Unit 2

Cellular Organization

Unit Map

2.A Membrane structure and function

2.A.1 Structure of model membrane

- In 1915, it was discovered that the membranes consisted of lipids and proteins.
- In 1935, Davson and Danielli proposed the first membrane model widely accepted, in which the cell membrane consisted of a lipid bilayer with hydrophilic coating of proteins on both sides which could also form pores.
- In the 1960s, Davson and Danielli's model was rejected following the use of electron microscopes to study cells.
- In 1972, Singer and Nicholson proposed proteins were embedded in the bilayer with only their hydrophilic ends exposed to the external aqueous solution and their hydrophobic regions embedded inside the membrane (fluid mosaic model).
- The freeze-fracture method of examining cells microscopically showed that the fluid mosaic model was accurate.

➢ **Fluid mosaic model**

Singer and Nicholson proposed fluid mosaic model of the cell membrane structure. The models of Davson, Danielli and Robertson couldn't explain some important experimental observations, such as why different membranes differed in structure and function and how the proteins can form the exterior of the membrane while they contain large hydrophobic regions.

S.J. Singer and Garth L. Nicholson proposed in 1972 the currently accepted model of the cell membrane, named the fluid mosaic model. This model retains the bilayer structure proposed by the two Dutch scientists E. Gorter and F. Grendel. The proteins are, however, in the bilayer and can move due to the membrane fluidity. They proposed that the lipid bilayer is organized in such a way that the hydrophilic part of the phospholipids are on the exterior of the lipid bilayer in contact with the water, while their hydrophobic tails face inward. The proteins float in this bilayer and can form pores and channels.

Membrane proteins have been studied by many investigators since then. Unwin and Henderson (1984) found that the portion of the proteins from the lipid bilayer is hydrophobic and often is arranged in a form of alpha-helix. This fluid mosaic model has remained the most accepted model for explaining the structure of the cell membrane since 1972. The freeze-fracture method of examining cells microscopically showed that the fluid mosaic model is an accurate description of cell membranes.

The fluid mosaic model continues to be refined. For example, the existence of membrane compartmentalization is also important for cell function. It is now well established that the plasma membranes contain protein-protein complexes, lipid rafts and pickets and fences formed by the actin-based cytoskeleton and can be polarized (apical and latero-basal compartmentalization in the epithelial cells).

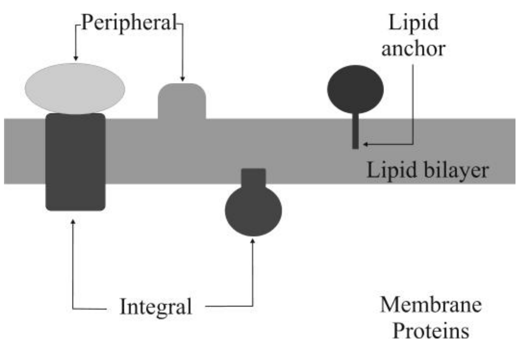

Figure 2.A.1-1
Showing the structure of the cell according to the fluid mosaic model, consisting of lipid bilayer that contains phospholipids, glycolipids and various integral and peripheral proteins accounts for selective permeability and active, passive transport mechanisms. Each phospholipid molecule has a head that is attracted to water (hydrophilic: hydro = water; philic = loving) and a tail that repels water (hydrophobic: hydro = water; phobic = fearing). Both layers of the plasma membrane have the hydrophilic heads pointing toward the outside; the hydrophobic tails form the inside of the bilayer.

2.A.2 Lipid bilayer and membrane protein diffusion

The plasma membranes of animal cells contain four major phospholipids (phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine and sphingomyelin), which together account for more than half of the lipid in most membranes. These phospholipids are asymmetrically distributed between the two halves of the membrane bilayer. The outer leaflet of the plasma membrane consists mainly of phosphatidylcholine and sphingomyelin, while phosphatidylethanolamine and phosphatidylserine are located in the inner leaflet. Phosphatidylinositol, fifth phospholipid, is also present in the inner half of the plasma membrane. It is a quantitatively minor membrane component and plays an important role in cell signaling. Phosphatidyl serine and phosphoionisitol have negatively charged head groups and are present at the cytosolic face of plasma membrane.

