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General Zoology

Cytology & Histology

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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 particular 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.

THE CELL 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:

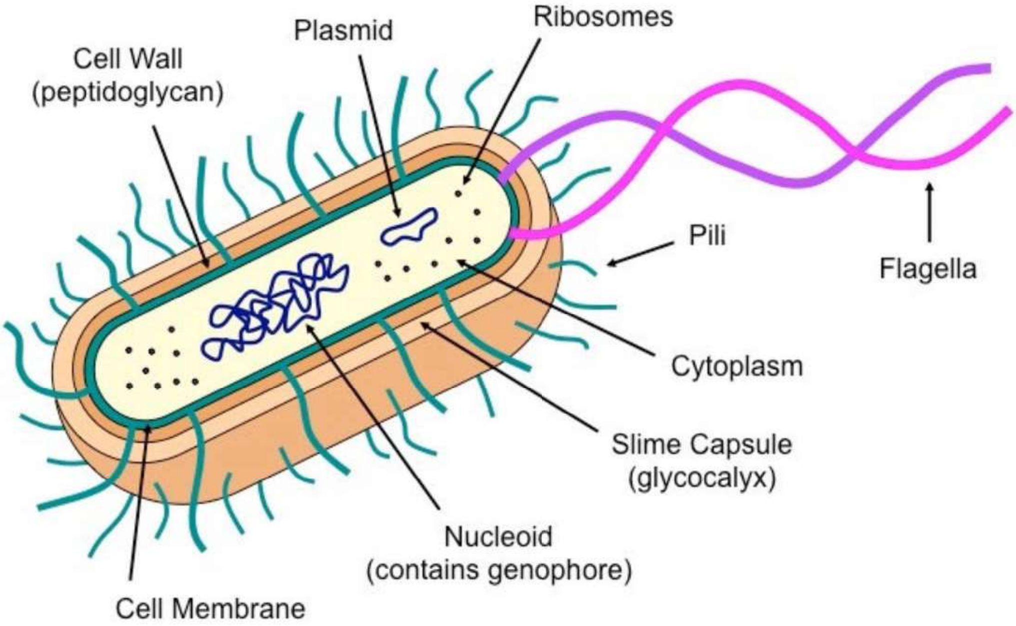

Figure 1: Prokaryotic cells structure.

Prokaryotic cells (Figure 1) 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:

