Physiology | Lecture 2 / A

Plasma Membrane

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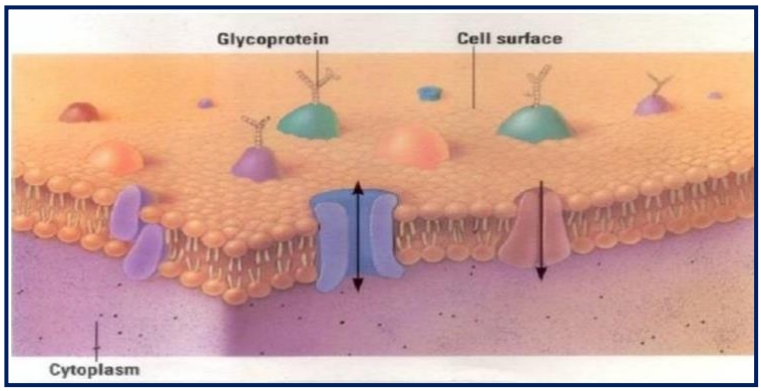
PLASMA MEMBRANE

■In this chapter, we will be talking about the *plasma membrane* , it's structure and function.



■ So , as we can see in this table :

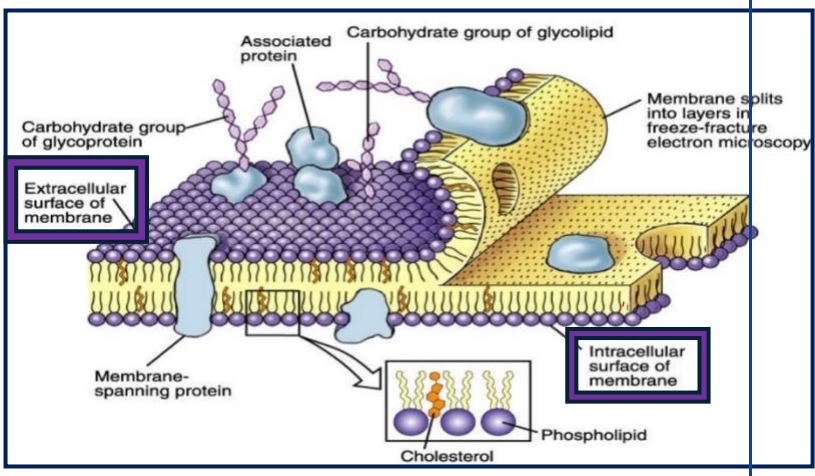
Membrane Structure	*Function*
Phospholipid Bilayer	▪ The phospholipids are arranged in a bilayer, with their polar, hydrophilic phosphate heads facing outwards, and their non-polar, hydrophobic fatty acid tails facing each other in the middle of the bilayer. ▪ This hydrophobic layer acts as a barrier to all but the smallest molecules (oxygen & Carbon Dioxide), effectively isolating the two sides of the membrane. ▪ Phospholipids can exchange position in the horizontal plane but not the vertical.
Integral Proteins	▪ Usually span from one side of the phospholipid bilayer to the other. ▪ Proteins that span the membrane are usually involved in transporting substances across the membrane (more detail below)
Peripheral Proteins	▪ These proteins sit on one of the surfaces (peripheral proteins). They can slide around the membrane very quickly and collide with each other, but can never flip from one side to the other. ▪ Proteins on the inside surface of plasma membrane are often involved in maintaining the cell's shape, or in cell motility. ▪ They may also be enzymes, catalysing reactions in the cytoplasm.
Glycoproteins	▪ Usually involved in cell recognition which is part of the immune system. They can also acts as receptors in cell signaling such as with hormones.
Cholesterol	▪ Binds together lipid in the plasma membrane reducing its fluidity as conferring structural stability

Bilayer structure is formed of lipids (most abundant are **phospholipids**) , also we have **cholesterol** molecules , beside

that we have a lot of types of **proteins** embedded in the plasma membrane and **glycoproteins** .

☆So we are going to analyze the function of these structures that we have in the plasma membranes.

-Lipids in Plasma membrane

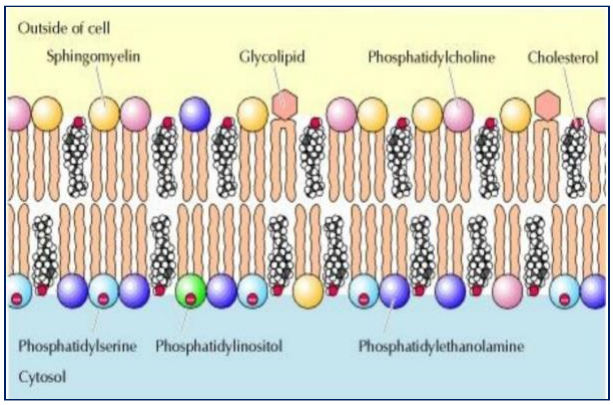


Plasma membrane is considered as a functional organelles , which is separating two compartments (**the Intracellular compartment from the Extracellular compartment**), that membrane is composed of a lipid Bilayer structure in which a lot of proteins are embedded .

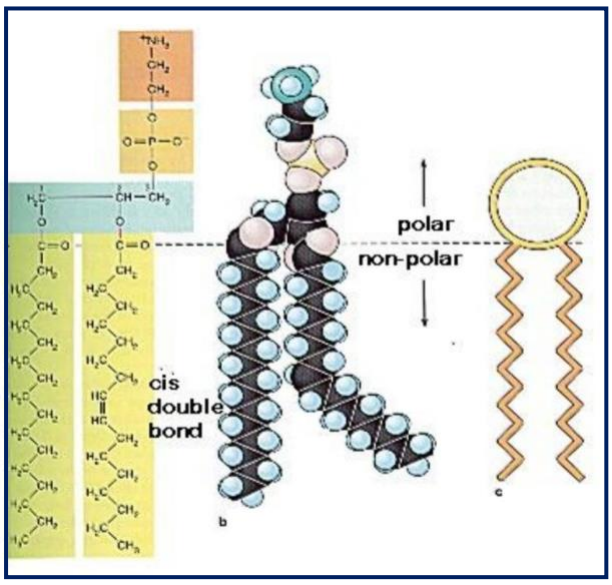
-Lipid function in Plasma membrane

this organelle is forming at **37°** degrees , which is the norml body temperature (***At the normal body temperature of 37 degrees the Membrane is in fluid state.***)

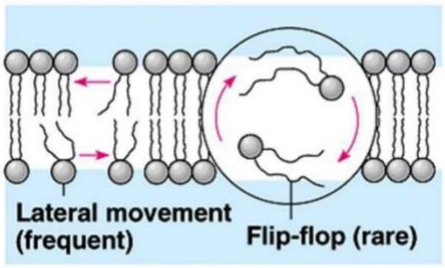
The fluidity is determined by the fatty acids as in the figure.



And once we are getting packing of these lipid structures ,we are not getting compact packing because of having double bonds at certain points over the fatty acids.
(The electrical properties of phospholipids Permit self assembly in a bilayer structure when found themselves in **Hydrophilic** medium).



