Transport Across Plasma Membrane Lecture - 1

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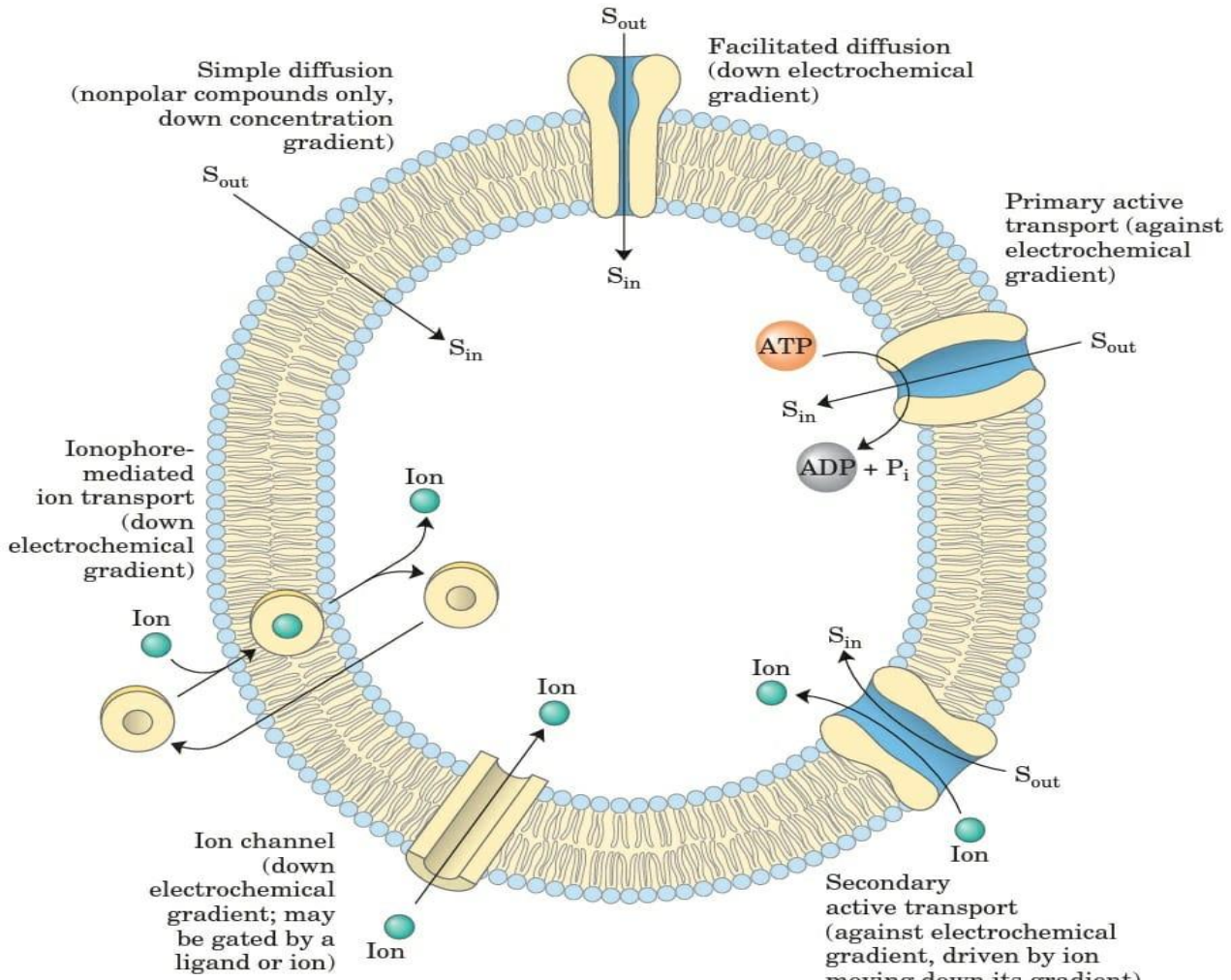
Types of transport across membrane



Summary of transport types.

Transport across membrane

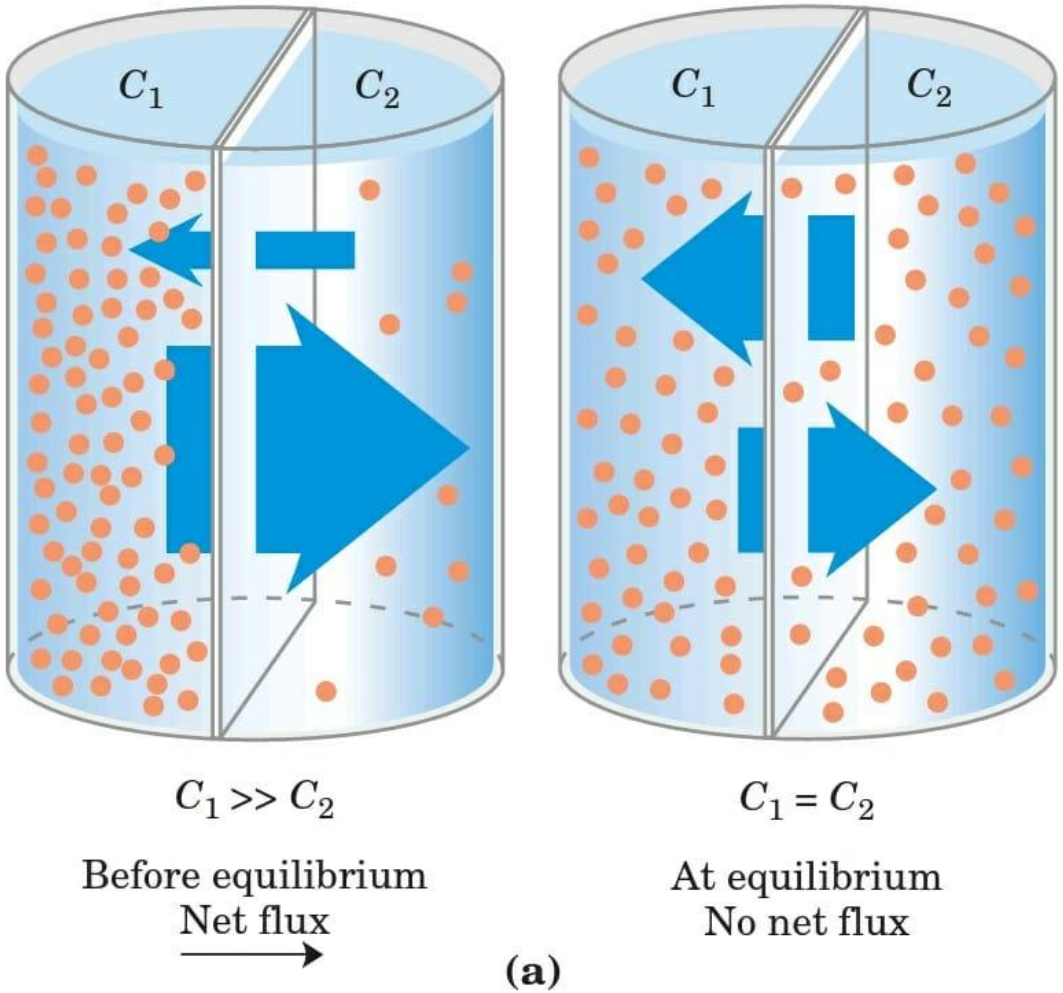
- It is of two types viz passive and active.

- **Passive transport:** It takes place along a concentration gradient from a region of higher concentration to that of lower concentration. It is of two subtypes.

- **1. Simple diffusion:** It doesn't require membrane proteins and is used for transport of gases in and out of cell.

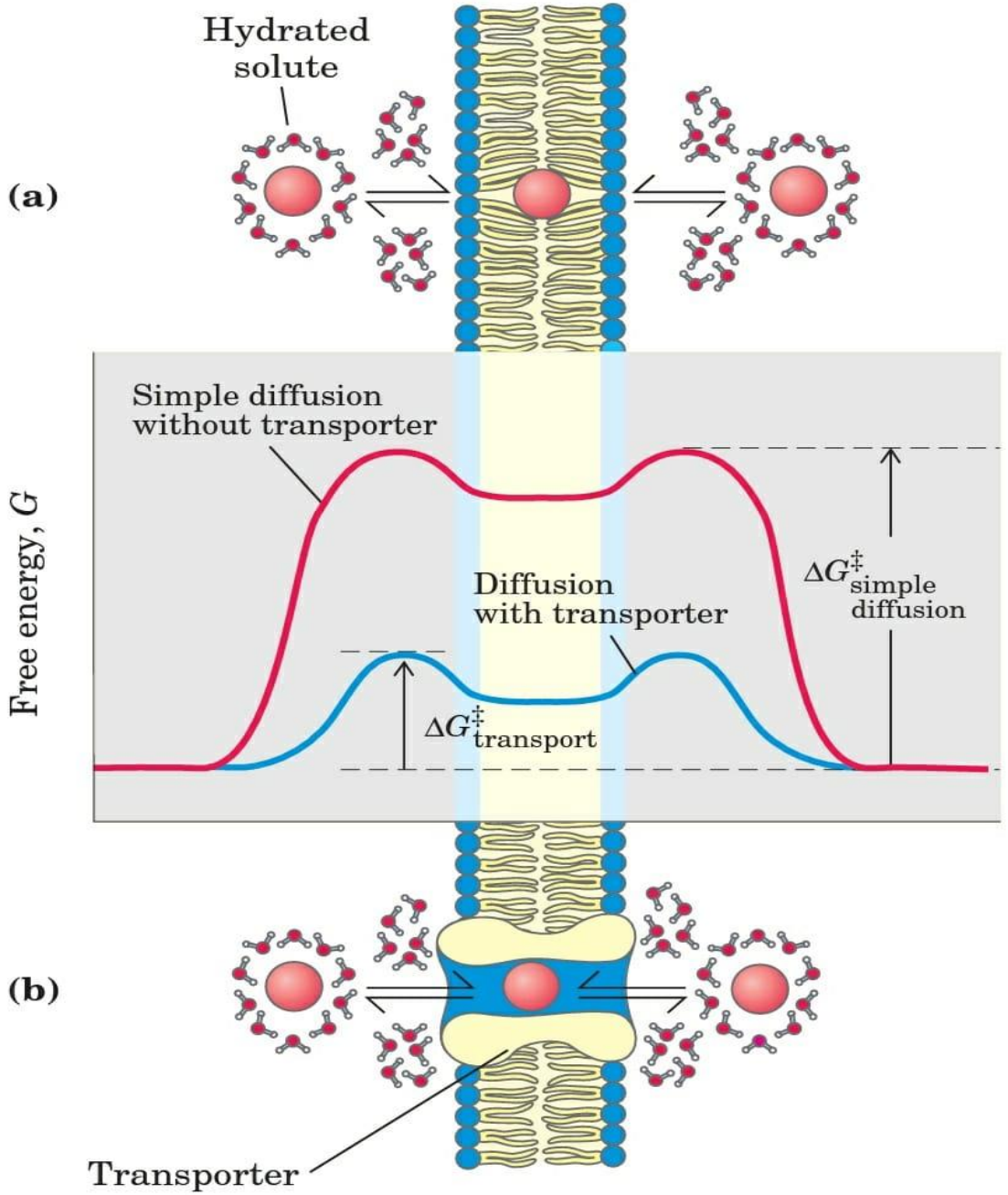
- **2. Facilitated diffusion:** It requires the presence of specific membrane proteins and is used for transport of molecules and ions that cannot cross the membrane due to their polarity.

