Physiology Sheet No. 3

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Remember:

Proteins embed the plasma membrane and other membrane bound organelles, and perform functions such as: Ion channels, enzymes, transporter, receptor, cell identity marker and linker which control the transport through the plasma membrane. Substances are transported across the plasma membrane by active & passive transport.

The lecture discussed two main topics:

1) control of membrane proteins activities through receptors.
2) Transport of ions across the plasma membrane.

control of membrane proteins activities:

(How to study this topic? understand the main idea only, the details will be discussed in the upcoming lectures) كيف ادرس هاد الموضوع؟ اقرأ وافهم الفكرة العامة ولا تتعمق بالتفاصيل حيث سيتم شرحها في المحاضرات القادمة

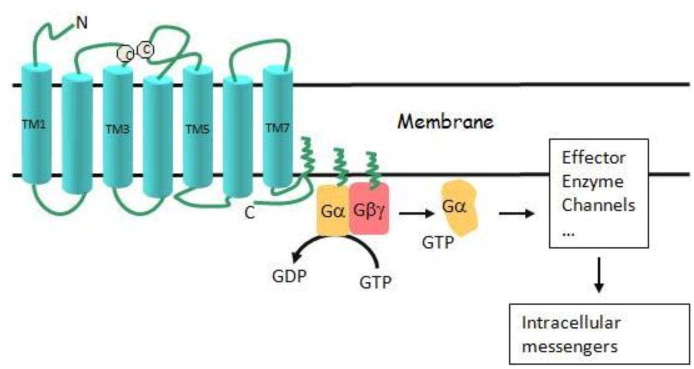
-**general mechanism**: ligand binds to its receptor (which is a type of proteins) and the receptor changes protein activities.

*ligands are signal molecules that bind to a specific receptor.

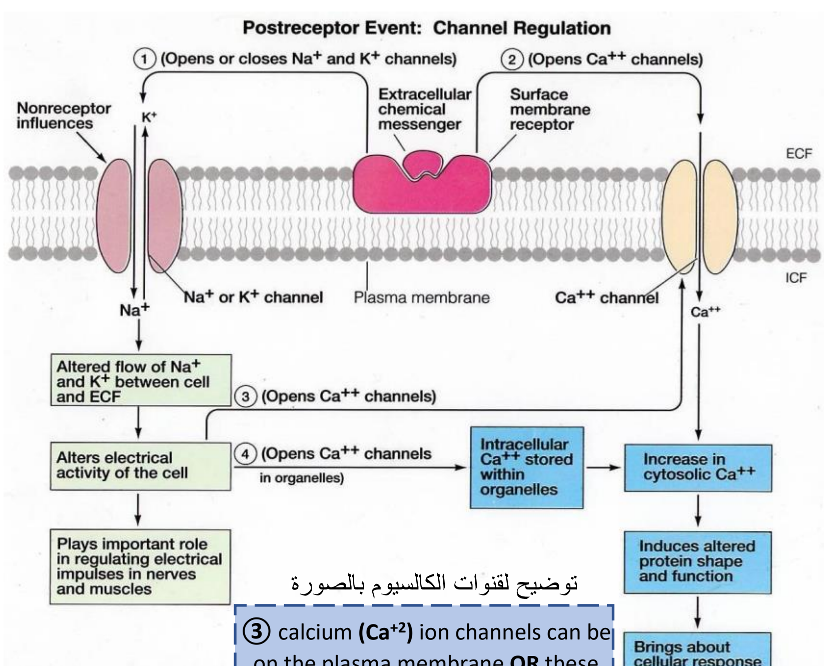
Receptors control → **ION CHANNELS**, **ENZYMES**, **VESICULAR TRANSPORT**

- ## Receptors & Channels:

-Receptors are linked to protein channels by a structure of protein complex known as effectors that cause chain reactions to get cellular response. e.g.(G-proteins).



-ligands bind to a receptor which causes the activation of proteins channels meaning opening the channels and changing the membrane permeability to certain ions.



