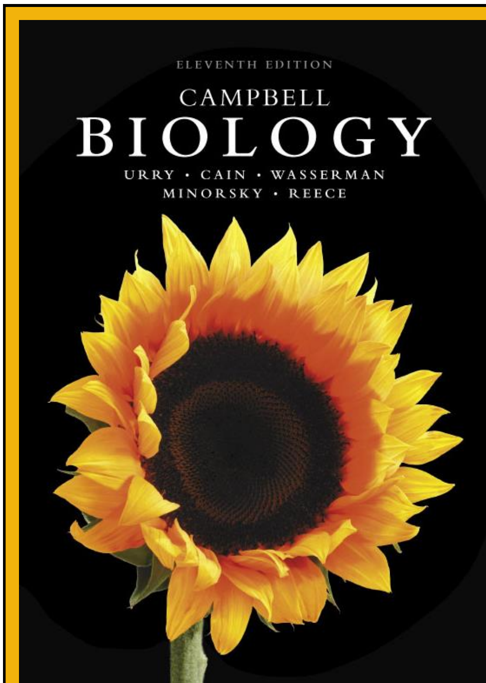


Chapter 5

The Structure and Function of Large Biological Molecules

Lecture Presentations by
Nicole Tunbridge and
Kathleen Fitzpatrick

The Molecules of Life

- All living things are made up of four classes of large biological molecules: ***carbohydrates***, ***lipids***, ***proteins***, and ***nucleic acids***
- **Macromolecules** are large molecules and are complex
- Large biological molecules have *unique properties* that arise from the *orderly arrangement of their atoms* (Structure-function)

Figure 5.1a

The scientist in the foreground is using 3-D glasses to help her visualize the structure of the protein displayed on her screen.

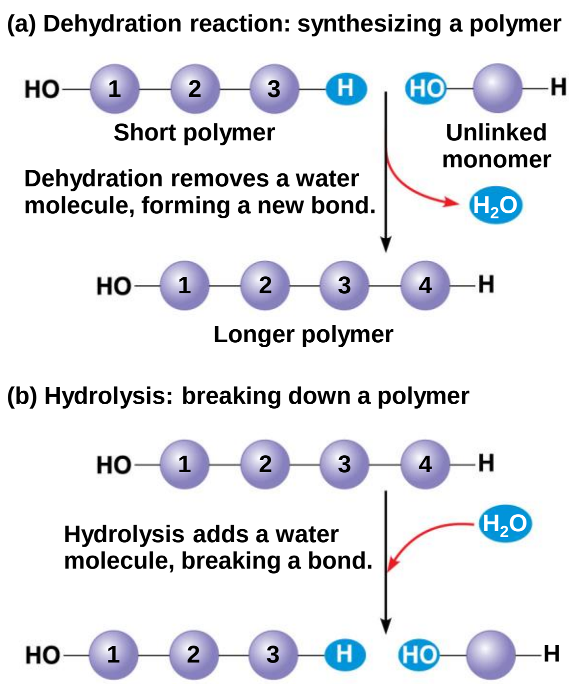
Concept 5.1: Macromolecules are polymers, built from monomers

- A **polymer** is a long molecule consisting of many similar building blocks
- The repeating units that serve as building blocks are called **monomers**
- Carbohydrates, proteins, and nucleic acids are polymers
- Lipids are not polymers

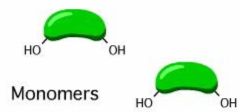
The Synthesis and Breakdown of Polymers

- **Enzymes** are specialized macromolecules that speed up chemical reactions such as those that make or break down polymers
- A **dehydration reaction** occurs when two monomers bond together through the loss of a water molecule *(SYNTHESIS)*
- Polymers are disassembled to monomers by **hydrolysis**, a reaction that is essentially the reverse of the dehydration reaction *(BREAKDOWN)*

Figure 5.2



Animation: Polymers



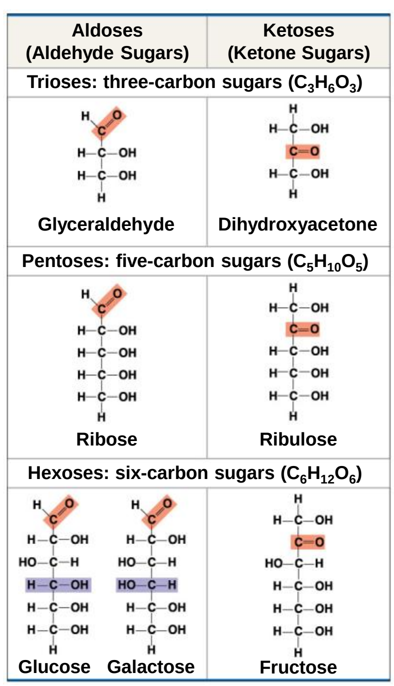
Concept 5.2: Carbohydrates serve as fuel and building material

- **Carbohydrates** include *sugars* and the *polymers of sugars*
- The simplest carbohydrates are **monosaccharides**, or simple sugars
- Carbohydrate macromolecules are **polysaccharides**, polymers composed of many sugar building blocks

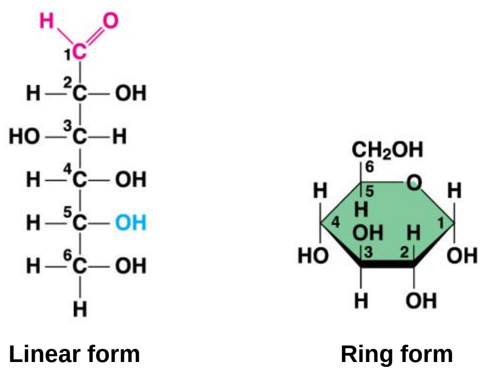
Sugars

- **Monosaccharides** serve as a major fuel for cells and as raw material for building molecules
- Monosaccharides have molecular formulas that are usually multiples of CH_2O
- **Glucose** ($C_6H_{12}O_6$) is the most common monosaccharide
- Monosaccharides are classified by
  - The location of the carbonyl group (as ald**ose** or ket**ose**)
  - The number of carbons in the carbon skeleton (tri**ose**, tetr**ose**, pent**ose**, hex**ose**, etc.)

Figure 5.3

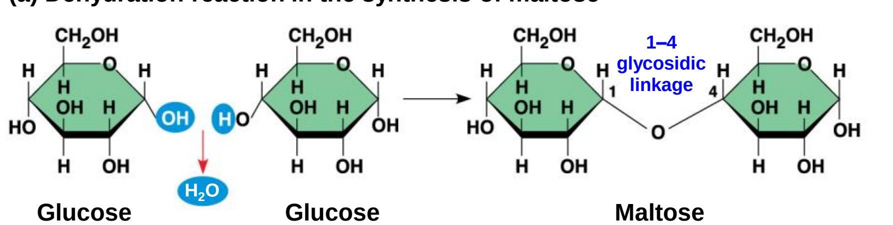


- In aqueous solutions many sugars form **rings**

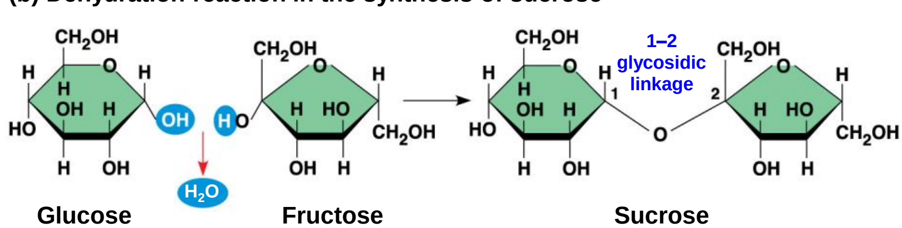


- A **disaccharide** is formed when a *dehydration reaction* joins two monosaccharides
- This covalent bond is called a **glycosidic linkage (bond)**