- It uses two types of proteins viz. Carriers and channels.



Simple diffusion

Role played by transporter



Carriers in facilitated diffusion

- They have following properties

1. They bind their substrates with high stereospecificity.

2. They catalyze transport at well below the limit of free diffusion.

3. They are saturable in the same sense as enzymes i.e. They have a substrate concentration above which there is no increase in rate of transport.

Channels in facilitated diffusion

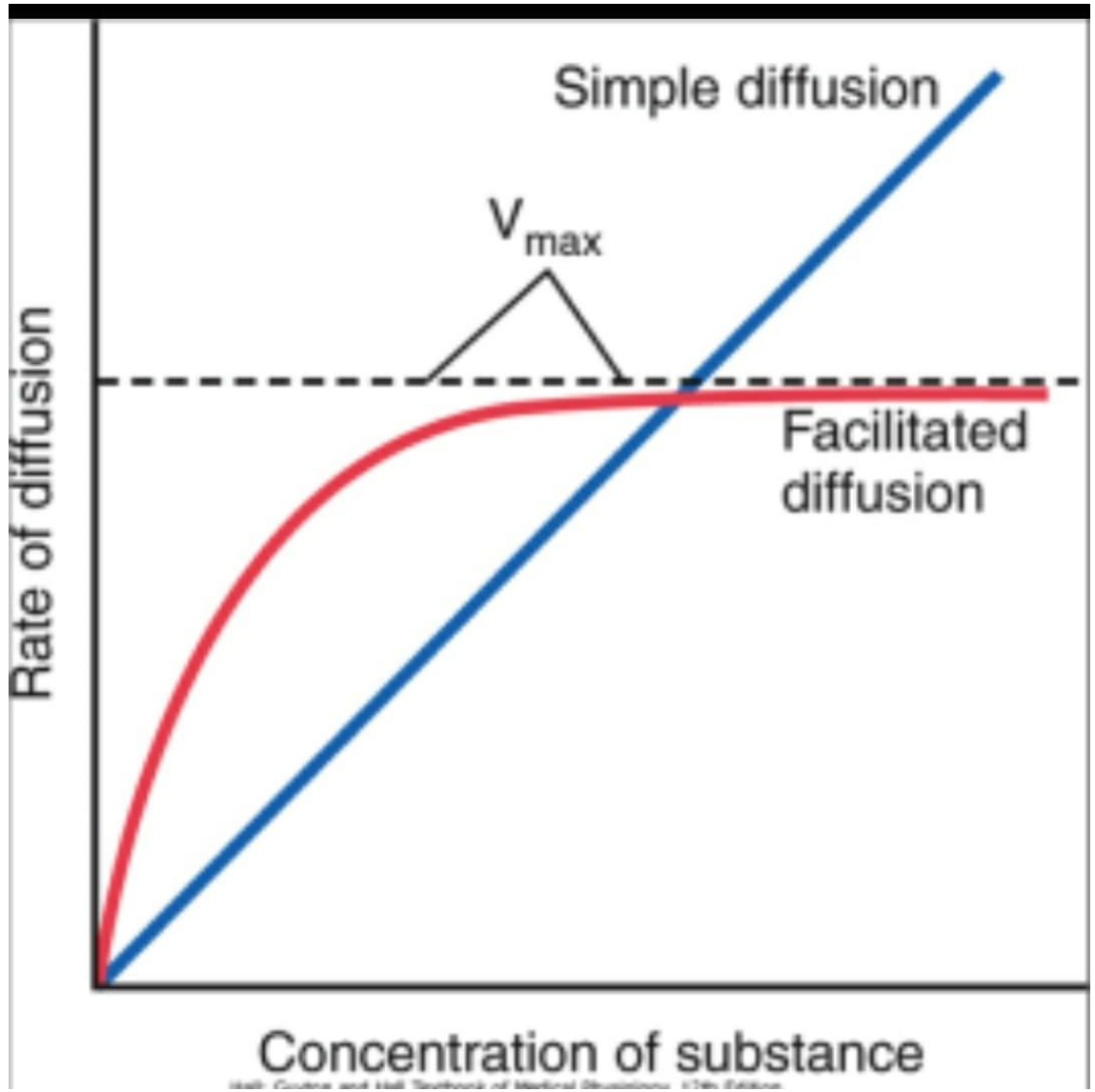
- They show following properties.

1. Their rate of transport is far higher than that of carriers.

2. Their rate of transport reaches limits of free diffusion.

3. They are less stereospecific.

4. They are not saturable i.e. they are not like enzymes or carriers.


Simple diffusion
V_{max}
Facilitated diffusion
Rate of diffusion
Concentration of substance

Examples of facilitated diffusion

- Glucose transport in erythrocytes is mediated by protein called as glucose transporter of erythrocytes and named as GLUT 1 to distinguish it from glucose transporters found in other cells.

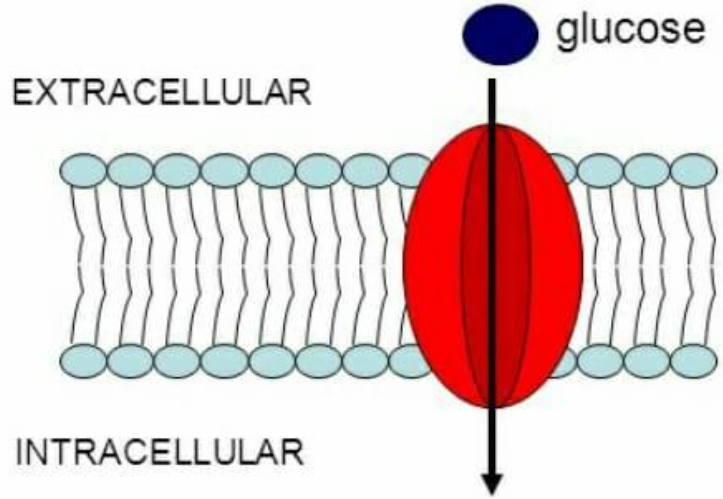
- It facilitates the entry of glucose in RBC at a rate that is 50000 times larger than rate of uncatalysed diffusion.

- It alongwith other members of GLUT family follows the features of facilitated diffusion discussed earlier.

1. High rate of diffusion down the concentration gradient.
2. Saturability
3. Stereospecificity.

GLUT – glucose transporter proteins

GLUT1 – red blood cells, adipose cells, muscle cells



GLUT4 – liver cells, adipose cells, muscle cells

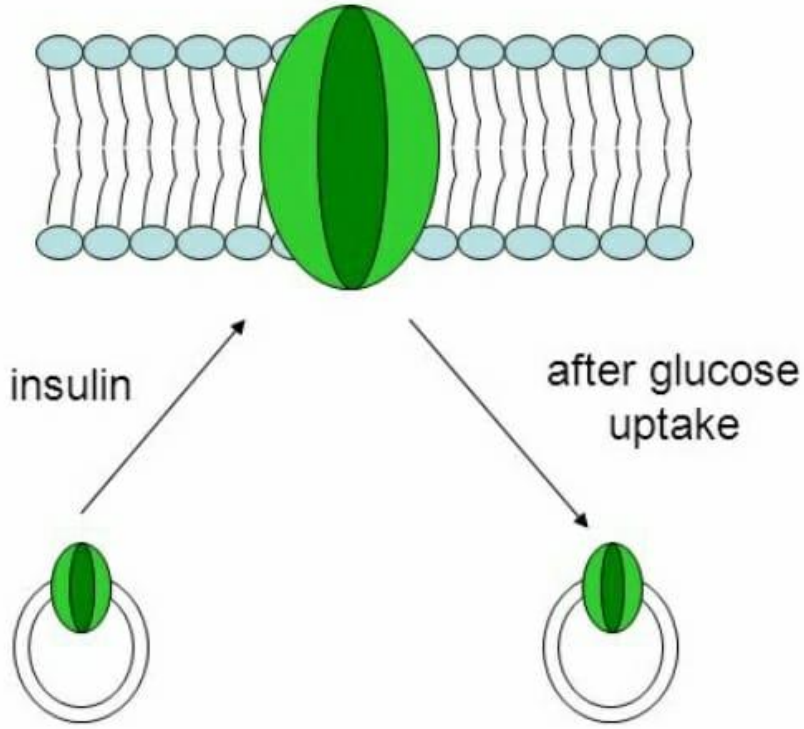


TABLE 11–4 Glucose Transporters in the Human Genome

Transporter	*Tissue(s) where expressed*	*Gene*	*Role*[*]
GLUT1	Ubiquitous	*SLC2A1*	Basal glucose uptake
GLUT2	Liver, pancreatic islets, intestine	*SLC2A2*	In liver, removal of excess glucose from blood; in pancreas, regulation of insulin release
GLUT3	Brain (neuronal)	*SLC2A3*	Basal glucose uptake
GLUT4	Muscle, fat, heart	*SLC2A4*	Activity increased by insulin
GLUT5	Intestine, testis, kidney, sperm	*SLC2A5*	Primarily fructose transport
GLUT6	Spleen, leukocytes, brain	*SLC2A6*	Possibly no transporter function
GLUT7	Liver microsomes	*SLC2A7*	–
GLUT8	Testis, blastocyst, brain	*SLC2A8*	–
GLUT9	Liver, kidney	*SLC2A9*	–
GLUT10	Liver, pancreas	*SLC2A10*	–
GLUT11	Heart, skeletal muscle	*SLC2A11*	–
GLUT12	Skeletal muscle, adipose, small intestine	*SLC2A12*	–

[*]Dash indicates role uncertain.

