Models for Structure of Membrane

Organization Of Lipids and Proteins

The following points highlight the top four historical models of plasma membrane. The models are:

1) Lipid & Lipid Bilayer models.
2) Unit membrane model (Protein - Lipid Bilayer - Protein)
3) Fluid Mosaic model.
4) Danielli model.

I Lipid and Lipid Bilayer model

This model explain the structure of Plasma membrane by Overton, Gorion and Grendel. Previously only indirect information was available to explain the structure of plasma membrane. In 1902, Overton observed that substances soluble in lipid could selectively pass through the membranes. On this basis he stated that plasma membrane is composed of a thin layer of lipid.

Subsequently, Gorter and Grendel in 1926, observed that the extracted from erythrocyte membranes was twice the amount expected if a single layer was present throughout the surface area of these cells. On this basis they stated that plasma membrane is made up of double layer of lipid molecules. These models of Gorter and Grendel could not explain the proper structure of plasma membrane but they put the foundation of future model of membrane structure.

II Unit membrane Model (Protein - Lipid bilayer - Protein)

This is also known as unit membrane model.

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This model was proposed by Danson Daniell and Robertson. When surface tension measurements made on the membranes, it suggests the presence of proteins. After the existence of proteins the initial lipid bilayer model proposed by Gorter and Grendel was modified. It was suggested that surface tension of cells is much lower than what one would expect if only lipid were involved.

It may also observed that if protein is added to model lipid water system, surface tension is lowered. This suggested indirectly the presence of proteins. On this basis Danielli proposed that plasma membrane contained a lipid bilayer with protein on both surface.

Initially they supposed that proteins existed as covalently bonded globular structures bound to the polar ends of lipids. Subsequently they developed the model in which the protein appears to be smeared over the hydrophilic ends of the lipid bilayer. This model makes its popularity for a long time.

With the availability of electron microscope later, fine structure of plasma membrane could be studied. Definite plasma membrane of 6nm to 10nm (10nm = 100 Å; 1nm = 10^{-6}mm) thickness was observed in surface of all cells, and plasma membranes of two adjacent cells were found to be separated by space, 1-15nm wide.

It was also observed that the plasma membrane of most of the cells appeared to be three layered. Two

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outer dense layers about 2.0 nm thick and the middle layer about 3.5 nm. The early ideas of Gorter and Grendel and those of Davson and Danielli were first formalized by Robertson in 1959 in the form of his unit membrane concept.

This membrane of unit membrane with three layers (two protein layer and one lipid bilayer) only supported the concept proposed earlier by Davson and Danielli. In this unit membrane the less dense middle layer corresponded to hydrocarbon chains of lipids. Thickness of unit membrane (10 nm) was found to be greater in plasma membrane than in intracellular membrane of endoplasmic reticulum or golgi complex.

III Fluid Mosaic model

To explain the structure plasma membrane various models have been put forward from time to time. But none was universally accepted. In this relation Gorter and Grendel, Davson and Danielli etc. proposed model for plasma membrane after that fluid mosaic model for plasma membrane was proposed which was universally accepted.

It was proposed by Singer and Nicholson (1912). This model postulates that lipid and integrated proteins are disposed in a sort of mosaic pattern and all the biological membranes have a quasi-fluid structure where both lipid and protein components are able to perform transitional movement within lipid bilayer.

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In this model, lipid molecule may exhibit intra-molecular movement or may rotate about their axis and may display flip-flop movement including transfer from one side of bilayer to the other. Thus this concept implies that main components of the membrane, i.e, lipids, proteins and oligosaccharides are held together by means of non-covalent interactions as suggested by Gitler (1972). A term amphipathy was coined by Hartley (1936) to the molecules having both hydrophilic and hydrophobic groups. Thus lipids and integrated proteins are amphipatic in nature.

Our present knowledge of plasma membrane is based on integration of data from chemical analysis and those from the study of biophysical properties with the help of various types of techniques. These have provided the main components which are integrated in plasma membrane. On this ~~reaction~~ relation, following four major techniques as discoveries have given support:

These are as follows

(i) Freeze fracture technique was used to study membrane. Freeze fractured electron microscope revealed the presence of bumps and depressions which are 7-8 nm. in diameter. This remains randomly distributed. These were later shown in Intramembrane protein particles which transverse the bilayer.

