Biochemistry

Biochemistry: is the study of the chemical composition and reactions of living matter.

Biological compounds fall into two major classes: organic compounds and inorganic compounds. Both are essential for life.

<u>Organic compounds</u>: contain carbon. Also, all organic compounds contain covalent bonds.

<u>Inorganic compounds</u>: do not contain carbon. These include water, salts and many acids and bases.

Inorganic compounds

Water: is the most abundant and most important inorganic compound found in living materials. It makes up 60% to 80% of most cells. Some of the life essential properties of water include:

1. high heat capacity: water absorbs and releases large amounts of heat before changing appreciably in temperature itself. It therefore helps prevent sudden changes in body temperature due to factor like sun and wind, muscle activity etc.

2. heat of vaporization: the changing of water from the liquid state to the gaseous state requires large amounts of heat be absorbed to break the hydrogen bonds that holds water molecules together. This is extremely important when we perspire.

3. polarity/solvent properties: water acts as a solvent for both organic and inorganic molecules. Note that Biochemistry is a "wet" chemistry. Biological molecules do not react chemically unless they are in solution.

Remember that water molecules are polar, they therefore tend to orient themselves with their slightly negative ends toward the positive ends of the solute. This attracts a solute and then surrounds it.

Water also forms hydration layers. These are layers of water molecules around large charged molecules (such as proteins) shielding them from other charged substances and preventing them from settling out of solution. When this happens, we refer to the mixture as a biological colloid. Examples would be cerebrospinal fluid and blood plasma.

4. reactivity: water serves as a reactant in many chemical reactions. Foods are digested by adding a water molecule to each bond to be broken. These reactions are called hydrolysis reactions. Water is also used when large protein or carbohydrate molecules are synthesized from smaller molecules. A water molecule is removed for every bond formed. This is called hydration synthesis.

5. cushioning: water surrounding certain body organs helps protect them from physical trauma. An example of this is cerebrospinal fluid around the brain.

Salts: a salt is an ionic compound containing cations other than H^+ and anions other than the hydroxyl ion (OH^-). Remember, when salts are dissolved in water, they dissociate into their component ions. All ions are electrolytes, i.e., substances that conduct an electrical current in solution

Acids/Bases: are also electrolytes in that they dissociate in water and can conduct an electrical current.

acids: are defined as a substance that releases hydrogen (H+) in detectable amounts. These are also defined as proton donors. Stomach acid (HCl) produced by stomach cells dissociates into a proton and a chloride ion: $HCl \rightarrow H^+$ (proton) + Cl^- (anion)..

Bases: are proton acceptors, that is they take up hydrogen ions. Common inorganic bases include the hydroxides such as magnesium hydroxide (milk of magnesia) and sodium hydroxide (lye). Hydroxides also dissociate in water. In this case they dissociate into hydroxyl ions (OH-) and a cation.
$NaOH \rightarrow Na^+$ (cation) + OH^- (Hydroxyl ion). What happens to the OH^- ? $OH^- + H^+ \rightarrow H_2O$

Biocarbonate ion (HCO3-) is an important base in the body and is particularly abundant in the blood Also, Ammonia (NH3), which is a common waste product of protein breakdown is also a base. By accepting a proton ammonia becomes an ammonium ion. $NH_3 + H^+ \rightarrow NH_4^+$.

The more hydrogen ions in a solution the more acidic the solution. Also, the more hydroxyl ions in a solution the more basic the solution hence the pH of a solution is defined as the negative logarithm of the hydrogen ion concentration (in moles per liter) Also written $-\log[H^+]$.

Acid/base concentration is measured in units called pH units. The pH scale runs from 0 to 14 with zero being the most acidic and 14 the most basic. A pH of 7 is neutral.

Note figure 2.12 in your textbook (Marieb). It shows the pH scale and give examples of the pH of common substances and body fluids.