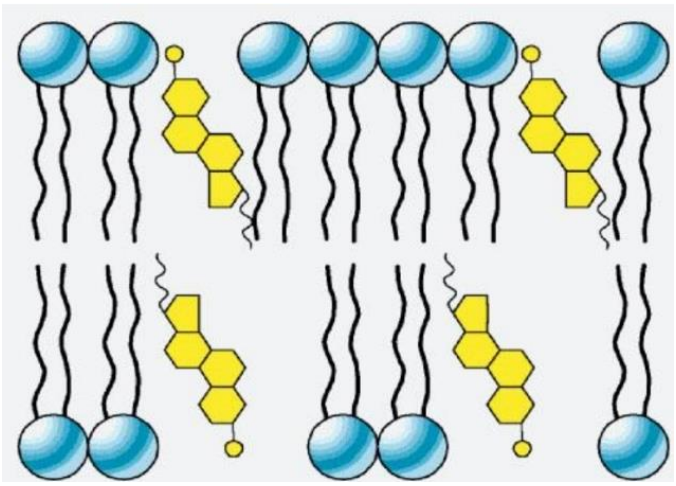
Because of the **fluidity** that we have at 37°, all the time we have movements of lipid particles along the membrane (2 types of them) which is called the **lateral movement** and is **more frequent** to occur .
Also we can have **flip-flop movements** which is more **rare movements** because of *the size* of the phospholipids.

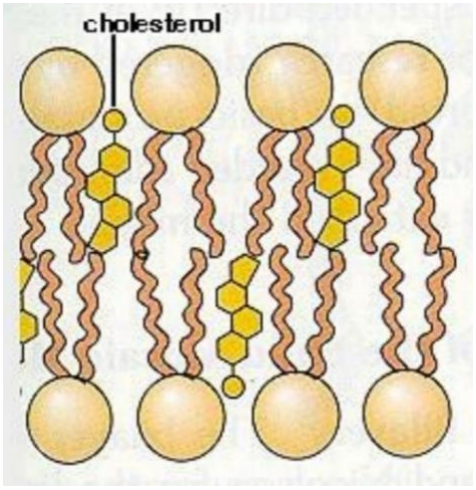


(a) Movement of phospholipids

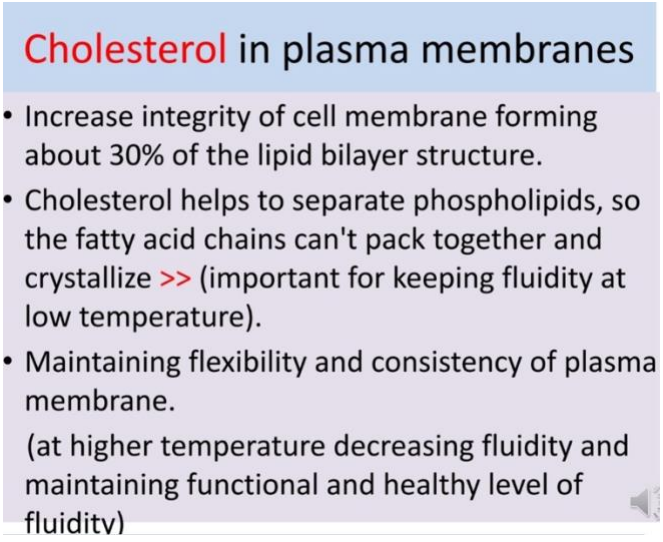
Cholesterol in plasma membranes

Beside phospholipids, we have **<u>cholesterol</u>** molecules embedded between phospholipids molecules, and they are also involved in ***controlling the fluidity*** of the plasma membranes .



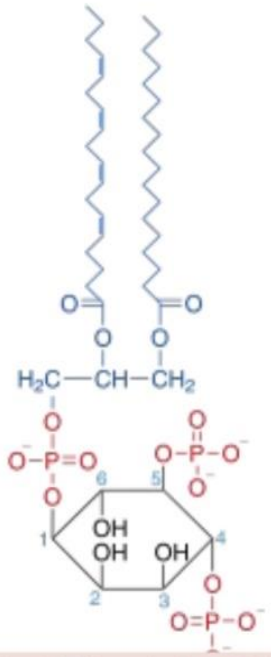


Cholesterol which is Separating phospholipids has an important role in keeping fluidity of that membrane . and it maintains the integrity of the plasma membrane.



PIP2 Functional phospholipids in Plasma

One of the phospholipids , which is found at the plasma membranes , has a functional Importance. the structure of that molecule is shown in the figure:-
We'll see the function of this molecule later ^^)



Phosphatidylinositol 4,5-bisphosphate (PIP2)

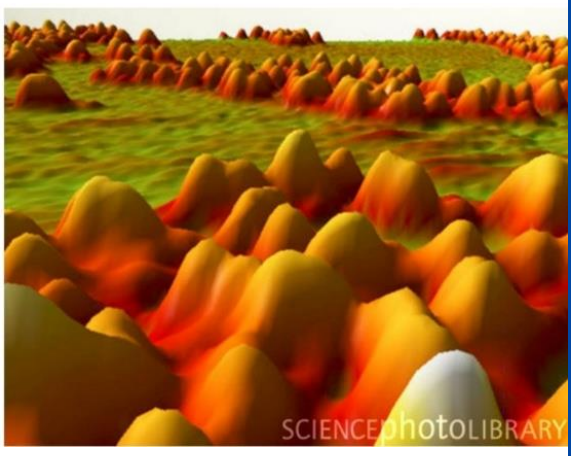
On the glycerol : at the carbon position 1&2 we have fatty acids, at the carbon position we have 3 a molecule with phosphate groups and its a sugar called ***inositol***.

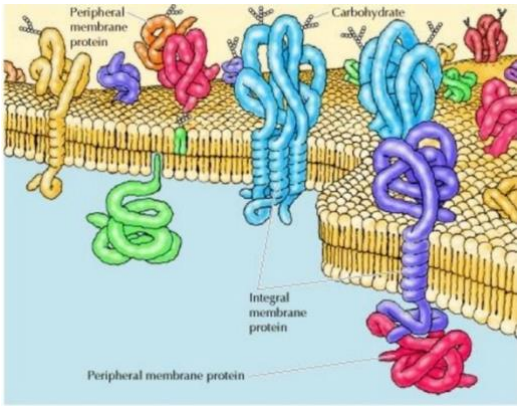
We will see the function of this molecule when we talk about signal transduction mechanism

Proteins in Plasma membrane

We have plenty of proteins that are found in the *plasma membranes*.

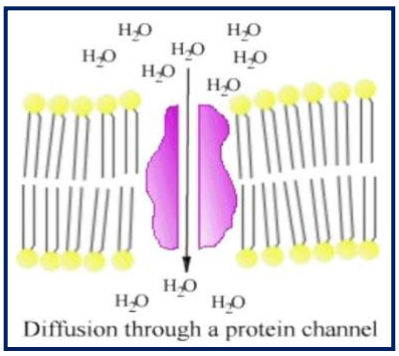
(as shown previously in the table above)
Many protein structures are found at the membrane.
Most of these have also a carbohydrate moiety. Some of these proteins are <u>penetrating the whole bilayer structure</u> (**integral** proteins) others are found at one <u>Surface</u> of the membrane (**peripheral** proteins).
These proteins perform specific functions .





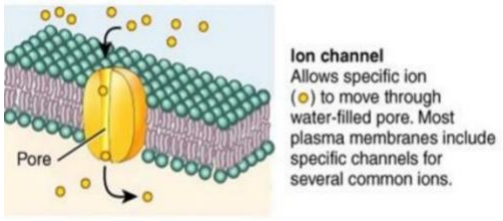
Proteins functions

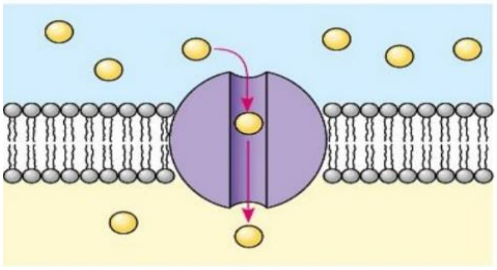
● Some proteins that span the membrane form a water filled Pathways (**Channels**) which enables water soluble substances to diffuse across the membrane through these Structures. Also, the hydrophilic particles cannot pass through the Lipid bilayer structure so they could pass the plasma membrane with the help of these channels.