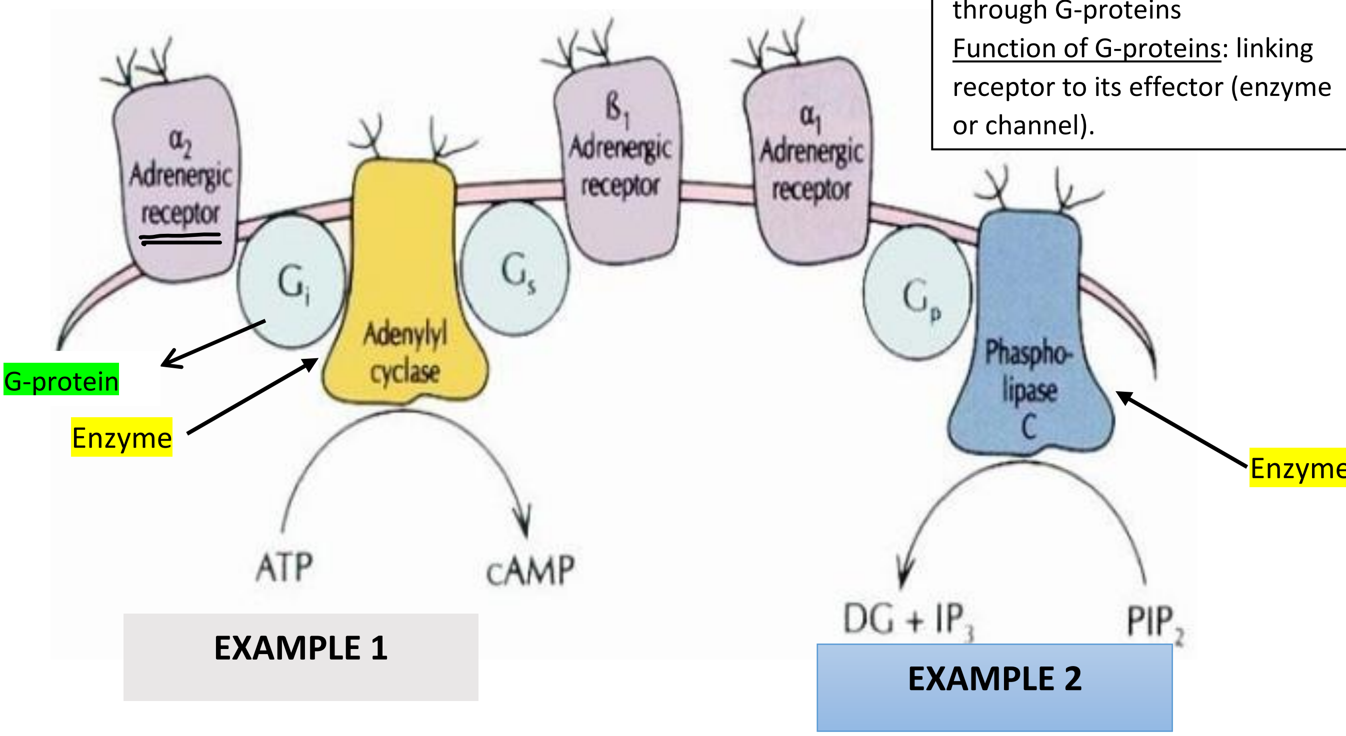
توضيح لقنوات الكالسيوم بالصورة

③ calcium (Ca^{+2}) ion channels can be on the plasma membrane **OR** these channels can be found in ④ organelle membrane(ER membrane)

For example: in this picture receptors activate sodium (Na^{+}) ion channel which leads to more diffusion of sodium from outside (higher concentration) to inside (lower concentration) OR activate potassium (K^{+}) ion channels that diffuse from inside to outside.
calcium (Ca^{+2}) ion can diffuse from outside to inside.
OR from inside to outside.
-see no.3 and 4 in the picture below.

- **Receptors & Activation of Enzymes:**
  - By controlling enzyme activities, concentration of certain substances can be modulated and controlled.
  - we have two examples:

Some of receptor are linked to enzymes (not only channels) through G-proteins
Function of G-proteins: linking receptor to its effector (enzyme or channel).

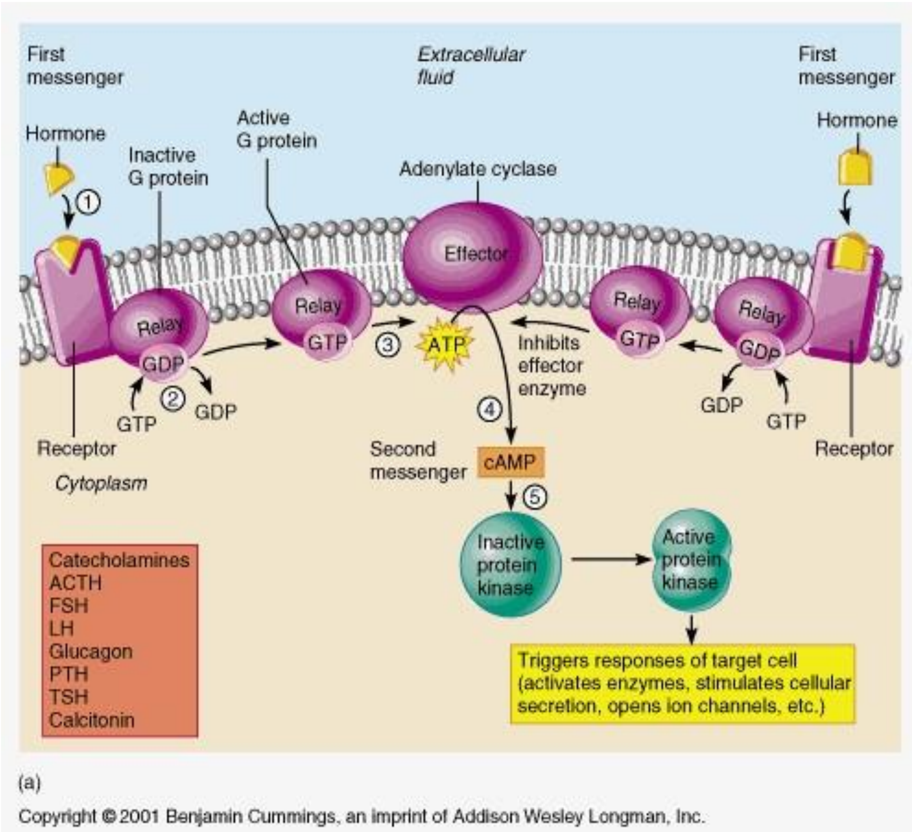


Enzyme name	**Adenylyl cyclase or (Adenylate cyclase)**	**Phospholipase C PL-C**
Enzyme function	**Convert** ATP to cAMP (adenosine triphosphate to cyclic adenosine monophosphate) By removing two phosphate groups. which **increases** concentration of cAMP inside the cell. **cAMP is known as second messenger and is used in cellular activity.	**Splits** PIP_2 to IP_3 and DG (Phosphatidylinositol bisphosphate to inositol triphosphate and Diacylglycerol). **IP_3 binds to a receptor that activates calcium channels that are located at membrane of ER(endoplasmic reticulum), which in its role activates the channel and increase the concentration of Ca^{+2} in the cytosol . (ca^{+2} move from ER to cytosol by)
Regulation mechanism	**Binding of ligand → enzyme activation → Increase in cAMP concentration** **OR** **Binding of ligand → enzyme inhibition → decrease in cAMP concentration**	**Binding of ligand → enzyme activation → Split PIP_2**

Details mentioned here read only! Just understand that substances concentration levels are controlled by enzyme regulation

التفاصيل المتعلقة ب وظيفة cAMP و IP_3 للقراءة فقط، المطلوب انو نعرف من خلال التحكم بنشاط الانزيمات يمكن التحكم بتركيز المواد داخل الخلية.

