Structure and Function of Biomembrane in Ion Channel

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Abstract— Conventional oxidation processes are used in water Viral ion channels are short auxiliary membrane proteins with a length of ca. 100 amino acids. They are found in enveloped viruses from influenza A, influenza B and influenza C (Orthomyxoviridae), and the human immunodeficiency virus type 1 (HIV-1, Retroviridae). The channels are called M2 (influenza A), NB (influenza B), CM2 (influenza C) and Vpu (HIV-1). Recently, in Paramecium bursaria chlorella virus (PBCV-1, Phycodnaviridae), a K. selective ion channel has been discovered. The viral channels form homo oligomers to allow an ion flux and represent miniaturised systems. Proton conductivity of M2 is established; NB, Vpu and the potassium channel from PBC-1 conduct ions; for CM2 ion conductivity is still under proof. This review summarises the current knowledge of these short viral membrane proteins. Their discovery is outlined and experimental evidence for their structure and function is discussed. Studies using computational methods are presented as well as investigations of drug protein interactions. Membranes play a central role in both the structure and function of all cells, prokaryotic and eukaryotic, plant and animal. Membranes basically define compartments, each membrane associated with an inside and an outside. If this were all they did, membranes would be considerably importance and Diversity of Membranes less interesting than they are. But, membranes not only define compartments, they also determine the nature of all communication between the inside and outside. This may take the form of actual passage of ions or molecules between the two compartments (in and out) or may be in the form of information, transmitted through conformational changes induced in membrane components. In addition, attached to membranes are many cellular enzymes. Some of these enzymes catalyze transmembrane reactions, involving reactants on both sides of the membrane or molecular transport. Others are involved in sequential reactions involving a series of enzymes which are concentrated in the plane of the membrane, thus facilitating efficient interactions. Still other enzymes have membrane-bound subs.

Keywords: Amino Acids, Viral, Prokaryotic, Eukaryotic, Enzymes, Molecular Transport

I. INTRODUCTION

A biomembrane or biological membrane is an enclosing or separating membrane that acts as a selective barrier, within or around the cell. It consists of a lipid bilayer with embedded proteins that may constitute close to 50% of membrane content. The cellular membranes should not be confused with isolating tissues formed by layer of cells, such as mucous and basement membrane. The membranes that are present in living organisms comprise the outer membrane (or membranes) of prokaryotic cells, and the outer and inner (numerous and varied) membranes of eukaryotic cells. They are responsible for a profusion of biological functions. Their many contributions to the life processes of cells explain why one third to one-half of all proteins encoded in the genome of various species is associated with Biomembrane. Appearance of lipid bilayers in the very early stages of the chemical origin of prebiotic systems permitted mixtures of biogenic molecules to become enclosed and therefore distinct from their environment. Acquisition of proteins (or of their prototypes) in these lipid bilayers would have permitted exchange of materials, energy and information across the primitive membranes and opened the way for the great variety of functions performed by present day Biomembrane.

Membranes play a central role in both the structure and function of all cells, prokaryotic and eukaryotic, plant and animal. Membranes basically define compartments, each membrane associated with an inside and an outside. If this were all they did, membranes would be considerably less interesting than they are. But, membranes not only define compartments, it also determine the nature of all communication between the inside and outside. This may take the form of actual passage of ions or molecules between the two compartments or may be in the form of information, transmitted through conformational changes induced in membrane components. In addition, attached to membranes are many cellular enzymes. Some of these enzymes catalyze transmembrane reactions, involving reactants on both sides of the membrane or molecular transport. Others are involved in sequential reactions involving a series of enzymes which are concentrated in the plane of the membrane, thus facilitating efficient interactions. Still other enzymes have membrane-bound substrates and/or are involved in the main-tenance or biosynthesis of the membrane. Most of the fundamental biochemical functions in cells involve membranes at some point, including such diverse processes as prokaryotic DNA replication, protein biosynthesis, protein secretion, bioenergetics, and hormonal responses.

Electron micrographs of mammalian cells reveal the wealth of membranous organelles which comprise a large part of the intracellular volume. It is now clear that the structural principles for all these membranes are basically the same. Furthermore, these structural similarities apply also to plant cell membranes and bacterial membranes. Such as the erythrocyte membrane, to other systems, tempered with a reasonable degree of caution. This caution is necessary because, paradoxically, one of the most salient points to be made about membranes is their remarkable diversity. This diversity is due primarily to the different functions of the proteins present in each membrane and to the way in which these proteins interact with each other as well as with cytoplasmic components. These interactions result in distinct morphologies, such as in the microvilli of the intestinal epithelium or the tubular endoplasmic reticulum, and may result in lateral inhomogeneities within a given membrane The main point is that there is a common ground for studying membranes in general, but that an appreciation for the subject

lies in large measure in the comprehension of the molecular and biological basis for the diversity in membrane structure and function.