Glucose transporters in diabetes mellitus type I

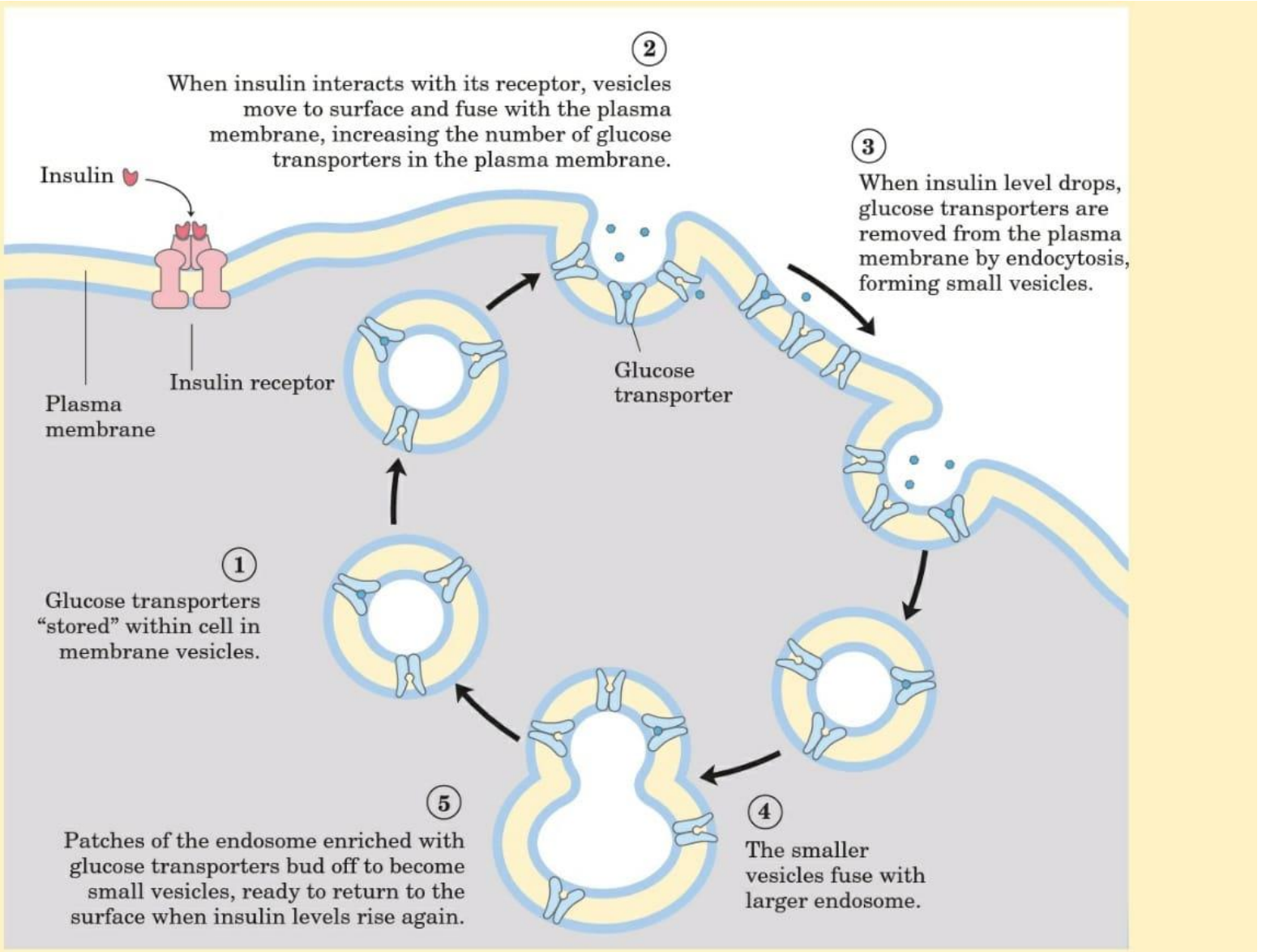
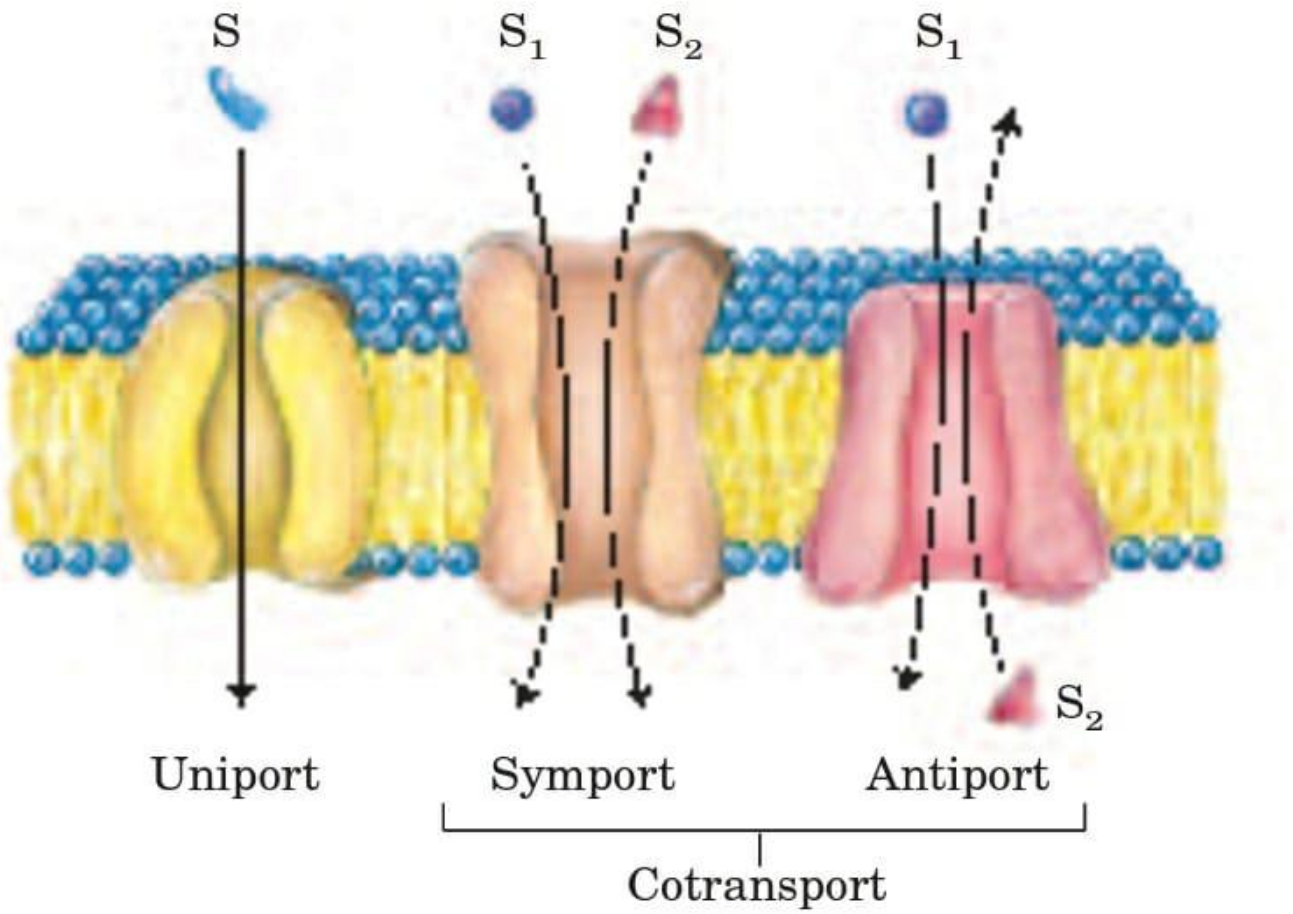
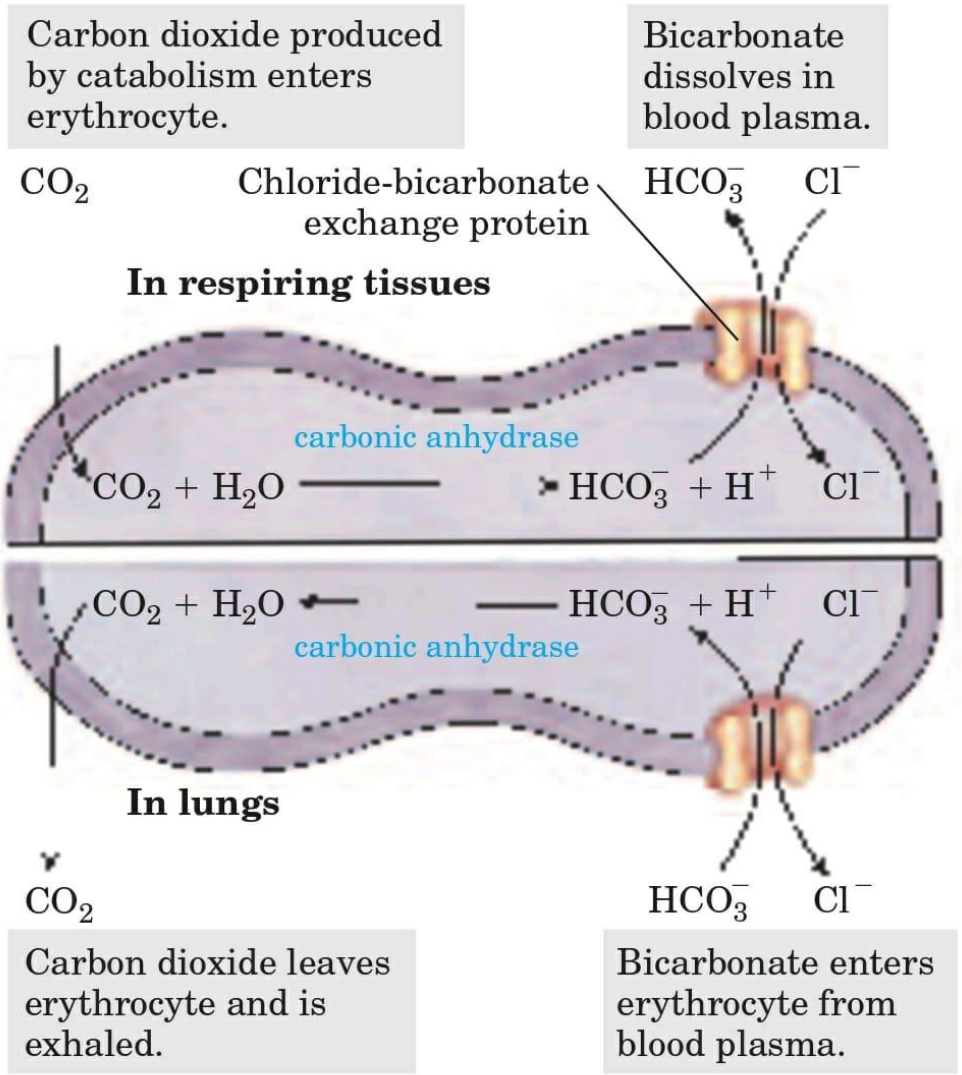


FIGURE 1 Regulation by insulin of glucose transport by GLUT4 into a myocyte.