Examples on Regulating Adenylate cyclase & cAMP **read only



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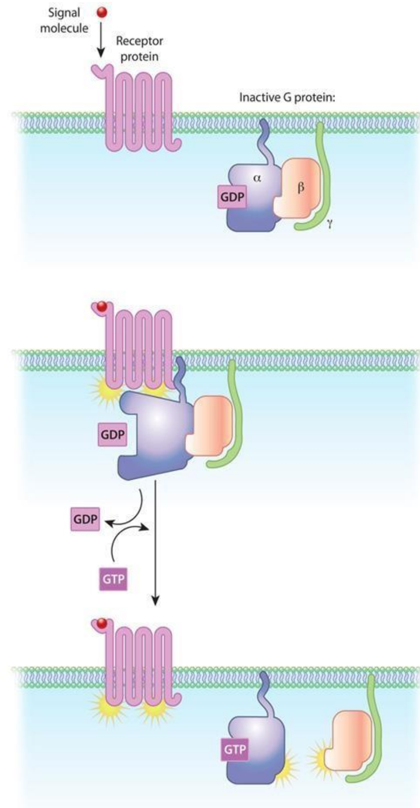
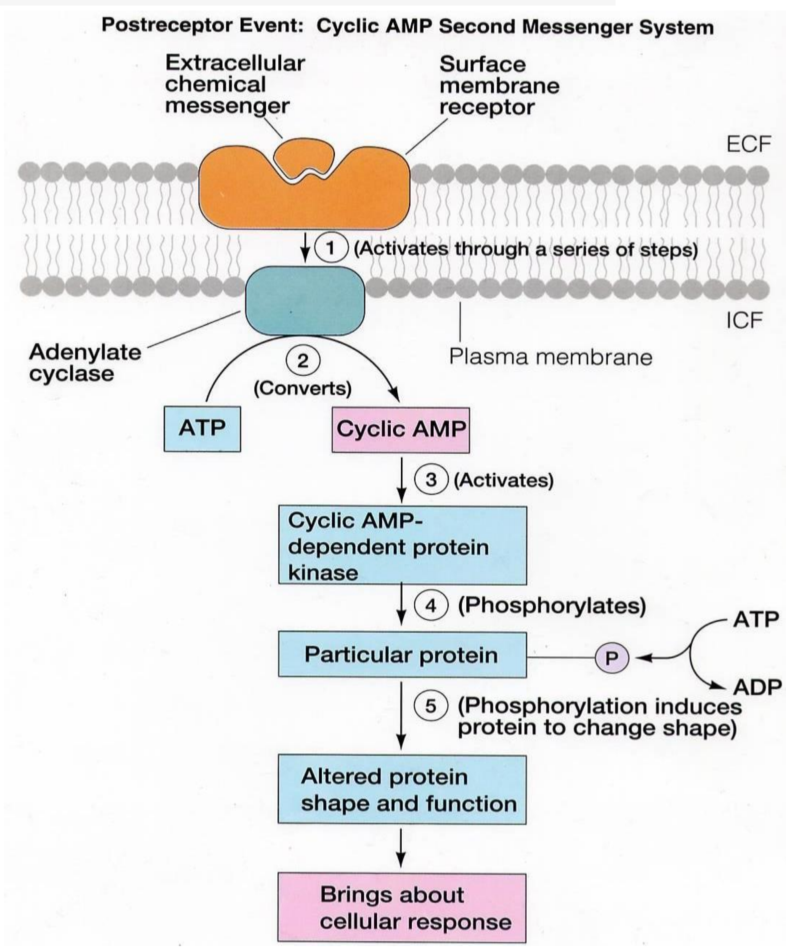




Examples on Regulating Phospholipase-C

Note that this is an example of changing the permeability of an organelle memebrane **(ER),** so its an example of changing the concentration of an ion (Ca^{+2}) inside the cell, as calcium will exit its stores in the ER and diffuse from inside (ER) to outside (cytosol) when calcium ion channels are activated by receptors.