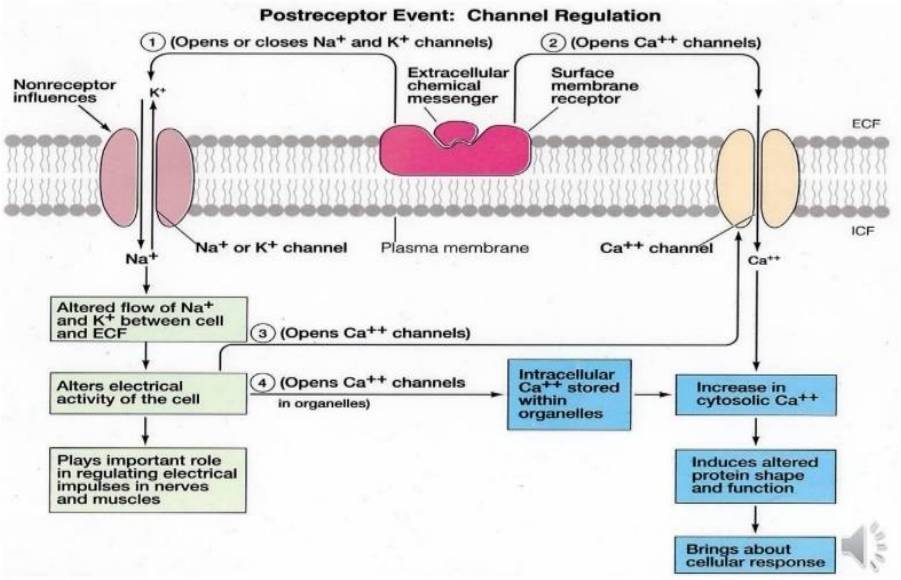
Channels that are at the plasma membrane are important for the **transportation of ion** from one side to another. One thing that you have to know is that these channels are **very specific** and **highly selective** , that means every ion has its own protein that is different from the other ones (Na+ can

Pass only through sodium channels and K+ can pass only Through K+ channels).

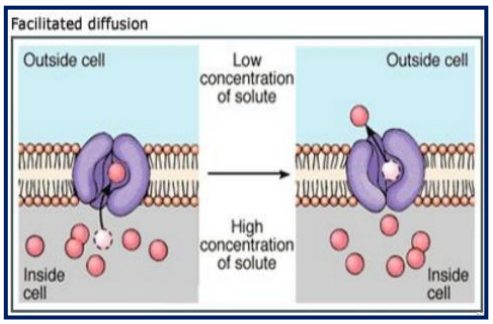


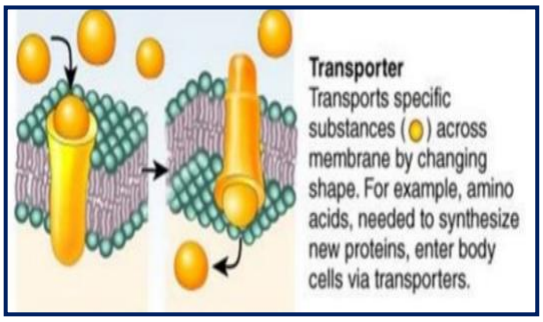


The activity of these channels is under controlling mechanisms that govern the channels activity. Some of These channels change their activity when the membrane potential is changed
(voltagedependent (sensitive) Channels). Other channels can open when a specific ligand Binds to its receptor and causes opening of channel (chemical gated channels).

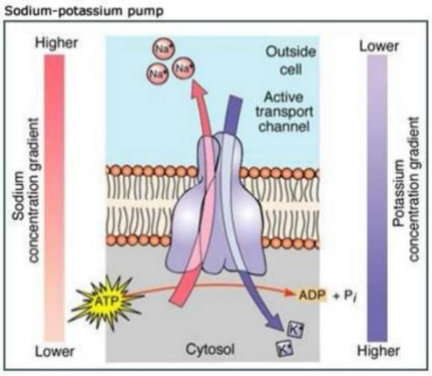


Other proteins serve as **Carrier molecules** which help other molecules (**bigger particles** such as glucose, galactose and fructose) to cross membrane. These Transport proteins are ***highly selective to substances***. They Bind to a substance and move it through the interstices to the other side of the membrane.

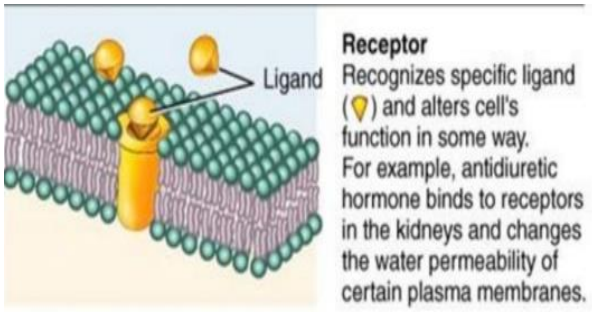




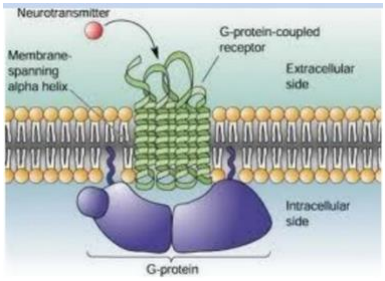
● We can even have carriers that helps ions to move across the membrane from the low concentration to the high concentration (**against their concentration gradient)** These carriers are called **ATP dependent carriers.**



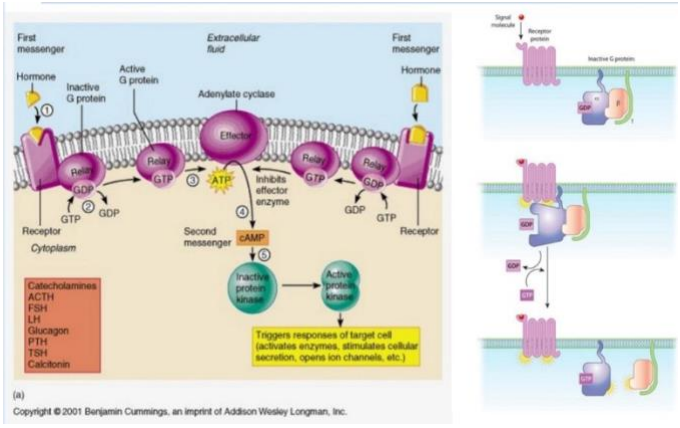
● Other proteins are **<u>Receptors</u>** for ligands found in the Extracellular fluid. The binding of ligand to receptor will
Initiate cellular events that alter the activity of the cell
(an ex. Activation of Na+ channels in striated muscle after binding of acetylcholine (Ach) to its receptor on the Muscle membrane). The receptors are important for communication between the control system and that specific cell.



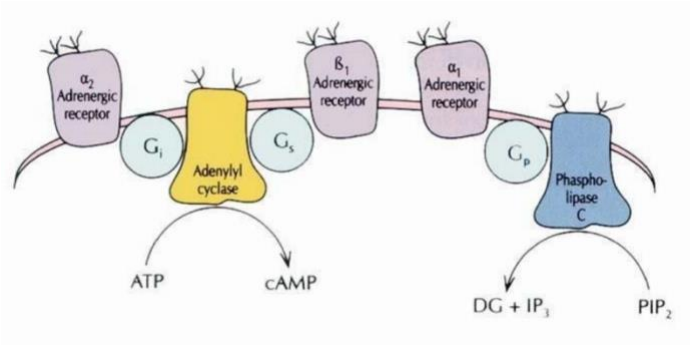
Some of these receptors are linked to other protein structures which are calld G Protein-receptors, they can modify the activity of certain structures like enzymes for example .