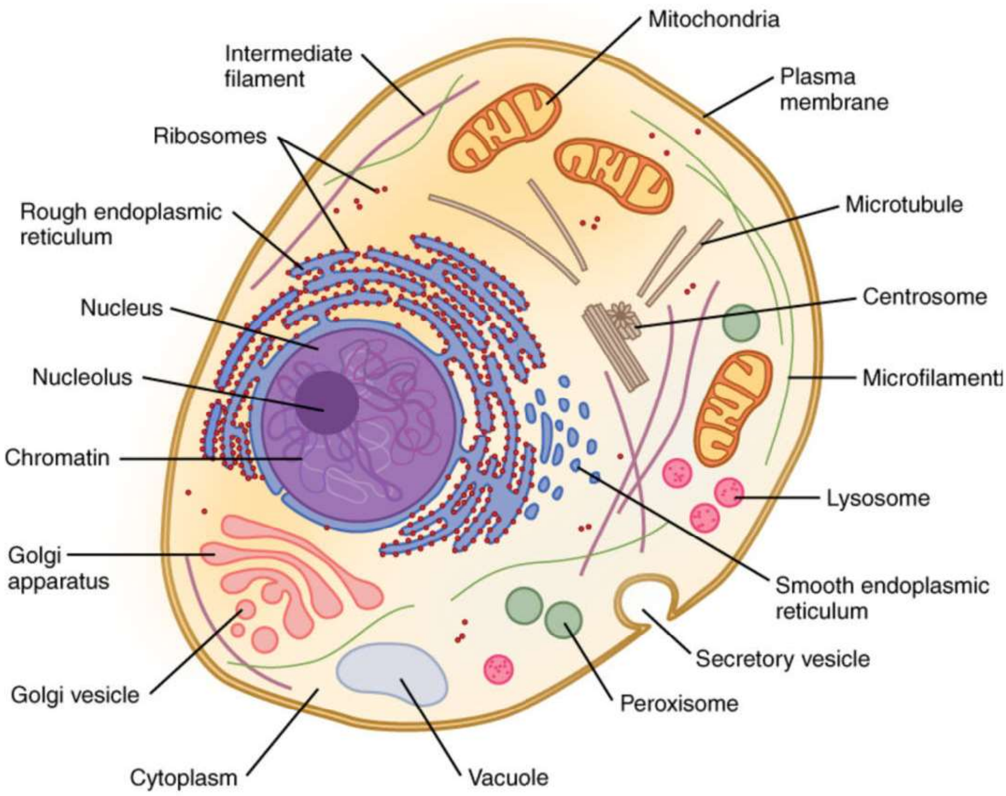

Figure 2: An eukaryotic cell containing the organelles and internal structures.

The internal organization of eukaryotic cell (Figure 2) 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 (3×10^{15}) corpuscles and a 60 kg human being has about 60×10^{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 contact with water.

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 3).

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 4).

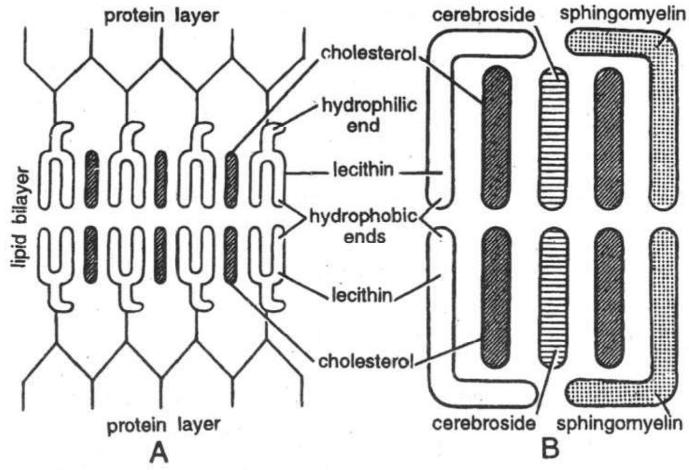

Figure 3: A phospholipids cholesterol complex of cell membrane

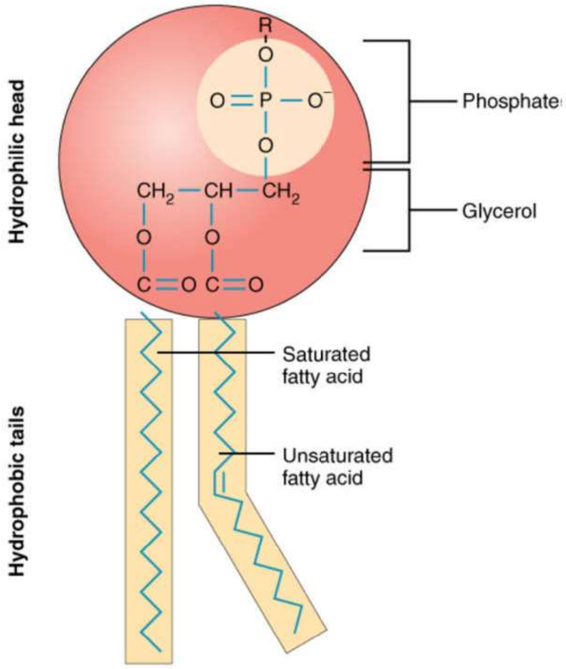

Figure 4: Phospholipid Structure. A phospholipid molecule consists of a polar phosphate "head," which is hydrophilic and a nonpolar lipid "tail," which is hydrophobic. Unsaturated fatty acids result in kinks in the hydrophobic tails.

Another arrangement of lipid molecule in a membrane is a bimolecular sheet, which isalso called a lipid bilayer (Figure 5). 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.