(a) Dehydration reaction in the synthesis of maltose



(b) Dehydration reaction in the synthesis of sucrose



Polysaccharides

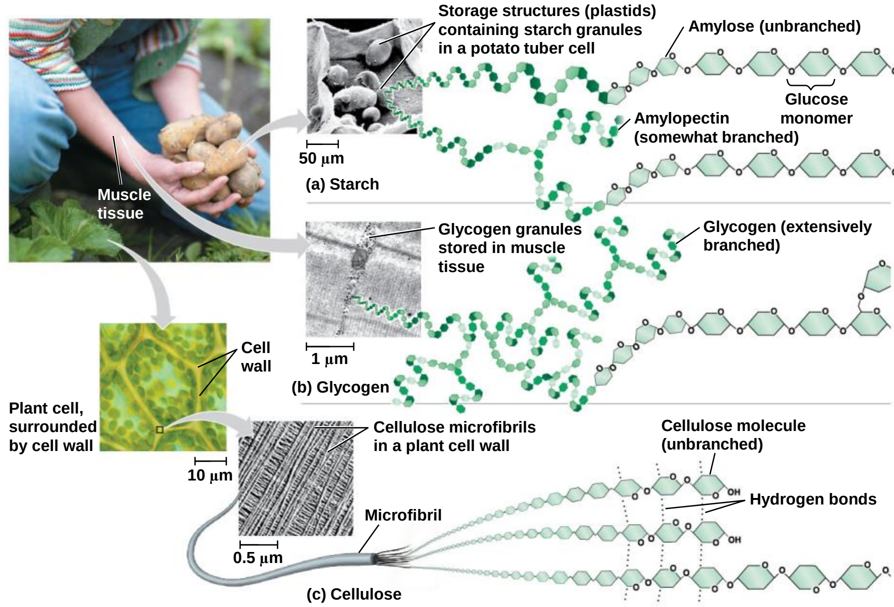
- **Polysaccharides**, the polymers of sugars, have storage and structural roles
- The architecture and function of a polysaccharide are determined by: *its sugar monomers* and *the positions of its glycosidic linkages*

Storage Polysaccharides

- **Starch** is a storage polysaccharide of plants
- Consists of glucose monomers
- Plants store extra starch as **granules** within chloroplasts and other plastids
- The simplest form of starch is **amylose**

- **Glycogen** is a storage polysaccharide in animals
- Consists of glucose monomers
- Glycogen is stored as granules in *liver* and *muscle*
- Hydrolysis of glycogen in these cells releases glucose when the demand for sugar increases

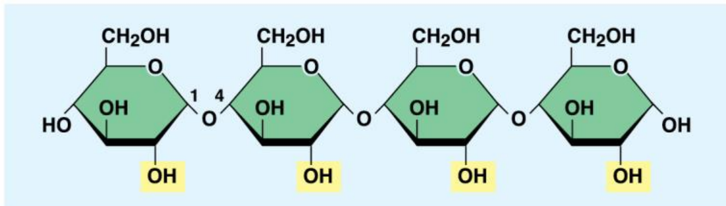
Figure 5.6



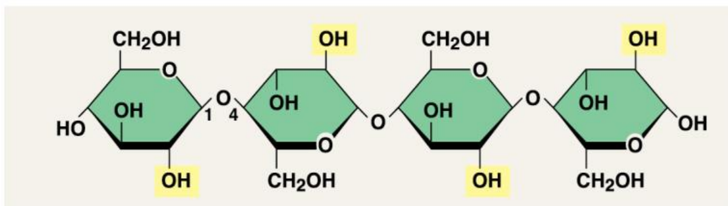
Structural Polysaccharides

- The polysaccharide **cellulose** is a major component of the *tough wall of plant cells*
- Like starch and glycogen, cellulose is a polymer of glucose, but the glycosidic linkages are different
- ***The difference is based on two ring forms for glucose: alpha (α) and beta (β)***

Figure 5.7b



(b) Starch and glycogen: 1–4 linkage of α glucose monomers



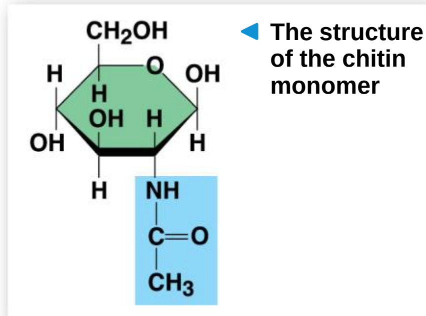
(c) Cellulose: 1–4 linkage of β glucose monomers

- Starch (α configuration) is largely **helical**
- Cellulose molecules (β configuration) are **straight** and **unbranched**
- Some hydroxyl groups on the monomers of cellulose can hydrogen-bond with hydroxyls of parallel cellulose molecules

- Enzymes that digest starch by hydrolyzing α linkages can't hydrolyze β linkages in cellulose
- The cellulose in human food passes through the digestive tract as "**insoluble fiber**"
- Some microbes use enzymes to digest cellulose
- Many herbivores, from cows to termites, have **symbiotic** relationships with these microbes

- **Chitin**, another structural polysaccharide, is found in the exoskeleton of arthropods (حشرات)
- Chitin also provides structural **support** for the cell walls of many fungi

Figure 5.8



The structure of the chitin monomer

Chitin, embedded in proteins, forms the exoskeleton of arthropods.

Class activity!

- How many molecules of water are needed to completely hydrolyze a polymer that is ten monomers long?
- 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?

Class activity!

- A dehydration reaction joins 2 molecules of glucose to form maltose. The formula for glucose is C6H12O6. What is the formula for maltose?

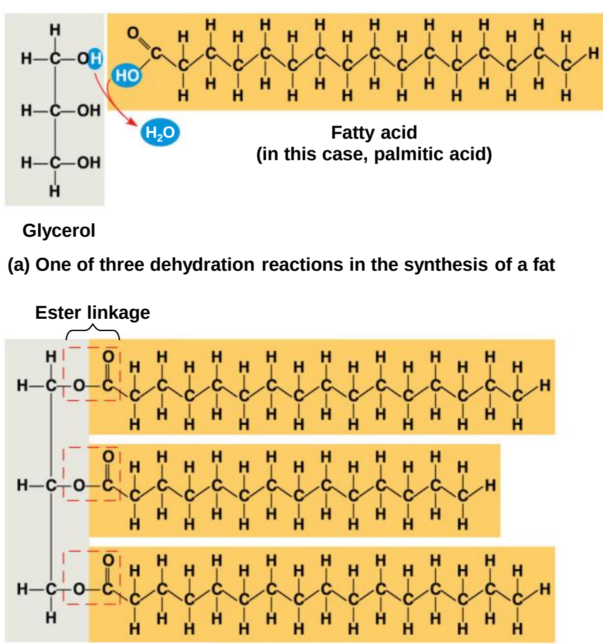
Concept 5.3: Lipids are a diverse group of hydrophobic molecules

