↓  
Changing the Conformation structure of the protein and make it loses its activity

**MAKE CONNECTIONS** Considering the chemical characteristics of the amino acids valine and glutamic acid (see Figure 5.14), propose a possible explanation for the dramatic effect on protein function that occurs when valine is substituted for glutamic acid.

➔ **Mastering Biology HHMI**  
Animation: Sickle-Cell Disease



### Sickle-Cell Disease: A Change in Primary Structure

Even a slight change in primary structure can affect a protein's shape and ability to function. For instance, **sickle-cell disease**, an inherited blood disorder, is caused by the substitution of one amino acid (valine) for the normal one (glutamic acid) at the position of the sixth amino acid in the primary structure of hemoglobin, the protein that carries oxygen in red blood cells. Normal red blood cells are disk-shaped, but in sickle-cell disease, the abnormal hemoglobin molecules tend to aggregate into chains, deforming some of the cells into a sickle shape (Figure 5.19). A person with the disease has periodic "sickle-cell crises" when the angular cells clog tiny blood vessels, impeding blood flow. The toll taken on such patients is a dramatic example of how a simple change in protein structure can have devastating effects on protein function.

➔ **Mastering Biology Interview with Linus Pauling: Winner of the Nobel Prize in Chemistry and the Nobel Peace Prize**



### What Determines Protein Structure?

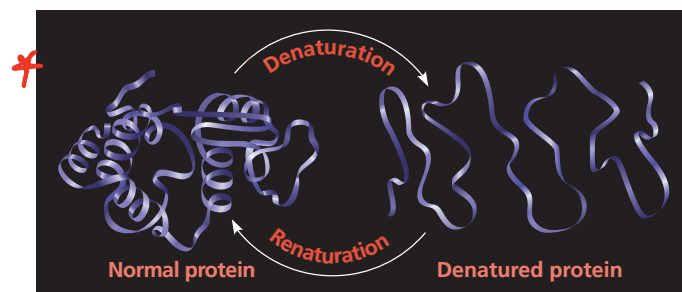
You've learned that a unique shape endows each protein with a specific function. But what are the key factors determining protein structure? You already know most of the answer: A polypeptide chain of a given amino acid sequence can be arranged into a three-dimensional shape determined by the interactions responsible for secondary and tertiary structure.

This folding normally occurs as the protein is being synthesized in the crowded environment within a cell, aided by other proteins. However, protein structure also depends on the physical and chemical conditions of the protein's environment. If the pH, salt concentration, temperature, or other aspects of its environment are altered, the weak chemical bonds and interactions within a protein may be destroyed, causing the protein to unravel and lose its native shape, a change called **denaturation** (Figure 5.20). Because it is misshapen, the denatured protein is biologically inactive.

Most proteins become denatured if they are transferred from an aqueous environment to a nonpolar solvent, such as ether or chloroform; the polypeptide chain refolds so that its

### ▼ Figure 5.20 Denaturation and renaturation of a protein.

High temperatures or various chemical treatments will denature a protein, causing it to lose its shape and hence its ability to function. If the denatured protein remains dissolved, it may renature when the chemical and physical aspects of its environment are restored to normal.



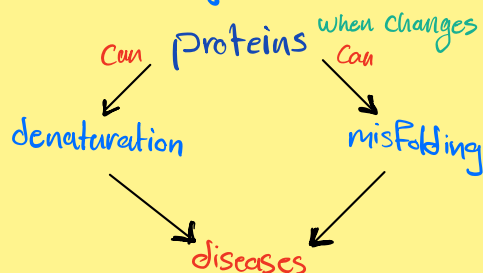
\* Some simple proteins can renature  
but most of the times the damage of the denaturation is permanent

\* وظيفة البروتين تعتمد على شكله

the structure & function of the protein are sensitive to physical & chemical conditions  
pH, temperature, salt concentration

## Denaturation

when the protein loses its native conformation & becoming biologically inactive



exist, where disulfide bridges are located, where ionic bonds can form, and so on. But how does protein folding occur in the cell?

## Protein Folding in the Cell

Biochemists now know the amino acid sequence for about 160 million proteins, with about 4.5–5 million added each month, and the three-dimensional shape for about 40,000. Researchers have tried to correlate the primary structure of many proteins with their three-dimensional structure to discover the rules of protein folding. Unfortunately, however, the protein-folding process is not that simple. Most proteins probably go through several intermediate structures on their way to a stable shape, and looking at the mature structure does not reveal the stages of folding required to achieve that form. However, biochemists have developed methods for tracking a protein through such stages and learning more about this important process.

