2(A)

PLASMA MEMBRANE

1972→ Jonathan Singer, Garth Singer Nicolson

Membrane is the boundaries of both around the cell and around distinct subcellular compartments. They act as selectively permeable barriers, allowing inside environment of cell or organelle to differ from outside. Membranes are involved in Function Like –

- Involved in signaling process. (By specific receptors)
- Transporting solutes.
- Energy Transduction.
- Scaffold for biochemical activities.
- Inter cellular interaction.

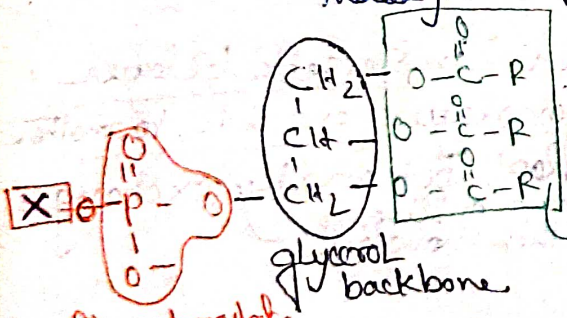
All membrane contains to basic components – Lipid & Protein. Some Contain – Carbohydrate.

MEMBRANE LIPID

Membrane contained different types of lipids and all are amphipathic (having hydrophobic + hydrophilic region) There are 3 main types of membrane lipids –

1. Glycerophospholipids / Phosphoglycerids –

Made by 3 components – i) Phosphorylated head group.
ii) Glycerol back bone
iii) Hydrocarbon Fatty acid chain.

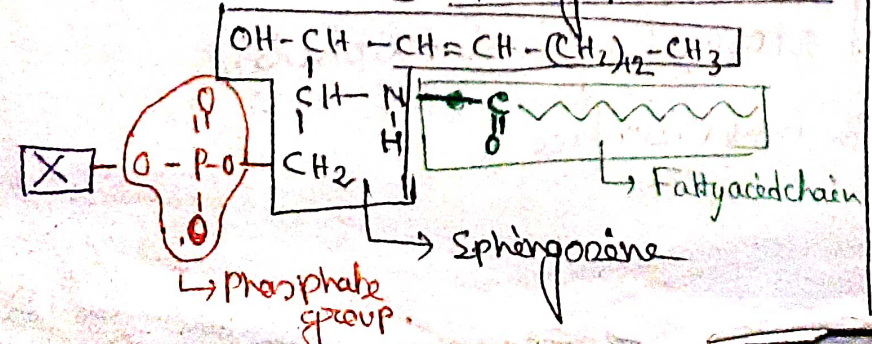


– Phosphatidyl choline
serine

2. Sphingolipid :-

Derivatives of Sphingosine, Amino alcohol containing long hydrocarbon chain. It can have phosphate group or not.

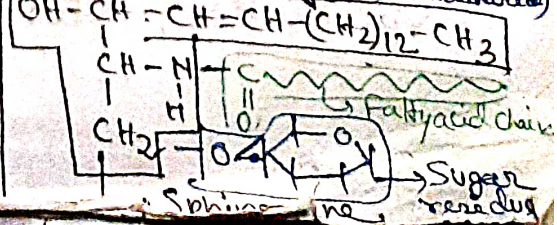
(a) Sphingophospholipid

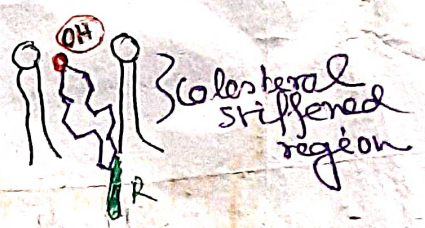


(b) Glycosphingolipid.

I) cerebroside → 1 (Simple Sugar)

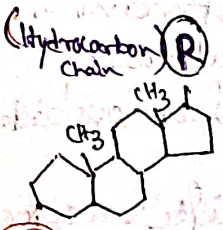
II) Ganglioside (2–8) (oligosaccharides)





3. STEROL:-

Sterol Cholesterol is major constitute of animal plasma membrane (absent in Prokaryot). Cholesterol is metabolic Precursor of Steroid hormone. having hydrophilic –OH group to membrane surface, remainder embedded in lipid layer. Hydrophobic rings Flat & rigid.



