PART (2): STRUCTURE AND MODELS OF BIOLOGICAL MEMBRANES

Biological membranes are sheet-like structures composed mainly of lipids and proteins. All biological membranes have a similar general structure. Membrane lipids are organized in a bilayer (two sheets of lipids making up a single membrane) that is approximately 60 to 100 Å thick. The proteins, on the other hand, are scattered throughout the bilayer and perform most membrane functions. Membranes are two-dimensional fluids: both lipids and proteins are constantly in motion. The ratio between lipid and proteins depends on the function of the cell, some examples of different cell membrane compositions are shown in the table below.

<table>
<thead>
<tr>
<th>Membrane</th>
<th>% By weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Protein</td>
</tr>
<tr>
<td>Myelin</td>
<td>18</td>
</tr>
<tr>
<td>Human erythocyte</td>
<td>49</td>
</tr>
<tr>
<td>Mouse liver</td>
<td>44</td>
</tr>
<tr>
<td>Ameba</td>
<td>54</td>
</tr>
<tr>
<td>Chloroplast spinach lamellae</td>
<td>70</td>
</tr>
<tr>
<td>Halobacterium purple membrane</td>
<td>75</td>
</tr>
<tr>
<td>Mitochondrial inner membrane</td>
<td>76</td>
</tr>
</tbody>
</table>
Membranes as Lipid Bilayers

All Biological Membranes are made of the same basic structure. This is composed of molecules called *Phospholipids*, which form a Phospholipid Bilayer. Phospholipids are *fats*. They are composed of *two Fatty Acid 'tails'* and *a Phosphate 'head'*. The Phosphate 'heads' are *Hydrophilic* whereas the Fatty Acid 'tails' are *Hydrophobic*, meaning that Phospholipids are *Amphipathic*.

When placed in water, *the 'heads' orientate themselves towards water molecules and the 'tails' away*, meaning that phospholipids will form a layer above water if left. If Phospholipid Molecules are completely surrounded by water, they may form a Bilayer.

A *Phospholipid Bilayer* consists of *two layers of Phospholipids* where the 'tails' point *inwards* and the 'heads' point *outwards*, towards water. One layer is like a mirror image of the other.

The Phospholipid Molecules are *not bonded together*, however, their *Amphipathic Nature* gives the Bilayer a degree of *stability*, since the Hydrophilic 'head' cannot easily through the Hydrophobic region created by the 'tails'. The *molecules can however move freely as a fluid in the plane of the Bilayer.*
Small, non-polar molecules can pass through the Phospholipid Bilayer since they can 'squeeze' between the Phospholipid Molecules and are not repelled by the hydrophobic region. Water molecules can also move through the Bilayer, despite being polar.

**Figure (3):** Schematic diagram of phospholipids’ molecule

**Figure (4):** Schematic diagram of phospholipids bilayer
Models of Biological Membranes Structure

1- Overton model (1895)

- Charles Ernest Overton is a very important figure in the development of a picture of cell membranes.
- He investigated the osmotic properties of cells and noticed in the late 19th century that the permeation of molecules through membranes is related to their partition coefficient between water and oil,
- He called the layers surrounding cells “lipoids” made from lipids and cholesterol.

Figure (5): Schematic diagram of Overtone model of plasma membrane.
They experimentally investigated the surface area of lipids. For this purpose they extracted the lipids from red blood cells of man, dog, rabbit, sheep, guinea pig, and goat in acetone.

- They concluded that cell membranes are made of *two opposing thin molecular layers*, and they proposed that this double layer is constructed such that *two lipid layers form a bilayer* with the *polar head groups pointing toward the aqueous environment*.

*Figure (6):* Schematic diagram of the cell membrane according to Gorter and Grendel (1925).

**Arguments of this model:** the attractive simplicity of Gorter’s and Grendel’s pictures is also its greatest weakness since *it fails to account for the manifold of functions attributed to cell membranes.*
- The earliest molecular model for the biomembrane structure including proteins.

- They took into account that the layers surrounding cells had a significant content of proteins adsorbed to the layers.

- As in the figure, a model of the cell membrane consisting of a lipid bilayer, with which a protein layer is tightly associated.

**Figure (7):** The cell membrane model according to Danielli and Davson (1935).

- In this model they proposed that:
  1. Proteins are adsorbed to the lipophilic layers surrounding cells. *The proteins possess hydrophobic interiors and a water-containing outer layer.*
  2. The lipid layer possesses amphiphilic or charged head groups. This implies that the lipid membrane also contains some water.
3. The water-containing regions of protein layers adsorbed on lipid layers are permeable for charged solutes, e.g., ions.

4. Divalent cations as calcium form complexes with lipids or proteins that reduce their interaction with water. Therefore membranes containing calcium are less permeable for ions.

5. Hydrophobic molecules such as ether penetrate the membranes through their lipophilic lipid part.

6. They used their model to interpret the observation of different membrane permeability of ions and hydrocarbons. In particular, they assumed that the membrane has both a lipophilic and a hydrophilic character.