Misfolding of polypeptides in cells is a serious problem that has come under increasing scrutiny by medical researchers. Many diseases—such as cystic fibrosis, Alzheimer's, Parkinson's, and mad cow disease—are associated with an accumulation of misfolded proteins. In fact, misfolded versions of the transthyretin protein featured in Figure 5.18 have been implicated in several diseases, including one form of senile dementia.

Even when scientists have a correctly folded protein in hand, determining its exact three-dimensional structure is not simple, for a single protein has thousands of atoms. The method most commonly used to determine the 3-D structure of a protein is **X-ray crystallography**, which depends on the diffraction of an X-ray beam by the atoms of a crystallized molecule. Using this technique, scientists can build a 3-D model that shows the exact position of every atom in a protein molecule (Figure 5.21). Nuclear magnetic resonance (NMR) spectroscopy, cryo-electron microscopy (cryo-EM; see Concept 6.1)

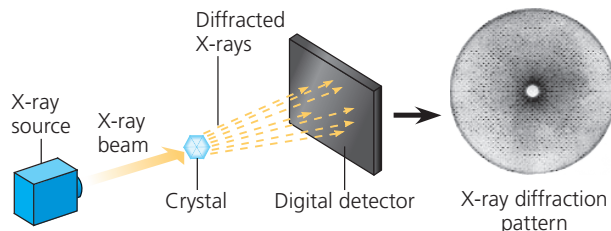
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## Figure 5.21 Research Method

### X-Ray Crystallography

**Application** Scientists use X-ray crystallography to determine the three-dimensional (3-D) structure of macromolecules such as nucleic acids and proteins.

**Technique** Researchers aim an X-ray beam through a crystallized protein or nucleic acid. The atoms of the crystal diffract (bend) the X-rays into an orderly array that a digital detector records as a pattern of spots called an X-ray diffraction pattern, an example of which is shown here.



**Results** Using data from X-ray diffraction patterns and the sequence of monomers determined by chemical methods, researchers can build a 3-D computer model of the macromolecule being studied, such as the four-subunit protein transthyretin (see Figure 5.18) shown here.