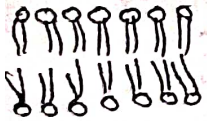
* Fatty acid Chain:-

Are the long chain of C atoms (having even no) like Palmitate C.16, Stearate C.18, unbranched, chain can be fully saturated with 'H' atom or may unsaturated one or more double bonds.

* LIPID BILYER:-

Phospholipid bilayer are Amphipathic / Amphophilic (hydrophilic and hydrophobic region). Hydrophobic fatty acid chains hidden inside micelle, hydrophilic head interact with water (Exoplasmic) & (Cytoplasmic).


Fig- Micelle


Lipid bilayer

Phospholipid bilayer in synthetic bilayer rarely migrate from one monolayer one side to another, the process known as - 'flip-flop' But radily exchange place with neighbors within monolayer by flippase

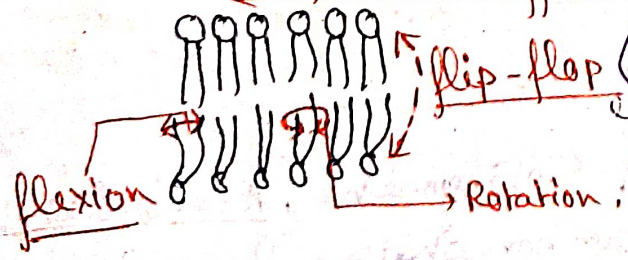


Fig- types of movements possible for phospholipid molecules in lipid bilayer

with the low conc. Mg++ ion concentration membrane reform outwardly / inner lipid layer ~ outer surface, water in inner surface

* Proteins can be extracted by detergent

MEMBRANE PROTEIN:→

Depending upon cell type & organelle within cell membrane contains different types of protein. They are classified into 3 type depending upon relationship to lipid bylayer—

① Integral or Transmembrane Protein:→

ⓐ Monotopic Pass entirely through lipid bilayer, domains
ⓑ Bitopic protrude from both extracellular & cytoplasmic side.
ⓒ Polytopic They are about 30% of all encoded protein.

Polytopic
- Signal receptor particle
- M, L Polypeptide of Bacterial reaction centre

- Freeze-Fracture/Freeze etching Technique-
  Distribution of protein in membrane shown by this technique ① membrane specimen Frozen quickly by liquid N_2 ② Fractured by sharp blow ③ exposed surface coated with platinum. ④ viewed in electron microscope.

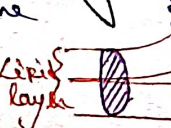
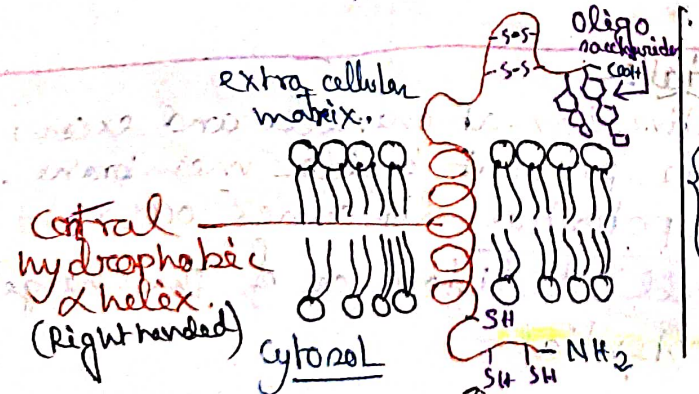


Fig - Freeze Fracture

Polytopic type also called Multiple membrane spanning protein (α helixes).
ex - Bacterio rhodopsin, found in photosynthetic bacterium, capture energy from light & use it to pump proton across membrane.



* Sulphydal groups don't form disulfide bond due to reducing environment of cytosol. SH maintain their reduce form.