Gastric juice and lemon juice = pH 2
coffee = pH 5
Urine = pH 5-8
milk = pH 6.5
Human blood = pH 7.4
seawater = pH 8.4
milk of magnesia = pH 10.5
oven cleaner = pH 13.5

Buffers

Living cells are extremely sensitive to changes in pH. In general, the acid -base balance of the body is regulated by the kidneys and lungs and by chemical systems called buffers.

Buffers resist large swings in pH by releasing hydrogen ions (acting as acids) when the pH begins to rise, and by binding hydrogen ions (acting as bases) when the pH begins to fall.

Because blood comes into contact with nearly every body cell, regulation of its pH is extremely critical. Normally blood pH varies within a very narrow range of 7.35 - 7.45. Variations greater than this often prove fatal.

Organic Compounds

Remember that earlier we said that organic compounds contain carbon and inorganic compounds do not. There are a few exceptions to this rule. Carbon dioxide, carbon monoxide, and carbides all contain carbon, however these compounds are considered to be inorganic.

Carbon makes the perfect elemental base for life because it is small and precisely electroneutral. Due to this fact carbon never gains or loses electrons. It always shares them. In addition, carbon only has 4 electrons in its outer valence shell. This allows it to form 4 covalent bonds with other elements. This allows carbon to be found it long chainlike molecules (fats), ring structures (carbohydrates and steroids) and several other structures.

Carbohydrates

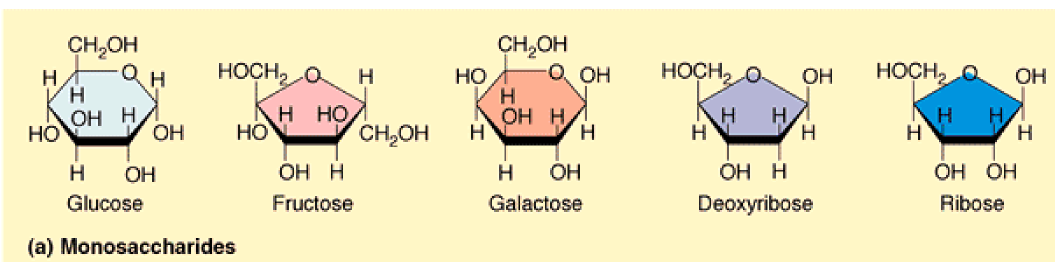
Carbohydrates are a group of molecules that includes sugars and starches. Carbohydrates usually represent about 1% - 2% of cell mass. Carbohydrates contain hydrogen, carbon, and oxygen. Generally, the hydrogen and oxygen atoms occur in the same 2:1 ratio as they do in water hence the term **Carbohydrate** (hydrated water).

Carbohydrates can be classified according to their size and solubility. Monosaccharide (one sugar), disaccharide (two sugars), and polysaccharide (many sugars). Monosaccharides are the building blocks of the other carbohydrates. In general, the larger the carbohydrate molecule the less soluble it is in water.

Monosaccharides

Also known as simple sugars are single chain or single ring structures containing 3 to 7 carbon atoms. Usually the carbon, hydrogen, and oxygen atoms occur in a 1:2:1 ratio giving a general formula for a monosaccharide as $(CH_2O)n$, where n is the number of carbon atoms. Monosaccharides are generically named according to their number of carbons. The most important monosaccharides in the body are the pentose (five carbon) and hexose (six carbon) sugars. the pentose deoxyribose is part of DNA and the hexose, glucose, is blood sugar.

Note that there are **isomers** of glucose, galactose and fructose. Isomers have the same molecular formula but their atoms are arranged differently giving them different chemical properties.



