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# Cytology

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# CYTOLOGY

# INTRODUCTION:

You developed from a single fertilized egg cell into the complex organism containing trillions of cells that you see when you look in a mirror. During this developmental process, early, undifferentiated cells differentiate and become specialized in their structure and function. These different cell types form specialized tissues that work in concert to perform all the functions necessary for the living organism. Cellular and developmental biologists study how the continued division of a single cell leads to such complexity and differentiation. Consider the difference between a structural cell in the skin and a nerve cell. A structural skin cell may be shaped like a flat plate (squamous) and live only for a short time before it is shed and replaced. Packed tightly into rows and sheets, the squamous skin cells provide a protective barrier for the cells and tissues that lie beneath. A nerve cell, on the other hand, may be shaped something like a star, sending out long processes up to a meter in length and may live for the entire lifetime of the organism. With their long winding appendages, nerve cells can communicate with one another and with other types of body cells and send rapid signals that inform the organism about its environment and allow it to interact with that environment. These differences illustrate one very important theme that is consistent at all organizational levels of biology: the form of a structure is optimally suited to perform functions assigned to that structure. Keep this theme in mind as you tour the inside of a cell and are introduced to the various types of cells in the body. A primary responsibility of each cell is to contribute to homeostasis. Homeostasis

is a term used in biology that refers to a dynamic state of balance within parameters that are compatible with life. For example, living cells require a water-based environment to survive in, and there are various physical (anatomical) and physiological mechanisms that keep all of the trillions of living cells in the human body moist. This is one aspect of homeostasis. When a particular parameter, such as blood pressure or blood oxygen content, moves far enough *out* of homeostasis (generally becoming too high or too low), illness or disease and sometimes death inevitably results.

## CHEMICTRY OF CELL & MACRMOLECULES STRUCTURE

In every life cell there are different compounds important for the body's structure and function. In general, these compounds are either inorganic or organic.

An **inorganic compound** is a substance that does not contain both carbon and hydrogen. A great many inorganic compounds do contain hydrogen atoms, such as water ($H_2O$) and the hydrochloric acid (HCl) produced by your stomach. In contrast, only a handful of inorganic compounds contain carbon atoms. Carbon dioxide ($CO_2$) is one of the few examples.

An **organic compound**, then, is a substance that contains both carbon and hydrogen. Organic compounds are synthesized via covalent bonds within living organisms, including the human body. Recall that carbon and hydrogen are the second and third most abundant elements in your body. You will soon discover how these two elements combine in the foods you eat, in the compounds that make up every cell of your body structure, and in the chemicals that fuel your functioning.

### (A) Inorganic compounds:

There are three groups of inorganic compounds essential to life: water, salts, acids, and bases. Organic compounds are covered later in the chapter.

#### 1- Water

As much as 70 percent of an adult's body weight is water. This water is contained both within the cells and between the cells that make up

tissues and organs. Its several roles make water indispensable to human functioning.

**Water as a Lubricant and Cushion:**

Water is a major component of many of the body's lubricating fluids. Just as oil lubricates the hinge on a door, water in synovial fluid lubricates the actions of body joints, and water in pleural fluid helps the lungs expand and recoil with breathing. Watery fluids help keep food flowing through the digestive tract and ensure that the movement of adjacent abdominal organs is friction free. Water also protects cells and organs from physical trauma, cushioning the brain within the skull, for example, and protecting the delicate nerve tissue of the eyes. Water cushions a developing fetus in the mother's womb as well.

**Water as a Heat Sink:**

A heat sink is a substance or object that absorbs and dissipates heat but does not experience a corresponding increase in temperature. In the body, water absorbs the heat generated by chemical reactions without greatly increasing in temperature.

Moreover, when the environmental temperature soars, the water stored in the body helps keep the body cool. This cooling effect happens as warm blood from the body's core flows to the blood vessels just under the skin and is transferred to the environment. At the same time, sweat glands release warm water in sweat. As the water evaporates into the air, it carries away heat, and then the cooler blood from the periphery circulates back to the body core.

## Water as a Component of Liquid Mixtures:

A mixture is a combination of two or more substances, each of which maintains its own chemical identity. In other words, the constituent substances are not chemically bonded into a new, larger chemical compound. The concept is easy to imagine if you think of powdery substances such as flour and sugar; when you stir them together in a bowl, they obviously do not bond to form a new compound. The room air you breathe is a gaseous mixture, containing three discrete elements nitrogen, oxygen, and argon and one compound, carbon dioxide. There are three types of liquid mixtures, all of which contain water as a key component. These are solutions, colloids, and suspensions.

For cells in the body to survive, they must be kept moist in a water-based liquid called a solution. In chemistry, a liquid solution consists of a solvent that dissolves a substance called a solute. Water is considered the "universal solvent" and it is believed that life cannot exist without water because of this. Water is certainly the most abundant solvent in the body; essentially all the body's chemical reactions occur among compounds dissolved in water. Because water molecules are polar, with regions of positive and negative electrical charge, water readily dissolves ionic compounds and polar covalent compounds. Such compounds are referred to as hydrophilic, or "water-loving." As mentioned above, sugar dissolves well in water. This is because sugar molecules contain regions of hydrogen-oxygen polar bonds, making it hydrophilic. Nonpolar molecules, which do not readily dissolve in water, are called hydrophobic, or "water-fearing."

## The Role of Water in Chemical Reactions:

Two types of chemical reactions involve the creation or the consumption of water: dehydration synthesis and hydrolysis. In **dehydration synthesis**, one reactant gives up an atom of hydrogen and another reactant gives up a hydroxyl group (OH) in the synthesis of a new product. In the formation of their covalent bond, a molecule of water is released as a byproduct (Figure 1).

This is also sometimes referred to as a condensation reaction. In **hydrolysis**, a molecule of water disrupts a compound, breaking its bonds. The water is itself split into $H^+$ and $OH^-$. One portion of the severed compound then bonds with the hydrogen atom, and the other portion bonds with the hydroxyl group. These reactions are reversible and play an important role in the chemistry of organic compounds.

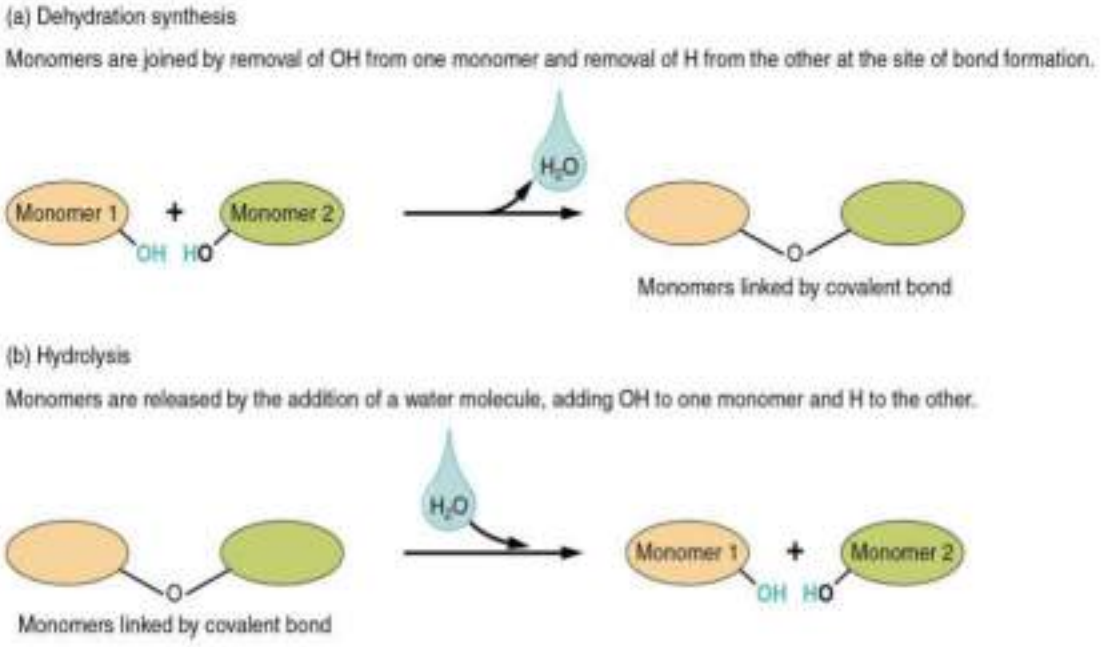



**Figure 1:** Dehydration Synthesis and Hydrolysis. Monomers, the basic units for building larger molecules, form polymers (two or more chemically bonded monomers). (a) In dehydration synthesis, (b) In hydrolysis

## 2- Salts:

Recall that salts are formed when ions form ionic bonds. In these reactions, one atom gives up one or more electrons, and thus becomes positively charged, whereas the other accepts one or more electrons and becomes negatively charged. You can now define a salt as a substance that, when dissolved in water, dissociates into ions other than H or OH. This fact is important in distinguishing salts from acids and bases, discussed next.

A typical salt, NaCl, dissociates completely in water (Figure 2). The positive and negative regions on the water molecule (the hydrogen and oxygen ends respectively) attract the negative chloride and positive sodium ions, pulling them away from each other. Again, whereas nonpolar and polar covalently bonded compounds break apart into molecules in solution, salts dissociate into ions. These ions are electrolytes; they are capable of conducting an electrical current in solution. This property is critical to the function of ions in transmitting nerve impulses and prompting muscle contraction. Many other salts are important in the body. For example, bile salts produced by the liver help break apart dietary fats, and calcium phosphate salts form the mineral portion of teeth and bones.

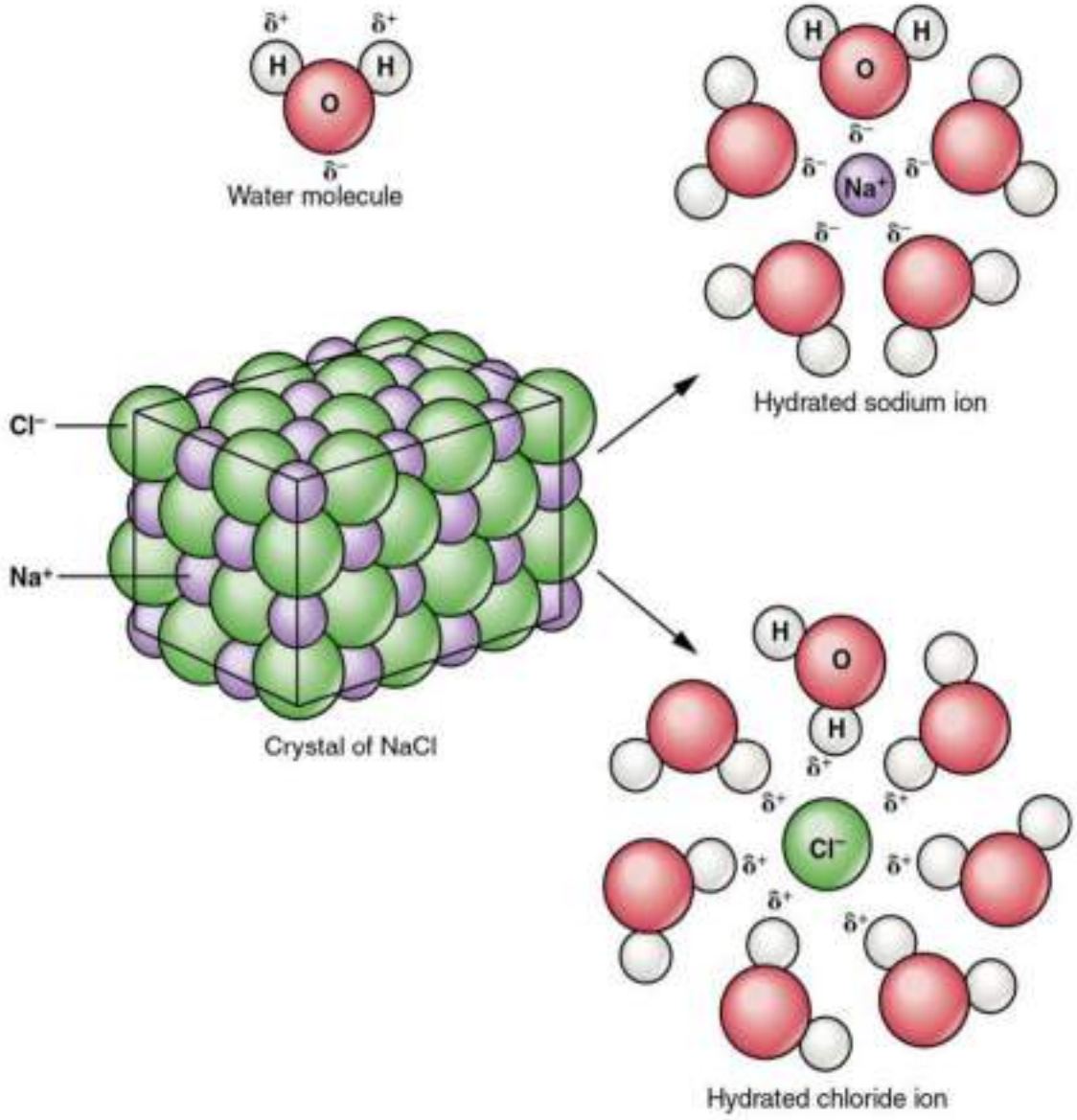



**Figure 2:** Dissociation of Sodium Chloride in Water. Notice that the crystals of sodium chloride dissociate not into molecules of NaCl, but into $Na^+$ cations and $Cl^-$ anions, each completely surrounded by water molecules.

## 3- Acids and Bases:

Acids and bases, like salts, dissociate in water into electrolytes. Acids and bases can very much change the properties of the solutions in which they are dissolved.

- **Acids:**

An **acid** is a substance that releases hydrogen ions $H^+$ in solution. Because an atom of hydrogen has just one proton and one electron, a positively charged hydrogen ion is simply a proton. This solitary proton is highly likely to participate in chemical reactions. Strong acids are compounds that release all their $H^+$ in solution; that is, they ionize completely. Hydrochloric acid (HCl), which is released from cells in the lining of the stomach, is a strong acid because it releases all of its $H^+$ in the stomach's watery environment. This strong acid aids in digestion and kills ingested microbes. Weak acids do not ionize completely; that is, some of their hydrogen ions remain bonded within a compound in solution. An example of a weak acid is vinegar, or acetic acid; it is called acetate after it gives up a proton.

- **Bases:**

A **base** is a substance that releases hydroxyl ions ($OH^-$) in solution, or one that accepts $H^+$ already present in solution. The hydroxyl ions or other base combine with $H^+$ present to form a water molecule, thereby removing $H^+$ and reducing the solution's acidity. Strong bases release most or all their hydroxyl ions; weak bases release only some hydroxyl ions or absorb only a few $H^+$. Food mixed with hydrochloric acid from the stomach would burn the small intestine, the next portion of the digestive tract after the stomach, if it were not for the release of bicarbonate ($HCO^-_3$), a weak base that attracts $H^+$ . Bicarbonate accepts some of the H protons, thereby reducing the acidity of the solution.

## (B) Organic compounds:

Organic compounds typically consist of groups of carbon atoms covalently bonded to hydrogen, usually oxygen, and often other elements as well. Created by living things, they are found throughout the world, in soils and seas, commercial products, and every cell of the human body. The four types most important to human structure and function are carbohydrates, lipids, proteins, and nucleotides. Before exploring these compounds, you need to first understand the chemistry of carbon.

### The Chemistry of Carbon

What makes organic compounds ubiquitous is the chemistry of their carbon core. Recall that carbon atoms have four electrons in their valence shell, and that the octet rule dictates that atoms tend to react in such a way as to complete their valence shell with eight electrons. Carbon atoms do not complete their valence shells by donating or accepting four electrons. Instead, they readily share electrons via covalent bonds.

Commonly, carbon atoms share with other carbon atoms, often forming a long carbon chain referred to as a carbon skeleton. When they do share, however, they do not share all their electrons exclusively with each other. Rather, carbon atoms tend to share electrons with a variety of other elements, one of which is always hydrogen. Carbon and hydrogen groupings are called hydrocarbons.

Many combinations are possible to fill carbon's four "vacancies." Carbon may share electrons with oxygen or nitrogen or other atoms in

a particular region of an organic compound. Moreover, the atoms to which carbon atoms bond may also be part of a functional group. A **functional group** (Table 1) is a group of atoms linked by strong covalent bonds and tending to function in chemical reactions as a single unit. You can think of functional groups as tightly knit "cliques" whose members are unlikely to be parted. Five functional groups are important in human physiology; these are the hydroxyl, carboxyl, amino, methyl and phosphate groups Carbon's affinity for covalent bonding means that many distinct and relatively stable organic molecules nevertheless readily form larger, more complex molecules. Any large molecule is referred to as **macromolecule** (macro- = "large"), and the organic compounds

**Table 1**: Illustrate the functional group structure and function

| Functional group | Structural formula | Importance |
|---|---|---|
| Hydroxyl | —O—H | Hydroxyl groups are polar. They are components of all four types of organic compounds discussed in this chapter They are involved in dehydration synthesis and hydrolysis reactions. |
| Carboxyl | O—C—OH | Carboxyl groups are found within fatty acids, amino acids, and many other acids. |
| Amino | —N—H2 | Amino groups are found within amino acids, the building blocks of proteins. |
| Methyl | —C—H3 | Methyl groups are found within amino acids. |
| Phosphate | —P—$O4^{2-}$ | Phosphate groups are found within phospholipids and nucleotides. |

# Biological Macromolecules:

## Synthesis of Biological Macromolecules:

**Biological macromolecules** are large molecules, necessary for life, that are built from smaller organic molecules. There are four major biological macromolecule classes (carbohydrates, lipids, proteins, and nucleic acids). Each is an important cell component and performs a wide array of functions. Combined, these molecules make up the majority of a cell's dry mass (recall that water makes up the majority of its complete mass). Biological macromolecules are organic, meaning they contain carbon. In addition, they may contain hydrogen, oxygen, nitrogen, and additional minor elements.

### a) Dehydration Synthesis

Most macromolecules are made from single subunits, or building blocks, called **monomers**. The monomers combine with each other using covalent bonds to form larger molecules known as **polymers**. In doing so, monomers release water molecules as byproducts. This type of reaction is **dehydration synthesis**, which means "to put together while losing water."( Figure 3).

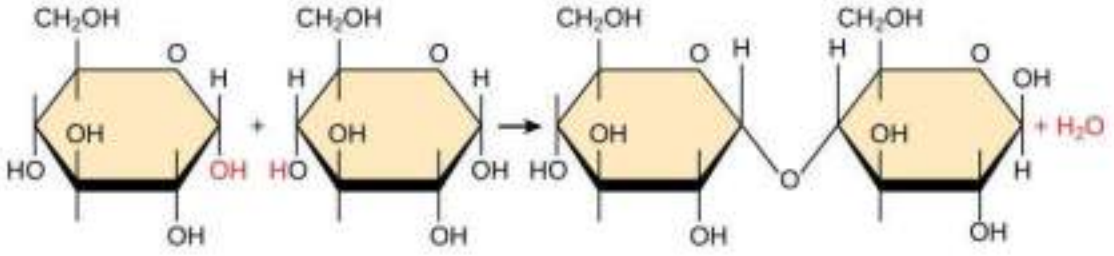



**Figure 3:** In the dehydration synthesis reaction above, two glucose molecules link to form the disaccharide maltose. In the process, it forms a water molecule.

In a dehydration synthesis reaction (Figure 3), the hydrogen of one monomer combines with the hydroxyl group of another monomer, releasing a water molecule. At the same time, the monomers share electrons and form covalent bonds. As additional monomers join, this chain of repeating monomers forms a polymer. Different monomer types can combine in many configurations, giving rise to a diverse group of macromolecules. Even one kind of monomer can combine in a variety of ways to form several different polymers. For example, glucose monomers are the constituents of starch, glycogen, and cellulose.

### b) Hydrolysis

Polymers break down into monomers during hydrolysis. A chemical reaction occurs when inserting a water molecule across the bond. Breaking a covalent bond with this water molecule in the compound achieves this (Figure 4). During these reactions, the polymer breaks into two components: one part gains a hydrogen atom ($H^-$) and the other gains a hydroxyl molecule ($OH^+$) from a split water molecule.

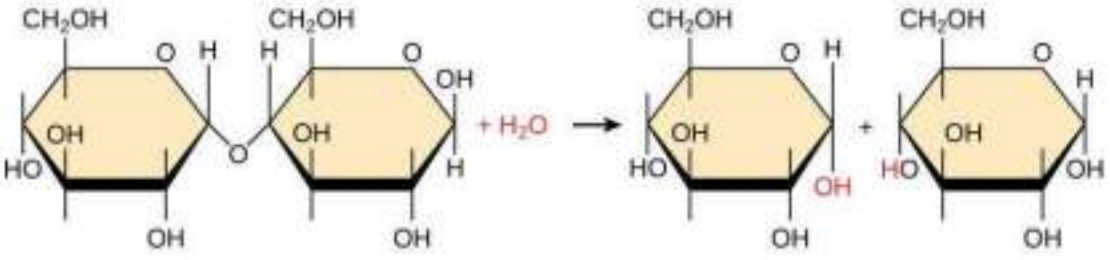



**Figure 4:** In the hydrolysis reaction here, the disaccharide maltose breaks down to form two glucose monomers by adding a water molecule. Note that this reaction is the reverse of the synthesis reaction in Figure 3.

Dehydration and **hydrolysis reactions** are catalyzed, or "sped up," by specific enzymes; dehydration reactions involve the formation of new bonds, requiring energy, while hydrolysis reactions break bonds and release energy. These reactions are similar for most macromolecules, but each monomer and polymer reaction is specific for its class. For example, catalytic enzymes in the digestive system hydrolyze or break down the food we ingest into smaller molecules. This allows cells in our body to easily absorb nutrients in the intestine. A specific enzyme breaks down each macromolecule. For instance, amylase, sucrase, lactase, or maltase break down carbohydrates. Enzymes called proteases, such as pepsin and peptidase, and hydrochloric acid break down proteins. Lipases break down lipids. These broken down macromolecules provide energy for cellular activities.

**Major biological macromolecule classes**

**(1) Carbohydrates**

The term carbohydrate means "hydrated carbon." Recall that the root hydro- indicates water. A carbohydrate is a molecule composed of carbon, hydrogen, and oxygen; in most carbohydrates, hydrogen and oxygen are found in the same two-to-one relative proportions they have in water. In fact, the chemical formula for a "generic" molecule of carbohydrate is $(CH_2O)_n$ . Carbohydrates are referred to as saccharides, a word meaning "sugars." Three forms are important in the body. Monosaccharides are the monomers of carbohydrates. Disaccharides (di- = "two") are made up of two monomers. **Polysaccharides** are the polymers and can consist of hundreds to thousands of monomers.

## a) Monosaccharides

**Monosaccharides** (mono- = "one"; sacchar- = "sweet") are simple sugars, the most common of which is glucose. In monosaccharides, the number of carbons usually ranges from three to seven. Most monosaccharide names end with the suffix -ose. If the sugar has an aldehyde group (the functional group with the structure RCHO), it is an aldose, and if it has a ketone group (the functional group with the structure RC(=O)R'), it is a ketose. Depending on the number of carbons in the sugar, they can be trioses (three carbons), pentoses (five carbons), and/or hexoses (six carbons). (Figure 5).

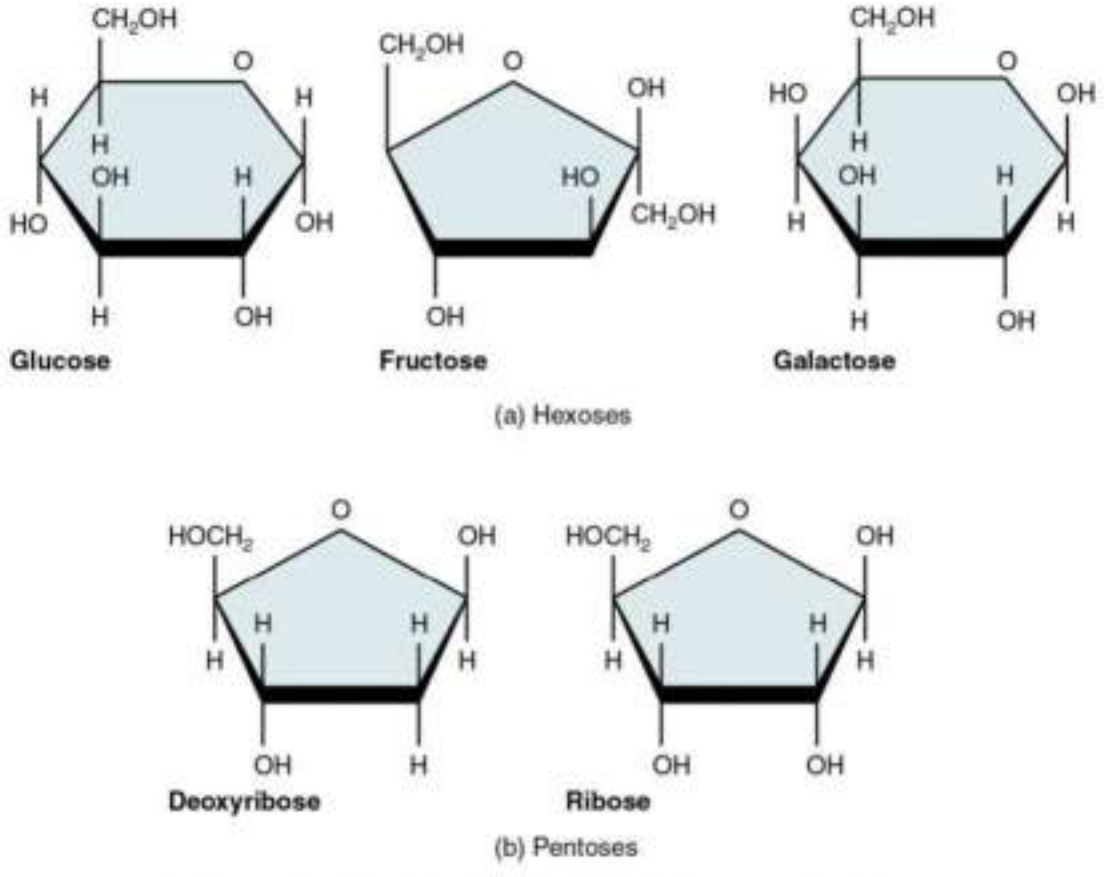



**Figure 5**: Illustrate five types of Monosaccharides.

**Functions of Monosaccharides:**

Monosaccharides are an energy source; most of them provide about 4 Calories per gram. Glucose is the main fuel for the body cells. Fructose participates in metabolism. Galactose is found in erythrocytes of blood of individuals. Ribose is part of deoxyribonucleic acid (DNA) in the chromosomes. Monosaccharides are non-essential nutrients, which means your body can produce all of those it needs for proper functioning from other nutrients, so you do not need to get them from food.

**Absorption of Monosaccharides and Their Effect on Blood Sugar Levels:**

Monosaccharides, like most nutrients are absorbed in the small intestine. They can be absorbed without previously being broken down by the intestinal enzymes. Glucose and galactose are absorbed easily, completely and faster than other carbohydrates, while fructose can be absorbed slowly and incompletely. After ingestion, glucose and galactose quickly raise the blood sugar, while fructose raises blood sugar only mildly and slowly.

During digestion, all carbohydrates have to be broken down into monosaccharides in order to be absorbed.

**b) Disaccharides**

A **disaccharide** is a pair of monosaccharides (di- = "two"). Disaccharides are formed via dehydration synthesis, and the bond linking them is referred to as a glycosidic bond (glyco- = "sugar").

Three disaccharides (Figure 6) are important to humans. These are sucrose, commonly referred to as table sugar; lactose, or milk sugar; and maltose, or malt sugar. As you can tell from their common names, you consume these in your diet; however, your body cannot use them directly. Instead, in the digestive tract, they are split into their component monosaccharides via hydrolysis.

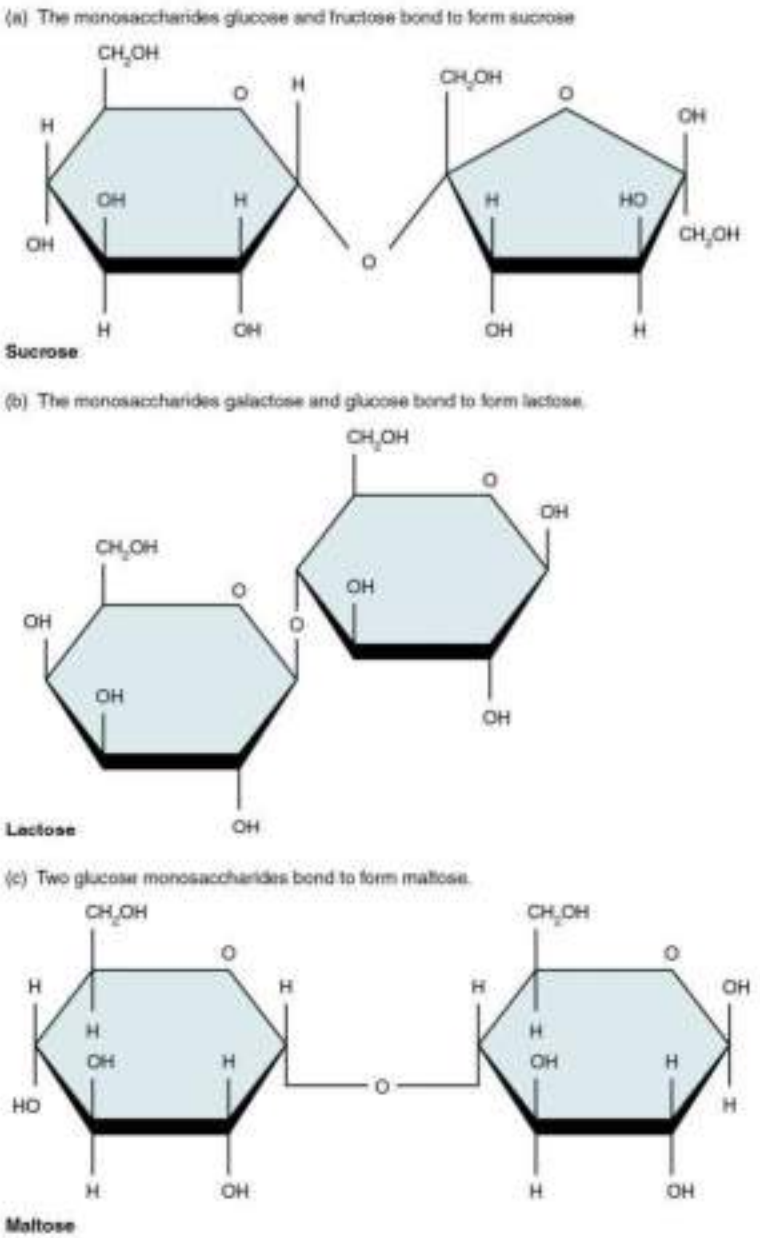



**Figure 6:** Three Important Disaccharides form by dehydration synthesis.

### c) Polysaccharides

A long chain of monosaccharides linked by glycosidic bonds is a **polysaccharide** (poly- = "many"). The chain may be branched or unbranched, and it may contain different types of monosaccharides. The molecular weight may be 100,000 daltons or more depending on the number of joined monomers. Starch, glycogen, cellulose, and chitin are primary examples of polysaccharides (Figure 7).

- **Starches** are polymers of glucose. They occur in long chains called amylose or branched chains called amylopectin, both of which are stored in plant-based foods and are relatively easy to digest.
- **Glycogen** is also a polymer of glucose, but it is stored in the tissues of animals, especially in the muscles and liver. It is not considered a dietary carbohydrate because very little glycogen remains in animal tissues after slaughter; however, the human body stores excess glucose as glycogen, again, in the muscles and liver.
- **Cellulose**, a polysaccharide that is the primary component of the cell wall of green plants, is the component of plant food referred to as "fiber". In humans, cellulose/fiber is not digestible; however, dietary fiber has many health benefits. It helps you feel full, so you eat less, it promotes a healthy digestive tract, and a diet high in fiber is thought to reduce the risk of heart disease and possibly some forms of cancer.

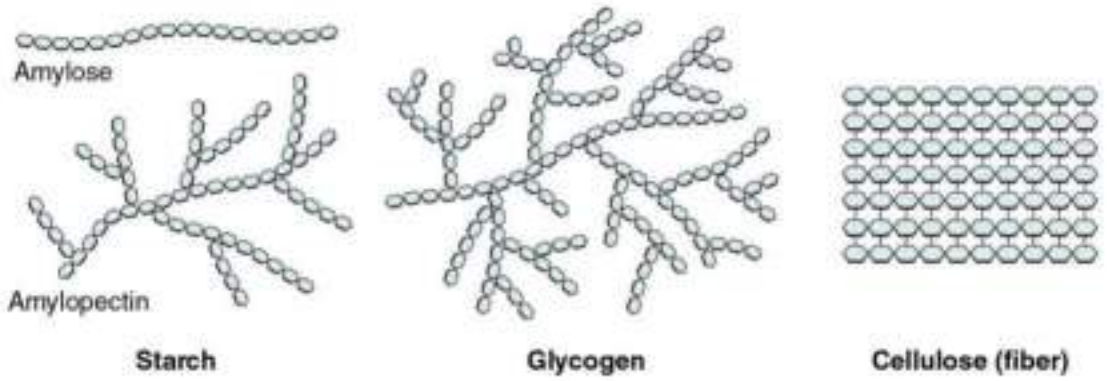



**Figure 7:** Three Important Polysaccharides. Three important polysaccharides are starches, glycogen, and fiber.

## Function of polysaccharides:

Nutrition polysaccharides are common sources of energy. Many organisms can easily break down starches into glucose. Polysaccharides have several roles. Polysaccharides such as starch, glycogen, and dextran's are all stored in the liver and muscles to be converted to energy for later use.

## Function of Carbohydrates:

The body obtains carbohydrates from plant-based foods. Grains, fruits, and legumes and other vegetables provide most of the carbohydrate in the human diet, although lactose is found in dairy products. Carbohydrates play a variety of extensive roles in all forms of life:

1- Although most body cells can break down other organic compounds for fuel, all body cells can use glucose. Moreover, nerve cells (neurons) in the brain, spinal cord, and through the peripheral nervous system, and red blood cells, can use only glucose for fuel.
2- Formation of the structural framework of RNA and DNA (ribonucleic acid and deoxyribonucleic acid).

3- -Form structural elements in the cell walls of plants (cellulose) and animals (chitin).

4- Carbohydrates are present in very small amounts in cells' structure for instance, some carbohydrate molecules bind with proteins to produce glycoproteins, and others combine with lipids to produce glycolipids, both of which are found in the membrane that encloses the contents of body cells.

## (2) Lipids

Lipids include a diverse group of compounds that are largely nonpolar in nature. This is because they are hydrocarbons that include mostly nonpolar carbon–carbon or carbon–hydrogen bonds. Non-polar molecules are hydrophobic ("water fearing"), or insoluble in water. Lipids perform many different functions in a cell. Cells store energy for long-term use in the form of fats. Lipids also provide insulation from the environment for plants and animals. For example, they help keep aquatic birds and mammals dry when forming a protective layer over fur or feathers because of their water-repellant hydrophobic nature. Lipids are also the building blocks of many hormones and are an important constituent of all cellular membranes. Lipids include fats, oils, waxes, phospholipids, and steroids.

### a) Fats and Oils

A fat molecule consists of two main components glycerol and fatty acids (Figure 8). Glycerol is an organic compound (alcohol) with three carbons, five hydrogens, and three hydroxyl (OH) groups. Fatty acids have a long chain of hydrocarbons to which a carboxyl group is

attached, hence the name "fatty acid." The number of carbons in the fatty acid may range from 4 to 36. The most common are those containing 12–18 carbons. In a fat molecule, the fatty acids attach to each of the glycerol molecule's three carbons with an ester bond through an oxygen atom

During this ester bond formation, three water molecules are released. The three fatty acids in the triacylglycerol may be similar or dissimilar. We also call fats **triacylglycerols** or **triglycerides** because of their chemical structure. Some fatty acids have common names that specify their origin. For example, palmitic acid, a **saturated fatty acid**, is derived from the palm tree. Arachidic acid is derived from *Arachis hypogea,* the scientific name for groundnuts or peanuts. Fatty acids may be saturated or unsaturated. In a fatty acid chain, if there are only single bonds between neighboring carbons in the hydrocarbon chain, the fatty acid is saturated. Saturated fatty acids are saturated with hydrogen. In other words, the number of hydrogen atoms attached to the carbon skeleton is maximized. Stearic acid is an example of a saturated fatty acid (Figure 9).

When the hydrocarbon chain contains a double bond, the fatty acid is **unsaturated**. Oleic acid is an example of an unsaturated fatty acid (Figure 10). Most unsaturated fats are liquid at room temperature. We call these oils. If there is one double bond in the molecule, then it is a monounsaturated fat (e.g., olive oil), and if there is more than one double bond, then it is a polyunsaturated fat (e.g., canola oil). When a fatty acid has no double bonds, it is a saturated fatty acid because it is not possible to add more hydrogen to the chain's carbon atoms. A fat

may contain similar or different fatty acids attached to glycerol. Long straight fatty acids with single bonds generally pack tightly and are solid at room temperature. Animal fats with stearic acid and palmitic acid (common in meat) and the fat with butyric acid (common in butter) are examples of saturated fats. Mammals store fats in specialized cells, or adipocytes, where fat globules occupy most of the cell's volume. Unsaturated fats help to lower blood cholesterol levels, whereas, saturated fats contribute to plaque formation in the arteries (Figure 11).

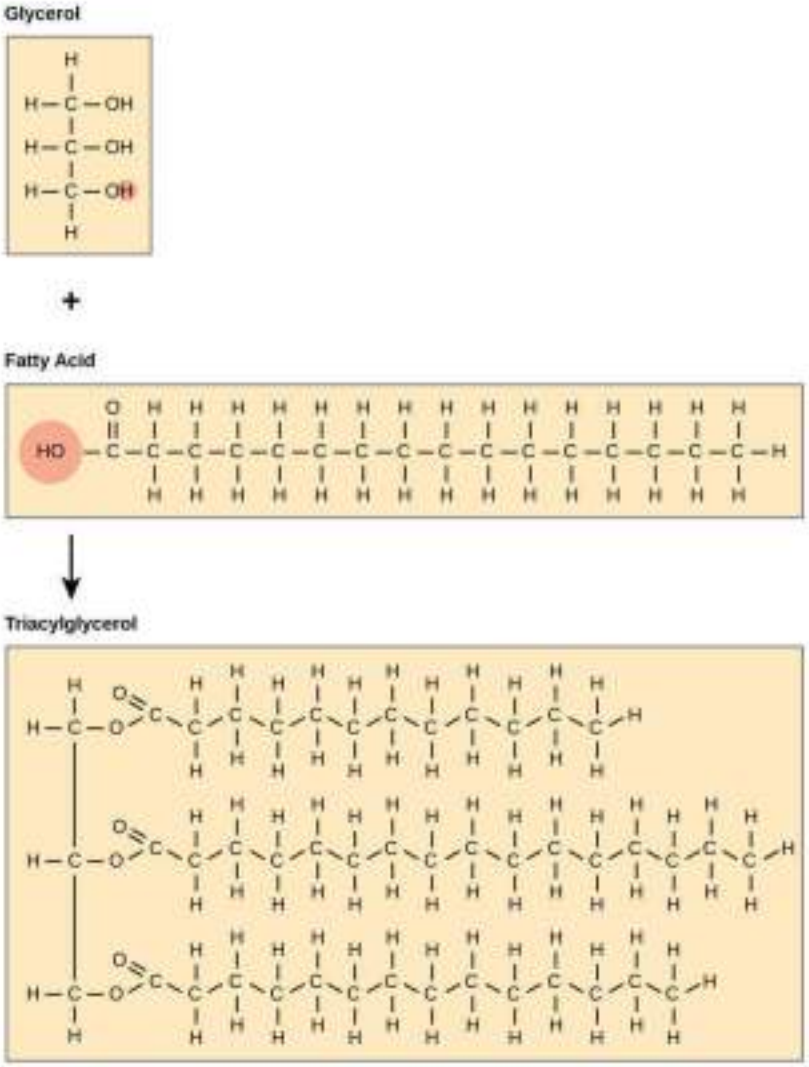



**Figure 8:** Joining three fatty acids to a glycerol backbone in a dehydration reaction forms triacylglycerol. Three water molecules release in the process.

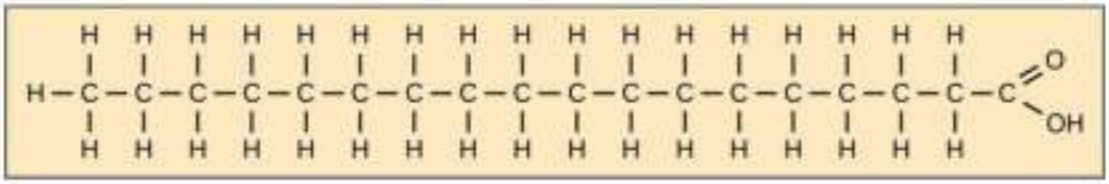


**Figure 9:** Stearic acid is a common saturated fatty acid.

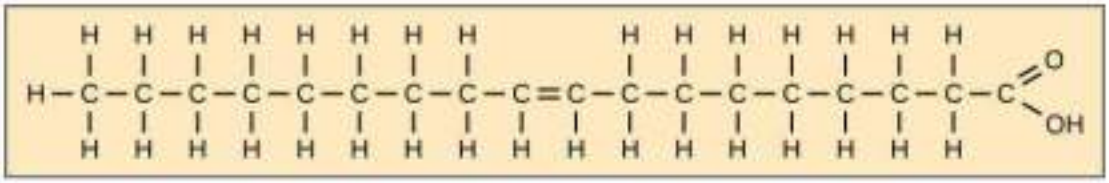


**Figure 10:** Oleic acid is a common unsaturated fatty acid.

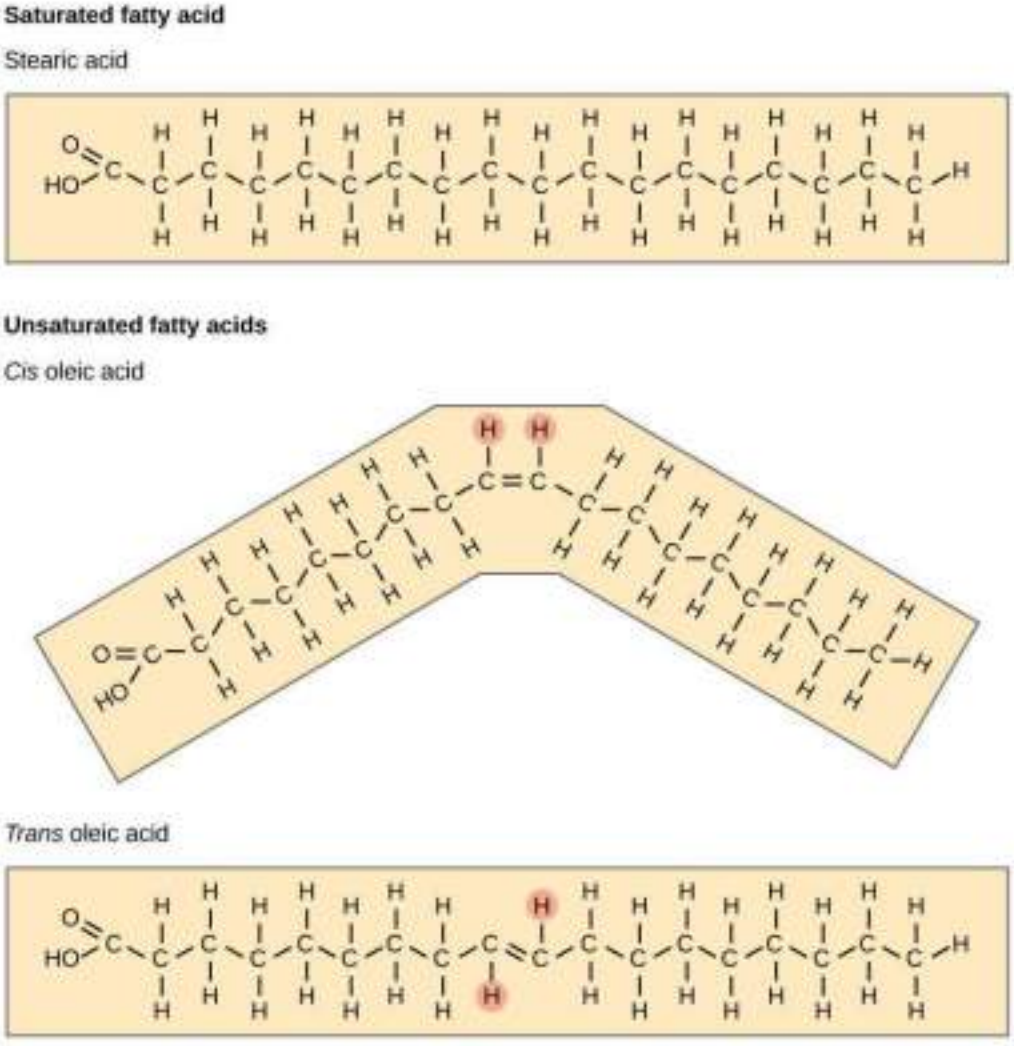



**Figure 11:** Saturated fatty acids have hydrocarbon chains connected by single bonds only. Unsaturated fatty acids have one or more double bonds.

## b) Phospholipids:

As its name suggests, a **phospholipid** is a bond between the glycerol component of a lipid and a phosphorous molecule. In fact, phospholipids are similar in structure to triglycerides. However, instead of having three fatty acids, a phospholipid is generated from a diglyceride, a glycerol with just two fatty acid chains (Figure 12). The third binding site on the glycerol is taken up by the phosphate group, which in turn is attached to a polar "head" region of the molecule. Recall that triglycerides are nonpolar and hydrophobic. This still holds for the fatty acid portion of a phospholipid compound. However, the phosphate-containing group at head of the compound is polar and thereby hydrophilic. In other words, one end of the molecule can interact with oil, and the other end with water. This makes phospholipids ideal emulsifiers, compounds that help disperse fats in aqueous liquids, and enables them to interact with both the watery interior of cells and the watery solution outside of cells as components of the cell membrane.

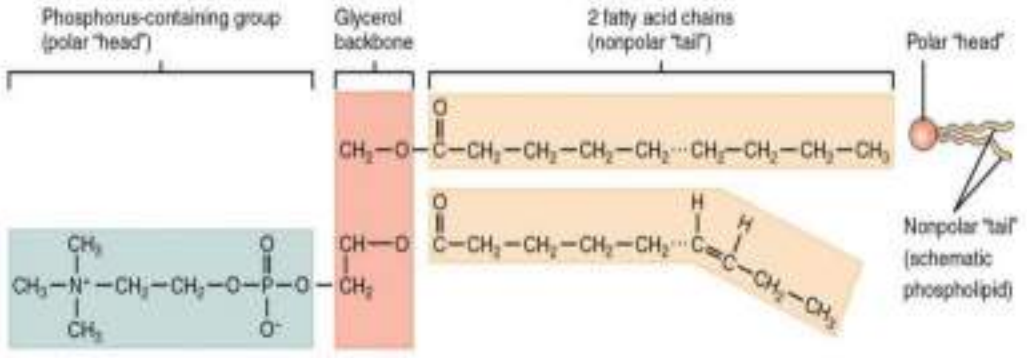



**Figure 12:** Phospholipid structure

### c) Steroids

A **steroid** compound (referred to as a sterol) has as its foundation a set of four hydrocarbon rings bonded to a variety of other atoms and molecules (Figure 13). Although both plants and animals synthesize sterols, the type that makes the most important contribution to human structure and function is cholesterol, which is synthesized by the liver in humans and animals and is also present in most animal-based foods. Like other lipids, cholesterol's hydrocarbons make it hydrophobic; however, it has a polar hydroxyl head that is hydrophilic. Cholesterol is an important component of bile acids, compounds that help emulsify dietary fats. In fact, the word root *chole–* refers to bile. Cholesterol is also a building block of many hormones, signaling molecules that the body releases to regulate processes at distant sites. Finally, like phospholipids, cholesterol molecules are found in the cell membrane, where their hydrophobic and hydrophilic regions help regulate the flow of substances into and out of the cell.

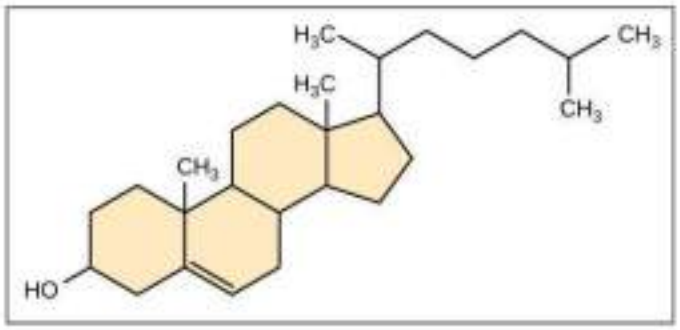
**Function of cholesterol:**

1- Cholesterol is composes about 30% of all animal cell membranes, is required to build and maintain membranes and modulates membrane fluidity over the range of physiological temperatures.
2- Cholesterol is maintaining cell membrane integrity so that animal cells do not need to build cell walls (like plants and most bacteria). The membrane remains stable and durable without being rigid, allowing animal cells to change shape and animals to move
3- Within cells, cholesterol is also a precursor molecule for several

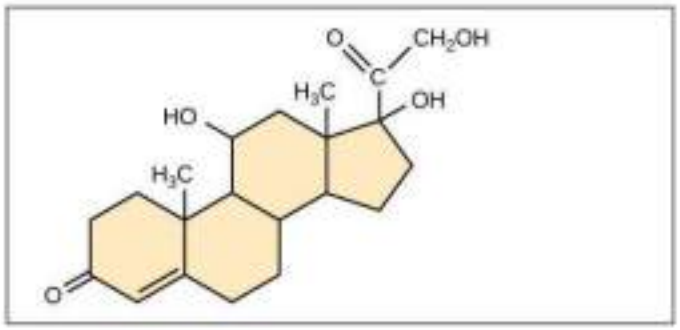
biochemical pathways. For example, it is the precursor molecule for the synthesis of vitamin D and all steroid hormones, including the adrenal gland hormones cortisol and aldosterone, as well as the sex hormones progesterone, estrogens, and testosterone, and their derivatives.

4- Cholesterol and phospholipids, both electrical insulators, can facilitate speed of transmission of electrical impulses along nerve tissue. For many neuron fibers.

5- All animal cells manufacture cholesterol, for both membrane structure and other uses, with relative production rates varying by cell type and organ function. About 20% of total daily cholesterol production occurs in the liver; other sites of higher synthesis rates include the intestines, adrenal glands, and reproductive organs.




Cholesterol




Cortisol

**Figure 13:** A steroid compound (referred to as a sterol)

### d) Prostaglandins:

Like a hormone, a **prostaglandin** is one of a group of signaling molecules, but prostaglandins are derived from unsaturated fatty acids (Figure 14). One reason that the omega-3 fatty acids found in fish are beneficial is that they stimulate the production of certain prostaglandins that help regulate aspects of blood pressure and inflammation, and thereby reduce the risk for heart disease.

Prostaglandins also sensitize nerves to pain. One class of pain-relieving medications called nonsteroidal anti-inflammatory drugs (NSAIDs) works by reducing the effects of prostaglandins.

