# BIOCHEMISTRY

INTRODUCTION

The Biochemistry Model Set can be used to build models of thousands of compounds including ATP, carbohydrates, lipids, nucleic acids, and proteins. It will help you visualize molecular structures, bonding, resonance, and relate the physical and chemical properties of the compound to its structure.

The atom models are easy to assemble by sliding the bond over the pole of the atom model and using a twisting motion to push the bond onto the pole. The poles on the atom models represent electron orbitals, a volume of space in which there is a probability of finding an electron with a certain amount of energy. As shown in Figure 1(A-C), the carbon atom has four valence electrons in the sp^3 orbitals. These orbitals are directed from the carbon nucleus toward the corners of a regular tetrahedron. A covalent bond is formed when an electron pair is shared between atoms by the overlap of orbitals. The scale of the bonds is 1.0 inch (25mm) = 1Å.

Figure 1: Bonding

(A)   (B)   (C)   (D)
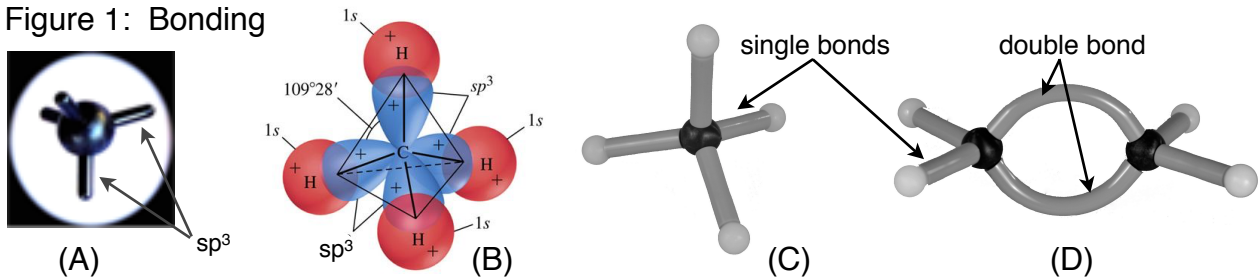
If two atoms share two pairs of electrons, the bond is said to be a double bond. There are two methods for representing double bonds. For a quick representation of the double bond in a molecule of ethane, use two 51mm gray links as show in Figure 1(D). A more exact representation of a double bond can be achieved using carbon atoms with three sp^2 hybrid orbitals and one unhybridized p orbital as shown in Figure 2(A). A double bond consists of one sigma (σ) bond and one pi (π) bond. The sigma bond is formed between two carbon atoms by the overlap of adjacent sp^2 orbitals as shown in Figure 2(B). The model of ethane, shown in Figure 2(C), has a black bond to represent the sigma bond.
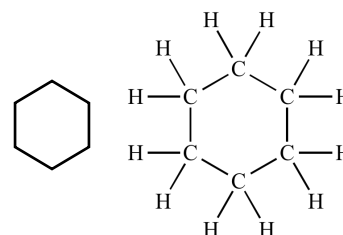
Figure 2: Sigma and Pi Bonds

(A)   unhybridized p orbital   (B)   (C) double bond
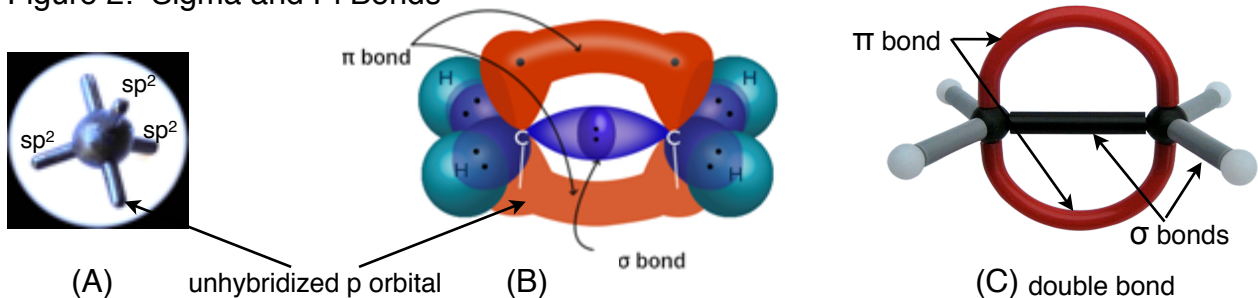
To form the C-C pi bond, the unhybirdized p orbitals overlap sideways as shown in Figure 2(B). Illustrate the pi bond using two red links to connect the adjacent unhybridized p orbitals.

Figure 3: Abbreviation For Cyclohexane

The carbon atom can unite with other carbon atoms to form a continuous chain, a branched chain, or a ring. Chemists often draw structural formulas for cyclic compounds as shown in Figure 3. A carbon atom is located at each vertex of the polygon. Note that every carbon atom has four bonds. When assembling biological molecules with ring structures, it is usually easier to begin by building the ring and then building outward from the ring.

Resonance is a way of describing delocalized electrons within certain molecules where the bonding cannot be expressed by one single Lewis structure. In resonance structures, two or more equivalent structures are possible, with identical positions of the atoms but different arrangements of the electrons. Figure 4(A) shows the structural formula for the amino acid, lysine. The electrons in the pi bond are delocalized and move forming a double bond with either oxygen atom or spreading out over the two oxygen atoms. Electron delocalization lowers the potential energy of the substance and thus makes it more stable than any of the contributing structures. In Figure 4(B), a pair of red links represents the delocalized electrons in lysine. Use the 5-pole atomic models of carbon (black) and oxygen (red) to construct the resonance structure of lysine.
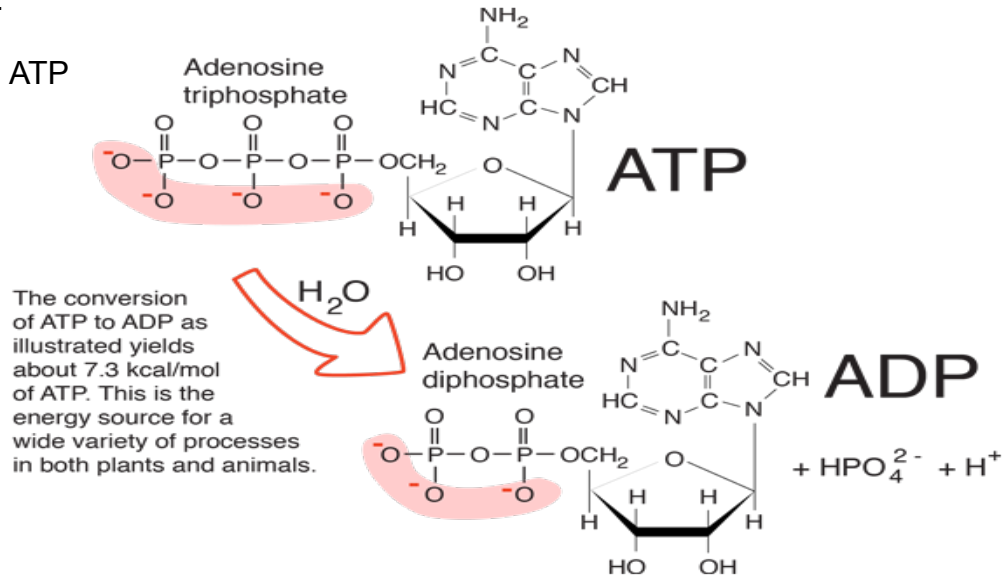
Figure 4: Resonance in Lysine

(A)

(B)
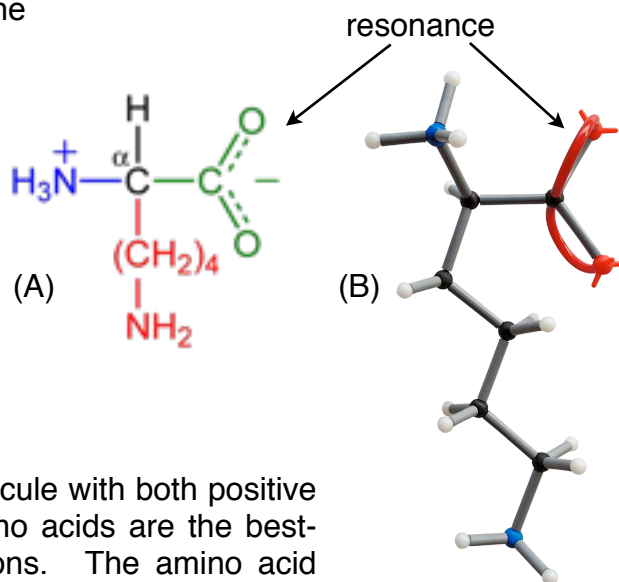
A zwitterion is a neutral molecule with both positive and negative charges. Amino acids are the best-known examples of zwitterions. The amino acid has both a basic amine group, $-NH_2$, and an acidic carboxylic acid group, $-COOH$. There is an internal transfer of a hydrogen ion from the $-COOH$ group to the $-NH_2$ group, leaving a neutral molecule with both a positive and a negative charge.