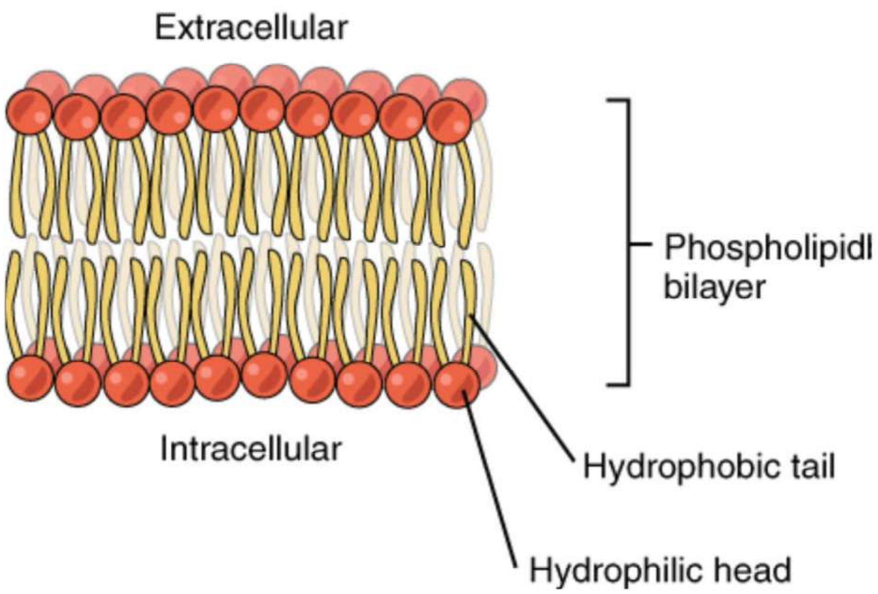

Figure 5: Phospholipid Bilayer. The phospholipid bilayer consists of two adjacent sheets of phospholipids, arranged tail to tail. The hydrophobic tails associate with one another, forming the interior of the membrane. The polar heads contact the fluid inside and outside of the cell.

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.

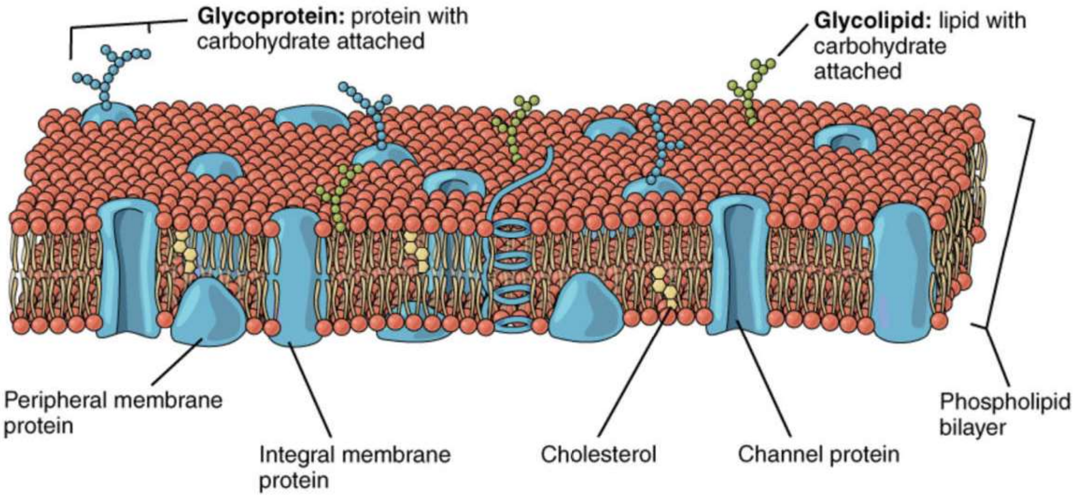

Figure 6: Cell Membrane. The cell membrane of the cell is a phospholipid bilayer containing many different molecular components, including proteins and cholesterol, some with carbohydrate groups attached.

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.

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 7).