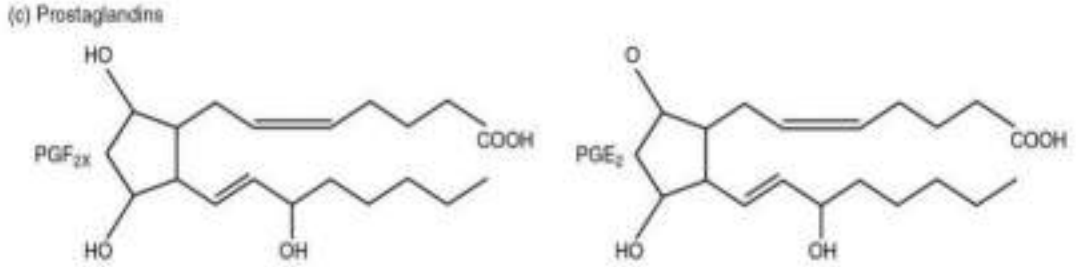



**Figure 14:** A prostaglandin structure

### (3) Proteins:

**Proteins** are one of the most abundant organic molecules in living systems and have the most diverse range of functions of all macromolecules. Proteins may be structural, regulatory, contractile, or protective. They may serve in transport, storage, or membranes; or they may be toxins or enzymes. Each cell in a living system may contain thousands of proteins, each with a unique function. Their structures, like their functions, vary greatly. They are all, however, amino acid polymers arranged in a linear sequence.

## (A) Types and Functions of Proteins:

**Enzymes**, which living cells produce, are catalysts in biochemical reactions (like digestion) and are usually complex or conjugated proteins. Each enzyme is specific for the substrate (a reactant that binds to an enzyme) upon which it acts. The enzyme may help in breakdown, rearrangement, or synthesis reactions. We call enzymes that break down their substrate's catabolic enzymes. Those that build more complex molecules from their substrates are anabolic enzymes, and enzymes that affect the rate of reaction are catalytic enzymes. Note that all enzymes increase the reaction rate and, therefore, are organic catalysts. An example of an enzyme is salivary amylase, which hydrolyzes its substrate amylose, a component of starch (Table 2).

**Hormones** are chemical-signaling molecules, usually small proteins or steroids, secreted by endocrine cells that act to control or regulate specific physiological processes, including growth, development, metabolism, and reproduction. For example, insulin is a protein hormone that helps regulate the blood glucose level. lists the primary types and functions of proteins (Table 2).

Proteins have different shapes and molecular weights. Some proteins are globular in shape, whereas others are fibrous in nature. For example, hemoglobin is a globular protein, but collagen, located in our skin, is a fibrous protein. Protein shape is critical to its function, and many different types of chemical bonds maintain this shape. Changes in temperature, pH, and exposure to chemicals may lead to changes in the protein's shape, leading to loss of function, or denaturation.

**Table 2:** Types of Enzymes and hormones, examples, and functions.

| Type | Examples | Functions |
|---|---|---|
| Digestive Enzymes | Amylase, lipase, pepsin, trypsin | Help in food by catabolizing nutrients into monomericunits |
| Transport | Hemoglobin, albumin | Carry substances in the blood or lymph throughout thebody |
| Structural | Actin, tubulin, keratin | Construct different structures, like the cytoskeleton |
| Hormones | Insulin, thyroxine | Coordinate different body systems' activity |
| Defense | Immunoglobulins | Protect the body from foreign pathogens |
| Contractile | Actin, myosin | Effect muscle contraction |
| Storage | Legume storage proteins, egg white (albumin) | Provide nourishment in early embryo development andthe seedling |

## Amino Acids:

- Amino acids are the monomers that comprise proteins. Each amino acid has the same fundamental structure, which consists of a central carbon atom, or the alpha ($\alpha$) carbon, bonded to an amino group ($NH_2$), a carboxyl group (COOH), and to a hydrogen atom. Every amino acid also has another atom or group of atoms bonded to the central atom known as the R group (Figure 15).
- Scientists use the name "amino acid" because these acids contain both amino group and carboxyl-acid-group in their basic structure. As we mentioned, there are 20 common amino acids present in proteins. Nine of these areessential amino acids in humans because the human body cannot produce them, and we obtain them from our diet. For each amino acid, the R group is different (Figure 16).

- The chemical nature of the side chain determines the amino acid's nature (that is, whether it is acidic, basic, polar, or nonpolar).
- A single upper-case letter or a three-letter abbreviation represents amino acids. For example, the letter V or the three-letter symbol Val represent valine (Figure 16).
- Just as some fatty acids are essential to a diet, some amino acids also are necessary. These essential amino acids in humans include isoleucine, leucine, and cysteine. Essential amino acids refer to those necessary to build proteins in the body, but not those that the body produces. Which amino acids are essential varies from organism to organism.
- The sequence and the number of amino acids ultimately determine the protein's shape, size, and function. A covalent bond, or peptide bond, attaches to each amino acid, which a dehydration reaction forms. One amino acid's carboxyl group and the incoming amino acid's amino group combine, releasing a water molecule. The resulting bond is the peptide bond (Figure 17).
- The products that such linkages form are peptides. As more amino acids join to this growing chain, the resulting chain is a polypeptide. Each polypeptide has a free amino group at one end. This end the N terminal, or the amino terminal, and the other end has a free carboxyl group, also the C or carboxyl terminal.
- While the terms polypeptide and protein are sometimes used interchangeably, a polypeptide is technically a polymer of amino

acids, whereas the term protein is used for a polypeptide or polypeptides that have combined together, often have bound non-peptide prosthetic groups, have a distinct shape, and have a unique function.

- After protein synthesis (translation), most proteins are modified. These are known as post-translational modifications. They may undergo cleavage, phosphorylation, or may require adding other chemical groups. Only after these modifications is the protein completely functional.

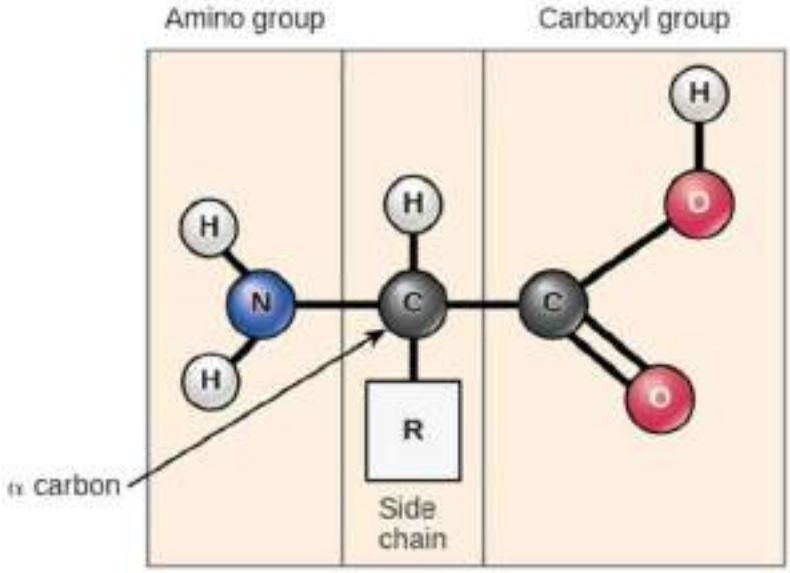



**Figure 15:** Amino acids have a central asymmetric carbon to which an amino group, a carboxyl group, a hydrogen atom, and a side chain (R group) attached.

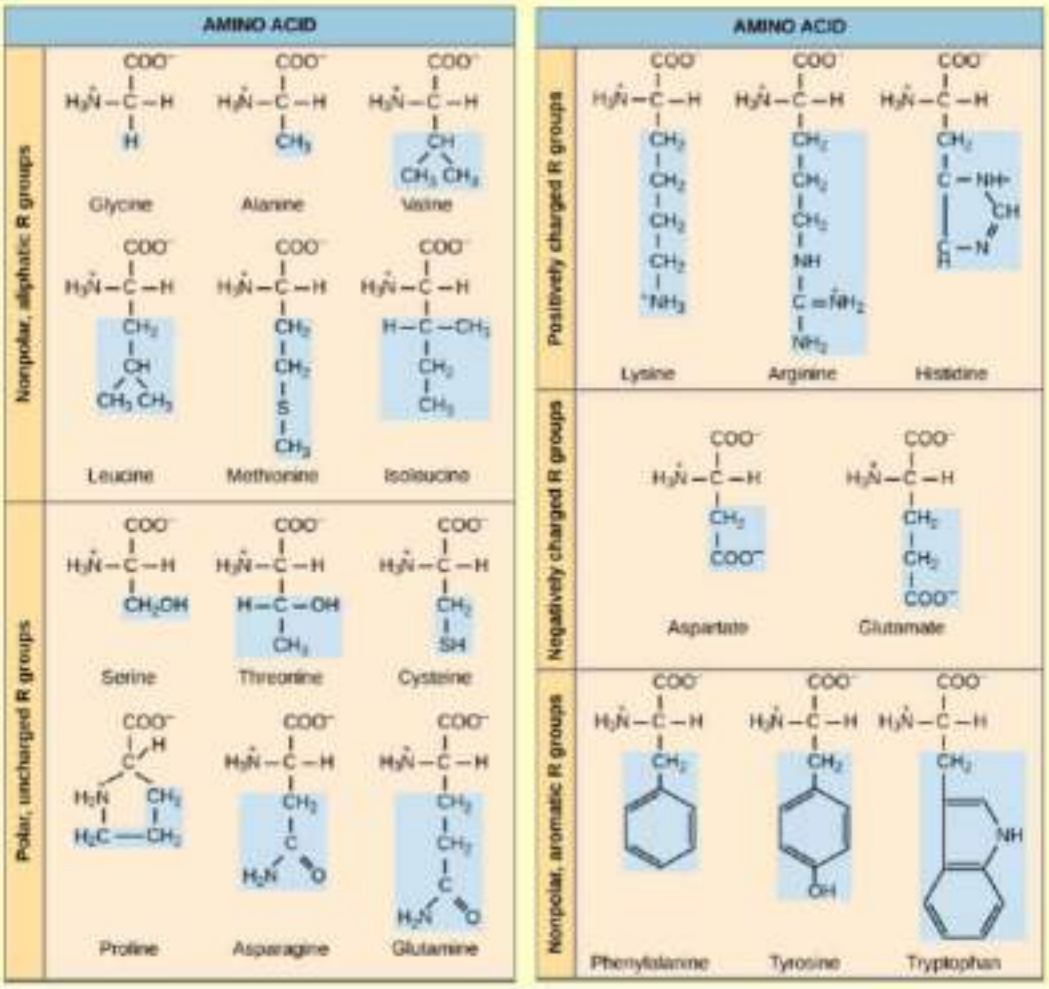



**Figure 16:** There are 20 common amino acids commonly found in proteins, each with a different R group (variant group) that determines its chemical nature.

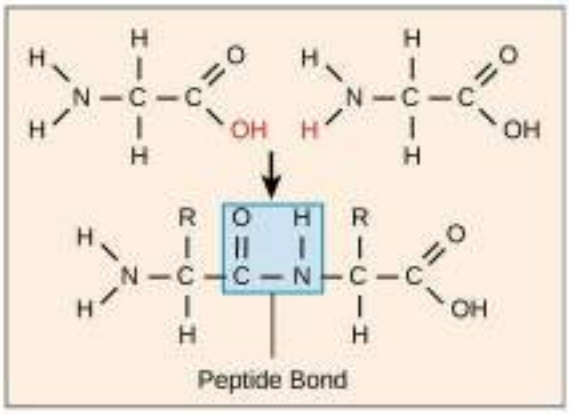



**Figure 17:** Peptide bond formation is a dehydration synthesis reaction. The carboxyl group of one amino acid is linked to the incoming amino acid's amino group. In the process, it releases a water molecule.

## (B) Protein Structure:

### 1- Primary Structure:

Amino acids' unique sequence in a polypeptide chain is its primary structure. For example, the pancreatic hormone insulin has two polypeptide chains, A and B, and they are linked together by disulfide bonds. The N terminal amino acid of the A chain is glycine; whereas, the C terminal amino acid is asparagine (Figure 18). The amino acid sequences in the A and B chains are unique to insulin.

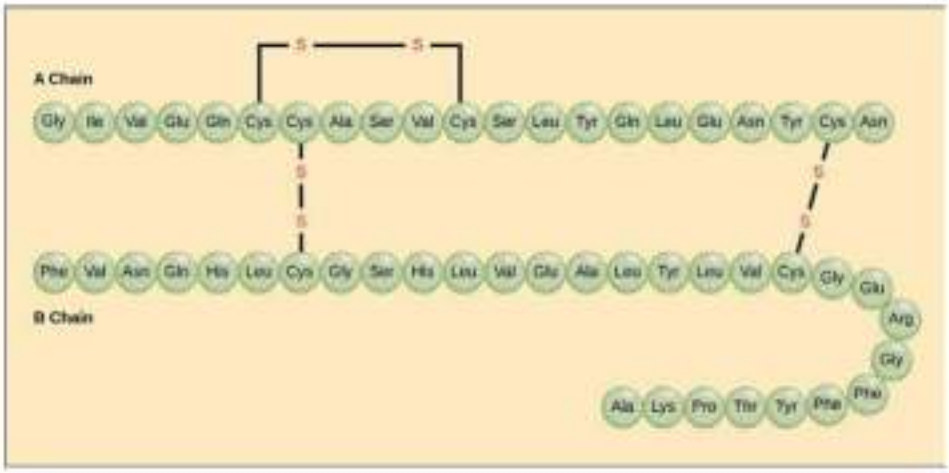



**Figure 18:** Bovine serum insulin is a protein hormone comprised of two peptide chains, A (21 amino acids long) and B (30 amino acids long).

### 2- Secondary Structure:

The local folding of the polypeptide in some regions gives rise to the secondary structure of the protein. The most common are the $\alpha$-helix and $\beta$-pleated sheet structures (Figure 19, 22). Both structures are held in shape by hydrogen bonds. The hydrogen bonds form between the oxygen atom in the carbonyl group in one amino acid and another amino acid that is four amino acids farther along the chain.

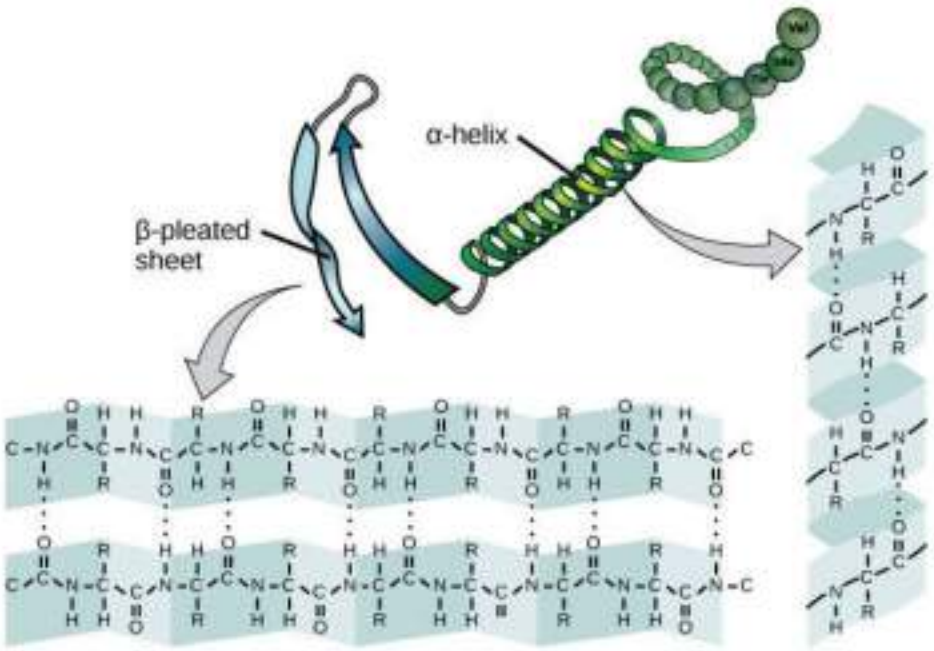



**Figure 19:** The *α*-helix and *β*-pleated sheet are secondary structures of proteins that form because of hydrogen bonding between carbonyl and amino groups in the peptide backbone.

## 3- Tertiary Structure:

The polypeptide's unique three-dimensional structure is its tertiary structure (Figure 20, 22). This structure is in part due to chemical interactions at work on the polypeptide chain. Primarily, the interactions among R groups create the protein's complex three-dimensional tertiary structure. The nature of the R groups in the amino acids involved can counteract forming the hydrogen bonds we described for standard secondary structures. For example, R groups with like charges repel each other and those with unlike charges are attracted to each other (ionic bonds). When protein folding takes place, the nonpolar amino acids' hydrophobic R groups lie in the protein's interior, whereas the hydrophilic R groups lie on the outside. Scientists also call the former interaction types of hydrophobic interactions.

Interaction between cysteine side chains forms disulfide linkages in the presence of oxygen, the only covalent bond that forms during protein folding.

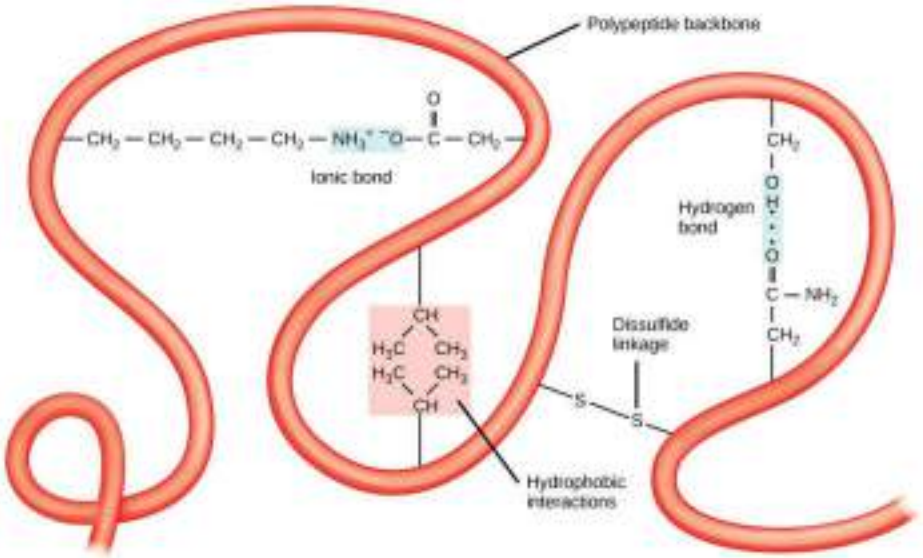



**Figure 20:** A variety of chemical interactions determine the proteins' tertiary structure. These include hydrophobic interactions, ionic bonding, hydrogen bonding, and disulfide linkages.

## 4- Quaternary Structure:

In nature, some proteins form from several polypeptides, or subunits, and the interaction of these subunits forms the quaternary structure. Weak interactions between the subunits help to stabilize the overall structure. For example, insulin (a globular protein) has a combination of hydrogen and disulfide bonds that cause it to mostly clump into a ball shape (Figure 21, 22). Insulin starts out as a single polypeptide and loses some internal sequences in the presence of post-translational modification after forming the disulfide linkages that hold the remaining chains together.

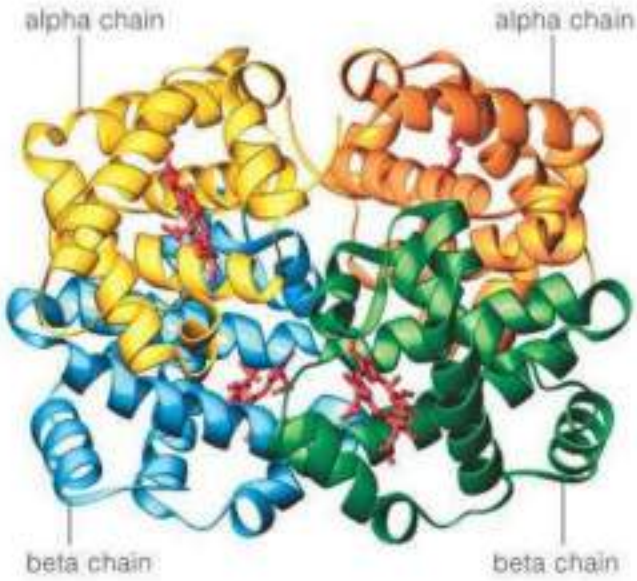



**Figure 21:** Insulin (a globular protein) quaternary structure.

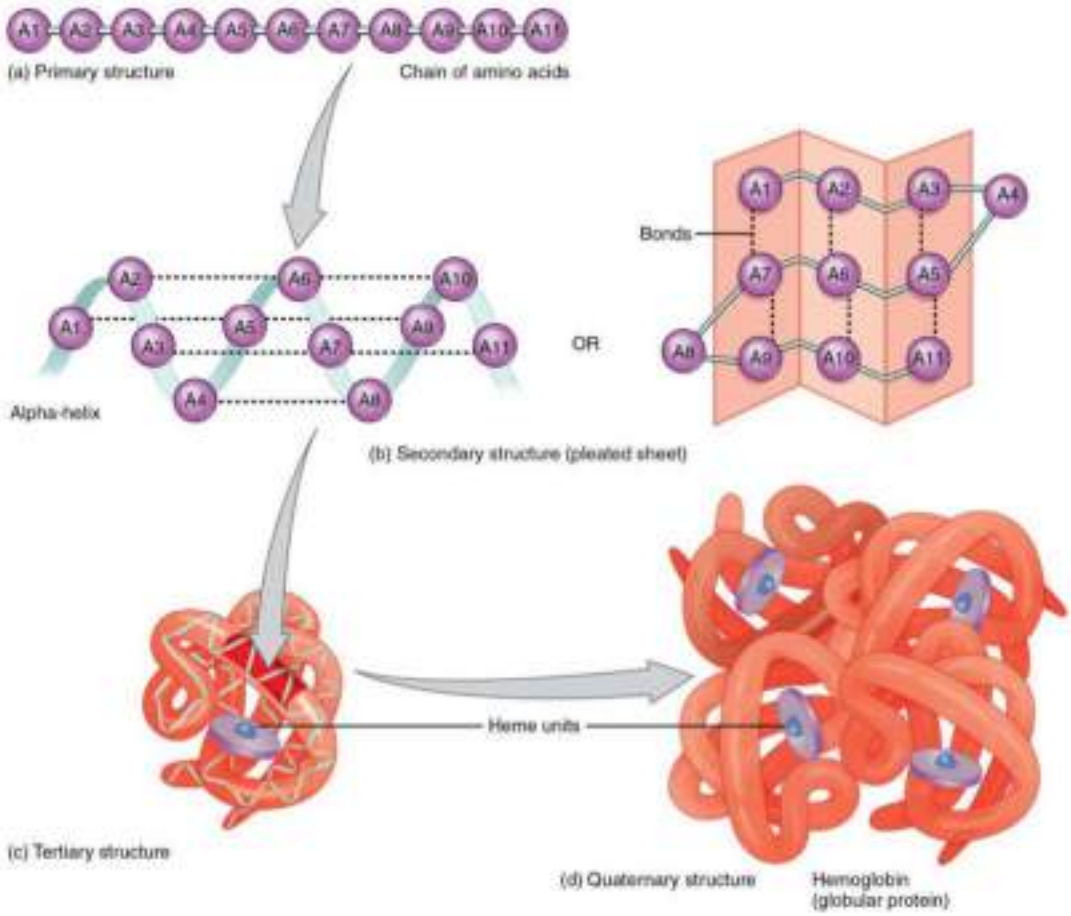



**Figure 22:** illustrates the four levels of protein structure (primary, secondary, tertiary, and quaternary)

## (4) Nucleotides

The fourth type of organic compound important to human structure and function are the nucleotides (Figure 23). A **nucleotide** is one of a class of organic compounds composed of three subunits: one or more phosphate groups a pentose sugar: either deoxyribose or ribose a nitrogen-containing base: adenine, cytosine, guanine, thymine, or uracil Nucleotides can be assembled into nucleic acids (DNA or RNA) or the energy compound adenosine triphosphate.

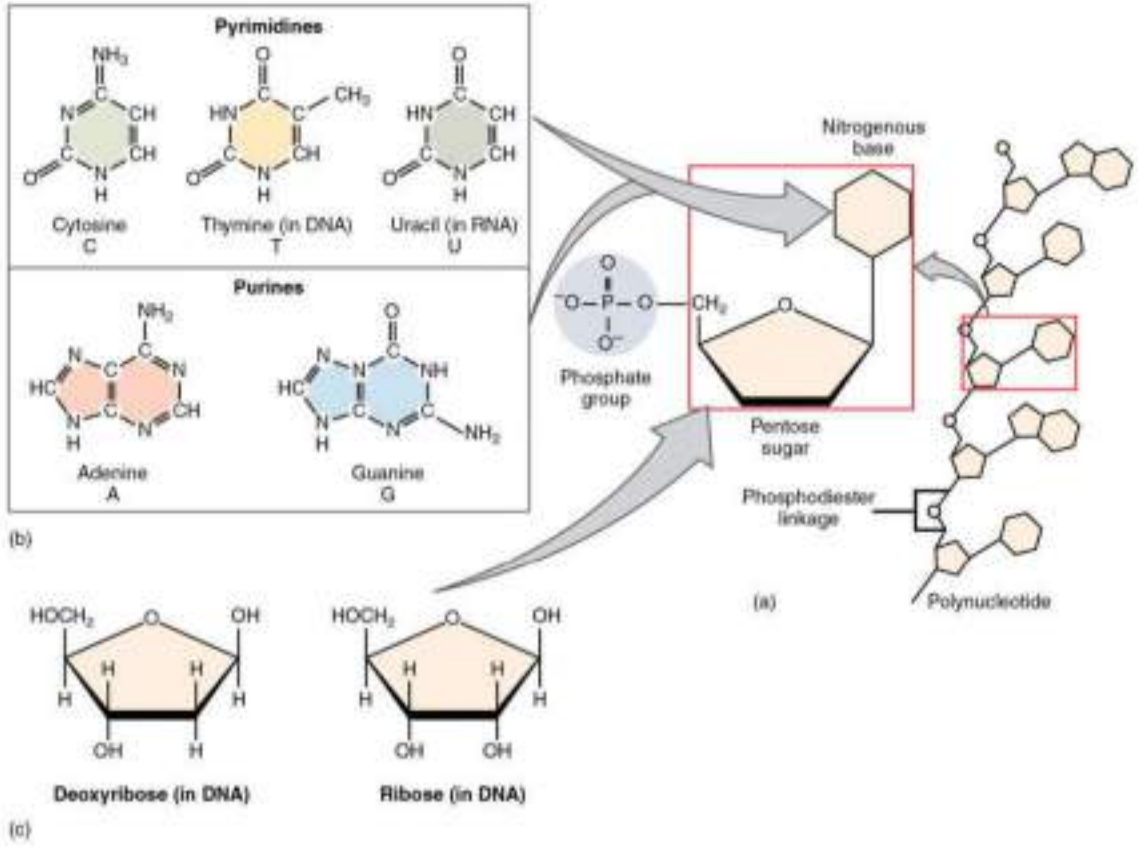



**Figure 23.** Nucleotides. (a) The building blocks of all nucleotides are one or more phosphate groups, a pentose sugar, and a nitrogen-containing base. (b) The nitrogen-containing bases of nucleotides. (c) The two pentose sugars of DNA and RNA.

**Adenosine Triphosphate:**

The nucleotide adenosine triphosphate (ATP) is composed of a ribose sugar, an adenine base, and three phosphate groups (Figure 24). ATP is classified as a high energy compound because the two covalent bonds linking its three phosphates store a significant amount of potential energy. In the body, the energy released from these high energy bonds helps fuel the body's activities, from muscle contraction to the transport of substances in and out of cells to anabolic chemical reactions.

When a phosphate group is cleaved from ATP, the products are adenosine diphosphate (ADP) and inorganic phosphate (P*i*). This hydrolysis reaction can be written:

$$ATP + H_2O \rightarrow ADP + Pi + energy$$

Removal of a second phosphate leaves adenosine monophosphate (AMP) and two phosphate groups. Again, these reactions also liberate the energy that had been stored in the phosphate-phosphate bonds. They are reversible, too, as when ADP undergoes phosphorylation. **Phosphorylation** is the addition of a phosphate group to an organic compound, in this case, resulting in ATP. In such cases, the same level of energy that had been released during hydrolysis must be reinvested to power dehydration synthesis. Cells can also transfer a phosphate group from ATP to another organic compound. For example, when glucose first enters a cell, a phosphate group is transferred from ATP, forming glucose phosphate ($C_6H_{12}O_6$—P) and ADP. Once glucose is phosphorylated in this way, it can be stored as glycogen or metabolized for immediate energy.

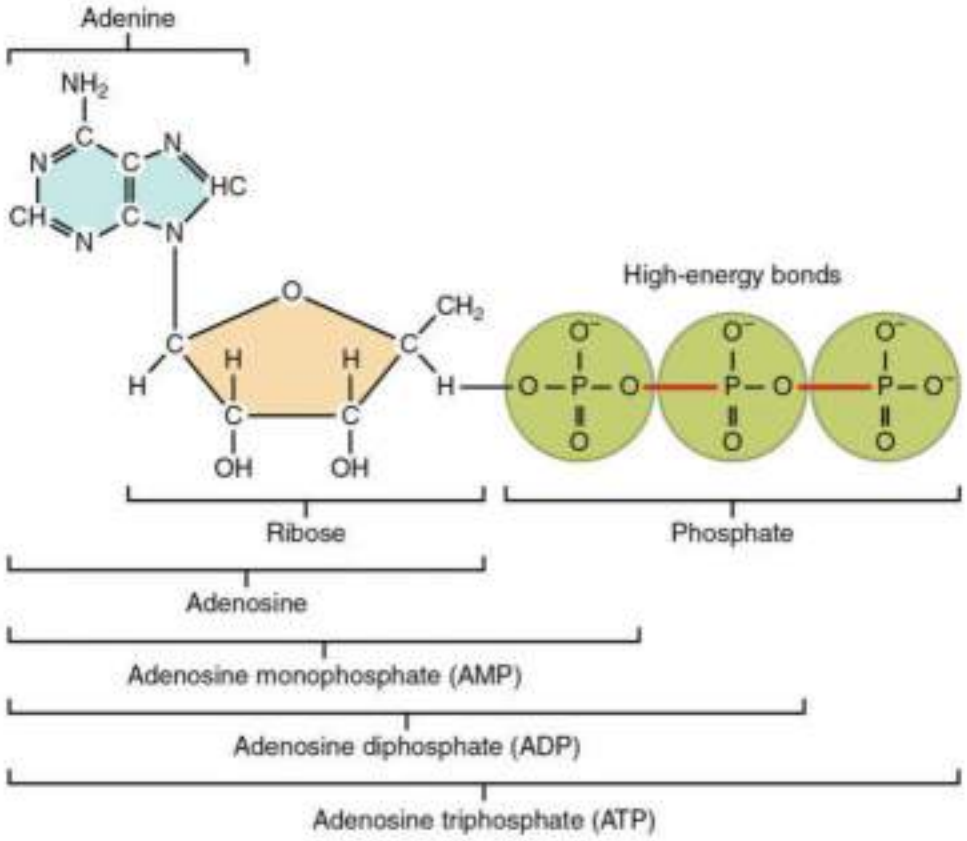



**Figure 24:** Structure of Adenosine Triphosphate (ATP)

## Nucleic Acids:

The nucleic acids differ in their type of pentose sugar. **Deoxyribonucleic acid (DNA)** is nucleotide that stores genetic information. DNA contains deoxyribose (so-called because it has one less atom of oxygen than ribose) plus one phosphate group and one nitrogen-containing base. The "choices" of base for DNA are adenine, cytosine, guanine, and thymine. **Ribonucleic acid (RNA)** is a ribose-containing nucleotide that helps manifest the genetic code as protein. RNA contains ribose, one phosphate group, and one nitrogen-containing base, but the "choices" of base for RNA are adenine, cytosine, guanine, and uracil. **Nucleic Acids will be discussed in the next chapter in details.**

# THE CELLULAR LEVEL OF ORGANIZATION & ORGANELLES STRUCTURES

## History and Origin of cell:

A cell was defined as "unit of biological activity delimited by a semi permeable membrane and capable of self-reproduction in a medium free of other living systems" by **Loewy and Siekevitz (1963)**.

The study of cell has been made possible with the help of light microscope. **Robert Hooke (1665)** with the help of light microscope discovered that a section of cork is made up of small cavities surrounded by firm walls. He used the term **"cell"** for the first time to describe his investigations on the "texture of a piece of cork". Later on **A. Van Leeuwenhoek (1632-1723)** observed various unicellular organisms and cells like bacteria, protozoan's, red blood cells and sperm etc. He observed nucleus in some erythrocytes, and all this was made possible with the improved microscopes. In **1809, Mirble M.** stated that all plant tissues are composed of cells. In the same year, importance of cells in living organisms was described by **J.B. Lamarck**. **Robert Brown** in **1831** observed nucleus in certain plant cells. *Mimosa* cells were boiled in nitric acid by **Dutrochet (1837)** to separate the cells to conclude that all organic tissues are composed of globular cells, united by simple adhesive forces. "All living organism are composed of cells" was stated by **Schwann, T. (1839)** after examining a variety of animals and plant tissues.

## Types of cells:

### (A) Prokaryotic Cells:

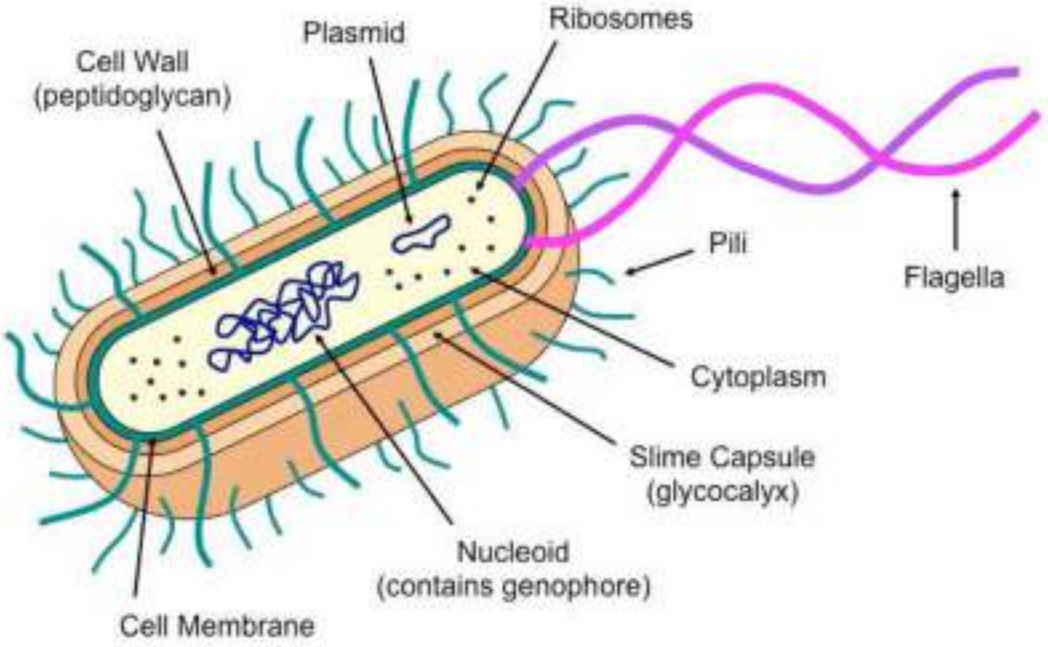



**Figure 25:** Prokaryotic cells structure.

Prokaryotic cells (Figure 25) are the most primitive cells and have simple structural organization. It has a single membrane system. They include bacteria, viruses, blue-green algae, mycoplasmas, rickettsias, spirochetes etc. Cyanobacteria or blue green algae are the largest and most complex prokaryote, in which photosynthesis of higher plants type have evolved. **Prokaryotes** are included in the kingdom **Monera** and the super kingdom **Prokaryota**. The Prokaryotes have the following characters:

(1) **The size** of prokaryotic cells ranges between 1 to 10 µm. They occur in a variety of forms.

(2) **Prokaryotic cell consists** of three main components:

I- **Outer covering:** It is composed of inner cell or plasma membrane,

middle cellwall and outer slimy capsule.

a. **Cell membrane:** Cell membrane made up of lipids and proteins, is thin and flexible and controls the movement of molecules across the cell. Respiratory enzymes are carried by it for energy releasing reactions. **Mesosomes**, the in-folds of plasma membrane bears respiratory enzymes and these are considered analogous to mitochondria of eukaryotic cells. Similarly, the pigments and enzymes molecules that absorb and convert the light into chemical energy in photosynthetic cells are also associated with the plasma membrane's in-folds called **photosynthetic lamella**. These lamellae are analogous to the chloroplast of eukaryotic cells. Plasma membraneplays role in replication and division of nuclear material. Since the in-folds remain continuous with the cell membrane, they are not considered as separate compartments. Thus, prokaryotic cell is non-compartmentalized.

b. **Cell wall :** It is a rigid or semi-rigid non-living structure that surrounds the cell membrane and its thickness ranges between 1.5 to 100 µm. Chemically it is composedof **peptidoglycans**. . Some bacteria such as mycoplasmas lack cell wall.

c. **Slimy capsule:** A gelatinous coat outside the cell wall is the slimy capsule. It is composed of largely of polysaccharides and sometimes it may have polypeptides and other compounds also. It protects the cell against desiccation, virus attacks, phagocytosis and antibiotics

II- **Cytoplasm:** Prokaryotic cytoplasm contains proteins, lipids,

glycogen and inorganic ions along with enzymes for biosynthetic reactions and ribosomes, tRNA and mRNA for protein synthesis. Prokaryotic cytoplasm has some special features as follows:

a. It lacks cell organelles like endoplasmic reticulum, mitochondria, Golgi apparatus, Centrosomes, vacuoles, Lysosomes, microfilaments, intermediate filaments and microtubules.
b. The only cytoplasmic organelle found in prokaryotic cells is the **ribosomes**. They are smaller than eukaryotic ribosomes i.e., 70S and lie free in the cytoplasm. They form poly-ribosomes at the time of protein synthesis. They are the sites of protein synthesis.
c. Like eukaryotic cells, the cytoplasm of prokaryotic cell does not show streaming movement or cyclosis.
d. Gas vacuoles are also formed in some prokaryotic cells.
e. The cell does not show phagocytosis, pinocytosis and exocytose, substances enter and leave the cell through the cell membrane.
f. They may contain deposits of polysaccharides or inorganic phosphates.

III- **Nucleoid:** Nuclear envelope is absent in prokaryotic cell and the genetic material lies directly into the cytoplasm. Such nuclear material is known as **nucleoid**. **Nucleoid** consists of greatly coiled single pro-chromosome. It shows the following special features:

a. A short and simple pro-chromosome is present which is attached at least at one point on cell membrane.
b. Mostly there is single copy of chromosome, the prokaryotic cell is haploid.

c. The DNA is naked as it is not associated with basic histone proteins. It is double stranded, helical and circular.

d. The amount of DNA is lesser than eukaryotic cell and it codes fewer proteins. Replication of DNA is continuous throughout the cell cycle. Transcription and translation occurs in cytoplasm and processing of mRNA is not required.

e. The processes like meiosis, gamete formation or fertilization are absent. Conjugation is seen in some bacteria.

f. Mitotic apparatus absent.

g. There is no nucleolus.

h. Cell membrane folds or mesosomes help to segregate the replicated products of chromosomes into daughter cells.

(3) **Plasmids:** In some prokaryotic cells, in addition to nucleoid, a small circular double stranded DNA molecule is present. It is called **plasmid**. Plasmids have 1000 to 30,000 base pairs and they generally encode proteins required by the organism to resist antibiotic and other toxic material.

(4) **Flagellum:** It is a whip like locomotory structure found in many bacteria. It is 150Å thick and 10 to 15µm long. As the flagellum does not have any surrounding membrane, it grows at the tip. It has two main parts: Filament and basal body.

a. **Filament-** Filament extends out of cell into the medium and it is composed of many intertwined spiral chains of the subunits of a protein called **flagellin**. Flagellin differs from actins or tubulin.

b. **Basal Body-** The basal body attaches the flagellum to the cell and generates the force to rotate it. It is composed of many

components and numerous proteins. It has shaft and hook.

(5) **Pili:** These are short, rod like non-motile processes or fimbriae present on many bacteria. These are formed of pilin protein. They are usually less than 10 nm thick. They help in attachment of bacteria to surfaces or food or to one another. Tubular sex Pili are present in some bacteria.

(6) Prokaryotic cells have all the biochemical mechanisms required to synthesize complex organic materials from simple organic precursors necessary for life. Thus, inspite of being simple in structure prokaryotes are more versatile in their syntheticactivities than eukaryotes.

## (B) Eukaryotic Cells:

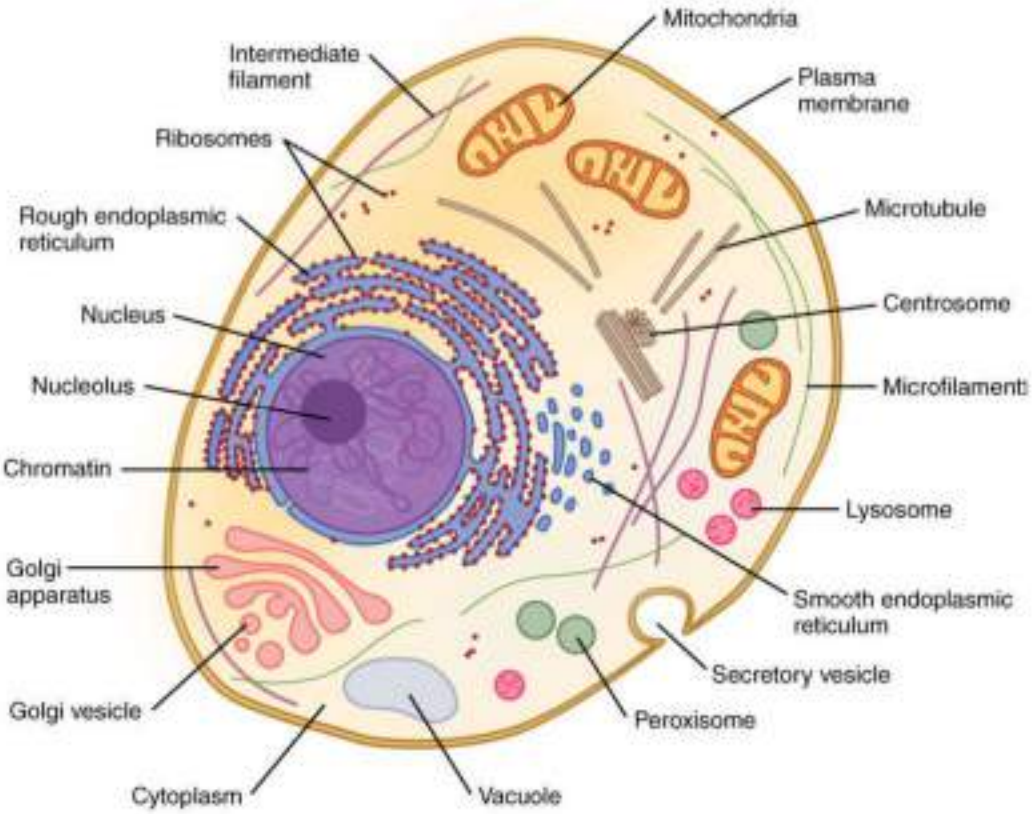



**Figure 26**: An eukaryotic cell containing the organelles and internal structures.

The internal organization of eukaryotic cell (Figure 26) is more developed than prokaryotic cells from which they are believed to have been evolved. They are evolved to have double membrane system. Primary membranes are the one that surrounds the cell, celled cell or plasma membrane and the secondary membrane surround the nucleus and other cellular organelles. Eukaryotic cells occur in protists, fungi, plants, and animals. Eukaryotic cells have the following characteristics:

(1) **Number-** In multicellular organisms the numbers of cells are correlated with the body size. The human blood contains about 30 quadrillion ($3 \times 10^{15}$) corpuscles and a 60 kg human being has about $60 \times 10^{15}$ cells. All multicellular organisms begin their life with a single cell "Zygote" and then become multicellular by its mitotic division during development.

(2) **Shape-** A cell may be spherical, cuboidal, oval, disc-like, polygonal, columnar, spindle like or irregular. Thus, cells acquire a variety of shapes not only in various organisms but also in different tissues of the same organism. The shape of cellis correlated with its functions like the shape of muscles and nerve cells are well adapted to their functions. Many factors such as cell functions, age of cell, presence or absence of cell wall, viscosity of cytoplasm etc. are responsible for various shapes of cells.

(3) **Size-** Most of the eukaryotic cells is microscopic and their size ranges between 10 to 100µm. Sporozoites of malaria parasite (*Plasmodium vivax)* is among the smallest cells having the size equal to 2µm long. While the Ostrich egg measures 175 × 120mm. Nerve cells are the longest having the size of its fiber to be of few

meterslong. Human cells generally range from 20 to 30µm.

(4) **Components of a cell-** Three main components of the eukaryotic cells are cellmembrane, cytoplasm, and nucleus. The cytoplasm and the nucleus further have several components. Various cell components are discussed below:

I- **Cell membrane-** Cell membrane, plasma membrane or plasmalemma is a thinelastic living covering that surrounds the cell keeping the cell contents in place, provides shape to the cell and controls the transfer of materials across it. It is composed of lipid-protein complex. It lacks respiratory enzymes. In many protists andanimal cells it allows endocytosis and exocytosis.

In certain protists, many fungi and all plant cells, the cell membrane is covered by a thick, rigid non-living cell wall that protects and supports the cell. In prokaryotes the cell wall surrounding the plasma membrane has a different structure in comparison to eukaryotes.

II- **Cytoplasm-** The cytoplasm or the cytosome is a semi-fluid, homogeneous, translucent ground substance known as cytoplasmic matrix or cytosol which is presentbetween the cell membrane and the nucleus. In the protozoan cell the outer firm layer of cytoplasm is called ectoplasm and the inner layer around the central fluid mass is called the endoplasm. The cytosol shows "cyclosis" or the streaming movement. The eukaryotic cytoplasm has the following features: -

**(A) Organelles:** The organized structures having the specific functions and capacity of growth and multiplication in some

cases are known as organelles. Mitochondria, centrosomes, Golgi bodies, plastids and vacuoles are the organelles that can be observed under light microscope, while endoplasmic reticulum, ribosome, microfilaments, microtubules, intermediate filaments, and micro bodies can only be seen under electron microscope. These organelles are often described as protoplasmic structures. The cells having cilia or flagella have their basal bodies at the bases are in the cytoplasm while rest of its part extends out of cytoplasm. These organelles are described as follows:

1- **Mitochondria**: The rod like or globule shaped structures scattered in the cytoplasm are found singly or in groups. They are bounded by **double membrane** of lipoproteins. The inner membrane gives out finger like structure known as **cristae** which partially subdivide the inner chamber of mitochondrion. On the inner surface of cristae are present mushroom like structures, **oxysomes** that are related tophosphorylation. The space between the membranes and its lumen is filled with mitochondrial **matrix**. Both the membranes and the matrix contain many oxidative enzymes and coenzymes. Since mitochondria contain DNA molecules and ribosomes, they synthesize certain proteins. They produce the energy and reserve it in the form of**adenosine triphosphate (ATP).**

2- **Endoplasmic reticulum:** The endoplasmic reticulum (ER) is a system of channels that is continuous with the nuclear membrane (or "envelope") covering the nucleus and composed

of the same lipid bilayer material. The ER can be thought of as a series of winding thoroughfares similar to the waterway canals in Venice. The ER provides passages throughout much of the cell that function in transporting, synthesizing, and storing materials. The winding structure of the ER results in a large membranous surface area that supports its many functions. Endoplasmic reticulum can exist in two forms: rough ER and smooth ER. These two types of ER perform some very different functions and can be found in very different amounts depending on the type of cell. Rough ER (RER) is so called because its membrane is dotted with embedded granules organelles called ribosomes, giving the RER a bumpy appearance.

1- **Ribosome's:** Ribosome is the minute spherical structures that originate in nucleolus and are found attached with the membrane of endoplasmic reticulum and in the cytoplasm. They are mainly composed of **ribonucleic acids (RNA) and protein**. They are mainly responsible for **protein synthesis**.

2- **Golgi bodies:** These are the stack of flattened parallel-arranged **sacs** and **vesicles** found in association of endoplasmic reticulum. They are composed of many **lamellae, tubules, vesicles and vacuoles**. Their membranes are supposed to be originated from ER and are composed of lipoproteins. In plant cells the Golgi complex is called **dictyosome** that secretes required materials for the formation of cell wall at the time of cell division. It helps in the formation of acrosome of sperms,

release of hormones, enzymes and other synthetic materials.

3- **Cilia, basal bodies and flagella:** Cilia are the minute structures covering the surface in some cells. Both cilia and flagella originate from the **basal bodies or blepharoplast** lying-in cytoplasm. They consist of nine outer fibrils with the two larger fibrils in the center. Each fibril consists of two microtubules or has **9+2**arrangement. Cilia and Flagella are the structure born by certain cells. They are composed of microtubules made of the protein **tubulin**. They have 9 + 2 plan of microtubule. Both grow at the base. They act as locomotory organelles, moves by their beats or undulations for they get the energy by breakdown of ATP molecule.

4- **Microtubules:** The ultra-fine tubules of protein (**tubulin**) traversing the cytoplasm of plant and animal cells providing the structural framework to the cell, determine the cell shape and general organization of the cytoplasm are known as microtubules. Tubules are made up of **13 individual filaments**. Microtubules help in transport of water and ions, cytoplasmic streaming (cyclosis) and the formation of spindles during cell division.

5- **Centrosomes:** (9+0) there is a clear zone around centrioles, near the nucleus, that includes a specialized portion of cytoplasm, called **centrospheres**. Its matrix is called kinoplasm that bears two rounded bodies the "centrioles". Each centriole consists of **nine fibrillar** units and each of them is found to contain **three microtubules** arrangedin a circle. Both

the centrioles are arranged at right angle to each other. Centrioles form the spindles of microtubules at the time of cell division. Centrioles are absent in plant cell and the spindle is formed without their help.

6- **Metaplasm:** The particles like vacuoles, granules and other cytoplasmic bodies such as ribonucleoprotein molecules.

7- **Basal granules:** The spherical bodies found at the base of cilia and flagellaare called the basal bodies. Each of them is composed of **nine fibrils** and each fibril consists of the three microtubules, out of which two enter the cilia or flagella.

**(B) Inclusions:** These are the **non-living or deutoplasmic structures** which are incapable of growth and multiplication. Common cell inclusions are stored organic materials such as starch grains, glycogen granules, aleurone grains, fat droplets, pigment granules and inorganic crystals. Cytoplasm is stores raw materials needed for the metabolism in both the cytoplasm and the nucleus. Many metabolic processes like biosynthesis of fatty acids, nucleotides, proteins, and oxidation take place in cytoplasm. It distributes the nutrients, metabolites and enzymes in a cell and brings about exchange of materials between the organelles as well as with the environmentor extracellular fluid.

**(C) Nucleus:** In a eukaryotic cell the genetic material is enclosed by a distinct **nuclear envelope** that forms a prominent spherical organelle the "Nucleus". The nuclear envelope bears **pores** for the exchange of materials between cytoplasmand nucleoplasm.

# PLASMA MEMBRANE

**History:** It had been shown by **Karl W. Nageli** (1817-1891) that the cell membrane is semi- permeable and is responsible for the osmotic and other related phenomena exhibited by livingcells. Before 1855, he used the term zellen membrane in his early papers. The term plasma membrane was used in 1855 by him to describe the membrane as a firm protective film that isformed by out flowing cytoplasm of an injured cell when protein rich cell sap came in contactwith water.

## Ultra-Structure of Plasma Membrane:

### A. Symmetrical Molecular Structure of Plasma Membrane:

Plasma membrane is a tripartite structure and is made up of three layers, having total thickness of 75Å. Two di-electronic layers are there, each of 25Å thickness, enclosing a middle dielectronic layer which is also 25Å thick. The middle layer is a tri-molecular layer oflipids having its non-polar hydrophobic groups facing inwards, whereas polar hydrophilic groups facing outwards. The hydrophilic polar groups are covered by a protein layer which is 20 to 25Å thick. The protein chains lie at right angles to the lipids (Figure 27).