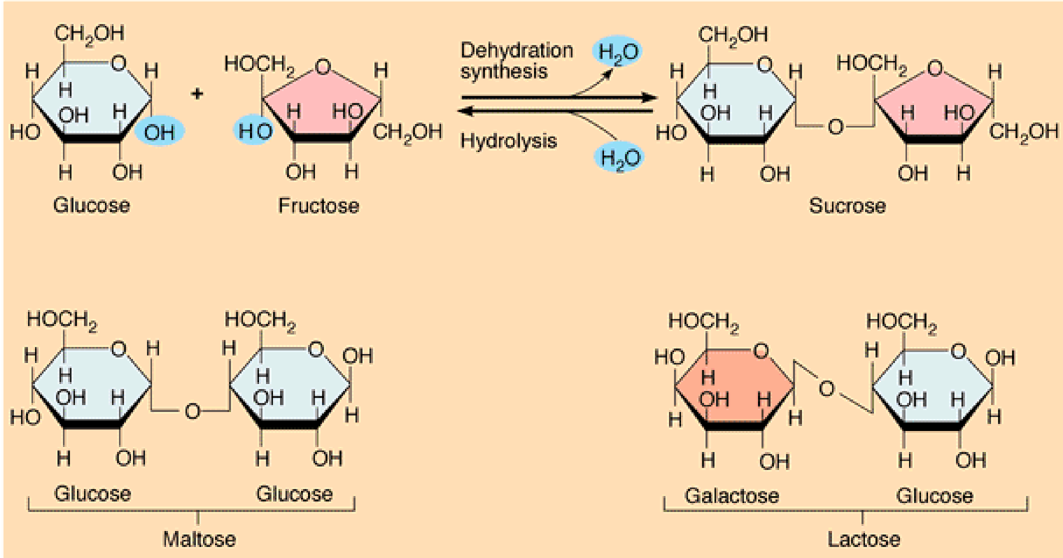
(a) Monosaccharides

Disaccharides

Disaccharides are double sugars that are formed by the joining of two monosaccharides. When the two monosaccharides join a water molecule is lost. This type of reaction is called **hydration synthesis**.

Important disaccharides in our diet include sucrose (galactose + fructose), lactose (glucose + galactose), and maltose (glucose + glucose)

Note that disaccharides are too large to pass through cell membranes so they must be digested into their simple sugar units before they can be absorbed through the digestive tract and into the blood. During this process a water molecule is added to each bond to be broken thus releasing the simple sugars. This process is called **hydrolysis**.



(b) Disaccharides

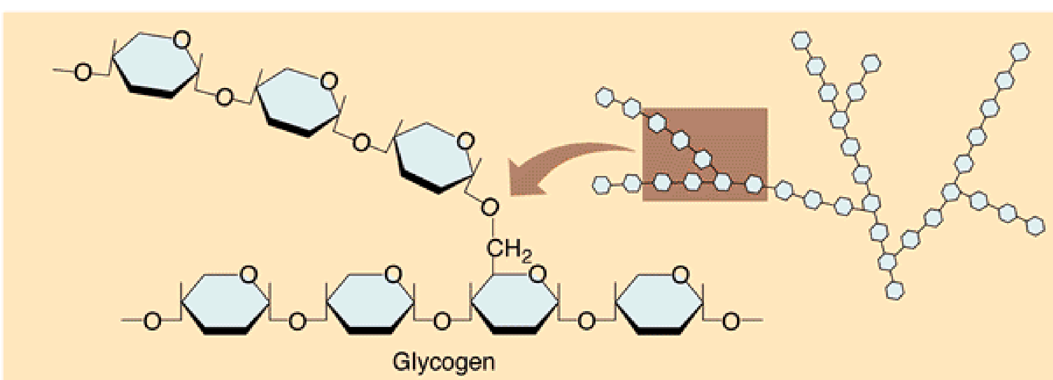
Polysaccharides

Polysaccharides are long chains of simple sugars. Because they are large, they are fairly insoluble and therefore are ideal for storage products. We are mainly concerned with two polysaccharides, starch and glycogen.

Starch: is a plant carbohydrate. When we eat starch it must be digested down to its glucose units before digestion. Cellulose is another plant polysaccharide however humans are unable to digest cellulose. It does help to make the bulk that helps move feces through the colon.