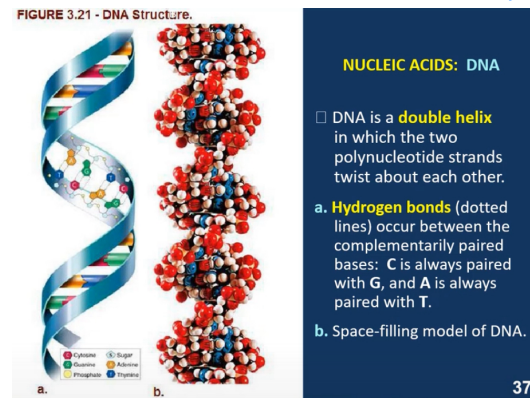
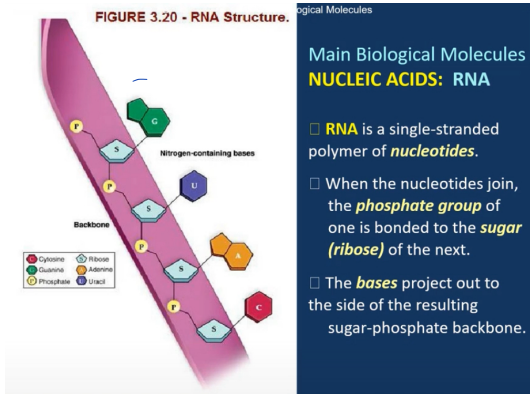
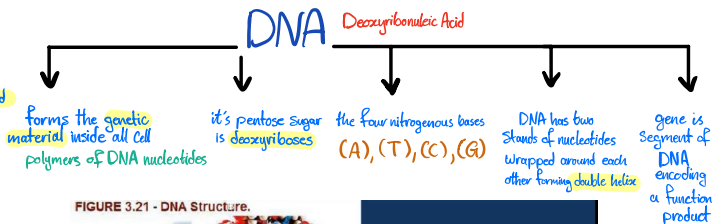
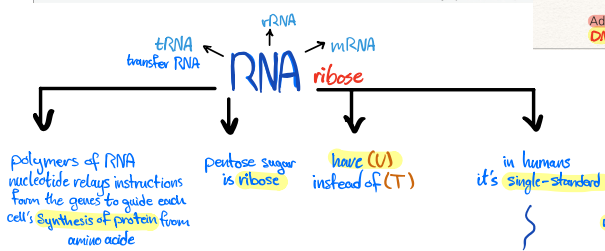
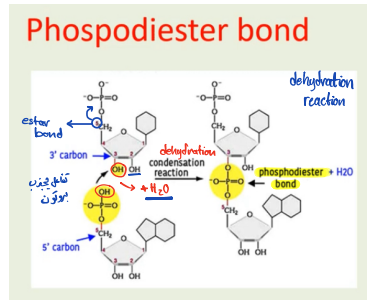
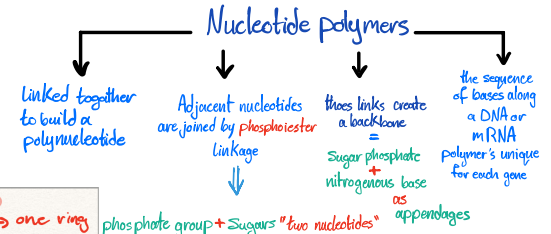
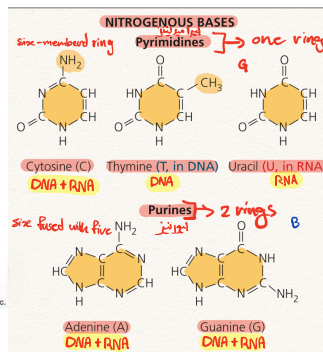
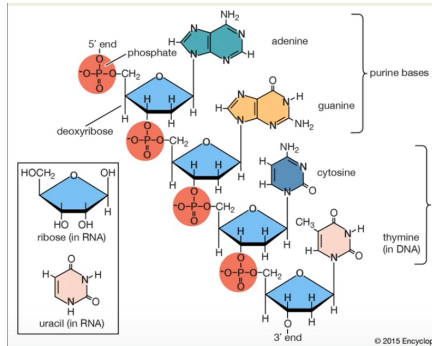
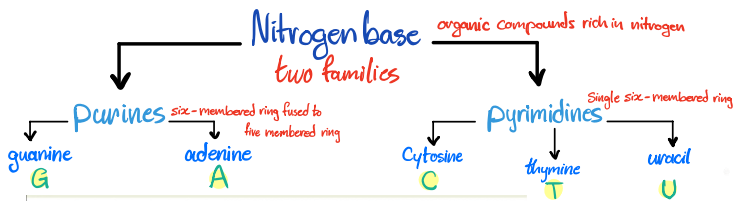
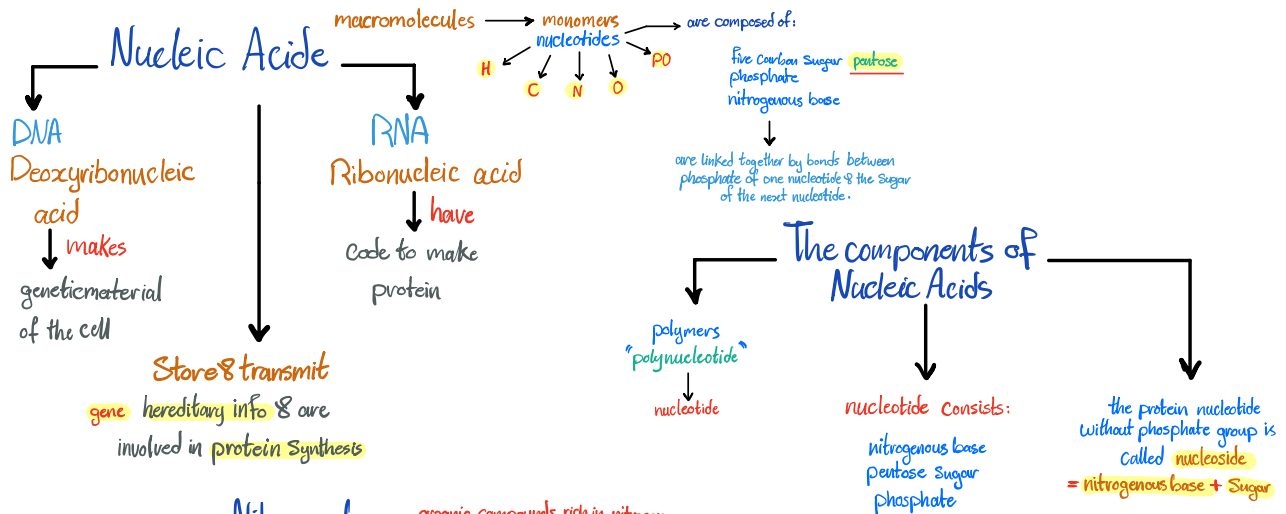
and bioinformatics (see Concept 5.6) are complementary approaches to understanding protein structure and function.

