Lecture 4 & 5: Biological macromolecules

Living systems are composed of various types of molecules. There are two main types: **Organic** and **Inorganic** molecules. All organic molecules contain carbon and those that don't are classified as Inorganic molecules. Organisms maintain reserves of small organic molecules that they can assemble into complex **Macromolecules** such as carbohydrates, lipids, proteins, and nucleic acids. These are the building blocks of the living organisms.

How are macromolecules formed?

Small molecules common to all organisms are ordered into unique macromolecules.

Many macromolecules consist of polymers. A **polymer** is a large molecule built up from smaller building block molecules, called monomers. **Monomers** (subunits) are the building block molecules. The inherent differences between human siblings reflect variations in polymers, particularly DNA and proteins. Macromolecules that make up living organisms are formed via polymerization.

Polymerization is the linking together of monomers to form polymers. Large organic molecules are often built from smaller ones by **condensation**, a process in which an enzyme covalently bonds two molecules together. A condensation reaction occurs via the loss of a small molecule, usually from two different substances, resulting in the formation of a bond. Polymerization in biological systems typical occurs via **dehydration synthesis.** Dehydration reaction is <u>synonymous with condensation</u> reaction except that dehydration reaction is limited to those condensations in which the small molecule is water. Dehydration synthesis is synonymous with dehydration reaction.

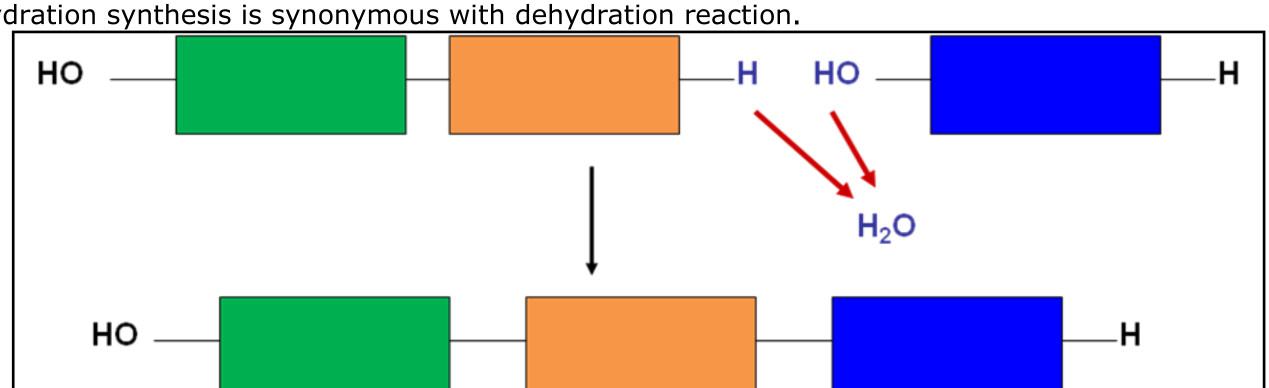


Figure: Condensation reaction. Three boxes represent molecules attached to each other that have free hydrogen and hydroxyl group. These groups can be utilized to form a bond via dehydration reaction, removing H_2O.

Energy is expended to polymerize so all condensation/dehydration reactions require an input of energy in order to move forward!!! Energy is expended to make polymers!

In biological systems, enzymes are required to polymerize without enzymes, no polymerization; so enzymes are required to make polymers. This process is known as Metabolism. Metabolism refers to activities by which cells acquire and use energy as they make and break apart organic compounds.

How are macromolecules broken or digested?

Hydrolysis, which is the reverse of condensation, breaks apart large organic molecules into smaller ones. Hydrolysis enzymes break apart polymers into monomers. By breaking the bonds between monomers, Hydrolysis liberates the energy that polymers contained during dehydration synthesis; thus, some of the energy required to polymerize is returned upon hydrolysis. Hydrolysis plays a very important role in the liberation of usable energy (ATP) within cells. Enzymes are employed in biological systems to effect most hydrolysis reactions. Example: Digestion of food involves numerous hydrolysis reactions.

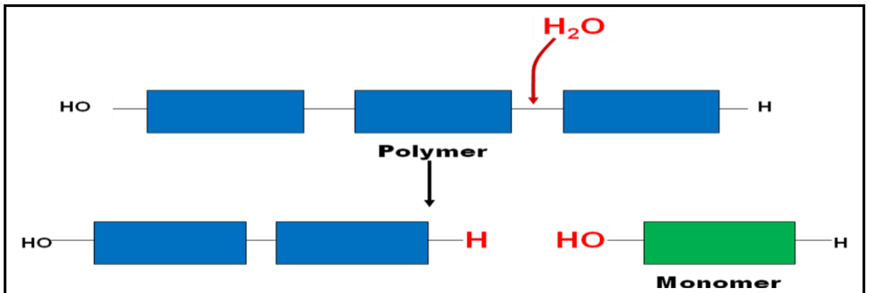
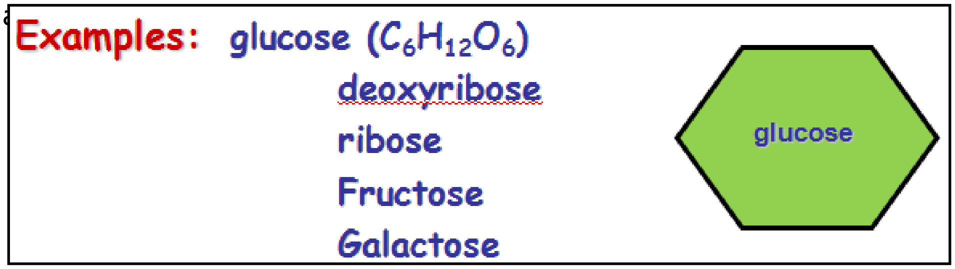


Figure: Hydrolysis reaction requires water to break the bond between two molecules and give back the free hydrogen and hydroxyl groups.