Glycogen: is the storage carbohydrate of animal tissue. It is found mainly in the liver and skeletal muscle. When blood sugar levels drop, the liver cells break down glycogen and release the glucose units into the blood.

When glucose is broken down and oxidized within cells there is a transfer of electrons. This relocation of electrons releases the bond energy stored in the glucose molecule and this energy is used to synthesize ATP. When ATP supplies in the body are sufficient, dietary carbohydrates are converted into glycogen or fat and stored.



(c) Portion of a polysaccharide molecule (glycogen)

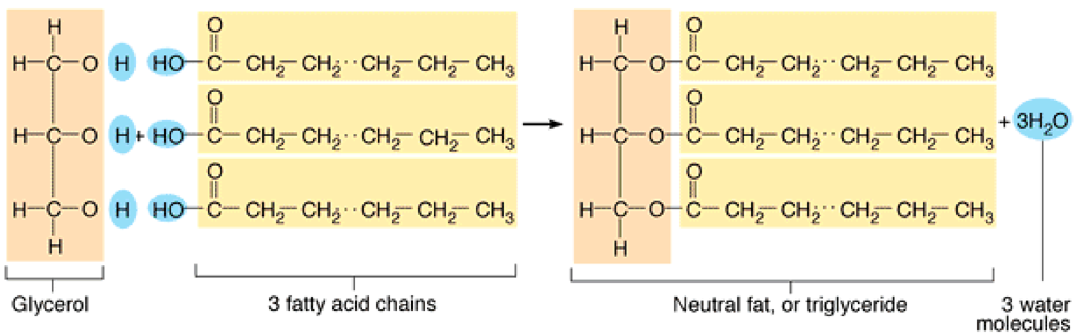
Lipids

Lipids are organic compounds that are insoluble in water but readily dissolve in other lipids and in organic solvents such as alcohol, chloroform, and ether. Lipids also contain hydrogen, carbon, and oxygen, but the proportion of oxygen is much lower. Also, many lipids contain phosphorus.

Lipids include neutral fats, phospholipids, and steroids

Neutral Fats (triglycerides)

Neutral fats are commonly known as fats when they are solid and as oils when they are liquid. These fats are composed of fatty acids and glycerol. Fat synthesis involves attaching three fatty acids to one glycerol molecule (via dehydration synthesis). This results in an E shaped molecule. Because of the 3:1 ration the neutral fats are also called triglycerides.



(a) Formation of a triglyceride

Fatty acids are linear chains of carbon and hydrogen atoms (hydrocarbons) with an organic group on one end. The hydrocarbon chains make neutral fats non-polar molecules. Since polar and non-polar molecules do not interact, oil (or fats) and water do not mix. Consequently, neutral fats are well suited for storing fuel (energy) in the body. Deposits of neutral fats are found mainly beneath the skin where they provide a layer of insulation.

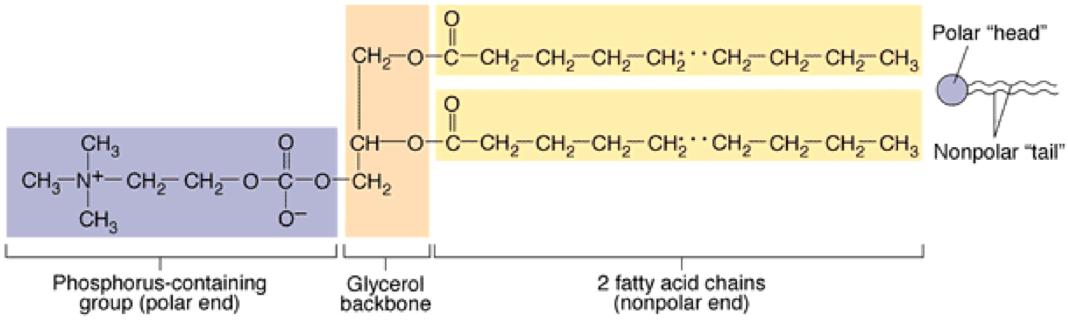
The length of the fatty acid chains and their degree of saturation determine how solid a neutral fat is at a given temperature. Fatty acid chains with only single covalent bonds between carbon atoms are referred to as **saturated**. Fatty acids that contain one or more double bonds between carbon atoms are called **unsaturated** (monounsaturated and polyunsaturated).

