B.Sc 1st Semester(Zoology Major)
Salbari College, Baksa(BTR)
Plasma Membrane: Structure and Function

By : J K Nath (Asst Professor)

Introduction to Plasma Membrane :

The outer walls of a house or car provide a strong, inflexible barrier that protects its human inhabitants from an unpredictable and harsh external world. You might expect the outer boundary of a living cell to be constructed of an equally tough and impenetrable barrier because it must also protect its delicate internal contents from a nonliving, and often inhospitable, environment. Yet cells are separated from the external world by a thin, fragile structure called the **plasma membrane** that is only 5 to 10 nm wide. It would require about 5000 plasma membranes stacked one on top of the other to equal the thickness of a single page of this study material.

Because it is so thin, no hint of the plasma membrane is detected when a section of a cell is examined under a light microscope. In fact, it wasn't until the late 1950s that techniques for preparing and staining tissue had progressed to the point where the plasma membrane could be resolved in the electron microscope. These early electron micrographs, such as those taken by J. D. Robertson of Duke University (**Figure 1**), portrayed the plasma membrane as a three layered structure, consisting of darkly staining inner and outer layers and lightly staining middle layer. All membranes that were examined closely—whether they were plasma, nuclear, or cytoplasmic membranes , or taken from plants, animals, or microorganisms—showed this same ultrastructure.

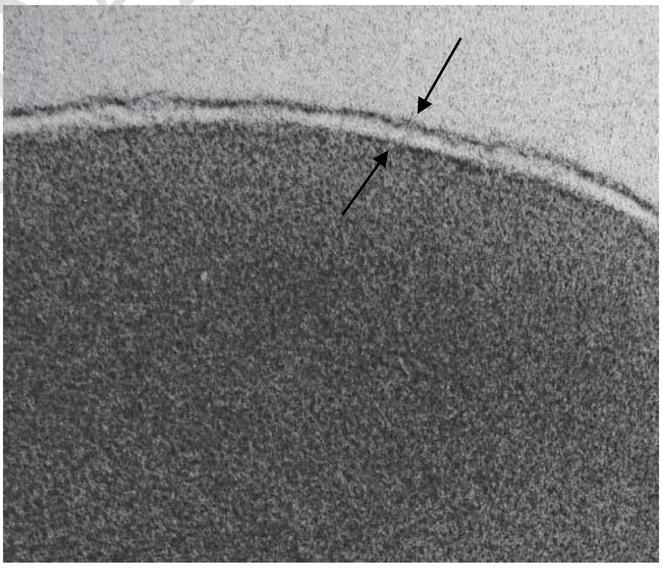

Figure 1: The trilaminar appearance of membranes

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Definition :

The plasma membrane, also referred to as the cell membrane, is a semi-permeable barrier that surrounds and encloses the contents of a cell. It is composed mainly of a phospholipid bilayer with embedded proteins and various molecules. The plasma membrane separates the cell's internal environment from the external surroundings, regulating the entry and exit of substances to maintain cellular integrity and facilitate communication with the external environment.

Functions of Plasma Membrane :

1)Compartmentalization : Membranes are continuous, unbroken sheets and it encloses the contents of the entire cell, whereas the nuclear and cytoplasmic membranes enclose diverse intracellular spaces. The various membrane bounded compartments of a cell possess markedly different contents. Membrane compartmentalization allows specialized activities to proceed without external interference and enables cellular activities to be regulated independently of one another.

2)Providing a selectively permeable barrier : Membranes prevent the unrestricted exchange of molecules from one side to the other. At the same time, membranes provide the means of communication between the compartments they separate.

3)Transporting solutes: The plasma membrane contains the machinery for physically transporting substances from one side of the membrane to another, often from a region where the solute is present at low concentration into a region where that solute is present at much higher concentration. The membrane's transport machinery allows a cell to accumulate substances, such as sugars and amino acids, that are necessary to fuel its metabolism and build its macromolecules. The plasma membrane is also able to transport specific ions, thereby establishing ionic gradients across itself. This capability is especially critical for nerve and muscle cells.

4)Responding to external stimuli : The plasma membrane plays a critical role in the response of a cell to external stimuli, a process known as **signal transduction** . Membranes possess **receptors** that combine with specific molecules(**ligands**)or respond to other types of stimuli such as light or mechanical tension.