The structure of some proteins is difficult to determine for a simple reason: A growing body of biochemical research has revealed that a significant number of proteins, or regions of proteins, do not have a distinct 3-D structure until they interact with a target protein or other molecule. Their flexibility and indefinite structure are important for their function, which may require binding with different targets at different times. These proteins, which may account for 20–30% of mammalian proteins, are called *intrinsically disordered proteins* and are the focus of current research.

## CONCEPT CHECK 5.4

1. What parts of a polypeptide participate in the bonds that hold together secondary structure? Tertiary structure?
2. Thus far in the chapter, the Greek letters  $\alpha$  and  $\beta$  have been used to specify at least three different pairs of structures. Name and briefly describe them.
3. Each amino acid has a carboxyl group and an amino group. Are these groups present in a polypeptide? Explain.
4. **WHAT IF?** Where would you expect a polypeptide region rich in the amino acids valine, leucine, and isoleucine to be located in a folded polypeptide? Explain.

For suggested answers, see Appendix A.

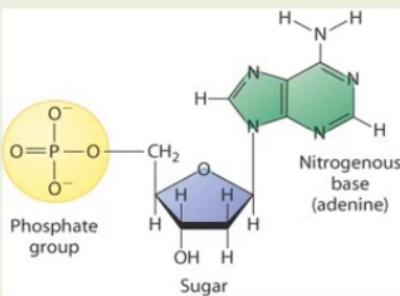




**Monomer of nucleic acids:** **nucleotide**

3 parts:

- sugar**
- phosphate**
- nitrogenous base**



Phosphate group

Sugar

Nitrogenous base (adenine)

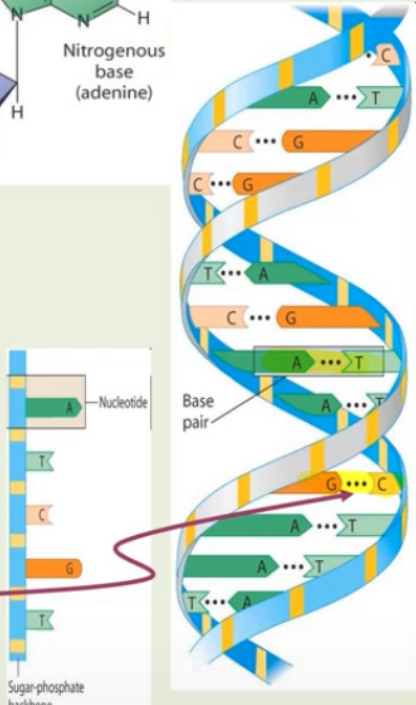
DNA is a double helix

- 4 bases **A= adenine T= thymine**
- C= cytosine G= guanine**
- base pairing rules

**A - T**      **C - G**

↓  
goes with U in RNA  
A - U → in RNA

- both strands are held together by **hydrogen bonds**



Nucleotide

Base pair

Sugar-phosphate backbone

TABLE 3.4		
DNA Structure Compared to RNA Structure		
	DNA	RNA
Sugar	Deoxyribose	Ribose
Bases	Adenine, guanine, thymine, cytosine	Adenine, guanine, uracil, cytosine
Strands	Double stranded with base pairing	Single stranded
Helix	Yes	No

## CONCEPT 5.5

# Nucleic acids store, transmit, and help express hereditary information

If the primary structure of polypeptides determines a protein's shape, what determines primary structure? The amino acid sequence of a polypeptide is programmed by a discrete unit of inheritance known as a **gene**. Genes consist of DNA, which belongs to the class of compounds called nucleic acids. **Nucleic acids** are polymers made of monomers called nucleotides.