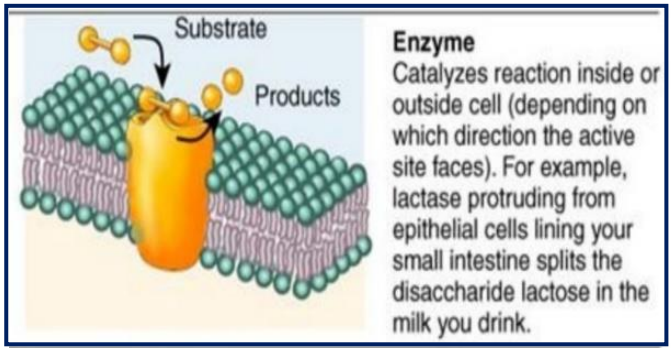
** ***In the figure, a receptor that can activate an enzyme called Adenylate cyclase***



There are many types of Gproteins that can be found at the inner part of the plasma membrane. These proteins are linking receptors to enzymes like adenyly cyclase as we mentioned before. Also, another type is Gp protein that links a receptor to an enzyme called PHASPHOLIPASE-C .

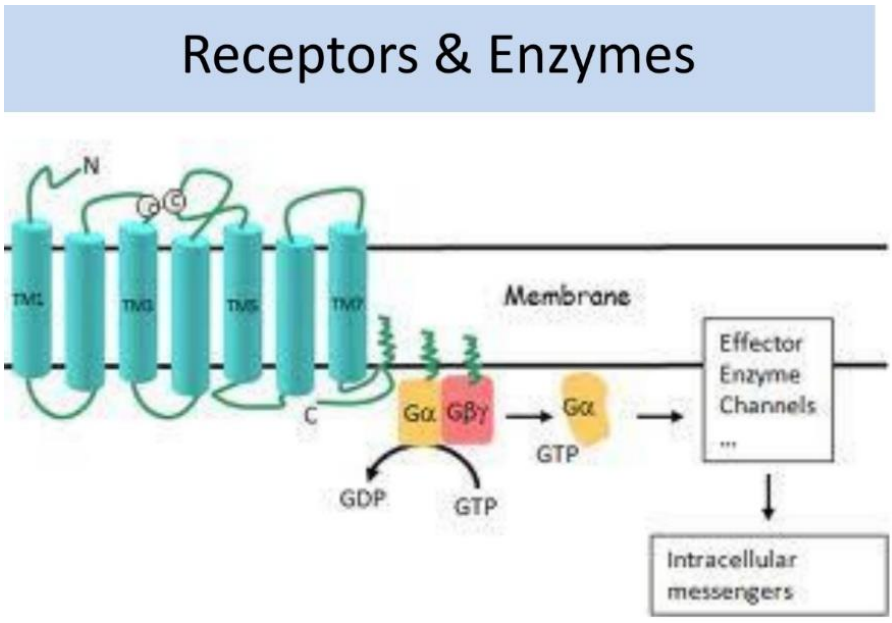


G- Proteins can act as activator or inhibitor like GS proteins which can stimulate the activity of the adenylase cyclase and GI protein which is inhibit the activity of the adenylase cyclase
●Other proteins function as **membrane bound enzymes**
Which control enzymatic reactions either inside or outside
The cell.

