Chapter 5

The Structure and Function of Macromolecules

Key Concepts

5.1 Most macromolecules are polymers, built from monomers

5.2 Carbohydrates serve as fuel and building material

5.3 Lipids are a diverse group of hydrophobic molecules

5.4 Proteins have many structures, resulting in a wide range of functions

5.5 Nucleic acids store and transmit hereditary information

Framework

The central ideas of this chapter are that molecular function relates to molecular structure and that the diversity of molecular structure is the basis for the diversity of life. Combining a small number of monomers or subunits into unique sequences and three-dimensional structures creates a huge variety of macromolecules. The table below briefly summarizes the major characteristics of the four classes of macromolecules.

Class	Monomers	Functions
Carbohydrates	Monosaccharides	Energy, raw materials, energy storage, structural compounds
Proteins	Amino acids	Enzymes, transport, movement, receptors, defense, structure
Nucleic acids	Nucleotides	Heredity, code for amino acid sequence
Lipids	Glycerol and fatty acids → fats; phospholipids; steroids (do not form polymers)	Energy storage, membranes, hormones

Chapter Review

Smaller organic molecules are joined together to form carbohydrates, lipids, proteins, and nucleic acids. These molecules, many of which are giant **macromolecules,** represent another level in the hierarchy of biological organization, and their functions derive from their complex and unique architectures.

5.1 Most macromolecules are polymers, built from monomers

Polymers are chainlike molecules formed from the linking together of many similar or identical small molecules, called **monomers.**

Synthesis and Breakdown of Polymers Monomers are joined by **condensation reactions** (or **dehydration reactions**), in which one monomer provides a hydroxyl group (−OH) and the other contributes a hydrogen (−H) to release a water molecule. With an input of energy and the help of enzymes, a covalent bond between the monomers is formed.

Hydrolysis is the breaking of bonds between monomers through the addition of water molecules. A hydroxyl group is joined to one monomer while a hydrogen is bonded with the other. Enzymes also control hydrolysis.

Diversity of Polymers Macromolecules are constructed from about 40 to 50 common monomers and a few rarer molecules. The seemingly endless variety of polymers arises from the essentially infinite number of possibilities in the sequencing and arrangement of these basic building blocks.

5.2 Carbohydrates serve as fuel and building material

Carbohydrates include sugars and their polymers.

Sugars **Monosaccharides** have the general formula of $(CH_2O)_n$. The number of these units forming a sugar varies from three to seven, with hexoses ($C_6H_{12}O_6$), trioses, and pentoses found most commonly. Sugar molecules may be enantiomers due to the spatial arrangement of parts around asymmetric carbons.

Glucose is broken down to yield energy in cellular respiration. Monosaccharides serve also as the raw materials for synthesis of other organic molecules and as monomers that are synthesized into disaccharides or polysaccharides.

■ INTERACTIVE QUESTION 5.1

Fill in the blanks to review the structure of monosaccharides.

You can recognize a monosaccharide by its multiple **(a)** __________ groups and its one **(b)** __________ group, whose location determines whether the sugar is an **(c)** __________ or a **(d)** __________. In aqueous solutions, most monosaccharides form **(e)** __________.

Sucrose, or table sugar, is a **disaccharide** consisting of a glucose and a fructose molecule. A **glycosidic linkage** is a covalent bond formed by a dehydration reaction between two monosaccharides.

Polysaccharides **Polysaccharides** are storage or structural macromolecules made from a few hundred to a few thousand monosaccharides. **Starch,** a storage molecule in plants, is a polymer made of glucose molecules joined by 1–4 linkages that give starch a helical shape. Most animals have enzymes to hydrolyze plant starch into glucose. Animals produce **glycogen,** a highly branched polymer of glucose, as their energy storage form.

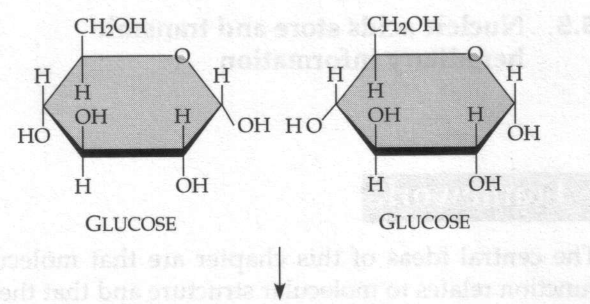
Cellulose, the major component of plant cell walls, is the most abundant organic compound on Earth. It differs from starch by the configuration of the ring form of glucose and the resulting geometry of the glycosidic bonds. In a plant cell wall, hydrogen bonds between hydroxyl groups hold parallel cellulose molecules together to form strong microfibrils.