(ii) Frye and Eddin (1970) labeled selectively the species specific proteins of human and mouse cells and then fused these cells of the two species to make a heterokaryon. After

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incubating the heterokaryons for 30-35 minutes at 37°c, human and mouse proteins in these heterokaryons were seen intermixing (as demonstrated by using specific antibodies), so that human and mouse proteins became randomly distributed suggesting that membrane proteins are mobile in the plane of the membrane.

(III) Patching and capping :- The process named patching and capping also provide evidence about the mobility of proteins within the lipid bilayer. This process suggested that, when ligands like antibodies have more than one sites for binding the specific proteins on the cell-surface, the proteins tend to aggregate into clusters through cross linking. This indicates that proteins diffuse laterally in the bilayer.

(IV) Flourescence recovery after bleaching (FRAP) has also been used for measuring rates of lateral diffusion of proteins. A cell surface protein of intrest is marked with a fluroscent ligand (eg antibody). The ligand is bleached in a small area by laser beam and the time taken for bleached and unbleached flourescent ligands to diffuse and mix is measured. The rate of diffusion of protein is not constant.

The evidences as above suggested that lipid bilayer has fluid properties enabling membrane proteins to diffuse rapidly. Rotational diffusion of proteins is possible. However no evidence of 'flip-flop' mechanism as suggested for lipids has been available for proteins. Later on it was suggested that

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not only proteins, but individual lipid molecules are also able to diffuse freely within the lipid bilayers.

And it was found true in synthetic as well as isolated biological membranes which were obtained from Mycoplasmas, bacteria & red blood cells. Initially this was demonstrated in the following two types of synthetic lipid bilayers i.e, liposomes and black membrane, liposomes are spherical vesicles.

These measures from 25nm to 1μm (1000nm) in diameter. Black membranes ~~not~~ extend across a hole in a partition between two aqueous compartments. The motion of individual lipid molecules could be measured by 'spin labeling". (The spin is unpaired electron creates a paramagnetic signal that can be detected by electron spin resonance (ESR) spectroscopy). The motion and orientation of spin labelled lipid can be deduced from the ESR spectrum. The lipid molecule can also rotate or readily exchange places within the same monolayer (10^7 times in a second) with a diffusion coefficient (D) of about 10^{-8} cm^2/sec. So that a lipid molecule could diffuse the length of a large bacterial cell (~2μm) in about one second.

Even when the lipid molecule is static, the hydrocarbon chains are flexible, similar results were obtained from isolated biological membranes, except that in the natural. On the basis of these facts, Singer & Nicholson proposed a hypothesis to explain the str. of plasma membrane. This is known as Fluid Mosaic model. Basically this model was modified by Robertson Davson.

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Modification of Fluid Mosaic Model:

On the basis of fluid-Mosaic model, it can be stated that cell membrane is a two dimensional oriented solution of integral proteins in the viscous phospholipids bilayer. Now recent work has cleared that although lipids and a fraction of the labeled protein population appear to diffuse freely, movement of other proteins is much more complicated than originally envisioned in the fluid mosaic model.

A substantial fraction of the protein is confined, at least transiently, to small domains in the membrane of a cell. Most probably by the propelation of cytoskeleton motors, a few membrane proteins undergo rapid, forward-directed transport towards the cell-edge. The transient confinement of integral proteins has been seen most clearly for certain cell adhesion molecules including cadherin and neural cell adhesion molecules and for receptors for nutrient and growth factors. Where proteins get confined, the domains are 300-500nm in diameter and the confinement lasts for 3-30 seconds. Recently such confinement of proteins has been explained by a 'membrane skeleton fence' model. On the basis of this membrane skeleton fence model it may be stated that a spectrin-like mesh work on the cytoplasmic side of the membrane sterically confines transiently some membrane spanning proteins.