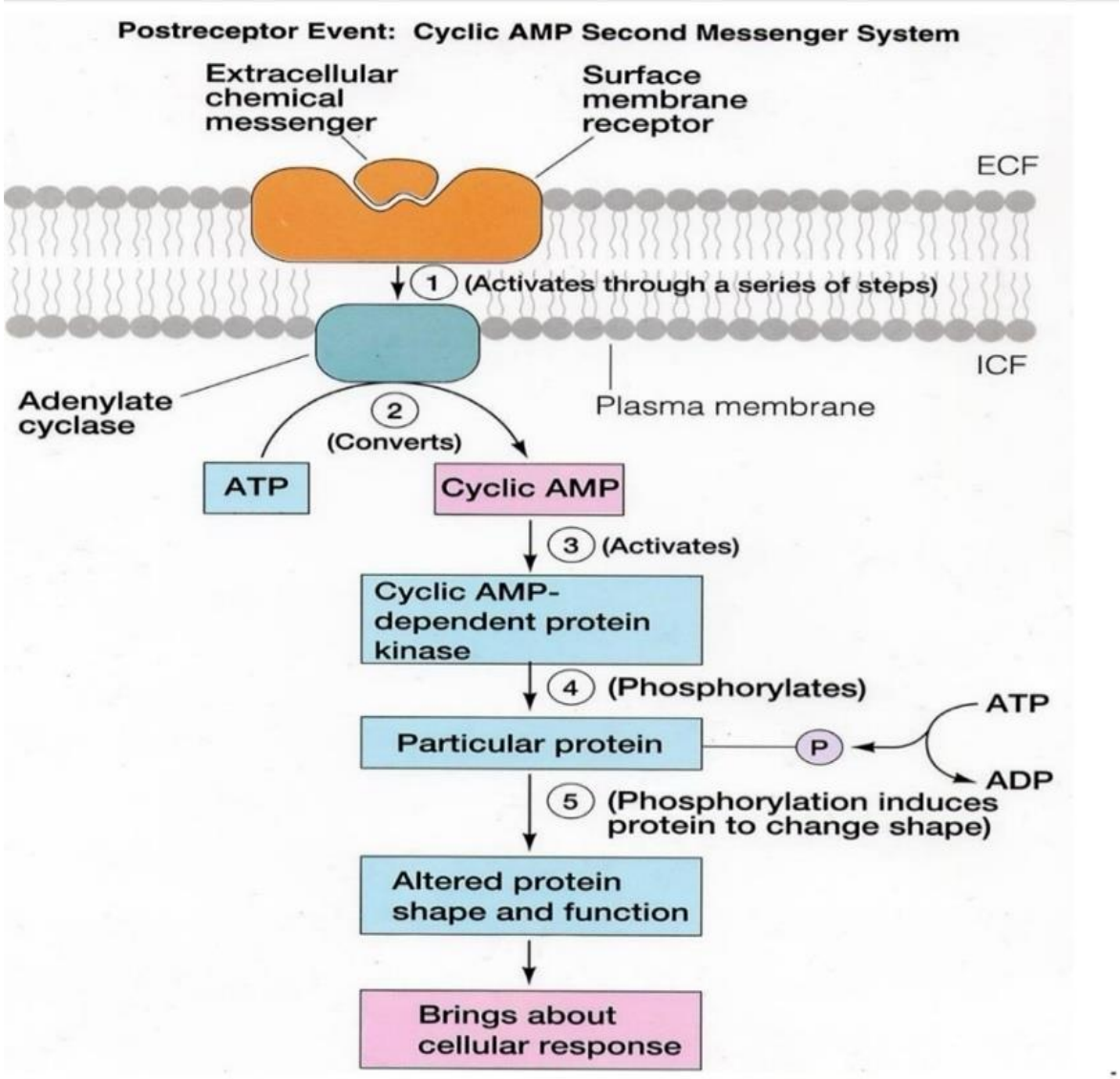


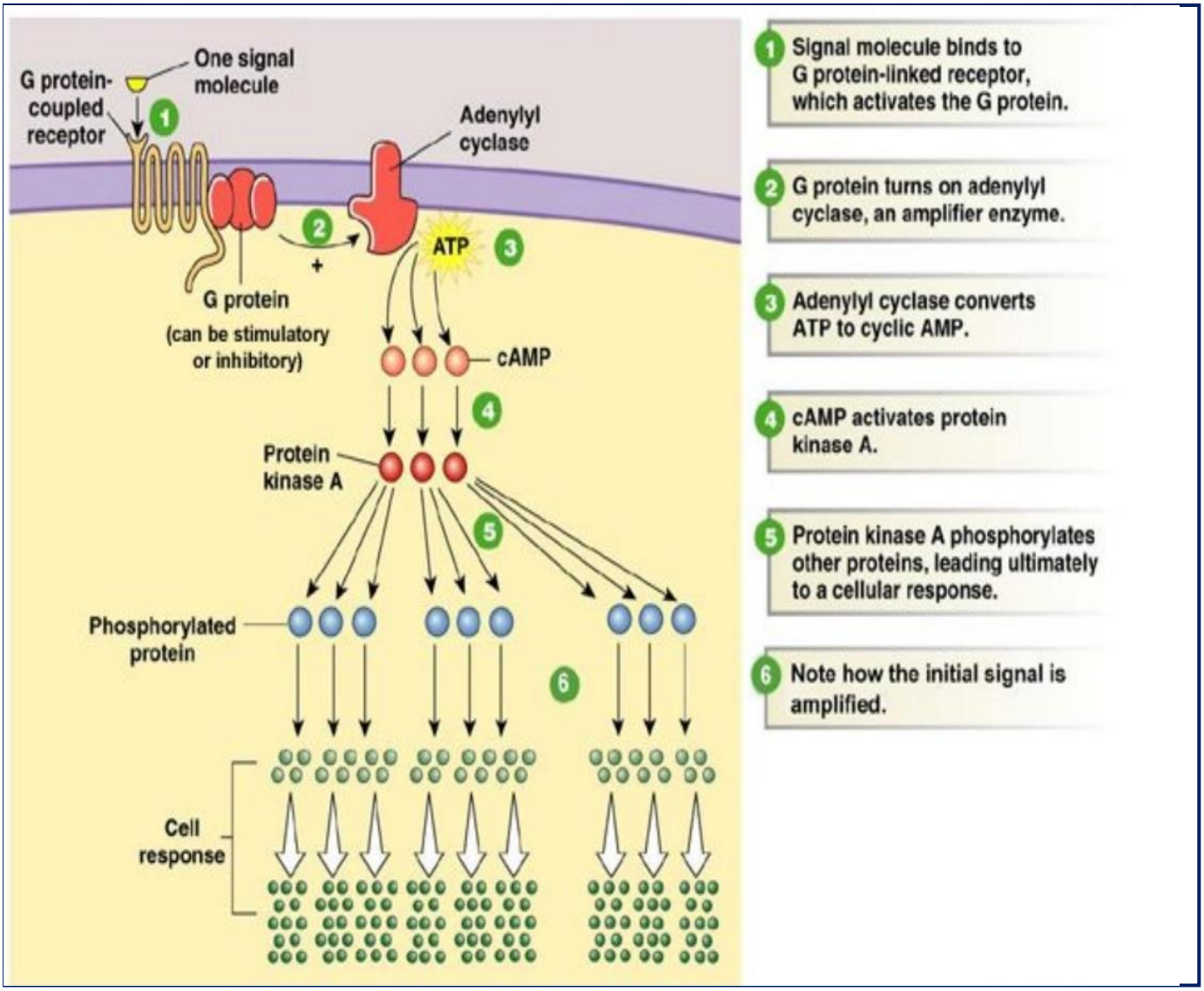
Some of the receptors that we have talked about are linked to certain structures which are Enzymes that can be found at that membrane.

By activating these enzymes, we're getting what we call **The Second Messenger**.



For example, by the activation of Adenylate cyclase we can convert ***ATP into cyclic AMP*** (the cyclic AMP is considered the second massenger) and this will bring some changes to the activity of the cell, now it can activate some cyclic AMP dependent proteins kinase. Once you get a kinase , you well get phosphoralation of a specific type of protein. By this process you are altering the shape and the function of these proteins and this would bring changes -cellular responses- by the activation of the enzyme


Postreceptor Event: Cyclic AMP Second Messenger System
Extracellular chemical messenger
Surface membrane receptor
ECF
1 (Activates through a series of steps)
ICF
Adenylate cyclase
Plasma membrane
2 (Converts)
ATP
Cyclic AMP
3 (Activates)
Cyclic AMP-dependent protein kinase
4 (Phosphorylates)
ATP
Particular protein
P
ADP
5 (Phosphorylation induces protein to change shape)
Altered protein shape and function
Brings about cellular response



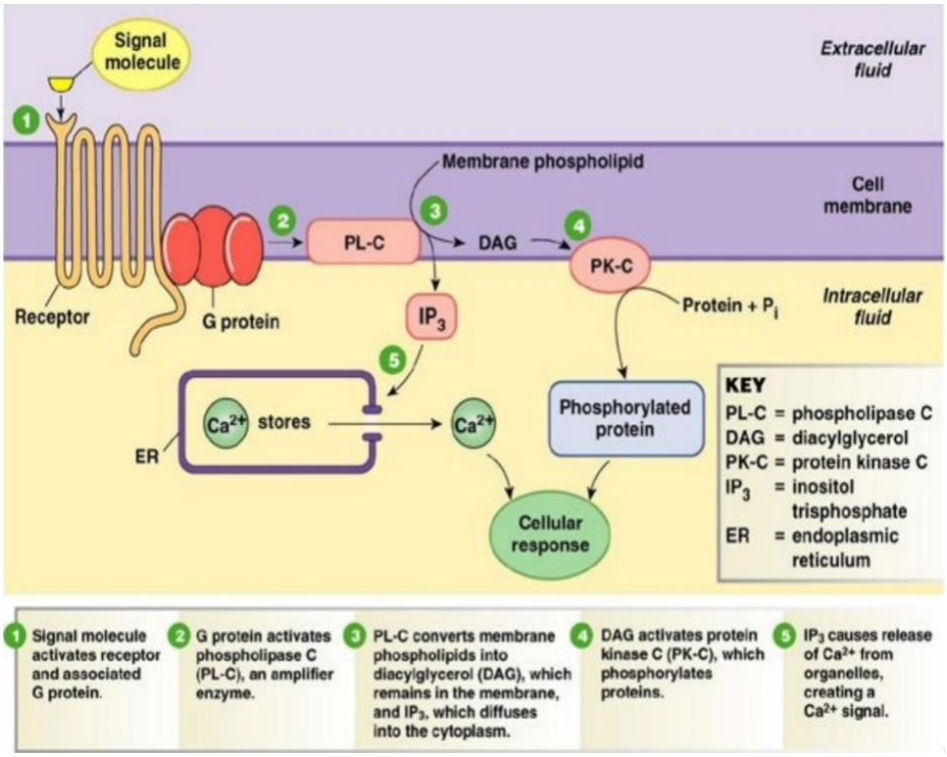
* The adenylyl cyclase converts <u>three</u> ATP into <u>three</u> cAMP ,each cAMPs activates proteins kinase

Protein Kinase can phosphorylate many specific targeted particles

So, we can get millions of responses by the activation of one molecule of Adenylyl cyclase