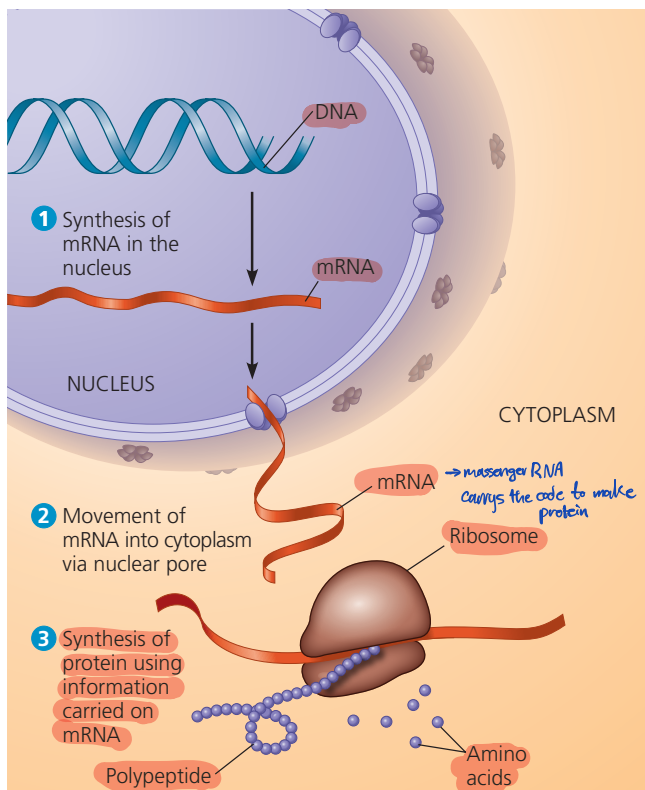
## The Roles of Nucleic Acids

The two types of nucleic acids, **deoxyribonucleic acid (DNA)** and **ribonucleic acid (RNA)**, enable living organisms to reproduce their complex components from one generation to the next. Unique among molecules, DNA provides directions for its own replication. DNA also directs RNA synthesis and, through RNA, controls protein synthesis; this entire process is called **gene expression** (Figure 5.22).

DNA is the genetic material that organisms inherit from their parents. Each chromosome contains one long DNA molecule, usually carrying several hundred or more genes. When a cell reproduces itself by dividing, its DNA molecules are copied and passed along from one generation of cells to the next. The information that programs all the cell's activities is encoded in the structure of the DNA. The DNA, however, is not directly involved in running the operations of the cell, any more than computer software by itself can read the bar code on a box of cereal. Just as a scanner is needed to read a bar code, proteins are required to implement genetic programs. The molecular hardware of the cell—the tools that carry out biological functions—consists mostly of proteins. For example, the oxygen carrier in red blood cells is the protein hemoglobin that you saw earlier (see Figure 5.18), not the DNA that specifies its structure.

How does RNA, the other type of nucleic acid, fit into gene expression, the flow of genetic information from DNA to proteins? A given gene along a DNA molecule can direct synthesis of a type of RNA called **messenger RNA (mRNA)**. The mRNA molecule interacts with the cell's protein-synthesizing machinery to direct production of a polypeptide, which folds into all or part of a protein. We can summarize the flow of genetic information as **DNA → RNA → protein** (see Figure 5.22). The sites of protein synthesis are cellular structures called ribosomes. In a eukaryotic cell, ribosomes are in the cytoplasm—the region between the nucleus and the cell's outer boundary, the plasma membrane—but DNA resides in the nucleus. Messenger RNA conveys genetic instructions for building proteins from the nucleus to the cytoplasm. Prokaryotic cells lack nuclei but still use mRNA to convey a message from the DNA to ribosomes and other cellular equipment that translate the coded information into amino acid sequences. Later, you'll read about other

▼ **Figure 5.22 Gene expression: DNA → RNA → protein.** In a eukaryotic cell, DNA in the nucleus programs protein production in the cytoplasm by dictating synthesis of messenger RNA (mRNA).



## ➔ Mastering Biology BioFlix® Animation: Gene Expression

functions of some recently discovered RNA molecules; the stretches of DNA that direct synthesis of these RNAs are also considered genes (see Concept 18.3).

## The Components of Nucleic Acids

Nucleic acids are macromolecules that exist as polymers called **polynucleotides** (Figure 5.23a). As indicated by the name, each polynucleotide consists of monomers called **nucleotides**. A nucleotide, in general, is composed of three parts: a five-carbon sugar (a pentose), a nitrogen-containing (nitrogenous) base, and one to three phosphate groups (Figure 5.23b). The beginning monomer used to build a polynucleotide has three phosphate groups, but two are lost during the polymerization process. The portion of a nucleotide without any phosphate groups is called a **nucleoside**.