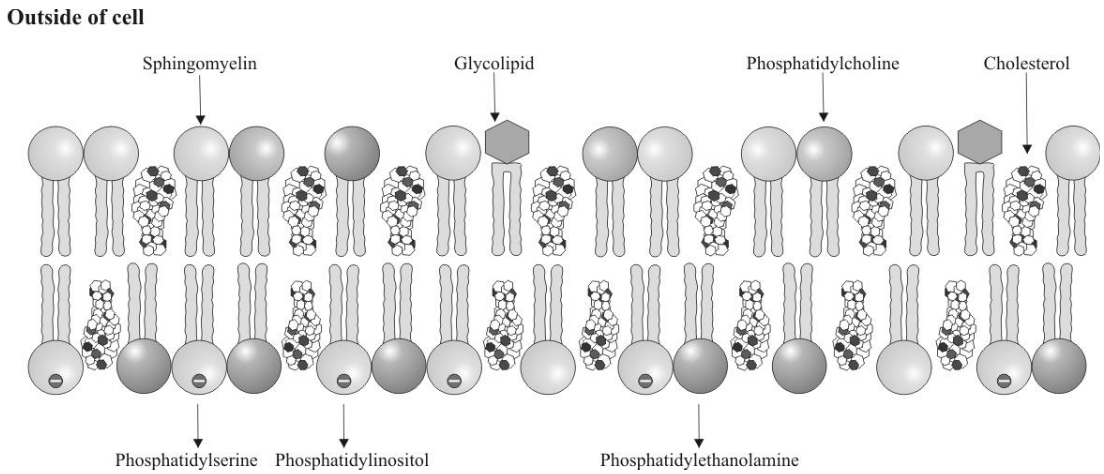

Figure 2.A.2-1
Lipid components of the membrane showing that the enter leaflets consist of phosphatidylcholine, sphingomyelin and glycolipids, whereas the inner leaflets contains phosphatidylethanolamine, phosphatidylserin, phosphatidylinosital. Cholesterol is distributed in both leaflets.

Cholesterol is distributed in both leaflets. The net negative charge of the head groups of phosphatidylserine and phosphatidylinositol is indicated. In addition to the phospholipids, the plasma membranes of animal cells contain glycolipids and cholesterol. The glycolipids are found exclusively in the outer leaflet of the plasma membrane, with their carbohydrate portions exposed on the cell surface. They are relatively minor membrane components, constituting only about 2% of the lipids of most plasma membranes. Cholesterol is a major membrane constituent of animal cells, being present in about the same molar amounts as the phospholipids.

Two general features of phospholipids bilayers are critical to membrane function

i. The structure of phospholipids is responsible for the basic function of membranes as barriers between two aqueous compartments. Because the interior of the phospholipids bilayer is occupied by hydrophobic fatty acid chains, the membrane is impermeable to water-soluble molecules, including ions and most biological molecules.

ii. Bilayers of the naturally occurring phospholipids are viscous fluids, not solids. The fatty acids of most natural phospholipids have one or more double bonds, which introduce kinks into the hydrocarbon chains and make them difficult to pack together. The long hydrocarbon chains of the fatty acids therefore move freely in the interior of the membrane, so the membrane itself is soft and flexible. In addition, both phospholipids and proteins are free to diffuse laterally within the membrane a property that is critical for many membrane functions.

Because of its rigid ring structure, cholesterol plays a distinct role in membrane structure. Cholesterol will not form a membrane by itself, but inserts into a bilayer of phospholipids with its polar hydroxyl group close to the phospholipid head groups. Depending on the temperature, cholesterol has distinct effects on membrane fluidity. At high temperatures, cholesterol interferes with the movement of the phospholipid fatty acid chains, making the outer part of the membrane less fluid and reducing its permeability to small molecules. At low temperatures, however, cholesterol has the opposite effect by interfering with interactions between fatty acid chains; cholesterol prevents membranes from freezing and maintains membrane fluidity. Although cholesterol is not present in bacteria, it is an essential component of animal cell plasma membranes. Plant cells also lack cholesterol, but they contain related compounds (phytosterols) that fulfill a similar function.