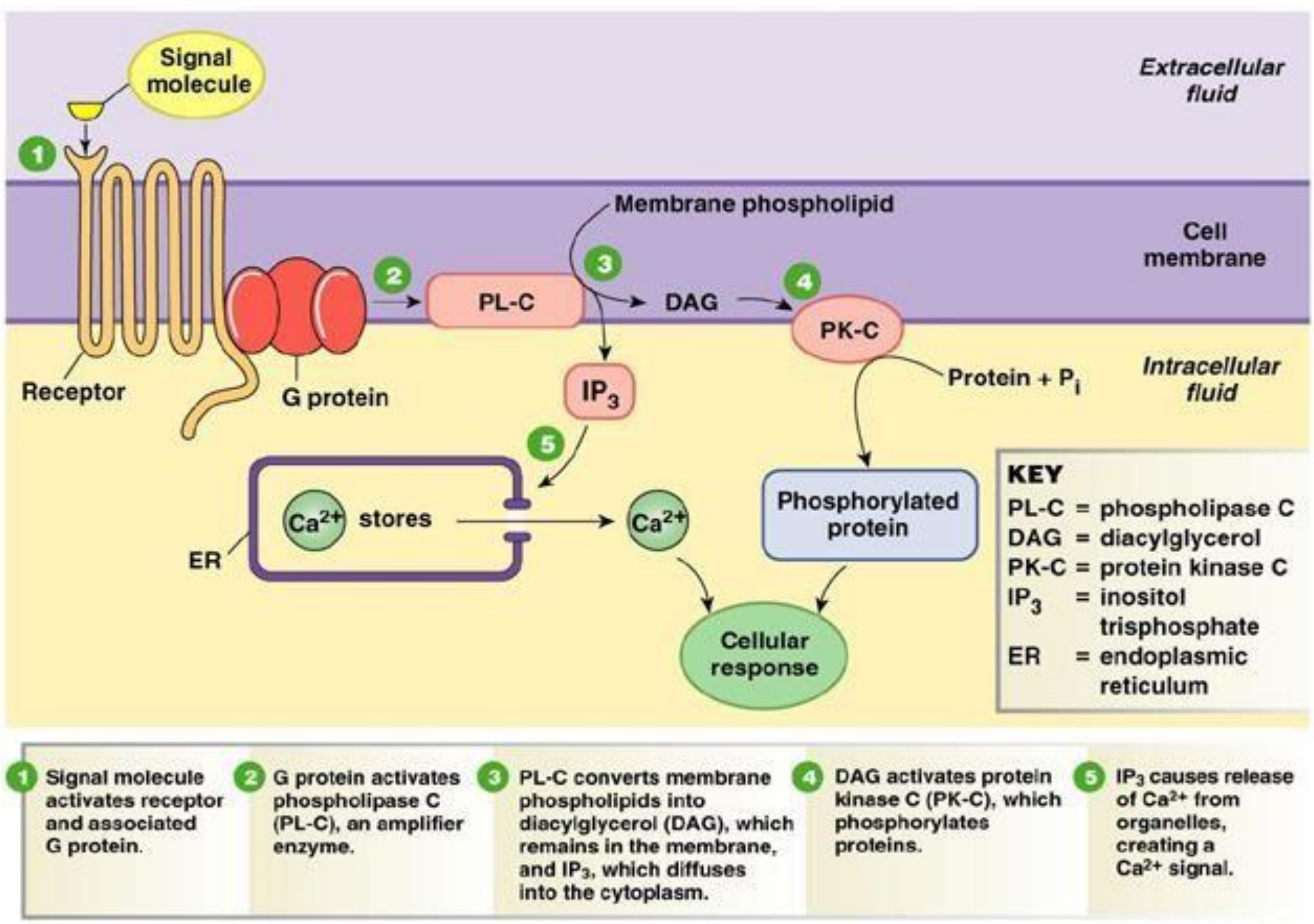


Fig. 6-12

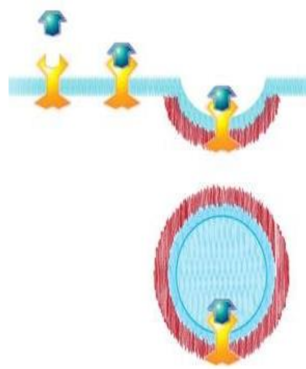
- **Receptors & <u>Vesicular Transport</u>:**

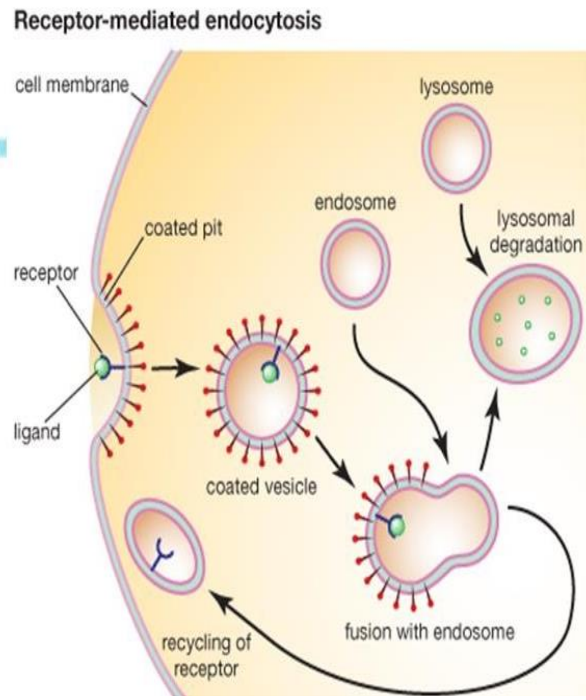
→ Endocytosis

→ Exocytosis

-regulation of endocytosis

-in receptor mediated endocytosis, receptor can <u>activate</u> endocytic processes by stimulating the formation of endocytic vesicles.