BIOCHEMICAL ENERGY

Adenosine triphosphate (ATP) is the high-energy molecule that stores the energy required for the metabolic reactions of life. The bonds between the phosphate groups of ATP can be broken by hydrolysis with the aide of an enzyme and water. This reaction is called hydrolysis which means to break using water. As shown in Figure 5, when the terminal phosphate bond is broken, ATP loses a phosphate group and becomes ADP, adenosine diphosphate. Food in the cells is gradually oxidized and the released energy is used to re-form the ATP. As a result the cell maintains a supply of this essential molecule.

Figure 5: ATP

The conversion of ATP to ADP as illustrated yields about 7.3 kcal/mol of ATP. This is the energy source for a wide variety of processes in both plants and animals.

To build the model of ATP, use Figure 6 and the phosphorus atom models with 6 poles. The 6 poles represent two sp orbitals and two unhybridized p orbitals required for resonance in ATP. The high-energy phosphate bonds are indicated with white bonds. There are several factors that explain why ATP is such a high energy molecule. ATP is stabilized by multiple resonance structures. The negative charge density associated with the three adjacent phosphate units of ATP destabilizes the molecule, making it higher in energy. Hydrolysis of the phosphate groups in ATP relieves some of the electrostatic repulsions and releases energy to do work. The products (ADP and P_i) are much lower in energy than the reactant (ATP).

Figure 6: Resonance in ATP

High-energy bonds (white)
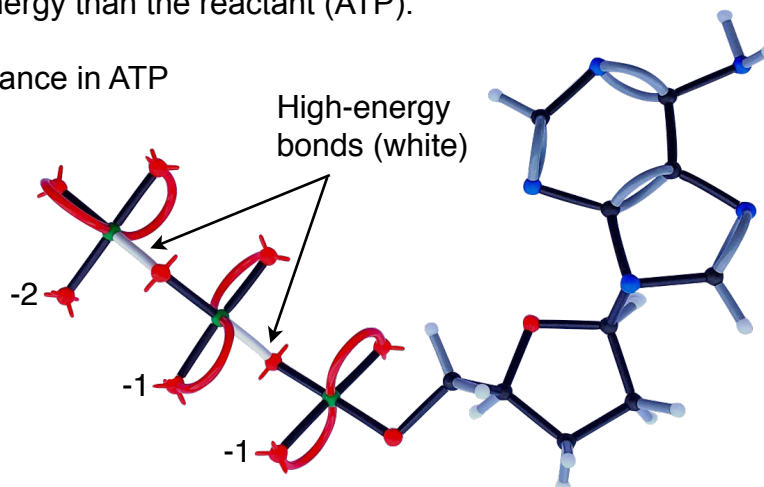
CARBOHYDRATES

The term carbohydrate was originally used to describe compounds that were hydrates of carbon because they contained carbon, hydrogen, and oxygen in a 1:2:1 ratio and had the empirical formula CH_2O. Carbohydrates can be classified on the basis of their structures. There are three groups of carbohydrates: monosaccharides, disaccharides, and polysaccharides. The monosaccharides are white, crystalline solids that contain an aldehyde or ketone functional group. They are subdivided into two classes, aldoses and ketoses, on the basis of whether they are aldehydes or ketones. They are also classified as a triose, tetrose, pentose, hexose, or heptose on the basis of whether they contain three, four, five, six, or seven carbon atoms. Table 1 lists some of the more common hexose and pentose carbohydrates.

| TABLE 1: CARBOHYDRATES		
Name	**Description**	**Structure**
Monosaccharide with a 6-Carbon Ring (hexose)		
Glucose	Glucose is the most abundant carbohydrate with the molecular formula $C_6H_{12}O_6$. It is also known as α-D-glucose or dextrose. It is made by green plants during photosynthesis from water and carbon dioxide, using energy from sunlight.	
Galactose	Galactose is less sweet compared to glucose. It differs from glucose in the location of the -OH group on the fourth carbon. β-D-galactose combines with α-D-glucose to form the disaccharide lactose.	
Monosaccharides with a 5-Carbon Ring (pentoses)		
Ribose	Ribose, found in RNA, has one oxygen atom attached to each carbon atom.	
Deoxyribose	Deoxyribose, found in DNA, is derived from the sugar ribose by the loss of an oxygen atom.	

Alpha and Beta Glucose

The arrangement of the atoms in the glucose molecule is important when determining its chemical nature. The structures in Figure 7 are planar cyclic representations called Haworth projections. Alpha and beta glucose are stereoisomers. They differ in the position of the -H and -OH groups on carbon 1′. Although the two isomeric forms have the same molecular formula, they are not similar in physical and chemical properties.

Figure 7: Alpha and Beta Glucose

α-D-glucose   β-D-glucose
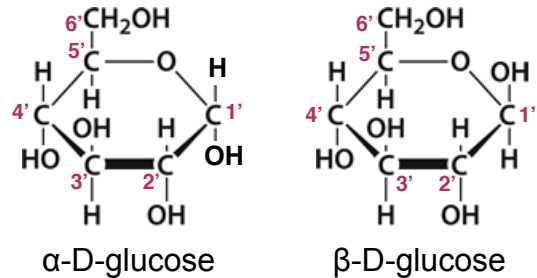
When building a model of glucose, it will not be a planar molecule as shown in a Haworth projection. The most stable conformation of glucose resembles a chair. As shown in Figure 8, carbon 1′ points downward and carbon 4′ points upward. If carbon 6′ is above the plane of the ring and the -OH group on carbon 1′ is on the opposite side of the ring (below the ring), it is α-D-glucose. If both carbon 6′ and the -OH group on carbon 1′ are above the plane of the ring, it is β-D-glucose.

Figure 8: Model of α-D-glucose
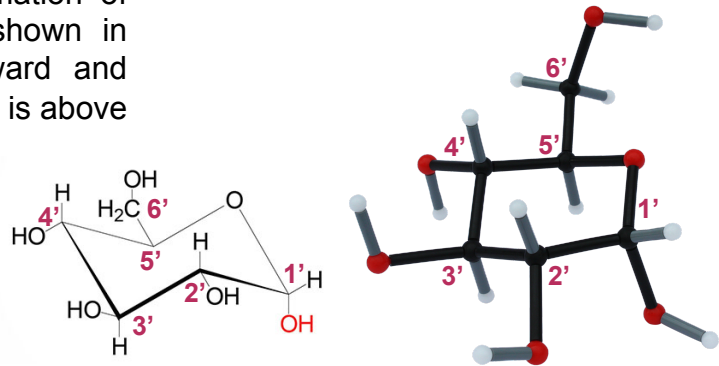

Disaccharides and Polysaccharides

Two monosaccharide sugar molecules can join together chemically to form a larger carbohydrate molecule called a double sugar, or disaccharide. The (1-4) glycosidic bond between two α-D-glucose molecules produces a disaccharide called maltose as shown in Figure 9. The production of a disaccharide is the result of a chemical reaction called a dehydration synthesis reaction. In such a reaction, the elements of water are removed and the glucose molecules are joined to form the disaccharide. One carbon on each participating monosaccharide is chemically bound together by oxygen. When a large number of α-D-glucose molecules are bonded with α-(1-4) glycosidic bonds, a polysaccharide called starch is formed. Starch can be easily broken down by enzymes.