Fig - Single Pass Transmembrane Protein

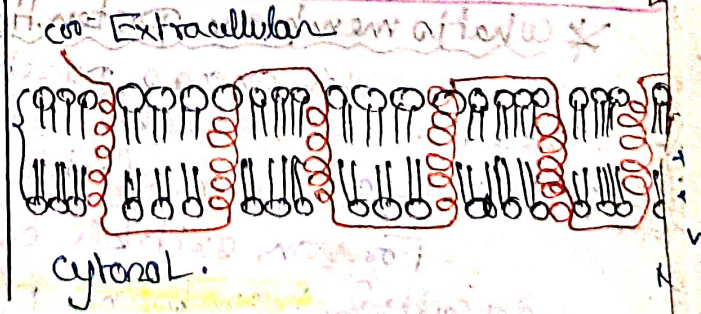


Fig. Multiple membrane Spanning region.

② Peripheral membrane Protein:-

(or with protein)
less tightly bound to lipid bilayer than integral (with polarised group)
proteins. Can remove peri. membrane protein by washing membranes with solution of High ionic strength.

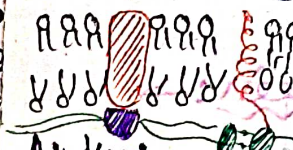


Fig- Peripheral protein

- They form fibrillar network, the 'cyto skeleton', provide mechanical support to membrane
- Some Functions as enzyme ex- ankyrin, Protein band
- Factors for transmembrane signals.
- specialized coats.

③ Lipid Anchored membrane Protein-

These are membrane proteins bound to membrane

① extracellular — by small, complex oligosaccharide links + Inositol embedded in lipid layer (GPI anchored protein)

② Intracellular/cytosolic — One or more hydrocarbon chains embeded in inner leaflet of lipid layer

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* What is membrane Potential:-

When excess positive ion at one side and excess negative ion at another side present beside membrane then a voltage or electric potential difference occur.

For non exitable cell the difference of the charge is called membrane potential.

* But in case of Nerve or Muscle cell Then same Potential reffered as Resting potential.

* PRINCIPLES OF MEMBRANE TRANSPORT

The plasma membrane is a selectively permeable barrier, some molecule like water, gas, urea can directly through bilayer, other molecules require presence of integral membrane transport proteins.

There are two means for the movement of substance -

① Passively by diffusion
② Actively by energy-coupled Transport process.

Both types of movement lead to net flux -

Net flux -

i) Influx - Movement of substance into the cell.
ii) Efflux - Substance movement out of the cell.

Carrier proteins allow solutes to cross the membrane only "passively" (downhill), Process called passive transport. uncharged molecule passes along with concentration gradient.

Carrier protein

Channel protein

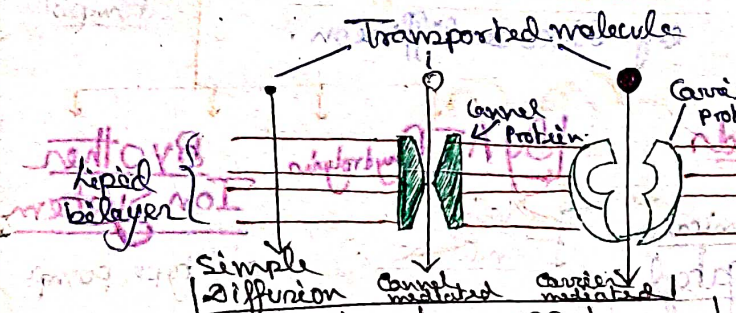
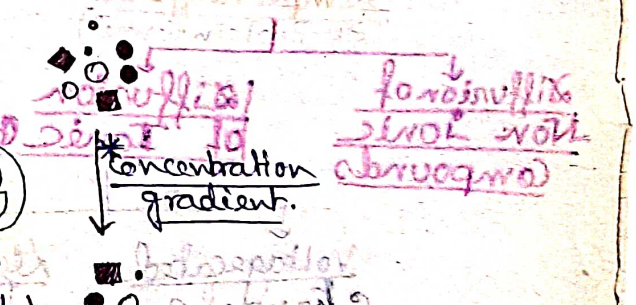
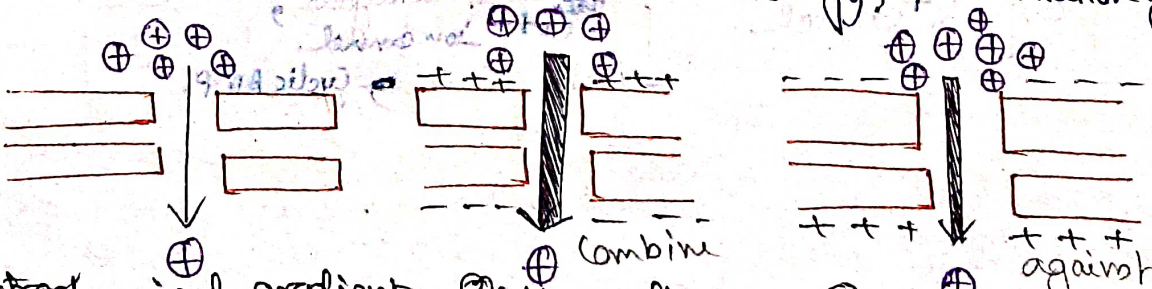