II. STRUCTURE OF BIOMEMBRANE

Structure and conformational properties of cell membranes, Singer and Nicholson model, integral proteins in membranes, conformational variations during ion transport, monitoring membrane potentials, Signal transduction and molecular reception.

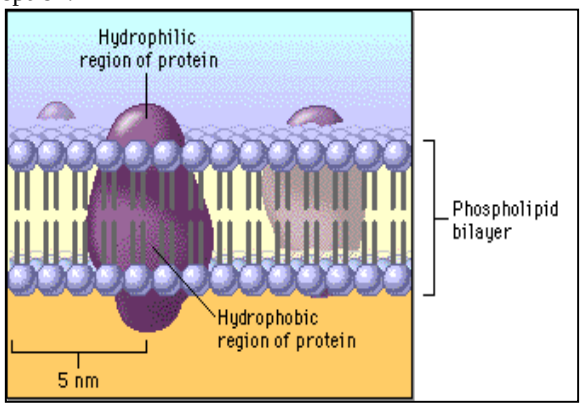


Fig. 2.1: Structure and conformational properties of cell membranes

Cell membrane is thin semi-permeable structure that surrounds the cytoplasm of a cell.

Cell membrane: Function and role

- To protect the integrity of the interior of the cell.
- Allow certain substances into the cell, while keeping other substances out via selective transport.
- Helps maintain its shape by serving as a base of attachment for the cytoskeleton in some organisms and the cell wall in others.
- Major components of Cell membrane:
- Proteins and lipids.
- Lipids range between 20 % to 80 % of the membrane; rest being proteins.
- Lipids provide flexibility; proteins maintain the cell's chemical climate and assist in the transfer of molecules across the membrane.

Cell Membrane lipids

The major components of natural membranes are lipids and cholesterol, with a small amount of other materials such as fatty acids. The relative amounts of these varies from membrane to membrane and even between organism.

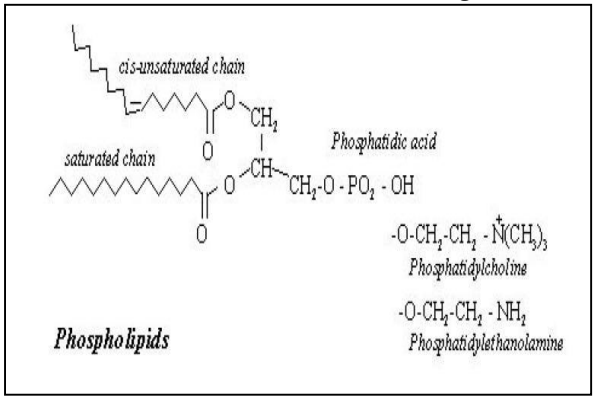


Fig. 2.2: The structures of lipids associated with membrane.

To the glycerol carbon atom 1 and 2 unsaturated and saturated fatty acid chain respectively are linked. To the C3 of glycerol moiety phosphate group is attached. Depending on type of group attached to C3 of glycerol the phospholipids can be phosphatidylcholine (choline attached), phosphatidyl ethanolamine (ethanolamine).

A. Types of Lipids in Membrane:

- Phosphatidylcholine (PC) is one of the most biologically prevalent lipid head group and is commonly used in biophysical studies.
- PC is zwitterionic having a negative charge on the phosphate group and a positive charge on the amine.
- Phosphaditic acid (PA), phosphatidylglycerol (PG) and phosphatidylserine (PS) are common negatively charged lipid head groups.
- Some head groups (PE) are smaller and are less hydrated which causes stress on the bilayer surface since the hydrocarbon chains are more exposed.
- Some lipid head groups on the outer leaflet of plasma membranes are modified with large carbohydrate moieties that act as signatures allowing cells to recognize each other.
- In terms of membrane protein structure, these head groups can participate in strong electrostatic and hydrogen-bonding interactions with the interfacial residues of membrane proteins, and their charge and hydration can directly influence the activity of peripheral membrane proteins.
- The hydrocarbon chains of lipids are usually 14-24 carbons long and, due to the mechanism of their synthesis, always have an even number of carbons.
- The chains tend to align parallel to each other stabilized by extended dispersion forces.
- Rotation can occur around the C-C bonds along the chains giving either a trans or gauche configuration