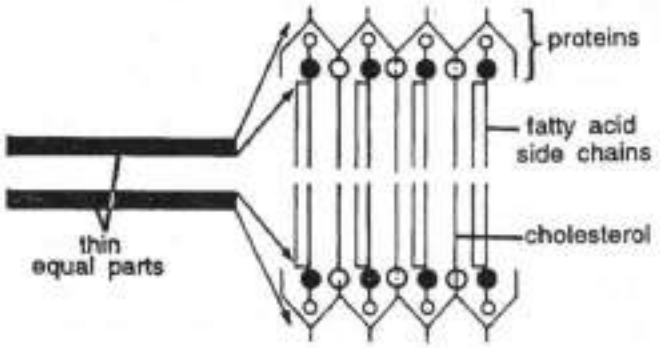



**Figure 27:** Symmetrical pattern of molecules in plasma membrane.

## B. Asymmetrical Molecular Structure of Plasma Membrane:

It is also a tripartite structure having a thick inner dielectronic component of 35-40 Å, a narrow outer dielectronic component of 25Å thickness, and a central dielectronic layer (bimolecular layer of lipids) which is 30Å wide; thus, total thickness comes to 90-95Å. In different types of cells, the thickness of plasma membrane varies. For example, in redblood corpuscles of rabbit, the plasma membrane is about 215 Å thick whereas, in intestinal epithelial cells it is 105 Å in thickness. Very small pores measuring about 10Å in diameter (smaller than pores of nuclear membrane) have been discovered in the membranes (Figure 28).

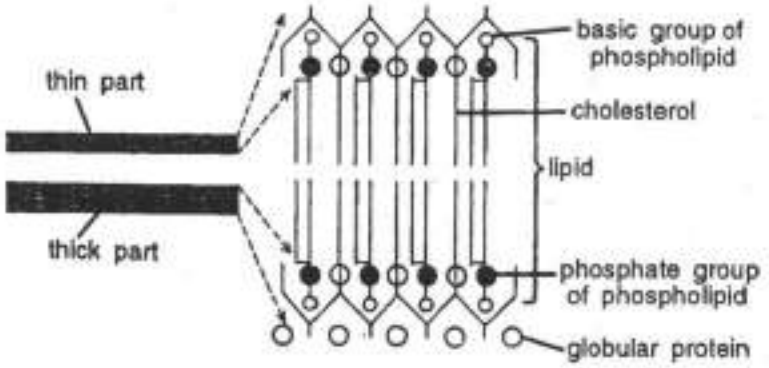



**Figure 28:** Asymmetrical pattern of plasma membrane.

## Chemical composition of plasma membrane:

Plasma membrane is primarily composed of protein and lipid, although carbohydrate is often present in association with protein (as glycoprotein) or lipid (as glycolipid). However, the relative proportions of protein and lipid vary considerably in membranes from different sources.

## I- Lipids:

The plasma membrane contains about 20 to 79% lipids mainly of three types like phospholipids, cholesterol, and glycolipids. The phospholipids which make up between 55% and 75% of the total lipid content, consists chiefly of lecithin and cephalin. The remainder consists of sphingolipids (with an amino group) and glycolipid conjugates with carbohydrates. Phospholipids derived from glycerol are called phosphoglycerides.

A phosphoglycerides is made up of two fatty acid chains, a glycerol backbone and a phosphorylated alcohol. The outer layer of phospholipids consists mainly of lecithin and sphingomyeline, while the inner layer is composed mainly of phosphatidyl ethanolamine and phosphatidyl serine (both are phosphoglycerides). The glycolipids (sugar containing lipids) are mainly in the outer half of the bilayer. Cholesterol is present in eukaryotes but not in prokaryotes. Plasma membrane of cells such aserythrocyte, liver cells and myelinated nerve cells are rich in cholesterol (Figure 29).

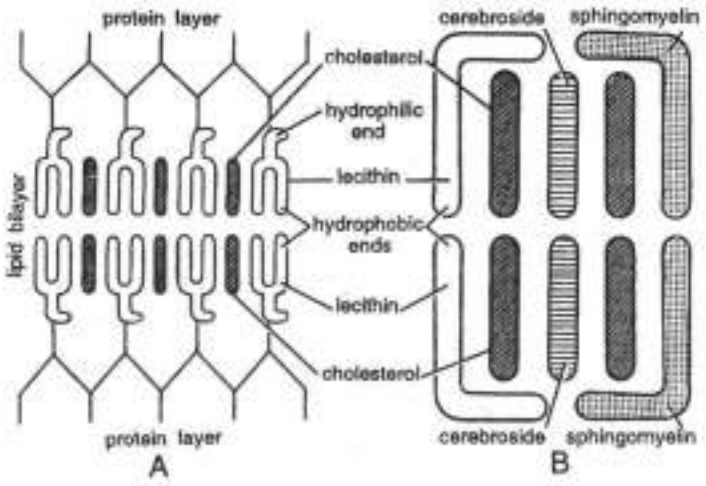



**Figure 29:** A phospholipids cholesterol complex of cell membrane

Membrane lipids are amphipathic molecules. They contain both a hydrophobic and hydrophilic moiety. Hydrophilic unit is also called the polar head groups, is represented by a circle and their hydrocarbon tails are depicted by straight or wavy lines. Polar head groups have affinity for water, whereas their hydrocarbons tails avoid water. This can be accomplished by forming a micelle, in which polar head groups are on the surface and hydrocarbon tails are directed inside (Figure 30).

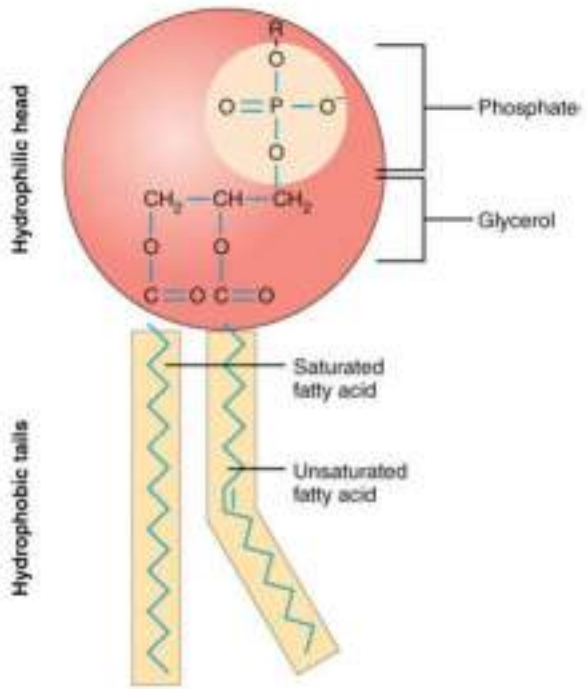



**Figure 30:** Phospholipid Structure. A phospholipid molecule consists of a polar phosphate "head," which is hydrophilic and a nonpolar lipid "tail," which is hydrophobic. Unsaturated fatty acids result in kinks in the hydrophobic tails.

Another arrangement of lipid molecule in a membrane is a bimolecular sheet, which isalso called a lipid bilayer (Figure 31). Phospholipids and glycolipids are key membrane constituents of bimolecular sheets. Hydrophobic interactions are the major driving force for the formation of lipid bilayer. The lipid bilayer of the membrane is interrupted only by the proteins that traverse it. This bilayer consists primarily of:

a. *Neutral Phospholipids and Cholesterol*: These include phosphatidylenoline, lecithin cerebroside, and sphingomyeline and phosphatidyl ethanolamine. They are without any electric charge at neutral pH and are closely packed in the bilayer along with cholesterol.

b. *Acidic Phospholipids*: These constitute about 5% to 20% fractions of the total phospholipids of plasma membrane. They are **negatively charged** and are associated with proteins by way of lipid-protein interactions. Common examples are phosphatidyl inositol, phosphatidylserine, sulpholipids, phosphatidyl glycerol and Cardiolipin. In plasma membrane, lipid fractions form permeability barrier and structural framework.

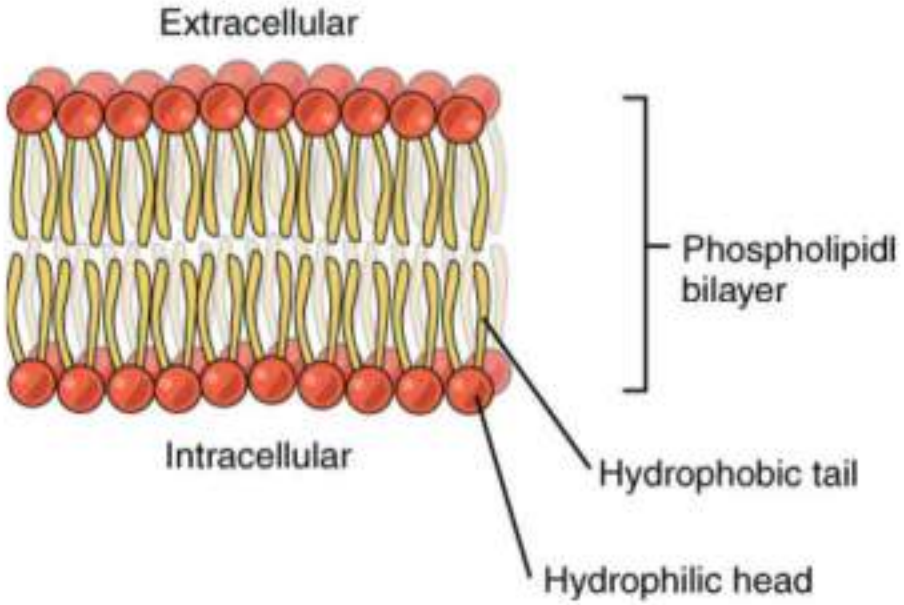



**Figure 31:** Phospholipid Bilayer. The phospholipid bilayer consists of two adjacent sheets of phospholipids, arranged tail to tail. The hydrophobic tails associate with one another, forming the interior of the membrane. The polar heads contact the fluid inside and outside of the cell.

## II- Proteins:

Proteins are the main component of plasma membrane (membrane sheath ). Myelin surrounding some nerve axons) is composed of about 80% lipids and 20% protein and presence of lipid makes myelin an excellent insulator. Eukaryotes membrane which serves primarily as permeability barriers possesses about 50% proteins and 50% lipid. Plasmamembrane that are actively involved in energy transfer, such as inner membrane of mitochondria, chloroplasts and membranes of aerobic prokaryotes have large amounts of proteins i.e. about 75%. They not only provide mechanical support but also act as carriers or channels, serving for transport. In addition, numerous enzymes, antigens and various kinds of receptor molecules are present in plasma membranes. Membrane proteins are classified as **integral (intrinsic) or peripheral (extrinsic)** according to the degree of their association with the membrane.

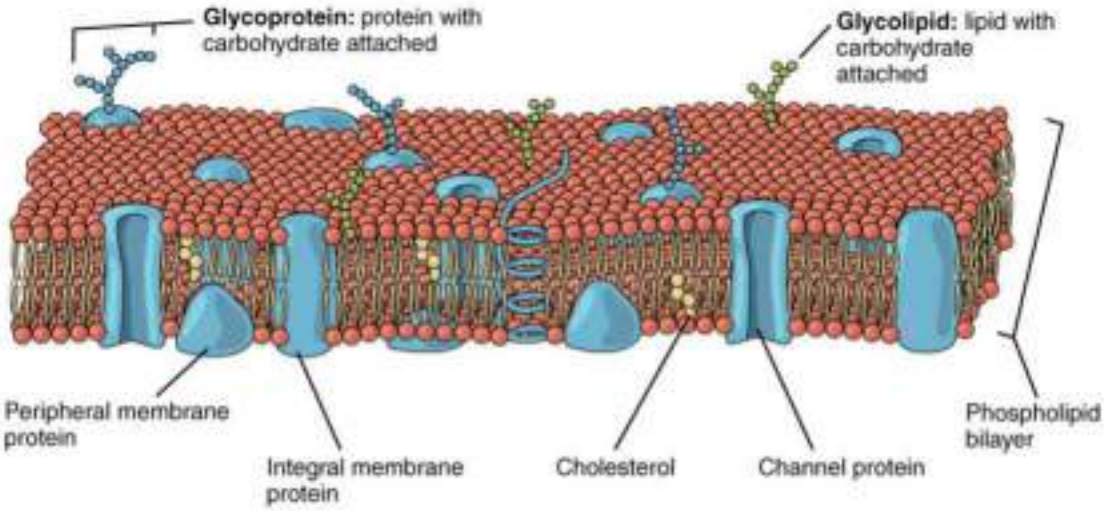



**Figure 32:** Cell Membrane. The cell membrane of the cell is a phospholipid bilayer containing many different molecular components, including proteins and cholesterol, some with carbohydrate groups attached.

a. ***Peripheral Proteins*:** They are also called extrinsic proteins associated with membrane surface. These can be separated by addition of salts, soluble in aqueous solutions and usually free of lipids. They are bound to the surface by electrostatic and hydrogen bond interactions. They form outer and inner layers of the lipid bilayer of plasma membrane. Common examples are cytochrome-C found in mitochondria, acetyl cholinesterase in electroplax membrane and spectrin found in erythrocytes.

b. ***Integral or Intrinsic Proteins*:** These proteins penetrate the lipid layer wholly or partially and represent more than 70% of the two protein types. Their polar ends protrude from the membrane surface while non-polar regions are embedded in the interior of the membrane. Usually, they are insoluble in water solutions and can be separate them from the membrane by detergents or organic solvents. The major integral proteins span the thickness of the membrane and have a small amount of carbohydrates on the pole at the outer surface. This protein appears to be involved in the diffusion of anions across the membrane. Integral proteins may be attached to the oligosaccharides to form glycoprotein or to phospholipid to form lipoproteins or proteolipids. Common intrinsic proteins are rhodopsin found in retinal rod cells and cytochrome oxidase found in mitochondrial membranes. Every protein in the cell membrane is distributed asymmetrically with respect to the lipid bilayer.

### III- Enzymes:

About 30 enzymes have been found in various membranes. Those most constantly found are 5'-nucleotidase, $Na^+$-$K^+$ activated ATPase, alkaline phosphatase, adenylcyclase, RNAse and acid phosphomonoestrase. $Na^+$-$K^+$ activated $Mg^+$ ATPase plays an important rolein the ionic exchange and may also act as carrier protein or permease across the plasma membrane. Some enzymes have a preferential localization. For example, alkaline phosphatase and ATPase are more abundant in bile capillaries, while disaccharides are present in microvilli of the intestine. Enzymes are asymmetrically distributed, for example in the outer surface of erythrocytes there are acetylcholinestrase, nicotinamide adenine dinucleotidase and $Na^+$-$K^+$ ATPase. In the inner surface there is NADH-diaphorase, G3PD, adenylate cyclase, protein kinase and ATPase

### IV- Carbohydrates:

The membranes of eukaryotic cells usually contain 2% to 10% carbohydrates in the form of glycolipids and glycoproteins. Hexose, hexosamine, fucose and sialic acid are the commonest carbohydrates found in the membrane. Plasma membranes of neuronal surface contain gangliosides (Lapertina, 1967) and are probably involved in the ion transfers. The distribution of oligosaccharides is also highly asymmetrical.

### V- Salts and water:

They are also present in cell membranes. Water in cell membranes forms parts ofmembrane structure as it does in all cell constituents.

## Models of plasma membrane structure:

### (1) Lamella-model of plasma membrane (Danielli-Davson model)

Danielli-Davson model (1934) (Figure 33, 34) suggested that the plasma membrane consists of twolayers of lipid molecules arranged radially with their hydrophobic hydrocarbon chains toward each other and with their respective polar groups arranged outwardly and inwardly throughout the entire double layer of lipid molecules. The polar ends of the lipid moleculesare associated with a monomolecular layer of polar globular protein molecule. The entire structure thus consisted of double layer of lipid molecule sandwiched between two continuous layers of protein. The lipid molecules are set at right angles to the surface and are so arranged in two layers that their non-polar hydrophobic fatty acid tails face each other, and their polar hydrophilic phosphate heads face the protein layer. The proteins involved were thought to be globular. Moreover, lamellar theory assumed the cell membrane to be a stable structure with little functional specificity and variability.

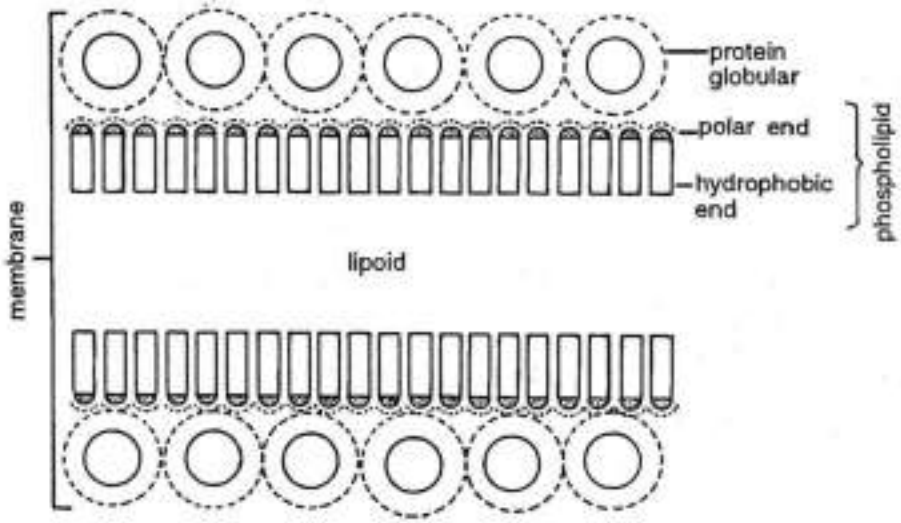



**Figure 33:** A schematic diagram of Davson-Danielli model.

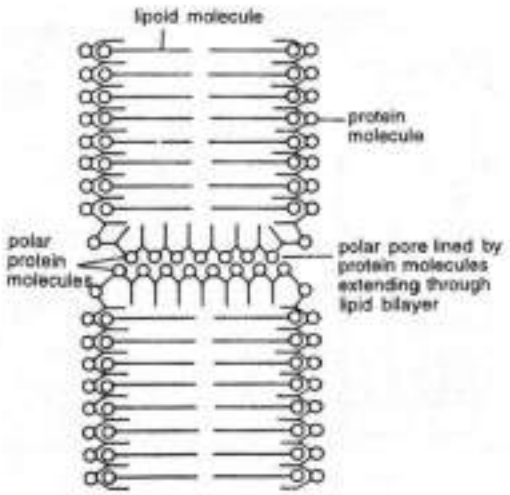



**Figure 34:** A modification of original Danielli-Davson model.

## (2) Miceller model of plasma Membrane:

According to the view of Hiller and Hoffman (1953) (Figure 35), plasma membrane consists of amosaic of globular subunits or micelles. If fatty acid molecules are completely surrounded by water, they may form aggregate called micelles in which the hydrophobic regions of fattyacid molecules are oriented toward the interior of the micelle away from the aqueous phase and their hydrophilic groups are at the surface in contact with the surrounding water. Micellesmay be in the form of small spheres of bimolecular layers. These micelles are closely packed together having a central core of lipid molecules and hydrophilic shell of polar groups. Each lipid micelle measures 40Å to 70Å in diameter. Protein component of the plasma membrane forms a monolayer on either side of the lipid micelles and is represented by globular type. The spaces between the globular micelles are thought to represent water filled pores which measures about 4Å in diameter. These pores are bounded partly by the polar groups of micelles and partly by the polar groups of associated protein molecules.

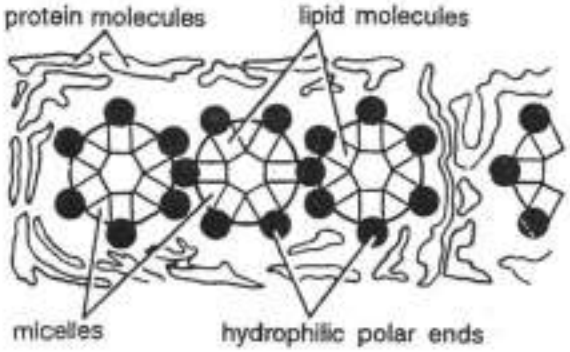



**Figure 35:** Plasma membrane based on Miceller theory (diagrammatic).

### (3) Fluid Mosaic Model of plasma membrane:

It was proposed by Singer and Nicholson (1972). The lipids are thought to be arranged primarily in a bilayer in which proteins are embedded to varying degrees. Singer classifies membrane proteins as peripheral or integral. The proteins varied in size and dissolved to varying degrees in the lipid matrix are able to diffuse laterally in the plane of membrane, and the entire structure is hence dynamic. In this model, lipid molecules may exhibit intra molecular movement or may rotate about their axis or may display flip-flop movement including transfer from one side of bilayer to the other.

The lipids, glycoprotein, and many of the intrinsic proteins of the membranes are amphipathic molecules. These amphipathic molecules constitute liquid crystalline aggregates in which the polar groups are directed toward the water phase and the non-polar groups are situated inside the bilayer. The lipid bilayer forms the structural matrix which serves as the permeability barrier of the membrane. In membranes with high lipid content, lipid bilayer is extensive and interrupted only occasionally by protein molecules, whereas in membranes with high

protein content, the extent of lipid bilayer is reduced. Thus, fluid mosaic model may describe the chemical composition of the molecular organization and ultra-structure of plasma membranes. This arrangement allows various enzymes and antigenic glycoprotein to have their active sites exposed to the outer surface of the membrane. The fluidity of membrane also implies that both the lipid and the protein have considerable freedom of movement within the bilayer. The fluidity of the lipid depends on the degree of saturation of the hydrocarbon chains and on the ambient temperature. A considerable proportion of the lipids in the membrane are unsaturated, so melting point of the bilayer is below body temperature (Figure 36)

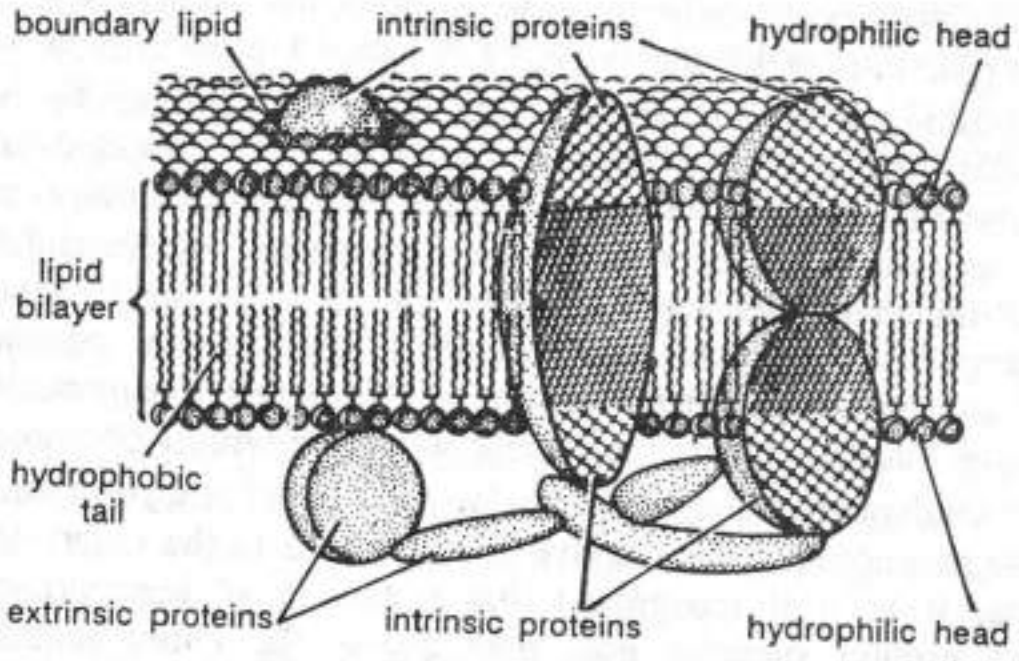



**Figure 36:** Plasma membrane based upon Fluid-mosaic model.

**Functions of Plasma Membrane:**

- It maintains the individuality and form of the cell.
- It keeps the cell contents in place and distinct from the environmental materials.
- It protects the cell from injury.
- It regulates the flow of materials into and out of the cell to maintain the concentration and kinds of molecules and ions in the cell. A cell remains alive as long as the cell membrane is able to determine which materials should enter or leave the cell.
- It forms organelles within the cytoplasm.
- Its junctions keep the cells together.
- It's infolds help in the intake of materials by endocytosis (pinocytosis andphagocytosis).
- It's out folds (microvilli) increase the surface area for absorption of nutrients. The outfolds also form protective sheaths around cilia and flagella.
- Its receptor molecules permit flow of information into the cell.
- Its oligosaccharide molecule helps in recognizing self from non-self.
- By controlling flow of material and information into the cell, the plasma membranemakes metabolism possible.
- It permits exit of secretions and wastes by exocytosis.
- It controls cellular interactions necessary for tissue formation and defense againstmicrobes.
- It helps certain cells in movement by forming pseudopodia as in Amoeba andleucocytes.

## Transport across the Cell Membrane

One of the great wonders of the cell membrane is its ability to regulate the concentration of substances inside the cell. These substances include ions such as $Ca^{++}$ , $Na^{+}$ , $K^{+}$ , and $Cl^{-}$; nutrients including sugars, fatty acids, and amino acids; and waste products, particularly carbon dioxide ($CO_2$), which must leave the cell. The membrane's lipid bilayer structure provides the first level of control. The phospholipids are tightly packed together, and the membrane has a hydrophobic interior. This structure causes the membrane to be selectively permeable.

A membrane that has **selective permeability** allows only substances meeting certain criteria to pass through it unaided. In the case of the cell membrane, only relatively small, nonpolar materials can move through the lipid bilayer (remember, the lipid tails of the membrane are nonpolar). Some examples of these are other lipids, oxygen and carbon dioxide gases, and alcohol. However, water-soluble materials like glucose, amino acids, and electrolytes need some assistance to cross the membrane because they are repelled by the hydrophobic tails of the phospholipid bilayer.

All substances that move through the membrane do so by one of two general methods, which are categorized based on whether or not energy is required. **Passive transport** is the movement of substances across the membrane without the expenditure of cellular energy. In contrast, **active transport** is the movement of substances across the membrane using energy from adenosine triphosphate (ATP).

### a. Passive Transport:

In order to understand how substances, move passively across a cell membrane, it is necessary to understand concentration gradients and diffusion. A **concentration gradient** is the difference in concentration of a substance across a space. Molecules (or ions) will spread/diffuse from where they are more concentrated to where they are less concentrated until they are equally distributed in that space. (When molecules move in this way, they are said to move down their concentration gradient.). **Diffusion** is the movement of particles from an area of higher concentration to an area of lower concentration. Having an internal body temperature around 98.6 F thus also aids in diffusion of particles within the body. Whenever a substance exists in greater concentration on one side of a semipermeable membrane, such as the cell membranes, any substance that can move down its concentration gradient across the membrane will do so. Consider substances that can easily diffuse through the lipid bilayer of the cell membrane, such as the gases oxygen ($O_2$) and $CO_2$ . $O_2$ generally diffuses into cells because it is more concentrated outside of them, and $CO_2$ typically diffuses out of cells because it is more concentrated inside of them. Neither of these examples requires any energy on the part of the cell, and therefore they use passive transport to move across the membrane. Because cells rapidly use up oxygen during metabolism, there is typically a lower concentration of $O_2$ inside the cell than outside. As a result, oxygen will diffuse from the interstitial fluid directly through the lipid bilayer of the membrane and into the

cytoplasm within the cell. On the other hand, because cells produce $CO_2$ as a byproduct of metabolism, $CO_2$ concentrations rise within the cytoplasm; therefore, $CO_2$ will move from the cell through the lipid bilayer and into the interstitial fluid, where its concentration is lower. This mechanism of molecules spreading from where they are more concentrated to where they are less concentration is a form of passive transport called simple diffusion (Figure 37).

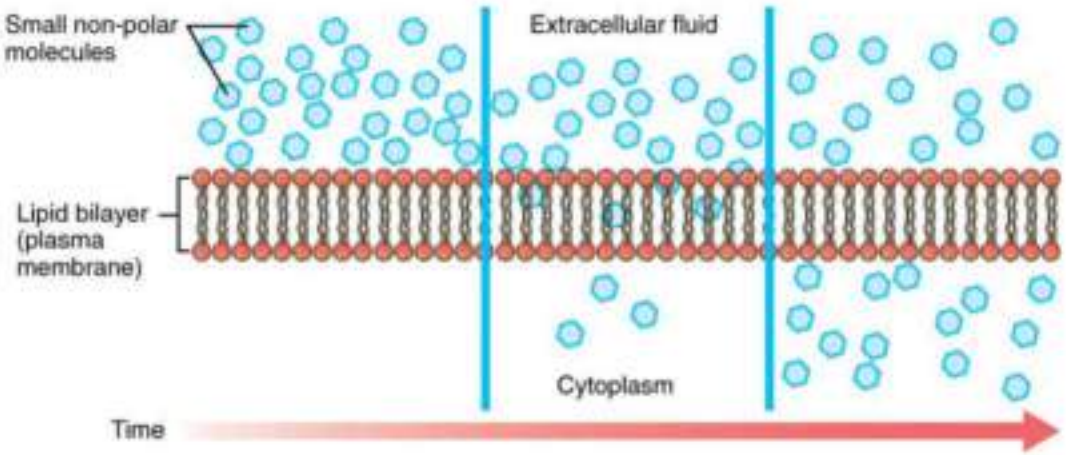



**Figure 37:** Simple Diffusion across the Cell (Plasma) Membrane. The structure of the lipid bilayer allows only small, non-polar substances such as oxygen and carbon dioxide to pass through the cell membrane, down their concentration gradient, by simple diffusion.

Solutes dissolved in water on either side of the cell membrane will tend to diffuse down their concentration gradients, but because most substances cannot pass freely through the lipid bilayer of the cell membrane, their movement is restricted to protein channels and specialized transport mechanisms in the membrane. **Facilitated diffusion** is the diffusion process used for those substances that cannot cross the lipid bilayer due to their size and/or polarity (Figure 38). A common example of facilitated diffusion is the movement of glucose

into the cell, where it is used to make ATP. Although glucose can be more concentrated outside of a cell, it cannot cross the lipid bilayer via simple diffusion because it is both large and polar. To resolve this, a specialized carrier protein called the glucose transporter will transfer glucose molecules into the cell to facilitate its inward diffusion.

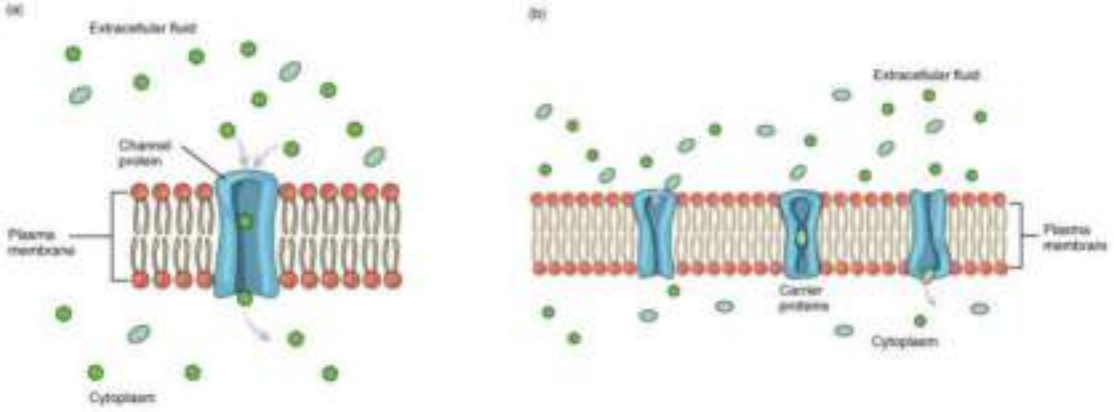



**Figure 38:** Facilitated Diffusion. Facilitated diffusion of substances crossing the cell (plasma) membrane takes place with the help of proteins such as channel proteins and carrier proteins.

In some cases, facilitated diffusion might move two substances in the same direction across the membrane, called a **"symport."** For example, in intestinal cells, sodium ions and glucose molecules are co-transported into the cells. In other cases, the facilitated diffusion might only require a tunnel-like channel for solutes, such as electrolytes (small, charged ions), to pass through the membrane (this is called a "uniport". As an example, even though sodium ions ($Na^{++}$) are highly concentrated outside of cells, these electrolytes are polarized and cannot pass through the nonpolar lipid bilayer of the membrane. Their diffusion is facilitated by membrane proteins that form sodium channels (or "pores"), so that Na ions can move down their concentration gradient from outside the cells to inside the cells. There

are many other solutes that must undergo facilitated diffusion to move into a cell, such as amino acids, or to move out of a cell, such as wastes. Because facilitated diffusion is a passive process, it does not require energy expenditure by the cell. Water also can move freely across the cell membrane of all cells, either through protein channels or by slipping between the lipid tails of the membrane itself. **Osmosis** is the diffusion of water through a semipermeable membrane (Figure 39).

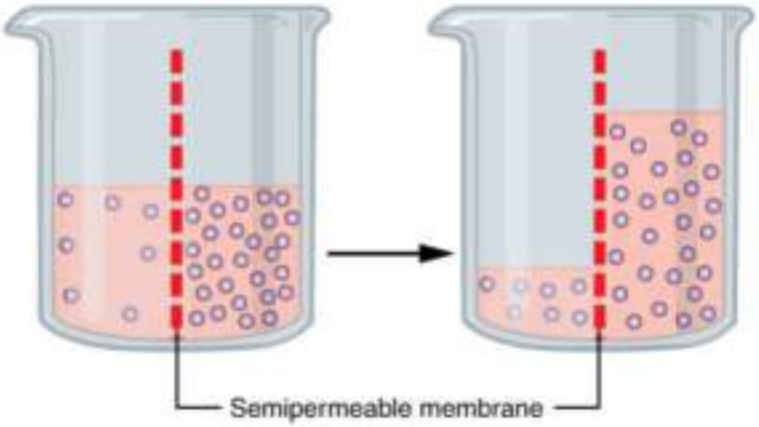



**Figure 39:**. Osmosis is the diffusion of water through a semipermeable membrane down its concentration gradient.

The movement of water molecules is not itself regulated by cells, so it is important that cells are exposed to an environment in which the concentration of solutes outside of the cells (in the extracellular fluid) is equal to the concentration of solutes inside the cells (in the cytoplasm). Two solutions that have the same concentration of solutes are said to be **isotonic** (equal tension). When cells and their extracellular environments are isotonic, the concentration of water molecules is the same outside and inside the cells, and the cells maintain their normal shape (and function). Osmosis occurs when there is an

imbalance of solutes outside of a cell versus inside the cell. A solution that has a higher concentration of solutes than another solution is said to be **hypertonic**, and water molecules tend to diffuse into a hypertonic solution (Figure 40). Cells in a hypertonic solution will shrivel as water leaves the cell via osmosis. In contrast, a solution that has a lower concentration of solutes than another solution is said to be **hypotonic**, and water molecules tend to diffuse out of a hypotonic solution. Cells in a hypotonic solution will take on too much water and swell, with the risk of eventually bursting. A critical aspect of homeostasis in living things is to create an internal environment in which all of the body's cells are in an isotonic solution. Various organ systems, particularly the kidneys, work to maintain this homeostasis.

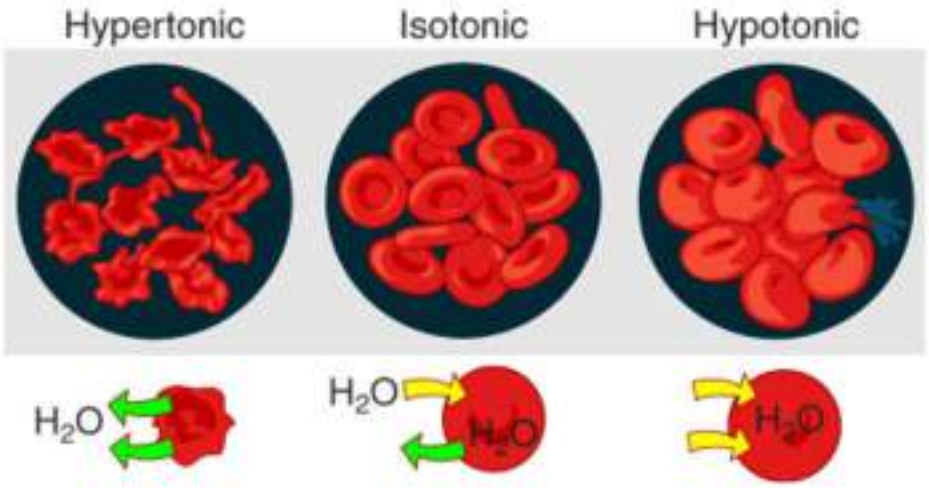



**Figure 40:** Concentration of Solutions. A hypertonic solution has a solute concentration higher than another solution. An isotonic solution has a solute concentration equal to another solution. A hypotonic solution has a solute concentration lower than another solution.

Another mechanism besides diffusion to passively transport materials between compartments is **Filtration**. Unlike diffusion of a substance from where it is more concentrated to less concentrated, filtration uses

a hydrostatic pressure gradient that pushes the fluid and the solutes within it from a higher-pressure area to a lower pressure area. Filtration is an extremely important process in the body. For example, the circulatory system uses filtration to move plasma and substances across the endothelial lining of capillaries and into surrounding tissues, supplying cells with the nutrients. Filtration pressure in the kidneys provides the mechanism to remove wastes from the bloodstream.

**b. Active Transport:**

For all the transport methods described above, the cell expends no energy. Membrane proteins that aid in the passive transport of substances do so without the use of ATP. During active transport, ATP is required to move a substance across a membrane, often with the help of protein carriers, and usually against its concentration gradient. One of the most common types of active transport involves proteins that serve as pumps. The word "pump" probably conjures up thoughts of using energy to pump up the tire of a bicycle or a basketball. Similarly, energy from ATP is required for these membrane proteins to transport substances molecules or ions across the membrane, usually against their concentration gradients (from an area of low concentration to an area of high concentration). The **sodium-potassium pump**, which is also called $Na^{++}/K^{+}$ ATPase, transports sodium out of a cell while moving potassium into the cell. The $Na^{++}$ /$K^{+}$ pump is an important ion pump found in the membranes of many types of cells. These pumps are particularly abundant in nerve cells, which are constantly pumping out sodium ions and pulling in potassium ions to maintain an electrical

gradient across their cell membranes. An **electrical gradient** is a difference in electrical charge across a space. In the case of nerve cells, for example, the electrical gradient exists between the inside and outside of the cell, with the inside being negatively charged (at around -70 mV) relative to the outside. The negative electrical gradient is maintained because each Na /K pump moves three Na ions out of the cell and two K ions into the cell for each ATP molecule that is used (Figure 41). This process is so important for nerve cells that it accounts for most of their ATP usage.

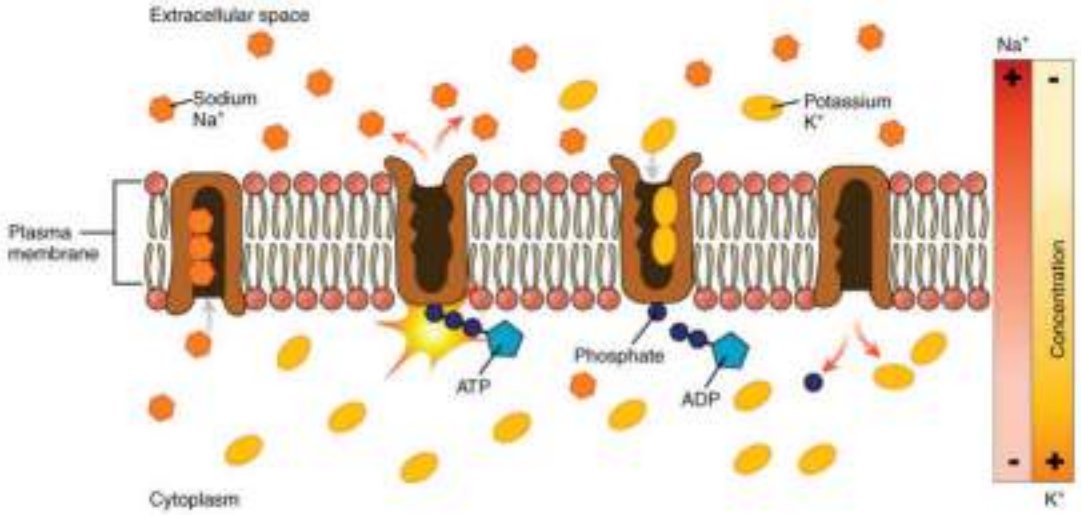



**Figure 41**: Sodium-Potassium Pump. The sodium-potassium pump is found in many cell (plasma) membranes.

Other forms of active transport do not involve membrane carriers. **Endocytosis** (bringing "into the cell") is the process of a cell ingesting material by enveloping it in a portion of its cell membrane, and then pinching off that portion of membrane (Figure 42). Once pinched off, the portion of membrane and its contents becomes an independent, intracellular vesicle. A **vesicle** is a membranous sac—a spherical and hollow organelle bounded by a lipid bilayer membrane. Endocytosis

often brings materials into the cell that must be broken down or digested. **Phagocytosis** ("cell eating") is the endocytosis of large particles. Many immune cells engage in phagocytosis of invading pathogens. Like little Pac-men, their job is to patrol body tissues for unwanted matter, such as invading bacterial cells, phagocytize them, and digest them. In contrast to phagocytosis, **pinocytosis** "cell drinking" brings fluid containing dissolved substances into a cell through membrane vesicles.

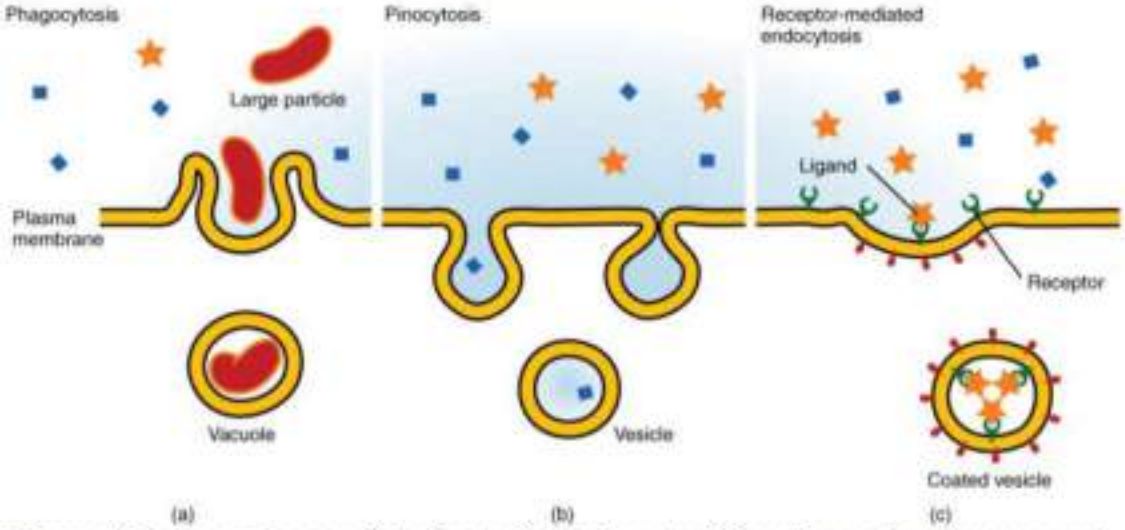



**Figure 42:** Three Forms of Endocytosis. Endocytosis is a form of active transport in which a cell envelopes extracellular materials using its cell membrane. (a) In phagocytosis, which is relatively nonselective, the cell takes in a large particle. (b) In pinocytosis, the cell takes in small particles in fluid. (c) In contrast, receptor mediated endocytosis is quite selective. When external receptors bind a specific ligand, the cell responds by endocytosing the ligand.

**Phagocytosis** and pinocytosis take in large portions of extracellular material, and they are typically not highly selective in the substances they bring in. Cells regulate the endocytosis of specific substances via receptor-mediated endocytosis. **Receptor mediated endocytosis** is endocytosis by a portion of the cell membrane that contains many

receptors that are specific for a certain substance. Once the surface receptors have bound sufficient amounts of the specific substance (the receptor's ligand), the cell will endocytose the part of the cell membrane containing the receptor-ligand complexes. Iron, a required component of hemoglobin, is endocytosed by red blood cells in this way. Iron is bound to a protein called transferrin in the blood. Specific transferrin receptors on red blood cell surfaces bind the iron-transferrin molecules, and the cell endocytoses the receptor-ligand complexes. In contrast with endocytosis, **exocytosis** (taking "out of the cell") is the process of exporting material using vesicular transport (Figure 43).

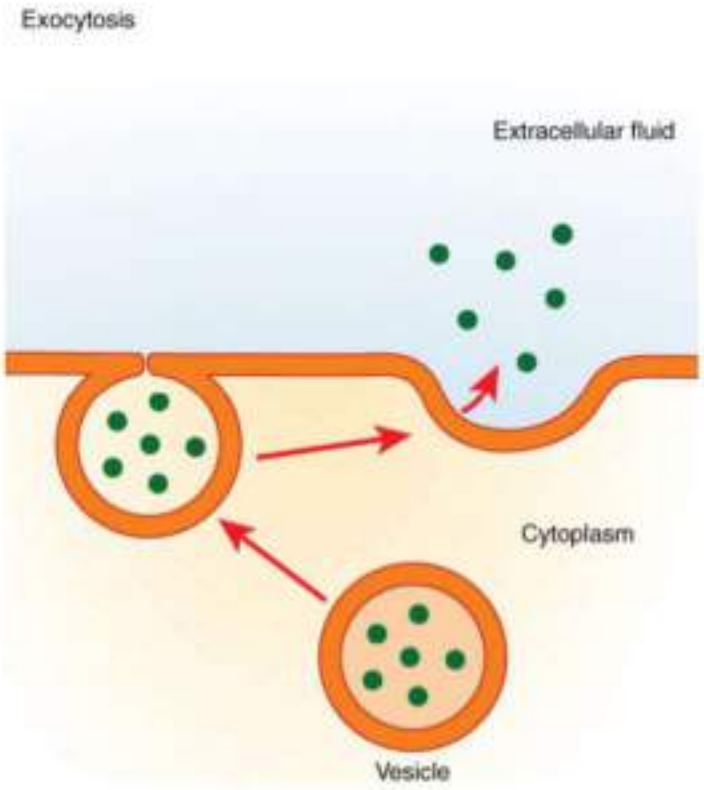



**Figure 43:** Exocytosis is much like endocytosis in reverse. Material destined for export is packaged into a vesicle inside the cell. The membrane of the vesicle fuses with the cell membrane, and the contents are released into the extracellular space.

Many cells manufacture substances that must be secreted, like a factory manufacturing a product for export. These substances are typically packaged into membrane-bound vesicles within the cell. When the vesicle membrane fuses with the cell membrane, the vesicle releases it contents into the interstitial fluid. The vesicle membrane then becomes part of the cell membrane. Cells of the stomach and pancreas produce and secrete digestive enzymes through exocytosis (Figure 43). Endocrine cells produce and secrete hormones that are sent throughout the body, and certain immune cells produce and secrete large amounts of histamine, a chemical important for immune responses.

# MITOCHONDRIA

**History:** Kölliker (1880) was the first who observed the mitochondria in insects muscle cells. He called them as 'sarcosomes'. Flemming (1882) named the mitochondria as 'fila'. Altmann in 1894 observed them and named them Altmann's granules or bioblasts. The term 'mitochondria' was applied by Benda (1897-98). They were recognized as the sites of respiration by Hogeboom and his coworkers in 1948. Lehninger and Kennedy (1948)reported that the mitochondria catalyze all the reactions of the citric acid cycle, fatty acid oxidation and coupled phosphorylation.

## Morphology of Mitochondria:

Morphologically mitochondria may be in the form of filaments or small granules. These may assume rod-like shape called chondriosomes which may enlarge or aggregate toform massive spheroid bodies called chondriospheres.

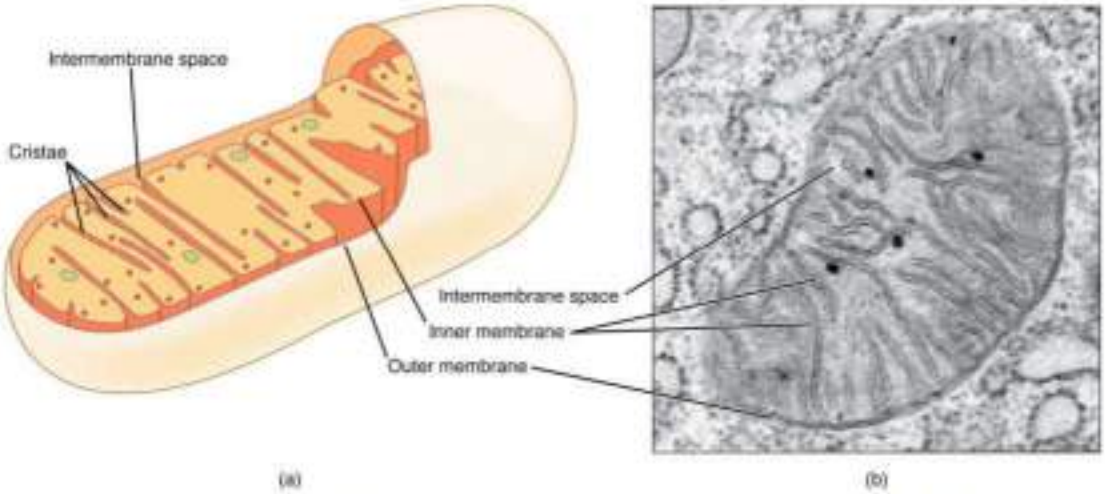



**Figure 44:** The mitochondria are the energy-conversion factories of the cell. (a) A mitochondrion is composed of two separate lipid bilayer membranes. (b) An electron micrograph of mitochondria.

1. **Position:** Mitochondria lie freely in cytoplasm, possessing power of independent movement and may take the form of filaments. In some cells they can move freely, carrying ATP where needed, but in others they are located permanently near the region of the cell where more energy is needed. E.g., in the rod and cone cells of retina mitochondria are located in the inner segment, in cells of kidney tubules they occur in the folds of basal regions near plasma membrane, in neurons they are located in the transmitting region of impulse, in certain muscle cells (e.g. diaphragm), mitochondria are grouped like rings or bracers around the I-band of myofibril. During cell division they get concentrated around the spindle.

2. **Number:** The number of mitochondria varies a good deal from cell to cell and from species to species. A few algae and some protozoan have only single mitochondria. Their number is related to the activity, age and type of the cell. Growing, dividing and actively synthesizing cells contain more mitochondria than the other cells. In Amoeba (*Chaos chaos),* there may be as many as 50,000 mitochondria. In rat liver cells, these are few in number, about 1000 to 1600. Some Oocytes contain as many as 3, 00,000 mitochondria.

3. **Size:** The average size of mitochondria is 0.5-1.0 μ in diameter and about 2-8 μ in length. In exocrine cells of mammalian pancreas, they are about 10 μ long and in oocytes of amphibian *Rana pipiens* are 20-40 μ long. Yeast cells have the smallest mitochondria.

**Ultra-structure of Mitochondria:**

The electron microscope shows the mitochondrion as the vesicles bounded by anenvelope of two-unit membranes and filled with a fluid matrix

1. **Membranes**: Both the inner and the outer mitochondrial membranes resemble the plasma membrane in molecular structure. Each of them is 60-70Å, trilamellar and composed of two layers of phospholipid molecules sandwiched between two layers ofprotein molecules. However, the two membranes differ in the kinds of protein and lipids they have and also in their properties. Both the outer and the inner membranes contain specific pumps or channels, for the transport of molecules through them. The membranes may be connected at adhesion sites through which proteins are transferredfrom the outer to the inner membrane. The outer and the inner membrane are separated from each other by a narrow space called the inter-membrane space or outer chamber or peri-mitochondrial space. It is about 80Å wide. It contains a clear homogeneous fluid.