Major Macromolecules

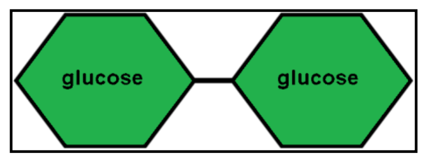
Carbohydrates

Carbohydrates are organic compounds that consist of carbon, hydrogen, and oxygen in a 1:2:1 ratio. Cells use different kinds of carbohydrates as structural materials, for fuel, and for storing and transporting energy. The three main types of carbohydrates in living systems are monosaccharides, oligosacch



Monosaccharides (one sugar unit) are the simplest type of carbohydrate, but they have extremely important roles as monomers of larger molecules. The molecular formula of monosaccharides is $(CH_2O)n$. The number of carbons (n in the formula above) varies between monosaccharide types, but for every carbon in a monosaccharide, there is also one water-molecule equivalent (H_2O in the formula). Glucose is the main "fuel" for bacteria, plants and animal cells.

Monosaccharides are the building blocks of more complex carbohydrates. For example, two monosaccharides can bond to form a **disaccharide** (two sugar unit).



Examples: **Sucrose (glucose+fructose) (Table Sugar)**
Lactose (glucose+galactose) (Milk Sugar)
Maltose (glucose+glucose) (figure Right)

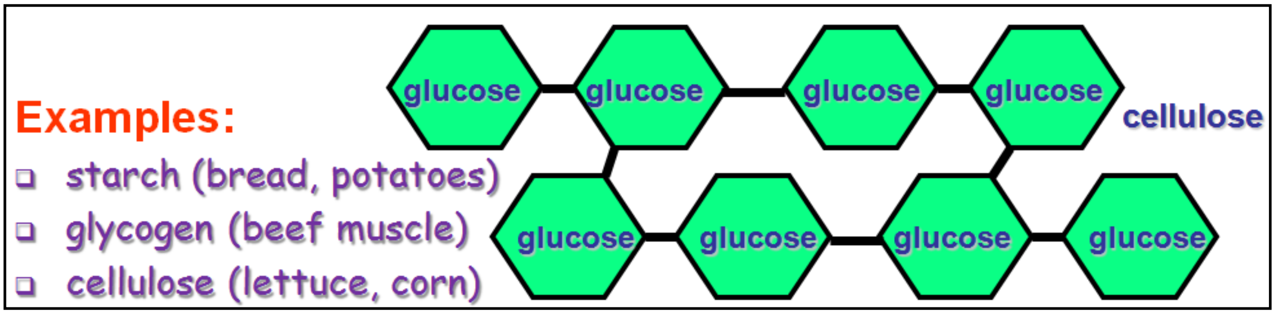
Before disaccharides can be used by organisms, they must be broken down into their monosaccharide units. The disaccharides have the molecular formula $C_{12}H_{22}O_{11}$.

A disaccharide is formed upon the formation of a glycosidic linkage (a type of bond) between monosaccharides. This glycosidic linkage forms via a dehydration reaction.

The "complex" carbohydrates, or **polysaccharides**, are straight or branched chains of many sugar monomers, often hundreds or thousands of them. There may be one type or many types of monomers in a polysaccharide (many sugar units). Most macromolecular carbohydrates are polysaccharides. Polysaccharides typically serve as **(i)** carbon and energy storage molecules (starch, glycogen) or **(ii)** as structural material (e.g., in plants, insects, and fungi).

Most plants make much more glucose than they can use. The excess is stored as starch inside cells that make up roots, stems, and leaves. Some starches are made of thousands of monosaccharide (glucose) units.

Potatoes, beans, and grains such as rice, corn, and wheat are examples of plants that store large quantities of starch. When sugars (fuel for energy) are in short supply, hydrolysis enzymes break the bonds between starch's monomers to release glucose subunits. Some common Polysaccharides and their characteristics are given below:



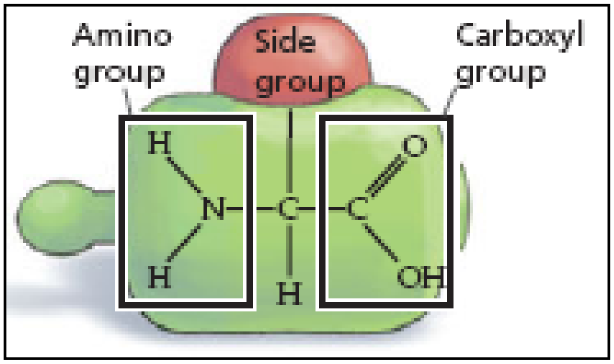
■ **Starch and Glycogen:**	■ **Cellulose:**	■ **Chitin**
• Starch is energy storage molecule in plants • Glycogen is energy storage molecule in animals. • Starch and glycogen can be digested by animals. **Glycogen:** Humans and some animals produce starch called glycogen in the liver. It is stored in the liver and in muscles. When extra energy is needed, the glycogen is broken down into glucose.	• Different bond formed than starch • Structural component in plants • Cannot be digested by animals **Cellulose** is a polysaccharide that is still more complex that the starches, but made up be only glucose units. The cell walls of plants are made of cellulose. The paper, cotton, and wood are made up of cellulose.	• Partly derived from non-sugars (nitrogen) • Composes exoskeletons of insects Long, unbranching chains of these monomers are linked by hydrogen bonds. As a structural material, chitin is durable, translucent, and flexible. It strengthens hard parts of many animals, including the outer cuticle of crabs, beetles, and ticks, and it reinforces the cell wall of many fungi.

Functions of Carbohydrates

- Providing energy and regulation of blood glucose
- Sparing the use of proteins for energy
- Breakdown of fatty acids and preventing ketosis
- Biological recognition processes
- Flavor and Sweeteners
- Dietary fiber, which is also a form of carbohydrate, is essential for the elimination of waste materials and toxins from the body

Proteins

Of all biological molecules, proteins are the most diverse in both structure and function. A tremendous number of different proteins, including some structural types, actively participate in all processes that sustain life. Amazingly, cells can make all of the thousands of different kinds of proteins they need from only **twenty** kinds of monomers called **amino acids**. Proteins are polymers of amino acids.