- **Lipids** are the only class of large biological molecules that <u>does not</u> include true polymers
- The unifying feature of lipids is that they do not like water and don't mix well with it (**HYDROPHOBIC**)
- Lipids consist mostly of hydrocarbon regions
- The most biologically important lipids are **fats**, **phospholipids**, and **steroids**

Fats

- **Fats** are made from two types of smaller molecules: glycerol and fatty acids
- *Glycerol is a three-carbon alcohol* with a hydroxyl group attached to each carbon
- A **fatty acid** consists of a carboxyl group attached to a long carbon skeleton

Figure 5.9

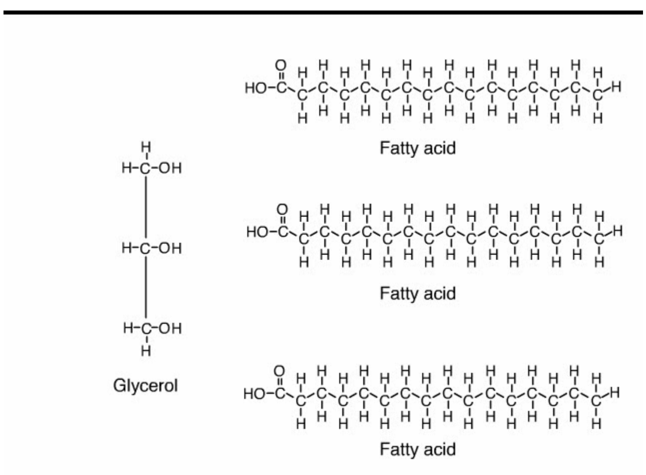


(a) One of three dehydration reactions in the synthesis of a fat

(b) Fat molecule (triacylglycerol)

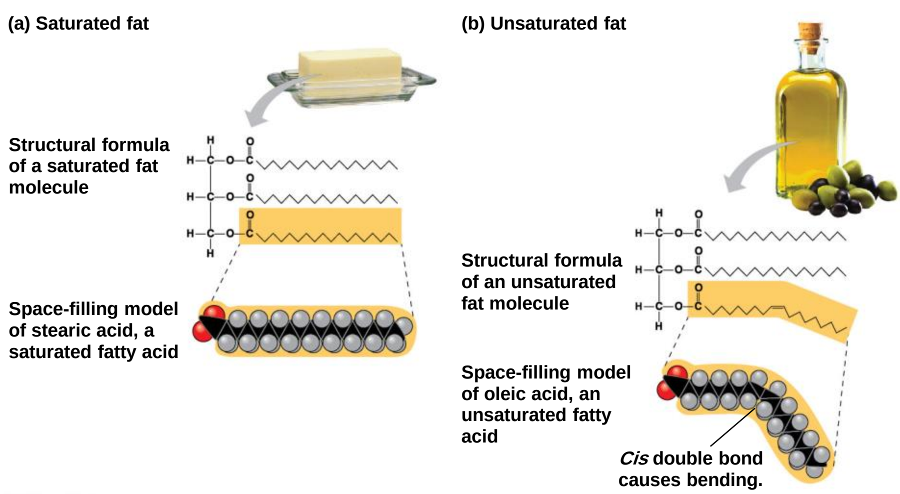
- Fats separate from water because water molecules hydrogen-bond to each other and exclude the fats
- In a fat, three fatty acids are joined to glycerol by an **ester linkage**, creating a **triacylglycerol**, or triglyceride
- The fatty acids in a fat can be all the same or different

Animation: Fats



- Fatty acids vary in length (number of carbons) and in the number and locations of double bonds
- **Saturated fatty acids** have the maximum number of hydrogen atoms possible and no double bonds
- **Unsaturated fatty acids** have one or more double bonds

Figure 5.10



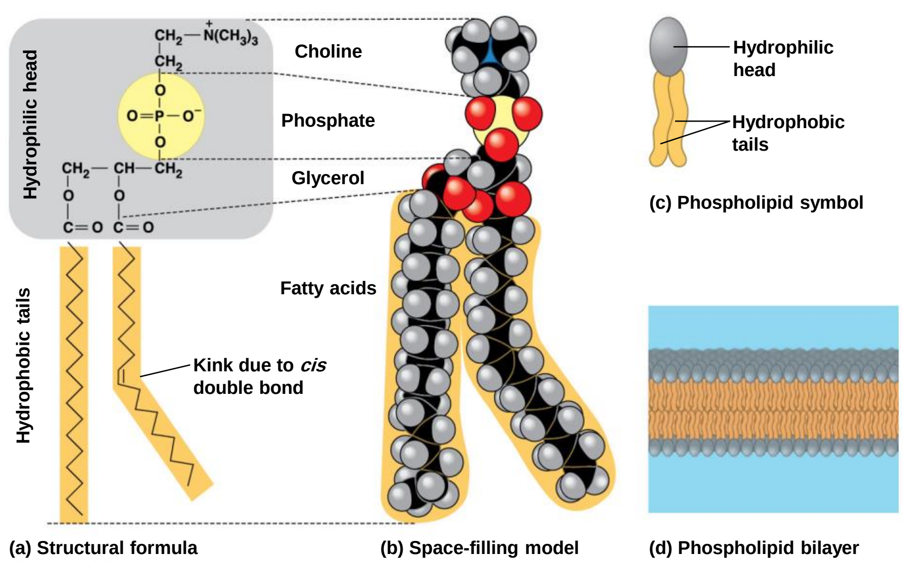
- Fats made from saturated fatty acids are called **saturated fats** and are *solid* at room temperature
- Most animal fats are saturated
- Fats made from unsaturated fatty acids are called unsaturated fats or oils and are *liquid* at room temperature
- Plant fats and fish fats are usually unsaturated

- The major function of fats is energy storage
- Humans and other mammals store their long-term food reserves in **adipose cells**
- Adipose tissue also cushions vital organs and insulates the body

Phospholipids

- In a **phospholipid**, two fatty acids and a phosphate group are attached to glycerol
- The two fatty acid tails are *hydrophobic*, but the phosphate group and its attachments form a *hydrophilic* head
- The molecule is therefore **AMPHIPATHIC** (both hydrophobic and hydrophilic)

Figure 5.11

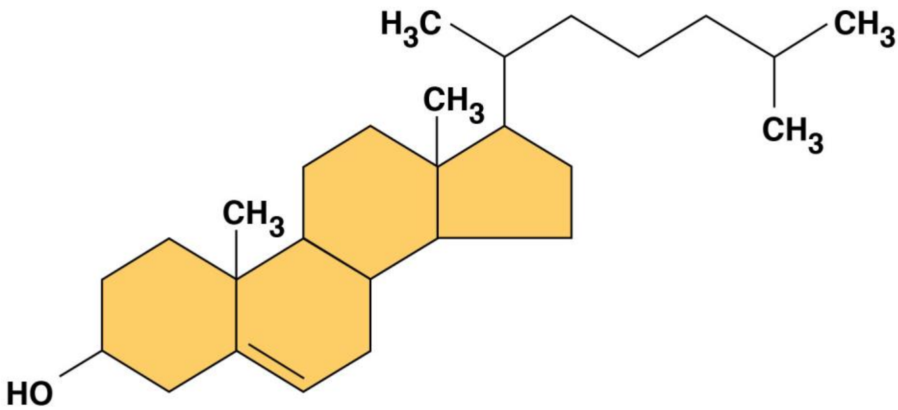


- When phospholipids are added to water, they self-assemble into double-layered sheets called **bilayers**
- At the surface of a cell, phospholipids are also arranged in a bilayer, with the hydrophobic tails pointing toward the interior
- The phospholipid bilayer forms a boundary between the cell and its external environment

Steroids

- **Steroids** are lipids characterized by a carbon skeleton consisting *of four fused rings*
- **Cholesterol**, a type of steroid, is a component in animal cell membranes and a precursor from which other steroids are synthesized
- A high level of cholesterol in the blood may contribute to cardiovascular disease
- Some hormones, such as sex hormones, are made from cholesterol

Figure 5.12



Class activity!