-regulation of exocytosis

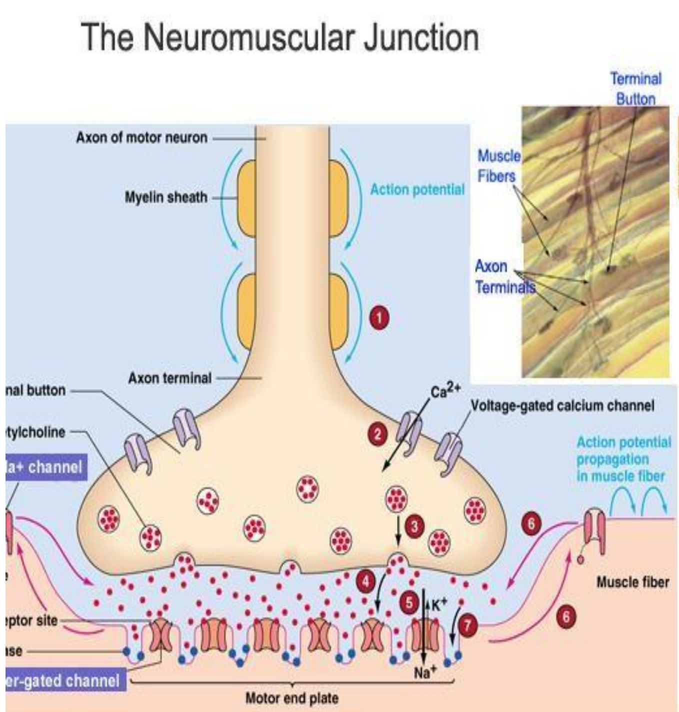
-an example of regulated exocytosis:

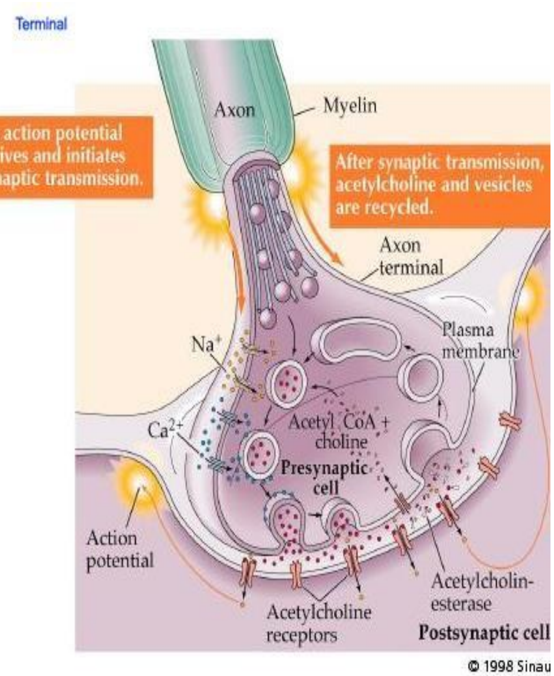
the synaptic transmission between two neurons

1) change of presynaptic membrane permeability to calcium ion (Ca^{+2})

2) increase in calcium concentration in axon terminal

3) more exocytosis by increasing the release of neurotransmitters.





Note: all details of receptor regulation processes will be discussed in signal transduction mechanisms, a topic will we take in upcoming lectures.

Remember: binding of a ligand to its receptor is common in all previous processes that have been mentioned.

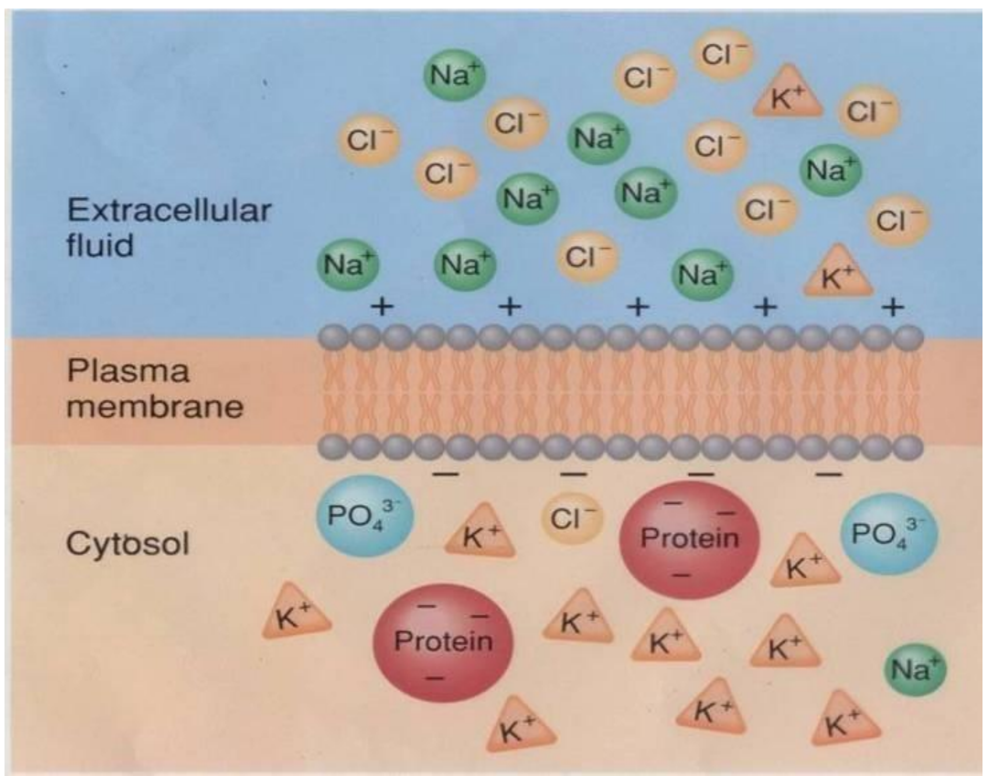
Transport of ions across the plasma membrane

شامل

-The lecture discussed a comprehensive understanding on diffusion of ions across the plasma membrane for **excitable cells** in a assumption that the plasma membrane would be permeable to one ion only.

-why we assumed that the membrane is permeabile to <u>one ion</u> only?
To study the movement of each indivisual ion across the membrane and the potential that's generated upon its movement.