Fig - down an electrochemical gradient.



Active transport (Uphill) require input of metabolic energy, to pump against concentration gradient



① electrochemical gradient with no membrane potential.

② With negative Potential inside.

③ With positive Potential inside

Combine

against.

- Electrochemical gradient = Concentration gradient + membrane potential (or electrical potential of membrane)

Can work combinedly (2nd case)

Can work against each other (3rd case)

* Diffusion through membrane:—

For diffusion, substrate must be present at higher conc. on one side than other, membrane must be permeable to substance. There are 2 factor for diffusion —
To measure polarity or non polarity of solute

① * Partial coefficient:— Solute

It is the ratio of solubility in a non polar solvent

e.g. Octanol or Vegetable oil (solute) mixed in water where non polar solvent mixed together.

Methyl alcohol = 0.78.

* Aquaporin - Integral protein, functions in Passive transport of water.

② Size of molecule:—

- Small size can pass, CO_2, O_2, H_2O, NO. Slips to adjacent Phospholipids.
- Larger can't pass like Sugar, Amino acid e.t.c.

TRANSPORT THROUGH MEMBRANE

- Passive transport:—
  - Simple Diffusion (By Protein Cannel)
    - Diffusion of Non Ionic Compounds
    - Diffusion of Ionic Compounds
      - By Voltage gated Channels
        - e.g. K^+ cannel
      - Chemical or Ligand gated Channels
        - e.g. Neurotransmitter as ligand, Ca^{++} ion cannel
        - Acetyl Coline → Cyclic AMP.
  - Facilitated Diffusion
    - e.g. Glucose diffusion.
- Active transport
  - By protein "Pumps"
    - By ATP hydrolysis
      - e.g. Na^+/K^+ Ion Cannel.
    - By other Ion System
      - e.g. P type pump H^+/K^+ ATPase. In Stomach

* VOLTAGE GATED CHANNELS

K^+ Cannels or Kv channels —

(Kcs A) These type of Cannels contain membrane associated helix, named S_1 to S_6, these two divided into —

① Pore domain — helix S_5 and S_6 and P segment (Portion of Polypeptide called pore helix). S_6 helix conformation determines wheather gate open or closed.

② Voltage sensor domain — Consisting of helices $S_1 - S_4$ that senses voltage across plasma membrane and that are homologous.

① Kv Cannels opens by change in voltage. S_4 helix contain several positively charged amino acid residues act as key element in voltage sensor.

② Under resting condition negative potential keeps gate closed.

③ Change in potential to more positive value ⇒ give electrical force to S_4 helix, that make change in S_4's position ↓ that's why '+' charges exposes cytoplasm to outside of cell.

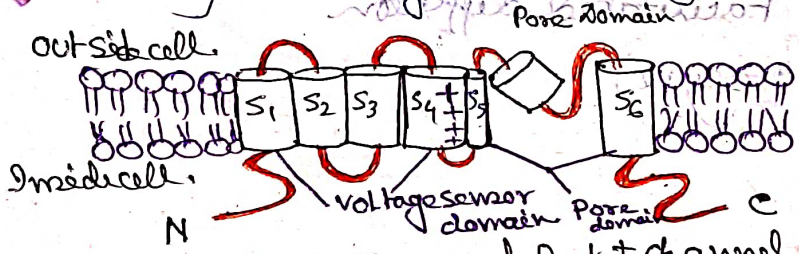


Fig - Eukaryotic voltage gated K^+ channel.