Enzymes that digest the α linkages of starch are unable to hydrolyze the β linkages of cellulose. Only a few organisms (some bacteria, microorganisms, and fungi) have enzymes that can digest cellulose.

Chitin is a structural polysaccharide formed from glucose monomers with a nitrogen-containing group and found in the exoskeleton of arthropods and the cell walls of many fungi.

■ INTERACTIVE QUESTION 5.2

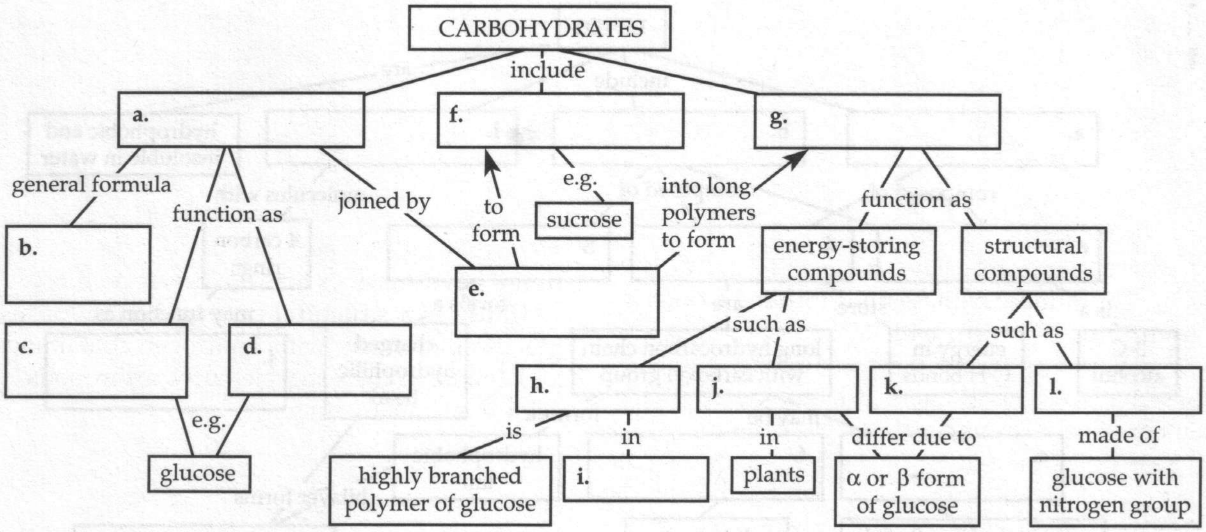
Circle the atoms of these two glucose molecules that will be removed by a dehydration reaction. Then draw the resulting maltose molecule with its 1–4 glycosidic linkage (between the number 1 carbon of the first glucose and the number 4 carbon of the second).



MALTOSE

■ **INTERACTIVE QUESTION 5.3**

Fill in the following concept map that summarizes this section on carbohydrates.



5.3 Lipids are a diverse group of hydrophobic molecules

Fats, phospholipids, and steroids are a diverse assemblage of macromolecules that are classed together as **lipids** based on their hydrophobic behavior. Lipids do not form polymers.

Fats **Fats** are composed of fatty acids attached to the three-carbon alcohol, glycerol. A **fatty acid** consists of a long hydrocarbon chain with a carboxyl group at one end. The nonpolar hydrocarbons make a fat hydrophobic.

A **triacylglycerol,** or fat, consists of three fatty acid molecules, each linked to glycerol by an ester linkage, a bond that forms between a hydroxyl and a carboxyl group. Triglyceride is another name for fats.