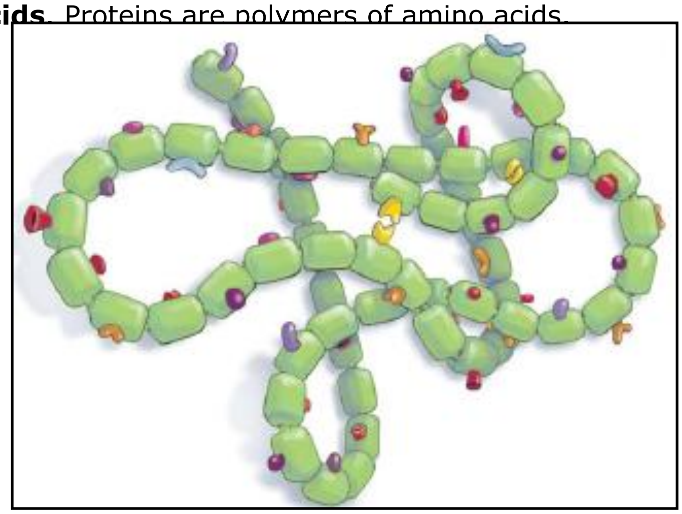
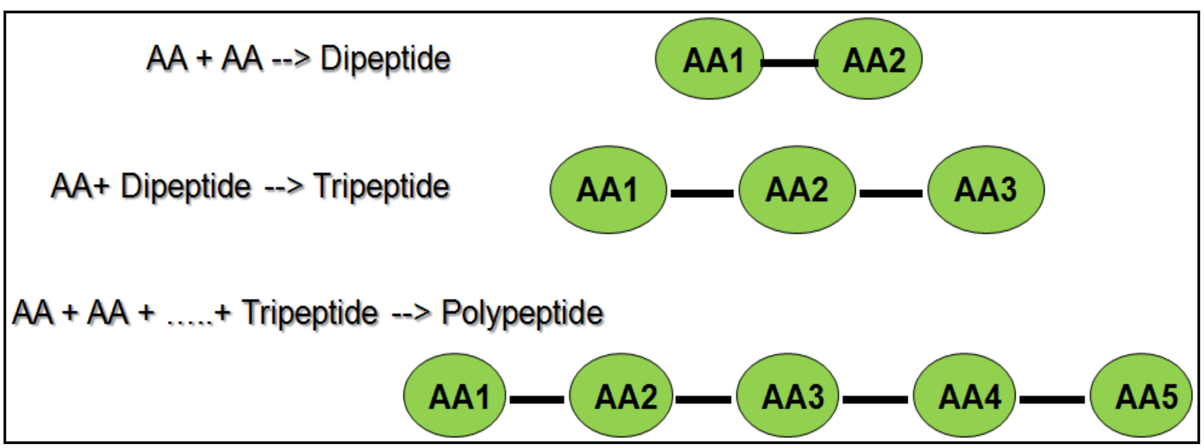
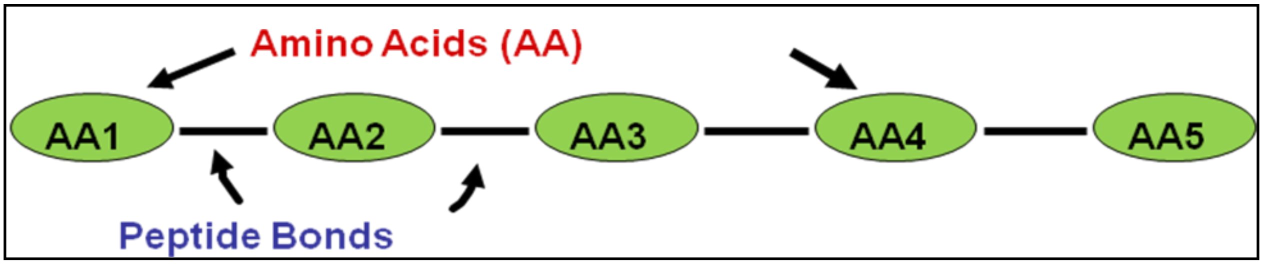


Figure: Individual amino acid(left) Protein composed of many amino acids (right)

Amino Acids

An amino acid (AA) is a small organic compound with an amine group(NH_3), a carboxyl group (COOH) (the acid), and one or more atoms called an "R group." In most amino acids, all three groups are attached to the same carbon atom. Amine group acts like a base, tends to be positive. Carboxyl group acts like an acid, tends to be negative. Side chain "R" group is variable, from 1 to 20. During protein synthesis, the amine group of one amino acid becomes bonded to the carboxyl group of the next to make a polypeptide chain.





Amino acids contain **carbon (C), hydrogen (H), oxygen (O), nitrogen (N) and sulfur (S)**

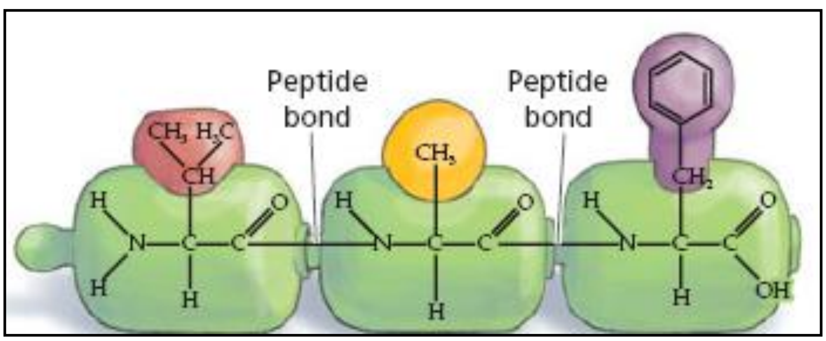
There are 20 different kinds of amino acids (AA)

Amino acids are divided into two groups- 1.Essential AA

2.Non-essential AA

1. An **essential amino acid** or **indispensable amino acid** is an amino acid that cannot be synthesized by the organism (usually referring to humans), and therefore must be supplied in the diet.
2. A **non-essential amino acid** is an amino acid that can be synthesized by the organism (usually referring to humans).So there is no deficiency of this AA in the body if they are not supplied in the diet.

   Protein synthesis involves covalently bonding amino acids into a chain. The bond that forms between two amino acids is called a **peptide bond**. Enzymes repeat this bonding process hundreds or thousands of times, so a long chain of amino acids (a polypeptide) forms.