Seven '+' charge side chain act as voltage sensor situated at every 3rd residue along the helix

e.g - Drosophila K^+ shaker

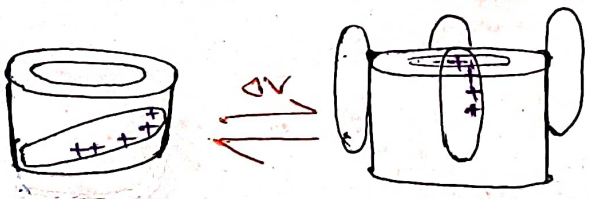


fig - S_4 helix moves like a paddle through lipid bilayer between intracellular & extracellular surface

④ After the channel is open for few milliseconds, movement of K^+ ion "Automatically" stopped by process known as inactivation.

Conserve penta-peptide - Gly - Tyr - Gly - Val - Thr
G - Y - G - V - T

* FACILITATED DIFFUSION -

In some case diffusion does not occur by diffusing through lipid bilayer. Some time it occurs through a membrane Spanning Protein - facilitative transporter. binding of solute to facilitative transporter to one side triggers conformational change of protein, exposing solute to other surface (without coupled to energy related system).

* Features -

- It only can move - 100 to 1000 solute/sec (whereas ion cannel can move millions/sec.
- Activity can be regulated.
- Important for entry & exit of polar solute.
  e.g. Glucose, Amino acids.

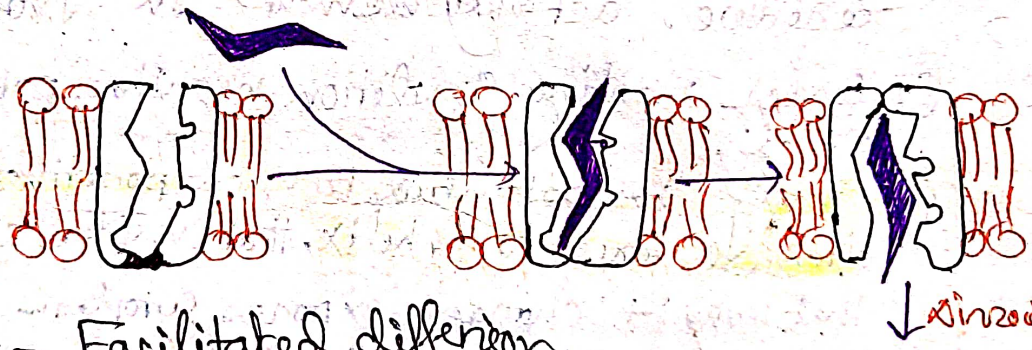
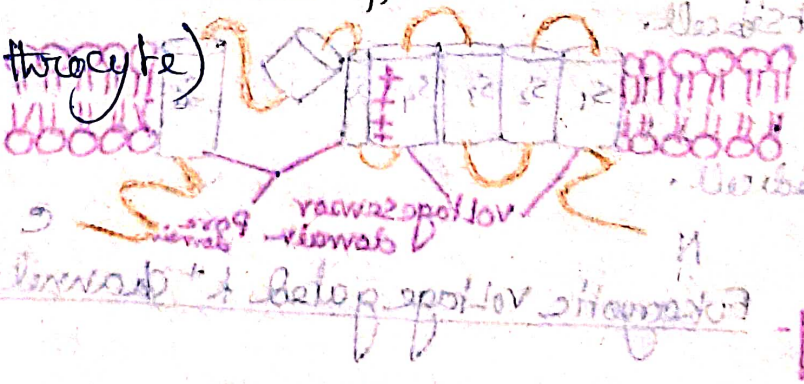
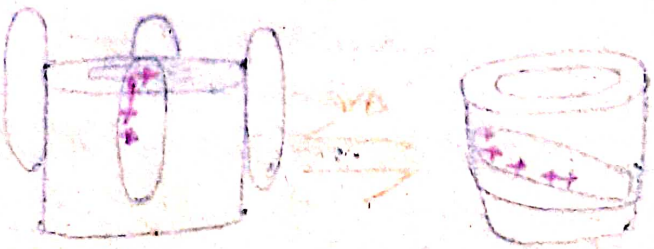


Fig :- Facilitated diffusion

(ie - Erythrocyte)





*ACTIVE TRANSPORT

Movement of Solute against a gradient requires input of energy. Endergonic movement of ions or other solute across membrane coupled to exargonic process like –

I) Hydrolysis of ATP.
II) Absorbance of light.
III) Transport of electron.
IV) Flow of some substances.