Figure 9: Dehydration Synthesis Reaction To Form Maltose

maltose
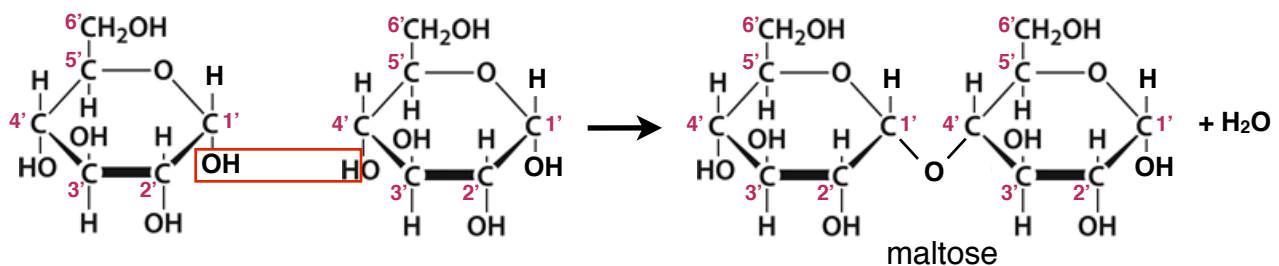
Two forms of the (1-4) glycosidic bond exists in nature, the alpha (α) bond and beta (β) bond. The beta bond is found in lactose, a disaccharide sugar composed of β-D-galactose and α-D-glucose that is found in milk. The model of the beta bond in α-lactose is shown in Figure 10. The beta bond makes α-lactose difficult to digest for individuals who show a low activity of the enzyme lactase. When many β-D-glucose molecules are bound with (1-4) glycosidic bonds, cellulose is formed. The beta bond in cellulose cannot be broken by human intestinal enzymes during digestion.

Figure 10: Beta Bond in Lactose
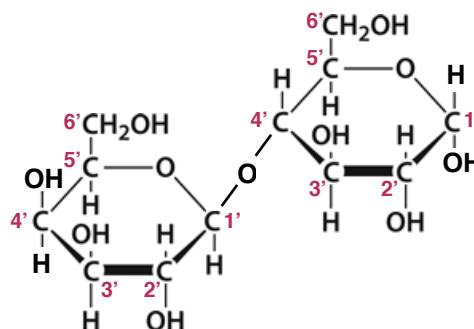
LIPIDS

Lipids are biomolecules that are soluble in organic non-polar solvents and are insoluble in water. Lipids are classified into two sub-groups of compounds. One diverse group of compounds do not have an ester functional group. This group includes fatty acids and steroids. The other group of compounds have an ester functional group and include triglycerides and phospholipids.

Fatty Acids

Fatty acids are carboxylic acids with long hydrocarbon chains. There are two types of fatty acids, saturated and unsaturated. Saturated fatty acids are long straight molecules that have all bonding positions between carbon atoms occupied by hydrogen atoms as shown in Figure 11. Studies have found that people whose diets are high in saturated fatty acids have a higher prevalence of coronary heart disease.

Figure 11: Saturated Fatty Acid - Lauric Acid

$$CH_3 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - \overset{\overset{\displaystyle O}{\displaystyle \|}}{C} - O - H$$
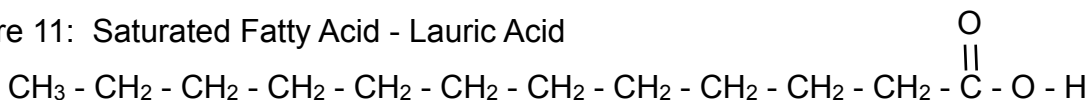
Unsaturated fatty acids, such as oleic acid, shown in Figure 12, have one or more double bonds between the carbon atoms. In the cis conformation, the hydrogen atoms attached to carbon atoms 9′ and 10′ are on the same side of the double bond, whereas in the trans conformation they are on opposite sides. The geometry of the cis double bond introduces a bend in the molecule. Most fatty acids found in nature are in the cis conformation.

Figure 12: Unsaturated Fatty Acid - Oleic Acid
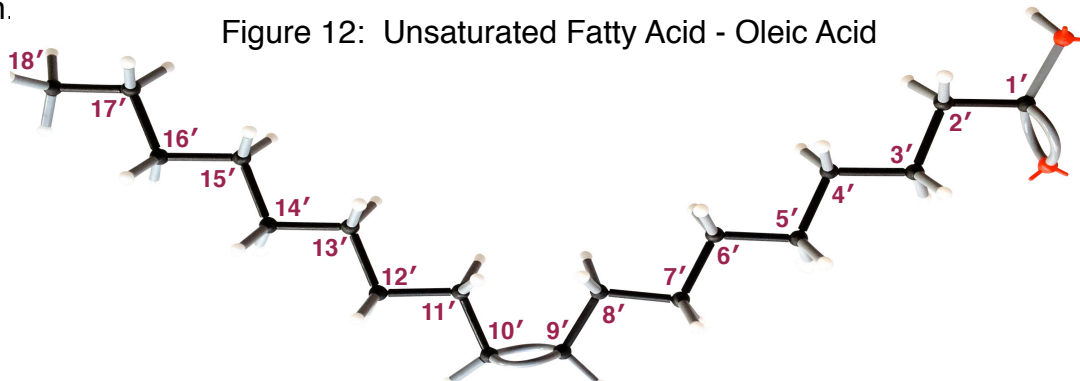
Steroids

The main feature of steroids is the fused ring system of three cyclohexanes and one cyclopentane. Steroids include such well-known compounds as cholesterol and the sex hormones, estradiol and testosterone.

Cholesterol, shown in Figure 13, performs several important functions in the body. It plays a role in maintaining the integrity and fluidity of cell membranes. Cholesterol is essential for making a number of critical hormones, bile, and vitamin D. High-density lipoprotein (HDL), sometimes referred to as "good cholesterol" is heavier than low-density lipoprotein (LDL) because it contains more protein and less cholesterol. It transports lipid molecules from the cells to the liver and helps lower the risk of developing cardiovascular disease. Low-density cholesterol can form deposits on the inner walls of blood vessels that harden and obstruct the flow of blood. This condition is known as atherosclerosis and can result in various heart diseases, strokes, and high blood pressure.

Figure 13: Cholesterol
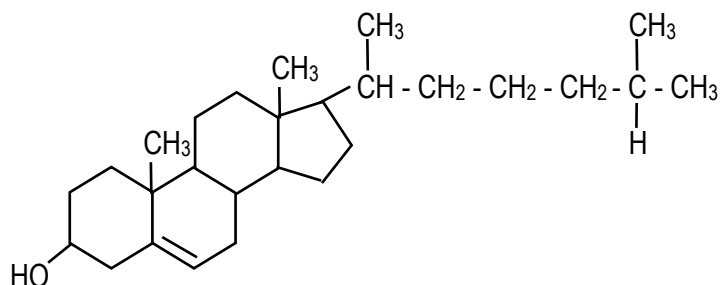
Estradiol, shown in Figure 14, is a form of estrogen, a sex hormone that is present in both males and females. In women, it is produced by the ovaries and plays a key role in the development and functioning of the reproductive system.