Fatty acids with double bonds in their carbon skeletons are called **unsaturated fatty acids.** The *cis* double bonds create a kink in the hydrocarbon chain and prevent fat molecules that contain unsaturated fatty acids from packing closely together and becoming solidified at room temperature. **Saturated fatty acids** have no double bonds in their carbon skeletons. Most animal fats are saturated and solid at room temperature. The fats of plants and fish are generally unsaturated and are called oils. Diets rich in saturated fats and in "*trans* fats" made in the process of hydrogenating vegetable oils have been linked to cardiovascular disease.

Fats are excellent energy storage molecules, containing twice the energy reserves of carbohydrates such as starch. Adipose tissue, made of fat storage cells, also cushions organs and insulates the body.

Phospholipids **Phospholipids** consist of a glycerol linked to two fatty acids and a negatively charged phosphate group, to which other small molecules may be attached. The phosphate head of this molecule is hydrophilic and water soluble, whereas the two fatty acid chains are hydrophobic.

The unique structure of phospholipids makes them ideal constituents of cell membranes. Arranged in a bilayer, the hydrophilic heads face toward the aqueous solutions inside and outside the cell, and the hydrophobic tails mingle in the center of the membrane.

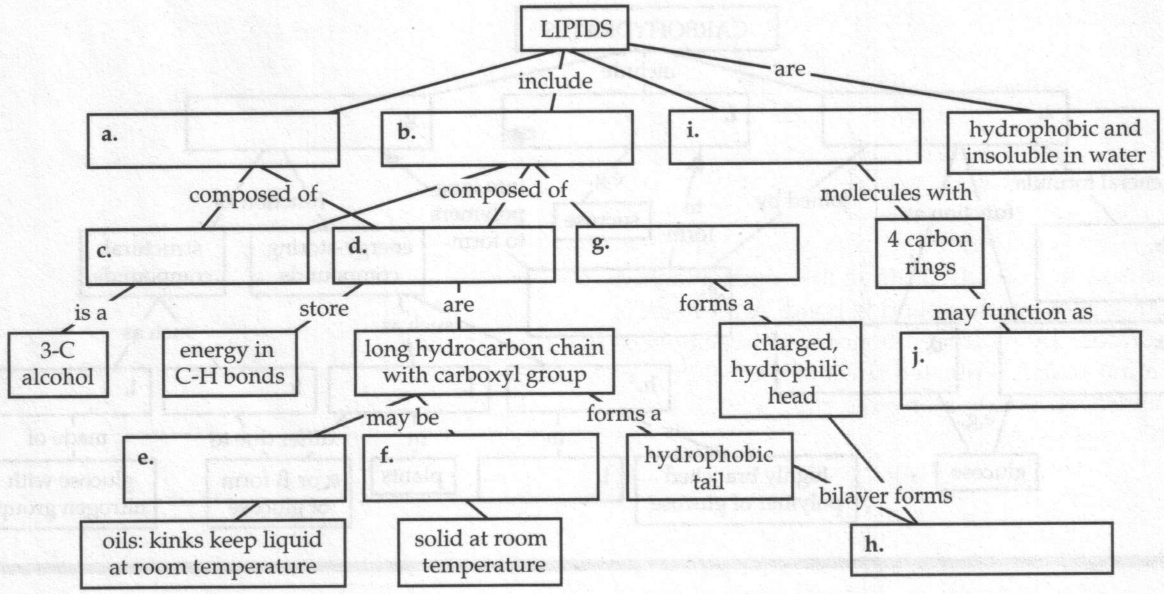
■ **INTERACTIVE QUESTION 5.4**

Sketch a section of a phospholipid bilayer of a membrane, and label the hydrophilic head and hydrophobic tail of one of the phospholipids.

Steroids **Steroids** are a class of lipids distinguished by four connected carbon rings with various functional groups attached. **Cholesterol** is an important steroid that is a common component of animal cell membranes and a precursor for other steroids, including many hormones.

■ INTERACTIVE QUESTION 5.5

Fill in this concept map to help you organize your understanding of lipids



5.4 Proteins have many structures, resulting in a wide range of functions

Proteins are central to almost every function of life. As **catalysts**, enzymatic proteins selectively speed up the chemical reactions of a cell.

Polypeptides A **polypeptide** is a polymer of amino acids. A **protein** consists of one or more polypeptide chains folded into a specific three-dimensional shape or conformation.