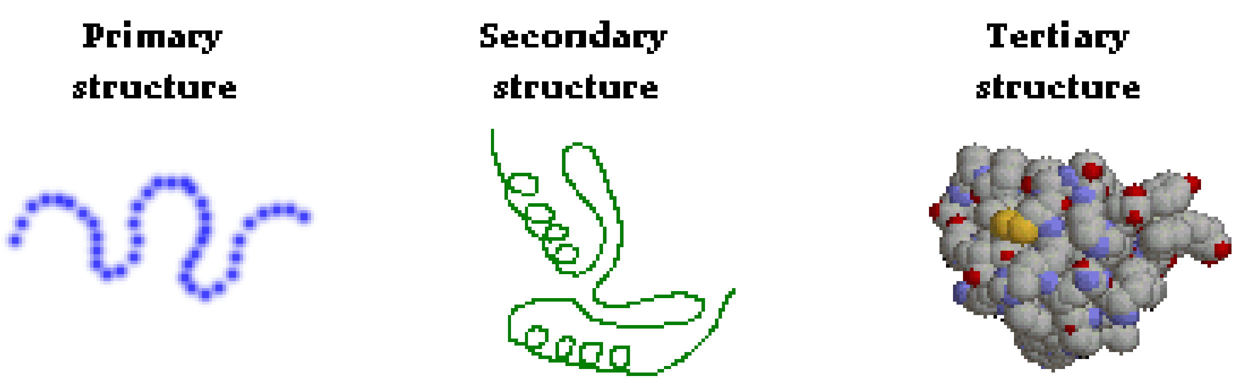
Important Facts

1. Most microorganisms and plants can biosynthesize all 20 standard amino acids, while animals (including humans) must obtain some of the amino acids from the diet. The amino acids that an organism cannot synthesize on its own are referred to as essential amino acids
2. In animals, amino acids are obtained through the consumption of foods containing protein. Ingested proteins are then broken down into amino acids through digestion, which typically involves denaturation of the protein through exposure to acid and hydrolysis by enzymes called proteases. Some ingested amino acids are used for protein biosynthesis, while others are converted to glucose through gluconeogenesis, or fed into the citric acid cycle. This use of protein as a fuel is particularly important under starvation conditions as it allows the body's own proteins to be used to support life, particularly those found in muscle. Amino acids are also an important dietary source of nitrogen.

Levels of Protein Structure

Structural features of proteins are usually described at four levels of complexity:

- **Primary structure:** the linear arrangment of amino acids in a protein and the location of covalent linkages such as disulfide bonds between amino acids.
- **Secondary structure:** areas of folding or coiling within a protein; examples include alpha helices and pleated sheets, which are stabilized by hydrogen bonding.
- **Tertiary structure:** the final three-dimensional structure of a protein, which results from a large number of non-covalent interactions between amino acids.
- **Quaternary structure:** non-covalent interactions that bind multiple polypeptides into a single, larger protein. Hemoglobin has quaternary structure due to association of two alpha globin and two beta globin polyproteins.



Nt. The primary structure of a protein can readily be deduced from the nucleotide sequence of the corresponding messenger RNA. Based on primary structure, many features of secondary structure can *be predicted with the aid of computer programs. However, predicting protein tertiary structure remains a very tough problem, although some progress has been made in this important area.*

Functions of Proteins

Main functions of Proteins

- Protein's main function is to build, maintain and repair all our body tissues, such as muscles, organs, skin and hair.
- Protein can also be used as energy source by body, but this usually only happens when carbohydrate and fat stores are in short supply.

Biological function of Protein

1. Protein acts as storage material of food and energy.
2. Many proteins are enzymes that catalyze biochemical reactions, and are vital to metabolism.
3. Proteins are molecular instrument through which genetic information is expressed.
4. They act as antibodies to prevent disease.
5. The milk proteins help the growth of infant mammals.
6. Like other biological macromolecules such as polysaccharides, lipids and nucleic acids, proteins are essential parts of organisms and participate in virtually every process within cells.
7. Many proteins are enzymes that catalyze biochemical reactions and are vital to metabolism.
8. Proteins also have structural or mechanical functions, such as actin and myosin in muscle and the proteins in the cytoskeleton, which form a system of scaffolding that maintains cell shape.
9. Other proteins are important in cell signaling, immune responses, cell adhesion, and the cell cycle.
10. Proteins are also necessary in animals' diets, since animals cannot synthesize all the amino acids they need and must obtain essential amino acids from food. Through the process of digestion, animals break down ingested protein into free amino acids that are then used in metabolism.

Lipids

Lipids are fatty, oily, or waxy organic compounds. Lipids are a structurally heterogeneous class of biological molecules that are, as their common characteristic, hydrophobic. Which means they are insoluble in water. The building blocks of lipids are fatty acids and glycerol. Lipids posses numerous C-H bonds (i.e., they are very hydrocarbon-like). Examples of lipids include: (i) Fats, (ii) Oils, (iii) Waxes, (iv) Phospholipids, and (v) Steroids, etc.

Lipids are similar to carbohydrates in that they contain only carbon, hydrogen, and oxygen. They differ from carbohydrates in one important way: no specific ratio (C:H:O). Many also serve as source of energy. In fact, a gram of fat can produce over twice as much energy as a gram of carbohydrate. Lipids are also a storage form of energy. The proportion of hydrogen to oxygen in carbohydrates is two to one. In lipid it is much higher.

Fats and oils

Fats are lipids with one, two, or three long chain fatty acids bonded (called an ester linkage) to a small alcohol called glycerol. When three fatty acids attach to a glycerol, the resulting molecule, which is called a triglyceride, is entirely hydrophobic.