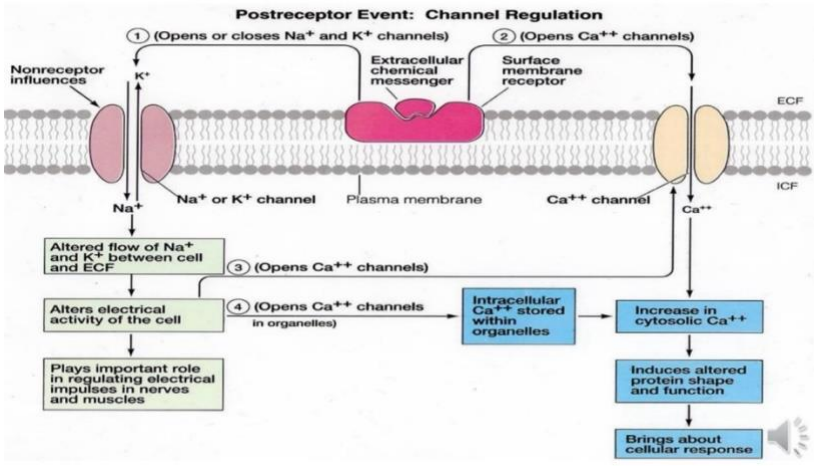
Another type of an enzyme that can be found at the plasma membrane and is activated by specific receptors Is called **PHASPHOLIPASE-C.** By the activating of this enzyme we can get splitting of a phospholipids (**PIP2** the functional phospholipid) to get **IP3**, which can cause changes inside the cell

(**IP3** can be called as a second Messenger).



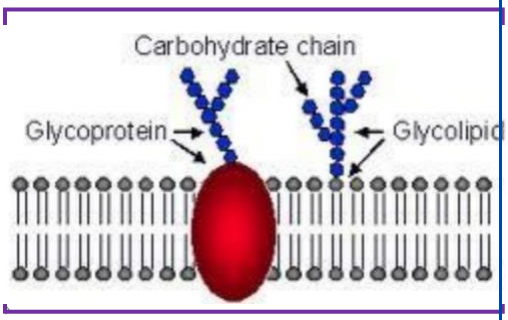
When some receptors bind into specific ligand it causes a specific activation of a channel , by activating this channel we are increasing transport of certain ion-for example-from one side to another side of the cell.

In this case, we are calling them(**ligand gated channels**.)

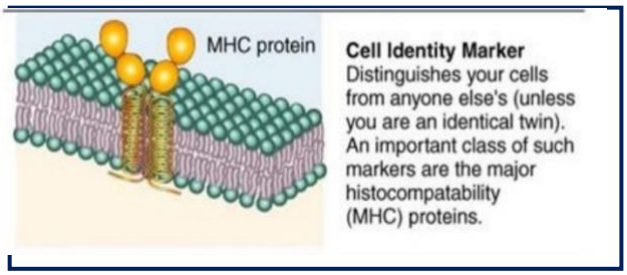


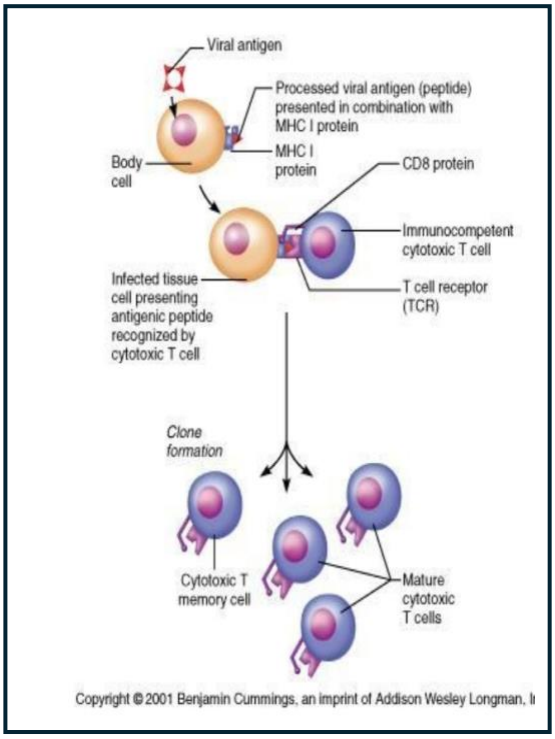
For example:if we activate sodium channels we are getting more transport of sodium ions from outside to inside or if we

have activated potassium channels we can get more transport of potassium from inside to outside.



We have **glycoproteins that has Carbohydrate chains** linked to the proteins, these are important for identifying cells (cell identity markers)
For example:antigens
***Note:each cell in our body has antigens**

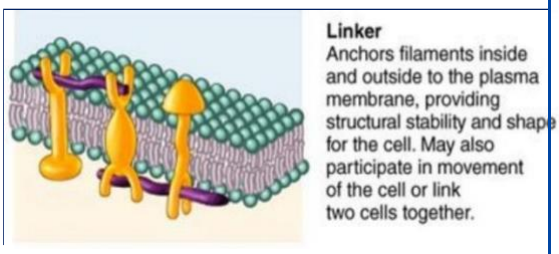




These antigens are important for helping our immune system recognize the self antibodies from the foreign antibodies.
That is important for the immune systems in our bodies.
A quick reminder:
((An antigen is a foreign substance that enters your body. This can include bacteria, viruses, fungi, allergens, venom and other various toxins. An antibody is a protein produced by your immune system. to attack and fight off these antigens.)

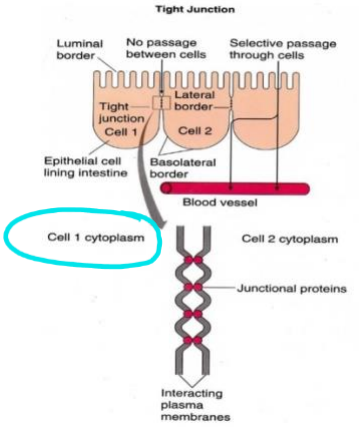
- Some proteins in the outer surface participate with

Carbohydrates to form adhesion molecules between the Cells in tissue structure known as ***C*ell *A*dhesion *M*olecules** (CAMs). One example of these molecules is cadherin.

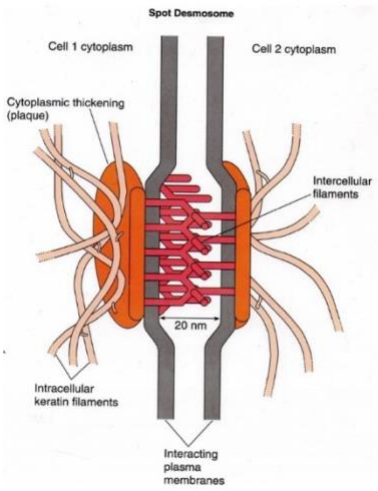


In Addition to the cohesion provided by ***CAMs*** and Extracellular matrix, some cells are directly linked by Specialized junctions. Such as desmosomes (adhering Junction), tight junction (impermeable junction), and gap Junction (communicating junction).

The ***impermeable junction*** (**tight**) is found between epithelial cells, which are joined together to form a sheet, which serve as high selective barrier that separates 2 different compartments. For ex. Epithelial cells that line the digestive tract separate the internal environment from the content of the hollow organs of the digestive system. Cells are held together by tight junctions, which form a tight belt around each cell and prevent passage of any substance between the cells.