Amino acids are composed of an asymmetric carbon (called the α carbon) bonded to a hydrogen, a carboxyl group, an amino group, and a variable side chain called the R group. At the pH in a cell, the amino and carboxyl groups are usually ionized. The R group confers the unique physical and chemical properties of each amino acid. Side chains may be either nonpolar and hydrophobic, or polar or charged (acidic or basic) and thus hydrophilic.

A **peptide bond** links the amino group of one amino acid with the carboxyl group of another. A polypeptide chain has a free amino group at one end and a free carboxyl group at the other. Polypeptides vary in length from a few to a thousand or more amino acids.

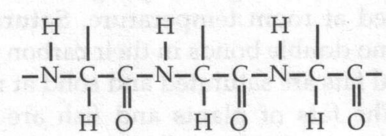
In the late 1940s and early '50s, Sanger determined the primary structure of insulin through the laborious process of hydrolyzing the protein into small peptide chains, determining their amino acid sequences, and then overlapping the sequences of small fragments created with different agents to reconstruct the whole polypeptide. Most of these steps are now automated.

■ INTERACTIVE QUESTION 5.6

a. Draw the amino acids alanine (R group—CH_3) and serine (R group—CH_2OH) and then show how a dehydration reaction will form a peptide bond between them.

b. Which of these amino acids has a polar R group? ________ a nonpolar R group? ________

c. What does this molecule segment represent? Note the N-C-C-N-C-C sequence.



Protein Conformation and Function Proteins have unique three-dimensional shapes created by the twisting or folding of one or more polypeptide chains. Protein conformation is dependent upon the interactions among the amino acids making up the polypeptide chain and usually arises spontaneously as soon as the protein is synthesized in the cell. The unique conformation of a protein, which results from its sequence of amino acids, enables it to recognize and bind to other molecules.

Primary structure is the unique, genetically coded sequence of amino acids within a protein.

Secondary structure involves the coiling or folding of the polypeptide backbone, stabilized by hydrogen bonds between the electronegative oxygen of one peptide bond and the weakly positive hydrogen attached to the nitrogen of another peptide bond. An **α helix** is a coil produced by hydrogen bonding between every fourth amino acid. A **β pleated sheet** is also held by repeated hydrogen bonds along the polypeptide backbone. This secondary structure forms when regions of the polypeptide chain lie parallel to each other.

Interactions between the various side chains (R groups) of the constituent amino acids produce a protein's **tertiary structure. Hydrophobic interactions** between nonpolar side groups clumped in the center of the molecule due to their repulsion by water, van der Waals interactions among those nonpolar side chains, hydrogen bonds between polar side chains, and ionic bonds between negatively and positively charged side chains produce the stable and unique shape of the protein. Strong covalent bonds, called **disulfide bridges,** may occur between the sulfhydryl side groups of cysteine monomers that have been brought close together by the folding of the polypeptide.

Quaternary structure occurs in proteins that are composed of more than one polypeptide chain. The individual polypeptide subunits are held together in a precise structural arrangement.

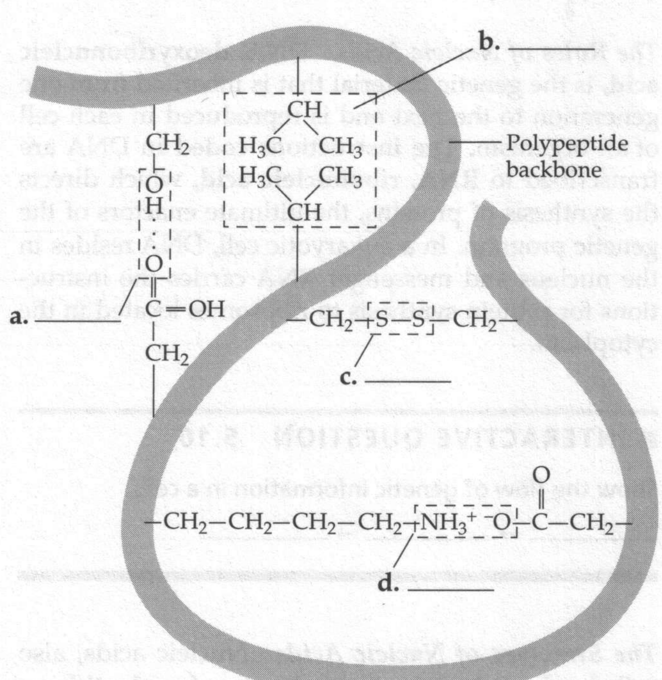
Even a slight deviation from the sequence of amino acids can severely affect a protein's function by altering the protein's conformation. A substitution of only one of the 146 amino acids in the primary structure of hemoglobin causes sickle-cell disease.