To understand the structure of a single nucleotide, let's first consider the nitrogenous bases (Figure 5.23c). Each nitrogenous base has one or two rings that include nitrogen atoms. (They are called **nitrogenous bases** because the nitrogen atoms tend to take up  $H^+$  from solution, thus acting as bases.) There are two families of nitrogenous bases: pyrimidines and purines. A **pyrimidine** has one six-membered ring of carbon and nitrogen atoms. The members of the pyrimidine family are cytosine (C), thymine (T), and uracil (U).

**Purines** are larger, with a six-membered ring fused to a five-membered ring. The purines are adenine (A) and guanine (G). The specific pyrimidines and purines differ in the chemical groups attached to the rings. Adenine, guanine, and cytosine are found in both DNA and RNA; thymine is found only in DNA and uracil only in RNA.

Now let's add the sugar to which the nitrogenous base is attached. In DNA the sugar is **deoxyribose**; in RNA it is **ribose** (see Figure 5.23c). The only difference between these two sugars is that deoxyribose lacks an oxygen atom on the second carbon in the ring, hence the name *deoxyribose*.

So far, we have built a nucleoside (base plus sugar). To complete the construction of a nucleotide, we attach one to three phosphate groups to the 5' carbon of the sugar (the carbon numbers in the sugar include ', the prime symbol; see Figure 5.23b). With one phosphate, this is a nucleoside monophosphate, more often called a nucleotide.

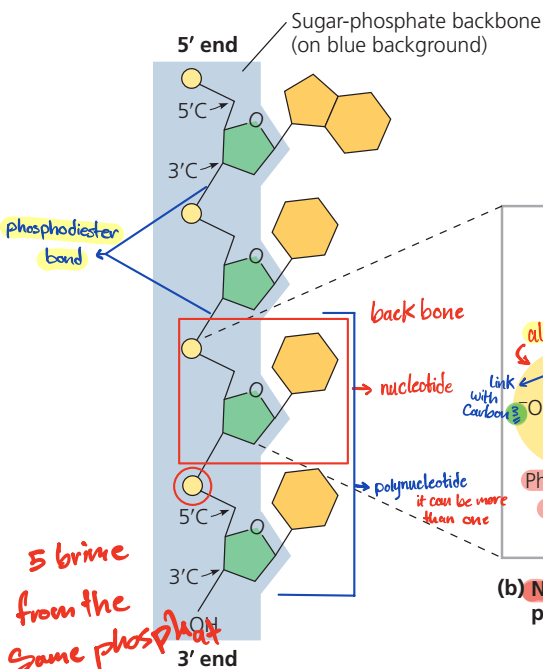
## Nucleotide Polymers

The linkage of nucleotides into a polynucleotide involves a condensation reaction. (You will learn the details in Concept 16.2.) In the polynucleotide, adjacent nucleotides are joined by a phosphodiester linkage, which consists of

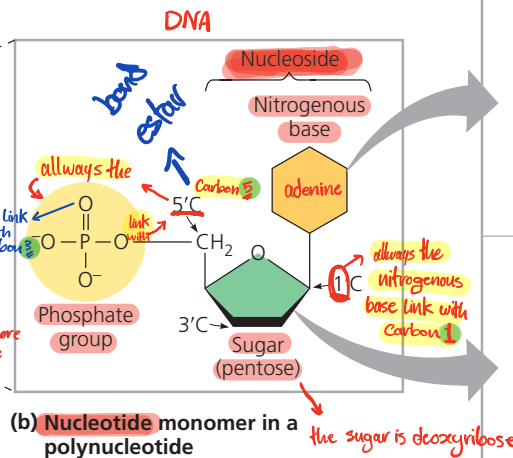
a phosphate group that covalently links the sugars of two nucleotides. This bonding results in a repeating pattern of sugar-phosphate units called the *sugar-phosphate backbone* (see Figure 5.23a). (Note that the nitrogenous bases are not part of the backbone.) The two free ends of the polymer are distinctly different from each other. One end has a phosphate attached to a 5' carbon, and the other end has a hydroxyl group on a 3' carbon; we refer to these as the *5' end* and the *3' end*, respectively. We can say that a polynucleotide has a built-in directionality along its sugar-phosphate backbone, from 5' to 3', somewhat like a one-way street. The bases are attached all along the sugar-phosphate backbone.