Chloride- Bicarbonate exchanger, an example of co transport system

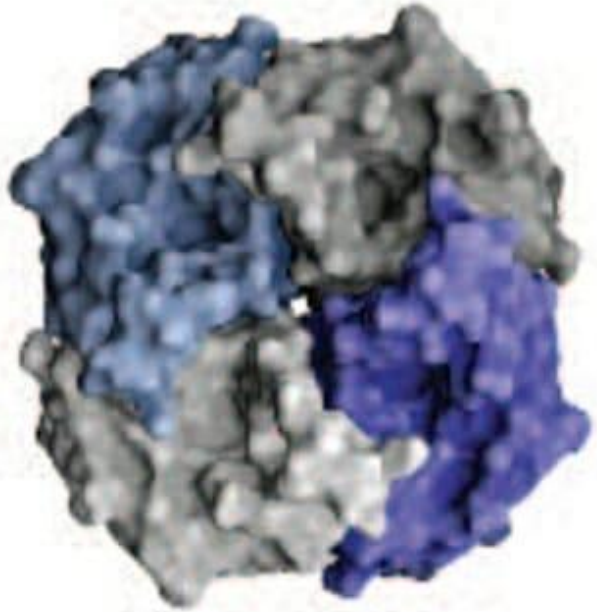


Chloride-Bicarbonate exchanger is antiporter

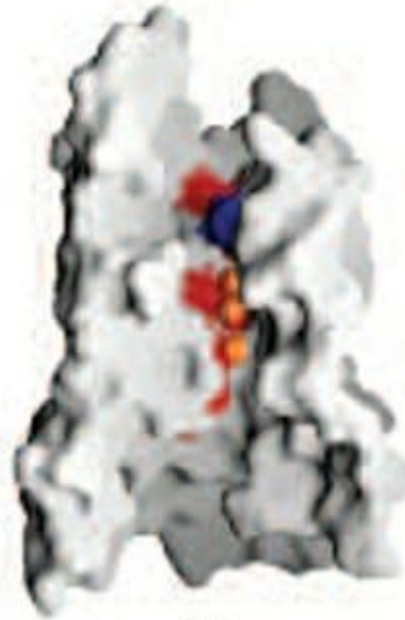


Aquaporins act as water channel in plasma membrane.

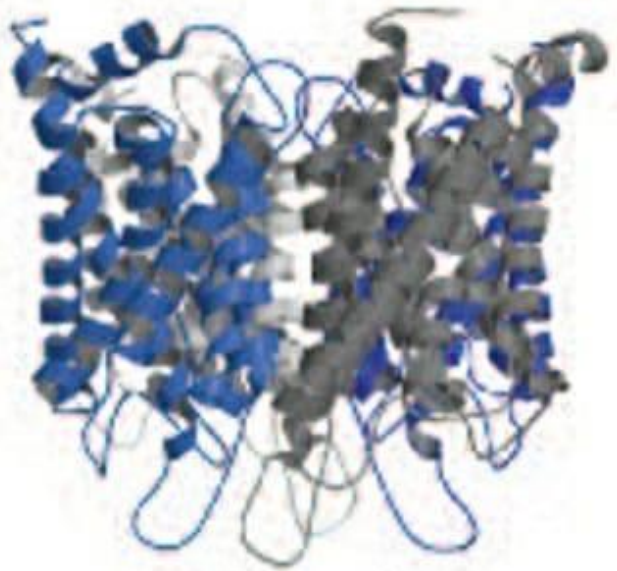
- They were discovered by Peter Agre.
- These are integral membrane proteins that act as channels for water transport into and outside the cell.
- They are responsible for activities related to water movements such as rapid swelling and shrinking of RBCs, concentration of urine in kidney etc.
- They are multimers and therefore example of type IV membrane proteins.
- They have a conserved sequence called as NPA i.e. Asn-Pro-Ala.
- It allows entry of water only and prevents entry of protons.



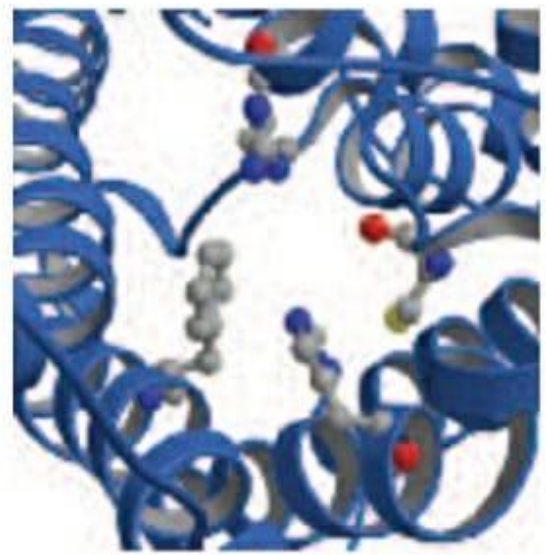
(a)



(c)



(b)



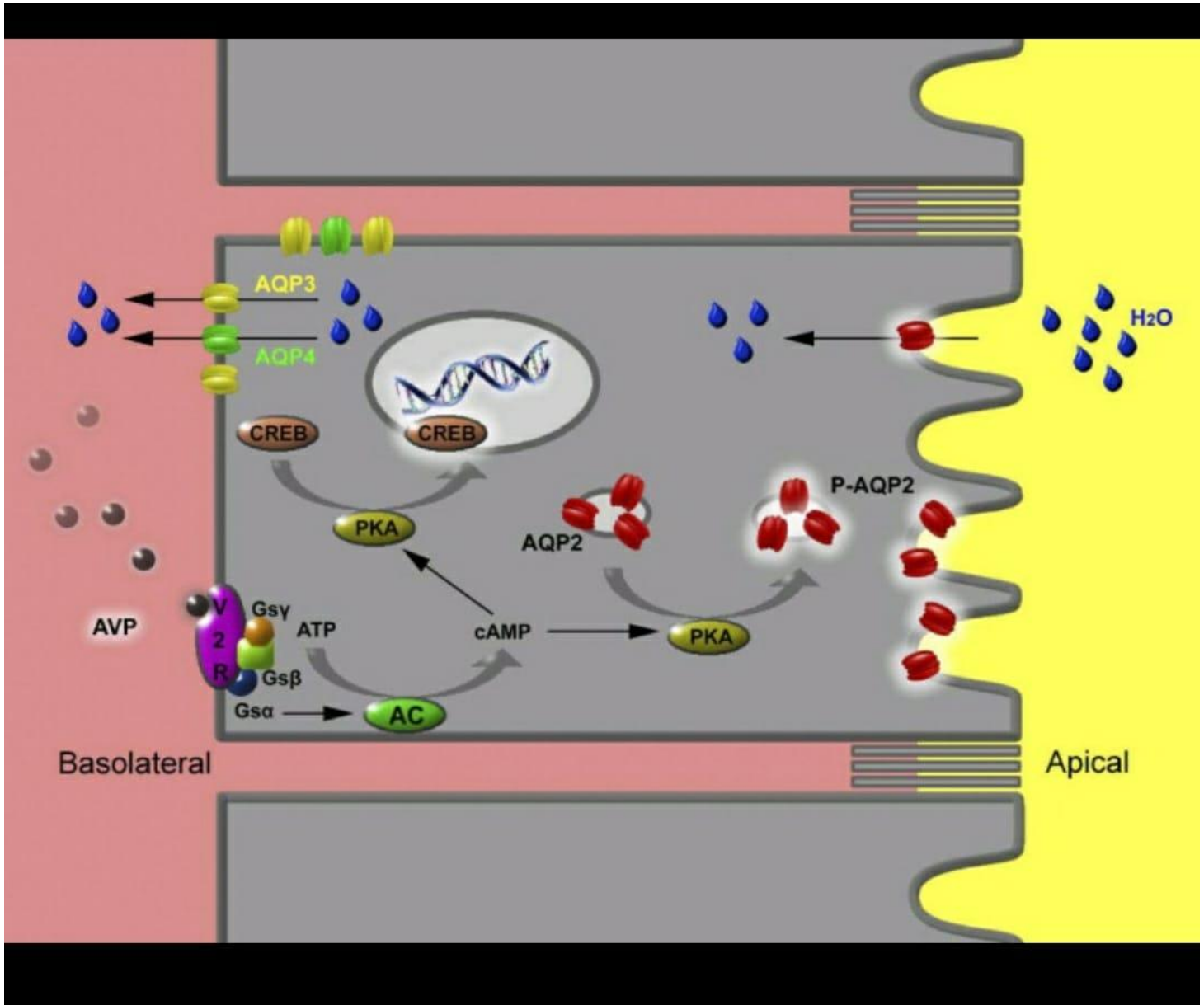
(d)

Structure of an aquaporin protein.