The interactions that create and maintain secondary and tertiary structure can be disrupted by changes in pH, salt concentration, temperature, or other aspects of the environment, and the protein may **denature,** losing its native conformation and thus its function.

The amino acid sequences of more than 100,000 proteins have been determined. Using the technique of **X-ray crystallography,** coupled with computer modeling and graphics, biochemists have established the three-dimensional shape of thousands of these molecules. Researchers have developed methods for following a protein through its intermediate states on the way to its final form and have discovered **chaperonins,** chaperone proteins that assist other proteins during the folding process, perhaps by providing a sheltered environment.

■ INTERACTIVE QUESTION 5.7

In the following diagram of a portion of a polypeptide, label the types of interactions that are shown. What level of structure are these interactions producing?



■ INTERACTIVE QUESTION 5.8

a. Why would a change in pH cause a protein to denature?

b. Why would transfer to a nonpolar organic solvent (such as ether) cause denaturation?

c. A denatured protein may re-form to its functional shape when returned to its normal environment. What does that indicate about a protein's conformation?

■ INTERACTIVE QUESTION 5.9

Now that you have gained more experience with concept maps, create your own map to help you organize the key concepts you have learned about proteins. Try to include the concepts of structure and function and look for cross-links on your map. One version of a protein concept map is included in the answer section, but remember that the real value is in the thinking process you must go through to create your own map.

5.5 Nucleic acids store and transmit hereditary information

Genes are the units of inheritance that determine the primary structure of proteins. **Nucleic acids** are polymers that carry and transmit this code.

The Roles of Nucleic Acids **DNA, deoxyribonucleic acid,** is the genetic material that is inherited from one generation to the next and is reproduced in each cell of an organism. The instructions coded in DNA are transcribed to **RNA, ribonucleic acid,** which directs the synthesis of proteins, the ultimate enactors of the genetic program. In a eukaryotic cell, DNA resides in the nucleus and messenger RNA carries the instructions for protein synthesis to ribosomes located in the cytoplasm.

■ INTERACTIVE QUESTION 5.10

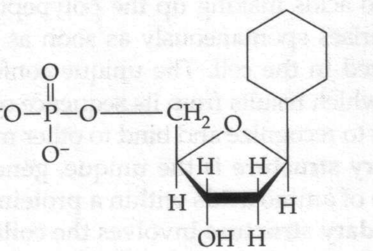
Show the flow of genetic information in a cell.

__________ → __________ → __________

The Structure of Nucleic Acids Nucleic acids, also called **polynucleotides,** are polymers of **nucleotides**—monomers that consist of a pentose (five-carbon sugar) covalently bonded to a phosphate group and a nitrogenous base. A monomer without the phosphate group is called a nucleoside. There are two families of nitrogenous bases. **Pyrimidines,** including cytosine (C), thymine (T), and uracil (U), are characterized by six-membered rings of carbon and nitrogen atoms. **Purines,** adenine (A) and guanine (G), add a five-membered ring to the pyrimidine ring. Thymine is only in DNA; uracil is only in RNA. In DNA, the pentose is **deoxyribose;** in RNA it is **ribose.**

Nucleotides are linked together into a polynucleotide by phosphodiester linkages, which join the phosphate of one nucleotide with the sugar of the next. The polymer has two distinct ends: a 5′ end with a phosphate attached to a 5′ carbon and a 3′ end with a hydroxyl group on a 3′ carbon. The nitrogenous bases extend from this backbone of repeating sugar-phosphate units. The unique sequence of bases in a gene codes for the specific amino acid sequence of a protein.

■ INTERACTIVE QUESTION 5.11



a. Label the three parts of this nucleotide. Indicate with an arrow where the phosphate group of the next nucleotide would attach to build a polynucleotide. Number the carbons of the pentose sugar.

b. Is this a purine or a pyrimidine?

c. Is this a DNA or RNA nucleotide?