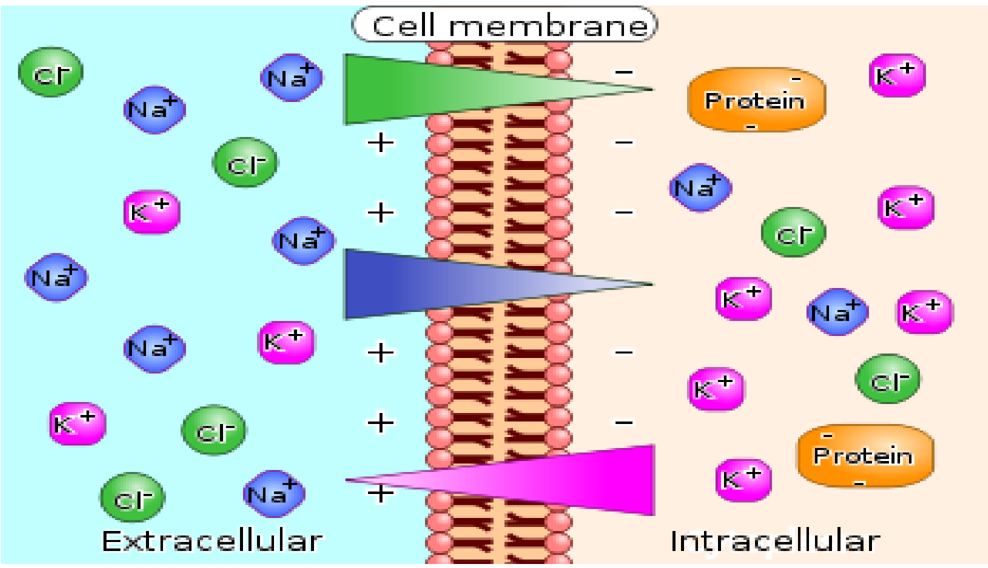
-the plasma membrane seperates two different compartments of different compositions.
-Cytosol has high concentration of proteins and potassium ions K^+
-Extracellular fluid has high concentration of sodium ions Na^+ and chloride ions Cl^-.



-difference in concentration for each ions mean:
High tendency for Na^+ and Cl^- to move from outside to inside of the cell.
& High tendency for K^+ to move from inside to outside of the cell.

Remember: ions move from areas of high concentration to low concentration (downhill).

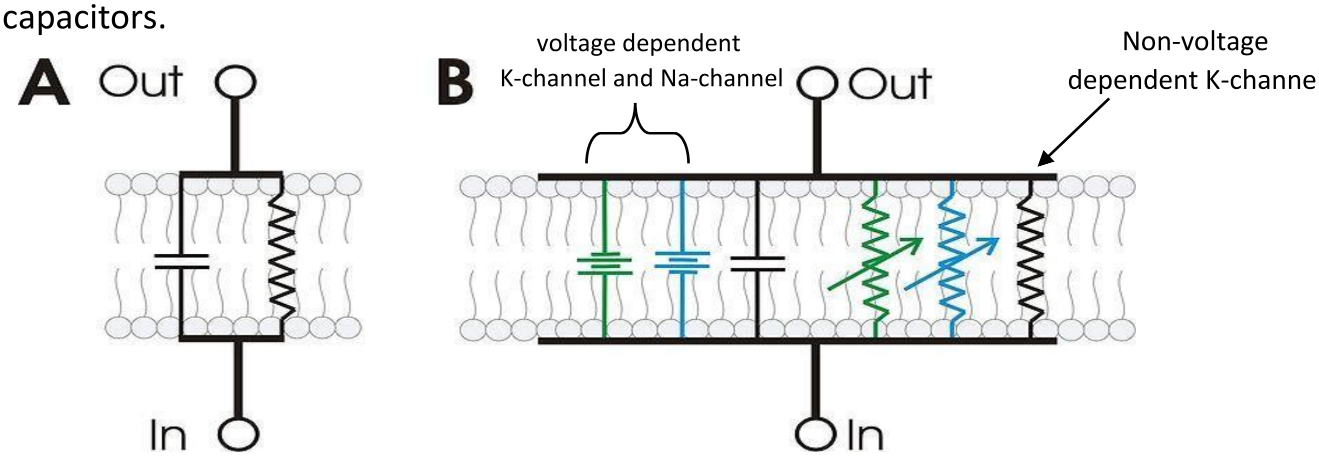
-assuming that the plasma membrane is highly permeable for one ion, the ion will move according to its concentration gradient across the plasma membrane, this movement will create electrical potential difference across the plasma membrane. (This electrical potential is just across the plasma membrane not deep inside the cells and the extra cellular fluid outside cell, in other words the potential is only on inner and outer surface of the membrane)



If membrane has **more active channel** to a certain ion than other, membrane will be **more permeable** for this ion.

- **Electrical properties of plasma membrane**

Plasma membrane in excitable cells is similar to an electrical device known as capacitors.