* Protein that carry active transport refferd as "Pumps"

*Hydrolysis of ATP – (PLASMA MEMBRANE)

Na⁺K⁺ pump is An ATPase
or
Sodium Potassium Pump

Jens Skou, 1957

Active transport drives movement of ion in only one direction, Na⁺/k⁺ ATPase responsible (Electrogenic) for Na⁺ ions actively pumped by antiporter out of cell against electrochemical gradient & pumping k⁺ in, by hydrolyzing ATP, to pump Na⁺ & k⁺. the positive charges of 2 ions balanced by negative charge by various anions. (cl⁻ ion outside, Protein & amino acid inside negatively charge)

* Ratio of Na⁺/k⁺ maintained as 3:2 (3 ion Na⁺ pumped out of cell & 2 k⁺ ions pumped in).

* Na⁺k⁺ ATPase :- Is electrogenic, Contributes directly operation of charges across membrane.

* Its 'P' type Ion pump – P Stands for Phosphorylation

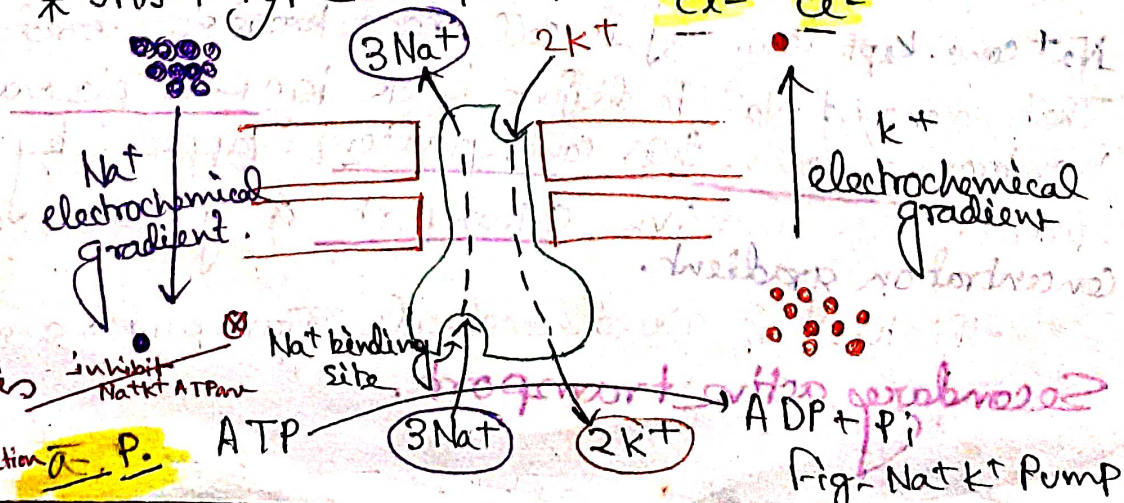


fig- Na⁺k⁺ Pump.

H^+/K^+ ATPase →

Inhibitor → Prilosec (Pump blocking drug)

Blockreceptor of parietal cell → Zantac, Pepcid (Acid blocking drug)