- Why are human sex hormones are considered lipids?
- 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?

Concept 5.4: Proteins include a diversity of structures, resulting in a wide range of functions

- Proteins make more than 50% of the **dry mass of most cells**
- Functions:
- Some proteins *speed up* chemical reactions (***Enzymes*** act as **catalysts** to accelerate reactions)
- Other protein functions include defense, storage, transport, cellular communication, movement, and structural support

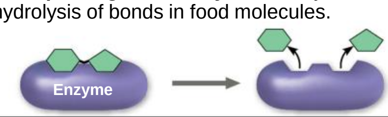
Figure 5.13a

Some Functions of Proteins

Enzymatic proteins

Function: ***Selective acceleration of chemical reactions***

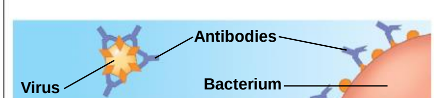
Example: Digestive enzymes catalyze the hydrolysis of bonds in food molecules.



Defensive proteins

Function: ***Protection against disease***

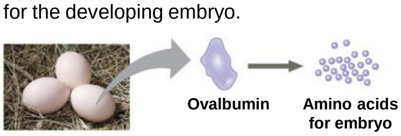
Example: Antibodies inactivate and help destroy viruses and bacteria.



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.

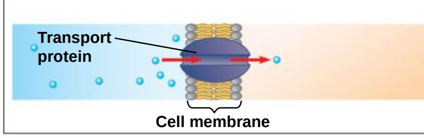
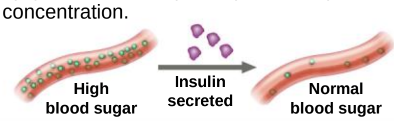


Figure 5.13b

Hormonal proteins

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

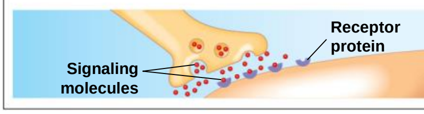
Example: Insulin, a hormone secreted by the pancreas, causes other tissues to take up glucose, thus regulating blood sugar concentration.



Receptor proteins

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

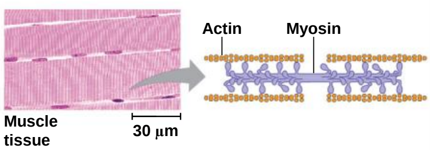
Example: Receptors built into the membrane of a nerve cell detect signaling molecules released by other nerve cells.



Contractile and motor proteins

Function: ***Movement***

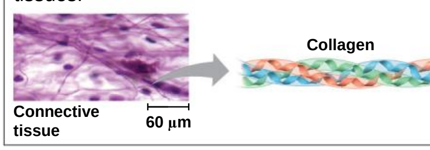
Examples: Motor proteins are responsible for the undulations of cilia and flagella. **Actin and myosin** proteins are responsible for the contraction of muscles.



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.



- Proteins are all made from the same set of **20 amino acids**
- **Polypeptides** are *unbranched* polymers built from these amino acids
- A **protein** is a biologically functional molecule that consists of one or more polypeptides

Amino Acid Monomers

- **Amino acids** are organic molecules with *amino* and *carboxylic acid* groups
- Amino acids differ in their properties due to differing *side chains*, called *R groups*

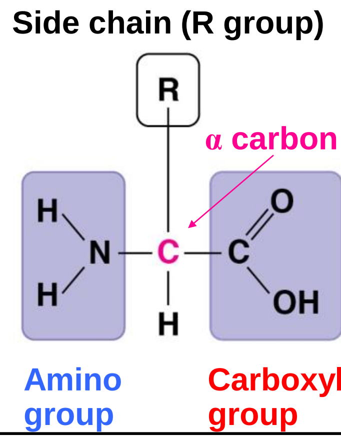
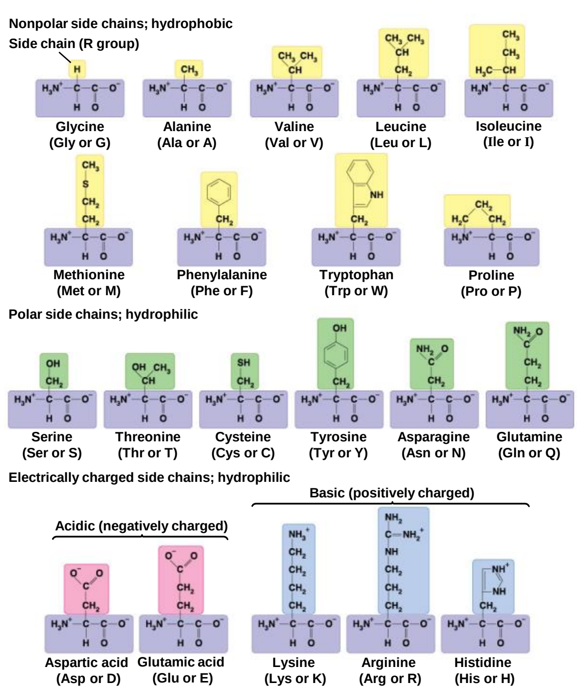


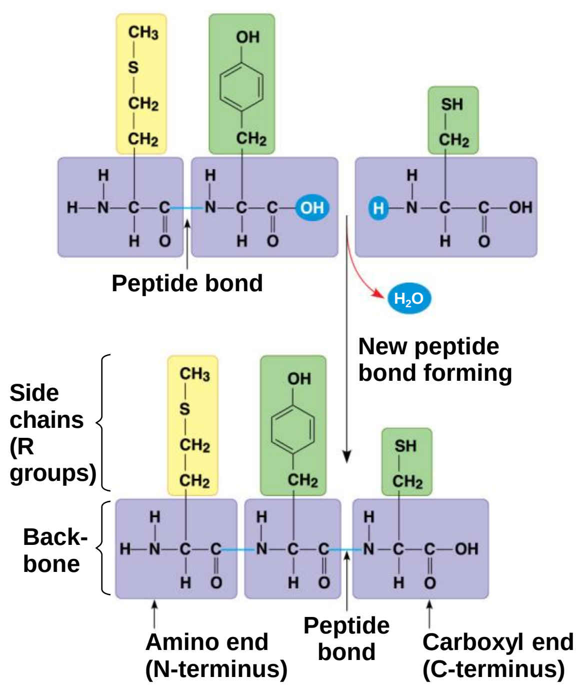
Figure 5.14



Polypeptides (Amino Acid Polymers)

- Amino acids are joined by *covalent bonds* called **peptide bonds**
- **A polypeptide is a polymer of amino acids**
- Polypeptides range in length from a few to more than 1,000 monomers
- Each polypeptide has a unique linear sequence of amino acids, with a carboxyl end (**C-terminus**) and an amino end (**N-terminus**)