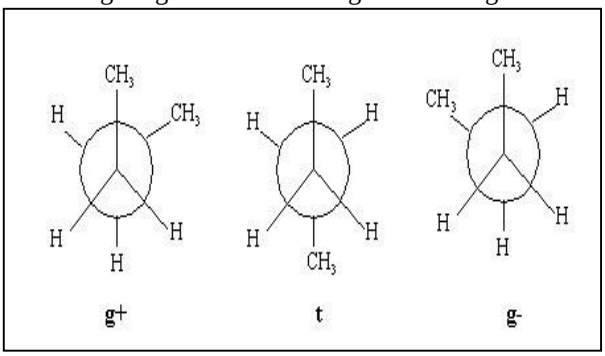
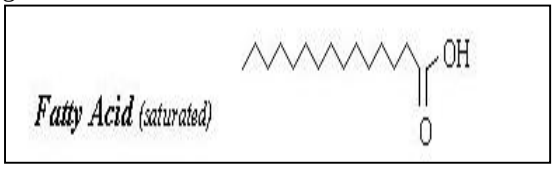


Fig. 2.3: The gauche and trans configuration.

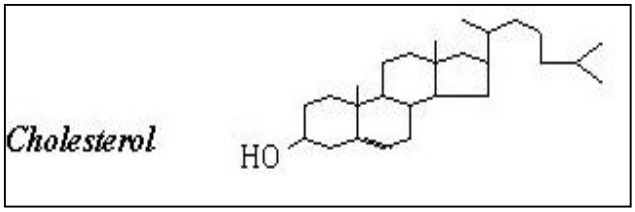
Trans configuration allows the chains to come into close proximity of each other whereas the gauche configuration introduces kinks in the chain increasing the distances between the kinked chain and its neighbor.

Fatty acids consist of a carboxylic group attached to a single14-24 CH2 chain:



- Difference between fatty acids and two-chained lipid molecules is that lipid can freely partition or flip-flop into membranes and distribute evenly in membrane.
- Because the pK of carboxylic group is shifted from ~3 to ~ 7 when embedded in membranes give the uncharged species some membrane solubility.

Cholesterol is a fused ring structure with a single polar hydroxyl group- can interact with groups on or close to the membrane surface:



1) Cholesterol has Varying affects on Membrane Fluidity:

- In fluid phase, cholesterol decrease the rotational freedom of the neighboring hydrocarbon chains and thus "stiffens" the membrane.
- In gel phases, cholesterol acts as a contaminant which decreases the order of the well-packed lipid chains.

2) Membrane's gel-fluid transition:

- The closeness of the lipid chains or their "packing" dictates many of the physical properties of the bilayer such as the lateral movement of the lipid chains, the permeability of the membrane to aqueous species and their gel to liquid phase transition.
- In the gel phase, the lipid chains are usually well-aligned with little rotation around the C-C bonds, which are predominantly in the trans position .This reduced number of gauche isomers leads to better chain packing that in turn results in an increase in bilayer thickness and a reduction in the rate of lateral diffusion of membrane components.
- In contrast, the fluid phase is characterized by relatively rapid diffusion of membrane components and lower bilayer thickness due to the larger number of gauche isomers on the hydrocarbon chains.

3) Membrane Proteins Function

- Structural proteins are attached to microfilaments in the cytoskeleton which ensures stability of the cell.
- Cell adhesion molecules allow cells to identify each other and interact, ex. proteins involved in immune response.
- Membrane receptor proteins serve as connection between the cell's internal and external environments.
- Transport proteins play an important role in the maintenance of concentrations of ions ex., carrier proteins and channel proteins.

4) Membrane Proteins: Main categories

- Integral membrane proteins which are permanently bound to the lipid bilayer.
- They can be defined as those proteins which require a detergent or some other a polar solvent to be displaced.
- Peripheral membrane proteins that are temporarily associated with lipid bilayer or with integral membrane proteins:
- They are temporarily attached either to the lipid bilayer to integral proteins by a hydrophobic, electrostatic, and other non-covalent interactions. Peripheral proteins dissociate following treatment with a polar reagent, such as a solution with an elevated pH or high salt concentrations.