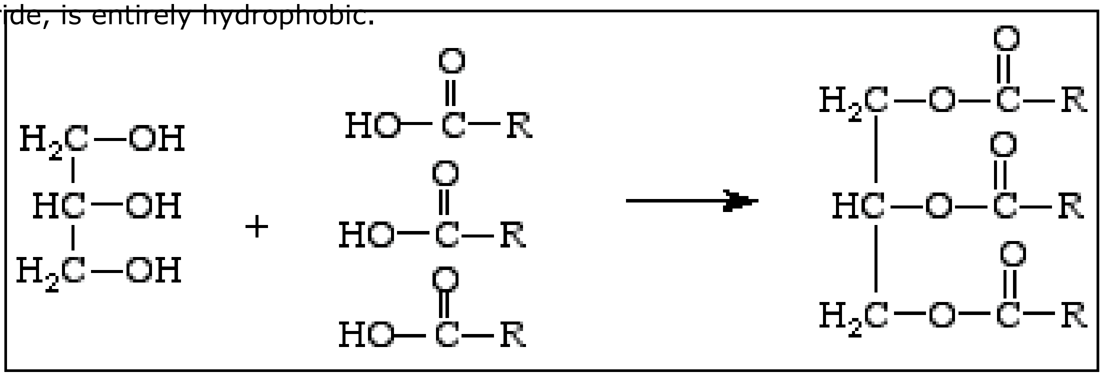


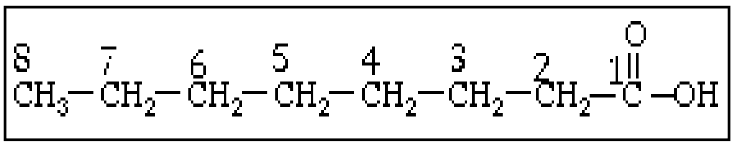
Figure: Showing triglyceride synthesized from one glycerol molecule and three fatty acids.

Fatty acids are long-chain hydrocarbons with a carboxyl group (-COOH) at one end.

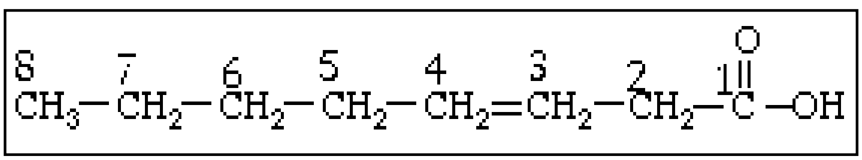
Fatty acids can be saturated or unsaturated. Saturated types have only single bonds in their tails. In other words, their carbon chains are fully saturated with hydrogen atoms. Saturated fatty acids have no C=C double bonds. Unsaturated fatty acids have one or more C=C double bonds. The tails of unsaturated fatty acids have one or more double bonds that limit their flexibility. Increasing the unsaturation of a fatty acid results in a decreasing melting point.

Fats and oils possess more energy per molecule and less hydration compared with carbohydrates, resulting in fats or oils possessing much more energy stored per unit mass or volume. During digestion, the fat or oil is broken down into these simple molecules (monomers). Fats and oils function in biological systems as energy storage molecules (e.g., nuts, seeds, and animals).

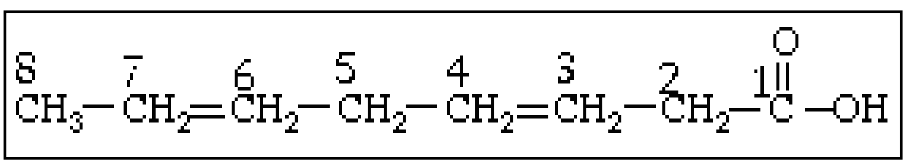
- Saturated fatty acids have no C=C double bonds. eg. Octanoic acid



- Unsaturated fatty acids have one or more C=C double bonds. eg. 3-octanoic acid



- Increasing the unsaturation of a fatty acid results in a decreasing melting point. eg, 3,6-octanoic acid



Fats

Fats are solid at ordinary temperatures. Generally, fats are produced by animals. In animals, fats are stored in adipose cells. Fats are also important as cushions for body organs and as an insulating layer beneath skin.

Oils

Oils are liquid at ordinary temperatures. Generally, oils are produced by plants. Some common vegetable oils are peanut, soybean, and corn oil.

Waxes

Both plants and animals produce waxes. The waxy coating on some plants leaves is an example of plant waxes. Beeswax is an example of a wax produced by an animal.

Phospholipids & Steroids

Phospholipids

Phospholipids differ from triacylglycerol in the sense that, one fatty acid (out of three) is replaced with a phosphate group, which in turn is bound to additional functional groups.

Structurally and functionally, the important thing about phospholipids is that these molecules are simultaneously hydrophobic (at one end, the fatty acid end) and hydrophilic (at the other end, the phosphate end). Phospholipids are the most abundant lipids in cell membranes, which have two layers of lipids.

Steroids

Steroids are lipids with a rigid backbone of four carbon rings and no fatty acid tails. All steroids possess a common ring structure. These ring structures vary by attached functional groups. Cholesterol is example of a steroid; cholesterol is a membrane component. The common steroid structure is the basis of sterol hormones including the human sex hormones (the estrogens and the androgens, including testosterone).