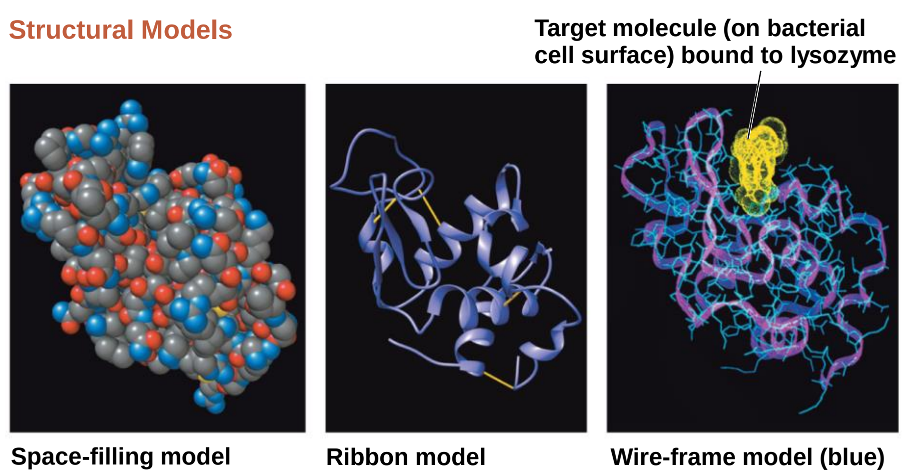
Figure 5.15



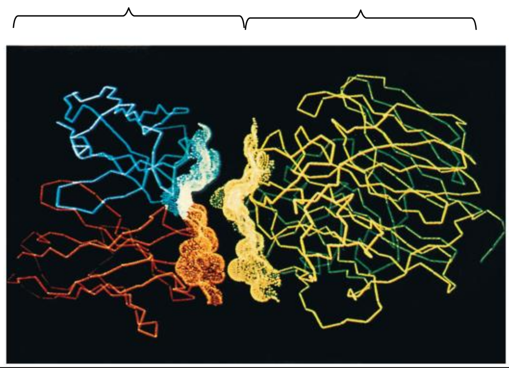
Protein Structure and Function

- The *specific activities* of proteins are due to their detailed *three-dimensional architecture*
- A functional protein consists of one or more polypeptides **precisely twisted, folded, and coiled into a unique shape**

Figure 5.16a



- The *amino acids sequence* determines a *protein's three-dimensional structure*
- A *protein's structure* determines how it works (*function*)
- The function of a protein usually depends on its ability to recognize and ***bind*** to other molecules



Four Levels of Protein Structure

- The ***primary structure*** of a protein is its unique sequence of amino acids
- ***Secondary structure***, found in most proteins, consists of coils and folds in the polypeptide chain
- ***Tertiary structure*** is determined by interactions among various side chains (R groups)
- ***Quaternary structure*** results when a protein consists of multiple polypeptide chains

Figure 5.18a

Primary Structure

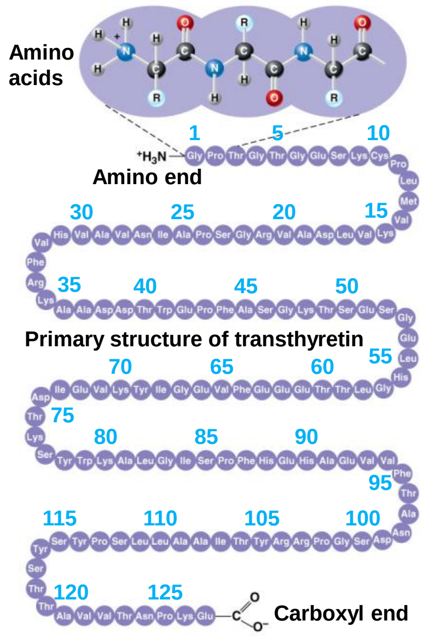
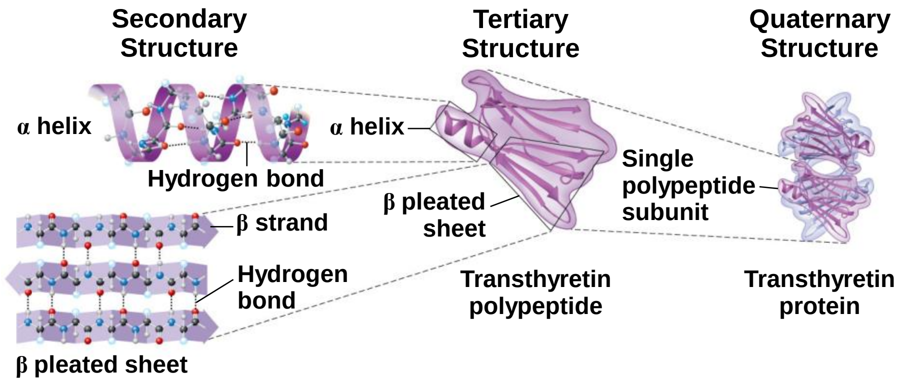


Figure 5.18b



- The **primary structure** of a protein is its *sequence of amino acids*
- Primary structure is like the *order of letters in a long word*
- Primary structure is determined *by inherited genetic information*
- E.g.

H_3N^+–Met-Tyr-Trp-Ala-Pro-Lys-Ala-Gly-Asp–COO^-

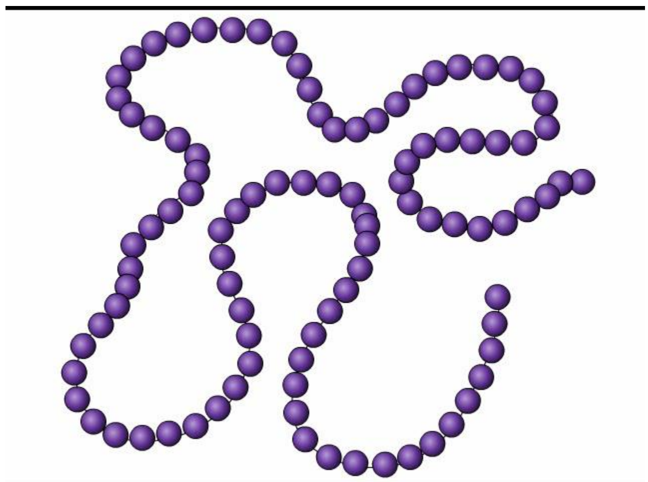
Is different from:

H_3N^+–Asp-Gly-Ala-Lys-Pro-Ala-Trp-Tyr-Met–COO^-

(Remember: RAT and TAR are different)

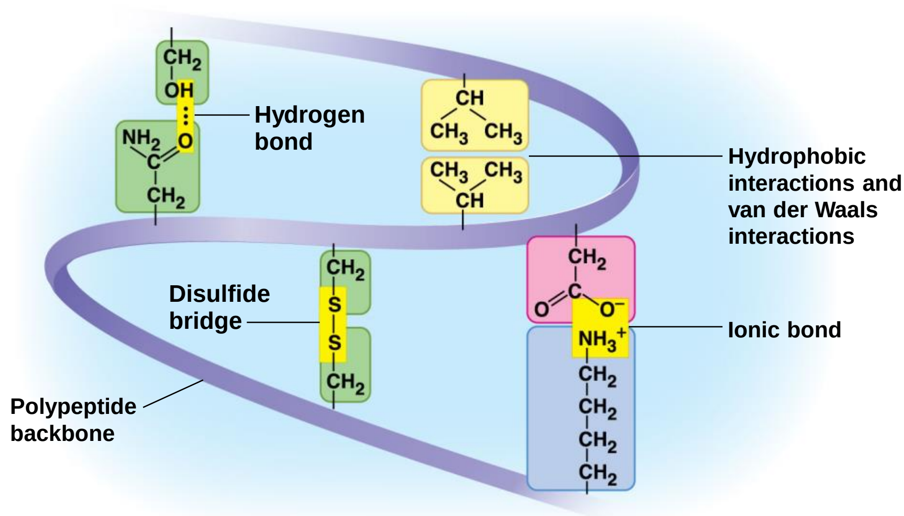
- The coils and folds of **secondary structure** result from hydrogen bonds between *repeating units of the polypeptide **backbone***
- Typical secondary structures are a *coil* called an ***α helix*** and a *folded structure* called a ***β pleated sheet***