TABLE 11–6 Aquaporins

Aquaporin	*Roles and/or location*
AQP-1	Fluid reabsorption in proximal renal tubule; secretion of aqueous humor in eye and cerebrospinal fluid in central nervous system; water homeostasis in lung
AQP-2	Water permeability in renal collecting duct (mutations produce nephrogenic diabetes insipidus)
AQP-3	Water retention in renal collecting duct
AQP-4	Cerebrospinal fluid reabsorption in central nervous system; regulation of brain edema
AQP-5	Fluid secretion in salivary glands, lachrymal glands, and alveolar epithelium of lung
AQP-6	Kidney
AQP-7	Renal proximal tubule, intestine
AQP-8	Liver, pancreas, colon, placenta
AQP-9	Liver, leukocytes
TIP	Regulation of turgor pressure in plant tonoplast
PIP	Plant plasma membrane
AQY	Yeast plasma membrane

Aquaporin and Diabetes insipidus

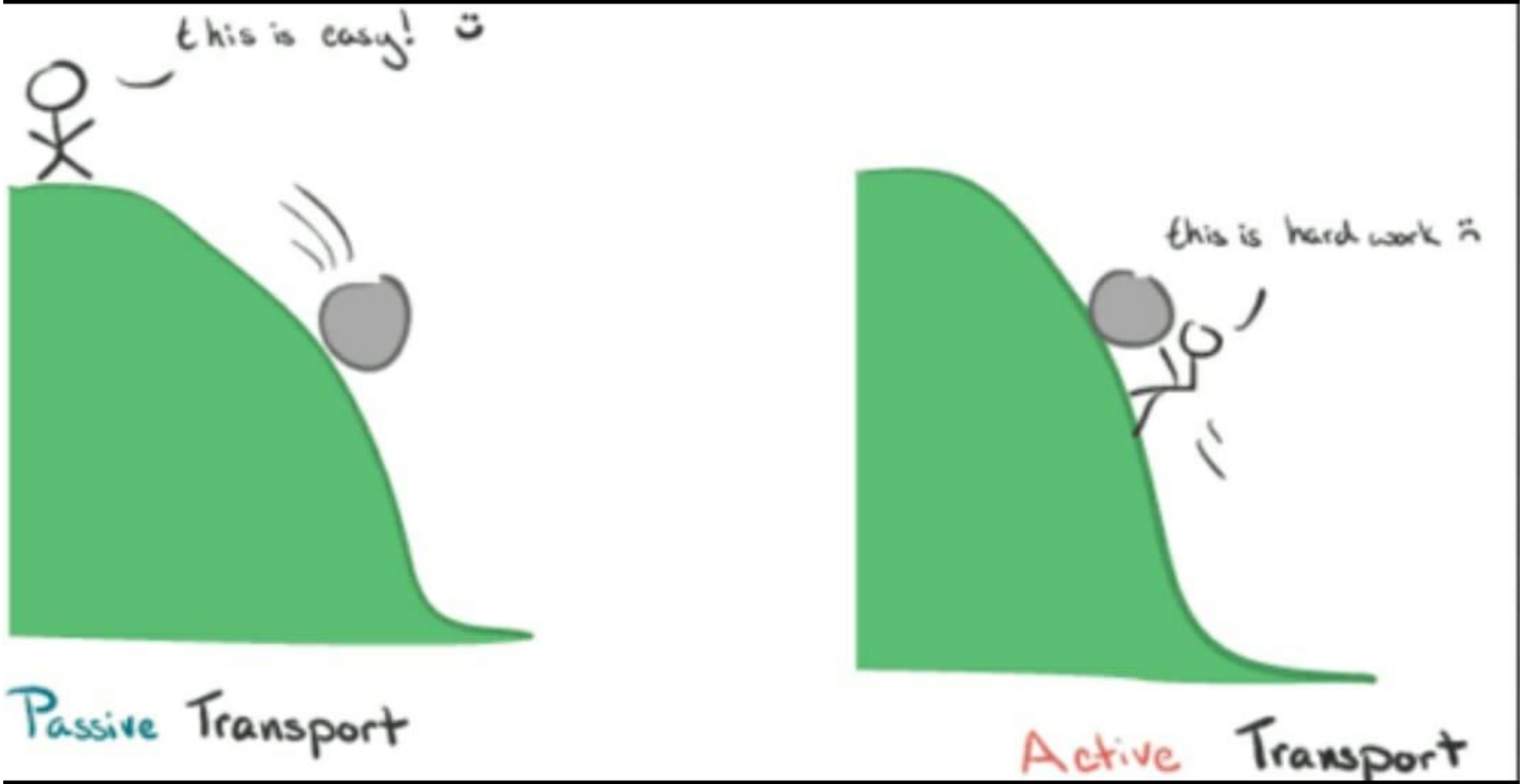


Active transport and it’s types.

- In passive transport, movement is always down the gradient thus it is a spontaneous process and doesn’t need energy.

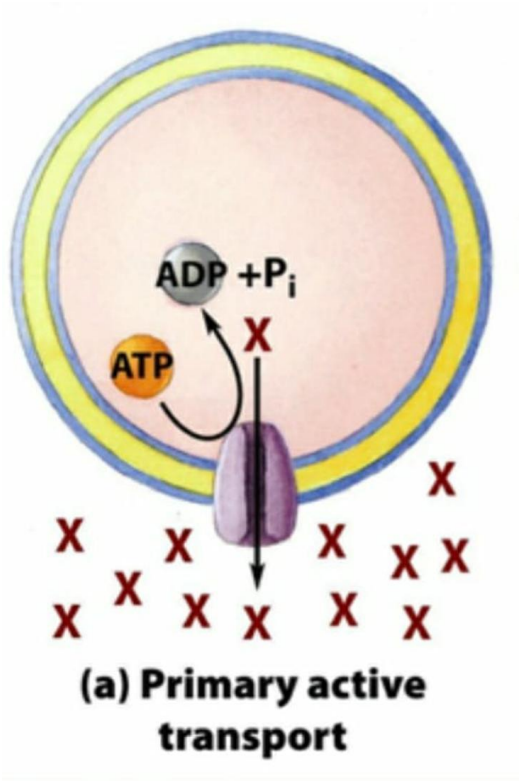
- In active transport, movement is always against the gradient thus it is a non spontaneous process. Therefore, it occurs only when coupled with an exergonic or energy yielding process such as

- absorption of sun light,
- breakdown of ATP,
- an oxidation reaction,
- a simultaneous movement of a solute down it’s electrochemical gradient.


this is easy! ☺
this is hard work ☹
Passive Transport
Active Transport

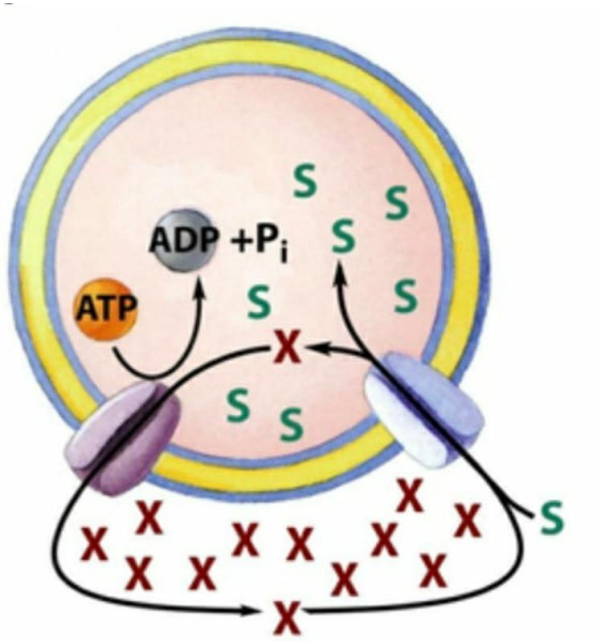
Types of active transport

1. **Primary active transport:** In this uphill movement of solutes is linked directly to an exergonic chemical reaction such as breakdown of ATP to ADP and Pi.



2. Secondary active transport :

It occurs when uphill or endergonic transport of one solute is coupled to the exergonic or downhill flow of a different solute that was originally pumped uphill by primary active transport.



(b) Secondary active transport

Examples of active transport

- There are many examples of primary active transport such as

1. P-type ATPases

2. F-type ATPases.

3. V-type ATPases

4. ABC transporters

P-type ATPases

- They are called so because they are integral membrane proteins found in plasma membrane.

- They are widely distributed in life forms. Some common examples are

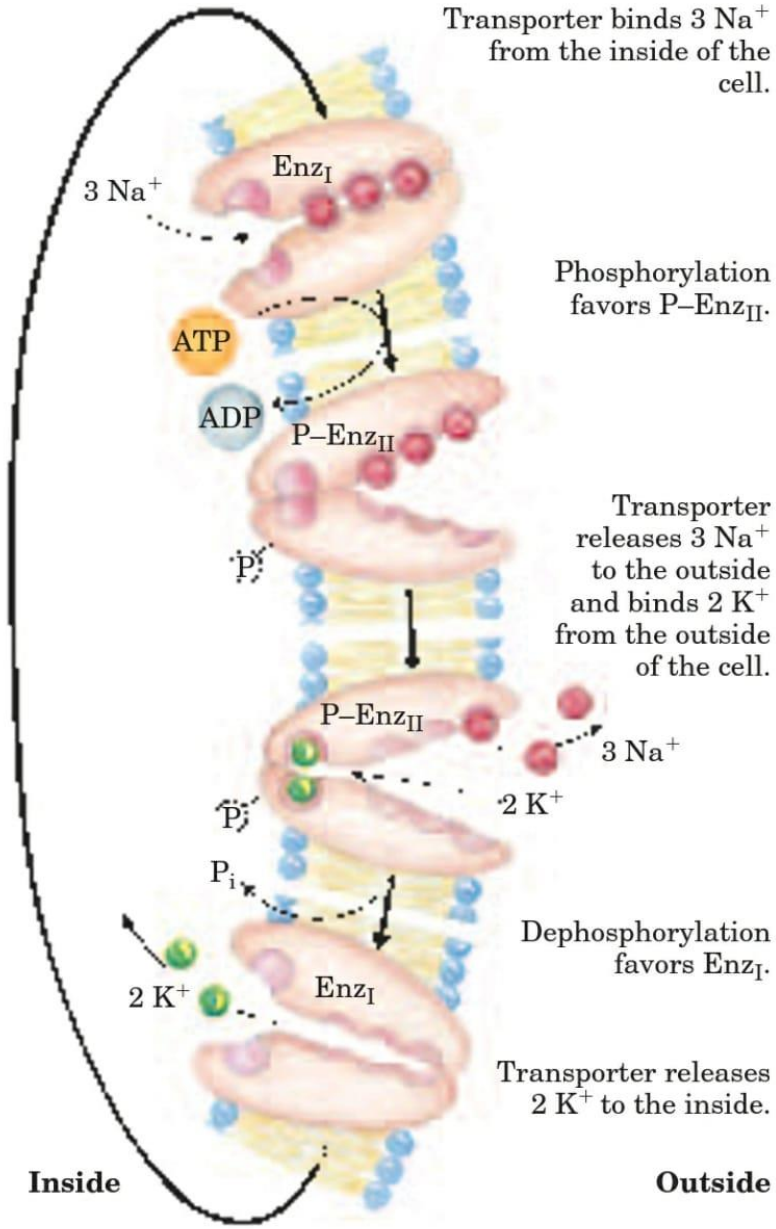
1. Sodium-Potassium ATPase, an antiporter of Sodium and Potassium ions.