The sequence of bases along a DNA (or mRNA) polymer is unique for each gene and provides very specific information to the cell. Because genes are hundreds to thousands of nucleotides long, the number of possible base sequences is effectively limitless. The information carried by the gene is encoded in its specific sequence of the four DNA bases. For example, the sequence 5'-AGGTAAGT-3' means one thing, whereas the sequence 5'-CGCTTAAAC-3' has a different meaning. (Entire genes, of course, are much longer.) The linear order of bases in a gene specifies the amino acid sequence—the primary structure—of a protein, which in turn specifies that protein's 3-D structure, thus enabling its function in the cell.

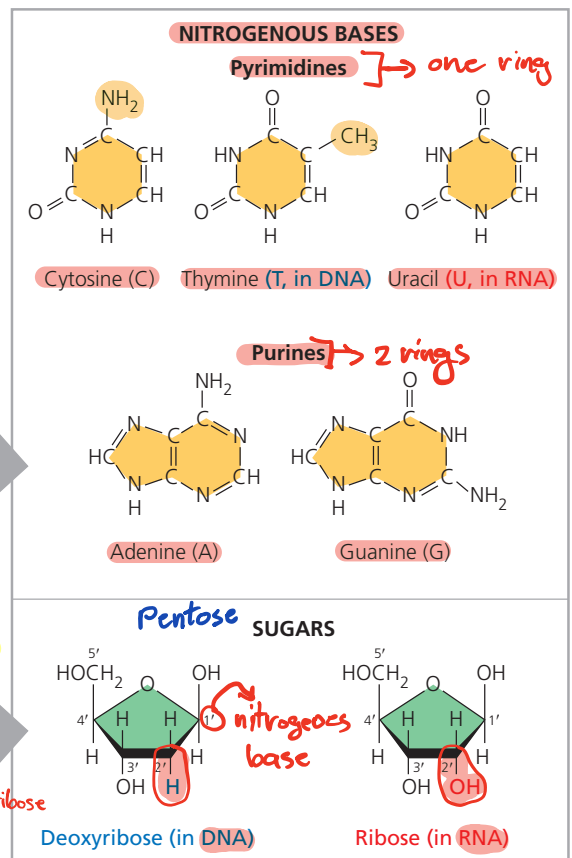
**Figure 5.23 Components of nucleic acids.** (a) A polynucleotide has a sugar-phosphate backbone with variable appendages, the nitrogenous bases. (b) In a polynucleotide, each nucleotide monomer includes a nitrogenous base, a sugar, and a phosphate group. Note that carbon numbers in the sugar include primes ('). (c) A nucleoside includes a nitrogenous base (purine or pyrimidine) and a five-carbon sugar (deoxyribose or ribose).