5)Intercellular interaction : Situated at the outer edge of every living cell, the plasma membrane of multicellular organisms mediates the interactions between a cell and its neighbors. The plasma membrane allows cells to recognize and signal one another, to adhere when appropriate, and to exchange materials and information. Proteins within the plasma membrane may also facilitate the interaction between extracellular materials and the intracellular cytoskeleton.

6)Energy transduction : Membranes are intimately involved in the processes by which one type of energy is converted to another type (energy transduction). The most fundamental energy transduction occurs during photosynthesis when energy in sunlight is absorbed by membrane bound pigments, converted into chemical energy, and stored in carbohydrates.

Structure of Plasma Membrane :

All plasma membranes, regardless of source, contain proteins as well as lipids. The ratio of protein to lipid varies enormously depends on cell types. For example, the plasma membrane of human RBC contains 43% lipid and 49% protein by weight whereas plasma membrane of mouse liver cells contains 54% lipid and 46% protein by weight. Carbohydrates are also present in plasma membranes and comprise only 5 to 10% of membrane mass. Carbohydrates bound either to proteins as constituents of glycoproteins or to lipids as constituents of glycolipids Carbohydrates are especially abundant in the plasma membranes of eukaryotic cells.

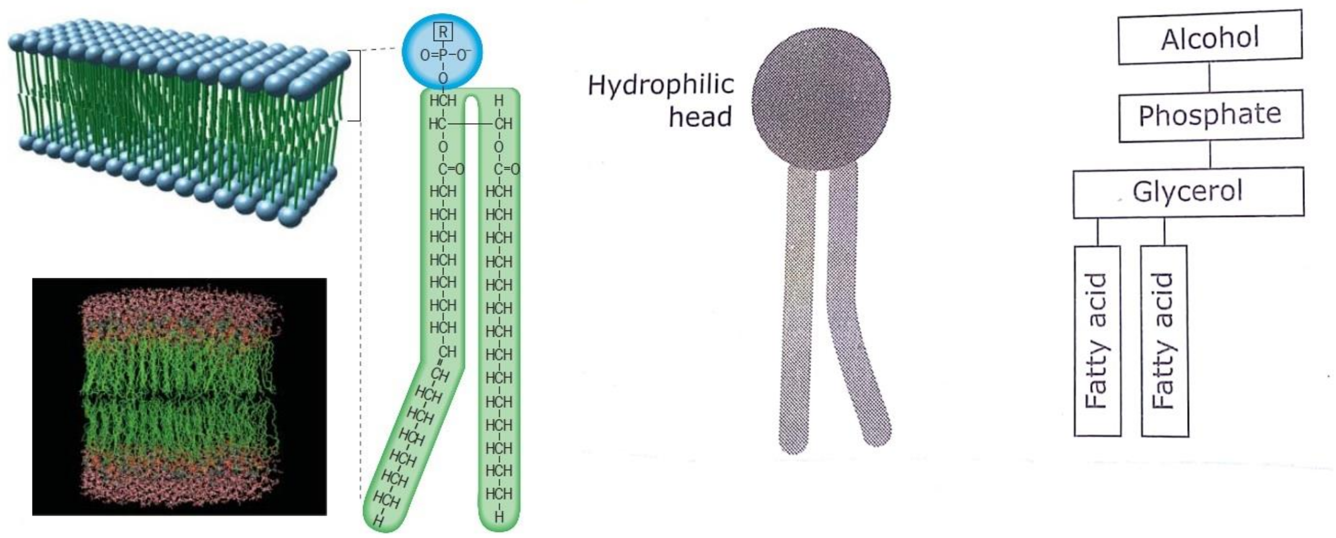
Lipid Bilayer :

The basic structure of the plasma membrane is the lipid bilayer. This bilayer is composed of two leaflets of amphipathic lipid molecules, whose polar head groups are in contact with the intra- or extracellular aqueous phase, where their non-polar tails face each other, constituting the hydrophobic interior of the membrane. The primary physical forces for organizing lipid bilayer are hydrophobic interactions. Three classes of lipid molecules present in lipid bilayer-phospholipids, glycolipids and sterol.