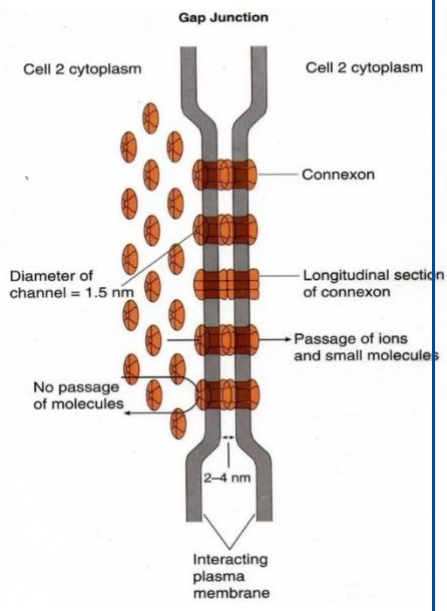


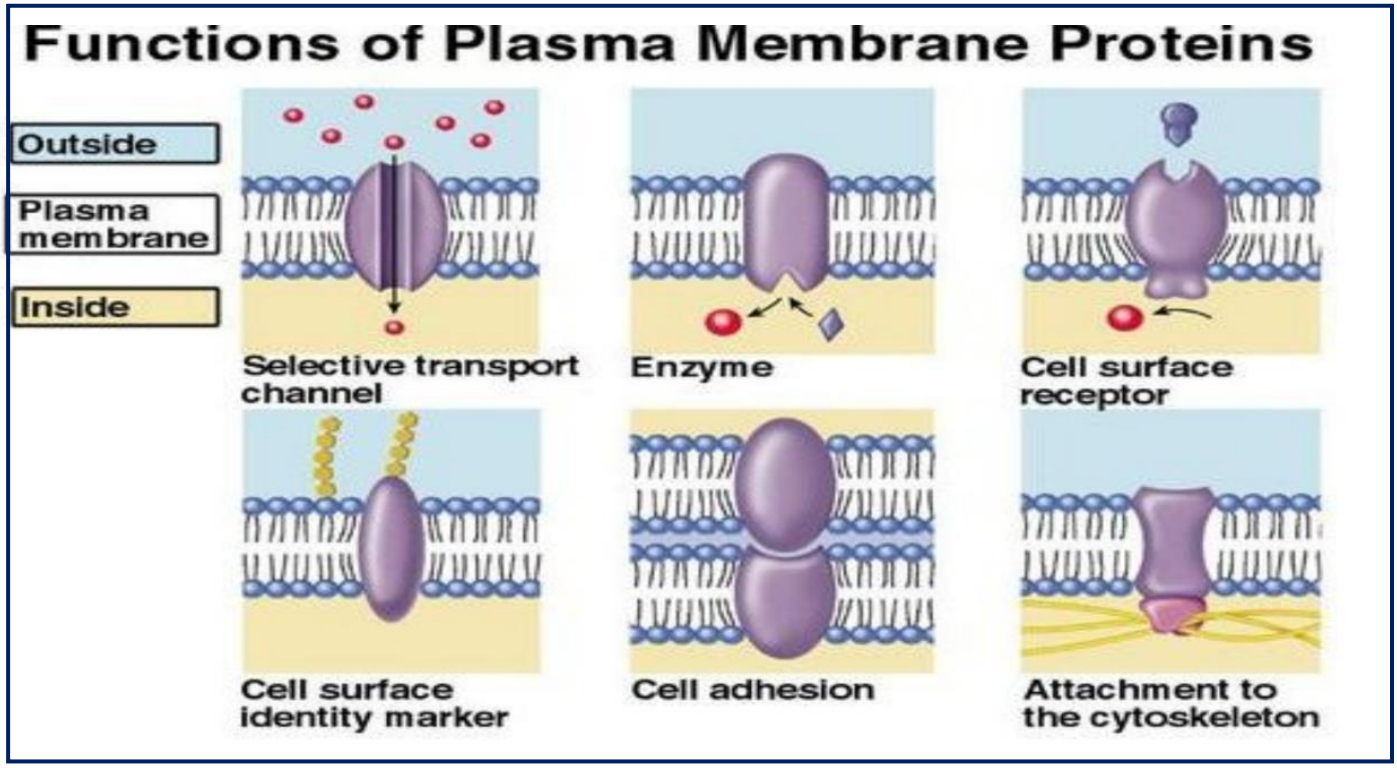
At the ***adhering junction*** (**desmosome**), filaments of unknown composition extend between the plasma membranes of two closely adjacent cells anchoring them together by maintaining a distance of about 20 nm between the two plasma membranes.



The ***communication junctions*** (**gap**) between the cells form small (tunnels) between adjacent cells which enable neighboring cell to communicate with each other. This tunnel is composed of protein known as connexons. These connexons extend outward from the plasma membrane to join other connexon from the adjacent cell. The tunnel permits small water soluble particles to pass between the connected cells. An example of this type of junction is found in the heart and between smooth muscle cells. This form of communication between neighboring cells has an importance in spreading the electrical activity *

(action potential) to adjacent cells and these cells are forming together a functional syncytium. This sort of communication enables synchronizing heart and smooth muscle activity.





Please check on the professor's handout, Very Important ..

University of Jordan
Faculty of Medicine
Department of Physiology and Biochemistry

Introduction to Physiology

Med I and Den I students 2023/2024

Outline for Cell Physiology and Transport through biological membranes.

Ref: **Textbook of Medical Physiology. Jordan Edition**, **By Guyton and Hall.**
Pp: 11-14, 47-59.

Plasma membrane as an organelle:

Lipids in plasma membrane:

The plasma membrane is a lipid bilayer in which proteins are impeded. The most abundant of these lipids are phospholipids (P-Choline and P-Ethanol-amine). The molecule of phospholipid has a polar electrical head containing negative charge of phosphate group oriented towards the periphery and two nonpolar fatty acid tails oriented toward the center of the lipid bilayer. The electrical properties of phospholipids permit self assembly in a bilayer structure when found themselves in hydrophilic medium. At the normal body temperature of 37 degrees C the membrane is in fluid state.

Membrane fluidity

The arrangement of the fatty acid tails in phospholipids plays a crucial role in determining the characteristics of the membrane, particularly its fluidity. More unsaturated fatty acids content give more fluidity to membrane and higher cholesterol content prevents extremes in fluidity of plasma membranes.

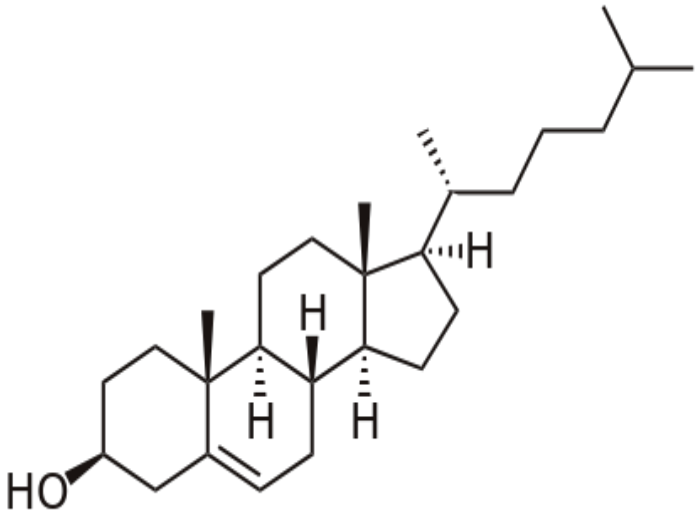
The saturated fatty acids lack double bonds and are therefore straight in shape. On the other hand, unsaturated fatty acids have one or more double bonds, resulting in a bent or kinked structure. The behavior of saturated and unsaturated fatty acid tails in phospholipids differs as the temperature decreases:

- At lower temperatures, the straight tails of saturated fatty acids can tightly pack together, creating a dense and relatively rigid membrane.

- In contrast, phospholipids with unsaturated fatty acid tails cannot pack as tightly due to the bent structure of the tails. As a result, a membrane composed of unsaturated phospholipids remains fluid at lower temperatures compared to one made up of saturated phospholipids.

Most cell membranes consist of a combination of phospholipids, some with two straight (saturated) tails and others with one straight and one bent (unsaturated) tail.