Animation: Secondary Protein Structure



- **Tertiary structure**, the *overall shape* of a polypeptide, results from *interactions between R groups*, (not interactions between backbone units)
- These interactions include **hydrogen bonds**, **ionic bonds**, **hydrophobic interactions**, and **van der Waals interactions**
- *Strong covalent bonds* called **disulfide bridges** may strengthen the protein's structure

Figure 5.18d



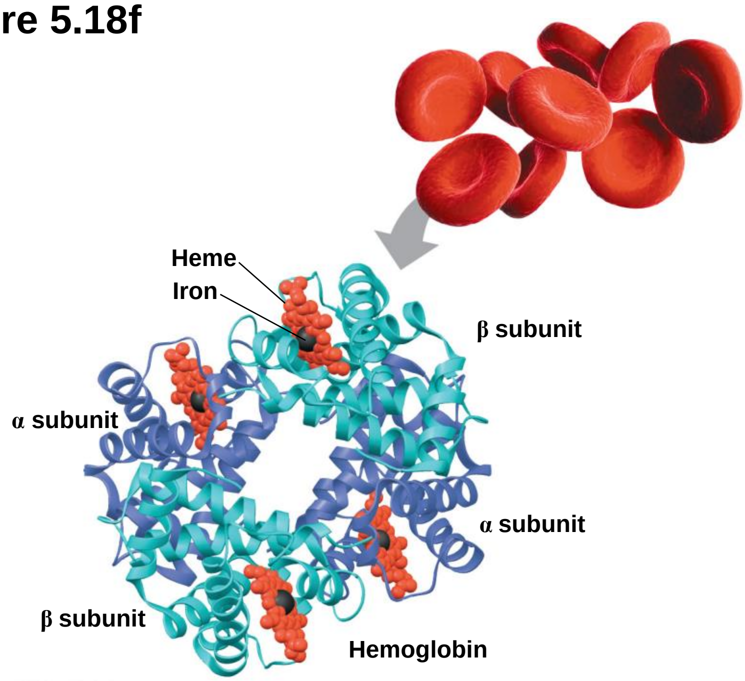
- **Quaternary structure** results when *two or more polypeptide chains form one macromolecule*

- E.g.

\- *Collagen* is a fibrous protein consisting of three polypeptides coiled like a rope

\- *Hemoglobin* is a globular protein consisting of four polypeptides: two α and two β subunits

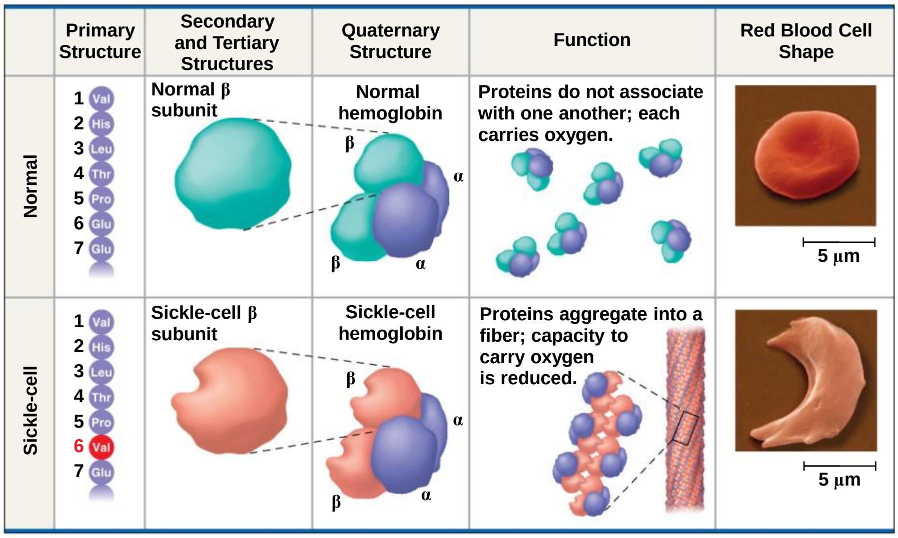
Figure 5.18f



Sickle-Cell Disease: A Change in Primary Structure

- *A slight change in primary structure can affect a protein's structure and ability to function*
- **Sickle-cell disease**, an inherited blood disorder, results from *a single amino acid substitution* in the protein hemoglobin
- The abnormal hemoglobin molecules cause the red blood cells to **aggregate** into chains and to deform into a **sickle shape**

Figure 5.19



Class activity!

- In a DNA double helix, a region along one strand has this sequence 5’-TAGGCCT-3’.
- Copy this sequence and write down the complementary strand, clearly indicating the orientation of the 2 strands.

Homework!

- Comparisons of amino acid sequences can shed light of the evolutionary divergence of related species. If you were comparing two living species, would you expect all proteins to show the same degree of divergence? Why or Why no?

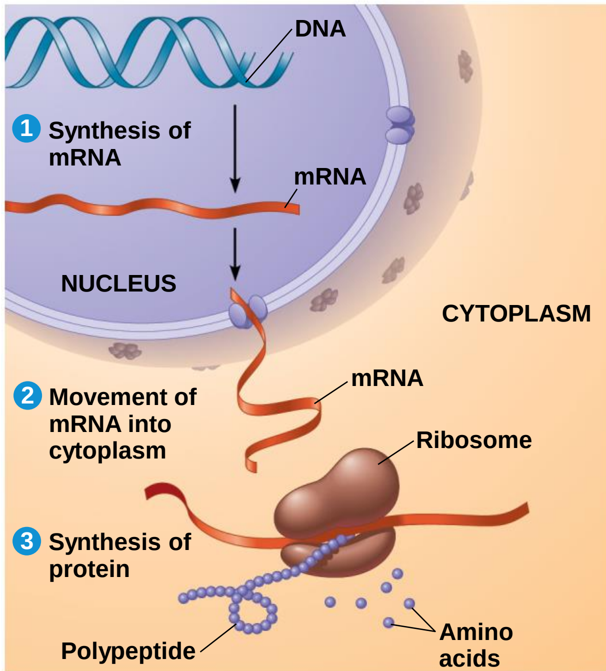
Concept 5.5: Nucleic acids store, transmit, and help express hereditary information

- The amino acid sequence of a polypeptide is programmed by a unit of inheritance called a **gene**
- Genes consist of DNA, a **nucleic acid** made of monomers called ***nucleotides***

The Roles of Nucleic Acids

- There are two types of nucleic acids
  - **Deoxyribonucleic acid (DNA)**
  - **Ribonucleic acid (RNA)**
- *DNA provides directions for its own replication*
- *DNA directs synthesis of messenger RNA (mRNA)* and, through mRNA, *controls protein synthesis*
- This process is called **gene expression**