   (i) ***Outer Membrane***- The outer membrane is smooth permeable to most small molecules, having trans-membrane channels formed by the protein 'porin'. It consists of about 50% lipid, including a large amount of cholesterol. It contains some enzymes but is poor in protein.

   (ii) ***Inner Membrane-*** The inner membrane is selectively permeable and regulatesthe movement of materials into and out

of the mitochondrion. It is rich in enzymes and carrier proteins permease. It has a very high protein/lipid ratio (about 4:1 by weight). It lacks cholesterol. Cardiolipin is closely associated with certain integral proteins and is apparently required for their activity.

2. **Matrix:** The space between the cristae called the inner chamber is filled with a gellike material termed the mitochondrial matrix. It contains proteins, lipids, some ribosomes, RNA, one or two DNA molecules and certain fibrils, crystals, and dense granules.

3. **Cristae:** The inner mitochondrial membrane bears plate like infoldings called the cristae. They extend inwards to varying degrees, and may fuse with those from the opposite side, dividing the mitochondrion into compartments. They are arranged in a characteristic manner in different cells. Normally they run at right angles to the long axis of the rod-shaped mitochondria. In cells of the proximal parts of the kidney tubules, the cristae are longitudinal folds parallel to the long axis of mitochondrion. Inmany protozoans, in insect flight muscles cells and in adrenal endocrine cells the cristae are tubular. Cristae are lamellar in hepatocytes. In heart muscle cells cristae arezig-zag (Figure 45).

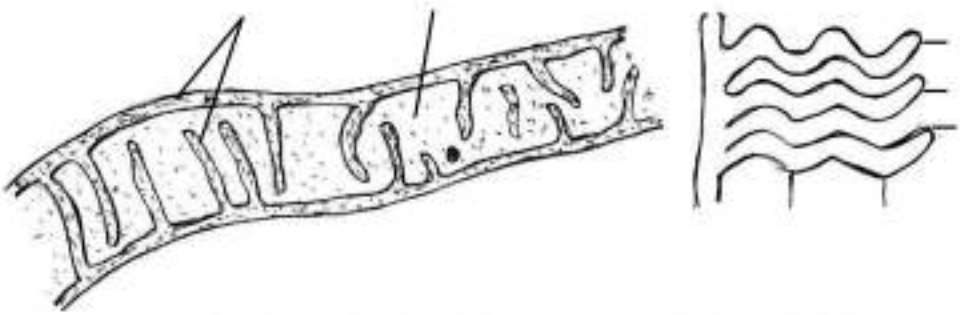


**Figure 45:** Cristae in a mitochondrion of an endothelial cell of human .

They also vary in number. The active cells may have numerous cristae whereas the inactive cells may have only a few. The cristae have in them a narrow intra-crista space. It is continuous with the inter-membrane space. The cristae greatly increase theinner surface of the mitochondrion to provide enough space for housing enzyme assemblies. The cristae also allow for expansion or swelling of mitochondria under different metabolic and environmental conditions

4. **Oxysomes:** The inner mitochondrial membrane bears minute regularly spaced particles known as the inner membrane subunits or elementary particles (EP) or oxysomes. An oxysome consists of three parts- a rounded head piece or F1 subunit joined by a short stalk to a base piece or F0 subunit located in the inner membrane. There may be 100,000 to 1000,000 oxysomes in a single mitochondrion (Figure 46).

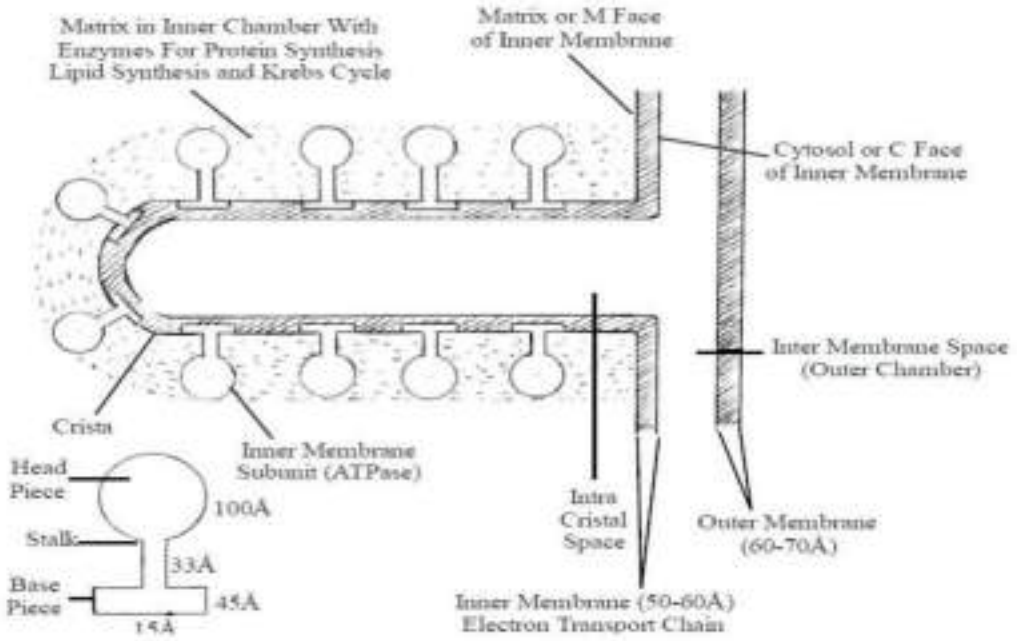



**Figure 46:** Detailed structure of a crista and an oxysome.

**Biogenesis of Mitochondria:**

The formation of new mitochondria has been explained with the following hypothesis.

1. **De Novo Synthesis**: According to this hypothesis mitochondria arises de novo from precursors in the cytoplasm.
2. **Origin from membrane**: This hypothesis proposes that the mitochondria arises from the invaginations of plasma membrane, endoplasmic reticulum, Golgi apparatus or nuclear envelop. The membrane invaginates and extends into the cytoplasm as a tubular structure. It gradually becomes curved and folded and forms a double walled structure, the mitochondrion.
3. **Develop from Micro bodies**: It is held that they mitochondria are developed by the accumulation of micro bodies in the cytoplasm. A micro body consists of a single outer membrane and a dense matrix with a few cristae which eventually develops into fully formed mitochondria.
4. **Prokaryotic Origin**: It is believed that mitochondria are originated from bacteria. It is supported by many evidences.
   (i) First is the localization of enzymes of respiratory chain, which in case of bacteria, are localized in plasma membrane which can be compared with the inner membrane of the mitochondrion.
   (ii) In some bacteria, plasma membrane forms membranous projections (called mesosomes) like cristae of mitochondria. These mesosomes possess respiratory chain enzymes.

(iii) The mitochondrial DNA is circular as it is in bacteria. Replication process of mitochondria is similar to bacteria.

(iv) Ribosomes in mitochondria are smaller and similar in size to that of bacterial ribosomes.

(v) Chloramphenicol inhibits the synthesis of protein in mitochondria as well as inbacteria. Furthermore, in the process of protein synthesis, mitochondria depend partially on mitochondrial matrix and DNA and partially on nucleus and cytoplasm of the eukaryotic cells. It exhibits the symbiotic nature of mitochondria. These evidence support the prokaryotic origin of mitochondria.

5. **Replication:** It is held that mitochondria are self-replicating organelles. New mitochondria arise by some type of splitting process from pre-existing mitochondria.

   The last hypothesis seems probable. Since the mitochondria have their own DNA and ribosomes, they can replicate new mitochondria. However, there is a nuclear control over the process as the mitochondria synthesize some of their proteins themselves and get others from the cytoplasm of the cell formed under the direction of the nuclear DNA

**Functions of Mitochondria:**

Mitochondria perform the following functions: -

1. Cell respiration takes place in mitochondria and so they are known as the 'powerhouse' of the cell. They bring about stepwise oxidation

of food stuffs or "low-grade" fuel of the cell and transfer the energy so released to the energy carrier ATP, the "high-grade" fuel of the cell. ATP is used to bring about the energy-requiring activities in the cells, namely, biosynthesis, active transport, transmission of nerve impulse, muscle contraction, cell growth and division and bioluminescence.

2. Mitochondria provide intermediates for the synthesis of important biomolecules such as chlorophyll, cytochromes, steroids etc.
3. Some amino acids are also formed in the mitochondria.
4. Mitochondria actively accumulate calcium ions as calcium phosphate precipitate. They regulate the calcium ions concentration in the cytoplasm by storing and releasing $Ca^{+}$. The calcium ions regulate numerous biochemical activities in the cell.

# ENDOPLASMIC RETICULUM

**History:** Early cytologists held that some sort of supporting network or cytoskeleton was present in the cells. It was given various names. Nissil substance, ergastoplasm, basophilic bodies, etc. In 1945, Porter, Claude and Fullman with the help of electron microscope noted a delicate membranous network in the cytoplasm. It was later called endoplasmic reticulum (ER) by Keith Porter in 1953. The ER originally seemed to be confined to the endoplasm of the cell, hence its name.

## Structure of Endoplasmic Reticulum:

In eukaryotic cells endoplasmic reticulum is generally the largest membrane which forms extensive system of intercommunicating membranous sacs or channels. It represents 30 to 60% of total membrane in a cell. The membrane of endoplasmic reticulum may or may nothave ribosomes attached to their outer membrane. Accordingly, these are classified as rough (RER) or smooth endoplasmic reticulum (SER). Rough endoplasmic reticulum is characterized by the presence of ribosomes of about 150Å in diameter and rich in protein and RNA. Smooth endoplasmic reticulum lacks ribosomes. It comprises three types of elements: cisternae, tubules, and vesicles (Figure 47).

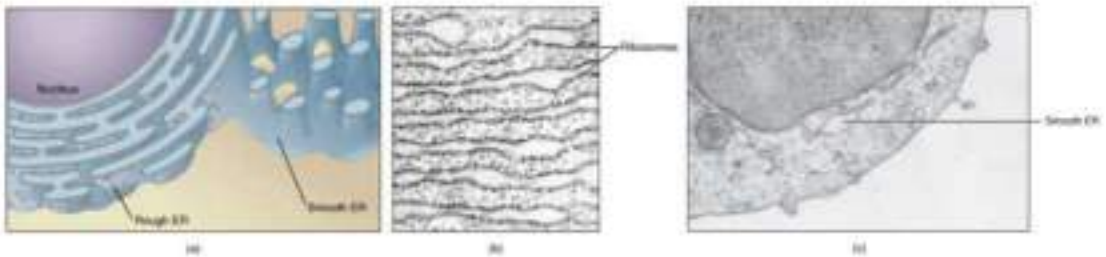


**Figure 47:** Endoplasmic Reticulum (ER).(a) The ER is a winding network of thin membranous sacs found in close association with the cell nucleus. (b) Rough ER is studded with numerous ribosomes, (c) Smooth ER synthesizes.

**Cisternae:** These are flattened, unbranched, sac like elements with about 40-50μm in diameter. They lie in stacks (piles) parallel to but interconnected with one another. They are separated from one another by cytosolic spaces. The small granular structures called the ribosomes may or may not be present on the surface of cisternae (Figure 48).

**Tubules:** These are irregular, branching elements, which form a network along with other elements. They are about 50-100□m in diameter and are often free of ribosomes (Figure 48).

**Vesicles:** These are oval, vacuole like elements, about 25-500□m in diameter. They often occur isolated in the cytoplasmic matrix. They are also free of ribosomes. A fluid calledthe endoplasmic matrix is present in the lumen of ER. All the elements of ER freely communicate with one another (Figure 48).

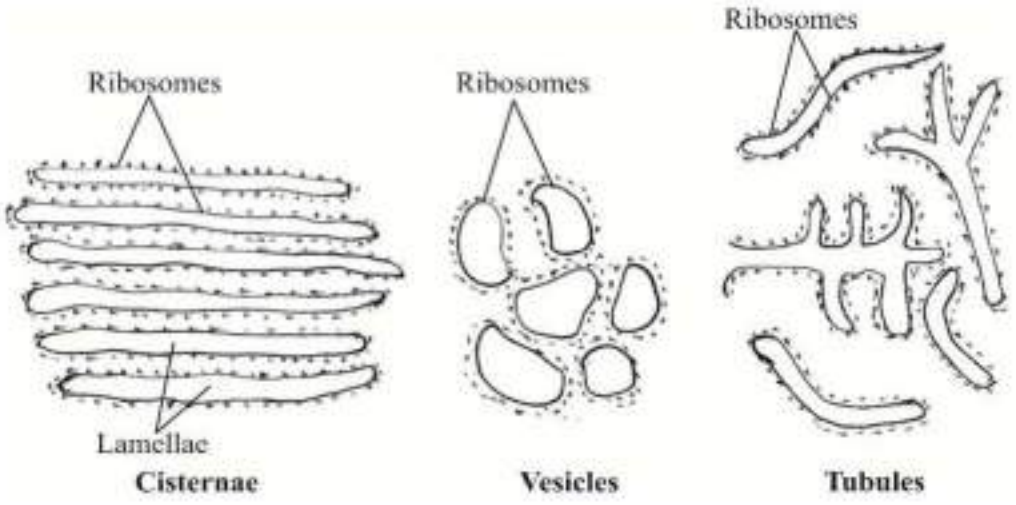



**Figure 48:** Various forms of ER.

**Ultra-structure of Endoplasmic Reticulum:**

The membrane bounding the cisternae, tubules and vacuoles of the ER is similar to the cell membrane. It is 50-60Å thick. The membranes of endoplasmic reticulum are composed of two layers of phospholipids molecules sandwiched by two layers of protein molecules like other membranes in the cell (Robertson, 1959). The ER membrane has a relatively high protein/lipid ratio. It is continuous with the cell membrane, Golgi membranes and outer membrane of the nuclear envelope. Certain cisternae open out by pores in the cell membrane. In the lumen of endoplasmic reticulum, secretary granules were observed by Palade (1956). The lumen acts as a passage for the secretary products. About 30-40 different enzymes are associated with the ER for the various synthetic activities. These may be located on the cytoplasmic surface or luminal surface or both. Membrane bound endoplasmic reticulum spaces varies in shape and sizes in different cell types (Figure 49). On the basis of absence or presence of ribosomes, two kinds of ER are found in cells.

**A. Smooth Endoplasmic Reticulum**: Ribosomes are absent on the walls of ER and so itappears smooth and hence called smooth or agranular ER. It mainly occurs as tubular forms. The tubules forms irregular lattices and measures about 500-1000Å in diameter. Smooth ER is commonly found in the cells involved in the synthesis of steroids or lipids i.e., non protein type of synthesis (Christensen and Fawcett, 1961) such as adrenal or sebaceous glands, gonadial interstitial cells. Certain cells with carbohydrate metabolism (e.g.,

liver cells), impulse conduction (e.g. muscle cells), with pigment production (e.g., retinal pigment cell) and electrolyte excretion (e.g., chloride cells of fish gills) are also have more of SER in them.

**B. Rough Endoplasmic Reticulum (RER):** It is characterized by the presence of ribosomes on the surface of reticulum and so it is also known as granular ER. It is in the form of flattened cisternae with the width of 400-500Å. RER occurs largely in the cells that are actively involved in the synthesis of proteins such as enzymes (e.g., pancreatic cells, plasma cells and liver cells) or mucus (goblet cells). In exocrine cells of pancreas, RER consists of reticular sheets and fenestrated cisternae in the basal region of the cell. These cisternae measures about 5-10 micron in length and their groups are 400-1000Å in diameter. In apical region of the cells, granular reticulum occurs in the form of vesicles. Granular and agranular ER are in continuity of their membranes in the regions of contact.

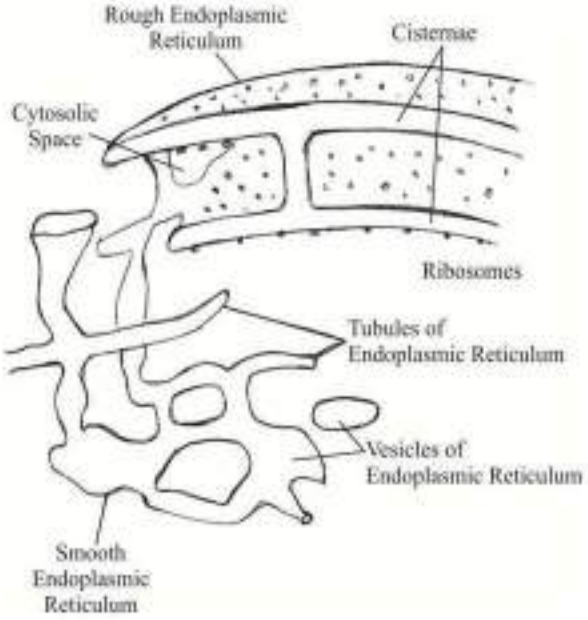



**Figure 49:** Various types of elements of endoplasmic reticulum.

**Functions of Endoplasmic Reticulum:**

**(A) Functions of smooth endoplasmic reticulum:**

1. **Surface for Synthesis:** The SER provides surface for the synthesis of fatty acids, phospholipids, glycolipids, steroids and visual pigments.
2. **Glycogen Metabolism:** The SER carries enzymes for glycogen metabolism in liver cells. Glycogen granules are attached in larger numbers to the outside of the SER's membranes in liver cells.
3. **Detoxification:** The SER has enzymes that are involved in the detoxification in the liver, i.e., converts harmful materials such as carcinogens and pesticides, into harmless ones for excretion by cell.
4. **Formation of organelles:** The SER produces Golgi apparatus, lysosomes, microbodies and vacuoles.
5. **Transport route:** The proteins shift from RER through SER to Golgi apparatus for further processing.
6. **Skeletal Muscle Contraction:** The sarcoplasmic reticulum in skeletal muscle cells release Ca2+ ions to cause contraction and absorbs Ca2+ ions to bring about relaxation.
7. **Fat Oxidation:** The SER membranes carry out the initial reactions in the oxidation of fats.

**(B) Functions of rough endoplasmic reticulum:**

1. **Surface for Ribosomes:** The RER provides a large surface for the attachment of ribosomes.
2. **Surface for synthesis:** The RER offers extensive surface on which protein synthesis can be conveniently carried on by ribosomes. The

newly formed proteins may enter the ER membranes, becoming a part of the membrane structure or pass into the ER lumen. The proteins becoming a part of ER membrane eventually move from the ER via membranes of other cell organelles, namely Golgi apparatus, secretary vesicles to become permanent plasma membrane proteins. The proteins entering ER lumen are packed for export.

3. **Packaging:** The proteins in ER lumen are processed and get enclosed in spherical membrane bound vesicles which get pinch off from the ER. These vesicles have various fates. Some remain in the cytoplasm as storage vesicles while others migrate to the plasma membrane and expel their contents by exocytosis. Some fuse with Golgiapparatus for further processing of their proteins for storage or release from the cell (Figure 50).
4. **Smooth ER Formation:** The RER gives rise to the smooth ER by loss of ribosomes.
5. **Formation of Nuclear Envelope:** The RER forms nuclear envelope around daughter cells in cell division.
6. **Formation of Glycoproteins:** The process of linking sugars to proteins to form glycoproteins starts in the RER and is completed in Golgi apparatus.

**Importance of Endoplasmic Reticulum:**

1. **Transport of Materials:** The ER facilitates transport of materials from one part of the cell to another thus forming the cell's circulatory system.

2. **Formation of Desmotubule:** Tubular extension, called desmotubule, extends through plasmodesmata to make ER continuous in the two adjacent plant cells.
3. **Support:** The ER acts as an intracellular supporting framework, the cytoskeleton thatalso maintains the form of the cell.
4. **Localization of Organelles:** It keeps the cell organelles properly stationed anddistributed in relation to one another.
5. **Surface for Synthesis:** The ER offers extensive surface for the synthesis of a varietyof materials.
6. **Storage of Materials:** The ER provides space for temporary storage of syntheticproducts such as proteins and glycogen.
7. **Exchange of materials:** The ER helps in the exchange of materials between thecytoplasm and the nucleus.
8. **Location of Enzymes:** A variety of enzymes is located in the ER membranes tocatalyze the biochemical reactions.

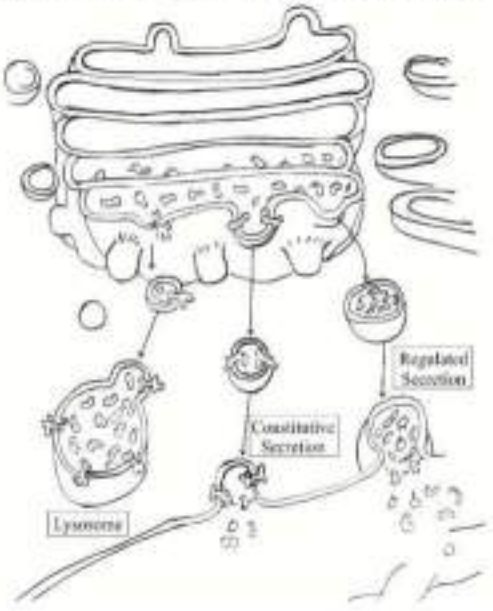



**Figure 50**: Transport of proteins from Golgi apparatus. Proteins are sorted and transformed in Golginetwork and transported in vesicles to their final destination.

# RIBOSOMES

**George E. Palade** (1953) was the first to observe dense particles or granules in animal cells under electron microscope. These were thus called as Palade's Particles. Later **Richard B. Roberts** named them **"ribosomes"** in 1958. **Tissieres and J.D. Watson** (1958) isolated ribosomes from E. coli for the first time. It was shown that ribosomes contain approximately equal amount of RNA and proteins

**Structure of Ribosome:**

Ribosomes are of two types **70S and 80S. 'S'** is **Svedberg unit**, a measure of particle size dependent on the speed with which the particles sediment in the ultracentrifuge. The **70S** ribosomes are found in the **prokaryotic cells** and in the **mitochondria and plastids** of eukaryotic cells. The **80S** ribosomes occur in the cytoplasm of the eukaryotic cells. Both the 70S and 80S ribosomes are similar in structure. They are small, spherical structures of which 70S ribosomes are around 200Å in diameter, while 80S are 250 to 300Å in diameter. They are porous and hydrated having two subunits, one is larger (140-160Å in diameter) having dome shaped structure and the other is smaller in size, found over the larger subunit, forming a cap like structure. The two subunits are separated by clefts (Palade and Kuff, 1966). **Membrane is absent around them**. The subunits occur separately in the cytoplasm, and join to form ribosomes only at the time of protein synthesis. Many ribosomes line up and join the mRNA chain. After the synthesis of protein, the ribosomes leave the mRNA chain and dissociate into subunits.

1. **70S Ribosome:** These are found in bacterial cells and have the molecular wt. $2.7 \times 10^{-6}$ daltons and sedimentation coefficient 70S. 70S ribosome consists of a large 50S subunit and a small 30S subunit. Each subunit is composed of rRNA and several basic proteins. The 50S subunit has two species of RNA: 23S and 5S and about 34 differentribosomal proteins. The 30S subunit has only one species of rRNA, i.e., 16S and about 21 different ribosomal proteins. They also occur in mitochondria and chloroplasts of eukaryotic cells (Figure 51).

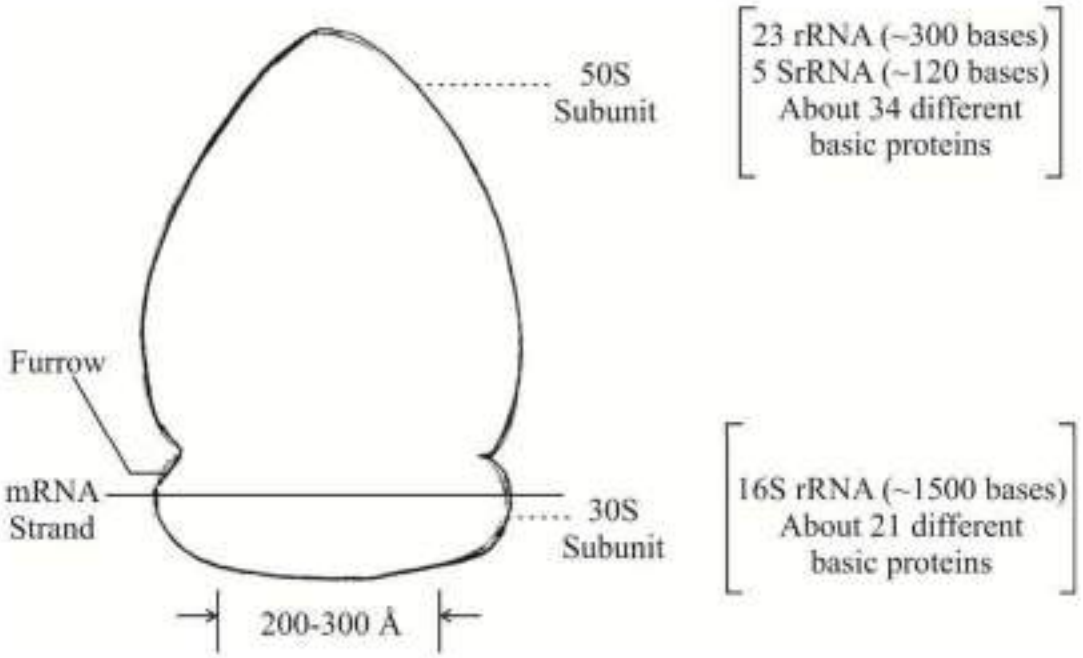



**Figure 51**: Structure of 70S ribosome of Escherichia coli.

2. **80S Ribosome:** Having the sedimentation coefficient 80S, these are somewhat larger and contain more RNA and proteins than 70S ribosomes. An 80S ribosome is over250 to 300Å in diameter. Their mol. wt. is $4 \times 10^{-6}$ Daltons. It consists of a large 60S subunit and a small 40S subunit. Each subunit is composed of rRNA and several

specific basic proteins. The 60S subunit has three species of rRNA: 28S, 5.8S and 5S and over 45 different ribosomal proteins. The 40S subunit has only one species of rRNA, i.e., 18S and over 33 different ribosomal proteins. They are found in eukaryotic cells (Figure 52)

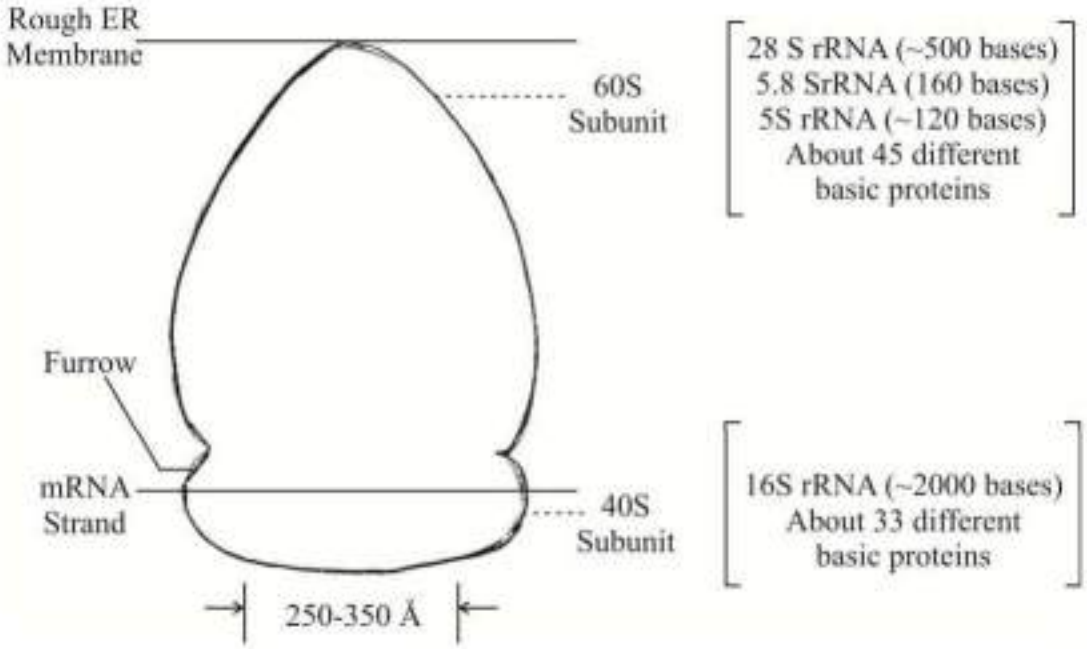



**Figure 52:** Structure of 80S ribosome of eukaryotic cell.

**Ultra-structure of ribosome:**

The ribosomes are composed of two subunits (one subunit is almost twice in size than the other) fitted together to form a complete unit of about 300Å in diameter. In 70S ribosome the 50S subunit is pentagonal compact particle of 160 to 180Å bearing a round concave area in its center of about 40 to 60Å that accommodates the small subunit. A small pore like transparent area is also present that inhibits the entrance of enzyme ribonuclease. Similar pores are present in 60S subunit of 80S ribosomes. The smaller subunits 30S of 70S and 40S of 80S ribosomes have irregular forms and are often divided into two portions which are

interconnected by a strand of 30 to 60 Å thicknesses. Ribosomes have a groove at the junction of large and small subunits. The mRNA is seated in the gap between both ribosomal subunits, where the ribosome protects a stretch of some 25 nucleotides of mRNA from degradation by ribonuclease. From this groove, a canal or tunnel extends through the large subunit and opens into the lumen of the endoplasmic reticulum. Polypeptides are synthesized in the groove between the two ribosomal subunits and pass through the tunnel of the large subunit into the endoplasmic reticulum (Figure 53).

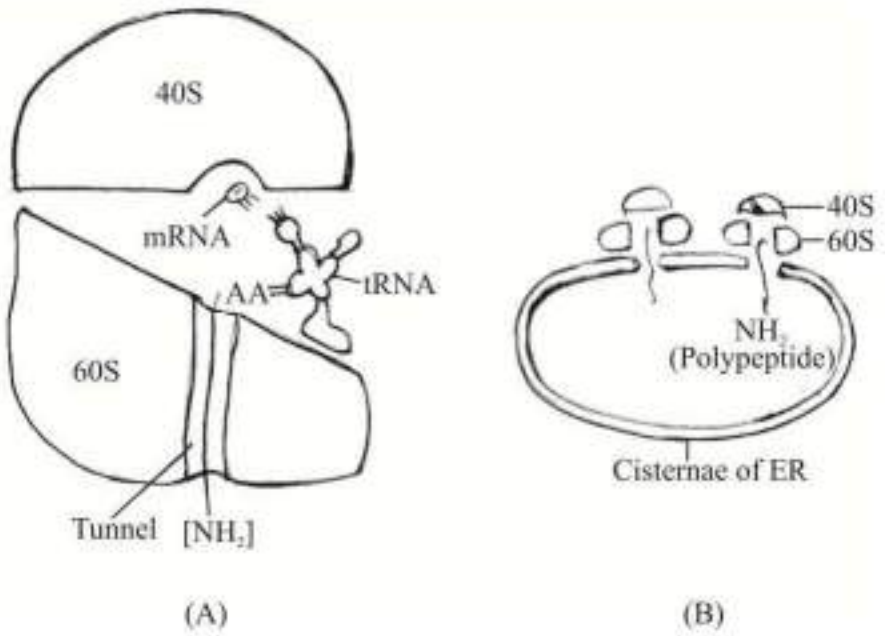



**Figure 53:** Ultra structure of ribosomes showing two subunits.

**Functions of Ribosome:**

1. **Attached Ribosomes:** The ribosomes provide space and enzymes for the synthesis of proteins in the cell. The ribosomes bound to the ER membranes synthesize:
   (i) integral proteins for cellular membranes.

(ii) lysosomal proteins.

(iii) secretary proteins for export as secretions.

2. **Free Ribosomes:** The free ribosomes produce structural and enzymatic proteins for use in the cell itself. These proteins include glycolytic enzymes and most extrinsic membrane proteins, such as spectrin.

**Importance of Ribosome:**

- Ribosomes are known as protein factories. Ribosomal RNA molecules possibly serve as a skeletal framework in the ribosomes.
- Smaller ribosomal subunit is required for the formation of initiation complex at the start of the protein synthesis. Whereas larger ribosomal subunit is necessary forpeptide bond formation and the elongation for the polypeptide.
- The ribosome function as a template in order to bring together various components involved in the synthesis of proteins. Ribosomes co-ordinate the interaction of t-RNA
- amino acid complex with m-RNA. This co-ordination results in the translation of genetic code forming specific proteins.
- Since free ribosomes are not involved in protein synthesis, they are transported through endoplasmic reticulum membranes and assembled into globules within the cisternae and canals in the cells that produce 'proteins for transport'. Proteins later appear in the form of granules outside the Golgi complex.

# GOLOGI APPARATUS

**History:** Camillo Golgi in 1898 discovered the Golgi apparatus in the nerve cells of barn owl and cat by metallic impregnation method. After it's discoverer's name, the Golgi apparatushas been variously named as Golgisome, Golgi material, Golgi membranes, Golgi body, etc.

**Structure of Golgi Bodies (Figure 54):**

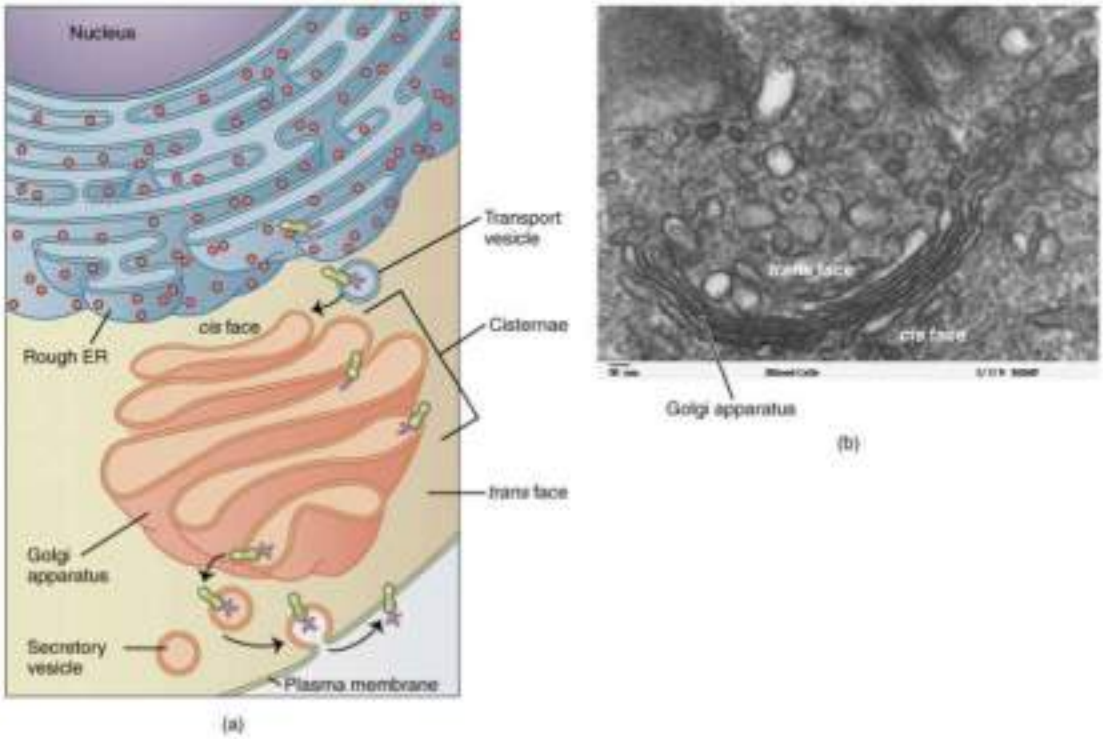



**Figure 54:** Golgi Apparatus. (a) The Golgi apparatus manipulates products from the rough ER, and produces new organelles called lysosomes. (b) An electron micrograph of the Golgi apparatus.

Golgi bodies varies in size and form in different types of cells, but they have similar organization in all kinds of cells. For example, it is well developed in secretory and nerve cells, but is rather small in muscle cells. Golgi bodies are compiled as a central stack (pile) of flattened sacs or cisternae and many peripheral tubules and vesicles.

1. **Cisternae:** The cisternae vary in number from 3 to 7 in most animal cells and from 10to 24 in plant cells. They are usually equally spaced in pile so that they are nearly parallel to one another, having 200-300Å wide inter-cisternal spaces containing alayer of parallel fibers called inter-cisternal elements. These support the cisternae and maintain regular spacing between them. The cisternae may be flat, but are often curved, having a distinct polarity with a convex face towards the cell membrane and concave face towards the nucleus. They are free of ribosomes and have swollen ends. They look like the smooth endoplasmic reticulum and are continuous with it at certainplaces. This suggests that the Golgi apparatus is derived from the smooth endoplasmicreticulum. A cisterna is about 0.5-1 μm in diameter and its cavity is about 100Å wide.It is fenestrated at the margin as here it passes into tubules. All the cisternae have a continuous lumen filled with a fluid.
2. **Tubules:** Short tubules arise from the periphery of the cisternae. Some of these enlarge at their ends to form vesicles.
3. **Vesicles:** The vesicles lie near the ends and concave surface of the Golgi complex. They are pinched off from the tubules of the cisternae. They are of three types: transitional, smooth or secretary and coated vesicles
   a. **Transitional Vesicles:** These are the small outgrowths formed from the transitional ER. They migrate to, converge and coalesce to cis face of Golgi, where they form new cisternae.
   b. **Smooth Vesicles:** These have smooth surface and contain secretions of the cell and so they are also called secretary

vesicles. They arise from the ends of the cisternae tubules.

c. **Coated vesicles:** These have rough surface, and they also arise from the cisternae tubules. They play a role in intracellular traffic of secretary protein molecules.

The Golgi complex has 3 functional regions: cis region that lies nearest the ER, medial region in the middle, and Tran's region with trans Golgi reticulum nearest to the plasma membrane. These regions have different enzymes which introduce different modifications to secretary and membrane proteins passing through them. The principal modification is glycosylation, i.e., addition of sugars to proteins, forming glycoproteins. Glycosylation starts in the ER and is completed in the Golgi complex. Modification of proteins in the Golgi apparatus also involves addition of lipids, forming lipoproteins (liposylation), and even the addition of other groups (Figure 55).

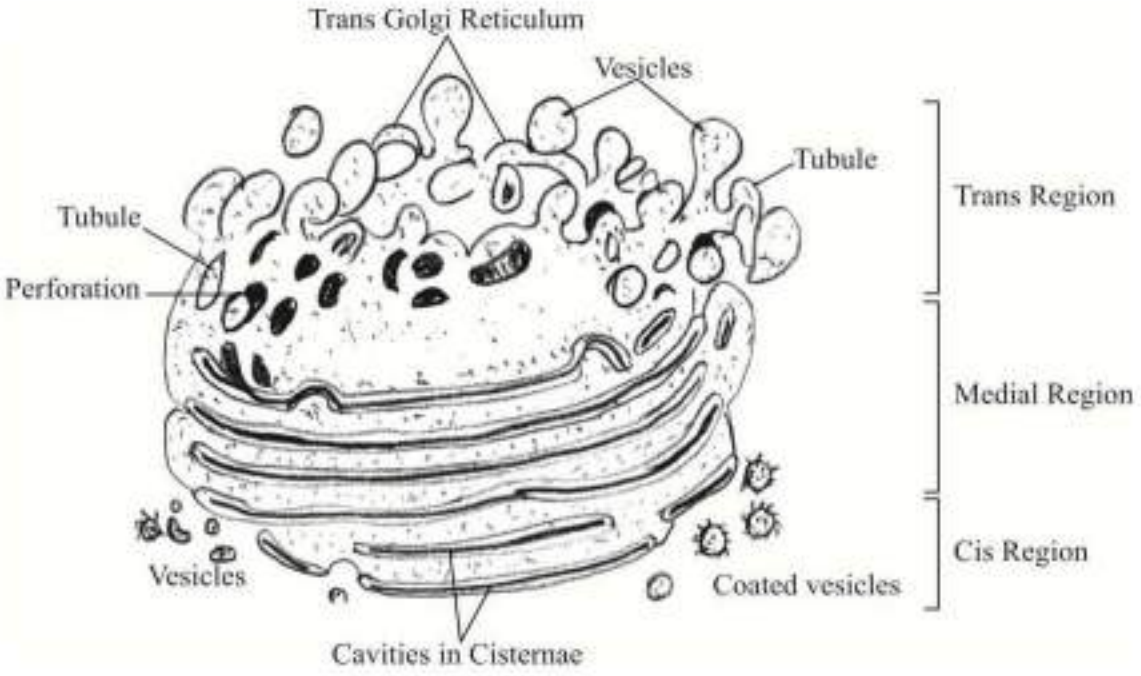



**Figure 55:** Thee-dimensional view of Golgi apparatus

**Functions of Golgi Bodies:**

1. **Formation of secretary vesicles:** The Golgi complex processes and packagesproteins and lipids coming from the ER for transport to other parts of the cell or out of the cell. Packaging involves wrapping the materials by a membrane, forming secretary vesicles. The materials so packed includes zymogen in pancreatic cells, mucus in goblet cells, lactoprotein in mammary gland cells, pigment granules in pigment cells, collagen in connective tissue cells, hormones in endocrine cells, etc.
2. **Synthesis of carbohydrates:** The Golgi apparatus synthesizes certain mucopolysaccharides from simple sugars.
3. **Formation of Glycoproteins:** The Golgi apparatus links the sugars with proteins coming from rough ER to form glycoproteins.
4. **Formation of Lipoproteins**: Lipids and proteins coming from the ER are complexed into lipoproteins in the Golgi apparatus.
5. **Addition to Cell Membrane:** The Golgi apparatus provides membrane material for the plasma membrane in pinocytotic and phagocytotic vesicles and for the formation of cleavage furrow during the division of animal cells. The transfer of membrane from the ER via transition vesicles, Golgi complex and secretary vesicles to the plasma membrane is called membrane flow.
6. **Membrane Transformation:** The Golgi apparatus changes one type of membrane into another type. Membranes are gradually modified from the ER type to one with characteristics of the plasma membrane as they shift through the Golgi complex.
7. **Formation of cell wall:** In some algae, cellulose plates for cell wall

is synthesized in Golgi complex. In higher plants the Golgi complex (a) synthesizes pectin and some carbohydrates necessary for the formation of cell wall and (b) produces some secretions such as mucilage, gums, etc.

8. **Formation of lysosomes:** The Golgi complex gives rise to primary lysosomes by budding. The lysosomes may also arise from ER.
9. **Acrosome Formation**: The Golgi complex gives rise to the acrosome in a sperm.
10. **Formation of Yolk and Cortical Granules**: The Golgi complex produces yolk and cortical granules in the eggs. Formation of yolk is called vitellogenesis.
11. **Formation of Nematocysts and Trichocysts**: The Golgi apparatus gives rise to the nematocysts in Hydra and perhaps also in other coelenterates, and trichocysts in ciliates such as Paramecium.
12. **Storage of Secretions:** The Golgi complex stores cell secretions such as proteins and lipids.
13. **Absorption of Materials:** Golgi apparatus absorbs materials from the environment. For example, cells of the intestinal lining use Golgi apparatus to absorb lipids from the intestine.
14. **Location of Enzymes:** A variety of enzymes is localized in the Golgi complex to helpin the cell's biochemical reactions.

**Importance of Golgi Bodies:**

The Golgi apparatus is often referred to as the "traffic police" of the cell because its enzymes sort out and modify cell's secretary proteins passing through its lumen and membrane proteins in its membranes and directs them to their proper destination.

# LYSOSOMES AND PEROXISOMES

**History:** Lysosome is an organelle which unlike other organelles, first became known through the biochemical studies and thereafter their morphological identifications were made. Christian de Duve, a Belgian cytologist and biochemist, in 1955 reported the presence of lysosomes in the cells by biochemical studies. Later on, Novikoff in 1956 observed these lysosomes as distinct cell organelles with the help of electron microscope.

**Structure of Lysosomes:**

Lysosomes (Figure 56) are round tiny bags filled with dense material rich in acid phosphatase (tissue dissolving enzymes) and other hydrolytic enzymes. They consist of two parts: (i) limiting membrane and (ii) inner dense mass.

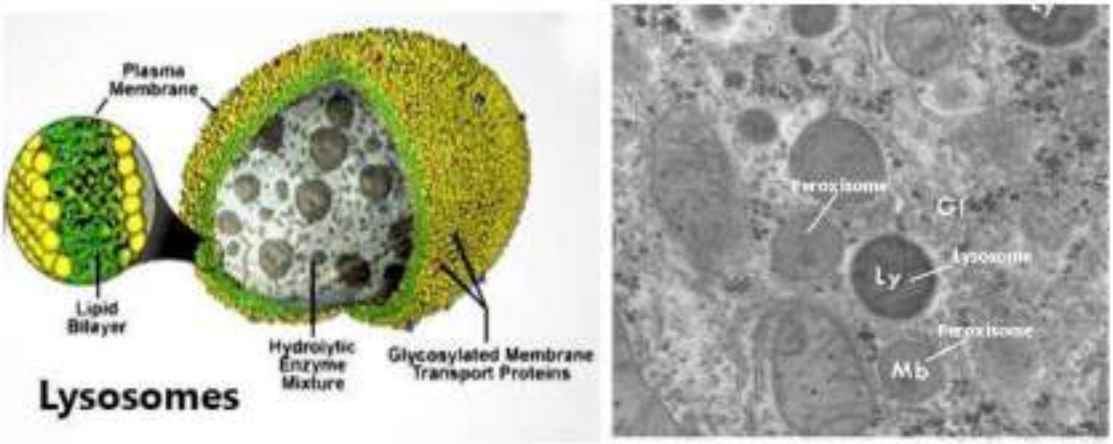



**Figure 56:** The structure of lysosomes

I- **Limiting membrane:** This membrane is single and is composed of lipoprotein Chemical structure is homologous with unit membrane of plasmalemma, consisting ofbimolecular layer.

II- **Inner dense mass:** This enclosed mass may be solid or of very dense contents. Some lysosomes have a very dense outer zone and a less dense inner zone. Some others have cavities or vacuoles within the inner granular material. Lysosomes are of varioustypes, and they help in intracellular digestion. Their contents vary with the stage of digestion.

**Kinds of Lysosomes:**

There are four types of lysosomes: primary, secondary, residual bodies and cyto-lysosome or autophagosome.

1. **Primary Lysosome (storage granules):** It is a small sac like body. Its enzymatic contents are synthesized by ribosomes and accumulated in ER. From there, they enter the Golgi region, where acid phosphatase reaction takes place. The GERL region, i.e., acid phosphatase rich region of Golgi maturing face is thought to be involved in the production of lysosomes. The primary lysosome comprises only one type of enzymeor another.
2. **Secondary Lysosome (digestive vacuole or heterophagosome)**: These are produced either from phagocytosis or pinocytosis of foreign material by the cell. Actually, within the cell, after phagocytosis or pinocytosis, the foreign bodies or extra-cellular substances are enclosed within the membrane and these membranes bound structures are known as **phagosome or pinosomes.** These ultimately fuse with primary lysosomes, thus forming secondary lysosome. This body having engulfed material within membrane has

also full complements of acid hydrolases (hydrolytic enzymes). The digested material of these lysosomes passes through the lysosomal membrane and is incorporated into the cell so that they may be reused in metabolic pathways.

3. **Residual bodies:** These are formed in case the digestion is incomplete. In some cells, such as Amoeba and other protozoa, these residual bodies are eliminated by defecation. Hence, lysosomes **having undigested material or debris** are called residual bodies. These bodies are formed due to lack of certain enzymes in lysosomes. These are rejected from the cell by exocytosis and some time in certain cells these bodies remain in cells for long time causing ageing. These residual bodies also cause diseases in man such as **fever, hepatitis, polynephritis, hypertension, congested heart failure** etc. If the debris which is mostly lipid in nature may accumulate and condense into concentric lamella, it forms myelin (Figure 57).
4. **Autophagic vacuole (cytolysosome or autophagosome):** In this case, the lysosome **digests a part of cell** (e.g., mitochondria or portion of ER) by the process of autophagy. For example, liver cell shows numerous autophagosome during starvation among which remnants of mitochondria occur. This is a mechanism by which the cell can achieve degradation of its own constituents without irreparable damage.

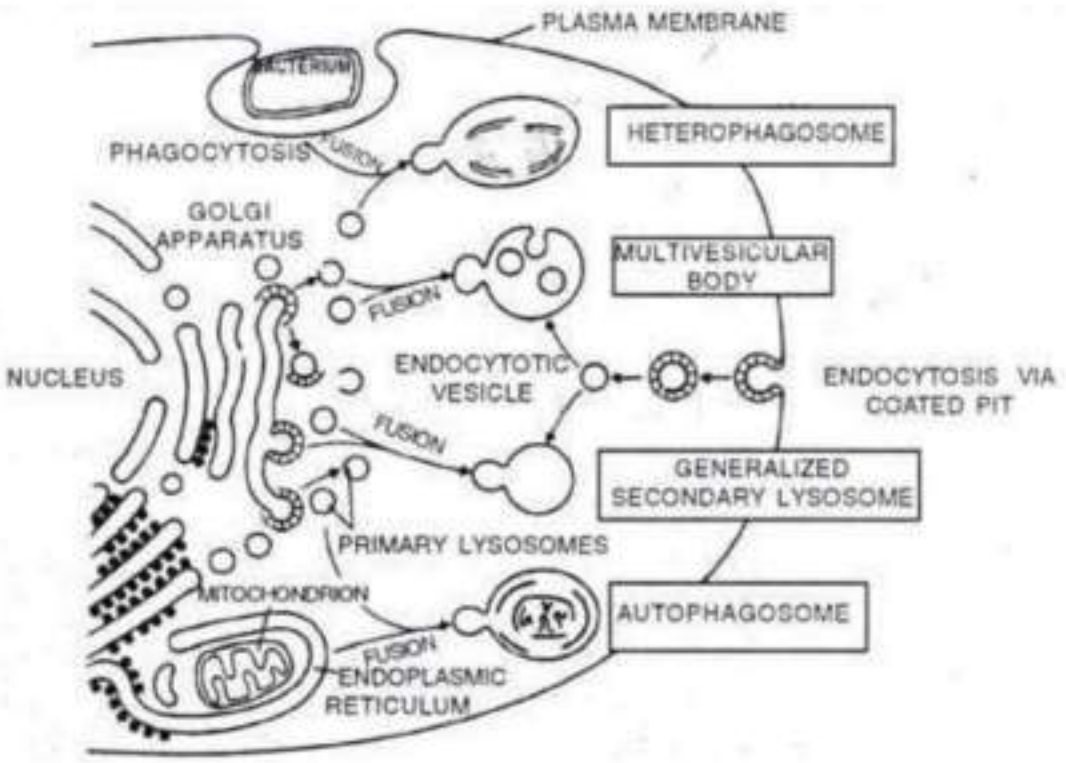



**Figure 57:** Formation of lysosomes and intracellular digestion in them.

## Chemical Nature of Lysosomes:

Chemically lysosomes are defined as a body rich in acid hydrolases. Acid phosphatase has been found in many cells of plant roots, fungi, liver, kidney, and endocrine glands. The lysosomal enzymes can break down all major biological macromolecules present in the cells or entering the cells from outside into their building block subunits by adding water. The common enzymes in the lysosomes are proteases, nucleases (deoxyribonuclease and ribonuclease), glycosidase, lipases, sulphatases and phosphatase, which hydrolyses proteins, nucleic acids, polysaccharides, lipids, organic sulphatases and organic phosphates respectively.