Figure 14: Estradiol

$\triangle$ = bonds oriented toward the viewer

$\blacktriangledown$ = bonds oriented away from the viewer
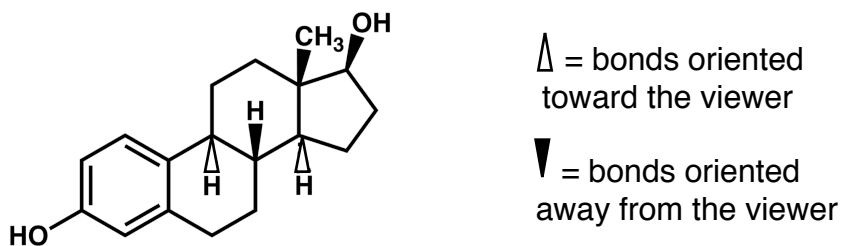
Testosterone, shown in Figure 15, is primarily secreted in the testicles of males and the ovaries of females, although small amounts are also secreted by the adrenal glands. In men, testosterone plays a key role in the development of male reproductive tissues and secondary sexual characteristics.
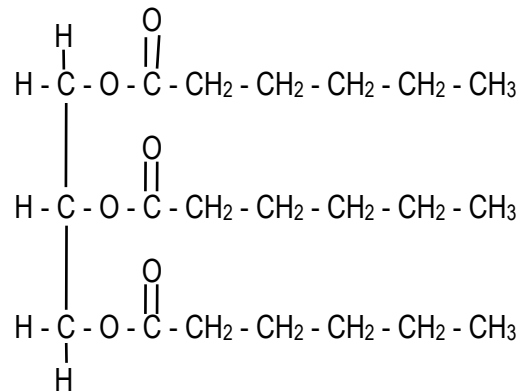
Figure 15: Testosterone
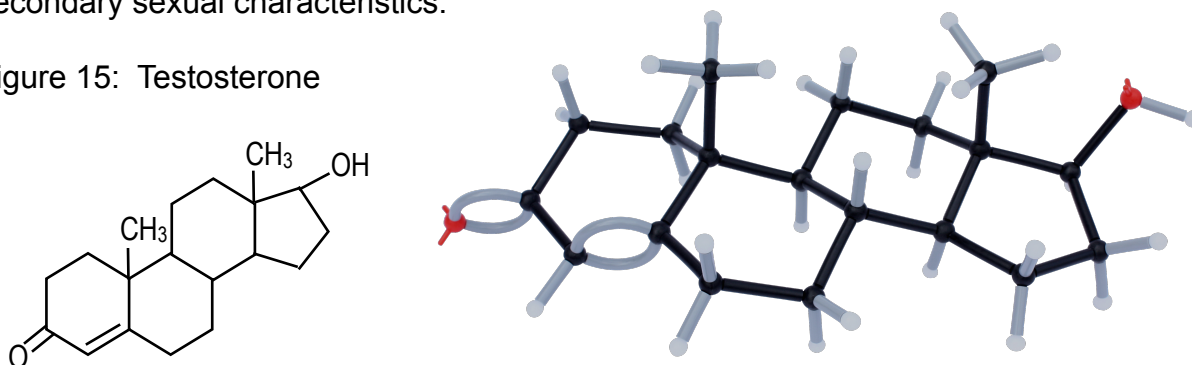
Triglycerides

Triglycerides are the most common type of lipid found in the body and in foods. Triglycerides include the edible fats and oils in our diets, substances such as olive oil, corn oil, peanut oil, butterfat, and lard. Fats and oils are made up of two different kinds of molecules, glycerol and three fatty acids. The structure of a triglyceride is shown in Figure 16. The three fatty acids may or may not be identical. The synthesis of a triglyceride is an ester synthesis reaction.
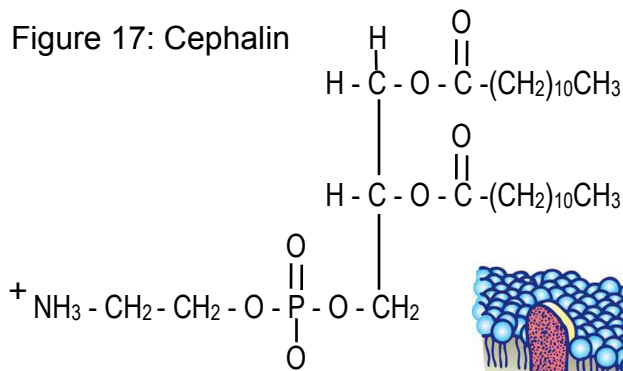
Figure 16: Triglyceride

$$H - \overset{\overset{\displaystyle H}{|}}{C} - O - \overset{\overset{\displaystyle O}{\|}}{C} - CH_2 - CH_2 - CH_2 - CH_2 - CH_3$$

$$H - C - O - \overset{\overset{\displaystyle O}{\|}}{C} - CH_2 - CH_2 - CH_2 - CH_2 - CH_3$$

$$H - \underset{\underset{\displaystyle H}{|}}{C} - O - \overset{\overset{\displaystyle O}{\|}}{C} - CH_2 - CH_2 - CH_2 - CH_2 - CH_3$$

Phospholipids

Phospholipids are esters of glycerol, two fatty acids, and phosphoric acid. Phospholipids are major components in the lipid bilayer of cell membranes. Cephalin, shown in Figure 17, is found in most cell membranes, particularly in brain tissues.
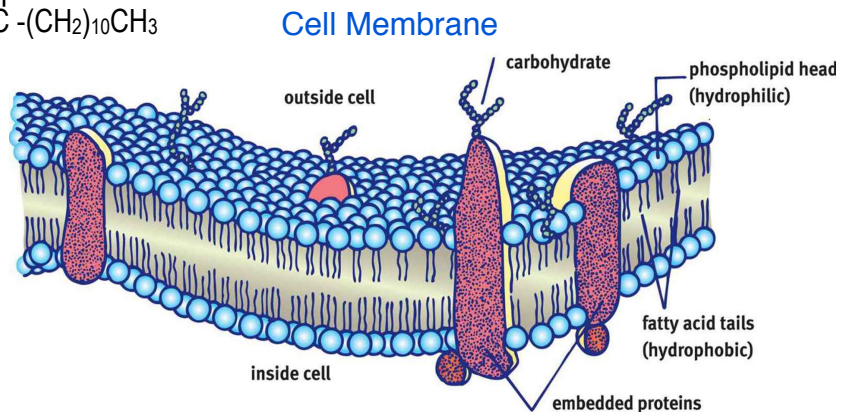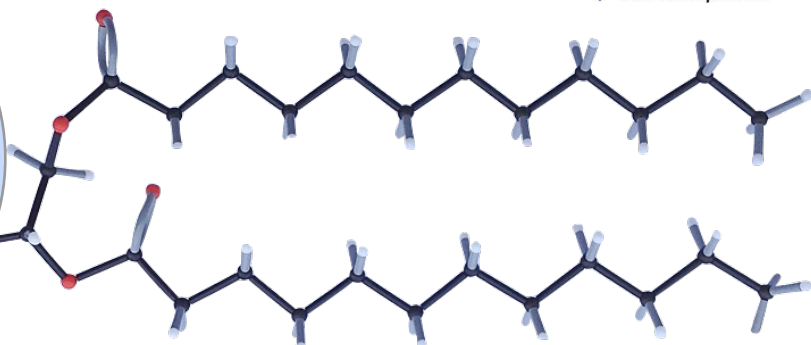
Figure 17: Cephalin

$$H - \overset{\overset{\displaystyle H}{|}}{C} - O - \overset{\overset{\displaystyle O}{\|}}{C} - (CH_2)_{10}CH_3$$

$$H - C - O - \overset{\overset{\displaystyle O}{\|}}{C} - (CH_2)_{10}CH_3$$

$$^+NH_3 - CH_2 - CH_2 - O - \overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O}{|}}{P}} - O - CH_2$$
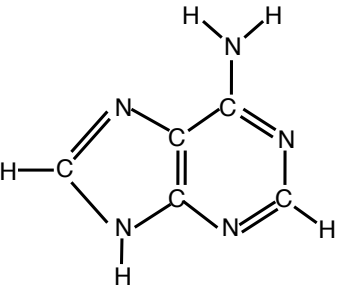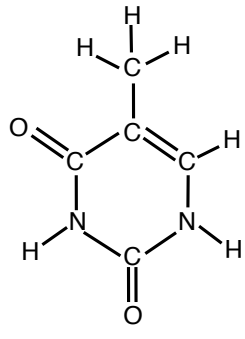
Cell Membrane