Animals possess an extra membrane constituent, apart from phospholipids, which aids in preserving fluidity. **Cholesterol**, a distinct lipid variety, is intricately interwoven within the phospholipids of the membrane, effectively reducing the impact of temperature fluctuations on fluidity.



The chemical structure of cholesterol is depicted in a diagram, showcasing three hexagonal shaped rings and one pentagon shaped ring. An OH group is connected to the first hexagonal ring, while a hydrocarbon chain is attached to the pentagon shaped ring.

Cholesterol plays a crucial role in regulating the fluidity of phospholipids within a membrane. At lower temperatures, it prevents the phospholipids from tightly packing together, thereby increasing fluidity. Conversely, at higher temperatures, cholesterol reduces fluidity, ensuring that the membrane maintains a functional and healthy level of fluidity. Ultimately, cholesterol broadens the temperature range at which the membrane can effectively function.

This lipid structure prevents water soluble molecules to pass through the bilayer, only lipid soluble substances can diffuse freely through the lipid membrane.

Proteins in plasma membrane:

Many protein structures are found at membrane. Most of these have also a carbohydrate moiety. Some of these proteins are penetrating the whole bilayer structure (integral proteins) others are found at one surface of the membrane (peripheral proteins).

The proteins which are impeded in the plasma membrane serve many functions that include:

- Some proteins that span the membrane form a water filled pathways (**Channels**) which enables water soluble substances to diffuse across the membrane through these structures. These channels are highly selective (Na+ can pass only through sodium channels and K+ can pass only through K+ channels). Not all the time the channel is opened. The activity of these channels is under controlling mechanisms that govern the channels activity. Some of these channels change their activity when the membrane potential is changed (voltage dependent (sensitive) channels). Other channels can open when a specific ligand binds to its receptor and causes opening of channel (chemical gated channels).
- Other proteins serve as **Carrier molecules** which help other molecules to cross biological membrane. These transport proteins are highly selective to substances. They bind to a substance and move it through the interstices to the other side of the membrane.
- Other proteins are **Receptors** for ligands found in the extracellular fluid. The binding of ligand to receptor will initiate cellular events that alter the activity of the cell. (an ex. Activation of Na+ channels in striated muscle after

binding of acetylcholine (Ach) to its receptor on the muscle membrane).

- Other proteins function as **membrane bound enzymes** which control enzymatic reactions either inside or outside the cell.
- Some proteins in the inner surface participate with cytoskeletal proteins to maintain cell shape.
- Some proteins in the outer surface participate with **Carbohydrates** to form adhesion molecules between the cells in tissue structure known as **C**ell **A**dhesion **M**olecules (CAMs). One example of these molecules is cadherin. In addition to the cohesion provided by CAMs and extracellular matrix, some cells are directly linked by specialized junctions. Such as desmosomes (adhering junction), tight junction (impermeable junction), and gap junction (communicating junction).

At the ***adhering junction*** (**desmosome**), filaments of unknown composition extend between the plasma membranes of two closely adjacent cells anchoring them together by maintaining a distance of about 20 nm between the two plasma membranes.

The ***impermeable junction*** (**tight**) is found between epithelial cells, which are joined together to form a sheet, which serve as high selective barrier that separates 2 different compartments. For ex. Epithelial cells that line the digestive tract separate the internal environment from the content of the hollow organs of the digestive system. Cells are held together by tight junctions, which form a tight belt around each cell and prevent passage of any substance between the cells.

The ***communication junctions*** (**gap**) between the cells form small tunnels between adjacent cells which enable neighboring cell to communicate with each other. This tunnel is composed of protein known as connexons. These connexons extend outward from the plasma membrane to join other connexon from the adjacent cell. The tunnel permits small water soluble particles to pass between the connected cells. An example of this type of junction is found in the heart and between smooth muscle cells. This form of communication between neighboring cells has an importance in spreading the electrical activity

(action potential) to adjacent cells and these cells are forming together a functional syncytium. This sort of communication enables synchronizing heart and smooth muscle activity.

Membranes and Transport:

Modalities of transport:

DIFFUSION:

Generally, dissolved particles found in solution are in constant movement. This random motion is due to thermal energy in particles that found themselves at a temperature above the absolute zero (in living systems about 310 degrees K). The random motion in liquids and gases will result in a random collision of particles with each other and with the wall. These haphazard collisions will cause a transfer of kinetic energy from one particle to another and change in the direction of motion. This continuous movement in liquids and gases is known as ***diffusion***.

Diffusion through biological membranes:

Particles can move across biological membrane by diffusion. This type of transport does **not** need consumption of energetic compounds (ATP). It is passive. Because of the lipid constituents of the membrane, only lipid soluble substances can diffuse through the lipid structures. Their diffusion depends on the solubility of particles in the lipid bilayer. Example: O2, CO2, NO and lipid particles can diffuse through the lipid structures.

While water soluble particles cannot pass the bilayer. But, they can be transported across membrane through protein channels. This type of transport is can also be characterized as ***simple diffusion (in some literature is considered as FACILITATD DIFFUSION*** by considering have a protein structure (channel) helped these particles to move across membrane. Also, there are some particles can NOT diffuse through membrane only with the help of a protein structures known as **carriers**. This type of diffusion of particles is known as **facilitated diffusion**.

Factors that influence simple diffusion:

- *Concentration*: More concentration of a substance means more kinetic energy in particles in a given compartment.

Intercellular communication and signal transduction mechanisms:

The coordination of cellular activities is critical for maintaining homeostasis and survival of living system as well as control of growth and development of the body as a whole. In addition to cellular communication between cells by gap junctions, control systems that are found in the body, such as endocrine system, nervous system, and paracrine cells release particles (ligands) that can bind to specific receptor at the target cell and change its activity.

Cellular events after ligand binding to receptor:

1. Activation of channels:
   When ligand binds to its receptor this activates membrane bound intermediary protein known as G protein (a protein composed of many subunits). The activation of G protein will induce opening of specific channel such as *chemical gated Na+ channels*. The opening of Na+ or K+ will change the potential difference across membrane, which in turn may cause activation (opening) of other type of channels known as voltage sensitive channels such as opening of *voltage gated Na+ channels or voltage gated Ca++ channels*.

2. Activation of second messenger system:
   Binding of specific ligand to its receptor may result in activation of second messenger that relays order through a series of biochemical events to induce changes in cell activity such as metabolic, secretory, or contractile responses according to cellular function.

c-AMP as second messenger:

Binding of ligand will induce activation of G protein freeing the α subunit of G protein which activates a membrane bound enzyme known as *adenylyl cyclase*. This enzyme converts **ATP** to **c-AMP**. The formed second messenger will activate *c-AMP dependent protein kinase* which phosphorylates particular protein which in turn bring responses inside cell. The process is

amplified inside the cell. Activation of one receptor may result in millions of end products of activated protein kinase enzyme.

Ca++ as second messenger:

Some G proteins activate other type of enzyme. In this pathway *phospholipase C* is activated. This enzyme breaks down **phosphatidyl inositol biphosphate** (PIP2)
(a phospholipid molecule that is anchored to the inner side of plasma membrane). The products of PIP2 breakdown are **diacylglycerol** (DAG) and **inositol triphosphate** (IP3). The IP3 induces release of **Ca++** from endoplasmic reticulum into the cytosol of the cell. Ca++ binds to and activates a protein called calmodulin. The activation of calmodulin triggers Ca++ dependent cellular responses by altering activity of other functional proteins inside target cells.

رسالة من الفريق العلمي:

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لا تَنسونا من صالحِ دعائِكم ولكم بالمِثل (^^

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