**Functions of Lysosomes:**

1. **Digestion of useful materials:** Intracellular digestion is a regular feature in protozoans and in lower invertebrates such as sponges and coelenterates. In thisprocess the organic substances (food particles) taken up by the cells in vacuoles (pinosomes or phagosome) from the environment are digested.
2. **Digestion of harmful materials:** The foreign particles, such as viruses, bacteria, and toxic molecules, are disposed of by hydrolyzing them in certain leucocytes and macrophages. This is called natural defense of the body. This activity of lysosomes is characteristic of higher animals.
3. **Digestion of unwanted materials:** The dead cells and debris that accumulate at the sites of injury are destroyed in some white blood cells. This is called natural scavenging of the body.
4. **Renewal of cells and organelles:** The old worn-out cells and cell organelles are broken down to make the component molecules available for formation of new cells. and cell organelles. Thus, the lysosomes facilitate the turn-over of cells in normal tissues and of organelles in normal cells.
5. **Feeding of starving animals:** Food to a starving animal is provided by digesting the stored food materials (proteins, lipids, and glycogen) and even the cells. This is called autophagy.
6. **Autolysis:** Autolysis caused by the lysosomal enzymes plays a role in normal developmental changes in both animals and plants. E.g.,

in the breakdown and absorption of tail during the metamorphosis of frog's tadpole. In autolysis, lysosome membrane ruptures and releases the enzymes into the surrounding cytoplasm. This kills and lyses the cell.

7. **Aid in fertilization:** The lysosome of sperms releases their enzymes to dissolve the egg membranes for the entry of the sperm into the ovum in fertilization. This is called extracellular digestion.

**Importance of Lysosomes:**

As lysosomes store the hydrolyzing enzymes of the cell, they digest the incoming food materials and remove the foreign bodies and their organelles no longer required. Their membrane prevents the enzymes from escaping into the cytoplasm and destroying it.

Malfunctioning of lysosomes may lead to diseases. Abnormal rupturing of lysosomal membrane and release of enzymes may cause blood cancer, sunburn, and genetic disorders. The degenerative changes in bones and joints associated with arthritis are suspected to be the result of abnormal release of enzymes from the lysosomes of the bone cells or lymph cellsinto the extracellular fluid.

# PEROXISOMES

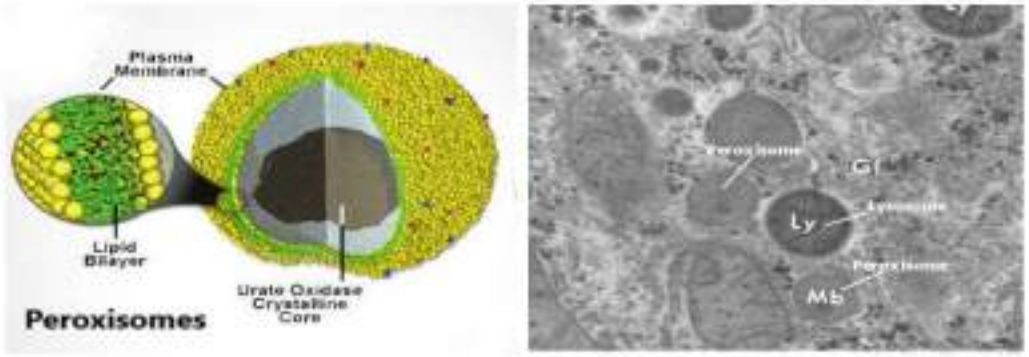



**Figure 58:** Structure of peroxisomes

**Peroxisomes** (Figure 58) are among the simplest of the subcellular organelles that are characteristic of all eukaryotic cells. With , 60 known enzymes in the matrix and ,45 documented integral or peripheral membrane proteins, it is a reasonable guess that this organelle has only , 125 proteins, which makes it much less complex than other organelles. The peroxisome derives its name from the fact that many metabolic enzymes that generate hydrogen peroxide as a by-product are sequestered here because peroxides are toxic to cells. Within peroxisomes, hydrogen peroxide is degraded by the enzyme, catalase, to water and oxygen.

Peroxisomes are surrounded by a single membrane, and they range in diameter from 0.1 to 1 mm. They exist either in the form of a network of interconnected tubules (peroxisome reticulum), as in liver cells, or as individual micro peroxisomes in other cells such as tissue culture fibroblasts. Peroxisome-Like Organelles Peroxisomes are related to specialized peroxisomes called glycosomes in parasites such as Trypanosomes, and to plant glyoxysomes, but are unrelated to hydro-genosomes, mitochondria, and chloroplasts. Collectively, peroxisomes,

glyoxysomes, and glycosomes are also referred to as microbodies.

**Peroxisome Distribution and Origin:**

Peroxisomes exist in all eukaryotes from single- and multi- cellular microorganisms, to plants and animals. Unlike mitochondria, nuclei, and chloroplasts, peroxisomes have no DNA. Consequently, all their proteins are encoded by nuclear genes. They are proposed to have originated from endosymbionts that subsequently lost their DNA, but the evidence for an endosymbiont origin is much weaker than it is for mitochondria and chloroplasts.

## Functions of Peroxisomes:

The principal function of peroxisomes is to house many metabolic pathways that are involved in various aspects of lipid metabolism. These include the following:

1- enzymes involved in the degradative oxidation (e.g., b-oxidation of very long chain fatty acids, 2-methyl-branched fatty acids, dicarboxylic acids, leuko- trienes, bile acid intermediates and cholesterol side chains, and both a- and b-oxidation of 3-methyl-branched chain fatty acids).

2- The early steps in the synthesis of ether glycero-lipids.

3- The formation of bile acids, dolichol, and cholesterol.

4- The catabolism of purines, polyamines, and amino acids, and the detoxification of reactive oxygen species such as hydrogen peroxide, superoxide anions, and epoxides. In methylotrophic yeasts, peroxisomes are also involved in the metabolism of methanol and methyl amines.

**Glycosomes** contain the glycolytic enzymes, in addition to enzymes common to most peroxisomes, whereas plant gloxysomes have some or all the glyoxylate pathway enzymes. Peroxisomes in the leaves of plants also participate in photorespiration. Despite the fragility of the organelle during bio- chemical purification, the peroxisome membrane is impermeable to small molecules such as NAD(H), NADP(H), acetyl-CoA, and even protons in vivo. Consequently, it is not surprising that the peroxisomal membrane has a number of transporters for fatty acids, fatty-acyl-CoA esters, metabolites, and ATP.

**Difference between Peroxisomes and Lysosomes:**

Peroxisome and Lysosome two organelles, filled with enzymes that catalyze different biochemical processes inside the cell. Also, the primary **Difference between Peroxisomes and Lysosomes** may be the enzymes they consist of and their features. Lysosomes contain enzymes, which degrade biopolymers like proteins, lipids, polysaccharides, and nucleic acids. Peroxisomes have enzymes for the oxidation of organic and natural compounds, the era of metabolic based energy. Both lysosomes and peroxisomes will be related structurally. But you can find the Difference between Peroxisomes and Lysosomes in proportions. Lysosomes are often large in comparison to peroxisomes and their dimensions vary together with the materials that are uptake into the organelle. Both organelles are usually enclosed by way of a single membrane.

# THE CYTOSKELETON

Much like the bony skeleton structurally supports the human body, the cytoskeleton helps the cells to maintain their structural integrity. The **cytoskeleton** (Figure 59) is a group of fibrous proteins that provide structural support for cells, but this is only one of the functions of the cytoskeleton. Cytoskeletal components are also critical for cell motility, cell reproduction, and transportation of substances within the cell. The cytoskeleton forms a complex thread-like network throughout the cell consisting of three different kinds of protein-based filaments: microfilaments, intermediate filaments, and microtubules (Figure 60).

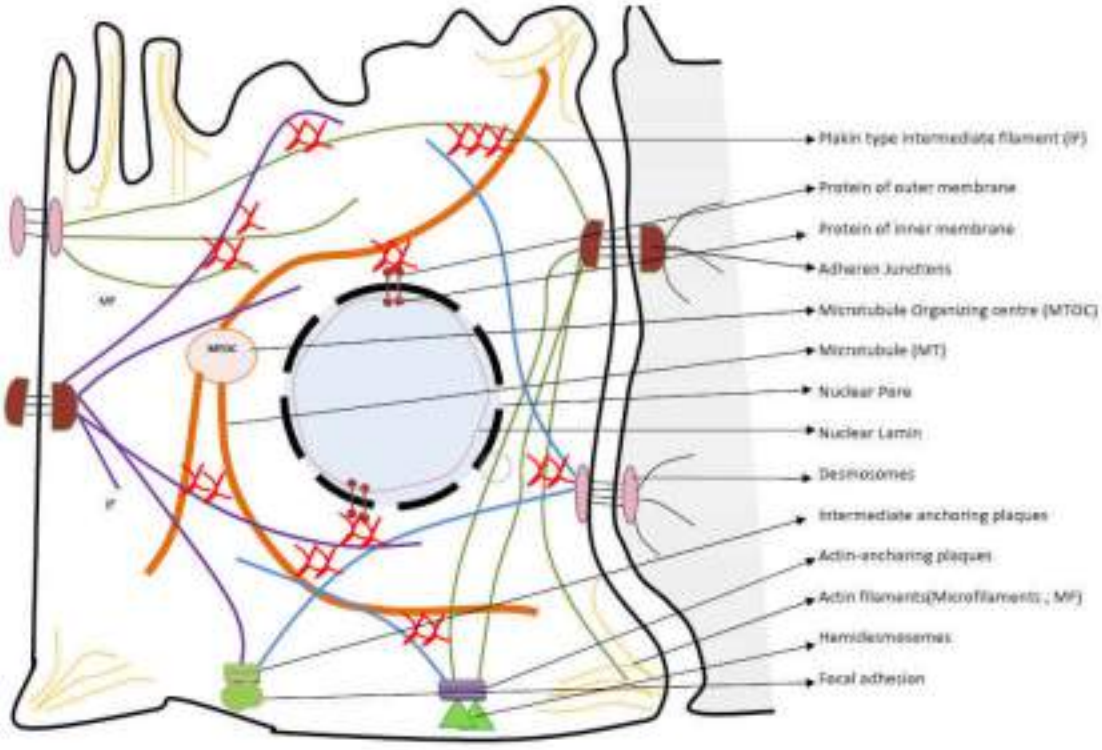



**Figure 59**: Cytoskeleton structures in cell.

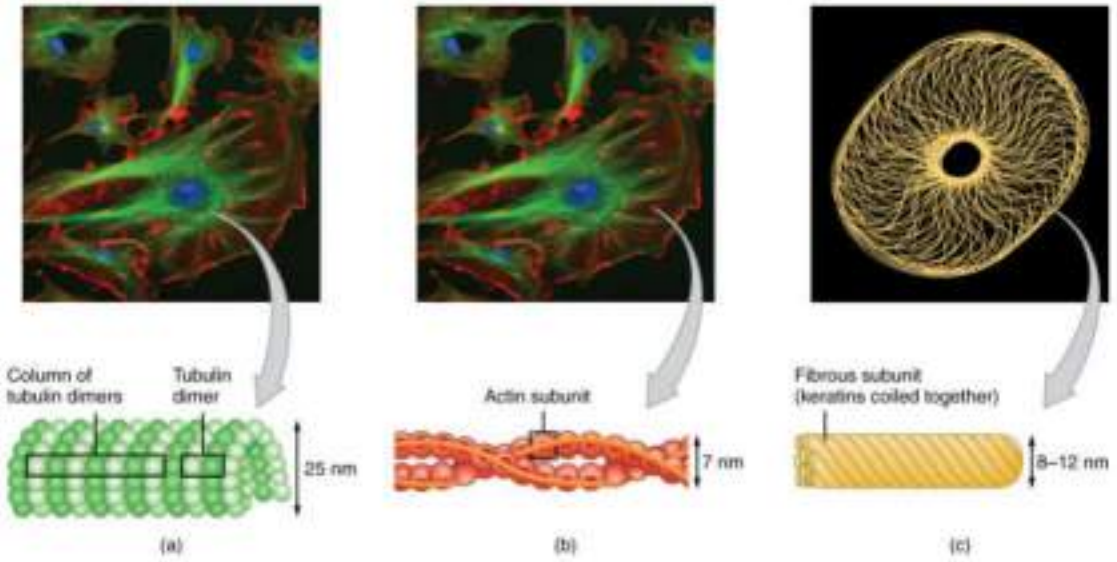



**Figure 60:** The Three Components of the Cytoskeleton. The cytoskeleton consists of (a) microtubules, (b) microfilaments, and (c) intermediate filaments. The cytoskeleton plays an important role in maintaining cell shape and structure, promoting cellular movement, and aiding cell division.

## Cytoskeleton functions:

The cytoskeleton plays an important role in maintaining cell shape and structure, promoting cellular movement, and aiding cell division.

1. To provide structural support in maintaining shape of the cells and resilience to tension and stress.
2. Intracellular transport of vesicle and movement of mRNA (refer to vesicular transport: from ER to Golgi apparatus to Plasma membrane) and translocation of organelles (to position various organelles within the cell).
3. The cytoskeletons also function as apparatus for cell motility by crawling movement (filopodia, lamellipodia) on substratum or swimming in aqueous medium through cilia or flagellar movement (microtubules) in single cell animals.
4. Motility: In multi-cellular organism, the contraction of muscles,

movement of sperms, neurons, WBC and phagocytes are some mentions.

5. It forms the most essential component of cell division machinery. Cytoskeletons are responsible for the alignment and separation of Chromatids and subsequent cytokinesis to form daughter cells.

**Structure of cytoskeleton:**

**1- Microtubules:**

**Structure of Microtubule:**

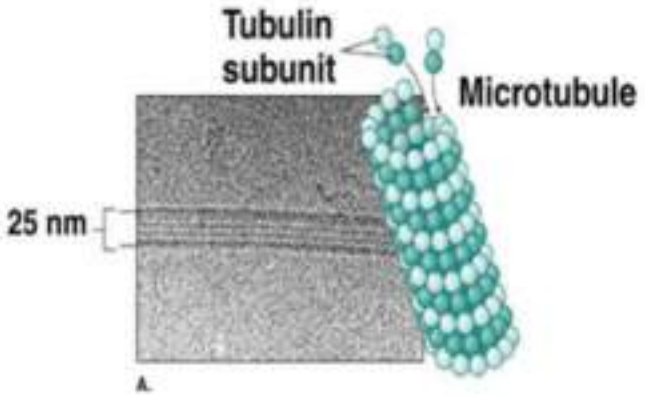



**Figure 61:** Structure of microtubules.

The microtubules are hollow, unbranched cylinders, generally about 200 to 270 Å thick and several micrometers long (the diameter of the microtubule fiber is 25 nm with GTP-αβ tubulin heterodimers as protein subunits (monomers). They may occur singly or in bundles and radiate from the centriole to the periphery of the cell. The microtubule is composed of 13 parallel proto- filaments that run its entire length and enclose a central lumen about 150 Å wide (Figure 61). Each proto filament is made up of a row of globular subunits that have a diameter of about 40to 50 Å. There may be cross bridges between adjacent microtubules.

**Functions of microtubules:**

1. **Form and support-** The microtubules form a part of cytoskeleton which (a) maintains the shape of the cell and (b) provides mechanical support to the cell. This role of microtubules is especially evident in cells having long processes such as the axopodia of certain protozoans and axons of nerve cells. Red blood corpuscles of non-mammalian vertebrates are kept flat by peripheral band microtubules.
2. **Movement-** The microtubules form the motile elements of cilia and flagella. These bring about locomotion in protists and cause currents in the environment of animals.
3. **Components of centriole and basal bodies-** The microtubules are components of centriole and basal bodies. The centriole give rise to the mitotic spindle and the basal bodies produce cilia and flagella.

   **Cilia** are found on many cells of the body, including the epithelial cells that line the airways of the respiratory system. Cilia move rhythmically; they beat constantly, moving waste materials such as dust, mucus, and bacteria upward through the airways, away from the lungs and toward the mouth. Beating cilia on cells in the female fallopian tubes move egg cells from the ovary towards the uterus.

   A **flagellum** (plural = *flagella*) is an appendage larger than a cilium and specialized for cell locomotion. The only flagellated

cell in humans is the sperm cell that must propel itself towards female egg cells.

4. **Formation of mitotic spindle-** The microtubules form the spindle and astral rays in cell division.
5. **Chromosome movement-** The chromosome fibers of spindle bring about movement of the chromosomes to the opposite poles of the cell in the anaphase.
6. **Cell differentiation-** The microtubules play a role in cell differentiation and determination of polarity.
7. **Intracellular transport-** Vesicles and protein molecules in the cell move along the "tracks" of microtubules. The movement is brought about by motor proteins kinesin and MAPIC (cytoplasmic dynin) powered by ATP.

**Importance of Microtubules:**

Microtubules are very important for the cells as they provide internal framework serving as cytoskeleton to determine and maintain the cell form. They also define pathway along which the particles move in cell. The mitotic apparatus consisting of spindle fibers and astral rays is in fact bundles of microtubules. The generation of bending movements in cilia and flagella is attributed to a sliding microtubule mechanism.

## 2- Microfilament:

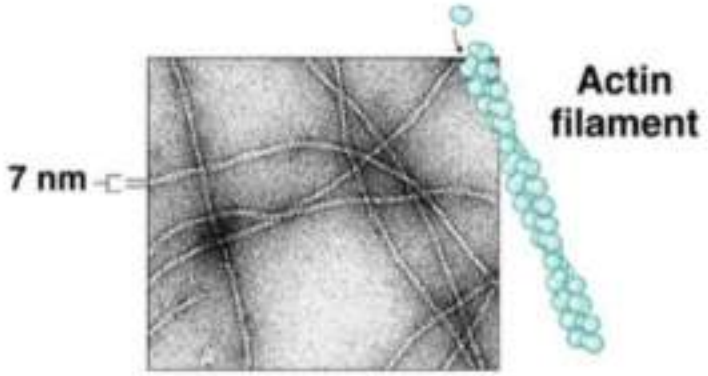



**Figure 62:** Structure of microfilaments.

In contrast with microtubules, the **microfilament** is a thinner type of cytoskeletal filament. The diameter of the microfilament or actin filament is 8 nm with ATP Actin molecules as protein subunits (monomers). (Figure 62). Actin, a protein that forms chains, is the primary component of these microfilaments. Actin fibers, twisted chains of actin filaments, constitute a large component of muscle tissue and, along with the protein myosin, are responsible for muscle contraction. Like microtubules, actin filaments are long chains of single subunits (called actin subunits). In muscle cells, these long actin strands, called thin filaments, are "pulled" by thick filaments of the myosin protein to contract the cell. Actin also has an important role during cell division. When a cell is about to split in half during cell division, actin filaments work with myosin to create a cleavage furrow that eventually splits the cell down the middle, forming two new cells from the original cell. The final cytoskeletal filament is the intermediate filament.

**Functions of microfilaments (Actin filaments):**

1. Membrane endocytosis during phagocytosis.
2. Vesicle transport along ER - GA – PM axis.
3. Locomotion for single cell organism: endoplasmic streaming.
4. Muscle Contraction: filament sliding.
5. Cytokinesis during cell division.

**3- Intermediate filament:**

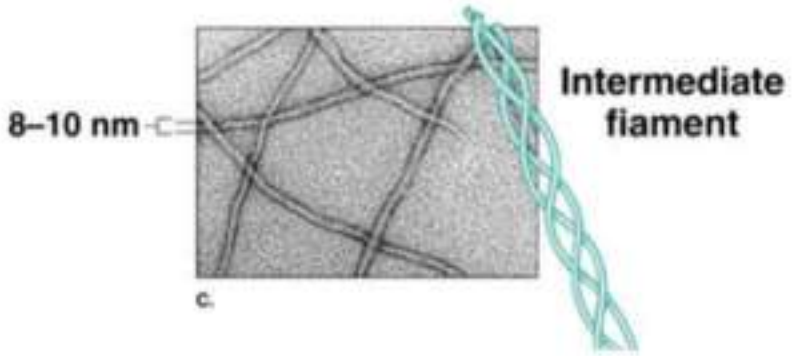



**Figure 63:** Structure of intermediate filaments.

As its name would suggest, an **intermediate filament** is a filament intermediate in thickness between the microtubules and microfilaments. The diameter of the intermediate filaments is 10-12 nm (Figure 63). Intermediate filaments are made up of long fibrous subunits of a protein called keratin that are wound together like the threads that compose a rope. Intermediate filaments, in concert with the microtubules, are important for maintaining cell shape and structure. Unlike the microtubules, which resist compression, intermediate filaments resist tension the forces that pull apart cells. There are many cases in which cells are prone to tension, such as when epithelial cells of the skin are compressed, tugging them in different directions.

Intermediate filaments help anchor organelles together within a cell and link cells to other cells by forming special cell-to-cell junctions.

**Functions of Intermediate filaments:**

1- Membrane mechanical support (nucleus inner membrane lined with Lamin A and C) and organizes nuclear content.
2- In cytosol, they form internal framework that supports the cell and add resilience of the cell.
3- They form the connecting network for cell attachment to their extra cellular matrix through hemidesmosomes and cell-cell adhesion through desmosomes.
4- They form the interconnecting link between cytoskeletons.

# CENTRIOLES

**History:** Van Benden in 1880 discovered centrosome in cells of certain parasites of cephalopods. Centrosome is the area of cytoplasm, often a clear zone, around the centriole. It is found lying in the center of the cell, near the nucleus, in the cytoplasm. In Metazoa, centrosome lies outside the nucleus, but in Protozoa it lies within the nucleus. It is lacking in some plant cells. T. Boveri in 1888 described centrosome in detail.

The substance of centrosome also called **kinoplasm** consists of two parts: smaller bodies or centrioles & Surrounding mass or centrosphere.

**Structure of Centriole:**

The centrioles usually occur as paired hollow cylinders which are about 0.2 nm in diameter and 0.3 to 0.5 nm in length. The two centrioles usually lie at right angles to each other.

The centriole is composed of nine sets of microtubules triplets arranged in a ring and embedded in a dense granular or amorphous, electron dense matrix (Figure 64, 65). There are no microtubules at the center of the ring giving the "9+0" pattern for the centriole. Each microtubule in a triplet is about 250Å wide. The triplets are tilted in such a way that each forms an angle of about 30 to 40° to the circumference of the cylinder, with the A sub tubule of each set nearest the center of the ring. Membrane around the centrioles is absent. Sometimes a granular disc, called satellites, appears around centriole.

All the triplets of centriole are similar and indistinguishable from one another. The three microtubules often called sub-tubules, of a triplet

are named A, B and C, beginning from the inside of the cylinder. A dense strand called A-C linker, connects the A sub-tubule of each triplet to the C sub-tubule of the adjacent triplet. These A-C linkers cause the tilt of the triplets from the radii of the cylinder. A fine radial fiber or spoke joins each A sub-tubule to the central hub of the cylinder. Each radial fiber has a dense thickening, the foot, near the A sub-tubule. This "cart-wheel" configuration though not always presents and when present it is often confined to the denser proximal end of the centriole. The C sub-tubules stop short of near upper ends and the peripheral tubules become doublet. B and C sub-tubules are C- shaped and their wall is completed by adjacent sub-tubules. Only 'A' sub-tubules are complete. The wall of 'A' sub-tubule is composed of 13 parallel proto-filaments which are made up of a row of □-□ tubulin dimers. A few proto-filaments are shared with the B-sub-tubule, which, in turn, shares a few of its proto-filaments with the C sub-tubule. Nine amorphous shapes of electron dense material with poorly defined outer limits are present around the centriole. These are called pericentriolar satellites (Figure 64, 65).

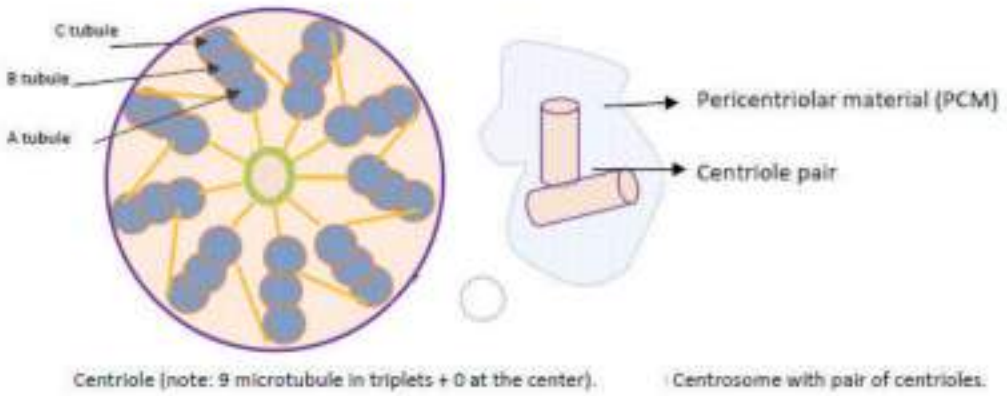



**Figure 64:** The centriole structure.

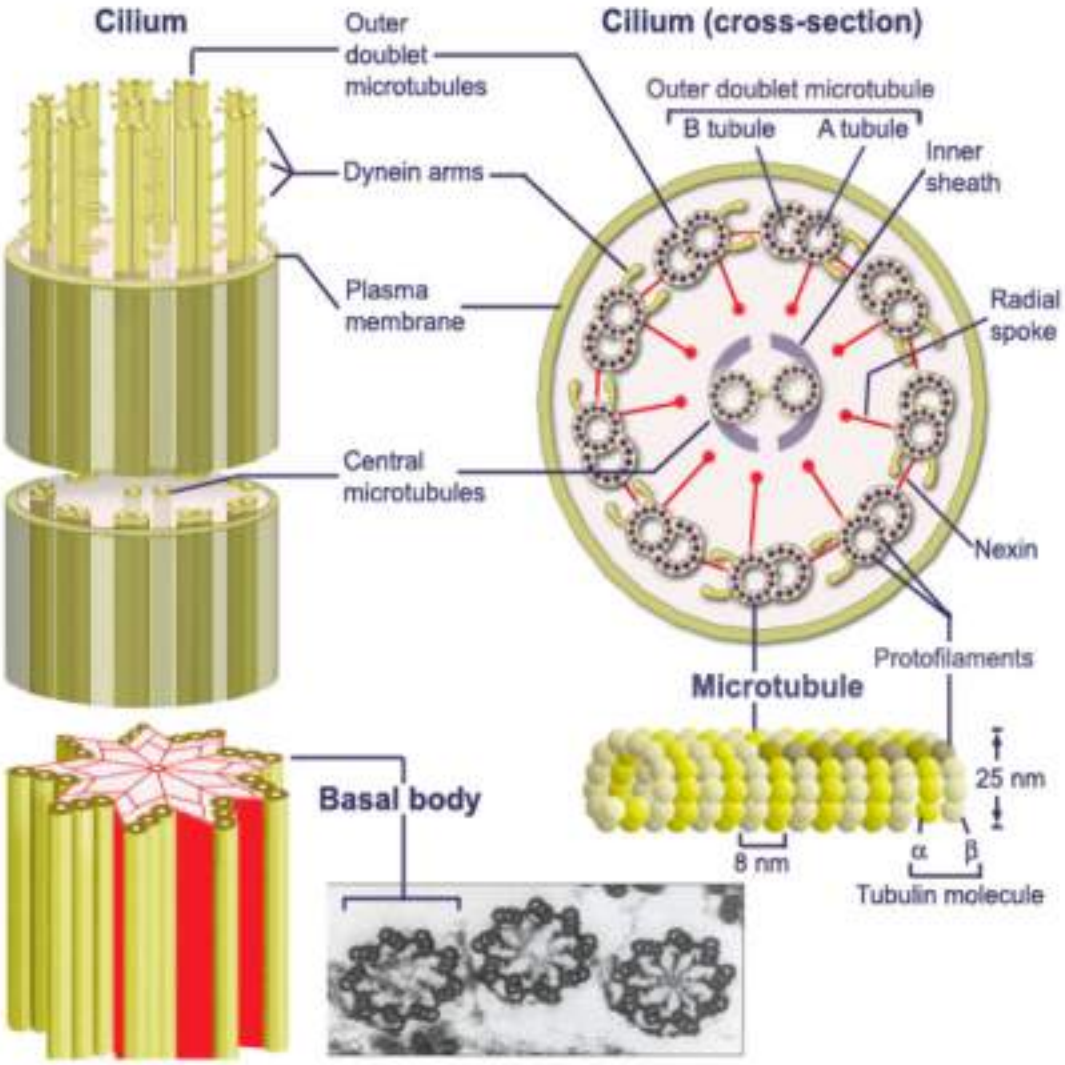



**Figure 65:** T.S. Centriole, cilium, and microtubule (showing faint 'cartwheel' pattern of fibrils).

## Chemical Composition:

The microtubule of the centriole is composed of a protein tubulin and some lipids having a high concentration of ATPase enzymes. They seem to contain RNA and a small DNA molecule. Proteins encoded by this DNA are presumably translated on cytosolic ribosomes and then incorporated into the centriole.

**Functions of Centriole:**

The centriole serves the following functions:

(i) They help in organizing spindle fibers and astral rays during mitosis and meiosis.

(ii) They provide basal bodies giving rise to cilia and flagella.

(iii)Pericentriolar material acts at the MTOC (microtubule organizing center) for thecytoplasmic microtubules.

**Importance of Centriole:**

Centriole is involved in the formation of spindle and astral rays which are responsible for the chromosomal movements during cell division. Also, centrioles give rise to basal bodies (kinetosome) or cilia or flagella.

# NUCLEUS

**History:** Nucleus was observed by a Dutch Microscopist, Antonie van Leeuwenhoek in 1710,as a centrally placed clear area in the blood cells of amphibians and birds. Fontana (1781) recorded an ovoid structure in each of the isolated epidermal cells of eel's skin. However, Robert Brown (1831) was the first to use the term nucleus for a prominent body present in the orchid cell. He stated that nucleus was the regular feature of the cells and initiated the concept of nucleated cells.

## Structure of Nucleus:

The nucleus consists of various parts. It is bounded by a thin but clearly defined covering, the **nuclear envelop** or karyotheca. Within the envelope is a clear fluid substance called **nucleoplasm** or nuclear sap or karyolymph is present in which the solutes of the nucleus are dissolved. Suspended in the nucleoplasm are network of protein-containing fibrils called **nuclear matrix**; fine intermingled nucleoprotein filaments collectively referred to as thechromatin; and one or more spherical bodies known as nucleoli (singular, nucleolus). There are no membranes or microtubules inside the nucleus (Figure 66)

- **Chemical Composition:** The nucleus is composed of about 9-12% DNA, 5% RNA, 3% lipids, 15% simple basic proteins such as histone or protamines, about 65% complex acid or neutral proteins, including enzymes such as polymerases for the synthesis of DNA and RNA, organic phosphates and inorganic salts or ions such as $Mg^{++}$, $Ca^{++}$ and $Fe^{++}$.

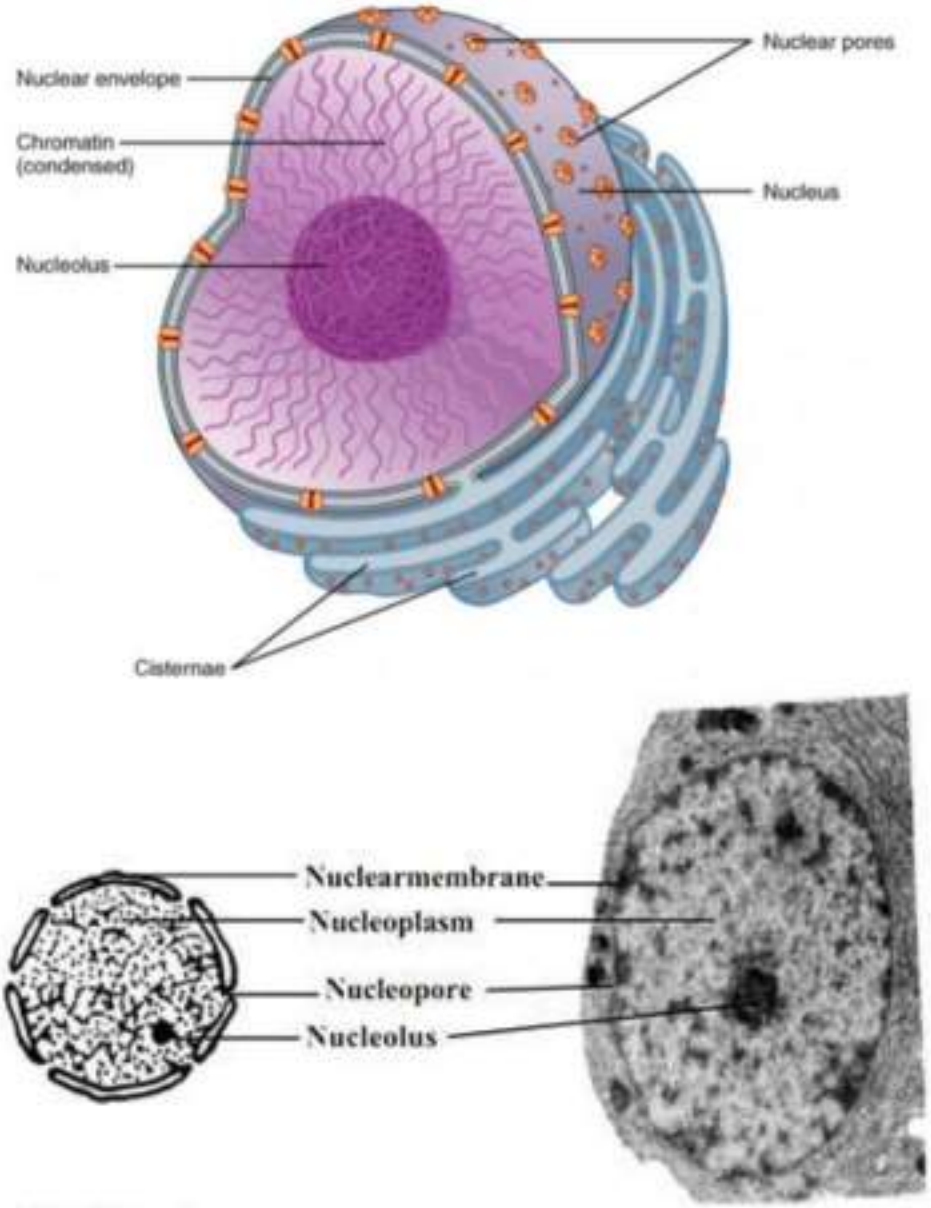



**Figure 66:** The Nucleus.

- **Functions:** The nucleus acts as a control center of the cell. It serves the following main functions:
  - It maintains the cell by directing the synthesis of structural proteins.
  - It regulates cell metabolism by directing the synthesis of enzymatic proteins.

- It contains genetic information for reproduction, development and behavior of the organism besides for structure and metabolism.
- It brings about cell replication when needed.
- It is the site for the formation of ribosome subunits.
- It brings about cell differentiation by keeping only certain genes operational.
- It develops genetic variations that result in evolution

## I- Nuclear Envelope:

The nuclear envelop separates the nucleoplasm from the cytoplasm. It consists of two-unit membranes: outer and inner. Each unit membrane is about 75Å thick and is a trilaminar lipoprotein like the plasma membrane. The two-unit membranes are separated by a space called the inter membrane or perinuclear space. It is about 250Å wide. The outer or cytoplasmic surface of the outer membrane is studded with ribosomes and polysomes and is rough. These ribosomes carry on protein synthesis. The outer membrane is continuous with RER at certain places. Thus, the perinuclear space is continuous with the channels of theRER. The inner membrane of the nuclear envelope is free of ribosomes, but has a dense layer, the nuclear lamina, closely associated with its inner or nucleoplasmic surface. The nuclear lamina is a 30 to 100 nm thick network of filaments composed of proteins named lamina A, B and C. The nuclear lamina supports the inner membrane and gives shape to it. It connects chromatin to the inner membrane, keeping most of the chromosomes in the periphery of the

nucleus. It also plays a role in the breakdown and reformation of nuclear envelope during mitosis (Figure 67).

**Nuclear Pores:** The nuclear envelope is generally perforated by minute apertures, the nuclear pores that control the passage of some molecules and particles. The pores are formed by fusion of the inner and outer membranes of the nuclear envelope. There may be 1000 to 10,000 pores per nucleus.

Each nuclear pore is fitted with an apparatus called the **pore complex** which fills considerable part of the pore. The pore complex is nearly cylindrical, projects into both cytoplasm and nucleoplasm, and projects beyond the rim of the pore over the nuclear envelope. The pore complex consists of two rings, the annuli, one located at the cytoplasmic rim of the pore and the other at the nucleoplasmic rim. Each annulus comprises eightsymmetrically arranged subunits and sends a spoke into the pore. The spoke encloses a channel about 100 to 200 Å wide. Ions and small molecules of the size of monosaccharide, disaccharides or amino acids pass freely between the nucleus and cytoplasm. The pore complexes do control the passage of larger molecules, such as RNA and proteins, and of ribosomal subunits. The pore complexes also act as a barrier to some molecules such as DNAof chromosomes.

**Functions:**

- It maintains the shape of the nucleus.
- It keeps the nuclear contents in place and distinct from cytoplasm.
- It regulates the flow of materials into and out of the nucleus by active transport andout pocketing.

- Its pores allow the exit of ribosomal subunits formed in the nucleolus and tRNA andmRNA synthesized on the chromosomes.

**II- Nucleoplasm:**

Nucleoplasm is a transparent fluid material in the nucleus. The chromatin fibers and nucleoli are suspended in it. It contains raw materials (nucleotides), enzymes (polymerases) and metal ions ($Mn^{++}$, $Mg^{++}$) for the synthesis of DNA and RNA. It also contains proteins and lipids. The proteins include basic histones and acidic or neutral non-histones that associate with the DNA molecules. There are proteins for the formation of ribosomal subunits also. The RNAs (rRNAs, tRNAs, mRNAs) and ribosomal subunits synthesized in the nucleoplasm pass into the cytoplasm via nuclear pores (Figure 67).

**Functions:**

- It is the seat for the synthesis of DNA, RNAs, ribosomal subunits, ATP, and NAD.
- It supports the nuclear matrix, chromatin material and nucleoli.
- It provides turgidity to the nucleus

**III- Nuclear Matrix:**

The nuclear matrix is a network of thin, criss-crossing, protein-containing fibrils that are connected at their ends to the nuclear envelope. It forms a sort of nuclear skeleton. It remains intact after the chromatin and DNA have been removed.

**Functions:**

- It maintains the shape of the nucleus.
- Chromatin fibers are anchored to nuclear matrix.
- The machinery for various nuclear activities, such as transcription and replication, isassociated with the matrix.
- It has also been implicated in the processing of newly formed RNA molecules andtheir transport through the nucleus.

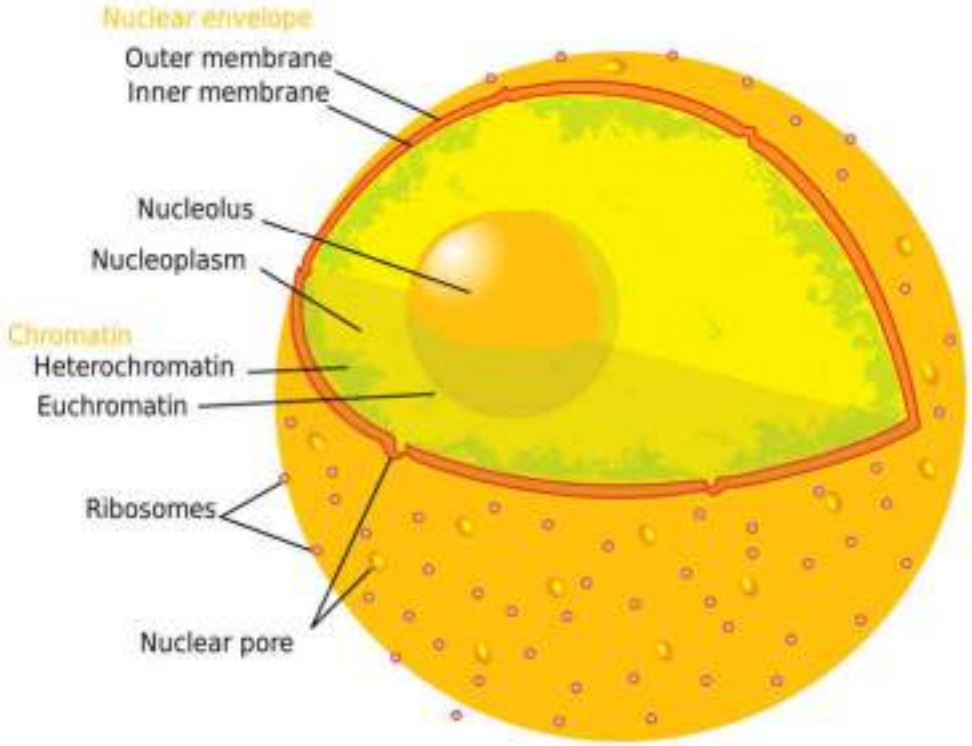



**Figure 67:** The nuclear structures.

## IV- Chromatin:

The term chromatin was first coined **by Flemming in 1879.** The chromatin occurs in an interphase (non-dividing) nucleus as fine filaments, the **chromatin fibers**. The fibers lie criss-cross to give the appearance of a diffuse network often referred to as the nuclear or chromatin reticulum. The chromatin occupies most of the nucleus. The chromatin fibers are simply extremely extended chromosomes. A chromatin fiber is normally about 100Å in diameter. A fiber thicker than 100Å appears to be coiled or folded, a fiber thinner than 100Å seems to have less protein content associated with it. Chromatin fibers typically appear approximately 250Å in diameter. During cell division, the chromatin fibers, by condensing and tight coiling, form short, thick, rod like bodies known as **chromosomes.**

Upon staining, this diffuse network of chromatin material shows light stained and dark stained areas. After cell division, the chromosomes change back into chromatin fibers. Most of the chromatin fibers become uncoiled, extended, and scattered in the nucleoplasm. These represent the **euchromatin** (true chromatin) of the interphase nucleus. They are stainedlightly.

The term **heterochromatin** is applied to those chromosomal regions that stain darker than others. They remain coiled and compacted in the interphase too. Heterochromatin represents relatively inactive parts of the chromosomes. It contains less DNA and more RNA than the euchromatin. Few mutations occur in this region. Little or no mRNA is synthesized here. Most of the DNA in heterochromatin is highly

repeated DNA, which is never, or very seldom, transcribed. Heterochromatin is of two types: **constitutive and facultative**. The DNA of constitutive heterochromatin is permanently always inactivated and remains in the condensed state. It occurs at several places: adjacent to the centromere of the chromosome, at the ends (telomeres) of the chromosomes, at certain portions within the euchromatin, and adjacent to the nuclear envelope. Facultative heterochromatin is partly condensed and inactivated. **One X-chromosome in female mammals is condensed to form the heterochromatic Barr body.**

**Nucleosomes:** In 1974, Kornberg and Thomas proposed that a chromatin fiber is a chain of similar subunits called nucleosomes (Figure 68). The nucleosome consists of a core particle wrapped by DNA strand. The core particle is an octamer of **8 histone molecules**, twoeach of the histones H2A, H2B, H3 and H4. The DNA strand forms 1½ or 1¾ turns around the core and consists of 140 nucleotides. Each nucleosome is connected to the next by a short DNA linker of 60 nucleotides. A nucleosome and a linker together have a total average length of 200 nucleotides and are together referred to as a chromatosome. A molecule of histone H1 is associated with each DNA linker, and it serves to pack nucleosomes together. Thus, a chromatin fiber is a chain of beads, a bead (nucleosome) is about 100Å wide and DNA linker is about 140Å long. Nucleosomes represent the lowest level of chromatin organization.Chromatin fiber appears about 250Å thick in electron micrographs. which suggests that the 100Å thick

chromatin fiber is either packed into a spiral or solenoids, containing 6 nucleosomes per turn or 6 nucleosomes are organized into a cluster, or super bead, thereby increasing the DNA packing by 5 folds. The thicker filament is maintained by H1 histone protein. The non-histone proteins do not occur in the nucleosome structure of chromatin. Nucleosomes are not formed in prokaryotes.

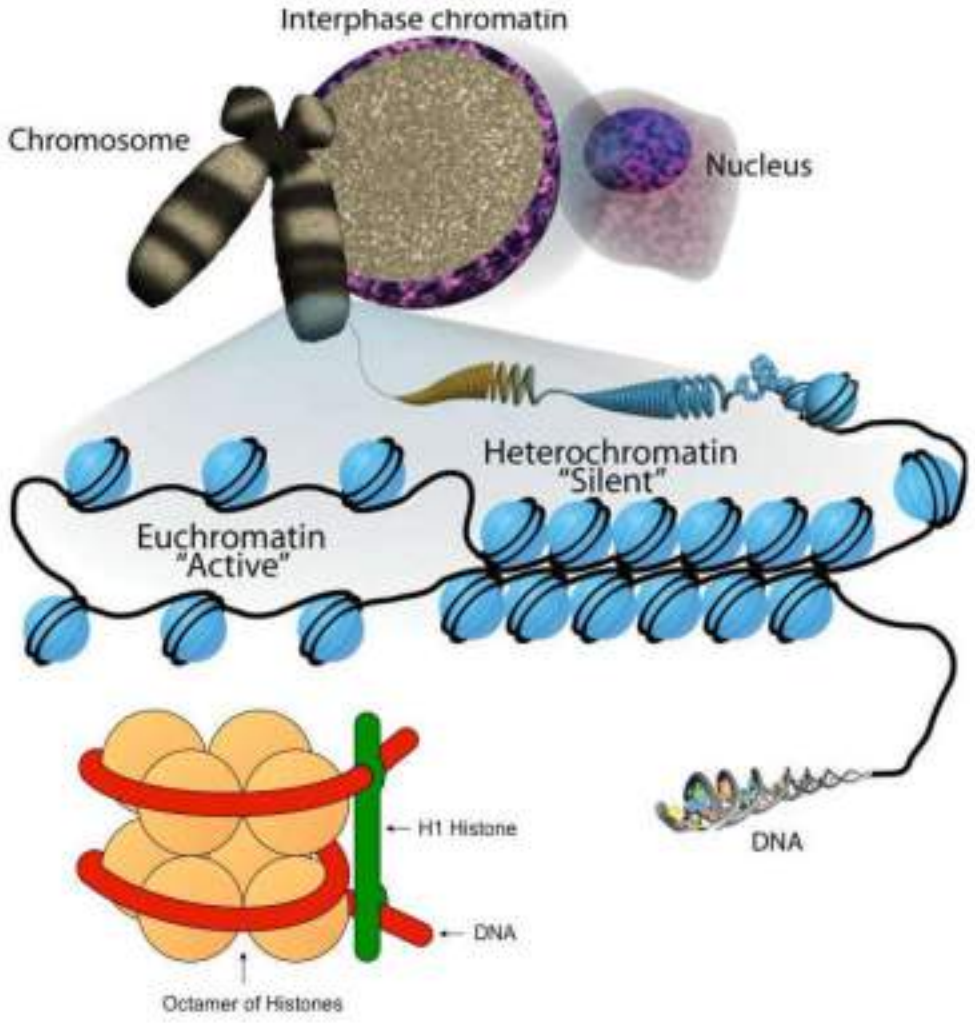



**Figure 68:** Chromatin and Nucleosome.

## Function:

The chromatin fibers form chromosomes during cell division.

## V- Nucleolus (Little Nucleus):

The nucleolus was discovered in 1781 by F. Fontana in the slime from the eel skin. It is present in the nucleus of most cells, but is inconspicuous or absent in sperm cells and in muscle cells. It is usually spherical but may have other forms. The number of nucleoli in a nucleus varies in different species. The nucleoli disappear during cell division, and are reformed at specific sites, the nucleolar organizers or nucleolar organizer regions (NORs), of certain chromosomes, the nucleolar chromosomes, at the end of cell division before the chromosomes become diffuse. Position of the nucleolus in the nucleus is often eccentric. However, it occupies a specific position on its chromosome.

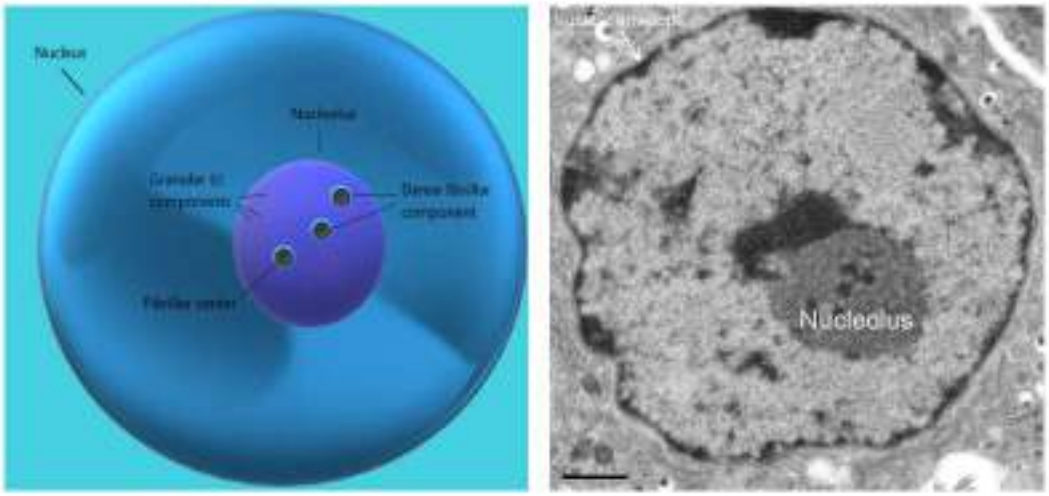



**Figure 69:** Nucleolus diagram and ultrastructure

The nucleolus (Figure 69) is a dense, somewhat rounded, dark staining organelle. It is without a limiting membrane. Calcium ions keep it intact. It consists of four regions.

1. Fibrillar Region or Nucleolonema- It contains indistinct fibrils about 50-100Å in diameter. The fibrils represent the long rRNA

precursor molecules in early stages of processing before the processing enzymes have cut off segments from them.

2. Granular Region- It contains spherical, electron dense particles, about 150-200 Å in diameter and with fizzy outline. The granules are ribosomal subunits (rRNA + ribosomal proteins) that are nearly ready for transport to the cytoplasm.
3. Amorphous Region or Pars Amorpha- It is a structure-less proteinaceous matrix in which the granular and fibrillar regions are suspended.
4. Nucleolar Chromatin- It consists of 100 Å thick chromatin fibers. The latter are a part of the nucleolar chromosome which follows a tortuous path through the granular and fibrillar components of the nucleolus. This part contains many copies of DNA that directs the synthesis of ribosomal RNA. The rest of the nucleolar chromosome lies in the nucleoplasm.

**Functions of Nucleus:**

- The nucleolus synthesizes and stores rRNA.
- It also stores ribosomal proteins received from the cytoplasm.
- It forms ribosomal subunits by wrapping the rRNA by ribosomal proteins. The ribosomal subunits pass out through the nuclear pores into the cytoplasm. Here the subunits join to form ribosomes when needed. Thus, it is the nucleolus which provides machinery (ribosomes) for protein synthesis.
- The nucleolus also plays a role in cell division.

**Importance of Nucleus:**

The nucleus is the control center of a cell. It regulates all metabolic activities of the cell and stores entire hereditary information. A cell without nucleus cannot survive.

**Organization of the Nucleus and Its DNA (Figure 70):**

Like most other cellular organelles, the nucleus is surrounded by a membrane called the **nuclear envelope**. This membranous covering consists of two adjacent lipid bilayers with a thin fluid space in between them. Spanning these two bilayers are nuclear pores. A **nuclear pore** is a tiny passageway for the passage of proteins, RNA, and solutes between the nucleus and the cytoplasm. Proteins called pore complexes lining the nuclear pores regulate the passage of materials into and out of the nucleus.