The above features of cell membrane, demanding revision of our original concept of fluid-mosaic model, were revealed through the use of atleast three new

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techiniques:

(i) Flourescence recovery after photo-blecching (FRAP
(ii) Single particle tracking (SPT)
(iii) Optical laser trap (OLT)

However, it is certain that the plasma membrane is an intriguing mix of dynamic activities, in which its components may randomly diffuse (as proposed in fluid mosaic model) or be confined transiently to small domains or experience highly directed movement. These features cause considerable lateral heterogeneity in the membrane

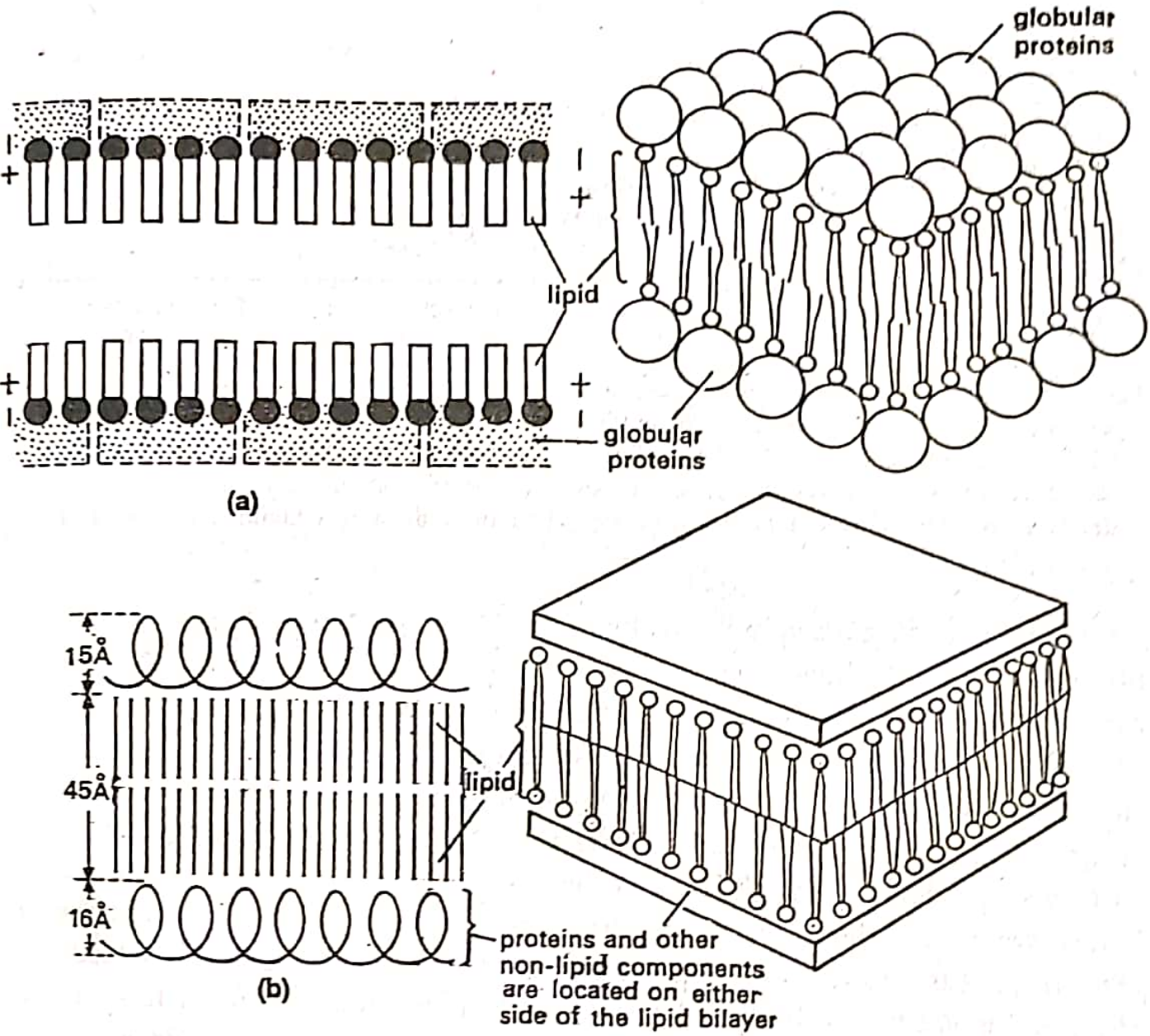

Fig. 14. Models of plasma membrane as proposed by (A) Davson and Danielli, (B) Robertson in each case : (a) a view of vertical section and (b) three dimensional view. (note the smear like protein layer on either side of lipid bilayer).