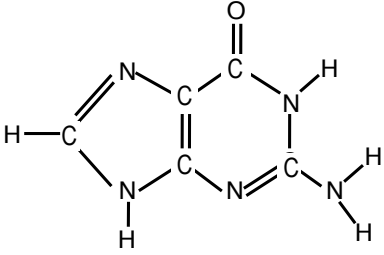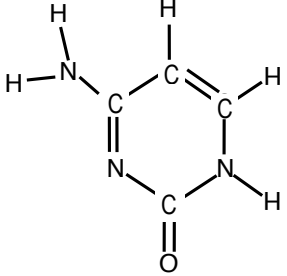phospholipid head
(hydrophilic - polar)
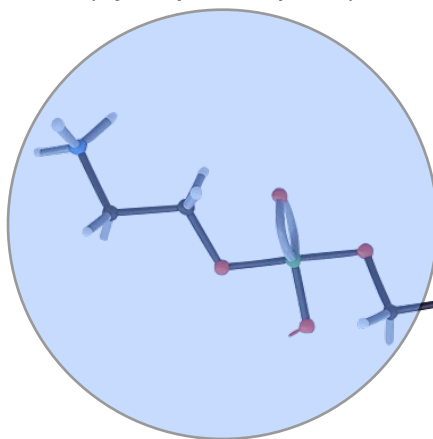
fatty acid tails
(hydrophobic - nonpolar)

8

NUCLEIC ACIDS

The two types of nucleic acids found in living cells are deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). Nucleic acids are composed of three major classes of compounds: phosphates, pentose sugars, and heterocyclic amines that together form a nucleotide. The pentose sugars, ribose and deoxyribose, are shown in Table 1. The molecular structures of the heterocyclic amines are shown in Table 2 below.

TABLE 2: HETEROCYCLIC AMINES			
Purines	**Structural Formula**	**Pyrimidines**	**Structural Formula**
Adenine		Thymine	
Guanine		Cytosine	

Dictated by specific hydrogen bonding patterns adenine-thymine and cytosine-guanine are always paired. The hydrogen bonding between adenine and thymine is shown in Figure 18.

Figure 18: Bonding Between Adenine and Thymine
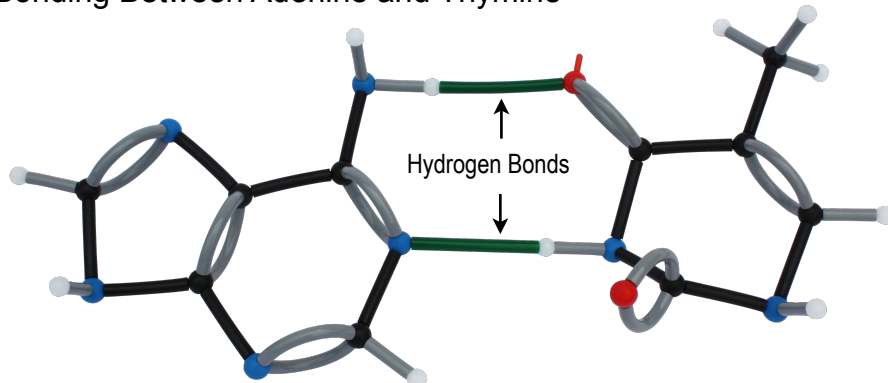
Structure of DNA and RNA

Deoxyribonucleic acid, DNA, is a double-stranded molecule. The best way to visualize DNA is as a very long twisted ladder. The sides of the ladder are composed of alternating phosphoric acid and deoxyribose molecules, running in opposite directions. The base pairs join to form the rungs of the ladder. The sequence of the base pairs is the genetic code for the entire cell.

Figure 19: DNA Molecule

Note: Nitrogen and oxygen atoms that have hydrogen bonds require the use of models with 4 poles.