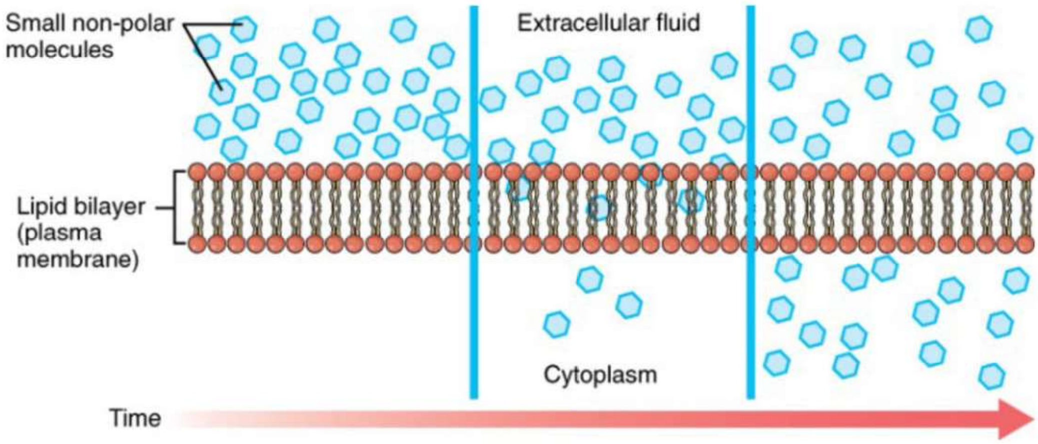

Figure 7: Simple Diffusion across the Cell (Plasma) Membrane. The structure of the lipid bilayer allows only small, non-polar substances such as oxygen and carbon dioxide to pass through the cell membrane, down their concentration gradient, by simple diffusion.

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 8). 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.

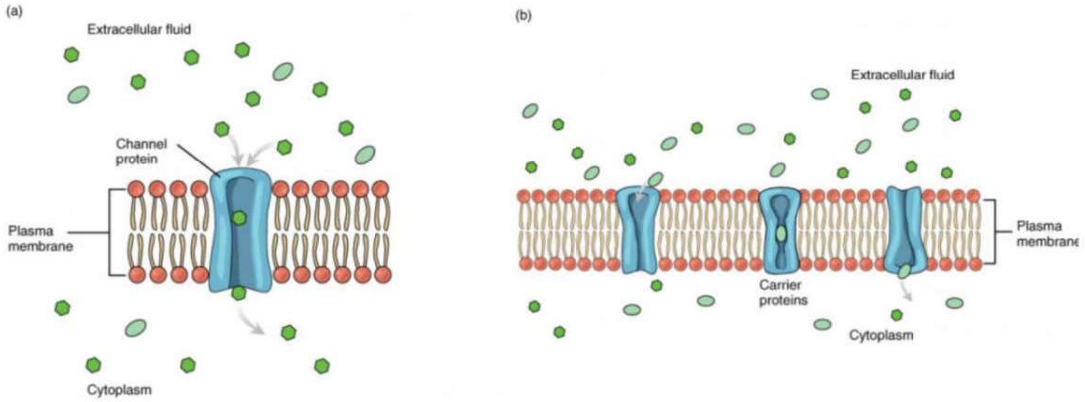

Figure 8: Facilitated Diffusion. Facilitated diffusion of substances crossing the cell (plasma) membrane takes place with the help of proteins such as channel proteins and carrier proteins.

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 9).

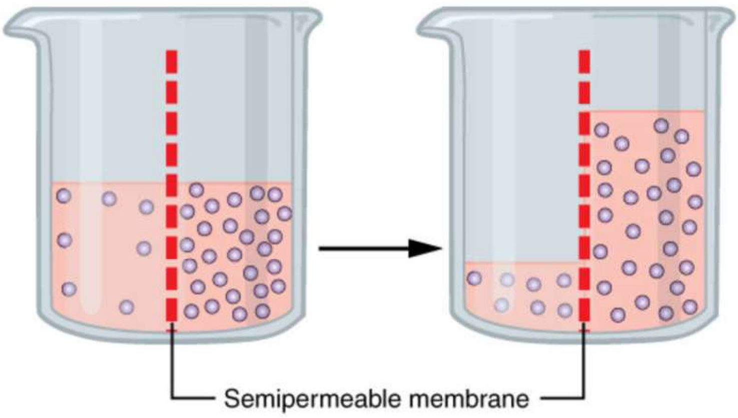

Figure 9:. Osmosis is the diffusion of water through a semipermeable membrane down its concentration gradient.

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 10). 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.