Inside the nuclear envelope is a gel-like nucleoplasm with solutes that include the building blocks of nucleic acids. There also can be a dark-staining mass often visible under a simple light microscope, called a **nucleolus** (plural = *nucleoli*). The nucleolus is a region of the nucleus that is responsible for manufacturing the RNA necessary for construction of ribosomes. The genetic instructions that are used to build and maintain an organism are arranged in an orderly manner in strands of DNA. Within the nucleus are threads of **chromatin** composed of DNA and associated proteins (Figure 3). Along the chromatin threads, the DNA is wrapped around a set of **histone** proteins. A **nucleosome** is a single, wrapped DNA histone complex. Multiple nucleosomes along the entire molecule of DNA appear like a

beaded necklace, in which the string is the DNA, and the beads are the associated histones. When a cell is in the process of division, the chromatin condenses into chromosomes, so that the DNA can be safely transported to the "daughter cells." The **chromosome** is composed of DNA and proteins; it is the condensed form of chromatin. It is estimated that humans have almost 22,000 genes distributed on 46 chromosomes

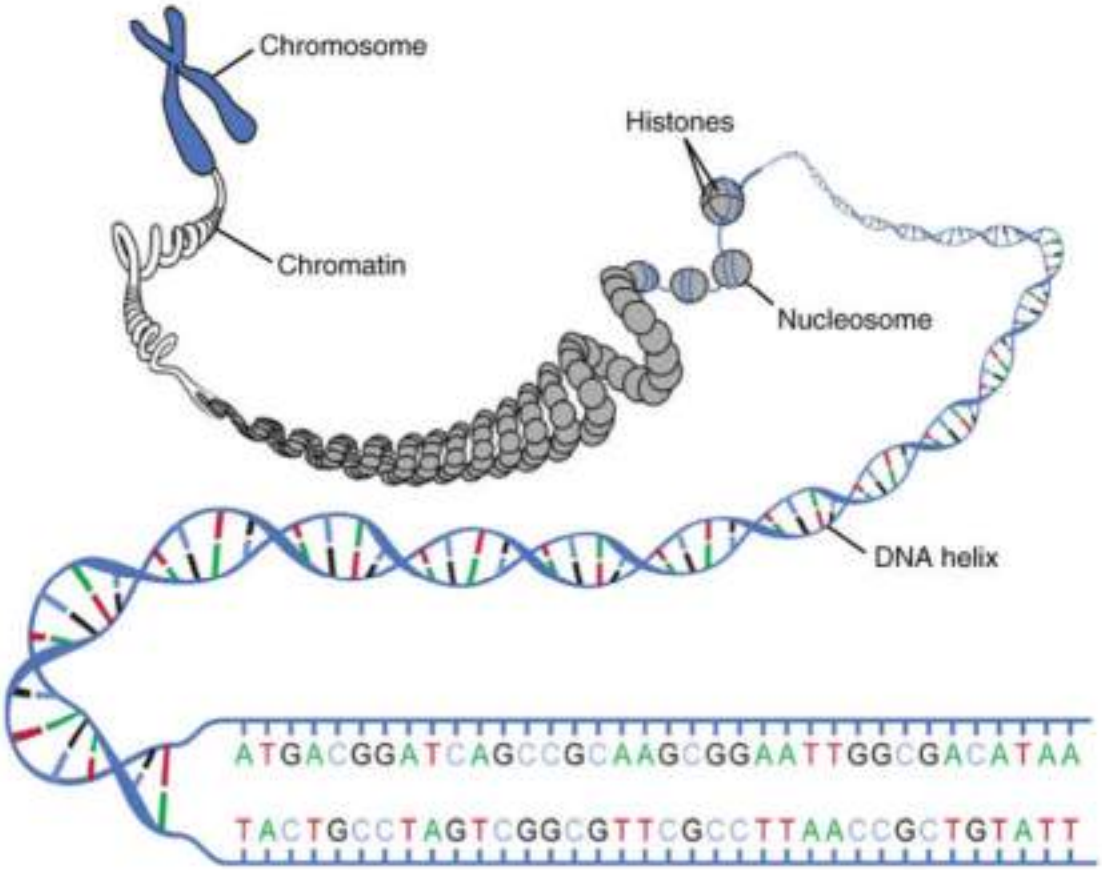



**Figure 70:** DNA Macrostructure. Strands of DNA are wrapped around supporting histones. These proteins are increasingly bundled and condensed into chromatin, which is packed tightly into chromosomes when the cell is ready to divide. Once synthesized, newly made ribosomal subunits exit the cell's nucleus through the nuclear pores.

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## CHROMOSOMES

**History:** W. Hofmeister in 1848, discovered nuclear filaments in the nuclei of pollen mother cells of *Tradescantia*. First accurate count of chromosomes was made by W. Flemming in 1882, in the nucleus of a cell. In 1884, W. Flemming, Evan Beneden and E. Strasburger demonstrated that the chromosomes double in number by longitudinal division during mitosis. Beneden in 1887 found that the number of chromosomes for each species was constant. The term "Chromosomes" was coined in 1888 by W. Waldeyer for the nuclear filaments. W.S. Sutton and T. Boveri suggested the role of chromosomes in heredity in 1902, which confirmed by Morgan in 1933.

**The structure of chromosomes varies in viruses, prokaryotes and eukaryotes as follows:**

A. **Viral chromosome-** In viruses there is a single chromosome bearing a single nucleic acid molecule (DNA or RNA) surrounded by a protein coat called Capsid. It may be linear or circular. The viruses having DNA as genetic material are called DNA viruses and those having RNA as genetic material are known as RNA viruses. A limited amount of genetic information is present in the viral chromosome which codes for little more than the production of more virus particles of the same kind in the host cell. In RNA viruses, often the RNA directs the synthesis of DNA complementary to itself by reverse transcription in the host. The RNA is then transcribed by the DNA for the formation of new virus particles. Such ribovirus is called

retrovirus. TheAIDS causing virus is a retrovirus.

B. **Prokaryotic chromosomes-** Prokaryotic chromosome (e.g., bacteria) has asingle and circular two-stranded DNA molecule which is not enveloped by any membrane. It lacks proteins and is in direct contact with the cytoplasm. The bacterial chromosome is packed into the nucleoid by some RNA that appears to form a core. It is attached to plasma membrane permanently at least at one point. In addition to the main chromosome some extra-chromosomal DNA molecules may also be present in most of the bacterial cells they are also double stranded and circular, but are much smaller in size. They are known as plasmids. The plasmid may occur independently in the cytoplasm of calls or may also be found in association of main chromosomal DNA and called as episome.

C. **Eukaryotic chromosomes-** The eukaryotic chromosomes are present in nucleus and in certain other organelles, like mitochondria and plastids. These chromosomes are called nuclear and extra nuclear chromosomes respectively.

Nuclear chromosomes are double stranded long DNA molecules of linear form. Proteins are associated with them. They are surrounded by nuclear envelope. More DNA isinvolved in coding far more proteins than the prokaryotic chromosomes.

Extra nuclear chromosomes are present in mitochondria and plastids. They are double stranded short DNA molecules of circular form. They lack protein association. Less genetic information is available for the

synthesis of only some particles of proteins for the organelles containing them. Other proteins are received from the cytoplasm where they are synthesized under the direction of nuclear chromosomes.

## Morphology of Chromosomes:

During the interphase stage, the eukaryotic chromosomes are extended into long and thin chromatin fibers where they lie criss-cross to form the **chromatin reticulum**. They replicate in the S-phase and become double. At this stage they consist of two chromatids that are held together at one point called **centromere** (Figure 71). At the time of cell division, the chromosomes condense and tightly coil up and become distinct at metaphase stage. The eukaryotic chromosomes vary in number, size, shape and position but they have remarkably uniform structure.

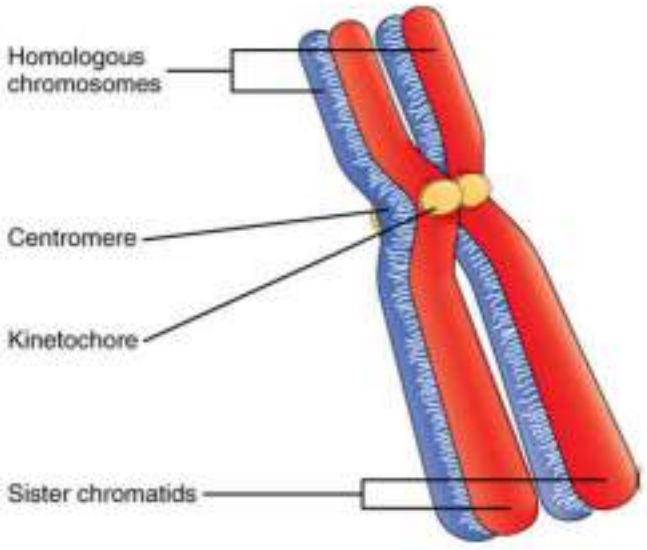


**Figure 71**: A Homologous Pair of Chromosomes with their Attached Sister Chromatids. The red and blue colors correspond to a homologous pair of chromosomes. Each member of the pair was separately inherited from one parent. Each chromosome in the homologous pair is also bound to an identical sister chromatid, which is produced by DNA replication, and results in the "X" shape.

1. **Number:** Eukaryotic chromosomes vary in number from two to a few hundred in different species. In a species all the individuals have same number of chromosomesin all of their cells, except the gametes. Since the chromosome number is constant for a species, it is helpful in determining and taxonomic position of thespecies.
2. **Size:** In a **species all the chromosomes are not of the same size.** Their size also varies from species to species. The particular chromosome of a species however has more or less a constant size. The organisms having fewer chromosomes have large sized chromosomes than those having many. Generally, plant chromosomes are larger than animal chromosomes and among plants the monocots have larger chromosomes than the dicots.
3. **Shape:** The chromosomes at metaphase stage look like slender rods that may be straight or curved to form an arc or a letter S. In anaphase stage they may assume J or V shapes, depending upon the position of the centromere.
4. **Position:** In a nucleus each chromosome is independent of all the other chromosomes in its location. Thus, they may occupy any region of the nucleus.
5. **Structure:** At **metaphase stage**, since the chromosome is a highly condensed nucleoprotein filament, it contains two greatly coiled sister chromatids. These chromatids that lie side by side along their length, are held together at a point called centromere, an area of the narrow region also called **primary constriction** of the metaphase chromosome. At the centromere each chromatid has a darkly staining, disc like, fibrous structure, called **kinetochore**, to which

spindle microtubules attach during cell division. Kinetochores are the sites where force is exerted to pull the chromatids towards the poles. One or more chromosomes may have additional narrow regions called the **secondary constrictions**. The part of the chromosome separated by secondary constrictions is termed as **satellite**. A chromosome with a satellite is called **sat chromosome**. The size and the shape of the satellite remain constant for a species. Secondary constrictions are associated with the nucleoli and are known as the **nucleolar organizers**. The chromosomes which have nucleolar organizing regions are known as the **nucleolar chromosomes** (Figure 72).

**Ends-** The ends of chromosomes are called **telomeres**. The function of telomere varies from the rest of the chromosome. On exposure to X-rays a chromosome may break and its pieces may rejoin, but no segment connects to the telomere, showing that the telomere has a polarity, and it, somehow "seals" the end (Fig. 7.1).

6. **Ultra-structure:** A chromatid contains a very fine filament called chromonema which is a single, long, double stranded DNA molecule. It is wrapped around histones to form **nucleosomes**. The nucleosome and non-histone proteins together form the chromatin fiber. The chromatin fiber has reactive groups, probably H1 histone molecules, which act as "folders" and crosslink the chromatin fiber changing it into a great coiled, compact metaphase chromatid.
7. **Chemical composition:** The chromatin in the eukaryotic chromosome consists chemically of about 35% DNA, about 60% proteins, about 5% RNA, some metal ions and certain enzymes.

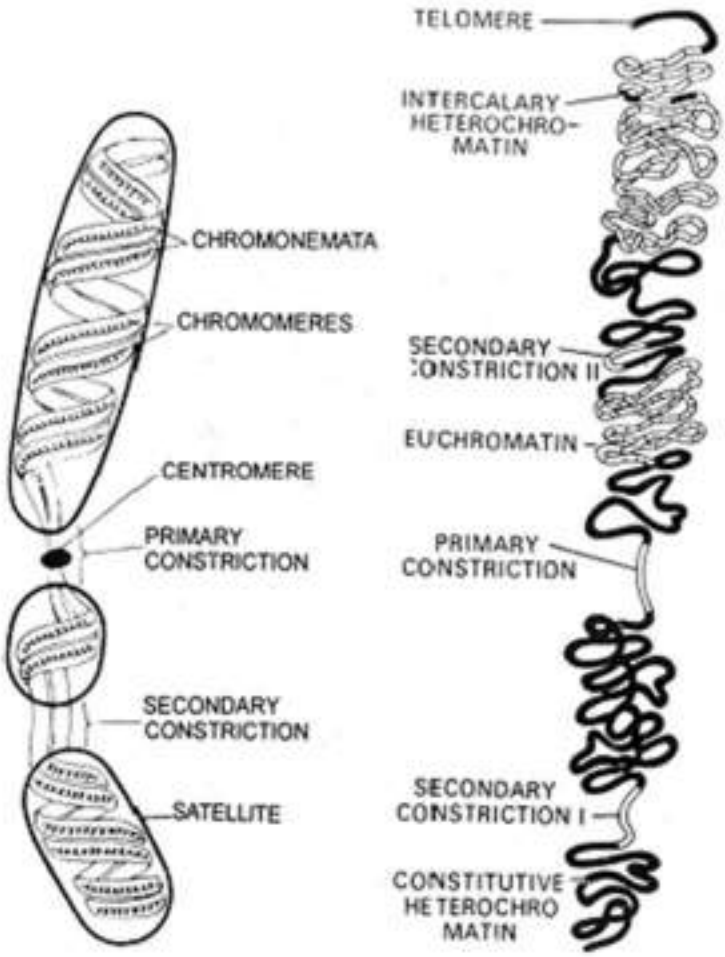


**Figure 72:** Detailed schematic structure of chromosomes.

**8- Types of chromosomes:** On the basis of the position and number of centromeres, chromosomes are classified as below (Figure 73):

**(i) Metacentric:** In metacentric chromosomes the centromere is at the middle of the chromosome, and the arms are equal. In anaphase the chromosome appears V-shaped. For example: human chromosome no. 3

**(ii) Submetacentric:.** In such chromosome, the centromere is near the center of the chromosome, and the arms are slightly unequal and in anaphase the chromosome appears J or L shaped. For

example: Human chromosome No. 1.

**(iii) Acrocentric:** In this type the centromere is near one end of the chromosome, and the arms are very unequal. For example: Human chromosome No. 4 & 5.

**(iv) Telocentric:** The centromere is at one end in such chromosomes, and the arms are on one side only. The chromosome remains rod shaped in anaphase also

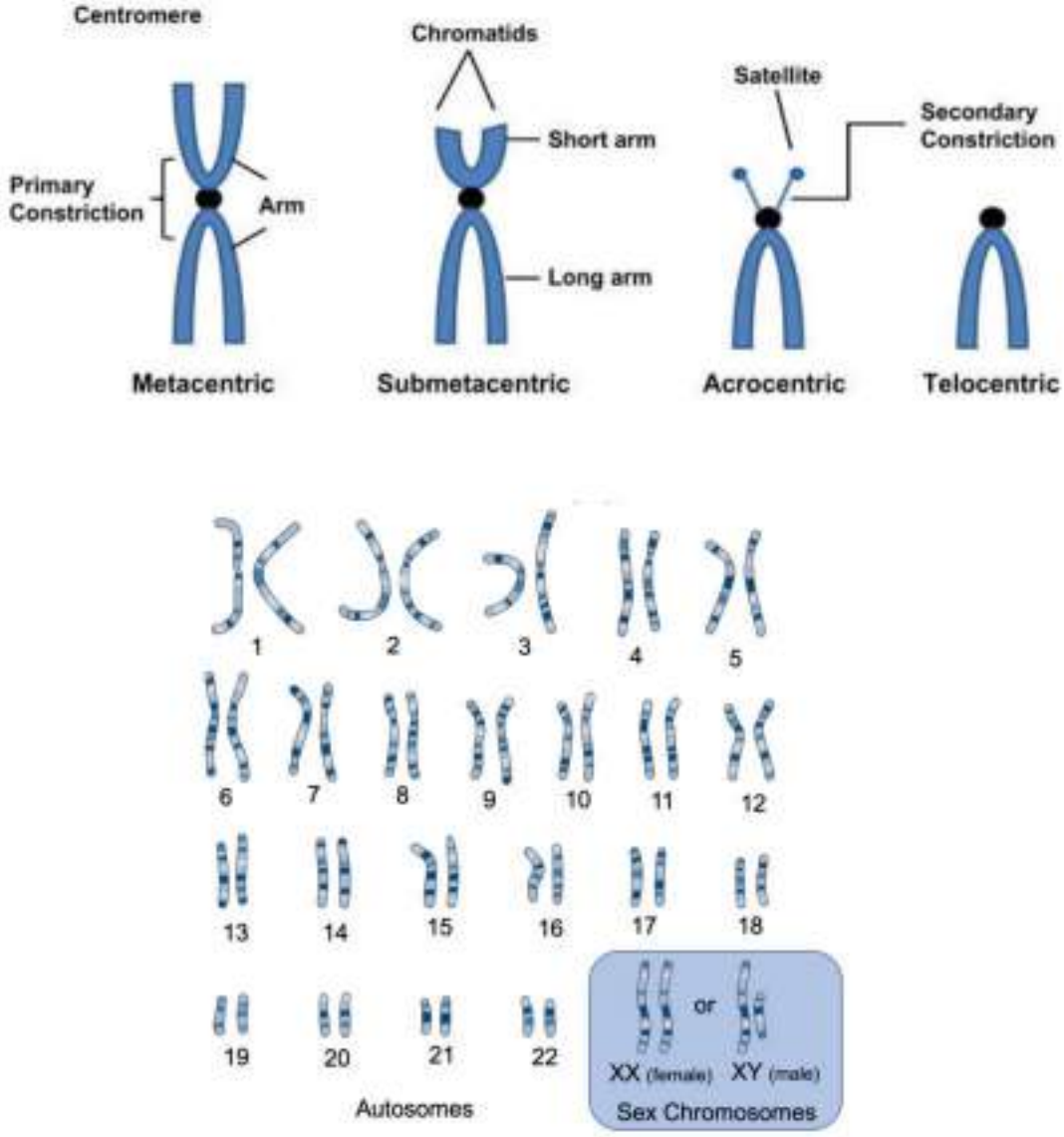


**Figure 73:** Types of chromosomes based on the position and number of centromeres and normal human karyotype.

**Depending upon the number of centromeres there are three types of chromosomes:**

(i) **Acentric:** The chromosome is without a centromere, which is formed by breakage of the chromosome. It does not attach to spindle microtubules, so it is lost in the cell division.

(ii) **Monocentric:** It is the chromosome with a single centromere, and it is the most common type.

(iv) **Dicentric:** It is the chromosome with two centromeres and is formed by the fusion of two chromosome segments each having a centromere. It is unstable and may break when the two centromeres are pulled to opposite poles in mitosis.

**Functions of Chromosomes:**

1- Chromosomes carry hereditary characters from parents to offspring.

2- They direct the synthesis of structural proteins and thus, help the cell grow, and divide.

3- By directing the formation of necessary enzymes, they control metabolism.

4- They guide cell differentiation during development.

5- They form nucleoli at nucleolar organizer sites in daughter cells.

6- They produce variations through changes in their genes and contribute to theevolution of the organisms.

7- They play role in sex determination.

8- They maintain the continuity of life by replication.

## Giant Chromosomes:

Giant chromosomes are special, enormously enlarged chromosomes about 100 times thicker than the ordinary mitotic chromosomes. These are seen in certain tissues of varied groups of animals and plants. They are easily visible under light microscope. The giant chromosomes are of two types: polytene and lampbrush.

### (A) Polytene Chromosomes:

Polytene chromosomes were first observed by **Balbiani** (1881) in **Chironomus** (a dipteran larva). Because of their large size showing numerous strands these are named as polytene chromosomes by **Kollar**. These banded chromosomes occur in the larval salivary glands (**salivary gland chromosomes**), midgut epithelium, and rectum and Malpighian tubules of various genera of dipterans.(Figure 74).

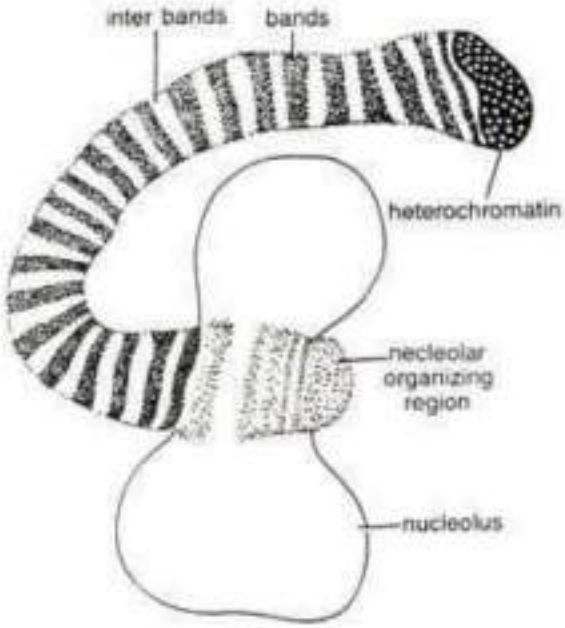


**Figure 74:** Structure of polytene chromosome showing nucleolar part.

These chromosomes are about 100-200 times larger than those of somatic chromosomes. They are roughly cylindrical and exhibit a distinct pattern of transverse striated structures consisting of alternate **darkly staining band** and **light staining interbands**. Dark bands are rich in DNA along with a small amount of RNA and basic proteins. They are genetically active. The inter-bands contain less of DNA but more acidic proteins and hence they are less active. The polytene chromosomes are formed by repeated replication of DNA without division of chromosome into daughter chromosomes. This amplification without separation is called **polytenization**. As a result, a thick bundle of parallel DNA molecules all having the same banding pattern across them is produced. Thus, there can be as many as several thousands of chromonemata in a giant chromosome.

**Functions of the Giant Polytene Chromosomes:**

- Polytene chromosomes carry genes which ultimately control physiology of an organism. These genes are formed of DNA molecules.
- These chromosomes also help in protein synthesis indirectly. The RNA present in the nucleolus serves as a means of transmission of genetic information to the cytoplasm, leading to the formation of specific protein

**(B) Lampbrush Chromosomes:**

These are the largest chromosomes which can be seen with naked eyes and are found in yolk rich **oocytic nuclei** of certain vertebrates such as fishes, amphibians, reptiles andbirds. They are characterized by the

fine lateral loops, arising from the chromomeres, during first prophase of meiosis. Because of these loops they appear like brush; that is why they are called **lampbrush chromosomes** first discovered by **Flemming** in 1882 and described in shark oocytes by **Ruckert** (1892). Lampbrush chromosome consists of longitudinal axis formed by a single DNA molecule along which hundreds of beads like chromomeres are distributed. Two symmetrical lateral loops (one for each chromatid) emerge from each chromomere, which are able to expand or contract in response to various environmental conditions. About 5 to 10% of the DNA is in the lateral loops. The axis having compacted DNA and tightly associated proteins is transcriptionally inactive. The loops consist of uncompacted DNA and proteins but have a good amount of RNA and they are transcriptionally active. A chromomere and its associated loop correspond with one gene.

In lampbrush chromosomes the DNA loops are the sites of intensive RNA synthesis. rRNA and mRNA are synthesized in large amount and the transcription of rRNA causes the enlargement of nucleolus, or formation of numerous additional nucleoli. Due to the synthesis of large amounts of proteins, fats, carbohydrates, and other molecules in the cytoplasm needed for further development of the embryo, the oocyte grows in size. Synthesis of proteins occurs near the loops (Figure 75).

**Functions of Lampbrush Chromosome:**

- Involved in the synthesis of RNA and proteins by their loops.
- Probably help in the formation of certain amount of yolk material for the egg.

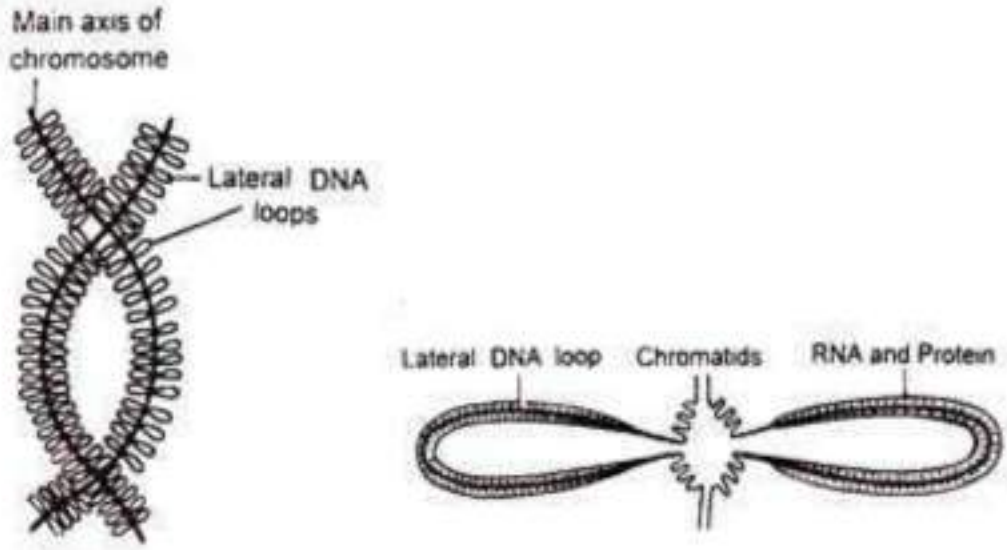


**Figure 75:** Detailed structure of lampbrush chromosome.

# CELL DIVISION

A multicellular organism starts its life as a single cell and it undergoes repeated division, thus, the growth and development of every living organism depends on the growth and multiplication of its cells. The cell increases in size due to growth and it is the characteristic feature of all the living organisms. After the cell attains maximum growth, it begins to divide. The vegetative growth of an organism takes place by an increase in the number of cells through cell divisions which follows the geometrical progression. The cell division is a continuous and dynamic process, and it involves the following three stages:

1. DNA or genome replication.
2. Nuclear division or karyokinesis.
3. Cytoplasmic division or cytokinesis.

The cell division is of two types on the basis of number of genomes present in the daughter cells in comparison to the dividing parent cell **mitosis** and **meiosis**.

1. ***Mitosis-*** The term mitosis was coined by **W. Flemming** in 1882. The multiplicationof a body cell into two daughter cells of equal size and containing the same number of chromosomes as in the parent cell is called mitosis or **somatic division**.
2. ***Meiosis-*** The term meiosis was first coined by **J. B. Farmer (1905) with J. E. Moore.** Meiosis occurs only in gonads (germ cells) during the formation of gametes like sperm and ovum. It is a process by means of which double number or 2N or diploid chromosomes is reduced to its half number or N or haploid (**reduction process).**

## Cell Cycle Stages, Mitosis & Cytokinesis: -

**Cell Cycle:** Every cell having the capacity to divide passes through a regular cycle of changes known as cell cycle. A cell starts its cycle in diploid condition.

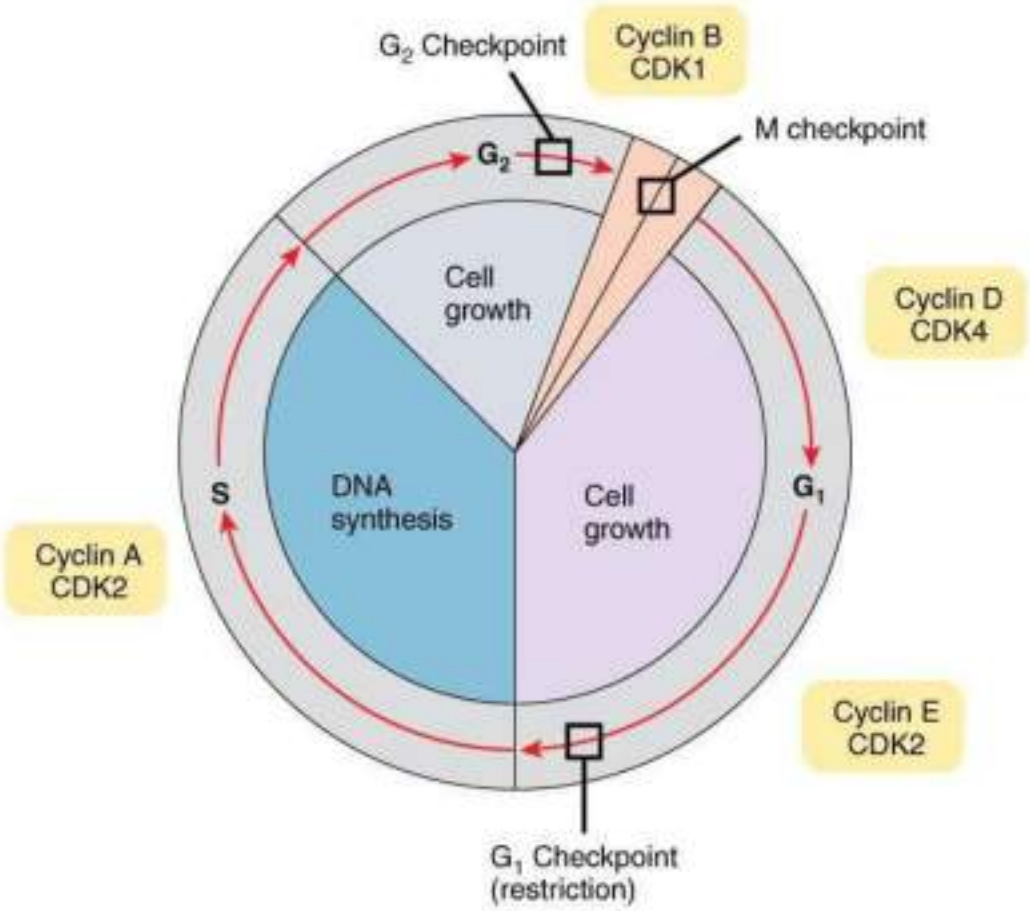


**Figure 76:** Cell cycle phases.

### Phases of cell cycle:

Cell cycle consists of two stages: A long un-dividing stage called **interphase or I-phase** and a short dividing stage **mitotic or M-phase.**

1. ***Interphase-*** The time between the end of telophase and the beginning of the next M- phase is called the interphase. It is a long stage that lasts for 10 to 30 hours. During this phase the cell grows

by synthesizing biological molecules such as lipids, proteins, carbohydrates, nucleic acids. Interphase is further divided into three sub phases or periods: first gap or G1 phase, synthetic or S phase and second gap or G2 phase.

(i) **$G_1$ phase-** The **gap between previous mitosis and beginning of DNA synthesis** is represented by $G_1$ phase. In this stage initial growth of a newly formed cell takes place. Various biological molecules (carbohydrates,proteins, lipids, including some non-histones, RNAs) are synthesized in this phase. Normal metabolism is carried out for the preparation for DNA replication that is to take place next to it. DNA synthesis does not occur in thisphase.

(ii) **S Phase-** During this **phase duplication of each chromosome** take place by replication of new DNA molecule on the template of the existing DNA. Synthesis of histone proteins and their mRNA, some non-histone proteins and formation of new nucleosome also occur in S-phase only. In most of the eukaryotes the S-phase lasts for 6 to 8 hours.

(iii)**$G_2$ Phase-** $G_2$ phase is the gap between DNA synthesis and nuclear division. RNA transcription and protein synthesis continues during this phase. Further growth of the cell and preparation for its division also takes place in this stage.During this stage the cytoplasmic organelles such as centrioles, mitochondria and Golgi apparatus are doubled, proteins for spindle and asters are synthesized and active metabolism stores energy for the next mitosis. It takes in most cells lasts for 2 to 5h.

2. ***Mitotic Phase-*** Interphase is followed by mitotic phase. During mitotic phase the already **duplicated chromosomes are equally distributed to the daughter cells** which contain exactly the same hereditary information as the parent cell. Though, the other cell components (organelles and molecules) are also divided approximately equally between the daughter cells, but not as precisely as the DNA. After the mitosis is over, the daughter cells enter the $G_1$ phase of the next cell cycle.

   During mitosis many structural and physiological changes take place in the cell, as the chromatin of the nucleus is packed into visible chromosomes, which are set free by breakdown of nuclear envelope. An extensive reorganization of the membranous components and cytoskeletal elements takes place. Endoplasmic reticulum and Golgi apparatus break down into small vesicles and stops the protein movement. Microtubules dissociate into tubulin dimers and are assembled into the spindle which occupies most of the cell and helps in the distribution of chromosomes into the daughter cells. Actin filaments get reorganized and form a contractile ring for the cytoplasmic division.

**Control of Cell Cycle:**

1. ***Nucleo-cytoplasmic Ratio-*** In 1910, **Hertwig** proposed that the cell division starts when the ratio between the volume of the nucleus and the volume of the cytoplasm is upset. As the cell grows, the synthesis of proteins, nucleic acids, lipids, and other cellular components takes place. During synthesis of these molecules, the

back-and-forth movements of materials through the nuclear and the cell membranes occurs. With the growth of the cell, its volume increases more than the surface of the nucleus and the cell, and at a critical point, the surface of the nucleus becomeinadequate for the exchange of materials between the nucleus and the cytoplasm required for further growth. The cell divides at this stage and regains the optimum and efficient nucleo-cytoplasmic ratio that allows the growth. Although the cell division usually occurs after a cell has grown to a certain size, there are important exceptions to this pattern.

2. ***Surface-Volume Ratio-*** With the growth of the cell size, its volume increases more than its surface area. All the materials of the cell required for its maintenance and growth are drawn through its surface. A stage will reach when the surface area is insufficient to supply the large volume of the cell. It is thought that there is a critical point at which the cell division starts, and the division of the cell greatly increases the surface without increasing the volume. This theory fails in case of starved cells, which may divide without doubling their size and form smaller daughter cells.
3. ***Nucleolus-*** Damage to nucleolus at a certain critical time (telophase or mid prophase) stops cell division.
4. ***Cyclic Nucleotides-*** Concentration of cAMP and cGMP vary regularly during the cell division. Concentration of cAMP is high during $G_1$ phase, but it falls as the cell entersthe S phase and mitosis. However, the concentration of cGMP often varies in the reverse pattern. Thus, addition or removal of any of these nucleotides can

start or stop entry of many cells into S phase and the subsequent M phase. The concentration of these cyclic nucleotides remains constant throughout the cell cycle in many cells. Also, plant cells do not have cyclic nucleotides. Based on these facts, cyclic AMP and GMP are no longer thought to regulate the cell cycle.

5. ***Phosphorylation-*** During cell cycle the phosphate groups are added to the histone groups particularly to $H_1$ as the cell enters S phase, increases during M phase, and are removed on the completion of mitosis before $G_1$ starts. Phosphate groups are also added and removed to non-histone proteins during cell cycle. Thus, it is believed that the changes in the histones and non-histones may have a role in the control of cell cycle because these proteins have been found to regulate the activity of genes in RNA transcription during interphase.
6. ***Cyclin:*** The concentration of the protein called cyclin appears to control mitosis as it builds up during interphase and is degraded during mitosis.

## MITOSIS DIVISION:

A German biologist Eduard Strasburger described mitosis for the first time in 1875.Same was described later in 1879 by Walther Flemming who also termed it "mitosis" in 1882.

It is the most common method of cell division in eukaryotes that takes place in somatic cells of the body and hence it is also known as somatic division. However, in gonadsit occurs in undifferentiated germ cells. In plants it takes place in the cells of meristematic tissues. The duration of mitosis on an average is from 30 minutes to 3 hours.

Mitosis (Figure 77) is defined as the division of a parent cell into two identical daughter cells eachwith a nucleus having the same amount of DNA, the same number and kind of chromosomes and the same hereditary instructions as the parent cell. Therefore, it is also known as the equational division. There are two main events involved in mitosis: Karyokinesis or divisionof the nucleus and cytokinesis or division of cytoplasm.

**Karyokinesis:**

In eukaryotes, karyokinesis is a complex process due to the presence of many chromosomes. It is a continuous process which may be divided into four stages: prophase, metaphase, anaphase and telophase.

1- **Prophase-** In an interphase cell the chromosomes are greatly extended and spread throughout the space in the nuclear compartment. Approximately 4 meters of DNA is organized into 46 duplicated chromosomes is present in the nucleus of a human G2 cell. The prophase is long and complex that lasts for about 50 minutes. It may be divided into 3 sub stages: early prophase, middle prophase and late prophase.

**A) Early prophase-** During the early prophase of mitosis the following events take place:

(i) The shape of cell becomes almost rounded and the cytoplasm becomes viscous.

(ii) The centrioles lie close to the nucleus and around them

assembles the short radiating microtubules by polymerization of the tubulin dimers. Both pairs of centrioles also called **diplosomes**, start moving to the opposite ends of the cell. The microtubules surrounding each pair of centrioles appear like a star body and are called the **aster**. The microtubules which are also termed as **astral rays**, are not in contact with the centrioles, but are separated from them by an amorphous zone of cytoplasm known as **pericentriolar cloud**. The microtubules stretching between the diplosomes moving apart increase in number and length by incorporating more tubulin dimers. Thus, asters shift theduplicated centrioles to the opposite ends of the cell from where the centriole pair will pass into separate daughter cells when cytokinesis occurs. Though thecentrioles have no role in the formation of the spindle, but they may be concerned with orienting the spindle.

(iii) Long microtubules assemble on one side of the nucleus to form mitotic spindle. **Microtubules are arranged in bundles called spindle fibers** and at each pole of the spindle lies the mother-daughter centriole pair.

(iv) The chromosomes that appear like threads in the nucleus gradually change into short, thick rods by loss of water and progressive coiling and become visible. Due to the duplication of DNA and chromosomal proteins during the interphase, each chromosome appears longitudinally double, consisting of two identical sister chromatids which are held

together at the narrow region called **primary constriction or centromere**. Each chromatid has a disc like structure at centromere, where the spindle microtubules join it. This disc is called as **kinetochore**.

**B) Middle prophase-** It includes the following events:

(i) The chromosomes further get shorter, thicker and their chromatids become uncoiled and finally they assume their characteristics sizes and become distinguishable individually.

(ii) **Nucleoli** progressively become smaller and **finally disappear.** Nuclear envelope begins to breakdown into small vesicles which disperse into the cytoplasm. The lamina dissociates into its protein subunits.

**C) Late Prophase-** This phase involves the following events:

(i) The nuclear envelope breaks completely thus, releasing the chromosomes and other nuclear contents into the cytoplasm.

(ii) The spindle gains their proper shape and size.

(iii) The growing spindles push the centriole pairs to the opposite ends of the cell.

**2- Metaphase-** The metaphase being short and simple lasts for 2 to 10 minutes and itinvolves the following events:

A. The spindle occupies the region of the nucleus.

B. The chromosomes move to the equatorial plane of the spindle.

C. Some spindle microtubules extend to and join the chromosomes. These are called chromosomal or kinetochore microtubules.

D. The chromosomes get aligned at the middle of the spindle in the form of a plate called equatorial or metaphase plate. This plate is formed by the kinetochores, the arms of the chromatids trailing away on the sides. It is at the right angles of the long axis of the spindle. During metaphase the chromosomes have fully aligned into a plate and await the separation of their chromatids.

3. **Anaphase-** Anaphase lasts only 2 to 3 minutes and it comprises the following events:

A. The **sister chromatids of each chromosome slightly separate** at the primary constriction so that their kinetochores stretch towards the opposite poles of thespindle. In all the chromosomes separation of chromatids occurs almost simultaneously. The **chromatids are now referred to as chromosomes** because they are no longer held to their duplicates.

B. After a short time, the chromatids separate completely from their formermates, and start moving to opposite poles of the spindle. As each chromosome is being pulled by its attached microtubules, its kinetochore leads and armstrail behind. As a result, the chromosomes are pulled into V, J and I shapes, depending upon the position of the kinetochore. (Metacentric, sub metacentric or telocentric respectively)

C. As the chromosomes move toward their respective poles, the two poles move farther apart by elongation of spindle.

The anaphase ends when all the chromatids reach the opposite poles.

Each pole of the spindle receives one chromatid from every metaphase chromosome, the two groups of chromatids have the same hereditary information.

4. **Telophase-** The telophase is long and complex and lasts for an hour or so. In this phase nucleus is reconstructed from each group of chromosomes. It involves the following events:
   a. The chromosomes at each pole unfold, and become long and slender. Finally, they become indistinguishable as were in an interphase cell.
   b. Nuclear envelope is reconstructed around each group of chromosomes gradually. First, the membrane vesicles associate with the individual unfoldingchromosomes, partially enclosing each chromosome. Then they fuse to form an envelope surrounding the entire set of chromosomes at each pole. The lamina proteins re-associate simultaneously with the reconstruction of nuclear envelope and form a complete lamina within the nuclear envelope
   c. Nucleolar material, composed of partially processed ribosomal subunits and processing enzymes, dispersed into the cytoplasm in the prophase return to the nucleolar organizer site and forms a small nucleolus. Processing of this preexisting material then continues. Transcription of new rRNA also begins at this time; it gradually speeds up until it attains the high level of characteristic of interphase cell. Along with this, the nucleolus grows and attains its normal size. The nucleolus reformed at telophase, thus

contains both old and new rRNA and ribosomal proteins.

With the transformation of chromosomes into chromatin and reconstruction of nucleoli, transcription of all the three RNA types gradually becomes normal.

The spindle begins to disappear, and the asters become small by depolymerization of microtubules and the centrioles take up their characteristic interphase position close to the one side of the nucleus. Short spindle microtubules persist for some time at the spindle equator to mark the region where the cytoplasm will later divide.

**Cytokinesis:**

Cytokinesis is the division of cytoplasm. It encloses the daughter nuclei formed by the karyokinesis in separate cells, thus completing the process of cell division. Cytokinesis is signaled at the metaphase by cytoplasmic movements that bring about equal distribution of mitochondria and other cell organelles in the two halves of the cell. Division occurs differently in animal cells and the plant cells.

**Significance of Mitosis:**

Mitosis has manifold significance-

- **Maintenance of Size**- Mitosis helps maintaining the size of the cell. A cell, when full grown, divides by mitosis instead of growing further.
- **Growth**- A fertilized egg develops into an embryo and finally into an adult by repeated mitotic cell division.

- **Maintenance of Chromosome Number**- Mitosis keeps the number of chromosomes equal in all the cells of an individual. Thus, mitosis provides a complete set of genetic information to each cell, since DNA is duplicated in S phase prior to mitosis.
- **Repair**- Mitosis provides new cells to replace the old worn out and dying cells.
- **Healing and Regeneration**- Mitosis produces new cells for the healing of woundsand regeneration.
- **Reproduction-** Mitosis brings about multiplication in the acellular organisms. In multicellular organisms also, it plays an important role in reproduction, asexual aswell as sexual.
- **Evidence of Basic Relationship of Organisms-** Mitosis, being essentially similar in many kinds of organisms, supports the basic relationship of all living things.

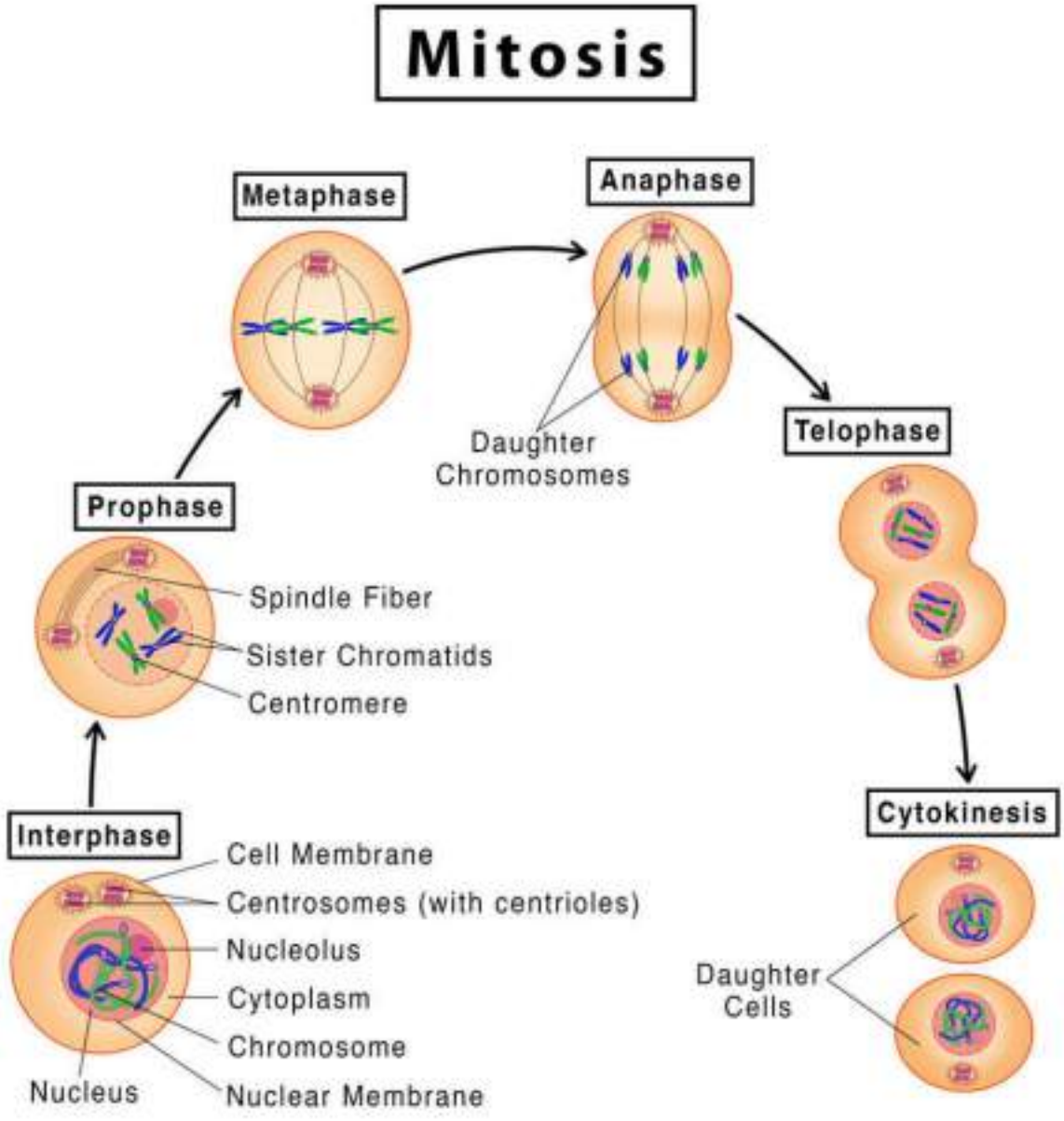


**Figure 77:** Mitosis division stages.

## MEOSIS DIVISION:

**In 1887**, August Weismann predicted on theoretical grounds that the number of chromosomes must be reduced by one-half during gamete formation. **Edouard Van Beneden** demonstrated reduction division in1887. J.B. Farmer and Moore introduced the term "meiosis" in 1905. Mitosis occurs in all kinds of eukaryotic cells, while meiosis is confined to certain cells and takes place at a particular time. Only the cells of sexually reproducing organisms undergo meiosis, and only special cells in the multicellular organisms switch over from mitosis to meiosis at the specific time in the life cycle. Meiosis produces gametes or gametic nuclei in animals, some lower plants, and various protists and fungus groups. Meiosis forms spore in higher plants. The spores give rise to gamete producing structure called gametophytes, which produces gametes by mitosis**.** Meiosis consists of two divisions that take place in rapid succession, with the chromosomes replicating only once. Thus, a parent cell produces four daughter cells, each having half the number of chromosomes and half of the nuclear DNA amount present in the parent cell. Meiosis is therefore also known as **reduction division**. The two divisions of meiosis are known as the first and the second meiotic divisions or **meiosis-I and meiosis-II**

### Meiosis Divisions:

### First meiotic division or Meiosis-I:

During the first meiotic division, the two homologous chromosomes of each pair separate from each other and go to separate daughter cells. This reduces the number of chromosomes from diploid to haploid

condition. **Meiosis-I** is therefore known as **heterotypicdivision**. The four phases of this division are called Prophase-1, metaphase-1, anaphase-1 and telophase-1.

1- **Prophase-.** The meiotic prophase-1 is more complex than the mitotic prophasebecause of the process of recombination that occurs in it. It also lasts much longer than the mitotic prophase in the same organism. It may extend over weeks, months or even years. Although it is more or less a continuous process, it is divided into 5 sub- stages: leptotene, zygotene, pachytene, diplotene and diakinesis (Figure 78).

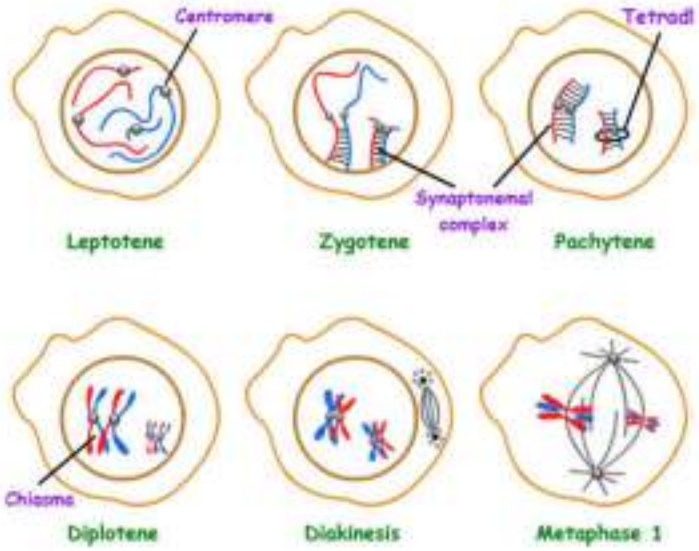


**Figure 78:** meiotic prophase-1 substages.

a. ***Leptotene-*** Leptotene begins when chromosomes appear as thin threads by condensation. The chromosomes become thicker as condensation proceeds. They lie jumbled up so that it is not possible to trace individual chromosomes. Each chromosome is double, consisting of two chromatids due to DNA replication during premeiotic interphase. However, the chromatids are

closely adhered together and are not distinguishable.

b. ***Zygotene-*** The homologous chromosomes come to lie side by side in pairs. The pairing of homologous chromosomes is called **Synapsis or conjugation**. A pair of homologous chromosomes lying together is termed as a **bivalent**. Pairing is so through that the corresponding ends and all the corresponding genes of the two homologous chromosomes lie exactly opposite to each other. The centrosome of the chromosomes also lies adjacent to one another. The chromatids are still not visible. A regular space of about 0.15 to 0.2 μm wide exists between the synapsed homologous chromosomes, bearing a highly specialized fibrillar organelle, **the synaptonemal complex** (Figure 79). The synaptonemal complex consists of three parallel and equally spaced longitudinal filaments flanked by chromatin and interconnected by short transverse filaments. The complex contains DNA and some specific proteinaceous material. It was discovered by Montrose J. Moses in 1955 in crayfish.

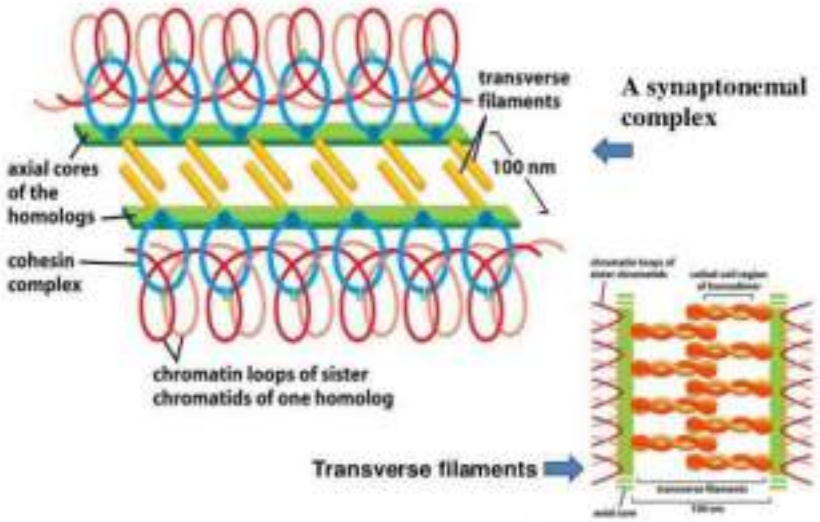


**Figure 79:** Synaptonemal complex.

c. ***Pachytene-*** The synapsed chromosomes continue to become short and thick. The chromatids of each synapsed chromosome slightly separate and become visible. A chromosome with two visible chromatids is known as dyad. A group of four homologous chromatids (two dyads) is called a tetrad. The number of tetrads equals the haploid number of chromosomes. The two chromatids of the same chromosomes are called are called sister chromatids and those of the two homologous chromosomes are called non-sister chromatids. The leptotene and the zygotene stages last for a few hours, the pachytene may take weeks, months or even years. It is prolonged because recombination or crossing over occurs in it.