2.A.3 Osmosis, ion channels, active transport, ion pumps

Mode of Transport across Plasma Membrane

The plasma membrane acts as a semi permeable barrier between the cell and the extracellular environment. This permeability must be highly selective to ensure that essential molecules such as glucose, amino acids and lipids can readily enter the cell that these molecules and metabolic intermediates remain in the cell and that waste compounds leave the cell. The selective permeability of the plasma membrane allows the cell to maintain a constant internal environment i.e. homeostasis. In all types of cells there exists a difference in ionic concentration with the extracellular medium. Similarly, the organelles within the cell often have a different internal environment from that of the surrounding cytosol and organelle membranes maintain this difference. Transport across the membrane may be passive or active. It may occur through the phospholipids bilayer or with the help of specific integral membrane proteins, called ***permeases or transport proteins.***

- **Passive transport**

  It is a type of diffusion in which an ion or molecule crossing a membrane moves down its electrochemical or concentration gradient i.e. they move from high concentration to low concentration. No metabolic energy is consumed in passive transport.

  Passive transport is of following three types

  i. **Osmosis** the plasma membrane is permeable to water molecules. The to and fro movement of water molecules through the plasma membrane occurs due to the differences in the concentration of the solute on its either sides. The process by which the water molecules pass through a membrane from a region of higher water concentration to the region of lower water concentration is known as ***osmosis.*** The process in which the water molecules enter into the cell is known as ***endosmosis,*** while the reverse process which involves the exit of the water molecules from the cell is known as ***exosmosis.*** In plant cells due to excessive exosmosis the cytoplasm along with the plasma membrane shrinks away from the cell wall. This process is known as ***plasmolysis.***

  ii. A cell contains variety of solutes in it, for instance, the mammalian erythrocytes contain the ions of potassium (K^+), calcium (Ca^{2+}), phosphate(PO_4^{3-}), dissolved hemoglobin and many other substances. If the erythrocyte is placed in a 0.9% solution of sodium chloride (NaCl), then it neither shrinks nor swells. In such case, because the intra-cellular and extra-cellular fluids contain same concentration and no osmosis takes place. This type of extra-cellular solution or fluid is known as ***isotonic solution or fluid.*** If the concentration of NaCl solution is increased above 0.9% then the erythrocytes shrink due to excessive exosmosis. The solutions which have higher concentrations of solutes than the intracellular fluids are known as ***hypertonic solutions.*** Further, if the concentration of NaCl solution decreases below 0.9% the erythrocytes will swell up due to endosmosis. The extra-cellular solutions having less concentration of the solutes than the cytoplasm are known as ***hypotonic solutions.*** Due to endosmosis or exosmosis the water molecules come in or go out of the cell. The amount of the water inside the cell causes a pressure known as ***hydrostatic pressure.*** The hydrostatic pressure which is caused by the osmosis is known as ***osmotic pressure***. The plasma membrane maintains a balance between the osmotic pressure of the intra-cellular and inter-cellular fluids.

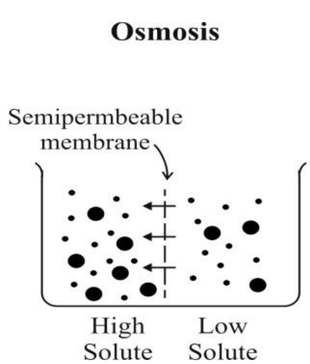

Figure 2.A.3-1
Figure showing the phenomenon of osmosis, a net movement of water across a selectively permeable membrane due to the difference in the solute concentration on both the sides of membrane. Water always flow from the solution with the lower solute concentration into the solution with higher solute concentration. When thinking about osmosis, we are always comparing solute concentrations between two solutions, and some standard terminology is commonly used to describe these differences; Isotonic: The solutions being compared have equal concentration of solutes. Hypertonic: The solution with the higher concentration of solutes. Hypotonic: The solution with the lower concentration of solutes.