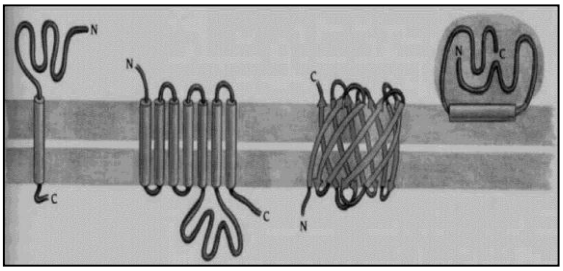


Fig. 2.4: Different arrangement of protein, spanning once or many time the membrane.

Some protein remains attached on one side of membrane. Secondary structure spanning membrane are generally alpha helices, sometimes beta sheets. Protein molecules are embedded in lipid layer and are arranged with 3 distinct regions, 1 hydrophobic TM segment and 2 hydrophilic regions.

B. Integral Membrane Proteins:

Integral polytopic proteins also known as TM proteins, are proteins that are permanently attached to the lipid membrane and span across the membrane .The TM regions are either beta-barrels (outer membranes of Gram- bacteria, mitochondria and chloroplasts and lipid-rich cell walls of a few Gram+bacteria) or alpha-helical (all types of biological membranes). Integral monotopic proteins are proteins that are permanently attached to the lipid membrane from only one side and do not span across the membrane.

C. Most TM elements arees helic

The two secondary structures that will satisfy all peptide backbone hydrogen bonds are sheets and -helices. All bitopic membrane proteins whose structures have solved cross the membrane as a helix. Mostly polytopic integral membrane proteins whose structures has solved cross the membrane by helices. A few cross by sheets.

1) Examples of bi and polytopic IMP

Transmembrane helical protein glycophorin, antibiotic gramicidin, hexose transporter, insulin and epidermal growth factor receptor, photosynthetic complexes, respiratory complexes, the potassium channel and bacterial rhodopsin

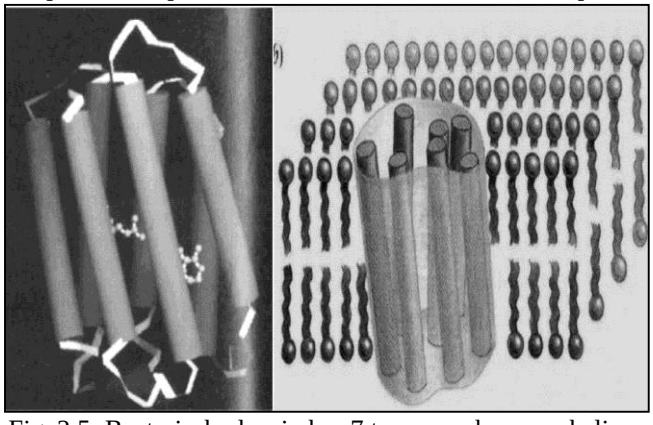


Fig. 2.5: Bacteriorhodopsin has 7 transmembrane a- helices hooked together by loops(

1) Bacteria rhodopsin are integral membrane proteins with seven transmembrane helices, the last of which contains the attachment point for retinal (a conserved lysine). Bacterial rhodopsins are a family of bacterial opsins. They provide light-dependent ion transport and sensory functions to a family of halophilic and other bacteria. The purple membrane of Halobacterium halobium contains Bacteriorhodopsin, a protein of 248 amino acids residues which binds retinal, the same photosensitive Pigment that is used to capture light in our eyes. Bacteriorhodopsin uses the energy of light to Pump protons across the membrane.\
2) What does rhodopsin do?

It's a light—driven protein pump. Trans-retinal gets into the helices - binds and absorbs a photon and changes to cis-retinal - as a consequence protons are pumped from the cytosol to the extracellular space, creating a proton gradient. This gradient is used to generate ATP and to transport ions and Molecules across the membrane

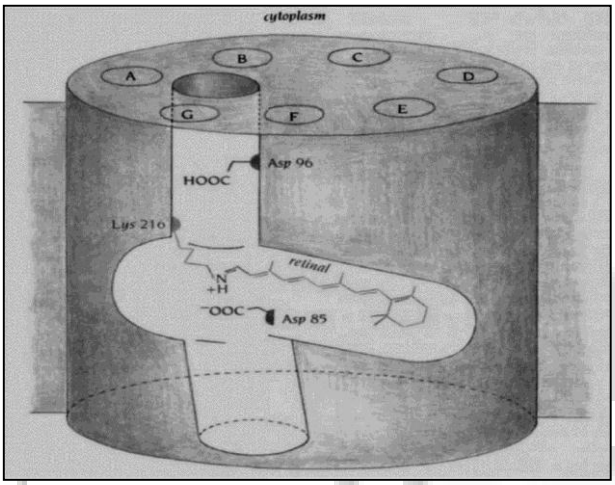


Fig. 2.6: Interaction of rhosdopsin with retinal wherein the conformation of retinal changes from trans to cis.