2. Calcium ATPase, an uniporter of Calcium ions.

3. Proton-Potassium ATPase, an antiporter of Hydrogen and potassium ions. It is found in parietal cells in stomach and pumps hydrogen ions outside the cell. It makes stomach acidic.

4. Bacteria use them to pump out toxic heavy metal ions such as Cadmium and Copper.

Sodium-Potassium ATPase.



(1) $ATP + Enz_I \longrightarrow ADP + P\text{-}Enz_{II}$

(2) $P\text{-}Enz_{II} + H_2O \longrightarrow Enz_I + P_i$

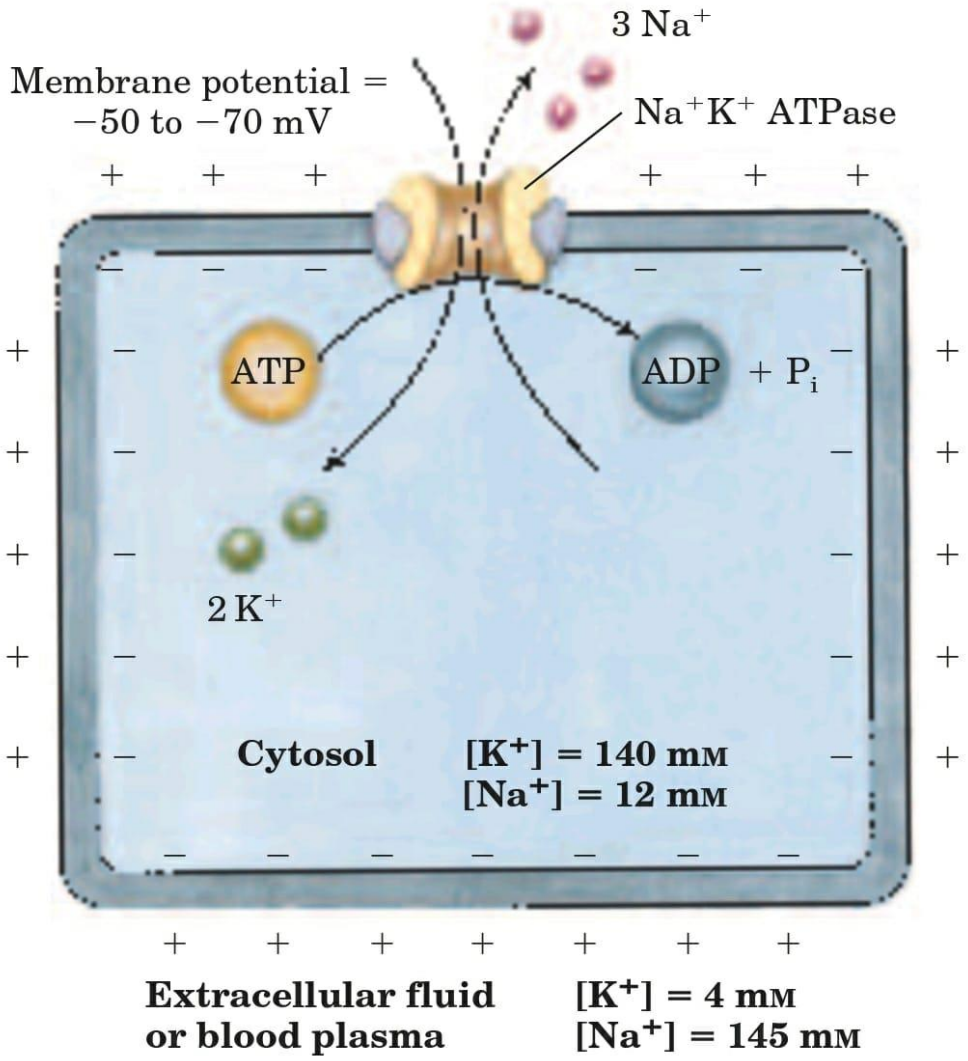
Sum: $ATP + H_2O \longrightarrow ADP + P_i$

Actions of this pump are responsible for lower concentration of Sodium ion inside the cell and higher concentration of potassium ions inside the cell.

1. Because of the charge imbalance it creates there is a net separation of charge across membrane.

2. Thus we see a transmembrane potential of -50 to – 70 mV with inside negative relative to outside.

3. Because this membrane potential is necessary for the for the prope function of the cell, about 25% of the total energy of cell is consumed by this pump alone.



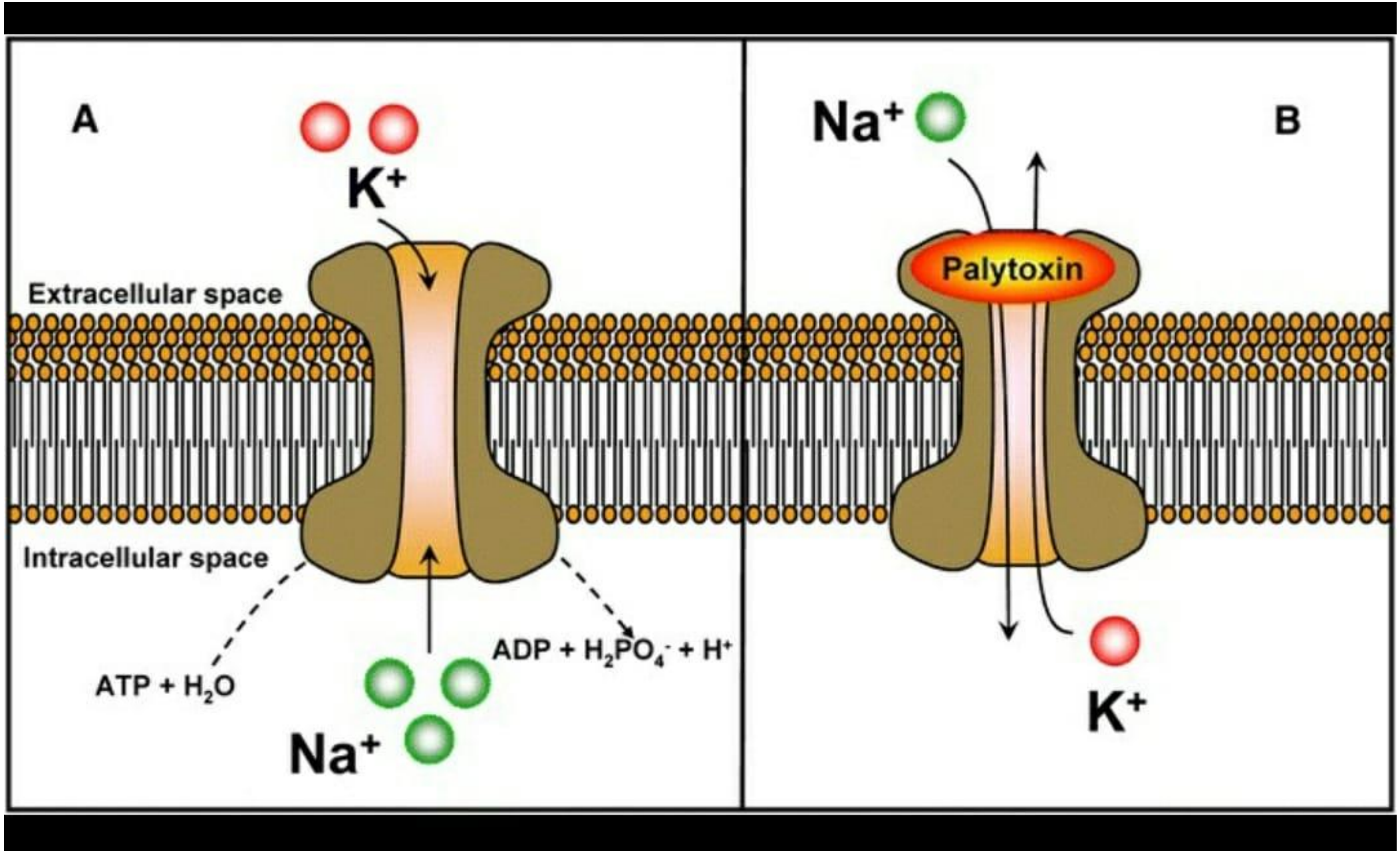
- **Ouabain,** it is a potent inhibitor of the pump and binds to the form that opens to the outside and locks in 2 Sodium ions.

- **Thus,** it prevents confirmation changes necessary for ion transport.