Phospholipids :

Phospholipids are made up of four components; an alcohol (glycerol or sphingosine), fatty acids, phosphate, and an alcohol attached to the phosphate. The fatty acid components are hydrophobic, whereas the remainder of the molecule has hydrophilic. There are two types of phospholipids: glycerophospholipids and sphingophospholipids Phospholipids derived from glycerol are called glycerophospholipids. Glycerophospholipids (or phosphoglycerides) contain glycerol, fatty acids, phosphate and an alcohol (e.g. choline). Phosphoglyceride molecules are classified according to the types of alcohol linked to the phosphate group. For example, if the alcohol is choline, the molecule is called phosphatidylcholine (also referred to as lecithin) and if serine, then it is called phosphatidylserine Phosphoglycerides are the most numerous phospholipid molecules found in plasma membranes.

Sphingophospholipids contain an amino alcohol called sphingosine instead of glycerol, a fatty acid, phosphate and an alcohol attached to the phosphate. In sphingophospholipid, the amino group of the sphingosine backbone is linked to a fatty acid by an amide bond, Sphingomyelin is the most abundant sphingophospholipid.



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Glycolipids :

Glycolipids contain carbohydrate (either monosaccharide or oligosaccharide) covalently attached to the lipid. These can derive from either glycerol or sphingosine. The simplest glycolipid, called a cerebroside, contains a single sugar residue such as glucose and galactose. The complex glycolipid, called a globoside, contains oligosaccharide.The glycol lipids are found exclusively in the outer leaflet of the plasma membrane, with their carbohydrate portion exposed on the surface.

Sterols :

The basic structure of sterol is a steroid nucleus, consisting of four fused rings, three with six cartons and one with five. It is planar, and relatively a rigid structure. Cholesterol is the major sterol present in the plasma membrane of animal cells. The plasma membrane of plant cells lacks cholesterol, but they contain other sterols like stigmasterol, sitosterol. With rare exceptions like Mycoplasma, bacterial plasma membrane also lacks cholesterol. The main function of cholesterol is to provide fluidity to the membrane.

Membrane Proteins :

Membrane proteins are responsible for most of the dynamic processes carried out by membranes, Most membrane proteins can be classified as being either **peripheral or integral**. Many of the proteins associated with membrane can be released from the membrane by relatively gentle extraction procedures, such as exposure to solutions of very high or low ionic strength or of extreme pH. These procedures interfere with weak non-covalent interactions between protein-protein or protein-membrane lipid, but leave the lipid bilayer intact; these proteins are referred to as **peripheral proteins (or extrinsic proteins)**. These proteins are bound to membranes primarily by electrostatic and hydrogen bond interactions and do not interact with the hydrophobic core of the phospholipid bilayer. They are usually bound to the membrane indirectly by interactions with integral membrane proteins or directly by interactions with lipid polar head groups: Most peripheral proteins are soluble in aqueous solution. Spectrin and ankyrin are very common examples of peripheral proteins present in the membrane of RBCs. Spectrin and ankyrin membrane proteins help determine the shape and flexibility of the RBC.