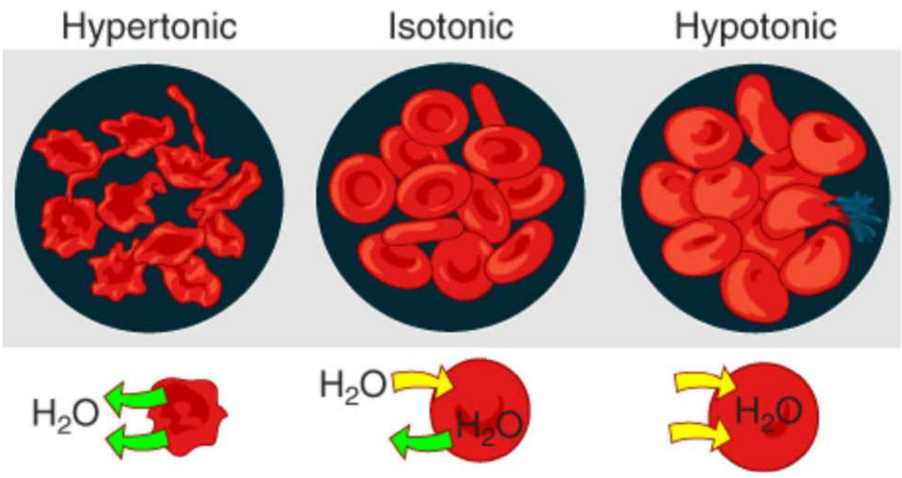

Figure 10: Concentration of Solutions. A hypertonic solution has a solute concentration higher than another solution. An isotonic solution has a solute concentration equal to another solution. A hypotonic solution has a solute concentration lower than another solution.

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 11). This process is so important for nerve cells that it accounts for most of their ATP usage.

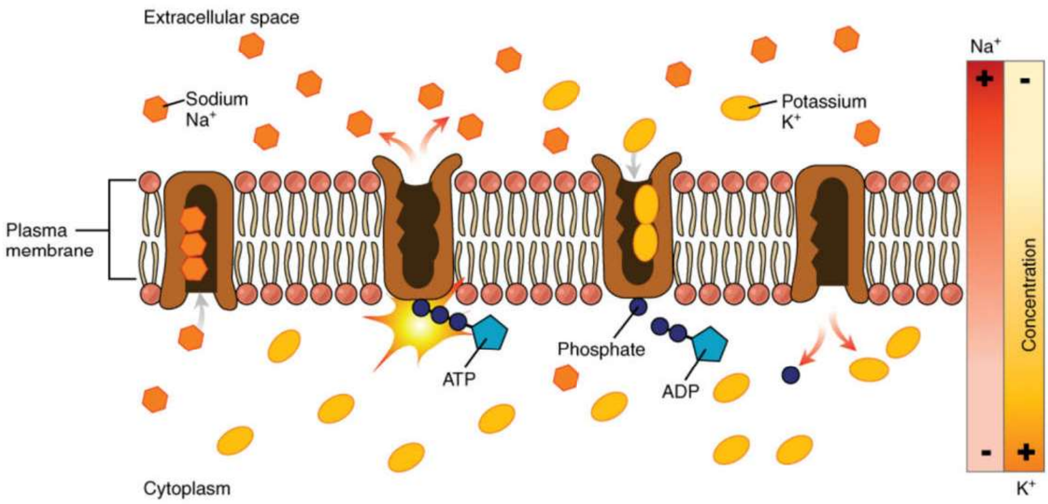

Figure 11: Sodium-Potassium Pump. The sodium-potassium pump is found in many cell (plasma) membranes.

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 12). 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.