Thymine nucleotide

Adenine nucleotide

Guanine nucleotide

Cytosine nucleotide
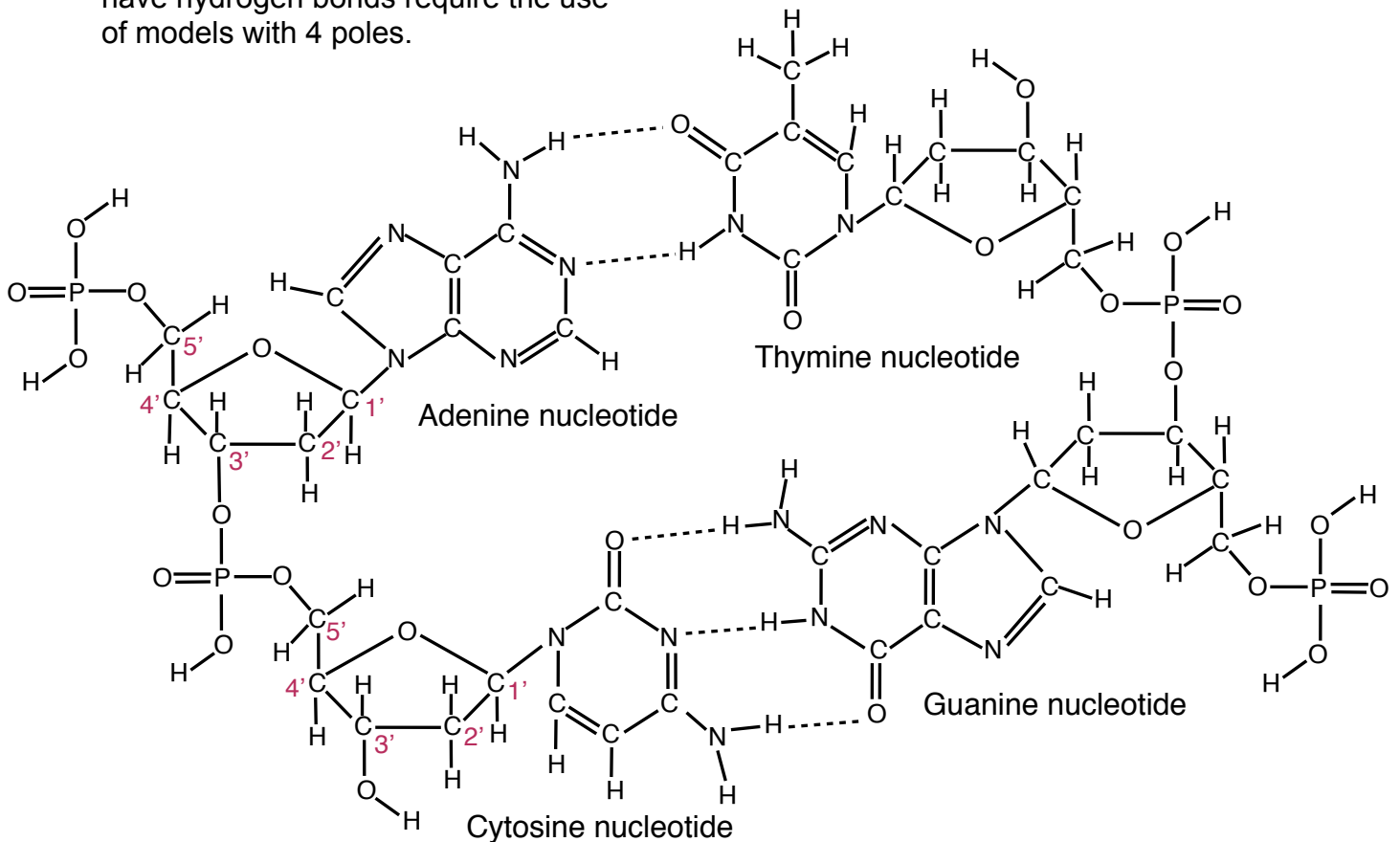
The molecule that "reads" the genetic code and is involved in the formation of proteins is ribonucleic acid, RNA. RNA is similar to DNA in that it is formed from nucleotides. However, RNA is a single-stranded molecule. Deoxyribose and thymine are not found in RNA. Two other molecules, ribose and uracil, are present. Ribose replaces deoxyribose, and uracil, shown in Figure 20, replaces thymine. Three general types of RNA exist: messenger, ribosomal, and transfer.
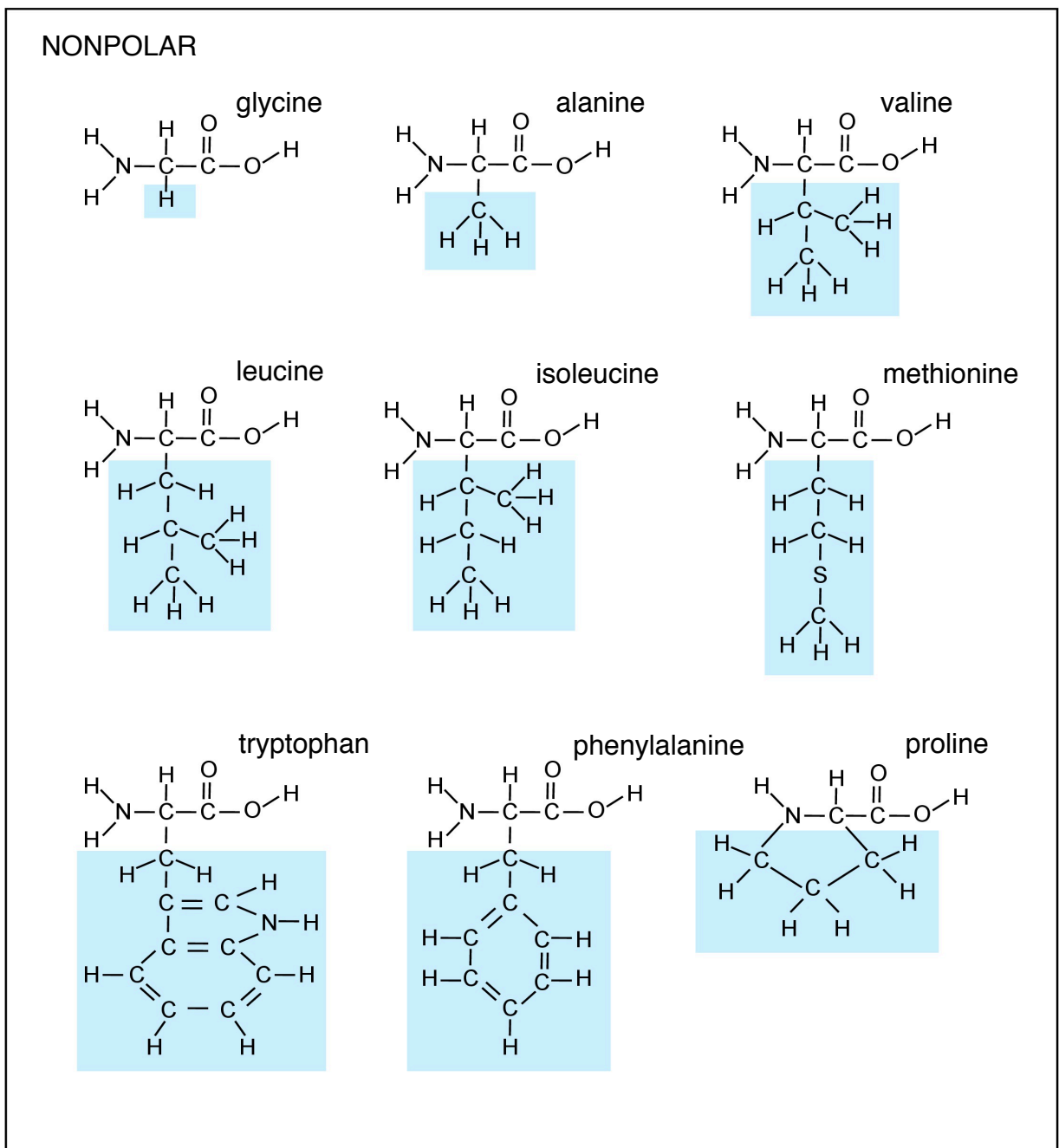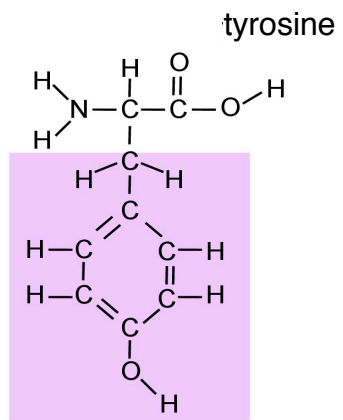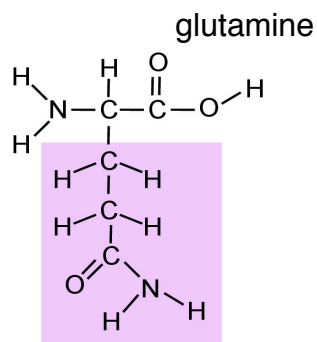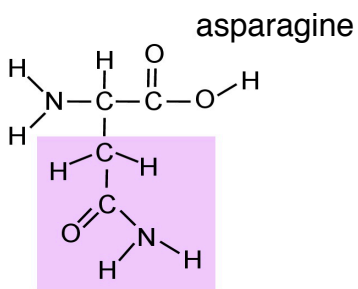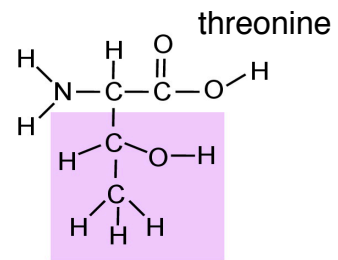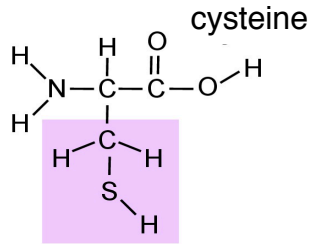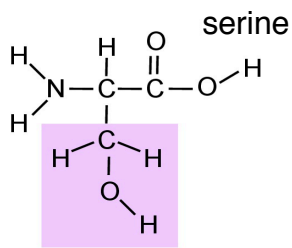
Figure 20: Uracil
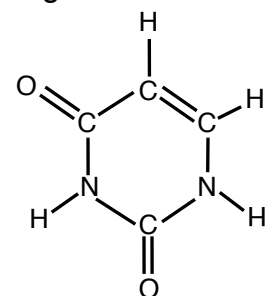
PROTEINS

Proteins are very large molecules composed of monomers called amino acids. Amino acids are compounds that contain two functional groups: an amine group (NH$_2$) and a carboxylic acid group (COOH). A side chain attached to the compound gives each amino acid a unique set of characteristics. Based on the side chain, the amino acids can be classified into 4 categories: nonpolar, polar, acidic polar, and basic polar.
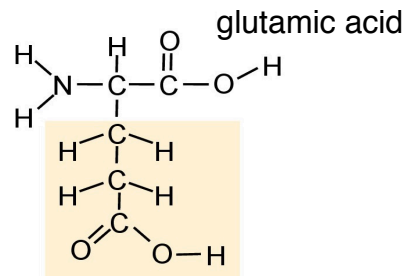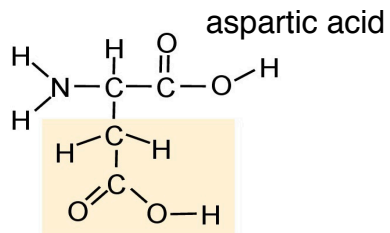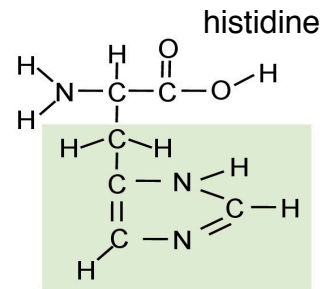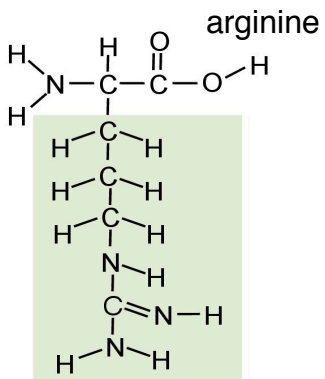
Figure 21: Twenty Amino Acids