III. CHANNELING

Gramicidin: channel protein
Gramicidin is an example of a channel.
Channels: Channels cycle between open and closed conformations. When open, a channel provides a continuous pathway through the bilayer, allowing flux of many ions.

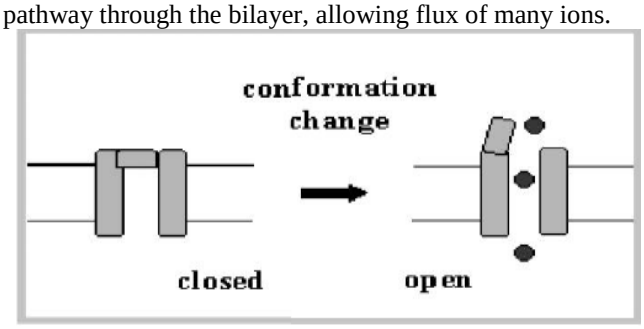


Fig. 3.1: channel proteins in action

A. Gramicidin: Channel Protein

It is an unusual peptide, with alternating D and L amino acids. In lipid bilayer membranes, gramicidin dimerizes and folds as a right handed helix. The dimer spans the bilayer.

The outer surface of the gramicidin dimer, which interacts with the core of the lipid bilayer, is hydrophobic. Ions pass through the more polar lumen of the helix.

With TM voltage clamped at some value, current (ion flow through the membrane) fluctuates each fluctuation, attributed to opening or closing of one gramicidin channel. A current increment corresponds to the current flow through a single channel. Gating of a gramicidin channel is thought to involve reversible dimerization. An open channel forms when two gramicidin molecules join end to end to span the membrane. This model is consistent with the finding that, at high concentrations of gramicidin, the overall transport rate depends on gramidicin.

B. Ion Channels

These move ions down their concentration gradient and are the fastest type of transport protein. Ion channels can be highly selective (e.g. only transporting Na+ ions) or more general, such as allowing through any cation.
Gated and Non-gated
Non-gated channels, such as the K+ channels involved in maintaining resting potential in neurones, allow ions through at all times, provided there is a concentration gradient for them to move down.

Gated channels will only 'open' under the correct circumstances, such as a certain membrane potential (voltage gated channels) or when an activating ligand binds to the channel (ligand gated channels).

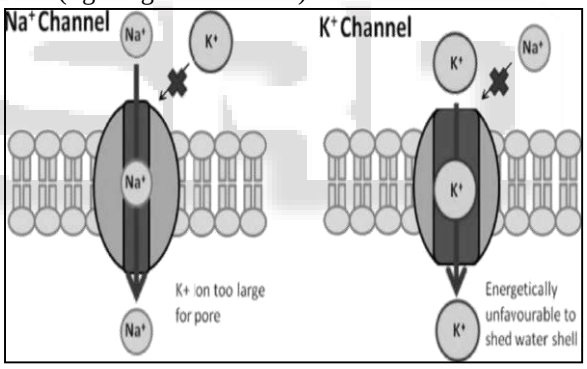


Fig. 3.2: Selectivity of ions to their channels. Ion

C. Channels

Ion selectivity and high ion conductance. The function of such ion channels is to allow specific inorganic ions, mainly K+,Na+,Ca2+, and Cl to diffuse rapidly across the lipid bilayer and balance differences in electric charge between the 2 sides of the membrane- the membrane potential Membrane Potential and selectivity First, it allows a cell to function as a battery, providing power to operate a variety of "molecular devices" embedded in the membrane. In electrically excitable cells such as neurons, it is used for transmitting signals between different parts of a cell. Opening and closing of ion channels at one point in the membrane produces a local change in the membrane potential, which causes electric current to flow rapidly to other points in the membrane. The membrane potential of resting cells is largely determined by K^+ which can move freely in or out through K^+ these channels are selective for K+ ions by a factor of 10,000 over Na+. The rate of selection is amazing...~10^8 ions per second. Selectivity implies strong interactions between K+ and the pore. Both K+

Ions and Na+ ions are spheres and featureless. K+> Na+ size wise so how can selectivity be so great.