Unsaturated (and short chain) fatty acids are liquid at room temperature. Humans mainly use these fats for cooking. **Monounsaturated** = olive oil and peanut oils
Polyunsaturated = corn oil, soybean oil, and safflower oils

Longer fatty acid chains and saturated fatty acids are solid at room temperature. Saturated fatty acids are common in animal fats such as butter and the fat in meats.

Phospholipids

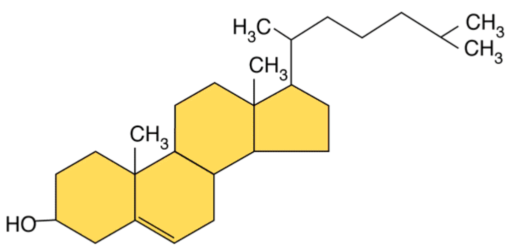
Phospholipids are modified triglycerides. Here one of the fatty acid chains has been replaced with a phosphorus containing group. It is this phosphorus containing group that give phospholipids their distinctive chemical properties. The hydrocarbon portion (tail) of the molecule is non-polar and interacts only with other non-polar molecules. The phosphorus containing portion (head) is polar and attracts other polar or charged particles, such as water or ions. Molecules with both polar and non-polar regions are said to be **amphipathic**. It is this distinct property that makes these molecules ideal for building cell membranes.



(b) Phospholipid molecule (phosphatidyl choline)

Steroids

Steroids are basically flat molecules made of four interlocking hydrocarbon rings. Steroids are fat soluble and contain little oxygen.



(c) Cholesterol

Cholesterol is the most important molecule in our steroid library. We ingest cholesterol when we eat animal products such as eggs, meat, and cheese. Our liver also produces cholesterol.

Cholesterol is absolutely essential for human life. It is found in cell membranes and is the raw material for vitamin D, steroid hormones, and bile salts.

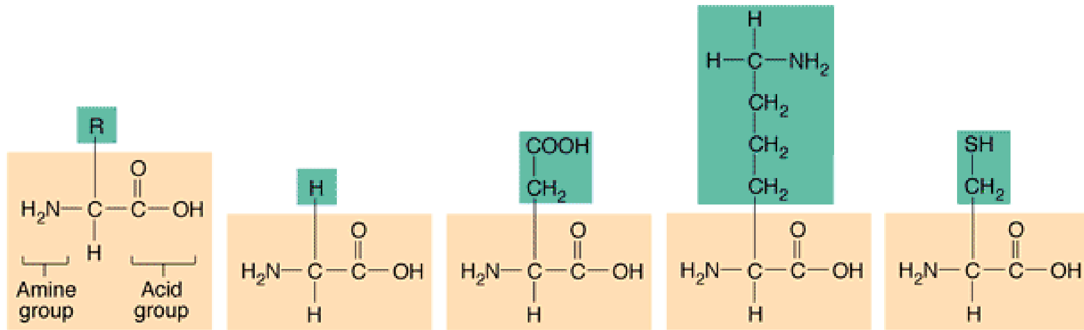
Eicosanoids

Eicosanoids are diverse lipids derived from a 20- carbon fatty acid (arachadonic acid) found in all cell membranes. The most important eicosanoids are the protaglandins which play roles in various body processes including blood clotting, inflammation, and labor contractions.

Amino Acids

Amino acids are the building blocks of proteins. There are 20 common types of amino acids. All amino acids have a basic amine group (—NH_2) and an organic acidic group (—COOH). This means that an amino acid can act as either an acid (proton donor) or a base (proton acceptor).

All amino acids are identical except for a side group known as the ***R group***. It is the R group that gives each amino acid its unique properties.