The DNA Double Helix DNA molecules consist of two chains of polynucleotides spiraling around an imaginary axis in a **double helix.** The two chains run in opposite 5′ to 3′ directions, an arrangement called **antiparallel.** In 1953 Watson and Crick first proposed this double-helix arrangement, which consists of two sugar-phosphate backbones on the outside of the helix with their nitrogenous bases pairing and hydrogen-bonding together in the inside. Adenine pairs only with thymine; guanine always pairs with cytosine. Thus, the sequences of nitrogenous bases on the two strands of DNA are complementary. Because of this specific base-pairing property, DNA can replicate itself and precisely copy the genes of inheritance.

DNA and Proteins as Tape Measures of Evolution Genes form the hereditary link between generations. Closely related members of the same species share many common DNA sequences and proteins. More closely related species have a larger proportion of their DNA and proteins in common. This "molecular genealogy" provides evidence of evolutionary relationships.

■ INTERACTIVE QUESTION 5.12

Take the time to create a concept map that summarizes what you have just reviewed about nucleic acids. Compare your map with that of a study partner or explain it to a friend. One version of a map on nucleic acids is included in the answer section. Refer to Figures 5.26 and 5.27 in your textbook to help you visualize polynucleotides and the double helix of DNA.

The Theme of Emergent Properties in the Chemistry of Life: A Review

At each stage in the hierarchy of levels from atoms through macromolecules, we have seen that novel properties arise with increasing structural organization.

Word Roots

con- = together (*condensation reaction:* a reaction in which two molecules become covalently bonded to each other through the loss of a small molecule, usually water)

di- = two (*disaccharide:* two monosaccharides joined together)

glyco- = sweet (*glycogen:* a polysaccharide sugar used to store energy in animals)

hydro- = water; **-lyse** = break (*hydrolysis:* breaking chemical bonds by adding water)

macro- = large (*macromolecule:* a large molecule)

meros- = part (*polymer:* a chain made from smaller organic molecules)

mono- = single; **-sacchar** = sugar (*monosaccharide:* simplest type of sugar)

poly- = many (*polysaccharide:* many monosaccharides joined together)

tri- = three (*triacylglycerol:* three fatty acids linked to one glycerol molecule)

Structure Your Knowledge

1. Describe the four structural levels in the conformation of a protein.
2. Identify the type of monomer or group shown by the formulas shown on the right. Then match the chemical formulae with their description. Answers may be used more than once.

________ 1. molecules that would combine to form a fat

________ 2. molecule that would be attached to other monomers by a peptide bond

________ 3. molecules or groups that would combine to form a nucleotide

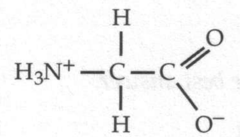
________ 4. molecules that are carbohydrates

________ 5. molecule that is a purine

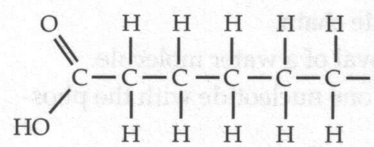
________ 6. monomer of a protein

________ 7. groups that would be joined by phosphodiester bonds

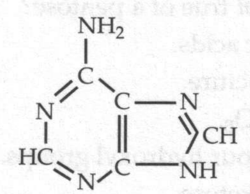
________ 8. most nonpolar (hydrophobic) molecule



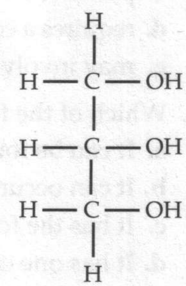
a. ________



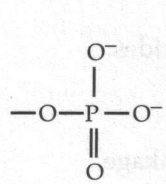
b. ________



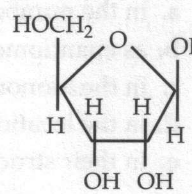
c. ________



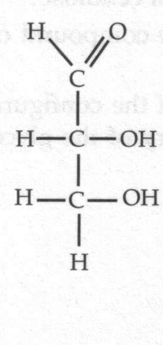
d. ________



e. ________



f. ________



g. ________

Test Your Knowledge

MATCHING: *Match the molecule with its type of molecule.*

________	1. glycogen	A. carbohydrate
________	2. cholesterol	B. lipid
________	3. RNA	C. protein
________	4. collagen	D. nucleic acid
________	5. hemoglobin	
________	6. a gene	
________	7. triacylglycerol	
________	8. enzyme	
________	9. cellulose	
________	10. chitin	