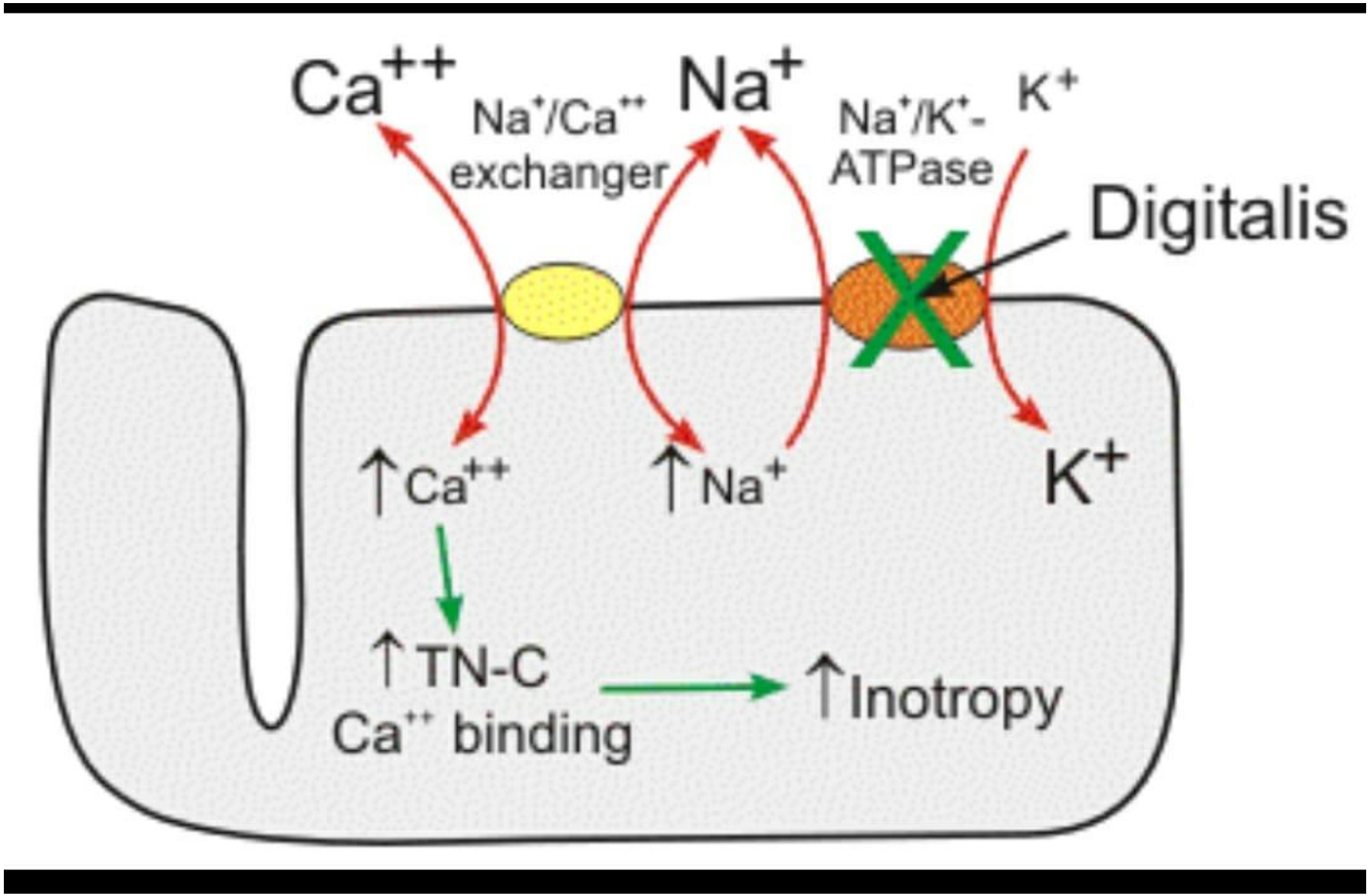
- **Palytoxin,** It is produced by a coral found around Hawaii islands.

- It binds to the proteins in the form that makes the ion binding sites accessible from both the sides.

- Thus, it converts a specific transporter into a non specific ion channel.


A
K+
Extracellular space
Intracellular space
ATP + H2O
ADP + H2PO4- + H+
Na+
Na+
B
Palytoxin
K+

- Digitalis has been used to treat congestive heart failure since introduction by William Withering in 1785.
- It’s active ingredient is called as digitoxigenin.
- It is a drug that is capable of strengthening the contraction of heart muscles without increasing the heart rate.
- Digitalis inhibits efflux of Sodium ions. It raises the intracellular sodium ions to high levels.
- This high intracellular sodium ion concentration forces the activation of Sodium-Calcium antiporter in the cardiac muscles.
- It causes efflux of Sodium ions and influx of calcium ions in the cardiac muscle cells.
- This elevated cytosolic calcium strengthens the contraction of cardiac muscles.


Ca++
Na+/Ca++ exchanger
Na+
Na+/K+- ATPase
K+
Digitalis
↑Ca++
↑Na+
K+
↑TN-C Ca++ binding
↑Inotropy

The Na^+ / K^+ ATPase pump is found on the plasma membrane of most animal cells, A mutation in the intrinsic phosphorylation site of the pump is most likely to affect.

(a) the outward movement of Na^+ only

(b) inward movement of K^+ only

(c) both the inward and outward movement of K^+ and Na^+

(d) has no effect on pump activity but affects its stability

P type Calcium pumps

- The cytosolic concentration of free calcium ion is usually below 100 nM. It is true for every cell.
- It is needed because concentration of Pi and PPi in cytosol is in mM range.

- They will combine with calcium ions if they are also present in cytosol and form insoluble calcium phosphate.
- This is negatively affect the performance of cell.

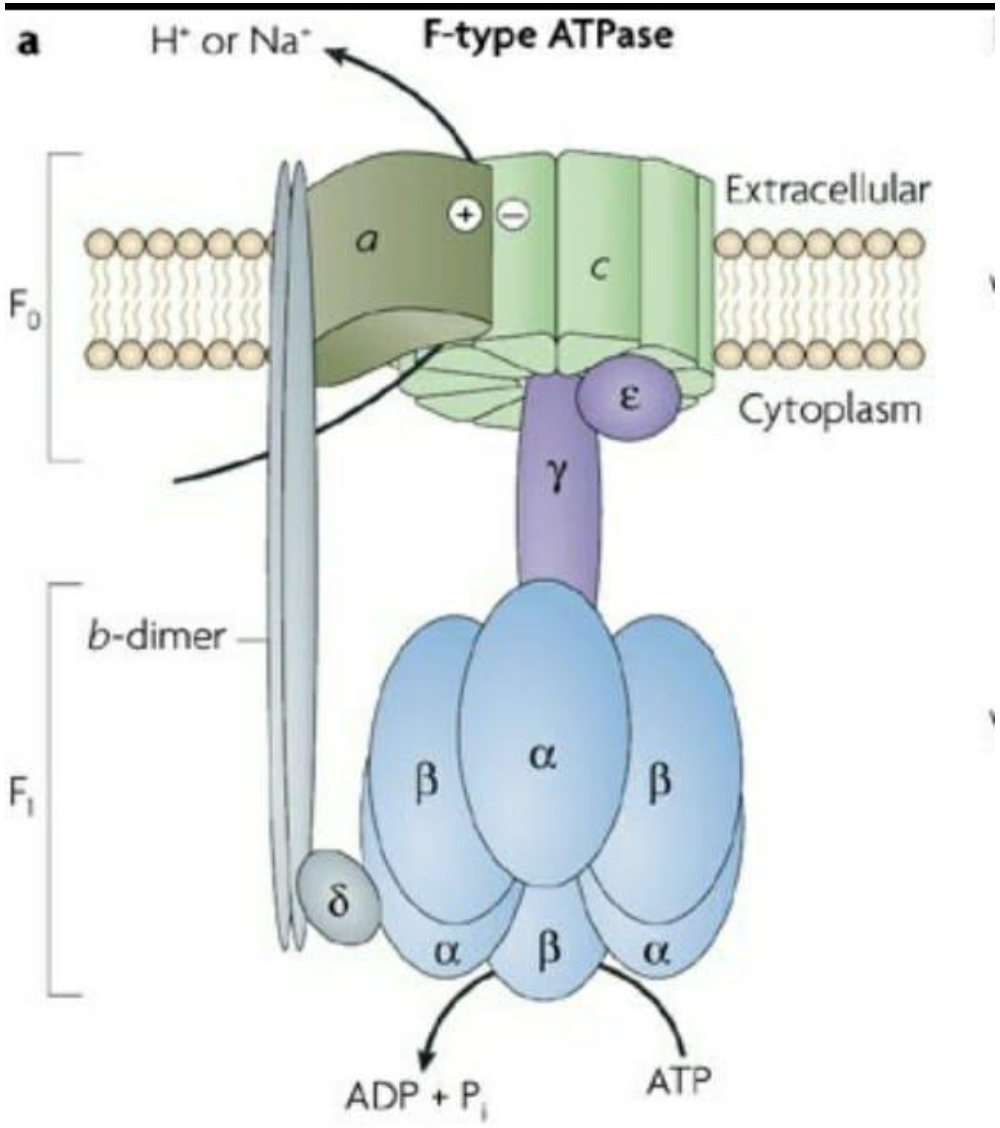
- To maintain this plasma membrane has a calcium pump in it. It pumps the calcium ions to extracellular side using the energy of ATP.