(a) Polynucleotide, or nucleic acid



(b) Nucleotide monomer in a polynucleotide



(c) Nucleoside components

Mastering Biology HHMI Animation: The Chemical Structure of DNA

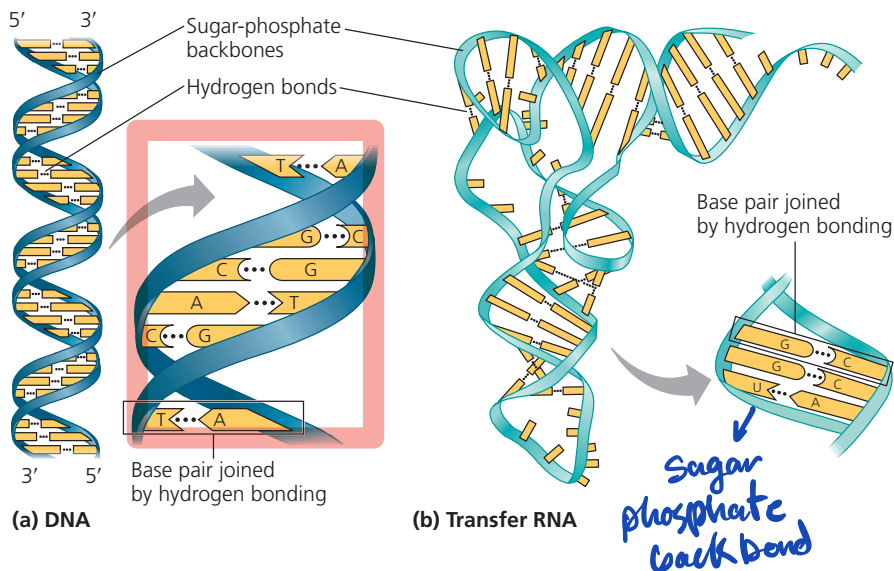




# Phospho diester bond

## ► Figure 5.24 The structures of DNA and tRNA molecules.

(a) The DNA molecule is usually a double helix, with the sugar-phosphate backbones of the antiparallel polynucleotide strands (symbolized here by blue ribbons) on the outside of the helix. Hydrogen bonds between pairs of nitrogenous bases hold the two strands together. As illustrated here with symbolic shapes for the bases, adenine (A) can pair only with thymine (T), and guanine (G) can pair only with cytosine (C). Each DNA strand in this figure is the structural equivalent of the polynucleotide diagrammed in Figure 5.23a. (b) A tRNA molecule has a roughly L-shaped structure due to complementary base pairing of antiparallel stretches of RNA. In RNA, A pairs with U.



► Mastering Biology HHMI  
Animation: Paired DNA Strands



## The Structures of DNA and RNA Molecules

A DNA molecule has two polynucleotides, or “strands,” that wind around an imaginary axis, forming a **double helix** (Figure 5.24a). The two sugar-phosphate backbones run in opposite 5' → 3' directions from each other; this arrangement is referred to as **antiparallel**, somewhat like a divided highway. The sugar-phosphate backbones are on the outside of the helix, and the nitrogenous bases are paired in the interior of the helix. The two strands are held together by hydrogen bonds between the paired bases (see Figure 5.24a). Most DNA molecules are very long, with thousands or even millions of base pairs. The one long DNA double helix in a eukaryotic chromosome includes many genes, each one a particular segment of the double-stranded molecule.

In base pairing, only **certain bases** in the double helix are compatible with each other. Adenine (A) in one strand always pairs with thymine (T) in the other, and guanine (G) always pairs with cytosine (C). Reading the sequence of bases along one strand of the double helix would tell us the sequence of bases along the other strand. If a stretch of one strand has the base sequence 5'-AGTCCG-3', then the base-pairing rules tell us that the same stretch of the other strand must have the sequence 3'-TCCAGGC-5'. The two strands of the double helix are **complementary**, each the predictable counterpart of the other. It is this feature of DNA that makes it possible to generate two identical copies of each DNA molecule in a cell that is preparing to divide. When the cell divides, the copies are distributed to the daughter cells, making them genetically identical to the parent cell. Thus, the structure of DNA accounts for its function of transmitting genetic information whenever a cell reproduces.

RNA molecules, by contrast, exist as single strands. Complementary base pairing can occur, however, between regions of two RNA molecules or even between two stretches of nucleotides in the same RNA molecule. In fact, base pairing within an RNA molecule allows it to take on the particular

three-dimensional shape necessary for its function. Consider, for example, the type of RNA called *transfer RNA (tRNA)*, which brings amino acids to the ribosome during the synthesis of a polypeptide. A tRNA molecule is about 80 nucleotides in length. Its functional shape results from base pairing between nucleotides where complementary stretches of the molecule can run antiparallel to each other (Figure 5.24b).

Note that in RNA, adenine (A) pairs with uracil (U); thymine (T) is not present in RNA. Another difference between RNA and DNA is that DNA almost always exists as a double helix, whereas RNA molecules are more variable in shape. RNAs are versatile molecules, and many biologists believe RNA may have preceded DNA as the carrier of genetic information in early forms of life (see Concept 25.1).

► Mastering Biology Animation: Nucleic Acid Structure

### CONCEPT CHECK 5.5

- DRAW IT** In Figure 5.23a, number all the carbons of the top three nucleotides (use primes), circle the nitrogenous bases, and star the phosphates.
- DRAW IT** A region along one DNA strand has this sequence of nitrogenous bases: 5'-TAGGCCT-3'. Write down its complementary strand, labeling the 5' and 3' ends.

For suggested answers, see Appendix A.



## Genomics and proteomics have transformed biological inquiry and applications

Experimental work in the first half of the 20th century established the role of DNA as the carrier of genetic information, passed from generation to generation, that specified the functioning of living cells and organisms. Once the structure