(2) ATP hydrolyzed and Phosphate transferred to protein

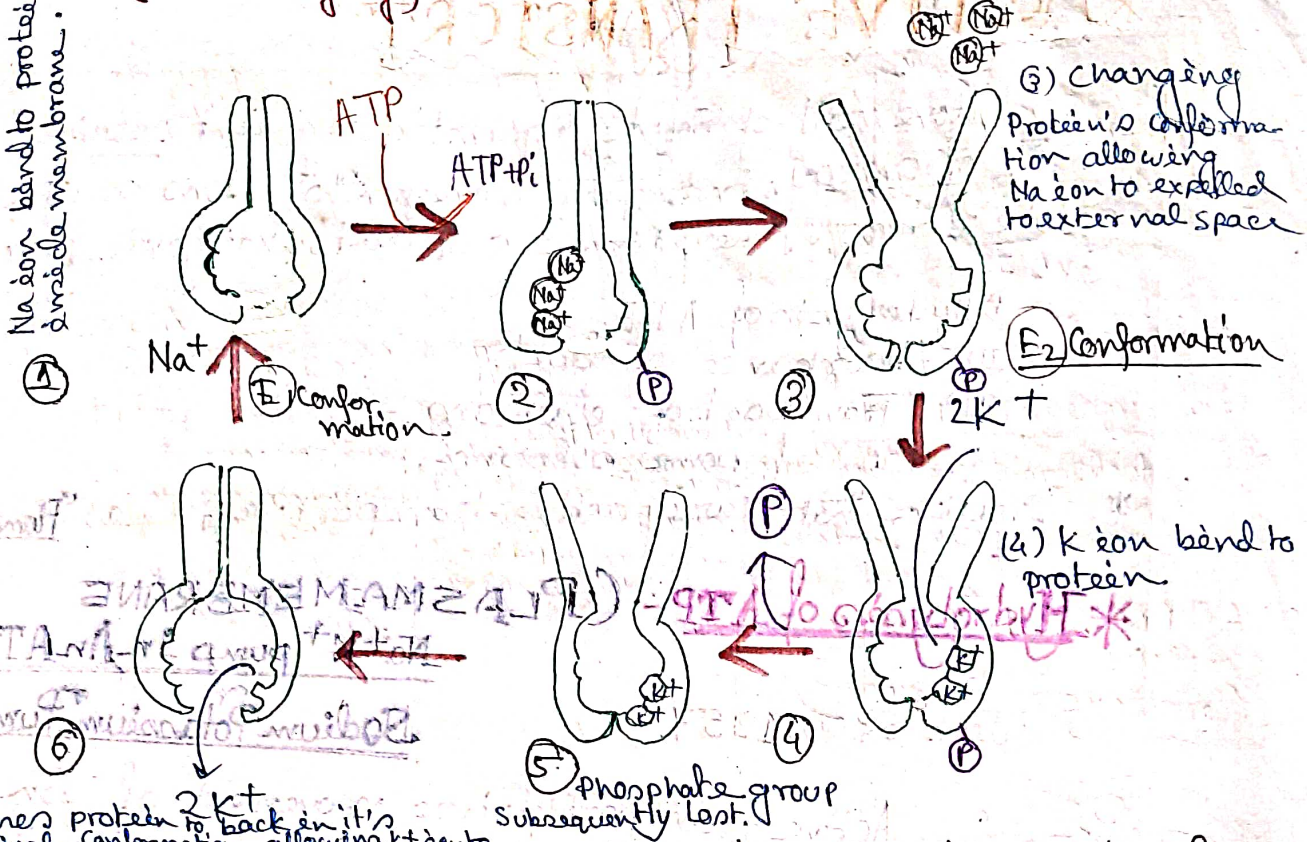


Fig- Schematic model of Na^+/K^+ ATPase transport cycle.

* Secondary Active transport – /Co-transport/ Coupling active transport –

Establishment of concentration gradients (of Na^+, K^+, H^+) provide a means by which free energy can stored in cell & utilize in various process like transport of other solutes.

*** Cotransport :–**

Movement of glucose against concentration gradient occurs by Cotransport with Na ion.

*** Secondary active Transport :–**

By primary Active transport (Na^+ K^+ ATPase) Na^+ conc. kept low in cell. The tendency of Na^+ to diffuse back to apical plasma membrane down their conc. gradient "tapped" by epithelial cell to drive Cotransport of glucose against concentration gradient.

This type of glucose molecule Transport named as Secondary active transport.

In this case 2 Na^+ molecules take 1 Glucose by Na^+/glu. Cotransporter and expose to epithelial cell & lower affinity for glucose & release. Then glucose molecule move out to blood stream by facilitated diffusion through Glucose Transporter.