-what you can see in the previous picture:

المبدأ الأساسي ***the plasma membrane in structure is similar to an electric circuit.**

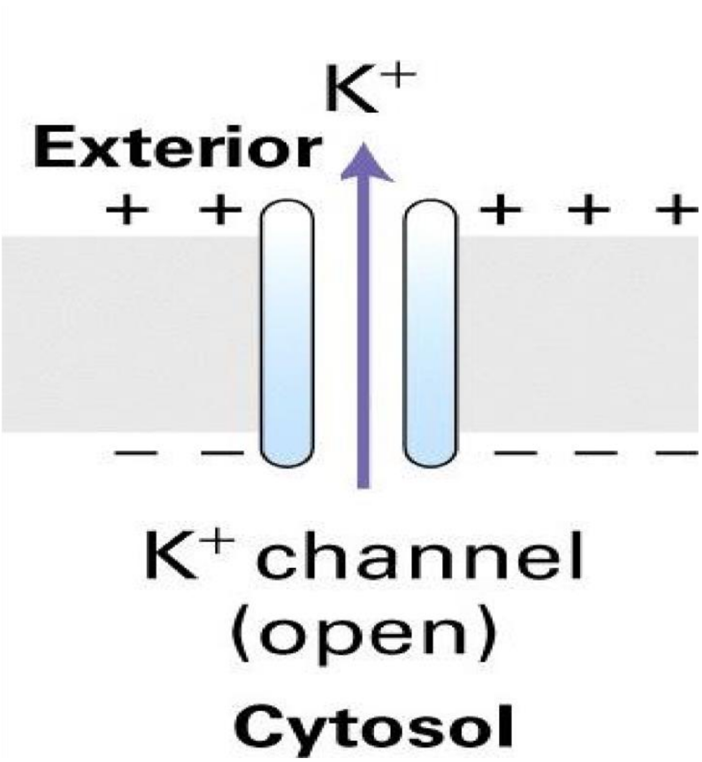
PART A there is a small patch of plasma membrane in an electric circuit that has a capacitor which acts as a separator of charges making the charge on the inside negative, charge on the outside positive, ion channel and high resistance to test the electric potential across plasma membrane.

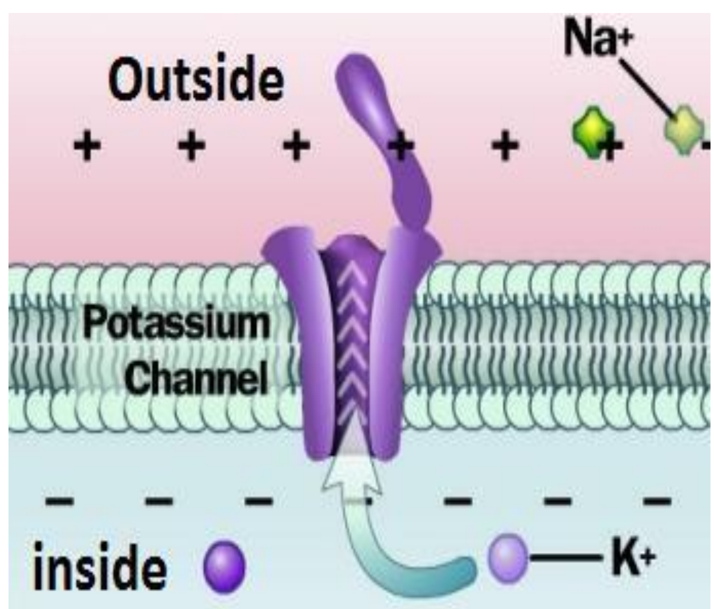
-PART B the number of ion channels in the plasma membrane has been increased so at least there's one sodium Na^+ channel and two potassium K^+ ion channels, the blue color represents voltage produced by concentration gradient of Na, the green color represents voltage produced by concentration gradient of K.

Permeability of ions and their potential

-potential of potassium ion:

-Assuming that the membrane is highly permeable to potassium ions K^+ only and has low permeability for sodium ions Na^+ and chloride ions Cl^-, the potassium will move according to its concentration gradient from inside of the cell to outside through **active** K^+ channels, the movement of potassium will create an electric potential, as the positive charge will be on the outer surface of the plasma membrane and the negative will be on the inner surface.

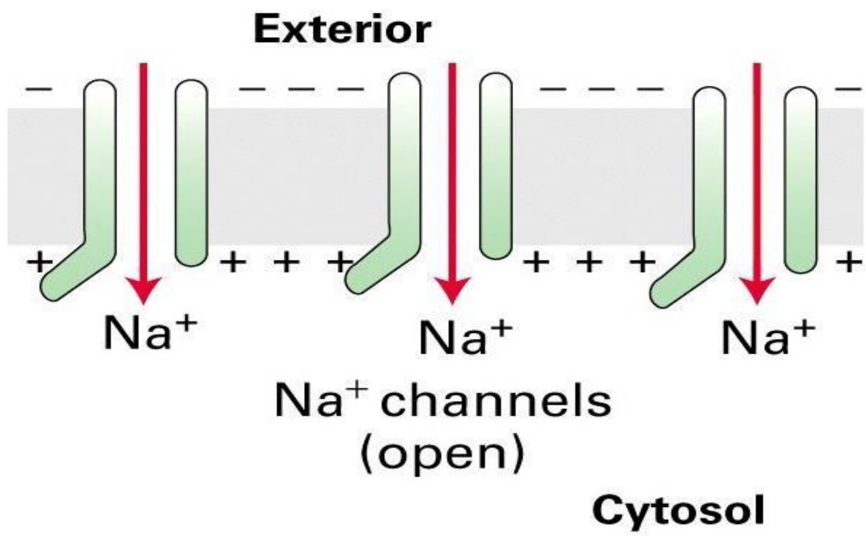




(The inside is negative regarding to the outside)

-potential of sodium ion:

-the same principle applies to sodium ions diffuse through Na^+ **active** ion channels in which we **assume** that the plasma membrane is highly permeable to Na^+ ions only and has low permeability for K^+ and Cl^- ions, the sodium will move according to its concentration gradient from outside of the cell to inside, the movement of sodium will create an electric potential, as the negative charge will be on the outer surface on the plasma membrane and the positive will be on the inner surface.



-the net diffusion of ions through channels will eventually stop due to **electro-chemical equilibrium**, in which there are two energies that act upon ions:

1) ***chemical energy*** created by concentration gradient across the membrane that pushes ions to move from high concentration to low concentration.