D. The K+ channel

The K+ channel is a tetramer molecule with one ion pore in the interface between the 4 subunits. The polypeptide chain of channel has 158 residues folded into 2 TM helices, a pore helix and a cytoplasmic tail of 33 residues. Perpendicular to the plane of the membranes Fits K+ perfectly not Na+.

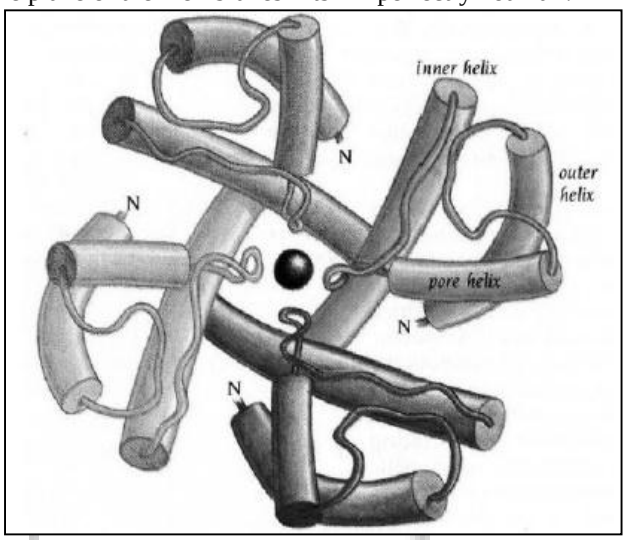


Fig. 3.3: Structure of potassium ion channel showing formation of pore due to arrangement of helices specific to potassium

E. Voltage Gated Channels

- These contain voltage sensing α helices made up of positively charged amino acid residues (each third residue has a positively charged side chain). When the channel is closed the positively charged α helices are attracted to the negative charges on the cytosolic side of the membrane, keeping the channel in a closed conformation, with the 'gate' segment of the protein blocking the channel pore.
- When the cytosol becomes more positive (during depolarisation of a neurone), the voltage sensing α helices are repelled and move towards the exoplasmic side of the membrane, inducing a conformational change in the gate segment of the ion channel and allowing ions to move through the pore.
- After a very short amount of time (0.5-1.0ms for Na+ channels, slightly longer for K+ channels), the voltage sensing helices return to their original position and the channel inactivating segment moves to block the pore.
- After repolarisation has taken place and the membrane is back to its resting potential, the channel inactivating segment is displaced and the channel returns to its original conformation.

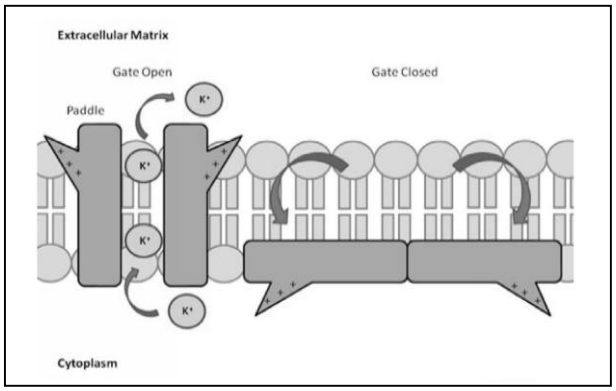


Fig. 3.4: Opening and closing of gated channel of potassium

F. Ligand Gated Channels

They are highly specific for one or two particular species of ion, e.g. the acetylcholine receptor at neurone synapses which transports Na+ and K+ ions. Acetylcholine diffuses across the synapse and then binds to the extracellular domain of the receptor, which induces a conformational change in the ion channel so that ions can pass through it. This conformational change is believed to be the rotation of α helices within the channel pore so that the large hydrophobic residues facing into the pore are replaced by small hydrophilic residues which can interact with the ions and allow them to move through the channel.

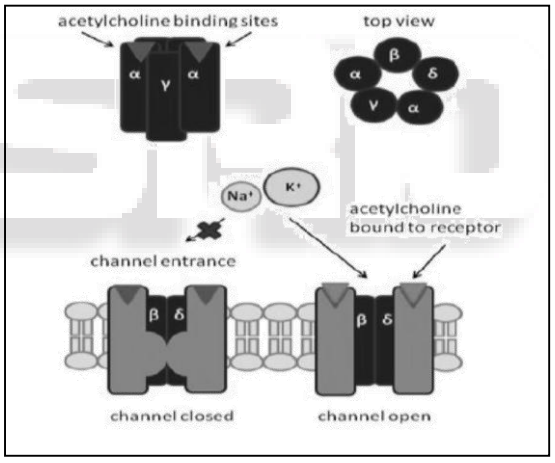


Fig. 3.5: Regulation of channel via Acetylcholine binding to its receptor

Carrier proteins cycle between conformations in which a solute binding site is accessible on one side of the membrane or the other.