MULTIPLE CHOICE: *Choose the one best answer.*

1. Polymerization is a process that
   a. creates bonds between amino acids in the formation of a peptide chain.
   b. involves the removal of a water molecule.
   c. links the sugar of one nucleotide with the phosphate of the next.
   d. requires a condensation or dehydration reaction.
   e. may involve all of the above.
2. Which of the following is *not* true of a pentose?
   a. It can be found in nucleic acids.
   b. It can occur in a ring structure.
   c. It has the formula $C_5H_{12}O_5$.
   d. It has one carbonyl and four hydroxyl groups.
   e. It may be an aldose or a ketose.
3. Disaccharides can differ from each other in all of the following ways *except*
   a. in the number of their monosaccharides.
   b. as enantiomers.
   c. in the monomers involved.
   d. in the location of their glycosidic linkage.
   e. in their structural formulas.
4. Which of the following is *not* true of cellulose?
   a. It is the most abundant organic compound on Earth.
   b. It differs from starch because of the configuration of glucose and the geometry of the glycosidic linkage.
   c. It may be hydrogen-bonded to neighboring cellulose molecules to form microfibrils.
   d. Few organisms have enzymes that hydrolyze its glycosidic linkages.
   e. Its monomers are glucose with nitrogen-containing appendages.
5. Plants store most of their energy as
   a. unsaturated fats.
   b. glycogen.
   c. starch.
   d. sucrose.
   e. cellulose.
6. What happens when a protein denatures?
   a. It loses its primary structure.
   b. It loses its secondary and tertiary structures.
   c. It becomes irreversibly insoluble and precipitates.
   d. It hydrolyzes into component amino acids.
   e. Its hydrogen bonds, ionic bonds, hydrophobic interactions, disulfide bridges, and peptide bonds are disrupted.
7. The α helix of proteins is
   a. part of the tertiary structure and is stabilized by disulfide bridges.
   b. a double helix.
   c. stabilized by hydrogen bonds and commonly found in fibrous proteins.
   d. found in some regions of globular proteins and stabilized by hydrophobic interactions.
   e. a complementary sequence to messenger RNA.
8. A fatty acid that has the formula $C_{16}H_{32}O_2$ is
   a. saturated.
   b. unsaturated.
   c. branched.
   d. hydrophilic.
   e. part of a steroid molecule.
9. Three molecules of the fatty acid in question 8 are joined to a molecule of glycerol ($C_3H_8O_3$). The resulting molecule has the formula
   a. $C_{48}H_{96}O_6$.
   b. $C_{48}H_{98}O_9$.
   c. $C_{51}H_{102}O_8$.
   d. $C_{51}H_{98}O_6$.
   e. $C_{51}H_{104}O_9$.

10. β pleated sheets are characterized by
- **a.** disulfide bridges between cysteine amino acids.
- **b.** parallel regions of the polypeptide chain held together by hydrophobic interactions.
- **c.** folds stabilized by hydrogen bonds between segments of the polypeptide backbone.
- **d.** membrane sheets composed of phospholipids.
- **e.** hydrogen bonds between adjacent cellulose molecules.

11. Cows can derive nutrients from cellulose because
- **a.** they can produce the enzymes that break the β linkages between glucose molecules.
- **b.** they chew and rechew their cud so that cellulose fibers are finally broken down.
- **c.** one of their stomachs contains bacteria that can hydrolyze the bonds of cellulose.
- **d.** their intestinal tract contains termites, which produce enzymes to hydrolyze cellulose.
- **e.** they can convert cellulose to starch and then hydrolyze starch to glucose.