2) ***electrical energy*** created by voltage gradient (potential) that was originally generated by movement of ions, this energy pushes ion in the **opposite direction** due to charge repulsion.تنافر الشحنات

For example: when sodium ions enter the cytosol and create potential with positive charge on the inside of the cell, the positive charge will prevent more ions to enter the cell by repulsion therefore the diffusion stops.

At equilibrium:
-the chemical concentration isn't equal across the membrane, so in this case for sodium ion the concentration is higher on the outside than on the inside.
-but the net diffusion of ions=0

- For any specific ion Potential generated by its movement can be measured by placing two electrodes on both (inner & outer) surfaces of the plasma membrane and **calculated** using the ***Nernest Equation.***

$$E = \frac{RT}{zF} \ln \frac{[C]out}{[C]in}$$

R = gas constant (1.987 cal mol^{-1} K^{-1})
T = absolute temperature (273.5 + T (ºC)
z = valence (ion charge)
F = Faraday's constant (9.6485x10^{4} C/mol)
$[C]out$: (outside concentration, Mm)
$[C]in$: (inside concentration, Mm)

at electro-chemical equilibrium:

$$\Delta G_{conc} + \Delta G_{volt} = 0$$

*ΔG_{volt}: electric energy

*ΔG_{conc}: chemical energy

*subtraction because the energies are opposite in directions.

$$zFV - RT \ln \frac{Co}{Ci} = 0$$

we multiplied by this constant to convert from ln to $\log_{10}$

$$V = \frac{RT}{zF} \ln \frac{Co}{Ci} = 2.3 \frac{RT}{zF} \log_{10} \frac{Co}{Ci}$$

**final equation

$$E_{ion} = 61.54\ mV \log_{10} \frac{[Co]}{[Ci]}$$

Concentration of Ions

Ion	Extracellular (mM)	Intracellular (mM)	Nernst Potential (mV)
Na^+	145	15	60
Cl^-	100	5	−80
K^+	4.5	160	−95
Ca^{2+}	1.8	10^{-4}	130

positive charge means the inner surface is positive regarding to the outer surface of the membrane

- **final note to keep in mind when using nernest equation:** the value z (valence) differs from ion to another in concern of charge (+,-) and number (1 or 2).

  -so the final equation can be used directly to calculate potential for K^+ and Na^+.

  الحسابات تختلف

  but calculations will differ for Cl^- and Ca^{+2}.

➢ Transport summary as mentioned in the slides:

Table 3.1 Transport of Materials Into and Out of Cells

Transport Process	Description	Substances Transported
Osmosis	Movement of water molecules across a selectively permeable membrane from an area of higher water concentration to an area of lower water concentration.	Solvent: water in living systems.
Diffusion	Random mixing of molecules or ions due to their kinetic energy. A substance diffuses down a concentration gradient until it reaches equilibrium.	
Diffusion through the lipid bilayer	Passive diffusion of a substance through the lipid bilayer of the plasma membrane.	Nonpolar, hydrophobic solutes: oxygen, carbon dioxide, and nitrogen; fatty acids, steroids, and fat-soluble vitamins; glycerol, small alcohols; ammonia. Polar molecules: water and urea.
Diffusion through membrane channels	Passive diffusion of a substance down its electrochemical gradient through channels that span a lipid bilayer; some channels are gated.	Small inorganic solutes, mainly ions: K^+, Cl^-, Na^+, and Ca^{2+}. Water.
Facilitated Diffusion	Passive movement of a substance down its concentration gradient via transmembrane proteins that act as transporters; maximum diffusion rate is limited by number of available transporters.	Polar or charged solutes: glucose, fructose, galactose, and some vitamins.
Active Transport	Transport in which cell expends energy to move a substance across the membrane against its concentration gradient through transmembrane proteins that act as transporters; maximum transport rate is limited by number of available transporters.	Polar or charged solutes.
Primary active transport	Transport of a substance across the membrane against its concentration gradient by pumps; transmembrane proteins that use energy supplied by hydrolysis of ATP.	Na^+, K^+, Ca^{2+}, H^+, I^-, Cl^-, and other ions.
Secondary active transport	Coupled transport of two substances across the membrane using energy supplied by a Na^+ or H^+ concentration gradient maintained by primary active transport pumps. Antiporters move Na^+ (or H^+) and another substance in opposite directions across the membrane; symporters move Na^+ (or H^+) and another substance in the same direction across the membrane.	Antiport: Ca^{2+}, H^+ out of cells. Symport: glucose, amino acids into cells.
Transport In Vesicles	Movement of substances into or out of a cell in vesicles that bud from the plasma membrane; requires energy supplied by ATP.	
Endocytosis	Movement of substances into a cell in vesicles.	
Receptor-mediated endocytosis	Ligand-receptor complexes trigger infolding of a clathrin-coated pit that forms a vesicle containing ligands.	Ligands: transferrin, low-density lipoproteins (LDLs), some vitamins, certain hormones, and antibodies.
Phagocytosis	"Cell eating"; movement of a solid particle into a cell after pseudopods engulf it to form a phagosome.	Bacteria, viruses, and aged or dead cells.
Pinocytosis	"Cell drinking"; movement of extracellular fluid into a cell by infolding of plasma membrane to form a pinocytic vesicle.	Solutes in extracellular fluid.
Exocytosis	Movement of substances out of a cell in secretory vesicles that fuse with the plasma membrane and release their contents into the extracellular fluid.	Neurotransmitters, hormones, and digestive enzymes.

THANK YOU 😊