There may be an intermediate conformation in which a bound substrate is inaccessible to either aqueous phase.

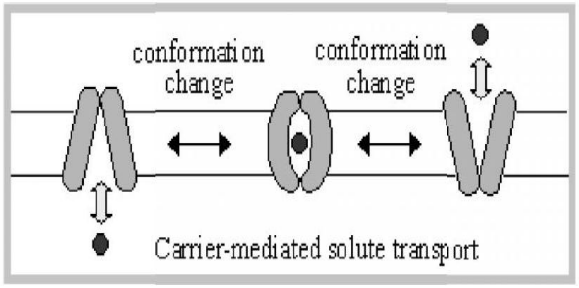


Fig. 3.6: Conformation change during carrier –mediated solute transport

IV. MEMBRANE PROTEINS AND THEIR FUNCTIONS

Now we come to the mosaic aspect of the fluid mosaic model. Somewhat like a tile mosaic, a membrane is a collage of different proteins, often clustered together in groups, embedded in the fluid matrix of the lipid bilayer. More than 50 kinds of proteins have been found so far in the plasma membrane of red blood cells, for example. Phospholipids form the main fabric of the membrane, but proteins determine most of the membrane's functions. Different types of cells contain different sets of membrane proteins, and the various membranes within a cell each have a unique collection of proteins.

Notice in Figure 6.1 that there are two major populations of membrane proteins: integral proteins and peripheral proteins. Integral proteins penetrate the hydrophobic interior of the lipid bilayer. The majorities are transmembrane proteins, which span the membrane; other integral proteins extend only partway into the hydrophobic interior. The hydrophobic regions of an integral protein consist of one or more stretches of nonpolar amino acid, usually coiled into α helices. The hydrophilic parts of the molecule are exposed to the aqueous solutions on either side of the membrane. Some proteins also have a hydrophilic channel through their center that allows passage of hydrophilic substances (see Figure 6.1). Peripheral proteins are not embedded in the lipid bilayer at all; they are appendages loosely bound to the surface of the membrane, often to exposed parts of integral proteins (see Figure 6.1).

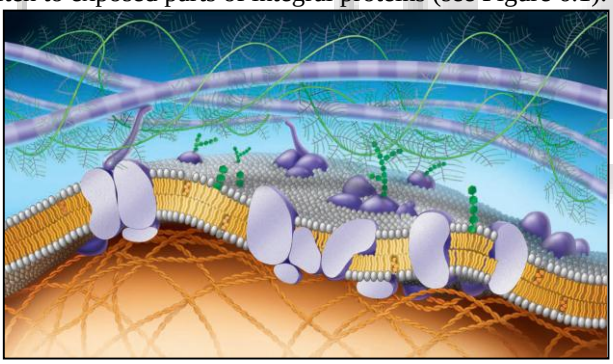


Fig. 4.1: Membrane Proteins and Their Functions

On the cytoplasmic side of the plasma membrane, some membrane proteins are held in place by attachment to the cytoskeleton. And on the extracellular side, certain membrane proteins are attached to fibers of the extracellular matrix, integrins are one type of integral protein). These attachments combine to give animal cells a stronger framework than the plasma membrane alone could provide.

A. Transport Left:

A protein that spansthe membrane may provide a hydrophilic channel across the membrane that is selective for a particular solute. Right: Other transport proteins shuttle a substance from one side to the other by changing shape. Some of these proteins hydrolyze ATP as an energy source to actively pump substances across the membrane.

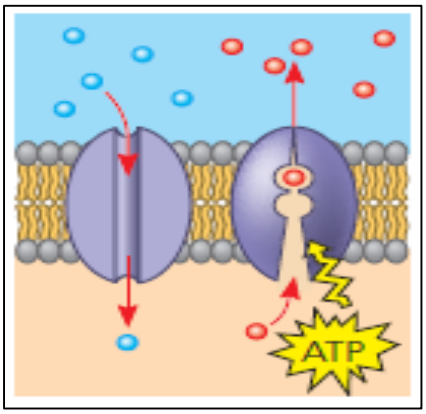


Fig. 4.2: Transport Left

B. Enzymatic Activity:

A protein built into the membrane may be an enzyme with its active site exposed to substances in the adjacent solution. In some cases, several enzymes in a membrane are organized as a team that carries out sequential steps of a metabolic pathway.