**Recombination** involves mutual exchange of the corresponding segments of non-sister chromatids of homologous chromosomes. It occurs by breakage and reunion of non-sister chromatid segments. Certain structures mediate the meiotic recombination by marking the sites of crossing over. These are known as **recombination nodules** (RNs). They are multicomponent proteinaceous ellipsoids found in association with the synaptonemal complex during prophase-I of meiosis (Carpenter, 1975b). The **synaptonemal complex**, aprotein structure, helps in recombination by keeping the homologous chromosomes in paired state for the required period and by containing and aligning the enzymes needed for breakage and union.

d. ***Diplotene-*** At this stage the homologous chromosomes separate

at many places. This is called disjunction. It occurs because the synaptic forces and the synaptonemal complex disappear. The chromatids become more distinct, and tetrads seem very clear. The homologous chromosomes do not separate at certain points. These points are called chiasmata. The chiasmata mark the sites where the exchange of chromatids occurred during pachytene. The number of chiasmata is related to the length of the chromosomes. Longer chromosomes have more chiasmata than the shorter ones. In case of single chiasmata, the bivalent looks like a cross; in case of two chiasmata, it looks like a ring; and in case of many it shows series of loops.

e. **Diakinesis-** In this stage the chromosomes condense again into short, thick rods. The chiasmata disappear by sliding towards the tips of chromosomes due to tight condensation. This process is called terminalization. The centrioles already duplicated in premeiotic interphase, move apart in pairs to the opposite ends of the cell. Asters form around each centriole pair. Spindle develops between the centriole pairs. The nucleolus disintegrates. The nuclear envelope breaks down into vesicles. The tetrads are released into the cytoplasm.

2- **Metaphase** I: The spindle shifts to the position that is earlier occupied by the nucleus. The tetrads scattered in the cytoplasm move to the equator of the spindle. Here, they align in two parallel metaphase plates, one formed by chromosomes and other by their homologous. The attachment of the tetrads to the spindle

microtubules in metaphase-I is different from that of mitotic metaphase chromosomes. Each homologous chromosome has two kinetochores, one for each of its two chromatids Both the kinetochores of a homologous chromosome connect to the same spindle pole. The two kinetochores of its homologue join the opposite spindle pole.

3- **Anaphase-I:** From each tetrad, two chromatids of a chromosome move as a unit (dyad) to one pole of the spindle, and the other two chromatids of its homologue migrate to the opposite pole. Thus, the two homologous chromosomes of each pair are separated in the anaphase-I of meiosis. The process is also called as **disjunction.** As a result, half of the chromosomes, which appear in early prophase, go to each pole. Thus, it is during anaphase-I that the real reduction in the chromosome number occurs. Each chromosome at the pole is still double and consists of two chromatids. Thus, the group of chromosomes at each pole though has only one member of each homologous pair still contains twice the haploid amount of DNA.

4- **Telophase I:** During telophase I, the chromosome at each pole of the spindle partly unfolds and elongate, and form a nucleus with nucleolus and nuclear envelope. The spindle and asters disappear.

The cytoplasm divides at its middle by constriction in an animal cell and by cell plate formation in a plant cell. This produces, two daughter cells, each with one nucleus. The nucleus of each daughter cell has received only one chromosome from each homologous pair. Thus, it has half the number of chromosomes, but double the

amount of nuclear DNA as each chromosome is double.

**Secone meiotic division or Meiosis-II:**

The meiosis-II is similar to mitosis as in this division, the two chromatids of each chromosome separate from each other and go to separate daughter cells. With the result, the number of chromosomes remains the same as produced by meiosis-I. Meiosis-II is, therefore, known as homotypic division. The four stages of this division are called prophase-II, metaphase-II, anaphase-II and telophase-II.

1- **Prophase-I:** When there is no interkinesis, the telophase-I spindle is replaced by two new spindles; and the centrioles and asters, if present, duplicate and one copy of each comes to lie at each pole of the new spindles. The telophase-I chromosomes move from the poles of the old spindle to the equators of the new spindles. If decondensation has occurred during telophase-I, the chromosome recondense to short rod lets as they migrate to the metaphase-II spindles.

2- If interkinesis is present, centrioles move apart and asters are formed around them. A spindle is formed between the centrioles. Chromosomes each consisting of two chromatids, appear in the nucleus. They are set free in the cytoplasm by breakdown ofthe nuclear envelope. Nucleus disappears.

3- **Metaphase-II**: The chromosomes get arranged at the equator of the spindle as a metaphase plate. The chromatids of each chromosome are joined at their kinetochores by chromosomal microtubules

extending from the opposite poles of the spindle as in mitosis

4- **Anaphase-II**: The two chromatids of each chromosome separate and move to the opposite poles of the spindles. Here they are called chromosomes. Each pole has **haploid number of chromosomes and haploid amount of DNA**. This amount is one-fourth of the DNA present in the original cell which entered meiosis.

5- **Telophase-I***:* The chromosome at each pole decondenses, and nuclear envelopedevelops around them. This produces two nuclei. Nucleolus is formed in each nucleus. Spindle and asters disappear. In cases that lack interkinesis, four nuclei are formed in telophase-II

**Cytokinesis:**

Cytoplasm divides at its middle by constriction in an animal cell and by cell plate formation in a plant cell. This produces two daughter cells. The later have half the number of chromosomes, and half the amount of nuclear DNA, i.e., in Reduction division is complete when this point is reached. The cells formed by meiosis-II in animals are mature gametes. They do not divide further. A gamete must fuse with another suitable gamete before a new individual can develop. The cells formed by meiosis-II in plants are the spores. The sporescan develop into new individuals without fusing in pairs. In fact the main difference between a spore and a gamete is the ability of the spore to develop directly into a new individual.

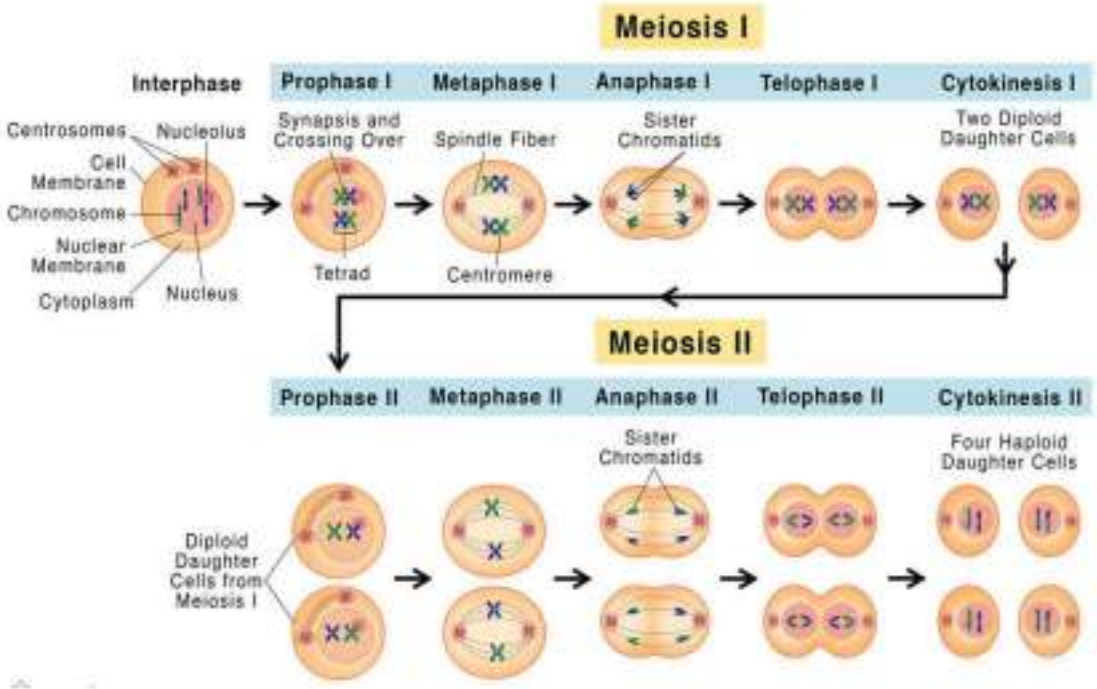


**Figure 80:** Stages of meiosis division.

# STRUCTURE AND TYPES OF NUCLEIC ACIDS

Deoxyribonucleic acid (DNA) and Ribonucleic acid (RNA) the principal **genetic materials** of living organisms are chemically called **nucleic acids**. Nucleic acid especially the DNA, a universal genetic material of most of the organisms, is having all the features required to be a good genetic material. DNA is a macromolecule and is a helically twisted double chain of poly deoxyribonucleotides.

In **prokaryotes** it occurs in **nucleoid** and as **plasmids**, both are **double stranded circular DNA**. In **Eukaryotes** most of the DNA is found in **chromatin of nucleus**. It is **linear**. Some small quantitative of DNA are found in **mitochondria and plastids** which is generally double stranded and circular RNA also acts as genetic material in majority of plant viruses.

**Features of DNA to act as genetic material:**

- Genetic material can **store information** used to control both the development andmetabolic activities of cell
- It should be **chemically stable** so that it can be replicated accurately during cell division
- It should be **transmitted for generations**
- It should be able to undergo **mutations providing genetic variability** required for theevolution.

## (A) Structure of DNA

Nucleic acid (DNA or RNA) first called nuclein by a Swiss chemist Friedreich Miescher (1869) as he removed nuclei from pus cells and isolated DNA i.e., "nuclein" from it. Nucleic acid (DNA or RNA) are macromolecules composed of repeating subunit called nucleotides

### Constitution of a nucleotide:

- A phosphate groups.
- A five-carbon sugar (ribose in RNA and deoxyribose in DNA).
- A cyclic nitrogen containing compound called a base (purines and pyrimidines).

Most commonly DNA occurs as a **double helix.** The two spiral strands of DNA are collectively called DNA duplex. Two separate and anti-parallel chains of DNA are wound around each otherin a **right-handed helical manner**. The DNA double helix comes to have two types of alternate **grooves major** and **minor** with the sugar phosphate backbone on the outer sides. The bases paired by hydrogen bonding are stocked on each other.

### Chemical Composition of DNA

Deoxyribonucleotides (monomer) of DNA are composed by three different types of chemicals (Figure 81).

(1) **Phosphoric acid ($H_3PO_4$)** has three reactive (-OH) groups of which two are involved informing sugar phosphate back bone of DNA.

(2) **Pentose sugar ($C_5H_{10}O_4$)** - DNA contains 2'-deoxy-D-ribose,

hence the namedeoxyribose.

(3) **Nitrogen bases**- DNA contained four different nitrogen bases (**A, G, C & T).** These fourbases are grouped in to two classes on the basis their chemical structure.

a. **Purine base:** Adenine and Guanine

b. **Pyrimidine bases:** Cytocine and uracil

(a) **Purine bases** - DNA has two types of purines (**adenine and guanine**). Each purine is a type of nitrogen base having a **double ring structure** (i.e., 9 member double rings with nitrogen at 1, 3, 7 and 9 positions).

Some of the common names of these bases reflect the circumstances of their discovery. Guanine, for example, was first isolated from guano (bird manure), and thymine was firstisolated from thymus tissue.

(b) **Pyrimidine bases**: DNA has two types of pyrimidine bases (**cytosine and thymine**). Each pyrimidine is a type of nitrogen containing base having a **single ring structure** (i.e.6 member rings with nitrogen at 1 and 3 positions).

**Nucleosides:** A nitrogenous base with a molecule of deoxyribose sugar (without phosphate group) is known as nucleosides. In nucleic acids, the nitrogen bases are covalently attached to the 1'-position of a pentose sugar ring with the help of glycosidic bond (Figure 82).

**Nitrogen base + sugar = nucleoside.**

- Adenine + deoxyribose = deoxyadenosine
- Guanine + deoxyribose = deoxyguanosine
- Cytosine + deoxyribose = deoxycytidine
- Thymine + deoxyribose = deoxythymidine

**Nucleotides-** A nucleotide is formed of one molecule of deoxyribose sugar, one molecule of phosphoric acid and anyone of the nitrogen base. Phosphoric molecule is attached to the 5th – carbon atom of deoxyribose ring with the help of phosphoester bond (Figure 82).

**Nucleosides + phosphoric acid = nucleotides**

Different nucleotides of DNA are as follows:

(1) Adenine + deoxyribose + phosphoric acid = deoxyadenylic acid or deoxyadenylate / dAMP

(2) Guanine + deoxyribose + phosphoric acid = deoxyguanylic acid or deoxyguanylate / dGMP

(3)Cytosine + deoxyribose + phosphoric acid = deoxycytidylic acid or deoxycytidylate / dCMP

(4)Thymine+deoxyribose+phosphoric acid = deoxythymidylic acid or deoxythymidylate / dTMP

**Table 3:** Nitrogen bases, their respective nucleosides, and nucleotides of DNA.

| Nitrogen base | Nucleoside (Nitrogen base + sugar) | Nucleotide (nucleocide +phosphate gp.) |
|---|---|---|
| Adenine (A) | A+S= Adenosine | Adenylic acid<br>adenosine monophosphate<br>(AMP) |
| Guanine (G) | G+S= Guanosine | Guanylic acid<br>Guanosine monophosphate<br>(GMP) |
| Thyamine<br>(T) | T+S = Thyamidine | Thyamidylic acid<br>Thyadine monophosphate<br>(TMP) |
| Cytosine<br>(C) | C+S = Cytidine | Cytidylic acid<br>Cytidine monophosphate<br>(CMP) |

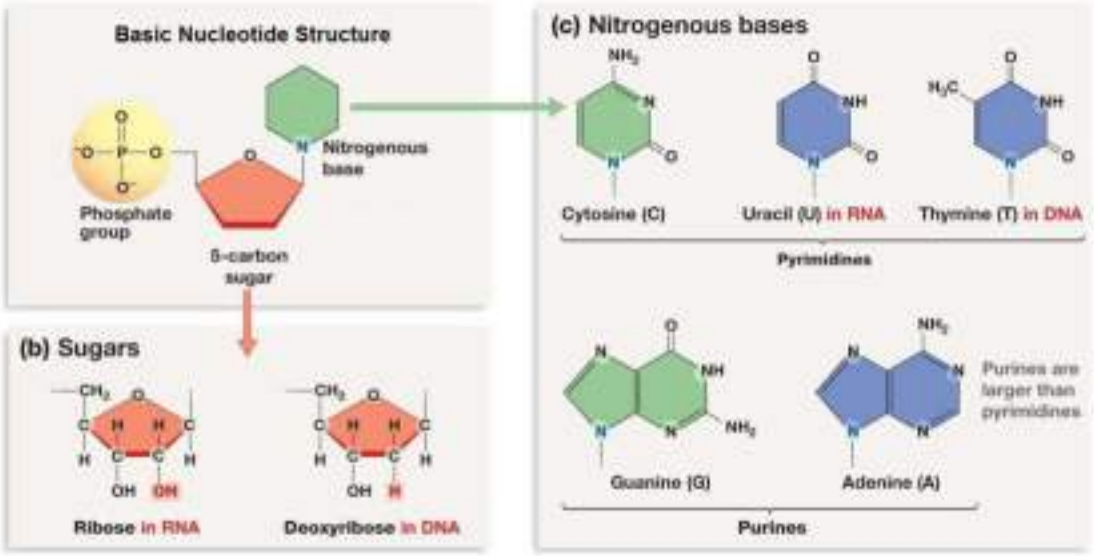


**Figure 81:** Chemical structure of nucleic acids (Nucleotide), (a) Nitrogen bases types and (b) Sugar structure.

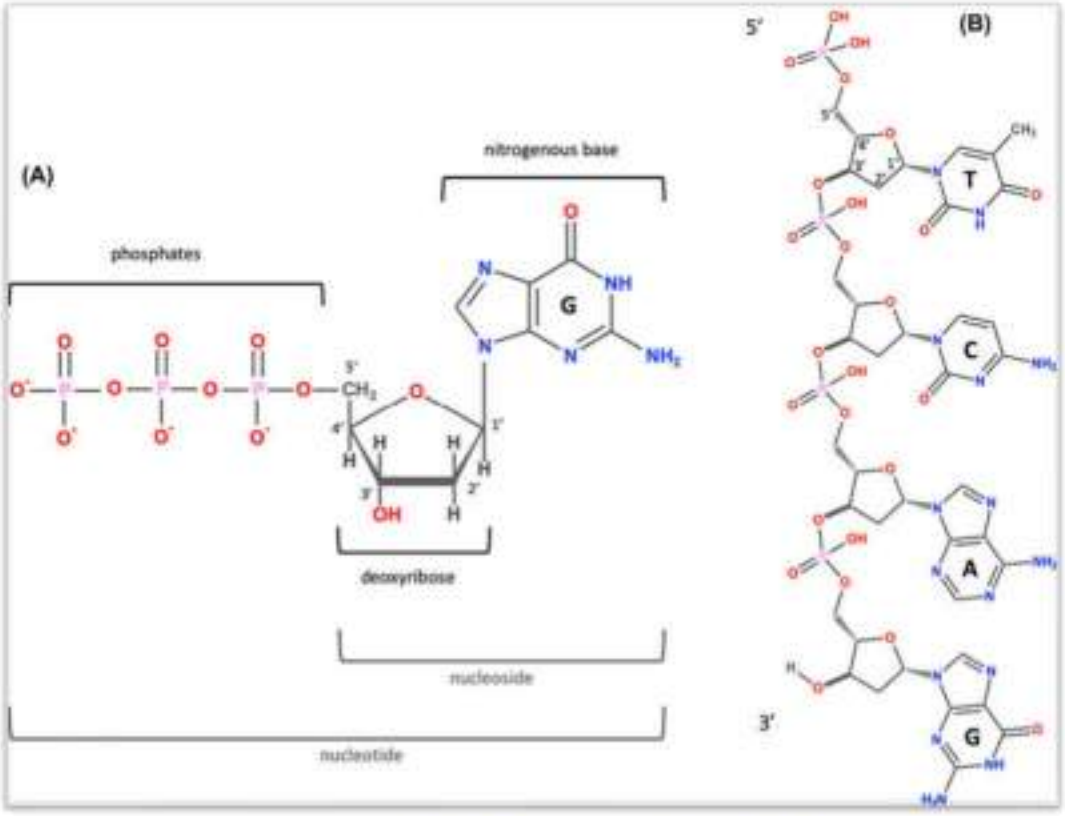


**Figure 82:** (a) Progressive formation of nucleoside to nucleotide (from lower to higher energy compounds, (b) Backbone of DNA. (The backbones are formed by 3 -to-5 phosphodiester linkages).

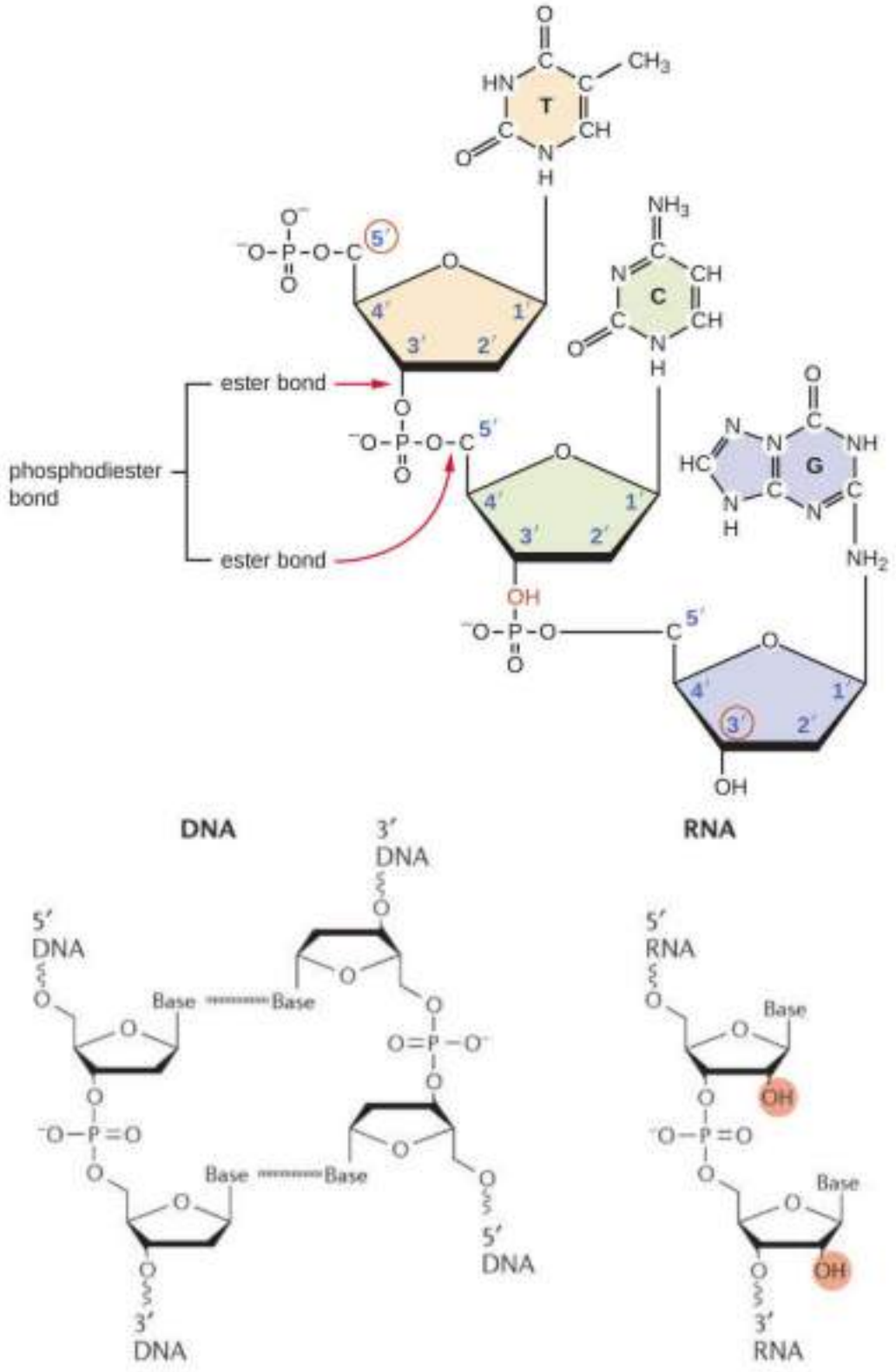


**Figure 83:** Chemical constituents of a nucleotide and DNA & RNA chain formation.

**Watson and Crick Double Helix Model of DNA:**

The structure of DNA was deduced by American **J. D. Watson** and **F.H.C. Crick** in 1953 for which they received the Nobel Prize in 1962. Their double- helix model of DNA structure model is widely accepted. Their double helix model of DNA was based on the data and information given by so many workers like **E. Chargaff, M.H.F. Wilkins, R. Franklin** and their coworkers. Main contributions in deducing this model were of: Chargaff's rule, Franklin's X-ray diffraction patterns and Kornberg's results

**Chargaff's rule-** In 1940's **Erwin Chargaff** analyzed base content of DNA using new chemical techniques and their observations and generalizations were called as Chargaff 's rule. Chargaff's rule strongly suggested that thymine and adenine as well as cytosine and guanine were present in DNA, always bonded to each other by H-bonds and shows some fixed inter relationship

- The proportion of A always equals that of T, and the proportion of G always equals thatof C or A = T and G = C.
- The amount of A, T, G, and C in DNA vary from species to species but A+T/G+C =constant for a particular species.

**Franklin's X-ray diffraction patterns-** Watson and Crick made use of the data of x-ray crystallographic of DNA structure from the studies of **M.H.F. Wilkins, R. Franklin,** and their coworkers. According to their data, DNA was a highly ordered, multiple stranded structure with repeating sub structure spaced every 3.4A° along the axis of the molecule.

**Korenberg's results**: Korenberg and his associates tried to synthesize DNA in a medium free ofDNA but in the presence of enzyme **DNA polymerase** and nucleotides-the building blocks of DNA. They found that in a DNA free medium with all necessary compounds DNA synthesis does not occur but the same happens i.e., DNA synthesis starts only when some DNA was added as a primer to the same medium.

**The important features of their model of DNA (Figure 84) are:**

a. Two helical polynucleotide chains are coiled around common axis, where the backbone isconstituted by sugar phosphate and the bases project inside.
b. The polynucleotide chains run in opposite directions. It means, if one chain has the polarity 5'P →3'OH, the other has 3'OH→5'P.
c. The two chains are held together by hydrogen bonds between their bases. Three hydrogen bonds occur between cytosine and guanine (C≡G) and two hydrogen bonds between adenine and thymine (A=T).
d. The diameter of the helix is $20A^0$ and bases are separated by 3.4 $A^0$ along the helix axisand related by a rotation of $36^0$.
e. The helical structure repeated after 10 residues on each chain, and intervals of 34 $A^0$

**Functions of DNA:**

1- DNA is genetic material which able to store information used to control both thedevelopment and metabolic activities of cells.
2- DNA can be replicated accurately during cell division and

transmitted for generations.

3- Crossing over during meiosis produces natural recombination of DNA which is passed onto next generation to produce variants in all sexually reproducing organisms.

4- DNA able to undergo mutations providing genetic variability required for evolution

5- Differentiation of various body parts is due to differential functioning of specific parts ofDNA.

6- Developmental stages occur in the life cycle of an organism by an internal clock of DNAfunctioning.

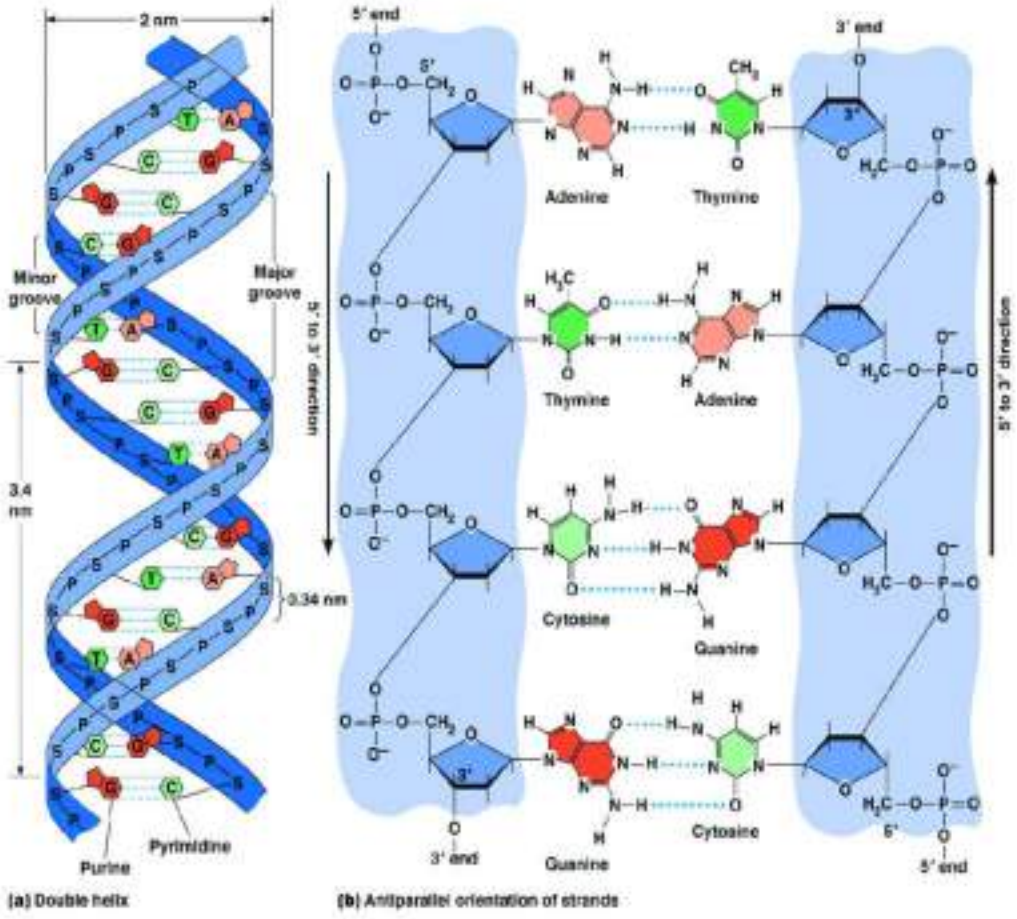


**Figure 84:** Watson and Crick Double Helix Model of DNA.

## Replication of DNA:

Replication is the process of formation of carbon copies on DNA. DNA functions as its own template. DNA replication is an autocatalytic function of DNA. During DNA replication the weak hydrogen bonds between nitrogen bases of the nucleotides separate so that the two polynucleotide chains of DNA separate and uncoil. The chains thus separated are complementary to one another. Each stand acts as a template and makes its own complimentary copy over it so that the new formed DNA duplex has one parental stand and one newly formed strand. This method of formation of new daughter DNA molecules is called semi-conservative method of replication (Figure 85).

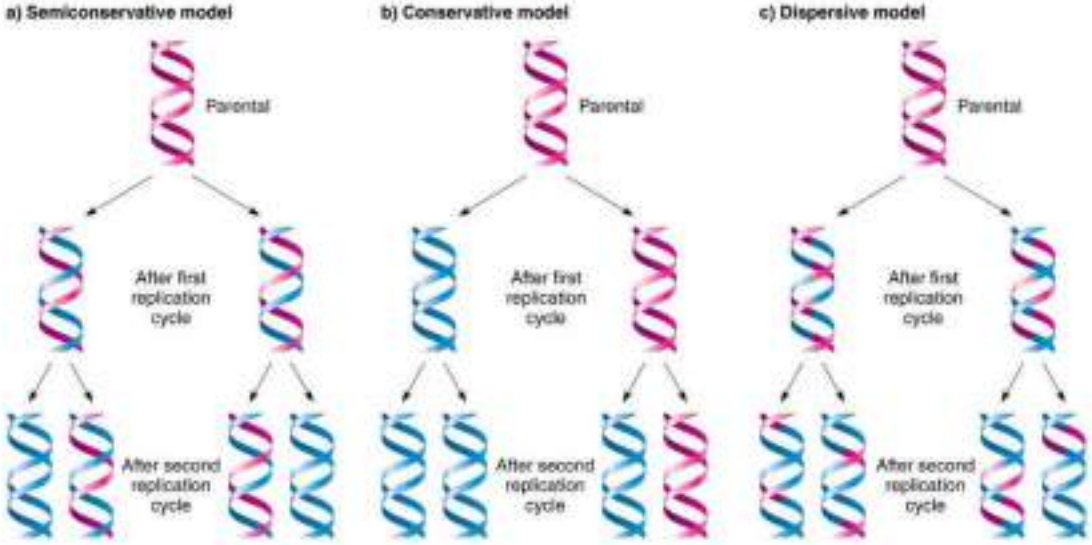


**Figure 85:** DNA replication.

**Mechanism of DNA Replication:**

DNA replication is the process of copying a DNA molecule and involves following four major steps:

1. Initiation of DNA replication.
2. Unwinding of helix.
3. Formation of primer strand.
4. Elongation of new strand.

1. **Initiation of DNA replication-** Replication is regulated by the rate of initiation. Replication of DNA in E. coli always begins at a definite site called **origin of replication**. The ***E. coli,*** origin of replication lies within the genetic locus **'ori'** and is bond to the cell membrane. 'Ori' contains four 9bp binding sites for the initiator protein (DnaA-ATP). The helicase DnaB (or mobilepromoter) binds and extends the single-stranded region for copying.

2. **Unwinding of helix-** Unwinding of DNA molecule into two strands results in the formation of Y shaped structure called **replication fork.** Due to unwinding positive super coiling has to be relieved by the **enzyme topoisomerase or DNA Gyrase**.

3. **Formation of Primer strand:** As the newly formed replication fork displaces the parental lagging strand, a mobile complex called a **primosome**, which includes the DnaB, Helicase and DNA primase help in the synthesizes **of RNA primers**. Both leading and lagging strand primers are elongated by **DNA polymerase III.** Need of primer is there to facilitate the action of DNA polymerase III as this

enzyme cannot initiate the process but can add activated deoxyribonucleotides to the 3' OH end of primer (Figure 86).

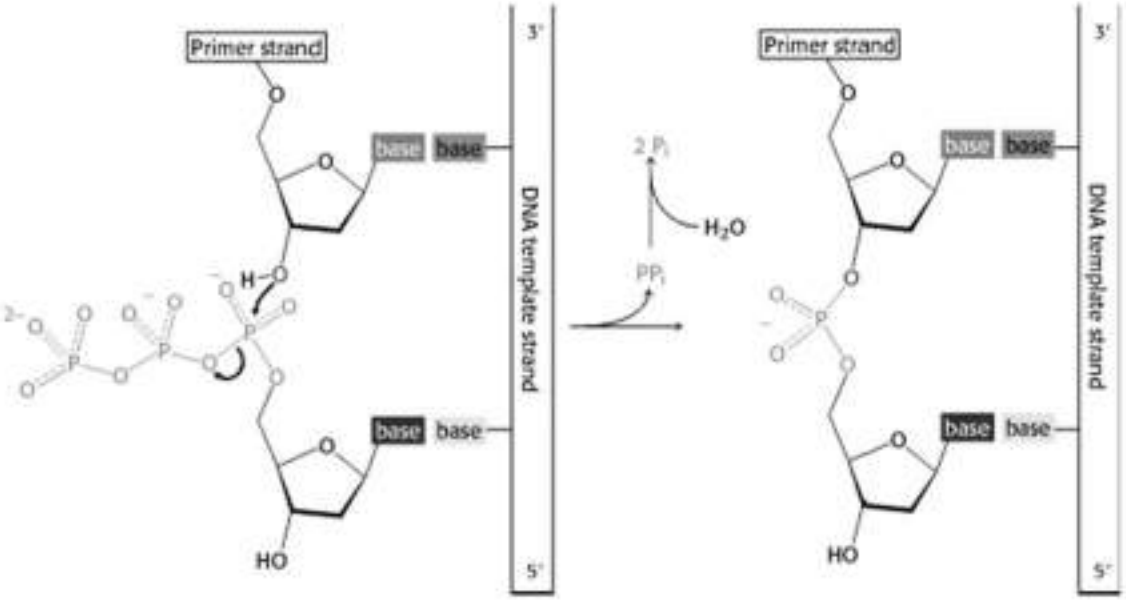


**Figure 86:** DNA Replication (Phosphodiester Bridge is catalyzed by DNA polymerases).

4. **Elongation of new strand:** after the formation of primer strand, DNA replication occurs in 5'→3'direction and complementary deoxyribonucleotides are added only to the free 3'OH end of the primer. A dimer of DNA polymerase III elongates both leading (3'→5') and lagging strands. The leading strand shows continuous replication while the lagging strand shows discontinuous replication. These short pieces of DNA replicated against lagging strand are known as **Okazaki fragments.** Okazaki fragments are 1000-2000 nucleotides long in prokaryotes. A separate RNA primer is used for the synthesis of each Okazaki fragments which, after replacing the RNA primers from deoxyribonucleotides, are later joined together with the help of **DNA ligase** or **DNA synthetase** forming a

continuous lagging strand. Hence DNA replication is semi-discontinuous as the leading strand is synthesized continuously and lagging strand is formed discontinuously in short pieces join later (Figure 87).

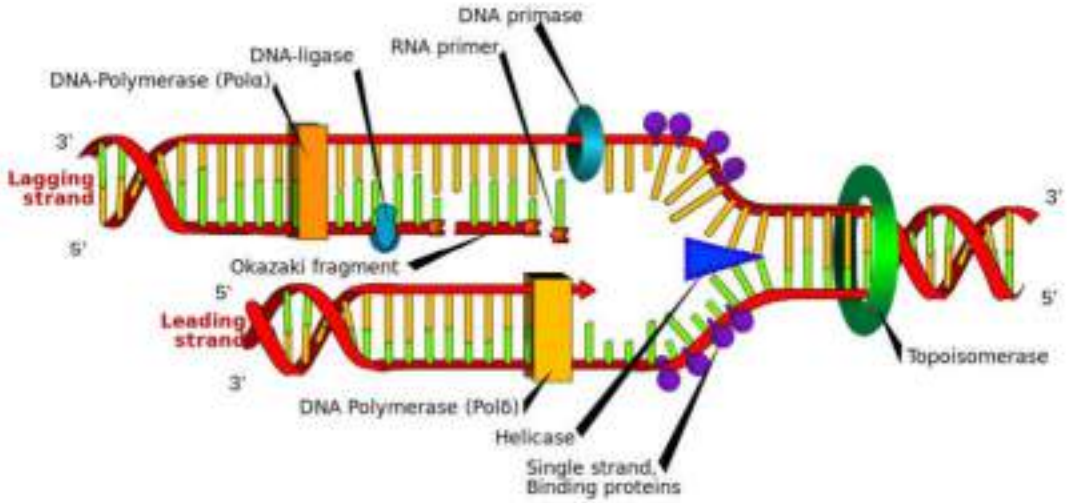


**Figure 87:** DNA Replication. During DNA replication, a number of different enzymes work together to pull apart the two strands so each strand can be used as a template to synthesize new complementary strands. The two new daughter DNA molecules each contain one pre-existing strand and one newly synthesized strand.

## Recombinant DNA:

The tools and technologies of molecular biology for breaking and rejoining DNA sequences from two or more different organisms are known as DNA recombinant technologies. These modified DNA fragments are called recombinant DNA. A recombinant DNA molecule is a vector in which the desired DNA fragment has been inserted to enable its cloning in an appropriate host. This is achieved by using specific enzymes (restriction enzymes) for cutting the DNA into suitable fragments and then for joining together the appropriate fragments by ligation.

## (B) Structure of RNA:

RNA is generally involved in protein synthesis but in majority of plant and some animal virusesit also acts as genetic material. There are two major types of RNA:

1. **Genetic RNA-** H. Fraenkel-Conrat showed that RNA present in **Tobacco Mosaic Virus** is its genetic material and this RNA is responsible for the infection in tobacco plant.

2. **Non- genetic RNA-** Prokaryotes and Eukaryotes where genetic information is contained in the DNA molecule, functions of such cells are performed by a different kind of nucleic acids called non-genetic ribonucleic acid. Non-genetic RNA is synthesized on DNA template. Suchnon genetic RNAs can be of many types like mRNA, r RNA, & t RNA.

### Chemical structure of RNA:

RNA is single stranded polyribonucleotide. Each ribonucleotide is made of:

- Phosphoric acid- $H_3PO_4$
- Ribose sugar- $C_5H_{10}O_5$
- Nitrogen base- Adenine (A), Guanine (G), Cytocine (C) and Uracil (U)

Many ribonucleotides join with each other by phosphor-ester bonds to make a linear chain of polyribonucleotide's. The chain will remain straight under all conditions in mRNA, may fold randomly in r-RNA or specifically to form t-RNA

**Types of RNA:**

The RNA is of following three major types: t RNA, mRNA and r RNA

**(1) Transfer RNA or t-RNA:**

It is also called **soluble or s-RNA**. There are over 100 types of t-RNA. t-RNA is the smallestRNA with 70-85 nucleotides and sedimentation co-efficient of 4S. It is about 10-15% of the total weight of tRNA of the cell. Each tRNA has a corresponding **anticodon** that can recognize the codon on mRNA and exhibit high affinity for specific activated amino acids combine with them and carry them to the site of protein synthesis

**Robert Holley** (1965) and his colleagues reported the complete nucleotide sequence of alanine tRNA of yeast. R. Holley (1965) first of all proposed a **clover leaf model for yeast $tRNA^{ala}$. Cloverleaf structure**-. Five parts or arms of cloverleaf structure are (Figure 88):

**(1) Acceptor stem or arm -** this is a region of the tRNA which acts as a site of attachment for the appropriate amino acid. It is also called **amino acid carrier arm**. It is formed by seven regular Watson & Crick base pairs between the 5' and 3' end of the tRNA. The **3' terminal end** of all tRNA is **always CCA-OH**. It is not base- paired and is the site of attachment of the amino acid. The amino acid is covalently bound through an ester linkage between the carboxyl group of the amino acid and the 3' hydroxyl group of the ribose of the tRNA.

**(2) Anti-codon loop or arm -** The anti-codon loop contains the three-nucleotide sequence that is complementary to the codon of mRNA

to which it corresponds. It consists of a total of 7 unpaired bases, three of which constitute the anti codon. With this site tRNA attaches to mRNA and helps in the transport of amino acids to the site of protein synthesis

(3) **DHU loop or D loop or arm -** The DHU loop is composed of three or four base pairs. It is depending on the species of tRNA. It is also variable in size containing 8 to 12 unpaired bases. The D-loop helps in binding of amino-acyl synthetase. It has modified bases called dihydrouridine hence named so.

(4) **T φC loop or arm-** is named so because of the presence of triplet sequence of pseudouridine (φ). It acts as ribosome recognize arm, help in determining the site of ribosome (A, P or E site) where the tRNA must come and attach during translation.

(5) **The extra arm-** is variable in nucleotides composition and is lacking entirely in some tRNA

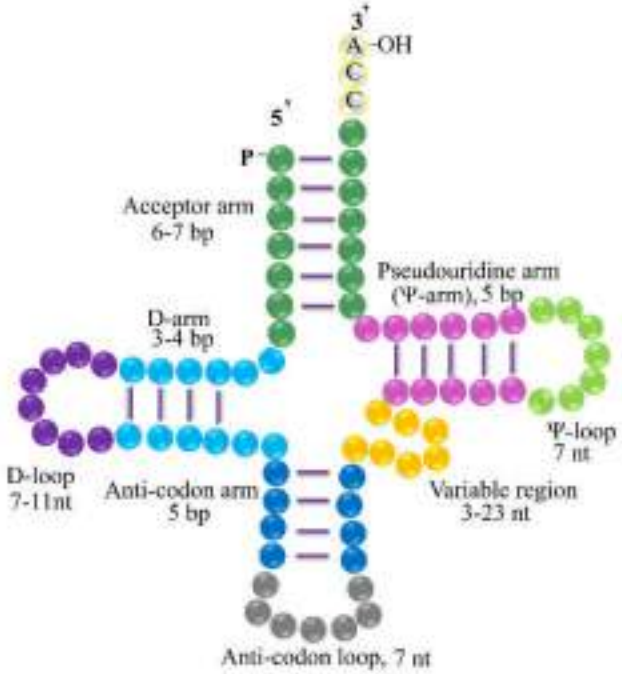


**Figure 88:** t-RNA structure.

**Functions of t-RNA:**

The tRNA plays important role in protein synthesis. T-RNA picks up a specific amino acid from the cytoplasm carries it to the site of protein synthesis and attaches itself to ribosome in accord with the sequence specified by mRNA. It transmits its amino acid to the polypeptide chain. In protein synthesis tRNA acts an adaptor molecule which is meant for transferring amino acids to ribosomes for synthesis of polypeptides. There are different tRNAs for different amino acids. Codons are recognized by anticodons of tRNA. They hold peptidyl chains over the mRNAs.

**(2) Messenger RNA or (mRNA):**

**The structure of mRNA:**

m-RNA is **always single stranded** having normal bases like A, G, U and C along with only afew unusual, substituted bases. There is never base pairing in mRNA. It functions as a templatefor protein synthesis it carries genetic information from DNA to a ribosome and helps to assemble amino acids in their correct order. Each amino acid in a protein is specified by a set of three nucleotides in the mRNA called **codons.** Both prokaryotic and eukaryotic mRNA contains three primary regions (Figure 89):

a) **5' untranslated region (5'UTR) -** the 5' untranslated region is a sequence of nucleotides atthe 5' end of the mRNA that does not code for the amino acid sequence of a protein. In **prokaryotic** (bacterial cell) mRNA contains a consensus sequence called the **Shine-Dalgarno sequence** (5'AGGAGGU3'), which serves as **the**

**ribosome binding site during translation**, it is formed of approximately 7 nucleotides upstream of the first or start codon. Eukaryotic mRNA has no such equivalent sequences in its 5' untranslated region. This is the sequence of the mRNA extending from the 5' end of the mRNA to the initiation codon. It is not translated into polypeptide sequence. It has a **function analogous to the function of a promoter on a gene**. Itwill direct the binding of the ribosome to the initiation codon.

b) **Protein coding region**- this region comprises the codon that specify the amino acid sequence of the protein. This region begins with a start codon and ends with a stop codon. This region has 3 regions namely initiation codon, coding region, stop codon.

- **Initiation codon-** it is always **AUG** and codes for a **methionine.** This is the triplet codonat which polypeptide synthesis begins. All polypeptides are synthesized with an amino terminal methionine.
- **Coding region-**this is the sequence of mRNA that contains **the consecutive triplet codons** that direct polypeptide synthesis. This region starts from the start codon and continue up to the stop codon. The coding region is often referred to as the open reading frame or ORF.
- **Stop codon-**this is the triplet codon that signals the **termination of translation**. There are three possible stop codon sequences **UAA, UAG, UGA**. Stop codons have no corresponding tRNA or amino acid.

c) **3' Untranslated region (3'UTR)-**This region of mRNA is the 3' un-translated region, a sequence of nucleotides at the 3'end of mRNA that is not translated into protein. This is the nucleotide sequence downstream from the stop codon. It extends from the stop codon to the 3' end of the mRNA. It does not code for amino acid sequence. It may function in stabilizing the mRNA. In eukaryotes it is transcribes as hnRNA which is converted into functional mRNA in the cytoplasm by removing introns (intervening sequences) and joining together exons (expressible sequences)

For the convenience the mRNA structure can be summarized as:

1. **Cap**- at 5' end, has methylated structure, does not translate
2. **Noncoding region-1**- has 10-100 nucleotides, rich in U and A bases, does not translate.
3. **The inititation codon**- AUG, codes for methionine amino acid
4. **The coding region**-about 1500 nucleotides on an average, translate proteins.
5. **Termination codon**- either of UAA, UAG or UGA ie present, helps in termination of translation
6. **Noncoding region-2**- made of 50-150 nucleotides, does not translate, has sequence likeAAUAAA
7. **Poly(A) sequence**- 200-250 A nucleotides, does not translate, makes tail of mRNA.

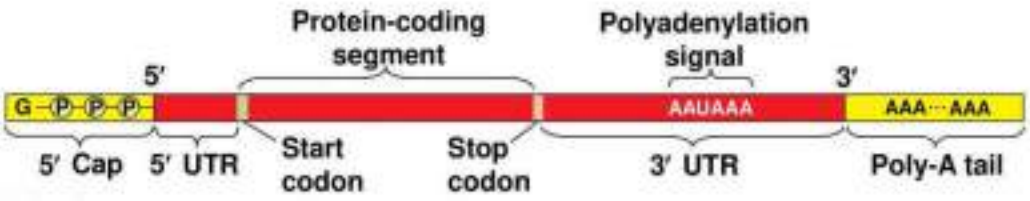


**Figure 89:** mRNA showing different regions.

**Functions of m-RNA:**

m-RNA carries coded information to be translation into polypeptide. It directly takes part in protein synthesis in a cell. In some viruses having RNA as genetic material, it may undergo reverse transcription to from compact genes which are used in genetic engineering. The phenomenon also occurs in nature and has added certain genes in the genomes.

**(3) Ribosomal rRNA (r-RNA):**

Ribosomal, stable, or insoluble RNA constitutes the largest part (up to 80%) of the total cellular RNA. It was reported by **Kuntz.** It is found primarily in the cytoplasm as well as organelle. In prokaryotes it is transcribed from ribosomal DNA which is a part of nuclear DNA but in eukaryotes ribosome is formed on nucleolar DNA. The genetic instruction contained in mRNA is translated into the amino acid sequences of polypeptides only with the help of ribosomes. Thus ribosomes play an integral part in the transfer of genetic information from genotype to phenotype. R-RNA is most stable type of RNA.

**Structure and processing of ribosome RNA**:

It forms about 80% of the total cellular RNA. r- RNA consists of a single stranded RNA which gets twisted over itself in certain regions due to complementary base pairing. R-RNA strand unfold on heating and refold on coiling. It is one the most stable RNA among all types of RNAs. R-RNA and ribo-proteins constitute ribosomes

In **eukaryotes** 4 types of rRNAs found are **28s, 18s, 5.85s, and 5s.** In the nucleolus of eukaryotes, RNA polymerase-I transcribes the rRNA

genes, which usually exit in tandem repeats to yield a long, single pre-rRNA which contains one copy each of the 18s, 5.8s and 28s sequences. Various spacer sequences are removed from the long pre-rRNA molecule by a seriesof specific cleavages. Many specific ribose methylations take place directed by small ribonucleoprotein particles (snRNPs) and the mature rRNA molecule fold and complex with ribosomal proteins. RNA pol. III synthesizes the 5srRNA from unlinked genes (Figure 90).

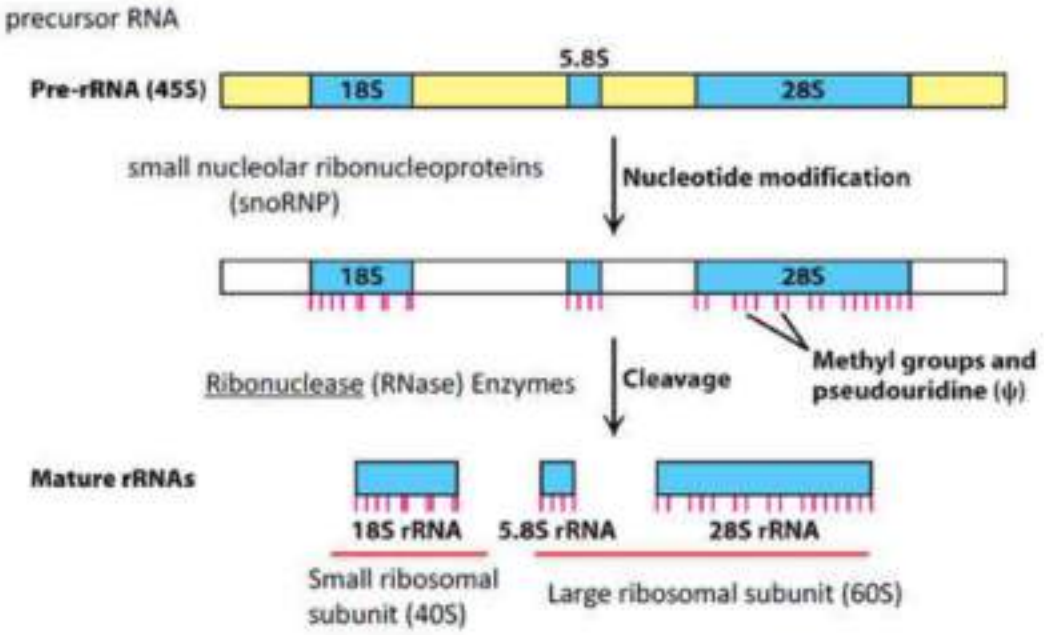


**Figure 90:** processing of rRNA in a eukaryotic cell.

## Functions of r-RNA:

r-RNA binds to protein molecules and give rise to ribosomes. 3'end of 18s rRNA (16s in prokaryotes) has unpaired nucleotides complementary to those of region or m-RNA, it is the site where ribosomes bind to mRNA during translation. 5s rRNA and surrounding protein complex provide binding site for tRNA.