POLAR

serine

cysteine

threonine

asparagine

glutamine

tyrosine

ACIDIC

aspartic acid

glutamic acid

BASIC

lysine

arginine

histidine
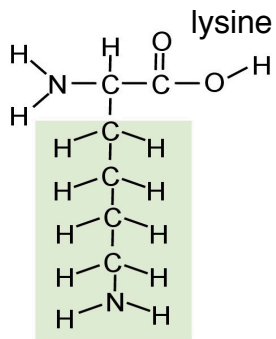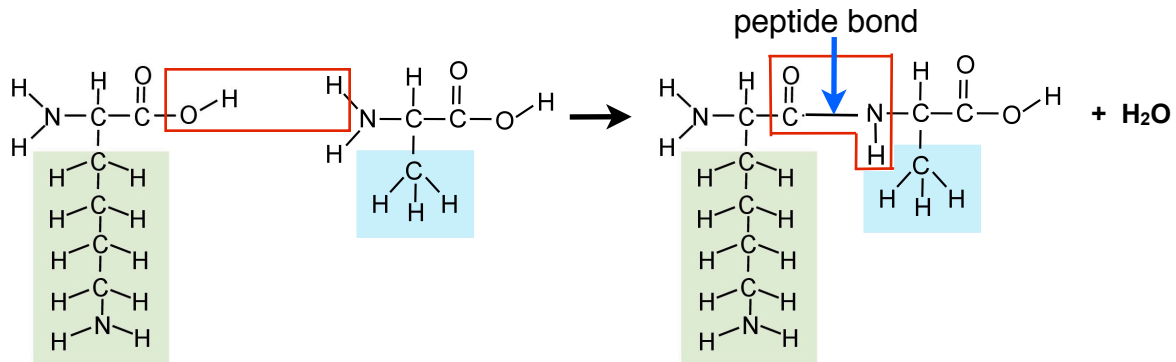
Peptide Bond

A peptide bond (or amide linkage) is a covalent bond formed between two amino acids when the carboxyl group of one amino acid reacts with the amine group of the other amino acid, causing the release of a molecule of water. This reaction is known as a dehydration synthesis or condensation reaction. The formation of the peptide bond between lysine and alanine is shown in Figure 22.

Figure 22: Formation of the Peptide Bond

The peptide bond length is consistent with partial double bond character. Because the bond between the carbonyl carbon and the nitrogen has a partial double bond character, rotation around this bond is restricted. The peptide bond presents a barrier to rotation which maintains the planar geometry of the bond. Electron delocalization lowers the potential energy of the substance and thus makes it more stable than any of the contributing structures. The contributing structures and the model of the resonance structure of the peptide bond is shown in Figure 23. Notice that the R-groups are on opposite sides of the peptide bond. The trans arrangement of the R-groups around the peptide bond predominates in proteins.

Figure 23: Peptide Bond

contributing structures

resonance model
of the peptide bond
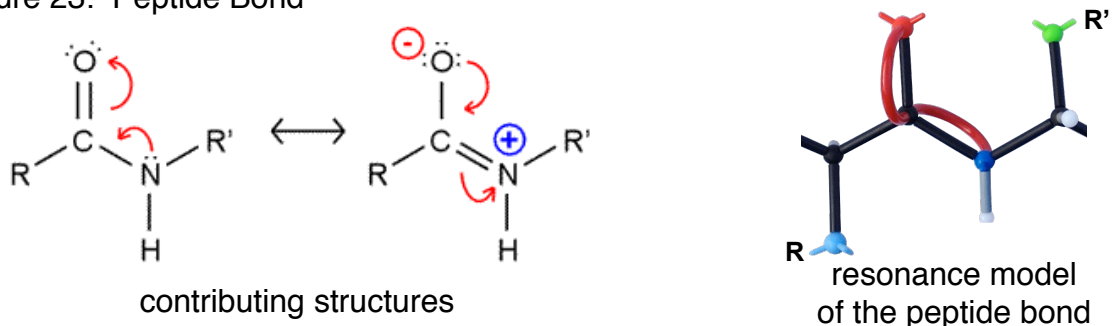
Primary Structure

Sometimes it is convenient to represent the R-group with a single model. The R-group models are color-coded to match the colors found in Figure 21. The nonpolar R-group is light blue; the polar R-group is purple; the acidic R-group is lime; and the basic R-group is orange.

Primary structure is used to describe the order of the amino acids joined together to make the polypeptide chain. The polypeptide chain is composed of amino acid residues, amino acids which have lost a water molecule in the dehydration synthesis reaction. An example of the primary structure of a polypeptide chain is shown in Figure 24.

Figure 24: Polypeptide

| Aspartic Acid | - | Glutamine | - | Lysine | - | Alanine | - | Glutamic Acid |
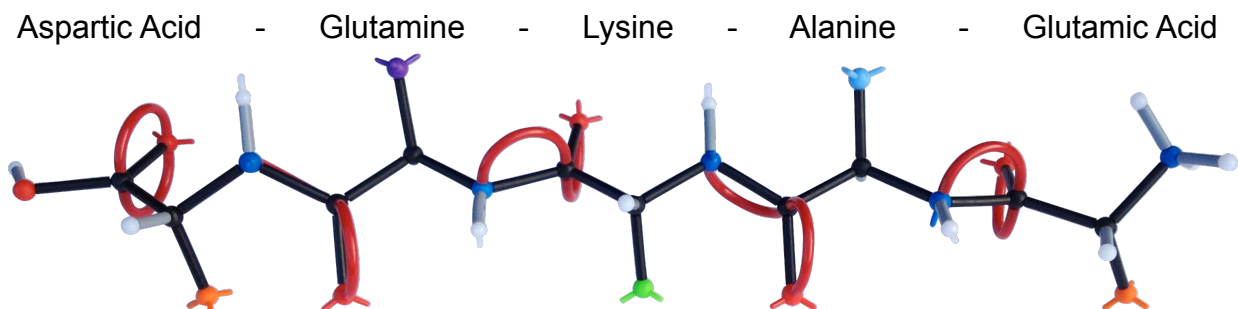
The R-groups alternate below and above the central axis of the polypeptide. The peptide bond is shown as a resonance structure with the delocalized electrons represented by red links. The resonance peptide bond is constructed using a 4-pole model for nitrogen and 5-pole models for carbon and oxygen.

Secondary Structure

The two most common secondary structures of a polypeptide chain are the alpha helix and the beta pleated sheet as shown in Figure 25. These secondary structures are held together by hydrogen bonds, formed between the lone pair of electrons on the oxygen atom and the hydrogen atom that is attached to the nitrogen atom. In the alpha helix, the polypeptide chain is coiled tightly in the fashion of a spring. The R-groups extend outward from the coil. The helix is stabilized by hydrogen bonds between the amine group of one amino acid and the carboxyl group on the fourth amino acid away from it. The alpha helix is a right-handed coil of amino acid residues. There are 3.6 amino acid residues in one complete turn of the helix.