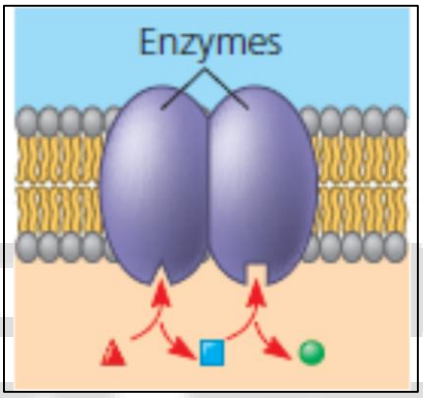


Fig. 4.3: Enzymatic Activity

C. Intercellular Joining:

Membrane proteins of adjacent cells may hook together in various kinds of junctions, such as gap junctions or tight junctions. This type of binding is more long-lasting than that shown in.

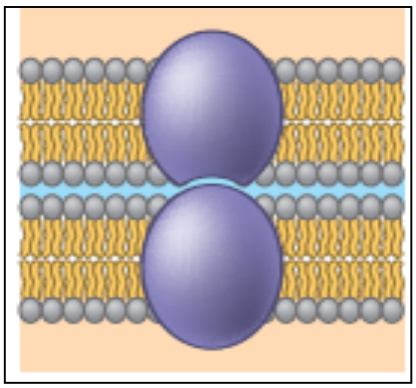


Fig. 4.4: Intercellular joining

D. Cell-Cell Recognition:

Some glycoproteins serve as identification tag that are specifically recognized by membrane proteins of other cells. This type of cell-cell binding is usually short-lived compared to that shown in.

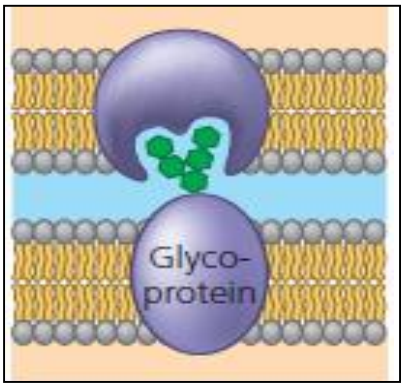


Fig. 4.5: Cell-Cell recognition

E. Signal Transduction:

A membrane protein have a binding site with a specific shape that fits the shape of a chemical messenger, such as a hormone. The external messenger (may cause the protein to change shape, allowing it to relay the message to the inside of the cell, usually by binding to a cytoplasmic proteins.

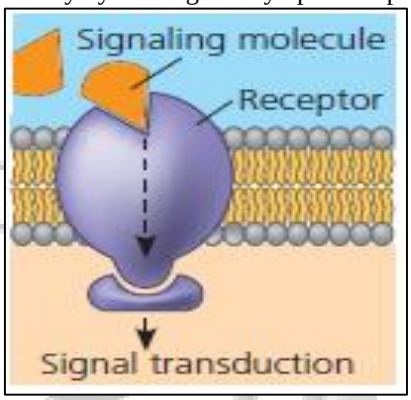


Fig. 4.5: Signal transduction

V. CONCLUSIONS

In this way we have studied about the structural and functional properties, classification, types and process of membrane with ion channels. The structure gives the detail information of biomembrane which includes glycosides, phospholipids. The core studies of different structures of biomembrane in the given above topics helps us to understand regarding the protection of integrity of the interior of the cell. It allows certain substances into the cell, while keeping other substances out via selective transport.

In this case study, we have looked at a few of the ways in which ion channels perform their function, notably to only allow a specific species of ion to cross the cell membrane efficiently. To achieve these, a fine balance must be established between, on the one hand, trying to attract a specific ion into the pore, and on the other hand, not binding to conducting ions too tightly so that ions do not stay stuck in the channel to block it. Because of this, even though different families of ion channels, such as ClCs and K^+ channels, have very different structures and ancestries, they end up sharing many common strategies for accomplishing their similar tasks. Both ClCs and potassium channels use vestibules of water to reduce the length of the membrane that needs to be crossed. They both expose their backbones to the permeating ions in order to create a favourable electrostatic environment for the ion without resorting to large binding energies. And they both need multiple ions present in their pore in order to conduct rapidly. Thus, despite their strikingly different structures, ClCs and K+ channels share many similarities.

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