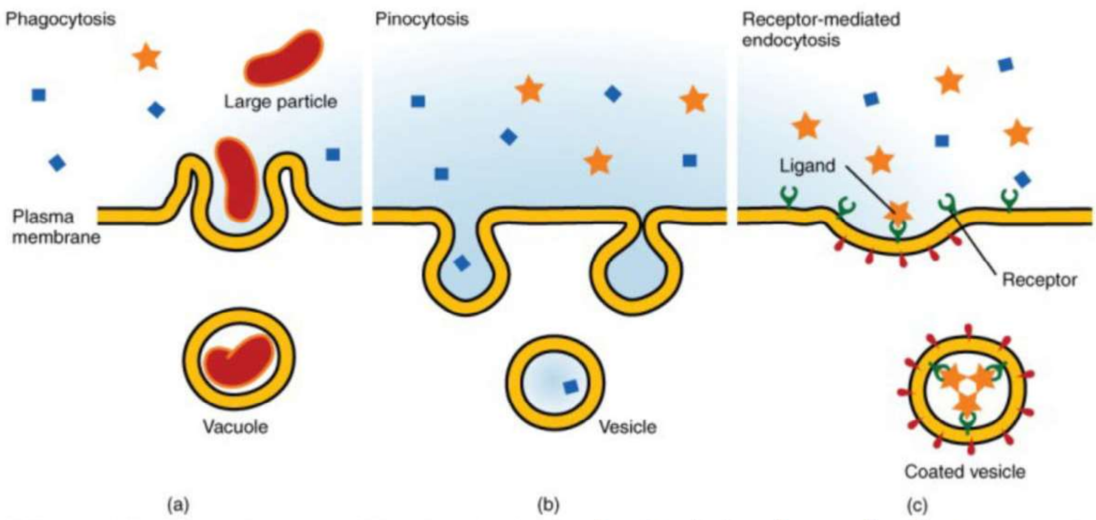

Figure 12: Three Forms of Endocytosis. Endocytosis is a form of active transport in which a cell envelopes extracellular materials using its cell membrane. (a) In phagocytosis, which is relatively nonselective, the cell takes in a large particle. (b) In pinocytosis, the cell takes in small particles 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 13).

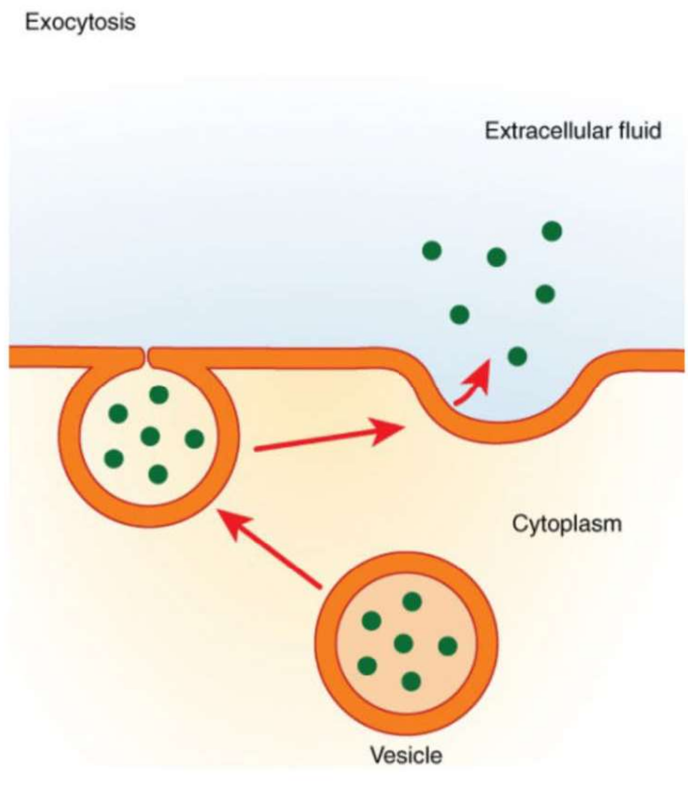

Figure 13: Exocytosis is much like endocytosis in reverse. Material destined for export is packaged into a vesicle inside the cell. The membrane of the vesicle fuses with the cell membrane, and the contents are released into the extracellular space.

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 13). 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.