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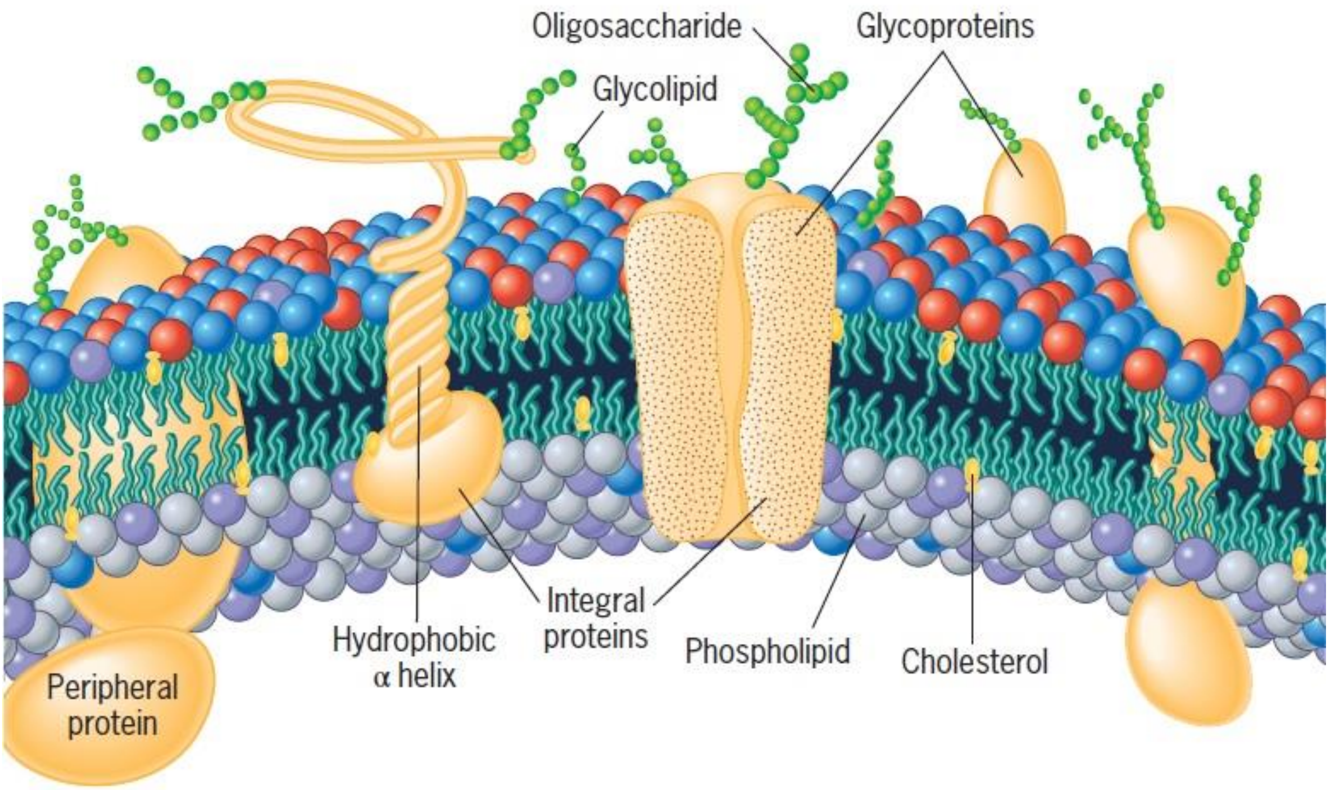
Proteins that are held in the lipid bilayer very tightly and cannot be released by relatively gentle extraction procedures are called **integral proteins (or intrinsic proteins)**. Integral membrane proteins are mostly transmembrane proteins which have one or more segments that are embedded in the phospholipid bilayer. Transmembrane proteins contain non-polar amino acid residues with hydrophobic side chains that interact with fatty acyl groups of the membrane phospholipids, thus anchoring the protein to the membrane. All transmembrane proteins are amphipathic. Example : **Glycophorin**.



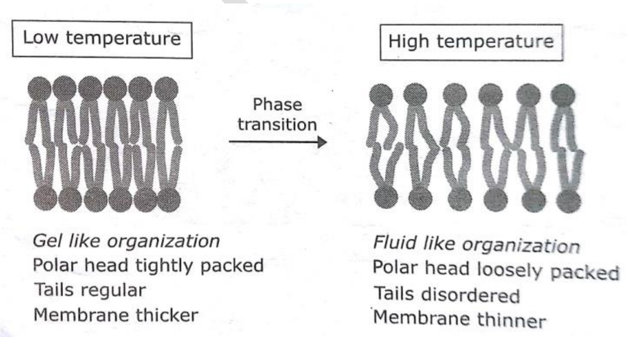
Motion of lipid molecules :

Lipid bilayer is not rigid and static structure. In a lipid bilayer, lipid molecules can rotate freely around their long axis called as rotational motion and can diffuse laterally within each leaflet called as lateral motion. The ability of lipids to diffuse laterally in a bilayer indicates that it can act as a fluid. The degree of bilayer fluidity depends on the lipid composition and temperature.

The transition of a lipid molecule from one leaflet to the other is called transverse diffusion or flip-flop movement. For such motion to occur, the lipid head group, which is polar and may be charged, must move into the hydrophobic interior of the bilayer. Hence, this process is not passive and requires energy. The thermodynamic barrier prevents rapid spontaneous transverse diffusion of phospholipids and is, therefore, a rare process. Several enzymes such as flippase, floppase and scramblase are required for transverse movement.