Figure 25: Secondary Structure of a Protein

alpha helix

beta pleated sheet (anti-parallel)
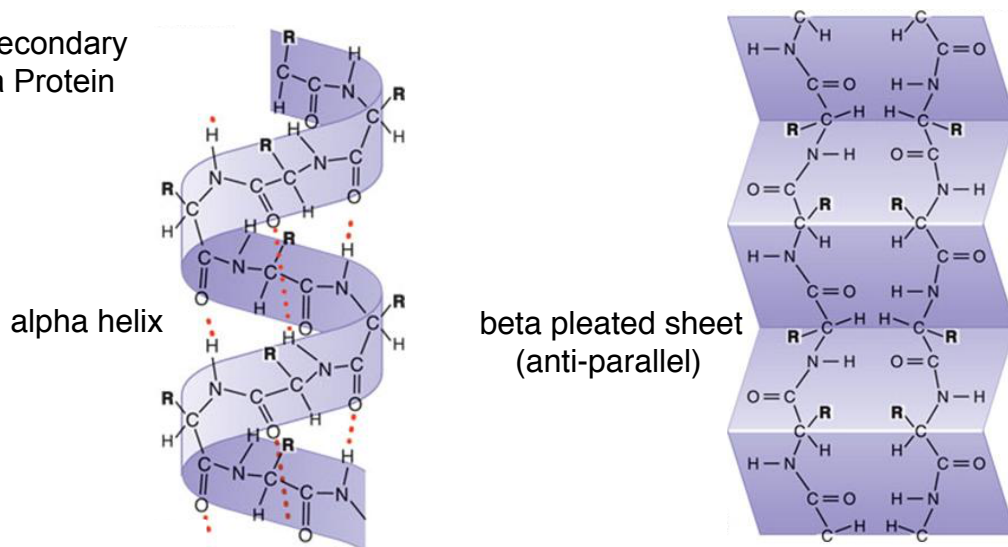
The beta pleated sheet is a secondary structure in which the polypeptide chains lie next to each other and are linked by hydrogen bonds between the N-H group and the C=O group. Pleated sheets are designated as parallel or anti-parallel based on the relative direction of the two interacting polypeptide chains. The parallel pleated sheet shown in Figure 26 has the polypeptide chains lying in the same direction.

Figure 26: Beta Pleated Sheet
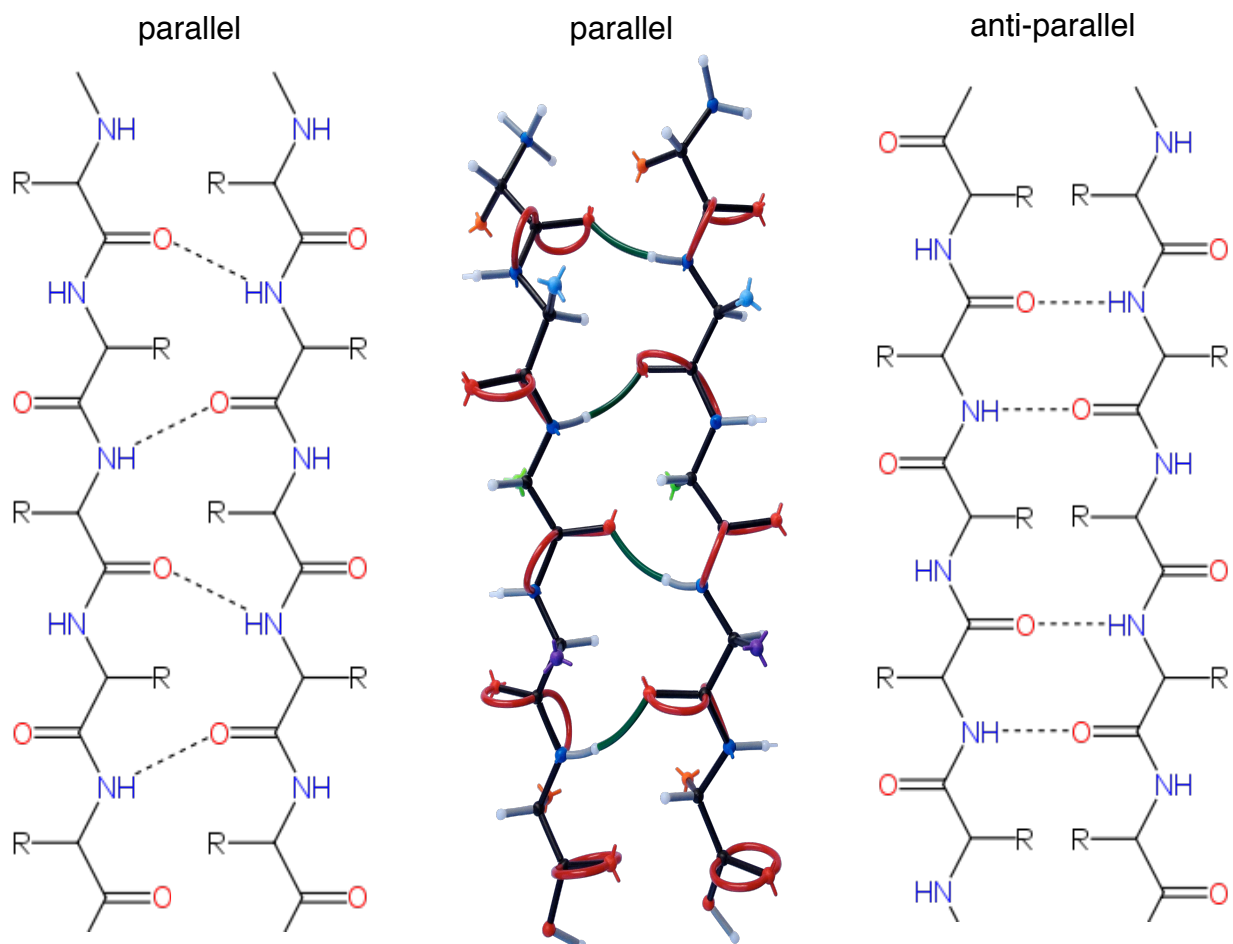
Tertiary and Quaternary Structure

The tertiary structure of a protein is a description of the folding of the polypeptide chain due to the interaction of R-groups. These interactions include hydrogen bonds between polar R-groups, ionic bonds between charged R-groups, hydrophobic interactions between nonpolar R-groups, and disulfide bonds. The quaternary structure describes the interactions between different peptide chains that make up the protein.

TABLE 3: THE BIOCHEMISTRY MODEL SET		
Model	**Description**	**Number**
Hydrogen, H	white, 1-pole represents 1s orbital	75
Carbon, C	black, 4-poles represent four sp^3 orbitals	40
Carbon, C	black, 5-poles represent three sp^2 orbitals and 1 unhybridized p orbital for double bond	10
Oxygen, O	red, 2-poles represent two sp^3 orbitals. Lone pairs of electrons are not shown.	25
Oxygen, O	red, 4-poles represent four sp^3 orbitals	16
Oxygen, O	red, 5-poles represent three sp^2 orbitals and 1 unhybridized p orbital for double bond	10
Nitrogen, N	blue, 3 poles represent three sp^3 orbitals. The lone pair of electrons is not shown.	15
Nitrogen, N	blue, 4-poles represent four sp^3 orbitals	5
Nitrogen, N	blue, 5-poles represent three sp^2 orbitals and 1 unhybridized p orbital for double bond	8
Phosphorus, P	green, 4-poles represent four sp^3 orbitals	2
Phosphorus, P	green, 5-poles represent three sp^2 orbitals and 1 unhybridized p orbital for double bond	4
Phosphorus, P	green, 6-poles represent two sp orbitals and 2 unhybridized p orbitals for resonance in ATP	3
Sulfur, S	yellow, 4 poles represent four sp^3 orbitals	2
Nonpolar R-Group	light blue	2
Polar R-Group	purple	2
Acidic R-Group	orange	2
Basic R-Group	lime green	2
Single bond, -H	gray, 25mm; use to link hydrogen atoms to the molecule	75
Single bond C-C, C-O, C-N	gray, 40mm; use with all atoms (except hydrogen) to hold the atoms securely in the molecule	28
Single bond	black, 40mm; designed to allow rotation around the single bond	55
Double bond	gray, 51mm	36
Pi bond	red, 83mm	20
High-energy bond	white, 40mm	3
Hydrogen bond	green 64mm hydrogen atom (attached to green hydrogen bond)	5 5
Bond length is scaled. 1 inch = 25mm and represents 1 angstrom		