Figure 5.22_3



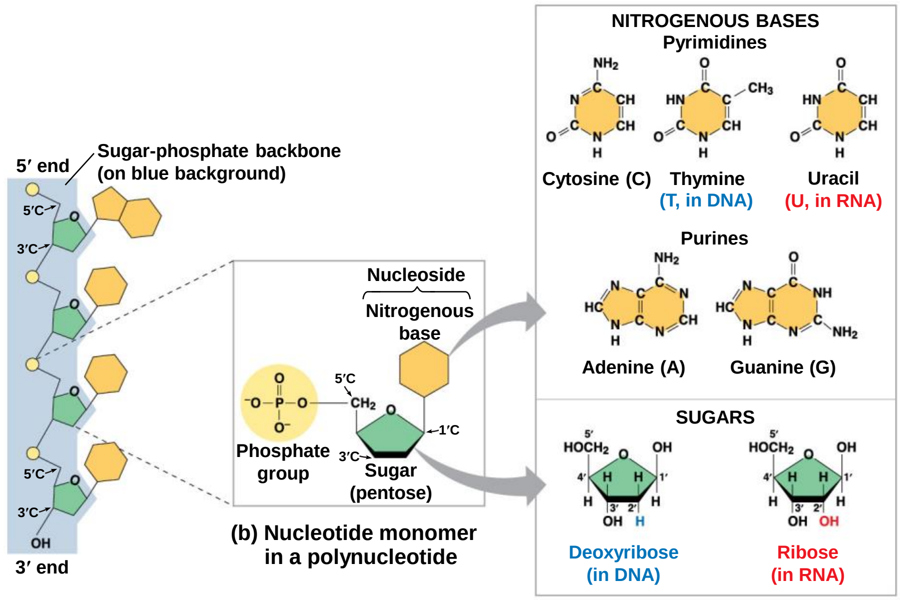
- Each gene along a DNA molecule directs synthesis of a messenger RNA (mRNA)
- The mRNA molecule interacts with the cell's protein-synthesizing machinery to direct production of a polypeptide
- The **flow of genetic information** can be summarized as ***DNA → RNA → protein***

The Components of Nucleic Acids

- Nucleic acids are *polymers* called **polynucleotides**
- Each polynucleotide is made of monomers called **nucleotides**
- Each nucleotide consists of a **nitrogenous base**, a **pentose sugar**, and one or more **phosphate groups**
- The portion of a nucleotide without the phosphate group is called a **nucleoside** (nitrogenous base + pentose sugar only)
- *Nucleoside* = nitrogenous base + sugar
- *Nucleotide* = nucleoside + phosphate group

- There are **two families** of nitrogenous bases
  - **Pyrimidines** (*cytosine (C)*, *thymine (T)*, and *uracil (U)*) have a single six-membered ring
  - **Purines** (*adenine (A)* and *guanine (G)*) have a six-membered ring fused to a five-membered ring
- In DNA, the sugar is **deoxyribose**; in RNA, the sugar is **ribose**

Figure 5.23

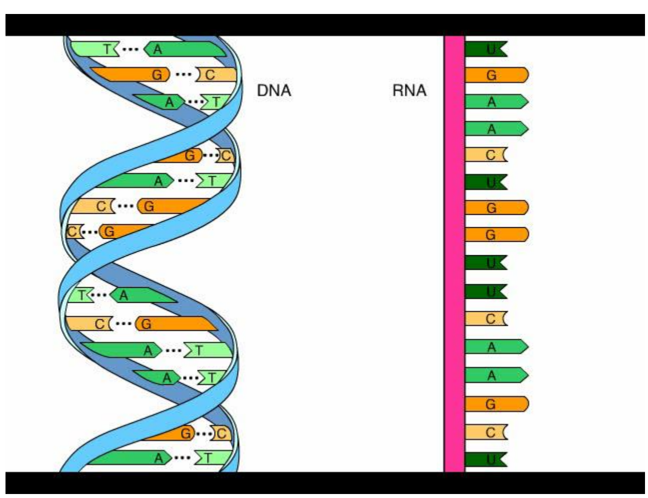


(a) Polynucleotide, or nucleic acid

(b) Nucleotide monomer in a polynucleotide

(c) Nucleoside components

Animation: DNA and RNA Structure



Nucleotide Polymers

- Nucleotides are linked together by **phosphodiester linkages** to build a polynucleotide
- A phosphodiester linkage consists of a *phosphate group that links the sugars of two nucleotides*
- These links create a ***backbone of sugar-phosphate*** units with nitrogenous bases as appendages
- The *sequence of bases* along a DNA or mRNA polymer is unique for each gene

The Structures of DNA and RNA Molecules

- DNA molecules have two polynucleotides spiraling around an imaginary axis, forming a **double helix**
- The backbones *run in opposite 5′ → 3′ directions* from each other, an arrangement referred to as **antiparallel**
- One DNA molecule includes many genes

- Only certain bases in DNA pair up and form hydrogen bonds: adenine (A) always with thymine (T), and guanine (G) always with cytosine (C)
- This is called ***complementary base pairing***
- This feature of DNA structure makes it possible to generate two identical copies of each DNA molecule in a cell preparing to divide

- RNA, in contrast to DNA, is *single-stranded*
- Complementary pairing can also occur between two RNA molecules or between parts of the same molecule
- In RNA, thymine is replaced by uracil (U), so **A can pair with U**
- RNA can also have other base pairing
- While DNA always exists as a double helix, RNA molecules are more variable in form

DNA and RNA Base Pairing Rules

DNA to DNA

- *Possible Bases:* Adenine, Thymine, Cytosine, Guanine
- G↔C, A↔T
- A and G are purines (double-ring), C and T are pyrimidines (single-ring)

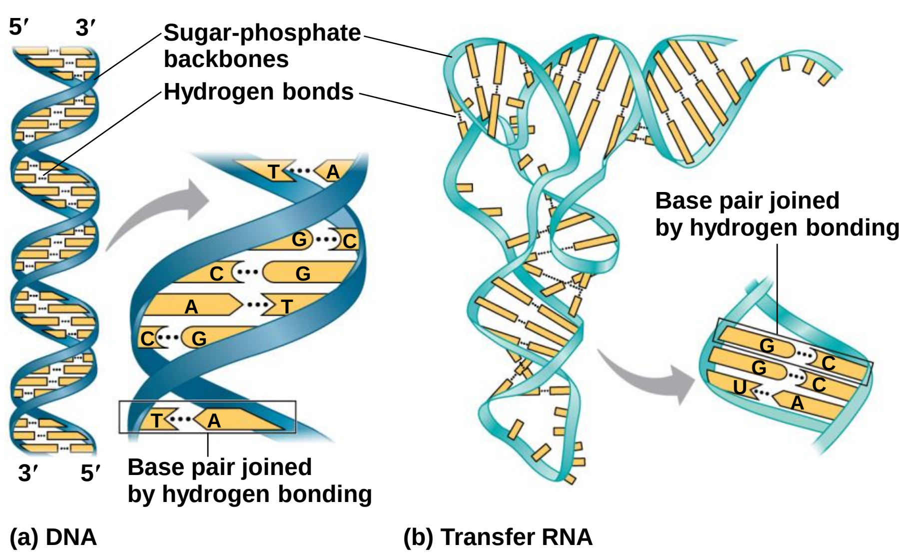
DNA to mRNA

- *Possible Bases:* Adenine, Thymine, Cytosine, Guanine, Uracil (RNA only)
- G↔C, A→U, T→A
- A and G are purines (double-ring), C, T, and U are pyrimidines (single-ring)

mRNA to tRNA

- *Possible Bases:* Adenine, Cytosine, Guanine, Uracil
- G↔C, A↔U
- A and G are purines (double-ring), C, T, and U are pyrimidines (single-ring)