Fluidity of a lipid bilayer :

The fluidity of the lipid-bilayer, the optimal value of which is a prerequisite for normal cell growth and function, depends on lipid composition and temperature. In general, an increase in the temperature tends to elevate membrane fluidity. Lowering of temperature causes a freely-flowing, low-viscous, fluid-like membrane structure to a more rigid, gel-like organization. This change is described as phase transition and the temperature at which this happens is called the transition temperature.



Fluidity of lipid bilayer also depends on chain length and the degree of unsaturation of its component fatty acid residues. Lipids with short or unsaturated fatty acyl chains undergo the phase transition at lower temperatures than lipids with long or saturated chains. Short chains have less surface area hence, a shorter chain length reduces the tendency of the hydrocarbon tails to interact with one another. Unsaturated fatty acyl chains have kinks, thus tend to adopt a more random, fluid state and form less van der Waals interactions with other lipids.

So, an increased proportion of unsaturated fatty acids than saturated fatty acids in the membrane increases the fluidity of bilayer at the reduced temperature.

Cholesterol is also a major determinant of membrane fluidity. The presence of cholesterol increases the order and rigidity. Its presence stabilizes the extended straight-chain arrangement of saturated fatty acids by van der Waals interactions. The presence of cholesterol is characteristic of the plasma membrane of animal cells, rather than plant cells. As a result, animal cell plasma membranes are less fluid (more rigid) than plant cell plasma membranes.

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Various Models of Plasma Membrane :

Various models have been proposed to elucidate the structure of membranes. These models have been proposed based on the extensive research carried out by different scientists enabling them to elucidate the structure of the membranes. The present-day perception of cell membrane is entirely based on the understanding of these past membrane models .

1)Overton Biomembrane Model:

Charles Ernest Overton played a very important role in the understanding of the picture of cell membranes. He studied the permeability of the cell membrane to a wide variety of substances, nearly 500 different plant and animal cell models. He noticed that substances that are non-polar in nature (ether soluble) did not result in the shrinking of cells, contrary to water soluble (polar) substances, irrespective of their molecular size. He reached to the conclusions what we know as the Overton's rules according to which the substances that are soluble in oil enter the living cells faster whereas substances that are highly soluble in water enter the cell slowly. Further, he proposed "Lipoidal theory" in 1899 according to which all living cells are covered by a thin layer of lipoid materials. He suggested that cholesterol and phospholipids could be the main components of cell membranes. Initial predictions related to lipid content as a major ingredient were justifiable, however, this model of cell membrane had several demerits e. g. there was no explanation for the movement of water and other hydrophilic substances across the cell boundaries and no idea related to energy dependent selective transport system.

2)Gorter and Grendel Model :

Gorter and Grendel were the first to propose that the lipids of the cell membrane are organised in a bimolecular lipid sheet. They experimentally calculated the surface area of lipids isolated from red blood cells from various animals like sheep, rabbit, goat and human in acetone. The red blood cells were chosen since these cells were known to lack internal membranes, they assumed that all lipids should come from the cell envelopes.

On comparing the surface area of the lipid to that of the red blood cells they found that surface area of the lipid was exactly twice to that of the red blood cell. They concluded that lipids of the cell membrane are organised in a bimolecular lipid sheet. They proposed the structure such that two lipid layers form a bilayer with the polar head (hydrophilic) groups pointing toward the aqueous exterior environment and non-polar (hydrophobic) ends of the lipids embedded in the centre. This model was named as 'bimolecular lipid leaflet model'.

No. of RBC = n
SA of 1RBC=X
Total surface area=nX

Then extract the lipid molecule of RBC and spread on water

↓

Surface area increased (double)

↓

2nX

Then conclude the PM consists of bilayer of lipid

Although the attempt for describing the structure of membrane and lipid bilayer concept was correct, however, there were some limitations were seen later in this model. The extraction technique used for lipid isolation could not extract erythrocyte lipids from the samples completely. Several mis-calculations happened in measuring the total area of the red blood cells and also this model unable to describe various crucial functions of the cell membrane.