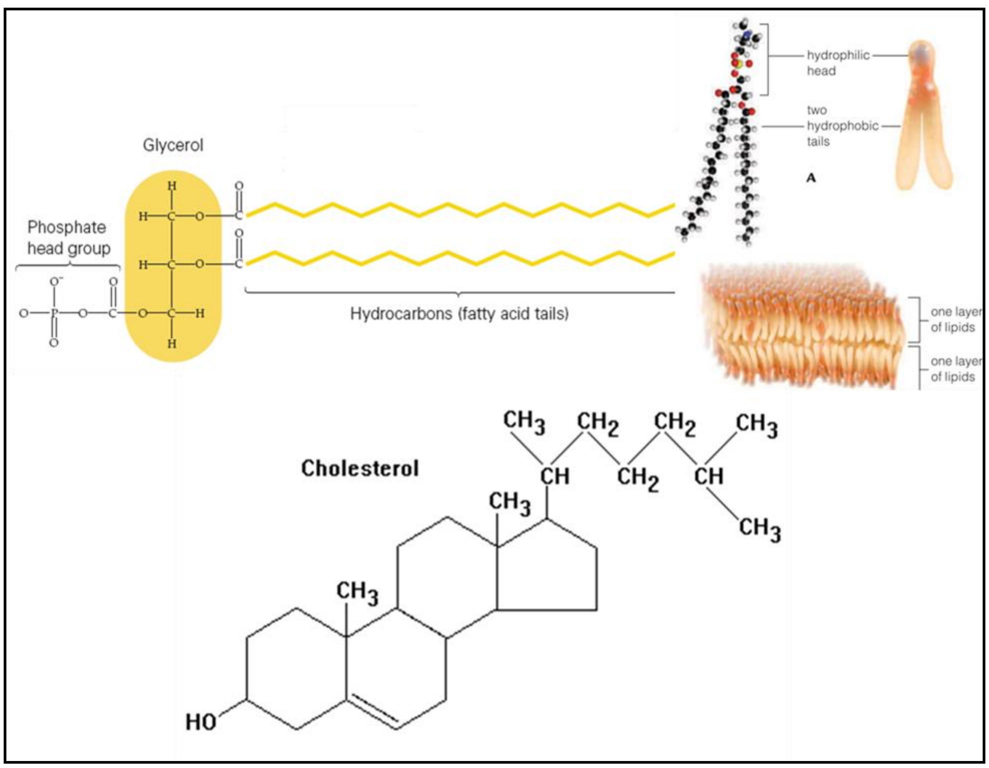


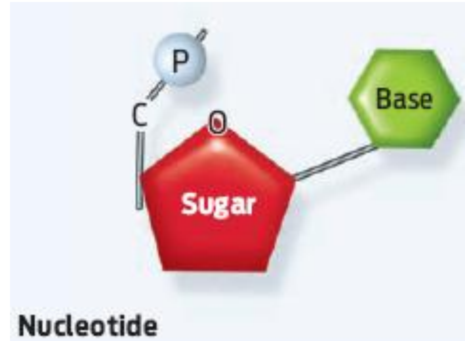
Figure: (Top left) molecule of Phospholipid consisting of a phosphate group attached to a diacylglycerol (glycerol attached to two fatty acids). (Top right) Showing phospholipid polar head and non polar tail. Many phospholipids stacked together to form the Lipid bilayer of cell membrane. (bottom) Molecule of Cholesterol.

Nutrition and Health facts regarding lipid consumption:

- Most of the lipid found in food is in the form of triacylglycerols, cholesterol and phospholipids.
- A minimum amount of dietary fat is necessary to facilitate absorption of fat-soluble vitamins (A, D, E and K) and carotenoids.
- Humans and other mammals have a dietary requirement for certain essential fatty acids, such as linoleic acid (an omega-6 fatty acid) and alpha-linolenic acid (an omega-3 fatty acid) because they cannot be synthesized from simple precursors in the diet. Both of these fatty acids are 18-carbon polyunsaturated fatty acids differing in the number and position of the double bonds.
- Most vegetable oils are rich in linoleic acid (safflower, sunflower, and corn oils). Alpha-linolenic acid is found in the green leaves of plants, and in selected seeds, nuts and legumes (particularly rapeseed, walnut and soy).
- Fish oils are particularly rich in the longer-chain omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).
- A large number of studies have shown positive health benefits associated with consumption of omega-3 fatty acids on infant development, cancer, cardiovascular diseases, and various mental illnesses, such as depression, attention-deficit hyperactivity disorder, and dementia. In contrast, it is now well-established that consumption of trans fats, such as those present in partially hydrogenated vegetable oils, are a risk factor for cardiovascular disease.
- The American Heart Association's Nutrition Committee strongly advises the **fat guidelines** for healthy Americans over age 2:
- Limit total fat intake to less than 25–35% of your total calories each day;
- Limit saturated fat intake to less than 7% of total daily calories;
- Limit trans fat intake to less than 1% of total daily calories;
- The remaining fat should come from sources of monounsaturated and polyunsaturated fats such as nuts, seeds, fish and vegetable oils; and
- Limit cholesterol intake to less than 300 mg per day, for most people.
- For example, a sedentary female who is 31–50 years old needs about 2,000 calories each day. Therefore, she should consume less than 16 g saturated fat, less than 2 g trans fat and between 50 and 70 grams of total fat each day (with most fats coming from sources of polyunsaturated and monounsaturated fats, such as fish, nuts, seeds and vegetable oils).

Nucleic acids

Nucleic acids are complex organic polymers that store and transfer genetic information within a cell. Inside a cell, they are the source of genetic information stored as chromosomes. **Nucleic acids** are composed of long chains of **nucleotides** linked by **dehydration synthesis.**



Types of Nucleic acids:

There are two types of nucleic acids which are polymers found in all living cells.

Deoxyribonucleic Acid (DNA) is found mainly in the nucleus of the cell

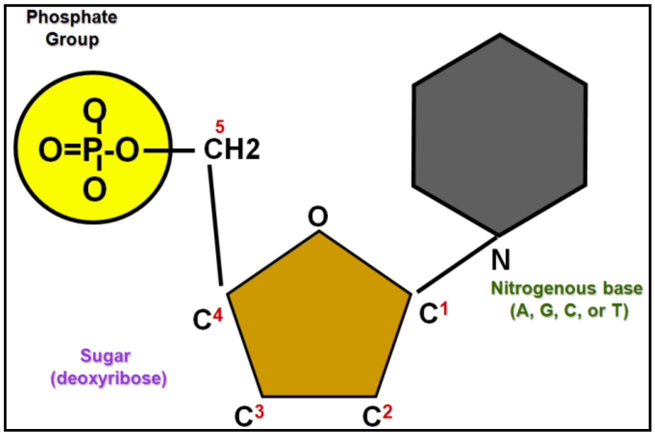
Ribonucleic Acid (RNA) is found mainly in the cytoplasm of the cell although it is usually synthesized in the nucleus.

DNA contains the genetic codes to make RNA and the RNA in turn then contains the codes for the primary sequence of amino acids to make proteins.