- **Arguments of this model**: Danielli and Davson did not exclude the possibility that the proteins may span the membrane such that a “mosaic” of protein-rich and lipid-rich regions is formed due to the lack of experimental evidence.
4- Robertson Model (1958)

- He basically confirmed the models of Gorter and Grendel (1925) and Danielli and Davson (1935) basing on microscopic evidence.
- In his review he carefully described the membrane structures of the different organelles including the double membrane layers of mitochondria and the cell nucleus as shown in figure (8).

![Diagram of lipid bilayer with protein layers]

**Figure (8):** Robertson (1959) collected electron microscopy images of many cells and organelles.

- All membranes of biological cells form a three layered structure and are about 7.5 nm thick. In Robertson’s view two protein layers are adsorbed to the lipid bilayer.

- **Arguments of this model:** Robertson’s model was sometimes incorrectly interpreted as that all membranes have the same composition. However, Robertson’s statement was merely meant to describe a common structure.
In the 1960s, the structures of a number of soluble proteins were solved by X-ray crystallography. Lenard and Singer (1966) found that many membrane proteins have a high $\alpha$-helical content. Also, electron micrographs revealed that labeled proteins form isolated spots in some membranes. Furthermore, they considered the role of hydrophobic amino acids in $\alpha$-helices. From this, Singer and Nicolson concluded that proteins may also span through membranes. This led to the famous Singer–Nicolson model (Singer and Nicolson, 1972) also known as the “fluid mosaic model.” This model can be summarized as follows:

- Membranes are constructed from lipids and proteins.
- The proteins form mainly two classes:
  
  (a) **Peripheral (extrinsic) proteins** are those proteins that are only loosely attached to the membrane surface and can easily be separated from the membrane by mild treatment (e.g., cytochrome c in mitochondria or spectrin in erythrocytes).
  
  (b) **Integral (intrinsic) proteins**, in contrast, cannot easily be separated from the lipids. They form the major fraction of membrane proteins.
Figure (9): The Mosaic-Fluid Membrane Model
- The structure forming unit (matrix) is the lipid double layer (bilayer). Membrane lipids, that the supporting structure, are *phospholipids*, *glycolipids* and *cholesterol*.

- Mosaic means an object comprised of bits and pieces embedded in a supporting structure. (1) membrane lipids form the supporting structure. (2) membrane proteins provide the bits and pieces. (3) both lipids and proteins may be mobile or 'fluid'.

- Carbohydrate Polymers may attach to parts of the membrane, forming *Glycolipids* when attach to Phospholipid Molecules and *Glycoproteins* when they attach to proteins. Both Glycolipids and Glycoproteins can act as *Cell Receptor Sites*. Hormones may bind to them, as may drugs, to instigate a response within the cell. They may also be involved in Cell Signalling in the Immune System.

- The Steroid Molecule *Cholesterol* gives the Plasma Membrane in some Eukaryotic Cells stability by *reducing the fluidity* and making the Bilayer more complete. Cholesterol helps control membrane fluidity by making the membrane Less fluid at warm temperatures (e.g. 37 C body temperature) by restraining the phospholipid movement and making the bilayer more fluid at lower (cool) temperatures by preventing close packing of phospholipids.
- *Type and Function of Integral proteins:*

(a) **Channel Protein**: Allow a substance to move across the membrane (EX all hydrogen ions to flow across membrane of electron transport chain)

(b) **Carrier Protein**: Selectively interacts with specific molecules or ions so it can cross membrane (EX Sodium and Potassium pump)

(c) **Cell Recognition Protein**: Called “glycoproteins”, allow cell to be recognized by body’s immune system

(d) **Receptor Protein**: Specifically shaped to a specific molecule (EX liver stores glucose after insulin binds to cell receptor)

(e) **Enzymatic Protein**: Catalyze specific reactions (EX ATP metabolism)

![Figure (10): The Mosaic-Fluid Membrane Model](image)
1. The fluid-mosaic model of the plasma membrane suggests that
A) cholesterols are always bad in nature  B) some proteins are free to move laterally through the membrane  C) phospholipids form a single lipid layer in the center of the membrane  D) the membrane has rigidity and flexibility

2. The plasma membrane is selectively permeable. This means that
A) only gasses and water can pass through it  B) small molecules can enter the cells  C) only certain substances can pass into or out of the cell  D) substances need carrier molecules to pass through it

3. Basic skeleton of the plasma membrane is formed by
A) strong muscles  B) bilayered phospholipid structure  C) water insoluble tails that face the exterior of the membrane  D) cholesterol and glucose

4. Why do the heads of the phospholipids point out and the tails point to each other?
A) The tails are nonpolar and form hydrogen bonds with each other  B) The tails are repelled by the aqueous environment  C) The heads are attracted to the water inside and outside  D) a and c  E) b and c

5. How are plasma membranes best described?
A) A double layer of phospholipid molecules with hydrophobic tails directed toward cytoplasm of the cell  B) A single layer of phospholipid molecules with water molecules attached along one side  C) A double layer of phospholipid molecules with hydrophilic heads directed toward each other  D) A double layer of phospholipid molecules with hydrophobic tails oriented toward each other  E) A single layer of phospholipids with tails pointed to the inside of the cell

1. To which group of organic compounds does A belong?  
2. To which group of organic compounds does B belong?  
3. To which group of organic compounds does C belong?