(a) Generalized structure of all amino acids (b) Glycine (the simplest amino acid) (c) Aspartic acid (an acidic amino acid) (d) Lysine (a basic amino acid) (e) Cysteine (a sulfur-containing amino acid)

Proteins

Proteins are long chains of amino acids joined together by hydration synthesis, with the amine end of one amino acid linked to the acid end of the next. The resulting bond produces a characteristic arrangement of linked atoms and is called a **peptide bond**. Two united amino acids are a dipeptide, three form a tripeptide, and ten or more form a polypeptide. The sequence of the linked amino acids results in a protein. Although there are only 20 amino acids the combinations and permutations allow for there to be thousands of different proteins.

Proteins compose 10% - 30% of cell mass and are the basic structural material of the body. Many proteins play vital roles in cell function. Proteins include enzymes, hemoglobin, contractile proteins in the muscles, and have the most varied functions of any molecules in the body. All proteins contain carbon, hydrogen, oxygen, and **nitrogen**. Many also contain sulfur and phosphorus.

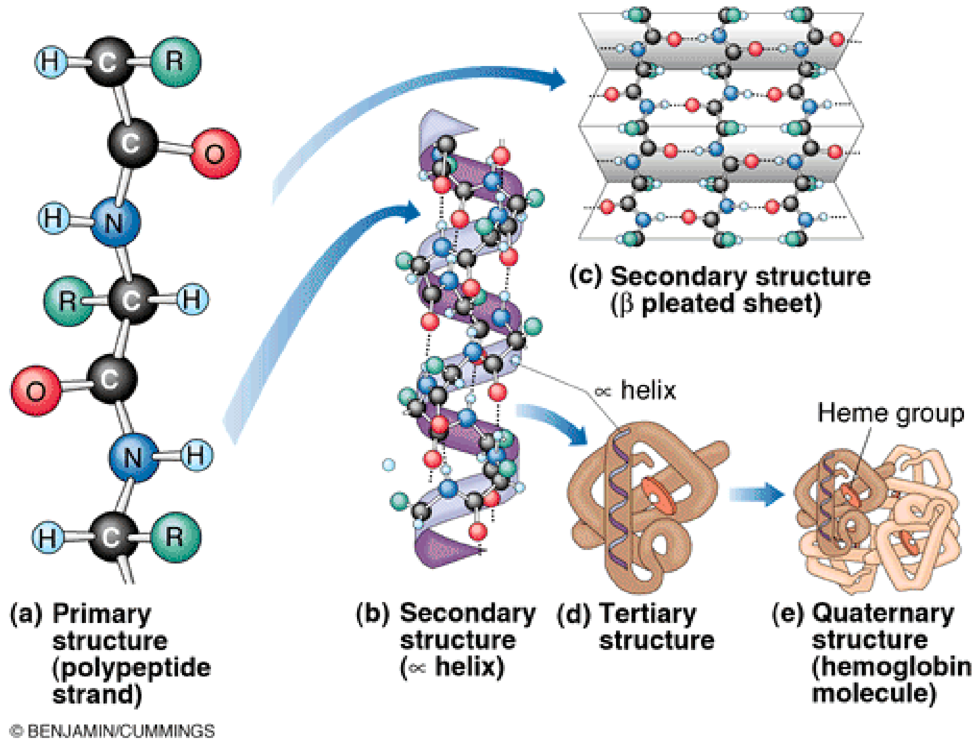
Proteins can be described in terms of 4 structural levels

The linear sequence of the amino acids making up the polypeptide chain is referred to as the primary structure. This is the backbone of the molecule and is similar to a string of beads.

Proteins do not exist as simple linear chains. Instead, they twist and bend upon themselves to form a complex secondary structure. The most common of these structures is the **alpha helix**. Another type of secondary structure is the **Beta pleated sheet**. Here the primary chains do not coil but rather are linked side by side by hydrogen bonds.