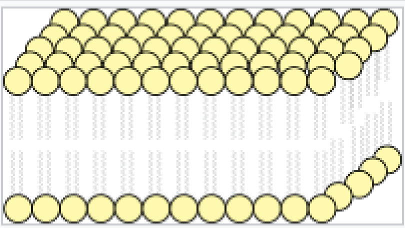

Diagram of the arrangement of amphipathic lipid molecules to form a lipid bi-layer. The yellow polar head groups separate the grey hydrophobic tails from the aqueous cytosolic and extracellular environments.

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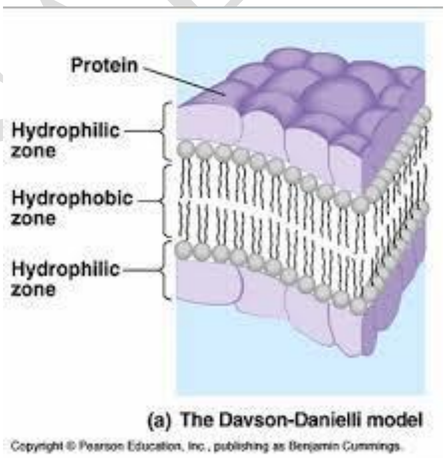
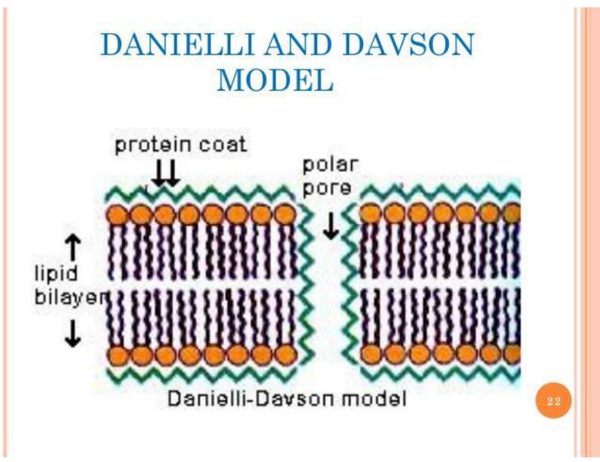
3)Sandwich Model by Davson and Danielli :

The ‘sandwich model’ or the ‘lamellar model’ of cell membrane as proposed by Jim Danielli and Hugh Davson (1935) relates the structure of the membrane to its chemical properties. After the Gorter and Grendel work on the bilayer structure of the lipids Harvey and Coley (1931) and Danielli and Harvey (1935) did an extensive study to study the surface tension of the cell membrane. They observe that the cell membrane showed lower surface tension compared to bimolecular lipid leaflet. Based on their observation they pointed out the presence of protein molecules adsorbed on the surface of lipid droplets which reduce the surface tension of droplets. In 1935 Jim Danielli and Hugh Davson proposed that biological membranes are made up of lipid bi-layers that are coated on both sides with absolute layer of protein (lipid bilayer sandwiched between two layers of protein). The hydrophilic polar heads of the lipid molecules are directed towards the proteins. The close association between the two is maintained by electrostatic forces. The hydrophobic non-polar tails of the two lipid layers are embedded in the centre where they are held together by hydrophobic bonds and van der Waals forces. The model assumed the cell membrane to be a stable structure with very little variability and functional specificity.

The Danielli Davson’s model also had several demerits due to which it was later on got modified by other researchers. This model showed that all the membranes have a constant lipid-protein ratio with uniform thickness and therefore, have symmetrical internal and external surfaces. The model could not explain the permeability of certain substances through the membrane.





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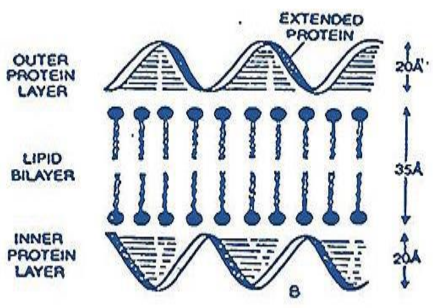
4)Robertson Unit Membrane Model :

So far all the cell membrane structures predicted were based on indirect studies. It was for the first time that Robertson proposed in 1959 his famous unit membrane model based on the experimental evidences from electron microscopy. The membranes were fixed with osmium tetra-oxide and potassium permanganate (KMnO4) which revealed a characteristic tri-laminar structure of the cell membrane consisting of two parallel outer dark (osmiophilic) layers and a central light (osmiophobic) layer.