Figure 5.24



Animation: DNA Double Helix

Concept 5.6: Genomics and proteomics have transformed biological inquiry and applications

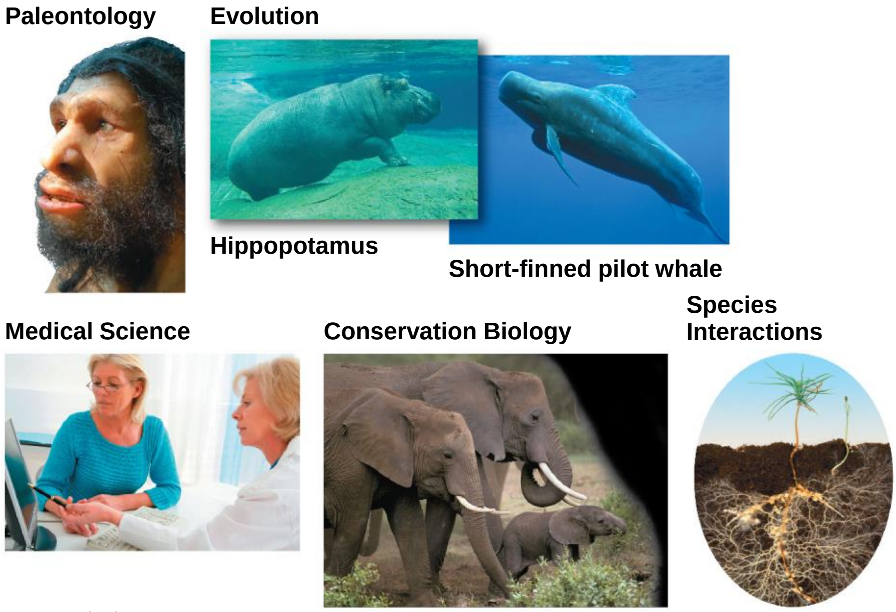
- Once the structure of DNA and its relationship to amino acid sequence was understood, biologists wanted to "decode" genes by learning their base sequences
- The first chemical techniques for **DNA sequencing** were developed in the 1970s and made better over the next 20 years
- The rapid development of faster and less expensive methods of sequencing was a side effect of the **Human Genome Project**
- Many genomes (including human) have been sequenced, generating large sets of data

Figure 5.25

- **Bioinformatics** uses *computer software* and other *computational tools* to deal with the data resulting from sequencing many genomes
- Analyzing large sets of genes or even comparing whole genomes of different species is called **genomics**
- A similar analysis of large sets of proteins including their sequences is called **proteomics**

Figure 5.26

MAKE CONNECTIONS: Contributions of Genomics and Proteomics to Biology



DNA and Proteins as Tape Measures of Evolution

- Sequences of genes and their protein products document the *hereditary background* of an organism
- Linear sequences of DNA molecules are passed from parents to offspring
- We can extend the concept of "molecular genealogy" to *relationships between species*
- Molecular biology has added a new measure to the toolkit of evolutionary biology

Figure 5.UN02a

➤ Human

➤ Rhesus monkey

➤ Gibbon

Species	Alignment of Amino Acid Sequences of β-globin
Human	1 VHLTPEEKSA VTALWGKVNV DEVGGEALGR LLVVYPWTQR FFESFGDLST
Monkey	1 VHLTPEEKNA VTTLWGKVNV DEVGGEALGR LLLVYPWTQR FFESFGDLSS
Gibbon	1 VHLTPEEKSA VTALWGKVNV DEVGGEALGR LLVVYPWTQR FFESFGDLST
Human	51 PDAVMGNPKV KAHGKKVLGA FSDGLAHLDN LKGTFATLSE LHCDKLHVDP
Monkey	51 PDAVMGNPKV KAHGKKVLGA FSDGLNHLDN LKGTFAQLSE LHCDKLHVDP
Gibbon	51 PDAVMGNPKV KAHGKKVLGA FSDGLAHLDN LKGTFAQLSE LHCDKLHVDP
Human	101 ENFRLLGNVL VCVLAHHFGK EFTPPVQAAY QKVVAGVANA LAHKYH
Monkey	101 ENFKLLGNVL VCVLAHHFGK EFTPQVQAAY QKVVAGVANA LAHKYH
Gibbon	101 ENFRLLGNVL VCVLAHHFGK EFTPQVQAAY QKVVAGVANA LAHKYH

Data from Human: http://www.ncbi.nlm.nih.gov/protein/AAA21113.1; rhesus monkey: http://www.ncbi.nlm.nih.gov/protein/122634; gibbon: http://www.ncbi.nlm.nih.gov/protein/122616

Figure 5.UN04

Summary

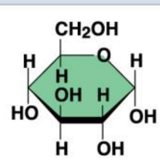
Components	Examples	Functions
 Monosaccharide monomer	Monosaccharides: glucose, fructose	Fuel; carbon sources that can be converted to other molecules or combined into polymers
	Disaccharides: lactose, sucrose	
	Polysaccharides: ▪ Cellulose (plants) ▪ Starch (plants) ▪ Glycogen (animals) ▪ Chitin (animals and fungi)	 ▪ Strengthens plant cell walls ▪ Stores glucose for energy ▪ Stores glucose for energy ▪ Strengthens exoskeletons and fungal cell walls

Figure 5.UN05

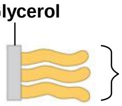
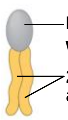
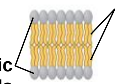
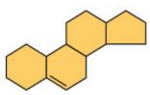
Components	Examples	Functions
Glycerol  3 fatty acids	Triacylglycerols (fats or oils): glycerol + three fatty acids	Important energy source  
 Head with P; 2 fatty acids	Phospholipids: glycerol + phosphate group + two fatty acids	Lipid bilayers of membranes  Hydrophobic tails; Hydrophilic heads
 Steroid backbone	Steroids: four fused rings with attached chemical groups	▪ Component of cell membranes (cholesterol) ▪ Signaling molecules that travel through the body (hormones)

Figure 5.UN06

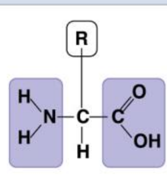
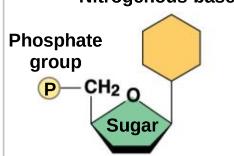
Components	Examples	Functions
 Amino acid monomer (20 types)	▪ Enzymes ▪ Defensive proteins ▪ Storage proteins ▪ Transport proteins ▪ Hormones ▪ Receptor proteins ▪ Motor proteins ▪ Structural proteins	▪ Catalyze chemical reactions ▪ Protect against disease ▪ Store amino acids ▪ Transport substances ▪ Coordinate organismal responses ▪ Receive signals from outside cell ▪ Function in cell movement ▪ Provide structural support

Figure 5.UN07

Components	Examples	Functions
 Nucleotide (monomer of a polynucleotide)	DNA:  ▪ Sugar = deoxyribose ▪ Nitrogenous bases = C, G, A, T ▪ Usually double-stranded	Stores hereditary information
	RNA:  ▪ Sugar = ribose ▪ Nitrogenous bases = C, G, A, U ▪ Usually single-stranded	Various functions in gene expression, including carrying instructions from DNA to ribosomes