Many proteins have a **tertiary structure**. This is seen when an alpha helix or a beta pleated sheet region fold upon one another to produce a more compact ball or globular molecule.

When two or more polypeptide chains are arranged in a regular manner to form a complex protein this protein is said to have a **quaternary structure**. Hemoglobin is an example of such a protein.



Fibrous Proteins

Fibrous proteins are extended and strand-like. Most exhibit only secondary structure, but some have quaternary structure as well. Collagen is a triple helix (a coiled coil) of three polypeptide chains that form a strong ropelike structure. Fibrous proteins are linear, insoluble in water, and very stable. These qualities are ideal for providing mechanical support and tensile strength to the body's tissues. Other fibrous proteins include keratin, elastin, titin, and the contractile proteins of muscles.

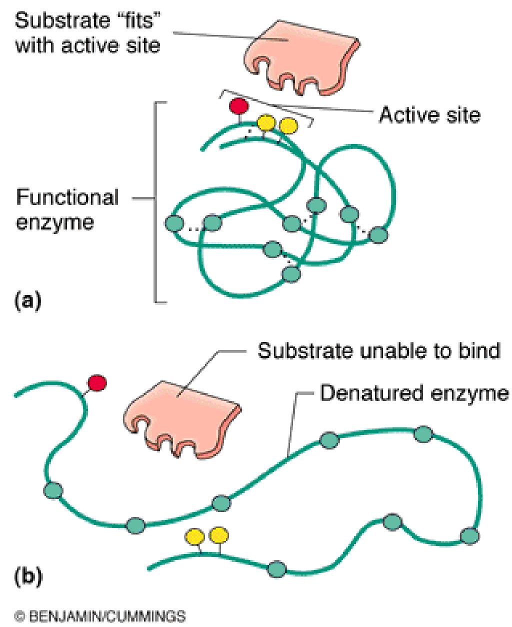
Globular Proteins

Globular proteins are compact, spherical porteins that have at least some tertiary structure (some have quaternary structure). These are water soluble, mobile, chemically active molecules. Many refer to these proteins as functional proteins. These proteins include antibodies, protein-based hormones and enzymes.

Refer to table 2.3 in your text (Marieb) for more information on protein structure.

Protein Denaturation

Although fibrous proteins are very stable, globular proteins are not. The activity of a globular protein depends on its specific three-dimensional structure and intermolecular bonds. Most of these bonds are hydrogen bonds, and hydrogen bonds are easily broken. When there are temperature extremes or drastic pH changes many of these bonds are broken and the globular protein will lose its specific shape. This is referred to as a **denatured** protein. Most forms of denaturation are reversible, however if the temperature change or Ph change is too severe the protein may be irreversibly denatured, that is, damaged beyond repair. The cooking of egg white is a good example of this. Denaturation is incompatible with the biologic function of the protein because it causes rearrangement of the protein’s **active site.**



Two groups of proteins, enzymes and molecular chaperones, are intimately involved in the normal functioning of all cells.

Enzymes

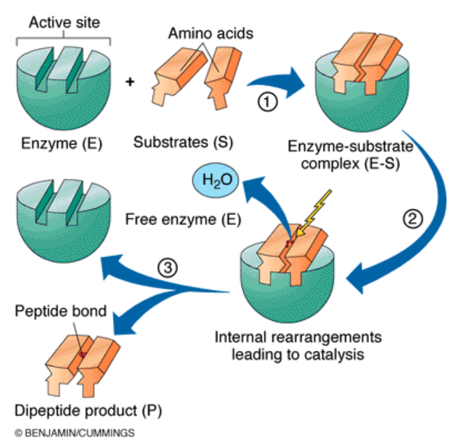
As mentioned earlier, enzymes act as catalysts to regulate and accelerate the rate of biochemical reactions. Without enzymes biochemical reactions proceed so slowly that for all practical purposes they do not occur at all. Enzymes increase the reaction rates by a factor of about 1 million.

Three steps are involved in the mechanism of enzyme action.