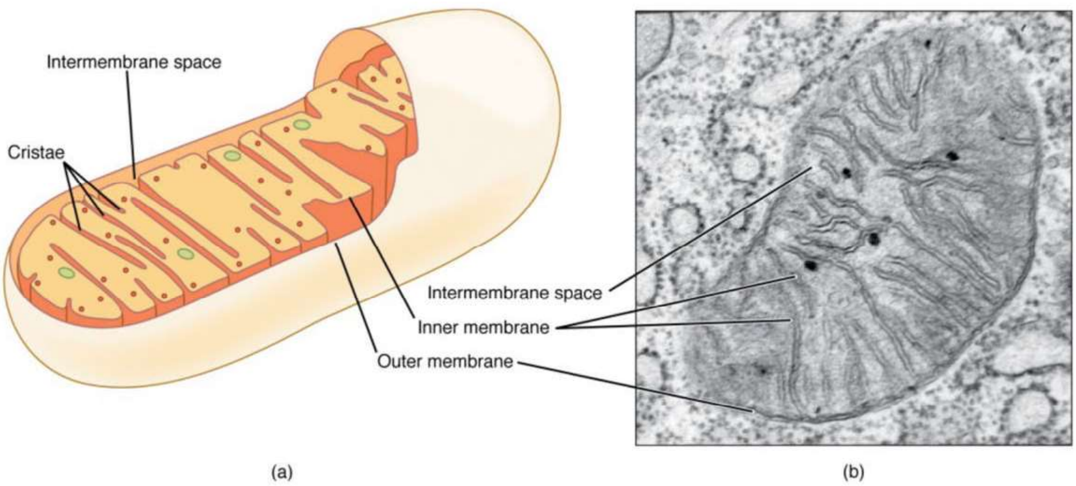

Figure 14: The mitochondria are the energy-conversion factories of the cell. (a) A mitochondrion is composed of two separate lipid bilayer membranes. (b) An electron micrograph of mitochondria.

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 andactively 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 15).

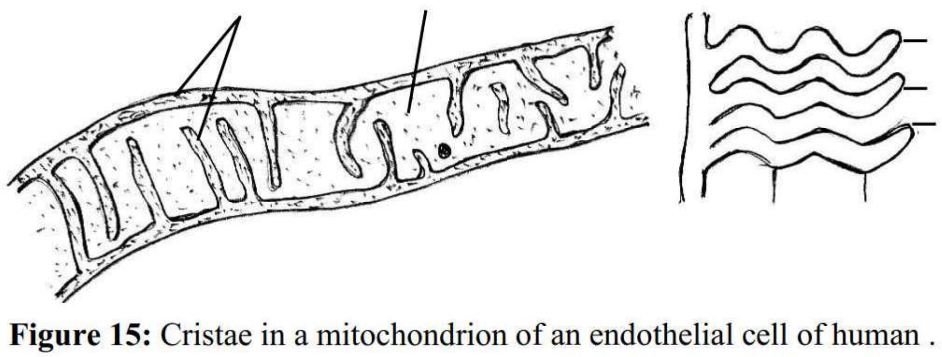

Figure 15: Cristae in a mitochondrion of an endothelial cell of human .

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 16).

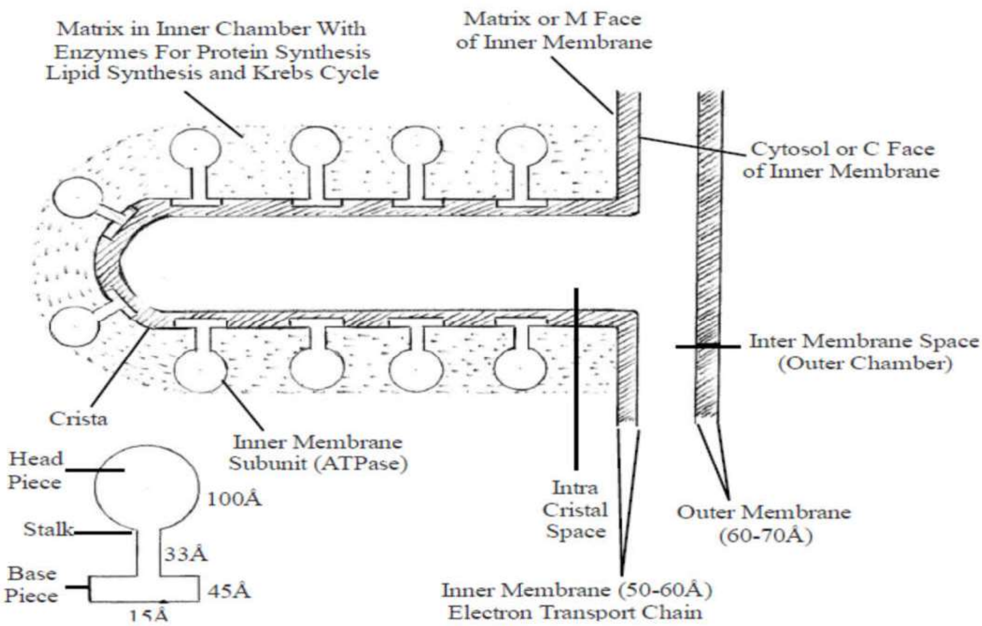

Figure 16: Detailed structure of a crista and an oxysome.

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 17).