12. Which of these molecules would provide the most energy (kcal/g) when eaten?
- **a.** glucose
- **b.** starch
- **c.** glycogen
- **d.** fat
- **e.** protein

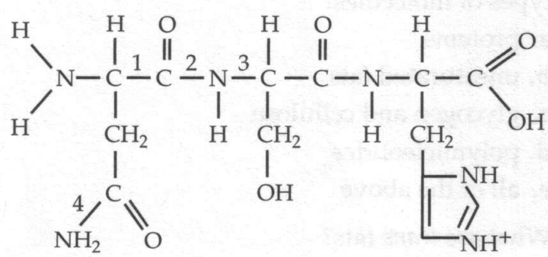
13. What *determines* the sequence of the amino acids in a particular protein?
- **a.** its primary structure
- **b.** the sequence of nucleotides in RNA, which was determined by the sequence of nucleotides in the gene for that protein
- **c.** the sequence of nucleotides in DNA, which was determined by the sequence of nucleotides in RNA
- **d.** the sequence of RNA nucleotides making up the ribosome
- **e.** the three-dimensional shape of the protein

14. Sucrose is made from joining a glucose and a fructose molecule in a dehydration reaction. What is the molecular formula for this disaccharide?
- **a.** $C_6H_{12}O_6$
- **b.** $C_{10}H_{20}O_{10}$
- **c.** $C_{12}H_{22}O_{11}$
- **d.** $C_{12}H_{24}O_{12}$
- **e.** $C_{12}H_{24}O_{13}$

15. How are the nucleotide monomers connected to form a polynucleotide?
- **a.** hydrogen bonds between complementary nitrogenous base pairs
- **b.** ionic attractions between phosphate groups
- **c.** disulfide bridges between cysteine amino acids
- **d.** covalent bonds between the sugar of one nucleotide and the phosphate of the next
- **e.** ester linkages between the carboxyl group of one nucleotide and the hydroxyl group on the ribose of the next

16. Which of the following would be the most hydrophobic molecule?
- **a.** cholesterol
- **b.** nucleotide
- **c.** amino acid
- **d.** chitin
- **e.** glucose

17. What is the best description of this molecule?



- **a.** chitin
- **b.** amino acid
- **c.** polypeptide (tripeptide)
- **d.** nucleotide
- **e.** protein

18. Which number(s) in the molecule in question 17 refer(s) to a peptide bond?
- **a.** 1
- **b.** 2
- **c.** 3
- **d.** 4
- **e.** both 2 and 4

19. If the nucleotide sequence of one strand of a DNA helix is GCCTAA, what would be the sequence on the complementary strand?
- **a.** GCCTAA
- **b.** CGGAUU
- **c.** CGGATT
- **d.** ATTCGG
- **e.** TAAGCC

20. Monkeys and humans share many of the same DNA sequences and have similar proteins, indicating that
a. the two groups belong to the same species.
b. the two groups share a relatively recent common ancestor.
c. humans evolved from monkeys.
d. monkeys evolved from humans.
e. the two groups first appeared on Earth at about the same time.

21. Which of the following would be the major component of the cell membrane of a fungus?
a. cellulose
b. chitin
c. cholesterol
d. phospholipids
e. unsaturated fatty acids

22. Hydrophobic as well as hydrophillic interactions would be important for which of the following types of molecules?
a. proteins
b. unsaturated fats
c. glycogen and cellulose
d. polynucleotides
e. all of the above

23. What are *trans* fats?
a. hydrogenated vegetable oils that have been identified with health risks
b. fats made from cholesterol that are components of plaques in the walls of blood vessels
c. fats that are derived from animal sources and are associated with cardiovascular disease
d. fats that contain *trans* double bonds and may contribute to atherosclerosis
e. polyunsaturated fats produced by removing H from fatty acids and forming *cis* double bonds

24. Which of the following is *not* a function performed by proteins?
a. transport of oxygen in blood
b. catalyst for metabolic reactions
c. protection against disease
d. signals and receptors
e. primary component of cell membranes

FILL IN THE BLANKS

1. The man who determined the amino acid sequence of insulin was ________.
2. Cytosine always pairs with ________.
3. Adenine and guanine are ________.
4. A pentose joined to a nitrogenous base and a phosphate group is called a ________.
5. The conformation of a protein is determined by its ________.
6. Proteins with more than one polypeptide chain have ________ structure.
7. The carbohydrate energy storage molecule of animals is ________.
8. Membranes are composed of a bilayer of ________.
9. The insoluble fiber listed on food packages consists primarily of ________.
10. Proteins that assist the proper folding of newly synthesized proteins are called ________.