1. The enzyme binds with the substance(s) on which it acts. These substances are called the substrates. Substrate binding occurs at the active site on the enzyme’s surface. This binding causes the active site to change shape so that the substrate and the active site fit together very precisely. This is known as the induced fit model.

2. The enzyme-substrate complex undergoes internal arrangements that form the product.

3. The enzyme releases the product of the reaction.



Molecular Chaperones

Molecular chaperones are globular proteins which help proteins achieve their functional three-dimensional structure. Some of the role played by molecular chaperones are:

Prevent accidental, premature, or incorrect folding of polypeptide chains and/or their association with other polypeptides.

Aid the desired folding and association process

Help to translocate proteins across cell membranes

Promote the beakdown of damaged or denatured proteins.

Nucleic Acids (DNA and RNA)

Nucleic acids are composed of carbon, oxygen, hydrogen, nitrogen, and phosphorus. They are also the largest molecules in the body.

Nucleic acids are composed of structural units called nucleotides, which are rather complex.

A nucleotide consists of three components joined together by dehydration synthesis: 1. a nitrogen containing base, 2. a pentose sugar, and 3. a phosphate group

It is the nitrogen containing base which gives each nucleotide type its specific characteristics. There are 5 types of nitrogen containing bases which contribute to nucleotide structure; 1. adenine (A), 2. guanine (G), cytosine (C), thymine (T), and uracil (U).

Adenine and guanine are large, two ring bases called purines
cytosine, thymine, and uracil are smaller, single ring bases called pyrimidines.

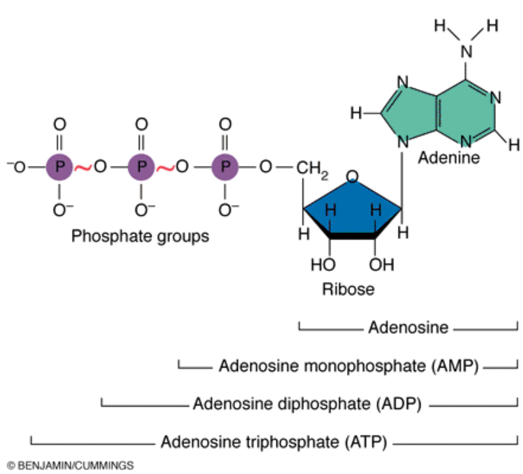
Nucleic acids typically include two major classes of molecules, 1. **deoxyribonucleic acid (DNA)** and 2. **ribonucleic acid (RNA)**.

DNA is a long, double stranded polymer. The bases found in DNA are adenine, thymine, guanine, and cytosine. The pentose sugar in DNA is deoxyribose, hence the name deoxyribonucleic acid. The two strands of a DNA molecule are linked together by hydrogen bonds between the nitrogen bases. The two strands also turn about one another forming a spiral, or helix. Since there are two helical strands the molecule is often referred to as a double helix. The bonding of these nitrogen base pairs is very specific. Adenine always bonds with thymine and guanine always bonds with cytosine; they are thus referred to as complementary bases. Also note that there are two hydrogen bonds between adenine and thymine, and three bonds between guanine and cytosine.

RNA molecules are single strands instead of double strands. RNA also replaces thymine with uracil, so in RNA the complementary base to adenine is uracil instead of thymine as in DNA. The sugar found in RNA is a ribose, again giving the molecule its name.

Adenosine Triphosphate

ATP is an adenine nucleotide to which two additional phosphate groups have been attached by **high-energy** phosphate bonds.



Although glucose is considered the most important cellular fuel, none of the chemical energy contained in its bonds is used directly to power cellular work. Instead, energy released during glucose breakdown is couple to ATP. The ATP then acts to provide energy that is immediately usable by all cells.

ATP is essential for life because it the molecule that drives cellular work. ATP drives the transport of certain solutes (amino acids) across cell membranes, activates contractile proteins in muscle cells, and provides energy required to drive endergonic reactions.