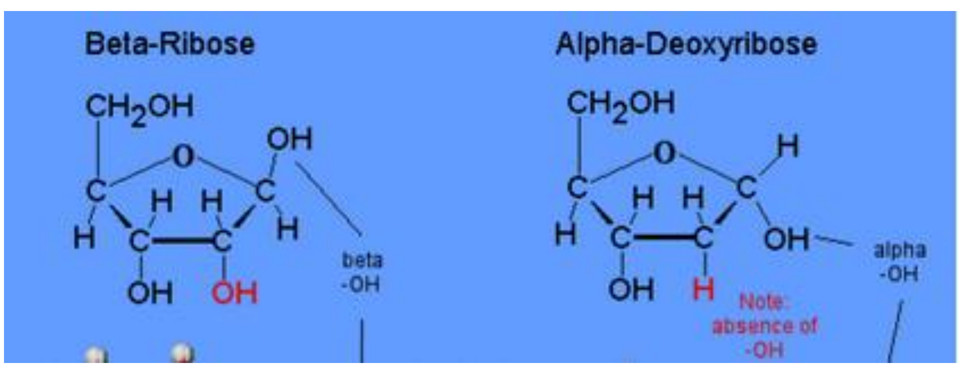
Chemical composition of Nucleic acids: Each Nucleotide is composed of three parts:

1. phosphate group (P)
2. pentose sugar known as ribose (5-carbon)
3. nitrogenous bases or amines

1. **Phosphate group:** A major requirement of all living things is a suitable source of phosphorus. One of the major uses for phosphorus is as the phosphate ion which is incorporated into DNA and RNA.



2. **Pentose sugar:** There are two types of pentose sugars found in nucleic acids. This difference is reflected in their names--deoxyribonucleic acid indicates the presence of deoxyribose; while ribonucleic acid indicates the presence of ribose. In the picture below, the structures of both ribose and deoxyribose are shown. Note the -OH on one and the red -H on the other are the only differences. The alpha and beta designations are interchangeable and are not a significant difference between the two.

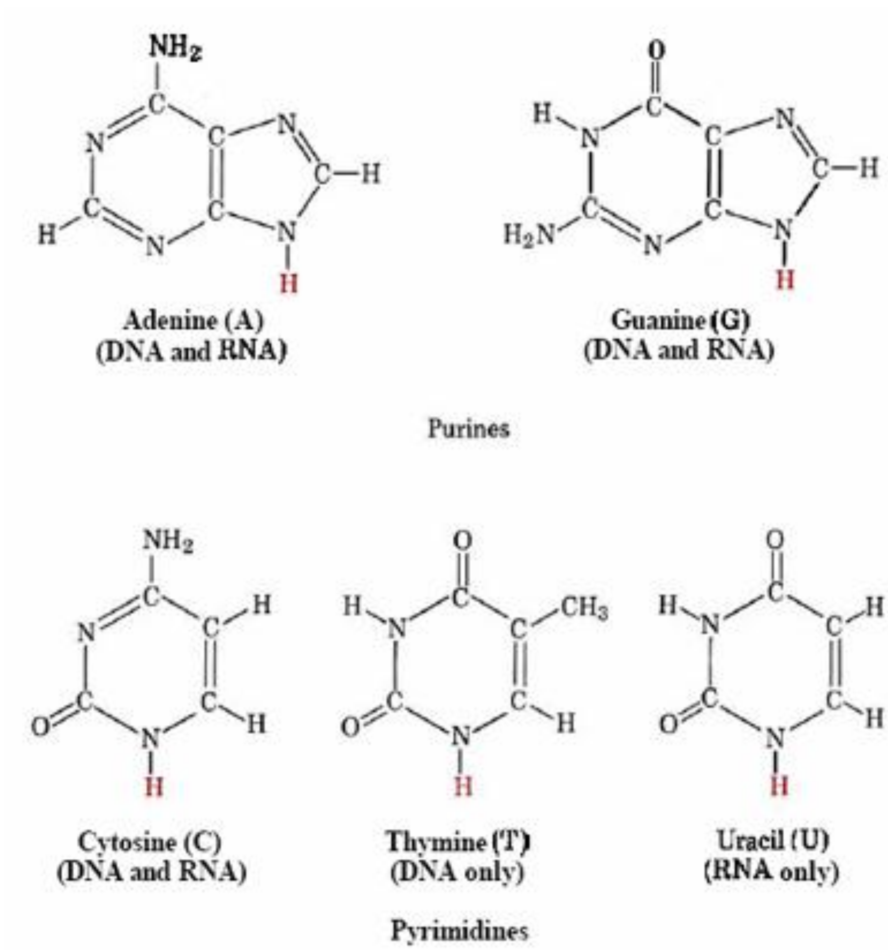


3. **Bases or Heterocyclic Amines:** Heterocyclic amines are sometimes called nitrogen bases or simply bases.

   The heterocyclic amines are derived from two root structures: purines or pyrimidines.

   The purine root has both a six and a five member ring; the pyrimidine has a single six member ring. There are two major purines, adenine (A) and guanine (G), and three major pyrimidines, cytosine (C), uracil (U), and thymine (T).

   The structures are shown in the graphic on the left. As you can see, these structures are called "bases" because the amine groups as part of the ring or as a side chain have a basic property in water



A major difference between DNA and RNA is that DNA contains thymine, but not uracil, while RNA contains uracil but not thymine. The other three heterocyclic amines, adenine, guanine, and cytosine are found in both DNA and RNA.

Secondary structure of DNA:

The secondary structure of DNA is actually very similar to the secondary structure of proteins. The protein single alpha helix structure held together by hydrogen bonds was discovered.