  iii. **Simple diffusion** is where a small molecule in aqueous solution dissolves into the phospholipids bilayer, crosses it and then dissolves into the aqueous solution on the opposite side. There is little specificity to the process. The relative rate of diffusion of the molecule across the phospholipids bilayer will be proportional to the concentration gradient across the membrane.

iv. Facilitated diffusion this is a special type of passive transport, in which ions or molecules cross the membrane rapidly because specific permeases in the membrane facilitates their crossing. Facilitated diffusion does not require the metabolic energy and it occurs only in the direction of a concentration gradient. Facilitated diffusion is characterized by the following special features

- The rate of transport of the molecule across the membrane is far greater than would be expected from a simple diffusion.
- This process is specific; each facilitated diffusion protein (called ***protein channel***) transports only a single species of ion or molecule.
- There is a maximum rate of transport, i.e., when the concentration gradient of molecules across the membrane is low, an increase in concentration gradient results in a corresponding increase in the rate of transport.

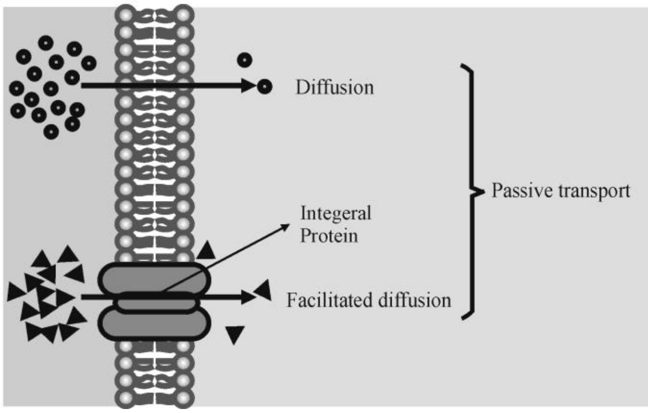

Figure 2.A.3-2
Figure showing phenomenon of facilitated diffusion that is a passage of molecules or ions across the biological membrane with the aid of integral proteins. Facilitated diffusion is a process whereby a substance passes through a membrane with a aid of an intermediary or a facilitator. Two major groups of integral proteins are involved-carrier protein and ion channel. The facilitator is an integral membrane protein that spans the width of the membrane. The force that drives the molecule from one side of the membrane to the other is the force of diffusion.

Examples of Facilitated Diffusion

- **Ionic transport through charged pores** Nerve conduction is propagated along the axonal membrane by action potential which regulates opening and closing of two main types of ion channels (i.e., channel proteins with water filled pores), Na^+ channels (or voltage-gated Na^+ channels) and K^+ channels (or K^+ leak channels). At the point of stimulation, there is a sudden and several hundred fold increase in permeability to Na^+, which reaches its peak in 0.1 millisecond (i.e., the membrane potential may depolarize from –90 mV and overshoot to + 50 mV). At the end of the period, the membrane again becomes essentially impermeable to Na^+, but the K^+ permeability increases and this ion leaks out of the cell, repolarising the nerve fiber. In other words, during the rising phase of the spike, Na^+ enter through the Na^+ channels and in descending phase K^+ is extruded through the K^+ channels. Such ion channels also occur in other types of cells such as muscle, sperm and unfertilized ovum. They are not coupled to an energy source (ATP), so the transport they mediate is always passive allowing specific ions mainly Na^+, K^+, Ca^{2+} and Cl^- to diffuse down their electrochemical gradient across the lipid bilayer. Further, an ion channel is made of integral proteins of neural membrane.

This protein has two functional elements

i. A selectivity filter which determines the kind of ion that will be transported
ii. A gate which by opening and closing the channel regulates the ion flow.

In both Na^+ and K^+ channels, the gating mechanism is electrically driven and is controlled by the membrane potential, without the need of other energy source. In the resting condition (steady state) both Na^+ and K^+ channels are closed. With depolarization, the Na^+ channel is opened and during repolarization, it closes again and K^+ channel opens. Calcium ion channels (Ca^{2+} channels) occur in axonal membranes and other membranes for the entrance of Ca^{2+} ions in the cell. Ca^{2+} ions have a fundamental role in many cellular activities such as exocytosis, endocytosis, secretion, cell