**Important features of RNA:**

- RNA is copied from one strand of the double helix called the template strand.
- RNA differs from DNA in that it is single stranded, has uracil inserted of thymine and has ribose sugar instead of deoxyribose ribose.
- Messenger RNA (mRNA) carries the genetic information that specifies a particular amino acid sequence of protein synthesized.
- mRNA bases constitute codons, each codon is made of three consecutive bases in a row.
- rRNA joins certain proteins to form ribosomes. Ribosomes physically support the other structures involved in protein synthesis, and some rRNA catalyses' formation of peptide bonds.
- tRNA is clover leaf-shaped and connects mRNA codon to an amino.
- In prokaryotes, RNA is translated as soon as it is transcribed while in eukaryotes, RNA is often altered (or modified) before it is actively translated.
- mRNA gains a modified nucleotide cap and a poly A tail.
- Many genes have intervening sequences called introns, which are not transcribed and cutout from the mRNA. The protein encoding sequences in mRNA, exons, are then reattached. Ribozymes are small RNAs with catalytic activity that can splice introns. They join proteins to form snurps, which associate to form spliceosomes.
- After being processed the RNA must be exported from the nucleus before it is translated.

## PROTEIN SYNTHESIS

The replication of DNA serves to carry genetic information from cell to cell and from generation to generation. This information is translated into protein that determines the phenotype of cell by controlling its biochemical reactions. Protein synthesis is the vital function of the cell where in the genetic information stored in DNA is passed on to RNA, especially mRNA by the process of **transcription.** All the three types of RNA i.e., mRNA, tRNA and rRNA together help in translating the coded information in the form of a polypeptide **(translation)**. The linear chain of amino acids translated is the primary protein which undergoes configurationally changes to form secondary, tertiary or quaternary proteins.

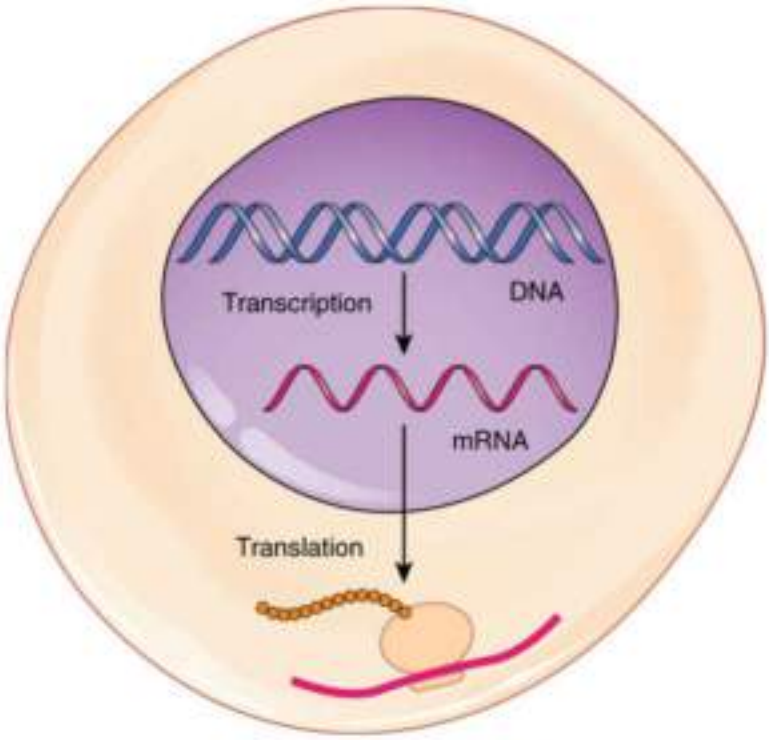


**Figure 91:** From DNA to Protein (central dogma): Transcription through Translation. Transcription within the cell nucleus produces an mRNA molecule, which is modified and then sent into the cytoplasm for translation.

**Protein Synthesis and its Mechanism:**

A gene expresses itself by protein synthesis. Protein synthesis is under direct controlof DNA in most cases or else under the control of genetic RNA where DNA is absent. Information for structure of a polypeptide is stored in a polynucleotide chain of DNA orRNA.

In 1958 **F. Crick** proposed that the concept of central dogma, which states that when a particular gene is expressed (control a function or a reactions) its information is copied into another nucleic acid (mRNA) which in turn directs the synthesis of specific proteins. So the central dogma was proposed as unidirectional flow of molecular information from DNA to mRNA and finally to polypeptide. Later a reverse of central dogma was also found in retroviruses. **H. Temin and D. Baltimore** (1970) reported that retro viruses operate a central dogma in reverse manner (inverse flow of information) or teminism inside host cells. This discovery was important in understanding cancer and hence, these two scientists were awarded Nobel Prize.

Genetic RNA of these viruses first synthesizes DNA through reverse transcription. This process is catalyzed by the enzyme reverse transcriptase. DNA then transfers information tomessenger RNA which takes part in translation of the coded information to from polypeptide.

**Necessary Materials:**

(1) **Amino acids**- there are some 20 amino acids and amides which constitute building blocks or monomers of proteins. They are found in the cellular pool or cytoplasm.

**The genetic code:** it is a set of rules defining how the four-letter code of DNA is translated into the 20-letter code of amino acids, which are the building blocks of proteins. The genetic code is a set of three-letter combinations of nucleotides called codons **(triplet),** each of which corresponds to a specific amino acid or stop signal. The concept of codons was first described by Francis Crick and his colleagues in 1961. There are 64 possible permutations, or combinations, of three-letter nucleotide sequences that can be made from the four nucleotides. Of these 64 codons, 61 represent amino acids, and three are stop signals. Although each codon is specific for only one amino acid (or one stop signal), the genetic code is described as degenerate, or redundant, because a single amino acid may be coded for by more than one codon. It is also important to note that the genetic code does not overlap, meaning that each nucleotide is part of only one codon-a single nucleotide cannot be part of two adjacent codons. Furthermore, the genetic code is nearly universal, with only rare variations reported (Figure 92, 93).

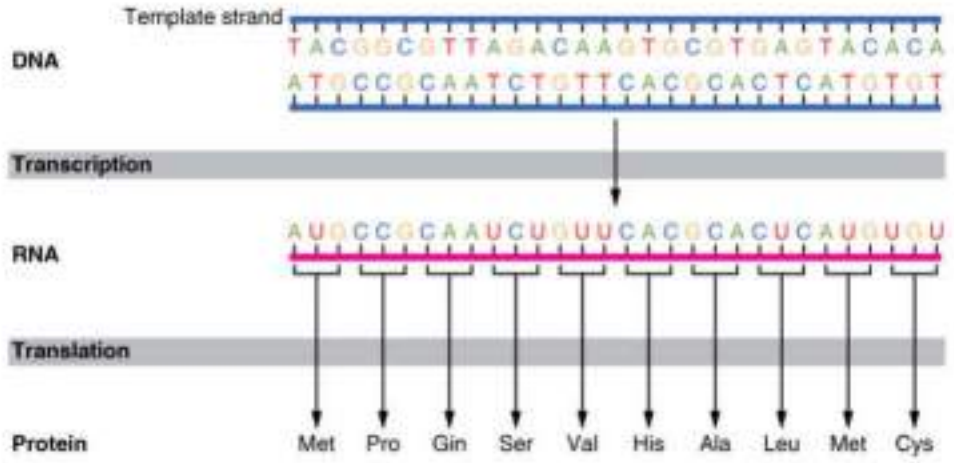


**Figure 92:** The Genetic Code. DNA holds all the genetic information necessary to build a cell's proteins.

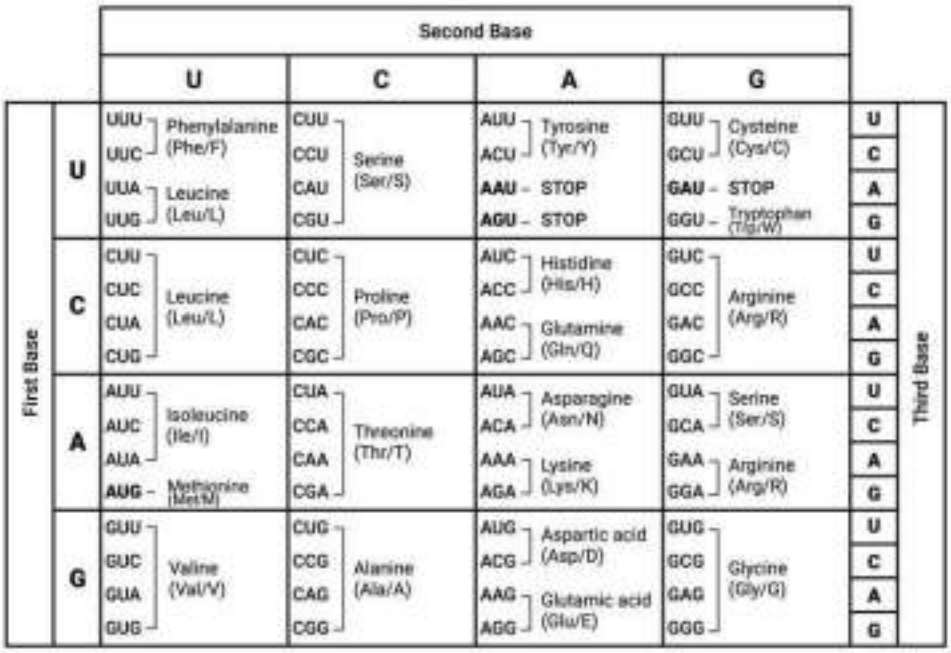


**Figure 93:** The 20 amino acids formation from 4 nucleotides.

**(2) Ribosome**- ribosome comprises two subunits which exists as separate subunits prior to the translation of mRNA and contain following sites (Figure 94):

- **P site (peptidyl site or D site- donor site) -** P site is jointly contributed by the two ribosomal subunits, most frequently occupied by peptidyl-tRNA or the tRNA carrying growing peptide chain. . The P-site is also referred to as the puromycin sensitive site. Puromycin is an antibiotic which shows similarities with a part of amino acyl-tRNA
- **A site (amino acyl site) -** A site is situated on the larger subunit of ribosome. It faces the tunnel between the two subunits, frequently occupied by amino acyl-tRNA, functions as acceptor for growing protein during peptide bond formation.
- **E-site** – the exit site, the ribosomal site harboring decylated

tRNA on transit out from the ribosome.

**The different parts of ribosomes, connected with protein synthesis are-**

a- **A tunnel**- It lies between the two subunits, acts as a place for mRNA

b- **The longitudinal groove**-is part of the longer subunits which acts as apassage of newly synthesized polypeptide

c- **Reactive sites**- P, A and E-site

d- **P-site-** acts as a donor of peptide chain to the newly coming tRNA

e- **A-site-** acts as a binding site for new tRNA with its amino acid for the elongation of polypeptide chain.

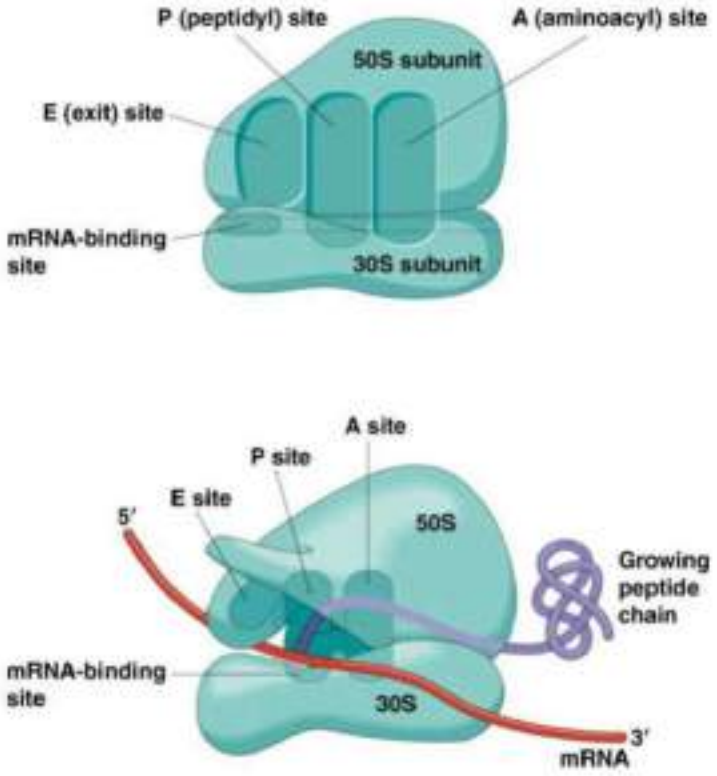


**Figure 94:** Different sites of ribosome (each with specified function).

(3) **mRNA-** carrying genetic information of DNA into cytoplasm for its translation

(4) **tRNA-** to transport the respective amino acids as per their anticodons against thecodons of mRNA

(5) **Enzymes-** amino acid activating system **(aminoacyl- tRNA synthetase),** Peptidepolymerase system

(6) **ATP-** as energy source

(7) **GTP-** for synthesis of peptide bonds

(8) Soluble protein initiation and transfer factors

(9) **Various inorganic cations** ($K^+$, $NH_4^+$, $Mg^{++}$ or $Mn^{++}$)

**Mechanism of protein Synthesis:**

Two major steps are involved in protein synthesis are:-

**I- Transcription**: involving transfer of genetic information from DNA to mRNA.

**II- Translation:** involving translation of the language of nucleic acid into that of apolypeptide.

**I- Transcription process:**

The transfer of genetic information from DNA to mRNA in general is known as transcription. The segment of DNA that takes part in transcription is called transcription unit. It has three components:

a) A promoter

b) The structural gene

c) A terminator

**a) A promoter-** promoter sequences are present upstream (5'end) of the structural genes of a transcription unit. The binding sites for

RNA polymerase lies within the promoter sequence. In prokaryotes 10bp upstream from the start point lies a conserved sequence described as 10 nucleotide sequences **TATAAT or "pribnow box"** and 35 nucleotide sequences **TTGACA as "recognitionsequence".**

b) **The structural gene**- structure gene is part of that DNA strand which has 3'→5'polarity as transcription occur in 5'→3' direction. The strand of DNA that directs the synthesis of mRNA is called **template or non-coding strand**. The complementary strand is called **non-template or coding strand,** it is identical in base sequence to RNA transcribed from gene, only with U in place of T.

c) **A terminator**- terminator is present at 3' end of coding strand and defines the end of the process of transcription. The base sequence of the mRNA molecule is complementary to that ofthe antisense strand which served as it template. Like DNA synthesis RNA synthesis also proceeds from 5' to 3' direction (5'→3').

**Transcription of mRNA in Eukaryotes (Figure 95):**

**Eukaryotes**-total 4 types of RNA polymerase, 3 types of RNA polymerase in nucleus, one inorganelles,

- **RNA-Polymerase** I: transcribes **rRNA ( 28S, 18S & 5.8S)**
- **RNA polymerase II:** transcribes **precursor of mRNA** (**hnRNA**- heterogeneous nuclear RNA)
- **RNA polymerase III:** transcribes **tRNA, 5SrRNA & snRNAs** (smallnuclear RNAs)

1. **Initiation**: binding of **RNA polymerase** to the **promoter region** with the help of an **Initiation Factor- Sigma factor** (binding of σ-

factor alter the property of enzyme; make to function as an initiation enzyme).

2. **Elongation**- RNA polymerase will keep on making a complementary strand against template strand with the help of ribonucleotides. The newly transcribed strand keeps separating and the DNA duplex keep on folding back instantaneously. During elongation, same RNA polymerase acts as elongation enzyme due to separation of σ- factor from it. **The direction of transcription is also from 5' 3'like replication**. So the template against which it is transcribed has polarity of 3'—5'.
3. **Termination**- after reaching the terminator region newly formed or nascent RNA falls off along with RNA polymerase. Termination is assisted by Rho-factor(ρ-factor)

   In eukaryotes the promoter site is recognized by presence of specific nucleotide sequence called **TATA box or Hogness box or Pribnow Box** (7 base pair long- TATAAA or TATAATs) located 19-27bp upstream to the start point. Another sequence is CAAT box present between -70 and -80bp. The nucleotide sequence at the two ends of all mRNA molecules is the same. Normally mRNA carries the codons of signal complete proteinmolecule (monocistronic mRNA) in eukaryotes, but in prokaryotes, it carries codons from several adjacent DNA cistron and becomes much longer in size (polycistronic mRNA).

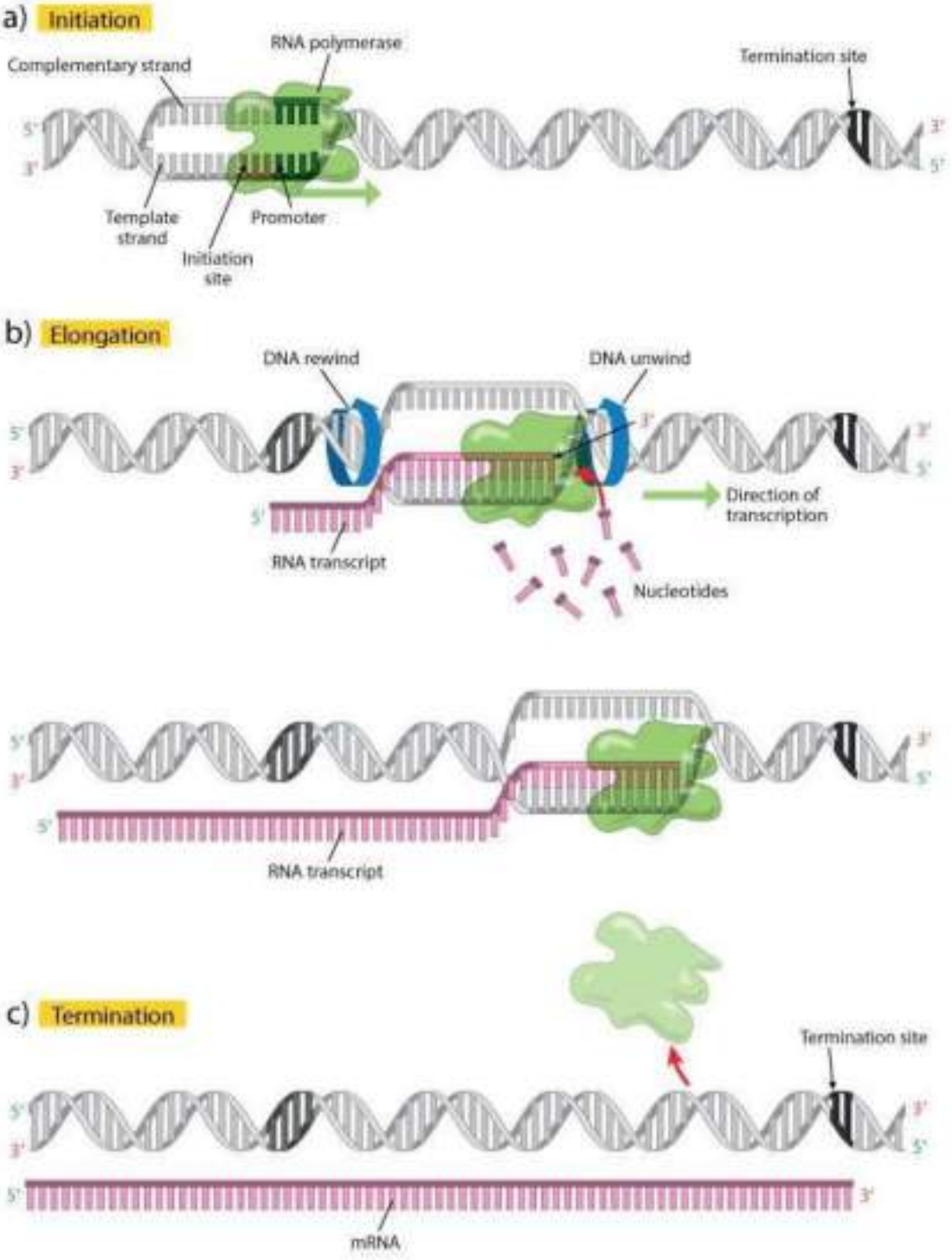


**Figure 95:** Eukaryotic cells transcription process.

**Processing of Eukaryotic Transcript (Figure 96):**

- **Splicing-** removal of **non-functional introns** and joining of all **functional exons** to make it a functional transcript. Splicing is important to remove the non-functional partof genetic information the DNA has kept but RNA does not need it. During copying from DNA, RNA does receive this non informative part in the form of introns but remove it with the help of some enzymes to make it functional.
- **Capping-** addition of methyl-guanosine triphosphate at 5' end of hnRNA
- **Tailing-** addition of 200-300 adenylated nucleotides at 3'end of hnRNA, addition of these nucleotides has no relation with the template.

The fully processed hnRNA is called mRNA, transported to the cytoplasm for translation.

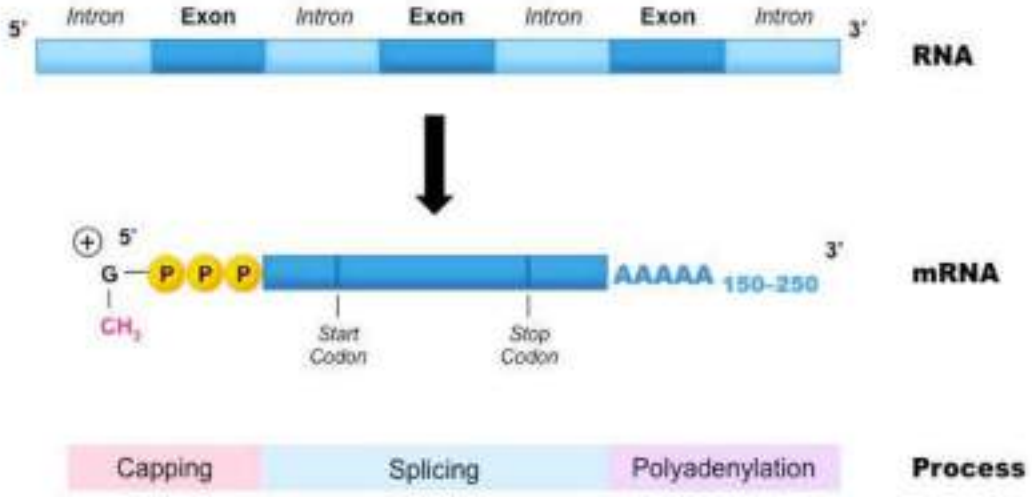


**Figure 96:** Processing of Eukaryotic Transcript

## II- Translation process:

### Components of Translation:

- **mRNA–** the mRNA serves at the template that will determine the sequence of aminoacids in the new polypeptide. It has following components:
  - 5' untranslated region or 5'UTR.
  - Initiation codon.
  - Coding region.
  - Stop codon.
  - 3' untranslated region or 3'UTR.
- **t-RNA-** tRNA, a clover leaf shaped molecule, delivers the correct amino acid to the ribosome as directed by the codon on the mRNA for incorporation into the polypeptide. It has following arms, each with specified function:
  - 3'amino acid carrier arm or acceptor arm with –CCA sequence.
  - Ribosome recognizing arm-to recognize A or P or E-site.
  - Anticodon arm- with 3 nucleotides to bind to complementary codon.
  - Enzyme recognizing arm- to recognize specific aminoacyl synthetase.
  - 5énd with G.
- **Ribosome-** protein synthesizing machinery, help in holding mRNA and tRNA for specific codon translation, has following components:
  - Smaller subunit ( 30S or 40S).

- Larger subunit ( 50S or 60S).
- Groove or tunnel between two subunits to hold mRNA.
- Three sites- P, A and E-site.
- Enzyme, peptidyl transferase, helps in peptide bond formation.

**General steps of eukaryote translation (Figure 97):**

1- **Activation of amino acids or charging of amino acids:** the amino acids attachment to the tRNA molecules is an active process and requires a lot of energy. In the presence of ATP, an amino acid combines with its specific amino acyl-tRNA synthetase; Mg2+ is also required in this reaction.

2- **Aminoacylation of tRNA or charging of tRNA:** It is the loading of tRNA with the activated amino acid.

3- **Initiation of translation**: In the first step there is binding of mRNA with smaller subunit of ribosome. Translation of Initiation codon (AUG) by a charged tRNA with Methionine (n-formyl methionine, f-Met, in prokaryote) amino acids takes place. It is followed by the translation of second codon by 2nd charged tRNA. After the translation of first two codons, the association of bigger subunit of ribosome takes place to form a complete translational complex. When two such charged tRNA comes close, the peptide bond between two amino acids, they carry, will take place with the help of a ribozyme called- Peptidyl transferase (23SrRNA molecule) enzyme. Formation of peptide bond between 1st& 2nd amino acid takes place. UTR- (Un- Translated-Regions) is the flanks of mRNA before Initiation and after the stop codon, which are not to be

translated, but they play role in efficient translation.

4- **Elongation:** The translated part of mRNA translocate from one to next codon. Regular addition of new amino acids takes place at A Polypeptide chain (PPC) keeps elongating at the expense of energy provided by GTP. PPC hangs in the groove of bigger subunit of ribosome on the P-site.

5- **Termination-** Binding of releasing factors to the stop codon helps in the release of polypeptide and terminates translation. Synthesis of polypeptide terminates when a nonsense codon of mRNA reaches the A-site. There are three nonsense codons- UAA, UAG & UGA. These codons are not recognized by any of the tRNAs. There is no tRNA having anticodon complementary to stop codon i.e., none of the tRNA has AUU, AUC or ACU anticodon. Finally, the ribosome encounters a stop codon. The polypeptide, tRNA and mRNA are released. The small and large subunits dissociate from one another.

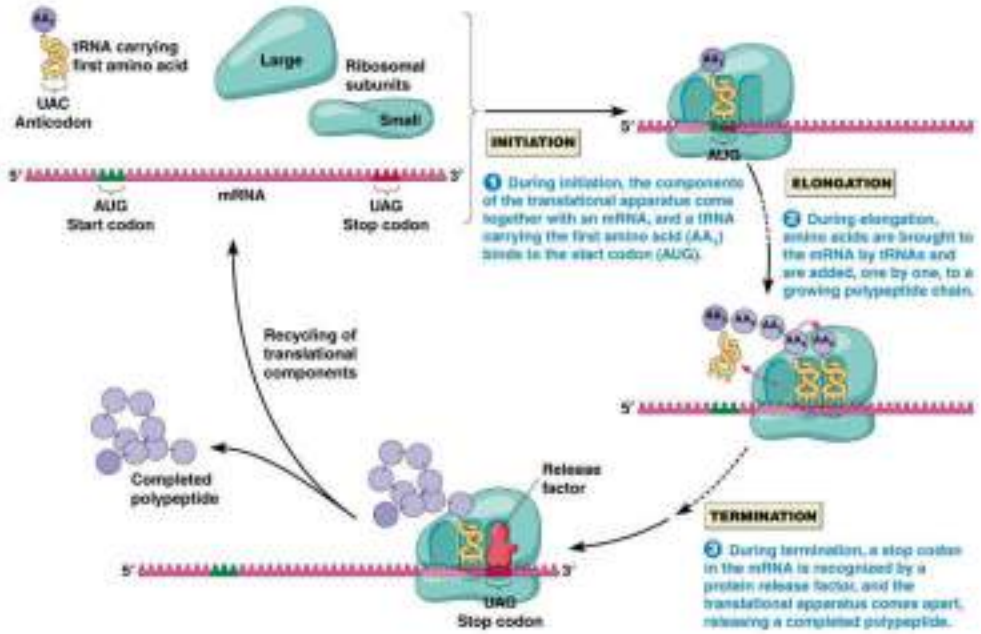


**Figure 97:** Eukaryote translation process.

## The operon:

According to the operon model, several gene codes for an enzyme in some metabolic pathways are located in sequence on chromosome. The expressions of structural genes are controlled by some regulatory genes. The **Operon means a unit of gene expression (Figure 98)** and regulation which typically includes:

1- **The structural genes:** also called cistron are any gene/s other than the regulatory genes, whose products or enzymes are involved in a specific biosynthetic pathway and whose expression is coordinately controlled.

2- **Operator sequence**: control elements such as an operator sequence, which is a DNA sequence that regulates transcription of the structural genes.

3- **Regulator gene (s):** the genes, whose products recognize the control elements e.g., a repressor which binds told regulates the operator sequence of the same operon.

Operon has structural and regulatory genes that function as a single unit, it includes the following:

- A regulator gene is located outside the operon codes for a repressor or Apo-repressor protein molecule.
- A promoter is a sequence of DNA where RNA polymerase attaches when a gene is to be transcribed.
- An operator is a short sequence of DNA where repressor binds,

preventing RNA polymerase from attaching to the promoter.

- Structural genes code for enzymes of a metabolic pathway and are transcribed as a unit.

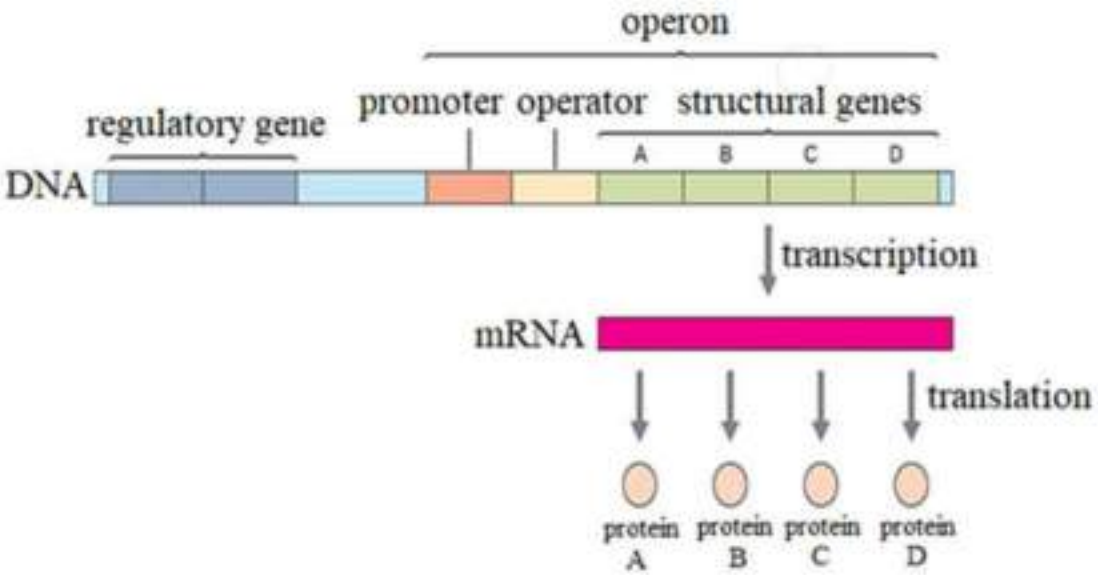


**Figure 98:** The operon structure.

# CELLULAR DIFERANTIATION

How does a complex organism such as a human develop from a single cell "a fertilized egg" into the vast array of cell types such as nerve cells, muscle cells, and epithelial cells that characterize the adult? Throughout development and adulthood, the process of cellular differentiation leads cells to assume their final morphology and physiology. Differentiation is the process by which unspecialized cells become specialized to carry out distinct functions.

## Stem Cells:

A **stem cell** is an unspecialized cell that can divide without limit as needed and can, under specific conditions, differentiate into specialized cells. Stem cells are divided into several categories according to their potential to differentiate. The first embryonic cells that arise from the division of the zygote are the ultimate stem cells; these stems cells are described as **totipotent** because they have the potential to differentiate into any of the cells needed to enable an organism to grow and develop. The embryonic cells that develop from totipotent stem cells and are precursors to the fundamental tissue layers of the embryo are classified as pluripotent. A **pluripotent** stem cell is one that has the potential to differentiate into any type of human tissue but cannot support the full development of an organism.

These cells then become slightly more specialized and are referred to as multipotent cells. A **multipotent** stem cell has the potential to differentiate into different types of cells within a given cell lineage or small number of lineages, such as a red blood cell or white blood cell.

Finally, multipotent cells can become further specialized oligopotent cells. An **oligopotent** stem cell is limited to becoming one of a few different cell types. In contrast, a **unipotent** cell is fully specialized and can only reproduce to generate more of its own specific cell type. Stem cells are unique in that they can also continually divide and regenerate new stem cells instead of further specializing. There are different stem cells present at different stages of a human's life. They include the embryonic stem cells of the embryo, fetal stem cells of the fetus, and adult stem cells in the adult. One type of adult stem cell is the epithelial stem cell, which gives rise to the keratinocytes in the multiple layers of epithelial cells in the epidermis of skin. Adult bone marrow has three distinct types of stem cells: hematopoietic stem cells, which give rise to red blood cells, white blood cells, and platelets (Figure 99); endothelial stem cells, which give rise to the endothelial cell types that line blood and lymph vessels; and mesenchymal stem cells, which give rise to the different types of muscle cells.

**Differentiation:**

When a cell differentiates (becomes more specialized), it may undertake major changes in its size, shape, metabolic activity, and overall function. Because all cells in the body, beginning with the fertilized egg, contain the same DNA, how do the different cell types come to be so different? The answer is analogous to a movie script. The different actors in a movie all read from the same script, however, they are each only reading their own part of the script. Similarly, all cells contain the same full complement of DNA, but each type of cell only

"reads" the portions of DNA that are relevant to its own function. In biology, this is referred to as the unique genetic expression of each cell. In order for a cell to differentiate into its specialized form and function, it need only manipulate those genes (and thus those proteins) that will be expressed, and not those that will remain silent. The primary mechanism by which genes are turned "on" or "off" is through transcription factors. A **transcription factor** is one of a class of proteins that bind to specific genes on the DNA molecule and either promote or inhibit their transcription (Figure 100).

In contrast, adult stem cells isolated from a patient are not seen as foreign by the body, but they have a limited range of differentiation. Some individuals bank the cord blood or deciduous teeth of their child, storing away those sources of stem cells for future use, should their child need it. Induced pluripotent stem cells are considered a promising advance in the field because using them avoids the legal, ethical, and immunological pitfalls of embryonic stem cells.

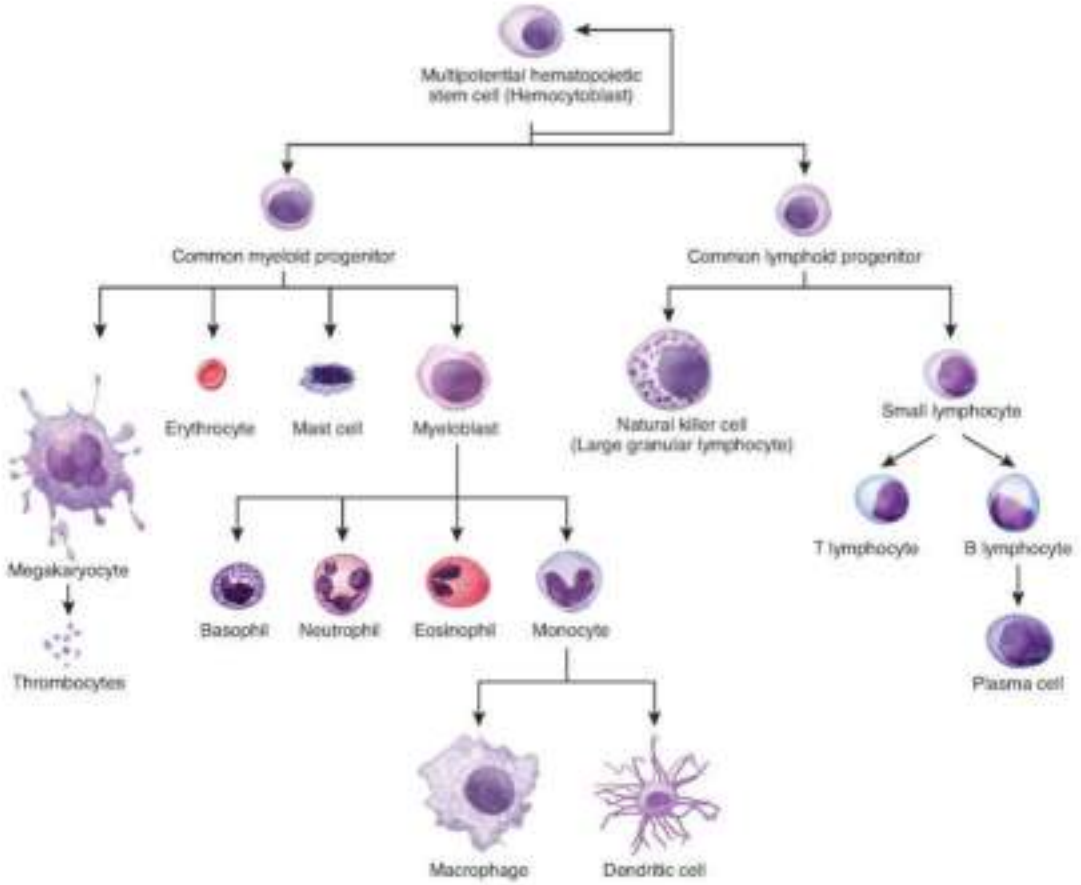


**Figure 99:** Hematopoiesis. The process of hematopoiesis involves the differentiation of multipotent cells into blood and immune cells. The multipotent hematopoietic stem cells give rise to many different cell types, including the cells of the immune system and red blood cells.

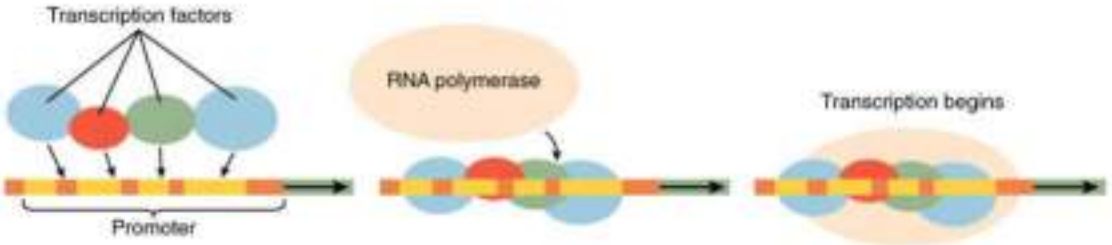


**Figure 100:** Transcription Factors Regulate Gene Expression. While each body cell contains the organism's entire genome, different cells regulate gene expression with the use of various transcription factors. Transcription factors are proteins that affect the binding of RNA polymerase to a particular gene on the DNA molecule.

# THE BIOGENESIS OF CELL ORGANELLES

Organelle biogenesis is the process by which new organelles are made. In a few cases, notably mitochondria and chloroplasts, some organelle proteins are encoded by the organelle's own genome. However, the amount of DNA in such organelles can encode only a very small number of the many proteins required. In practice, the study of organelle biogenesis includes the mechanisms by which proteins and lipids, newly synthesized elsewhere in the cell, are delivered to organelles and the process by which organelles are divided between daughter cells during mitosis. In general, it is thought that new organelles are derived by proliferation of preexisting organelles. However, for some organelles on the secretory and endocytic pathways, e.g., the Golgi complex, the extent to which they can be made de novo by a cell without a preexisting organelle or template remains a subject of controversy.

**The mechanisms for organelle biogenesis:**

The mechanisms for organelle biogenesis in the secretory and endocytic pathways (Figure 101). includes:

**A) Vesicular traffic:**

A coated vesicle buds from a donor organelle, loses its coat and fuses with an acceptor organelle. The coat made up of cytosolic proteins (denoted by black ovals and gray circles - refer to legend for designations of individual factors) both deforms the donor membrane to form the vesicle and sorts into the vesicle only those proteins

(checked boxes) selected for delivery. Vesicle fusion with the acceptor membrane requires formation of a SNARE complex. Thus, the vesicle must contain a v-SNARE which forms a complex with a cognate t-SNARE in the acceptor membrane.

**B) Maturation:**

An organelle is formed from the preceding organelle in a pathway by retrieval of those proteins (hatched boxes) which should not be in the final organelle, using retrograde vesicular traffic to deliver them to an earlier stage in the pathway. Additional proteins (stippled boxes) may be delivered to the organelle by vesicular traffic from other sources (e.g., to endocytic compartments from the biosynthetic/secretory pathway). It should be noted that an organelle may be formed and/ or maintain its composition by a mixture of the two mechanisms. Thus, when organelles are formed by anterograde vesicular traffic, retrieval may still be used to ensure that mis-sorted proteins are returned to their correct residence.

**Organization into Complex Structures**

Organelle biogenesis is not simply a question of delivering newly synthesized proteins and lipids to a specific intracellular site but may also require the establishment of a complex architecture.

A dramatic example of this is seen in the case of the Golgi complex where it is clear that the observed morphology in part reflects the interaction of the structure with the cytoskeleton via appropriate motor proteins and in part the function of matrix proteins in the organization

of the cisternae. A further complication, particularly for organelles on the secretory and endocytic pathways, is the requirement to maintain morphological form and associated functional integrity despite the large volume of through traffic of both proteins and lipids. In the case of the Golgi complex, there has long been a debate about how secreted proteins pass through it. The work of Rothman and colleagues suggested anterograde vesicular traffic between the Golgi cisternae. However, electron microscopy studies of large macromolecules, including algal scales and collagen aggregates favored a maturation model with new cisternae forming on the cis-side and mature ones fragmenting from the trans-side. The cisternal maturation model has been refined to encompass data on retrograde vesicular traffic in COPI coated vesicles such that the present consensus is that most, if not all, anterograde movement through the Golgi complex is the result of cisternal progression with retrograde vesicular traffic ensuring that the polarized distribution of Golgi enzymes in the cisternal stack is maintained (Figure 101).

A recent three-dimensional reconstruction of the Golgi complex from data obtained by high voltage electron microscopy has suggested that tubular and vesicular structures can bud at every level of the Golgi stack. Structurally, using conventional electron microscopy techniques, and functionally, the trans-Golgi network can be distinguished from the cisternal stack and is defined as the site for sorting to different post-Golgi destinations. Both clathrin-coated vesicles and noncoated tubular structures appear to bud from the trans-Golgi network.

Experiments in which secreted proteins tagged with green fluorescent protein have been imaged as they leave the Golgi complex in living cells have shown that large tubular carriers are particularly important for constitutive traffic to the cell surface.110 In many neuroendocrine cell types, regulated secretory granules are also formed at the trans-Golgi network. Despite the biogenesis of such organelles being amongst the first to be studied by radiolabeling pulse-chase techniques, the mechanisms by which proteins are sorted into these granules remain unclear, with "sorting for entry" and "sorting by retention" models still the subject of much debate.

In the endocytic pathway, the biogenesis of individual organelles has been less well studied with the exception of lysosomes and the yeast vacuole. This has partly been due to the pleiomorphic morphology of endosomes, partly to the difficulty of identifying marker proteins that, at steady state, are mainly localized in endosomes and partly because the molecular mechanisms of membrane traffic through the pathway have only started to be understood in the last few years. As in the secretory pathway, vesicular traffic between individual organelles does not explain all steps in the pathway. Clathrin-coated vesicles budding from the plasma membrane comprise a very important, but not sole, mechanism of delivery from the plasma membrane to early endosomes (defined historically as the first endosomal compartment to be entered by endocytosed ligands). Traffic from early to late endosomes, found deeper within the cell, has been studied extensively and is mediated by large endocytic carrier vesicles which some regard as matured early endosomes. Delivery from late endosomes to lysosomes involves direct

fusion between the two organelles. Such fusion is SNARE-mediated and results in a hybrid organelle from which lysosomes are reformed. In addition to heterotypic fusion between late endosomes and lysosomes, the endocytic pathway is characterized by the occurrence of homotypic fusions between early endosomes and between late endosomes. These homotypic fusion events are also SNARE-mediated and allow continuous remodeling of these organelles. Organelles in the late endocytic pathway are characterized by the presence of numerous internal vesicles, leading to the alternative description of late endosomes as multivesicular bodies. Some cell surface receptors are sorted into such vesicles after internalization from the plasma membrane and prior to degradation. Recently, insights have been gained into the molecular mechanisms by which proteins are sorted into these vesicles, which have a different lipid composition from the limiting membrane of the organelle. Such mechanisms include partitioning into lipid microdomains, dependent on the composition of trans-membrane

domains, and ubiquitination of cytoplasmic tail domains followed by recognition of the ubiquinated domain by protein complexes involved in inward vesiculation.

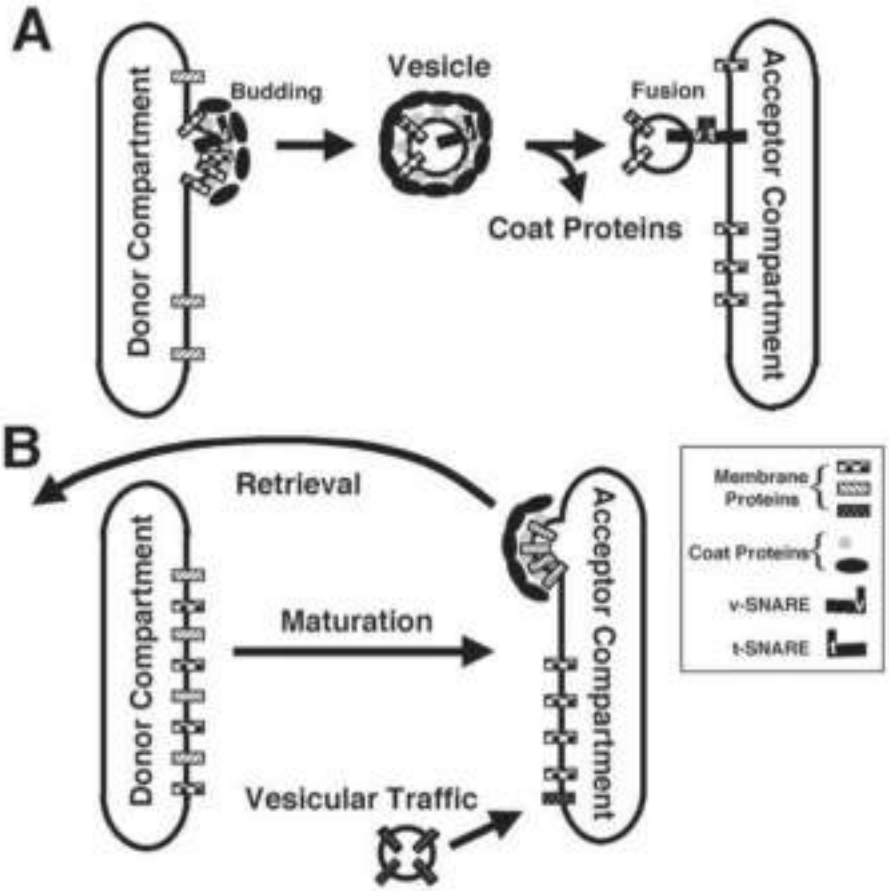


**Figure 101**: The mechanisms for organelle biogenesis in the secretory and endocytic pathways.

## Organelle Inheritance

Organelle biogenesis is closely linked to organelle inheritance in cell division. During the cell cycle, each organelle must double in size, divide and be delivered appropriately to the daughter cells. In summarizing a large amount of earlier work, Warren and Wickner categorized two organelle inheritance strategies that have been described. The first is **stochastic**, relying on the presence of multiple copies of an organelle randomly distributed throughout the cytoplasmand the second is **ordered**, often, but not always, using the mitotic spindle as a means of partitioning (Figure ١٠2).

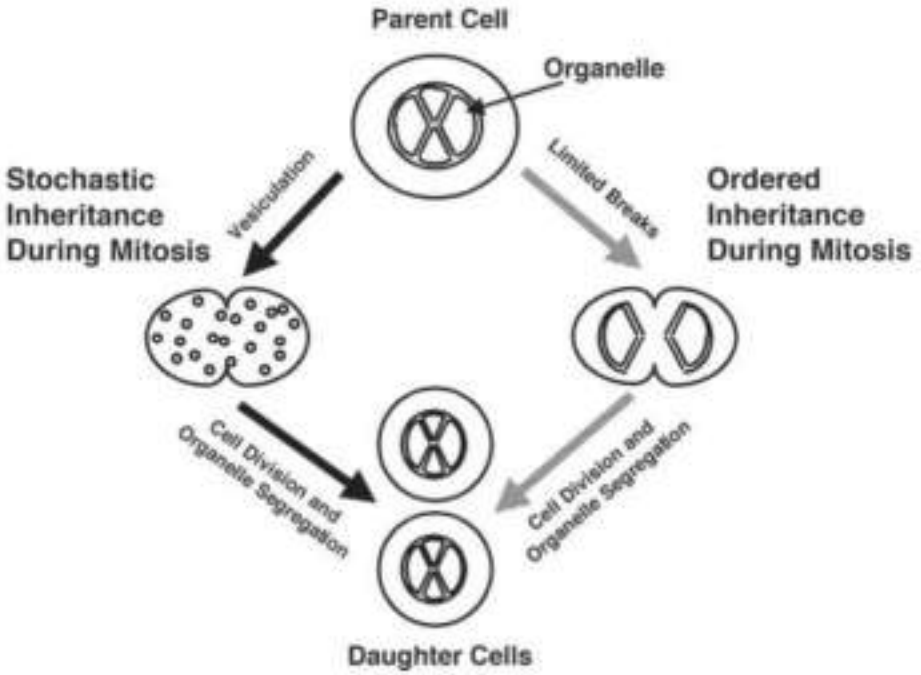


**Figure 102:** Mechanisms for organelle inheritance during mitosis. In the **"stochastic inheritance"** model (solid arrows), an organelle, shown here as an anastomosed, reticular network with all the membrane having a common composition, vesiculates to form many vesicles. These are apportioned by chance to the daughter cells where the organelle is reassembled. It has been estimated that the Golgi complex of a fibroblastic cell would, if completely vesiculated, generate ~80,000 vesicles of 0.1μm diam. In the **"ordered inheritance"** model (hatched arrows), specific and limited breaks in the organelle occur such that, once the fragments are correctly aligned in the dividing cell, each daughter receives half.

The morphology of many organelles may differ in different cell types, which itself may be related to the use of one or other of these strategies to a greater or lesser extent. Mitochondria, for example are, in many cells, multiple copies of small bean shaped structures, but in the budding yeast *S. cerevisiae* form an extensive tubular reticulum beneath the plasma membrane which partitions in an ordered way into the bud. The steady-state morphology of mitochondria which continuously grow, divide and fuse throughout the cell cycle is itself largely

determined by the frequency of fission events and fusion. It should be noted that growth and division of mitochondria also requires coordination of these processes for the inner and outer membranes. In contrast to mitochondria, the endoplasmic reticulum is always a single copy organelle, albeit a dynamic reticulum. This breaks down into tubular vesicular elements during cell division to a variable extent. It often fragments little, thus segregation of equal amounts into daughter cells during mitosis may rely mainly on the uniform and extensive distribution of the endoplasmic reticulum network throughout the cytoplasm of the mother cell. In *S. cerevisiae* the endoplasmic reticulum becomes anchored at the bud tip pulling the network into the bud as it enlarges. Whereas the bulk of the endoplasmic reticulum often does not fragment during mitosis, inheritance of the nuclear envelope, the outer membrane of which is continuous with the endoplasmic reticulum, is more complex since it has to break down during mitosis of animal cells to allow separation of the chromatids.

Perhaps the greatest recent controversy concerning organelle inheritance relates to how the Golgi complex is divided between daughter cells at mitosis. Two models have been proposed to explain this. In the first, proposed by Warren, the Golgi complex breaks down into vesicle clusters and shed vesicles which are distributed stochastically between the daughter cells where they reassemble in telophase. Cell-free assays have led to the identification of some of the molecular machinery for disassembly and reassembly. In the second model, proposed by Lippincott-Schwartz, endoplasmic reticulum is the

partitioning unit, with the Golgi complex merging with the endoplasmic reticulum during prometaphase and emerging from it during telophase. A key observation in developing this second model was that inhibition of traffic from the endoplasmic reticulum to the Golgi complex results in disintegration of the latter.

Some of the discrepancies between the two models may be resolved by data from Warren's group who have shown that whilst Golgi membrane enzymes may, to a greater or lesser extent, redistribute to the endoplasmic reticulum during mitosis, matrix proteins do not, thus allowing the disassembled matrix to become the partitioning units on which the Golgi complex is reassembled after mitosis.

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