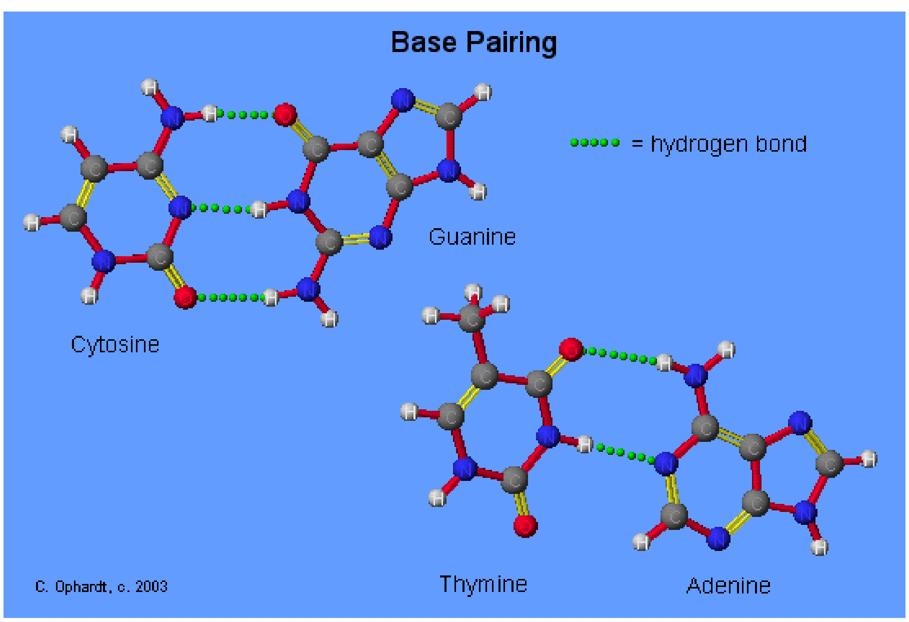
In addition, chemical studies by E. Chargaff indicate several important clues about the structure of DNA. In the DNA of all organisms:

1. The concentration of adenine equals that of thymine.
2. The concentration of guanine equals that of cytosine.

Base Pairing Principle

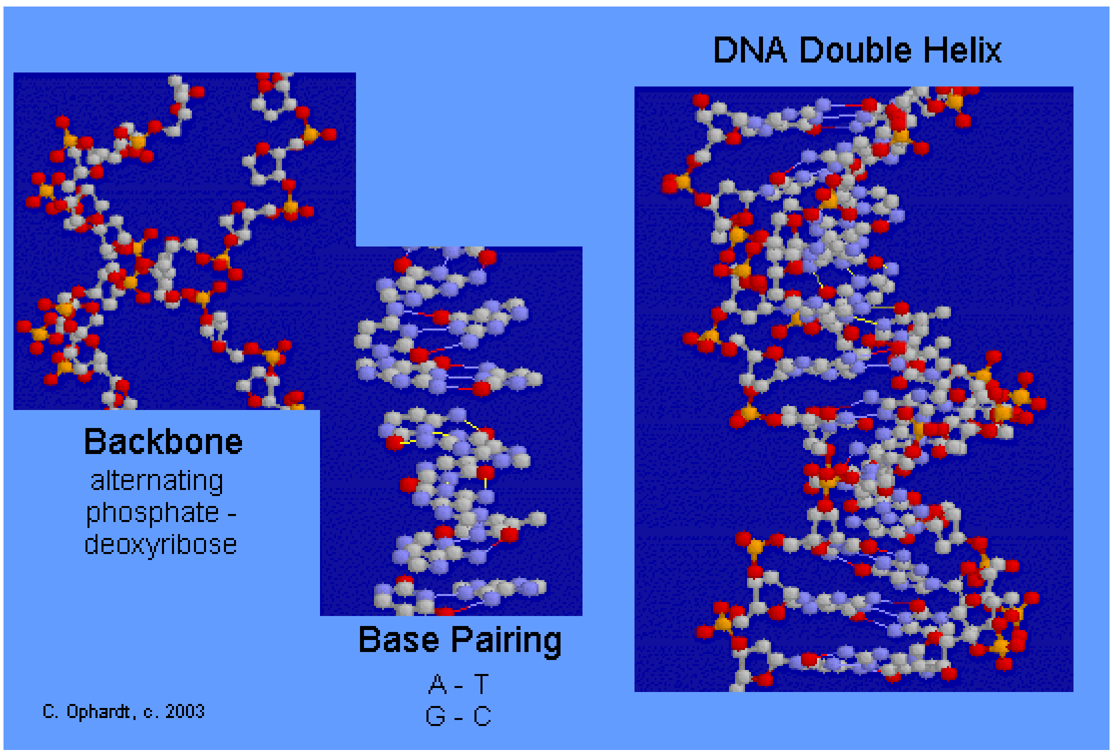
The Base Pairing Principle is that adenine pairs with thymine (A - T) and guanine pairs with cytosine (G - C)

The base pairing is called complementary because there are specific geometry requirements in the formation of hydrogen bonds between the heterocylic amines. Heterocyclic amine base pairing is an application of the **hydrogen bonding principle**. In the structures for the complementary base pairs given in the graphic on the left, notice that the thymine - adenine pair interacts through two hydrogen bonds represented as (T=A) and that the cytosine-guanine pair interacts through three hydrogen bonds represented as ($C\underline{=}G$).



DNA Double Helix

The double-stranded helical model for DNA is shown in the graphic on the left. The easiest way to visualize DNA is as an immensely long rope ladder, twisted into a cork-screw shape. The sides of the ladder are alternating sequences of deoxyribose and phosphate (backbone) while the rungs of the ladder (bases) are made in two parts with each part firmly attached to the side of the ladder. The parts in the rung are heterocyclic amines held in position by hydrogen bonding. Although most DNA exists as open ended double helices, some bacterial DNA has been found as a cyclic helix. Occasionally, DNA has also been found as a single strand. But RNA is always single stranded. That's why DNA is more stable than RNA.



Difference between DNA and RNA:

	DNA	RNA
Structural Name:	Deoxyribonucleic Acid	Ribonucleic Acid
Function:	Medium of long-term storage and transmission of genetic information.	Transfer the genetic code needed for the creation of proteins from the nucleus to the ribosome. This process prevents the DNA from having to leave the nucleus, so it stays safe. Without RNA, proteins could never be made.
Structure:	Typically a double- stranded molecule with a long chain of nucleotides.	A single-stranded molecule in most of its biological roles and has a shorter chain of nucleotides.
Bases/Sugars:	Long polymer with a deoxyribose and phosphate backbone and four different bases: adenine, guanine, cytosine and thymine.	Shorter polymer with a ribose and phosphate backbone and four different bases: adenine, guanine, cytosine, and uracil.
Base Pairing:	A-T (Adenine-Thymine), G-C (Guanine-Cytosine)	A-U (Adenine-Uracil), G-C (Guanine-Cytosine)