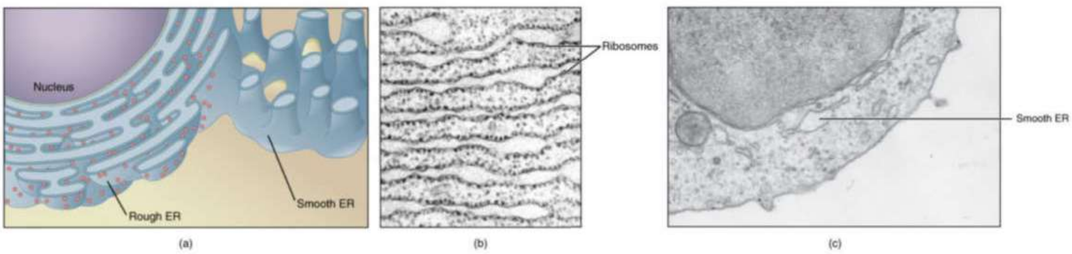

Figure 17: Endoplasmic Reticulum (ER).(a) The ER is a winding network of thin membranous sacs found in close association with the cell nucleus. (b) Rough ER is studded with numerous ribosomes, (c) Smooth ER synthesizes.

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 18).

Tubules: These are irregular, branching elements, which form a network along with other elements. They are about 50-100 nm in diameter and are often free of ribosomes (Figure 18).

Vesicles: These are oval, vacuole like elements, about 25-500 nm 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 18).

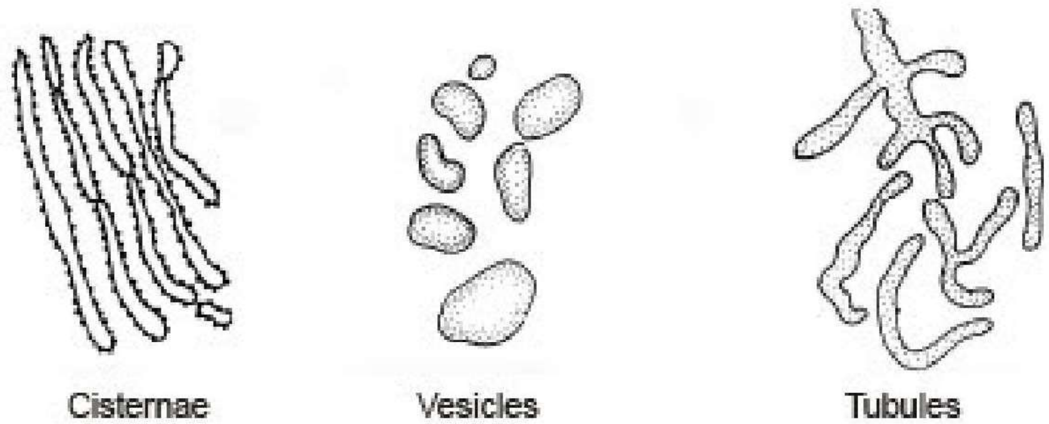

Figure 18: Various forms of ER.

Ultra-structure of Endoplasmic Reticulum:

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.

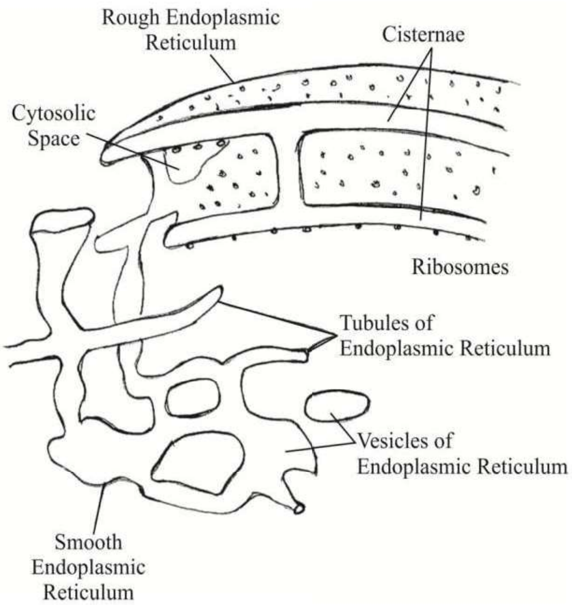

Figure 19: Various types of elements of endoplasmic reticulum.

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.