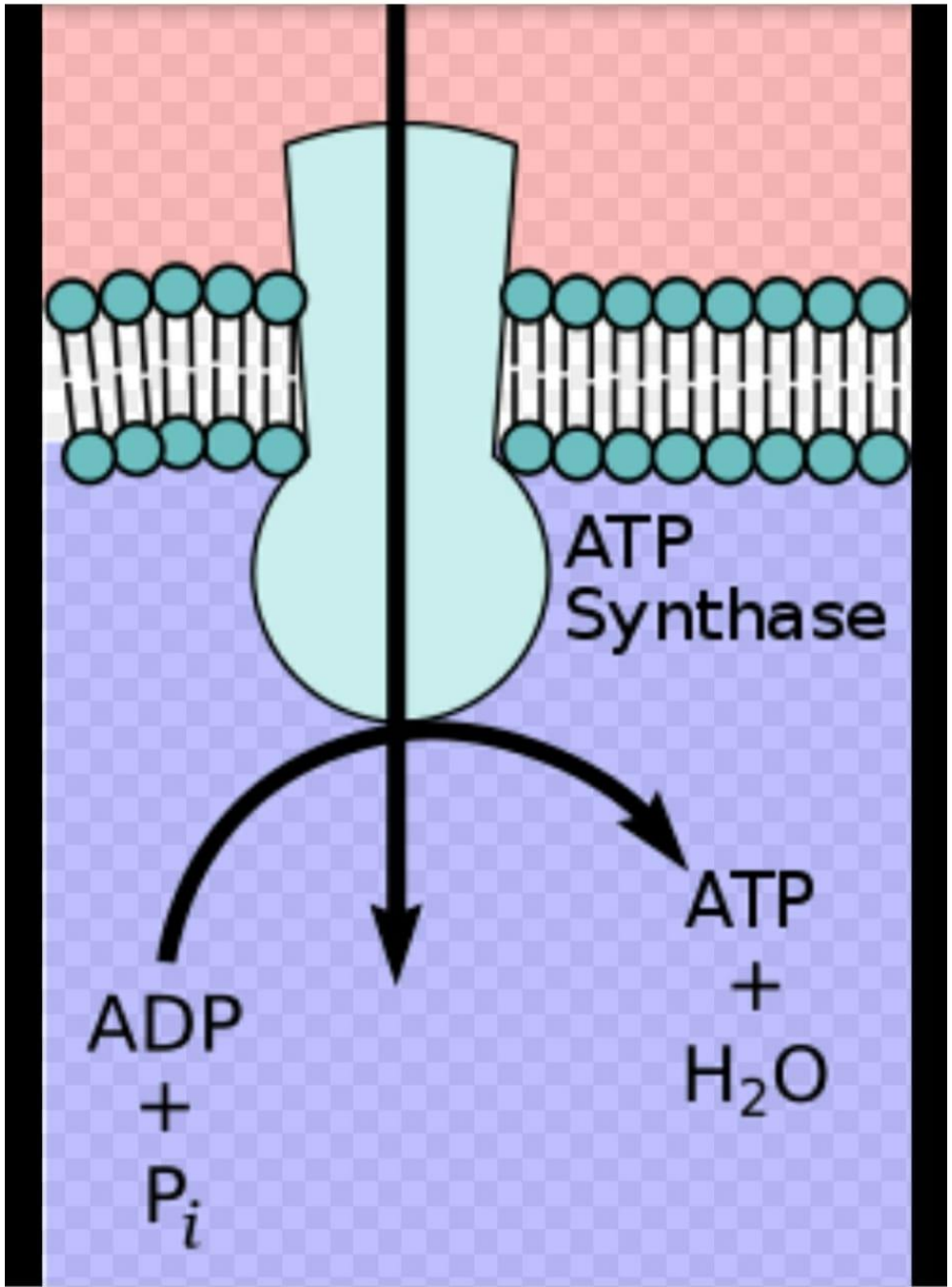
- In addition endoplasmic reticulum membrane also has a calcium pump to transport calcium ions from cytosol into ER lumen using the energy of ATP hydrolysis.

- This pump is also found in the ER of myocytes or muscle cells and is called as sarcoplasmic calcium pump.

F type ATPases

- They are called so because they are involved in ATP synthesis process as energy coupling factor.
- Their basic function is to pump protons uphill using the energy of ATP. Thus, they came to be called as ATPases.
- They usually have two different components Fo and F1 components and thus also called as FoF1ATPase.
- They are found in all the organisms ranging from eubacteria to humans.
- Archaebacteria have a closely homologous system called as AoA1 ATPase.
- The reaction catalysed by these pumps is reversible. Which means they can use the proton gradient for production of ATP. In this role they are primarily called as ATP synthase.


a
H+ or Na+
F-type ATPase
Extracellular
Cytoplasm
a
c
ε
γ
F0
b-dimer
F1
β
α
β
δ
α
β
α
ADP + Pi
ATP


ATP
Synthase
ADP
+
Pi
ATP
+
H2O

V type ATPases

- They are called so because they are found in the membrane of vacuoles.
- They pump protons against their concentration gradient using energy of ATP hydrolysis.

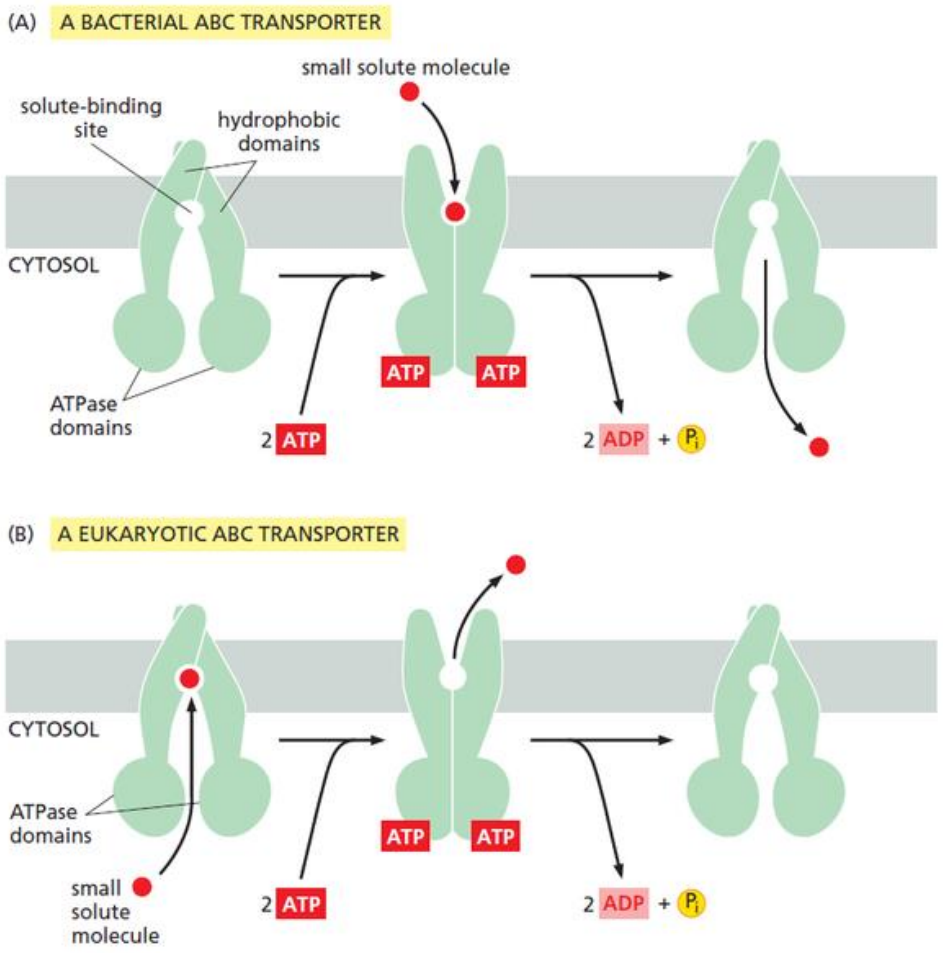
- They are responsible for

1. Acidification of lysosome and endosomes.
2. Acidification of Golgi complex.
3. Acidification of secretory vesicles.
4. Acidification of vacuoles in fungi and in higher plants.

- They have a structure that resembles the F type ATPases so they are also called as VoV1 ATPases.

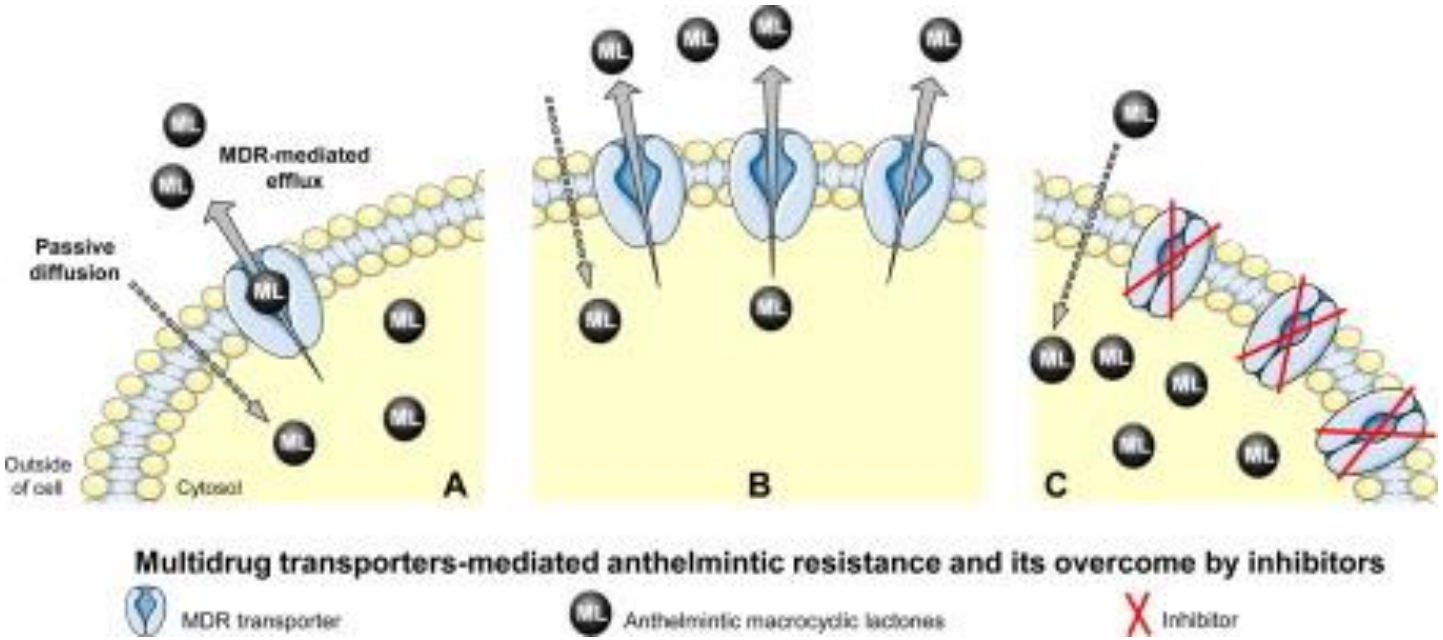
ABC Transporters

- It is acronym for transporters that have ***ATP-binding cassette domains.***
- They are found in all forms of life i.e. microbes, plants, fungi and animals.



- In humans, ABC transporters have following roles
    1. Involved in maintaining lipid bilayer.
    2. Transport of sterols, sterol derivatives and fatty acids.

- In humans, they are also involved in drug resistance against some chemotherapy drugs and some anti helminthic drugs.



- MDR transporter has broad substrate specificity for hydrophobic compounds including drugs such as vinblastine, Adriamycin and doxorubicin etc.
- By pumping these drugs out of the cells, it prevents the accumulation of drugs in cells.
- As a result, drugs fail to show their effects.

- They are also responsible for ***antibiotic resistance in microbes.***

Thank you