The thickness of osmiophilic layers measured was 2.0-2.5nm and that of the osmiophobic layers measured was 2.5-3.5 nm. The total thickness of the trilaminar structure measured 6.5- 8.5 nm. This value when compared with the thickness predicted on the basis of chemical studies was same. The tri-laminar structure (dark-light-dark) was presumed to be universal for all cell membranes including the endoplasmic reticulum, hence the name unit membrane model. Robertson proposed that the unit membrane structure consisted of a bimolecular lipid leaflet sandwiched between outer and inner layers of dense protein. He also proposed that all bio membranes are either made of a unit membrane or a multiple of unit membrane.

Robertson model was basically the confirmation of earlier two models i.e. Gorter & Grendel (1925) model and Danielli Davson (1935) sandwich model. However, Robertson's model was sometimes incorrectly interpreted as that all membranes have the same composition. Cell membrane, membranes of endoplasmic reticulum, golgi complex and lysosomes are unit membranes while nuclear membrane, membranes of mitochondria and plastids are double unit membranes. However, Robertson's statement was merely meant to describe a common structure.



ROBERTSON'S MODEL

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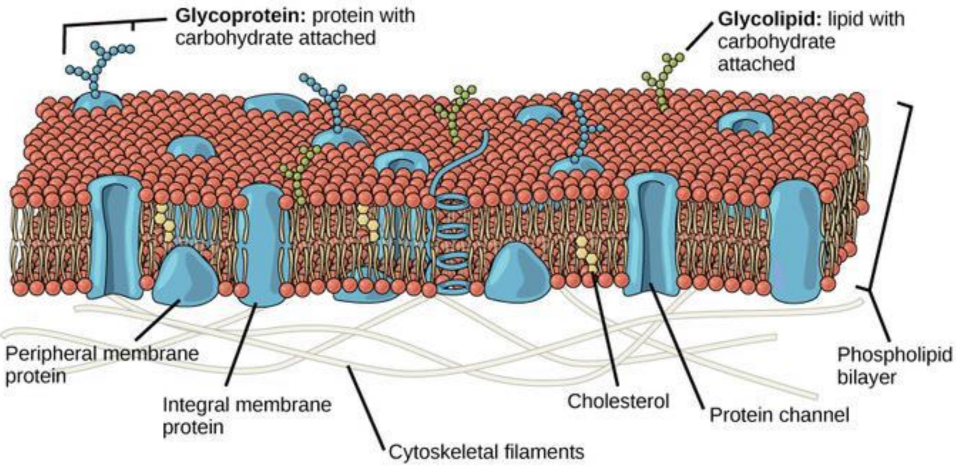
5)Fluid Mosaic Model :

S.J. Singer and G. Nicholson in 1972 presented the most widely accepted model till date the 'fluid mosaic model' which is the culmination of all the membranes models predicted earlier. According to the fluid mosaic model membranes are two-dimensional solutions of oriented lipids and globular proteins. The concept of lipid bilayer remains as such as predicted in earlier studies however the presence of protein as continuous sheath on either surface of lipids was reformed. In this mosaic model the proteins are present both on the surface of the lipid membrane as well as found embedded in the lipid bilayer or span through the membrane. The proteins present on the surface are more hydrophilic in nature and are called as the Peripheral proteins, non-covalently linked to the polar heads of phospholipids molecules. Peripheral proteins are loosely attached to the membrane surface and can easily be separated from the membrane by mild treatment. The proteins found embedded in the matrix are called as the Integral proteins. They are hydrophobic in nature having affinity for the hydrophobic tails of phospholipids on interior of the layer. Integral proteins form the major fraction of membrane proteins nearly 70% of the total protein and cannot easily be separated from the lipids as compared to the peripheral proteins. Several integral proteins form a tunnel like passage which allows for the movement of water and water soluble substances. The lipid bilayer has two important role one it acts as a solvent for integral membrane proteins and second it acts as a permeability barrier. Membrane lipids and proteins are free to diffuse laterally provide flexibility and dynamism to the membrane.The fluid mosaic model of cell membrane is still the widely accepted model.



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