Low Conc. of Na^+ in Epithelial cell maintained by Na^+/k^+ ATPase on basolateral membrane

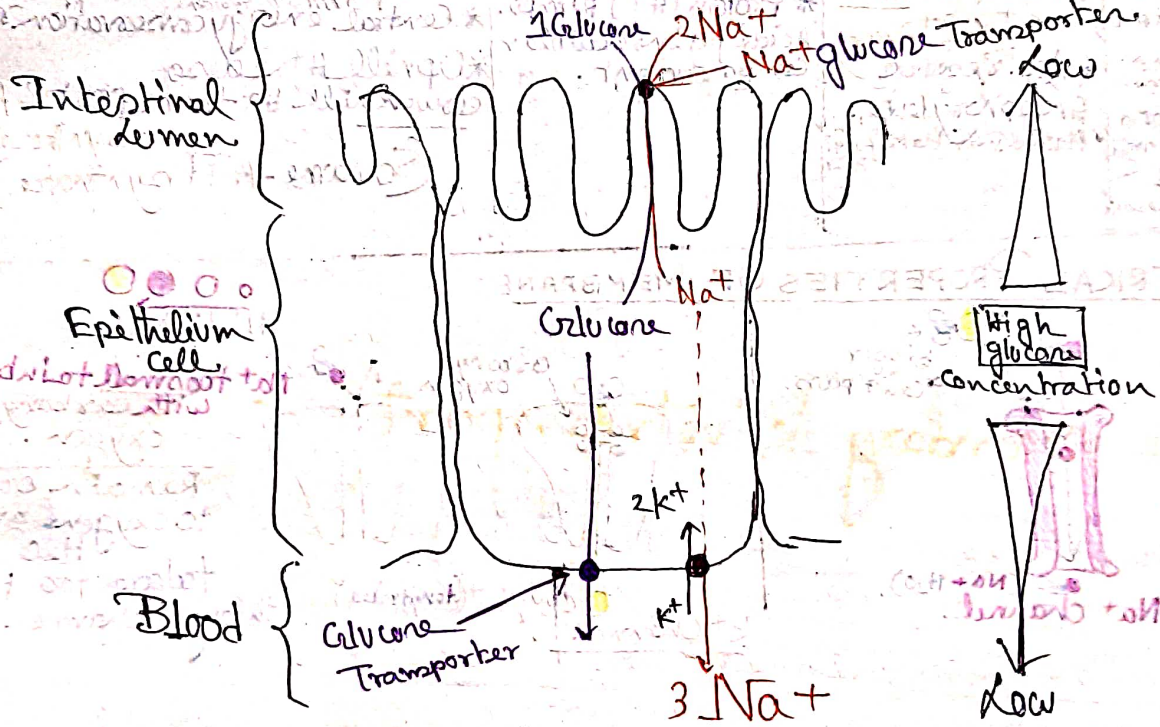
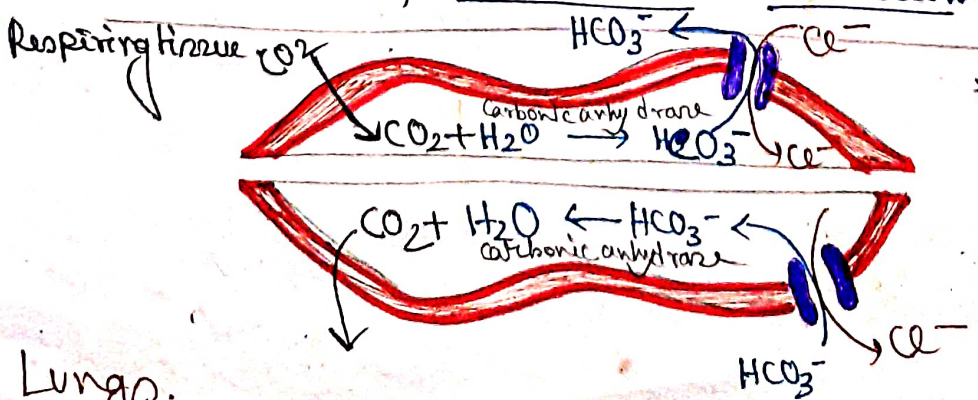


Fig:- Secondary Active Transport. (use of energy stored in ionic gradient).

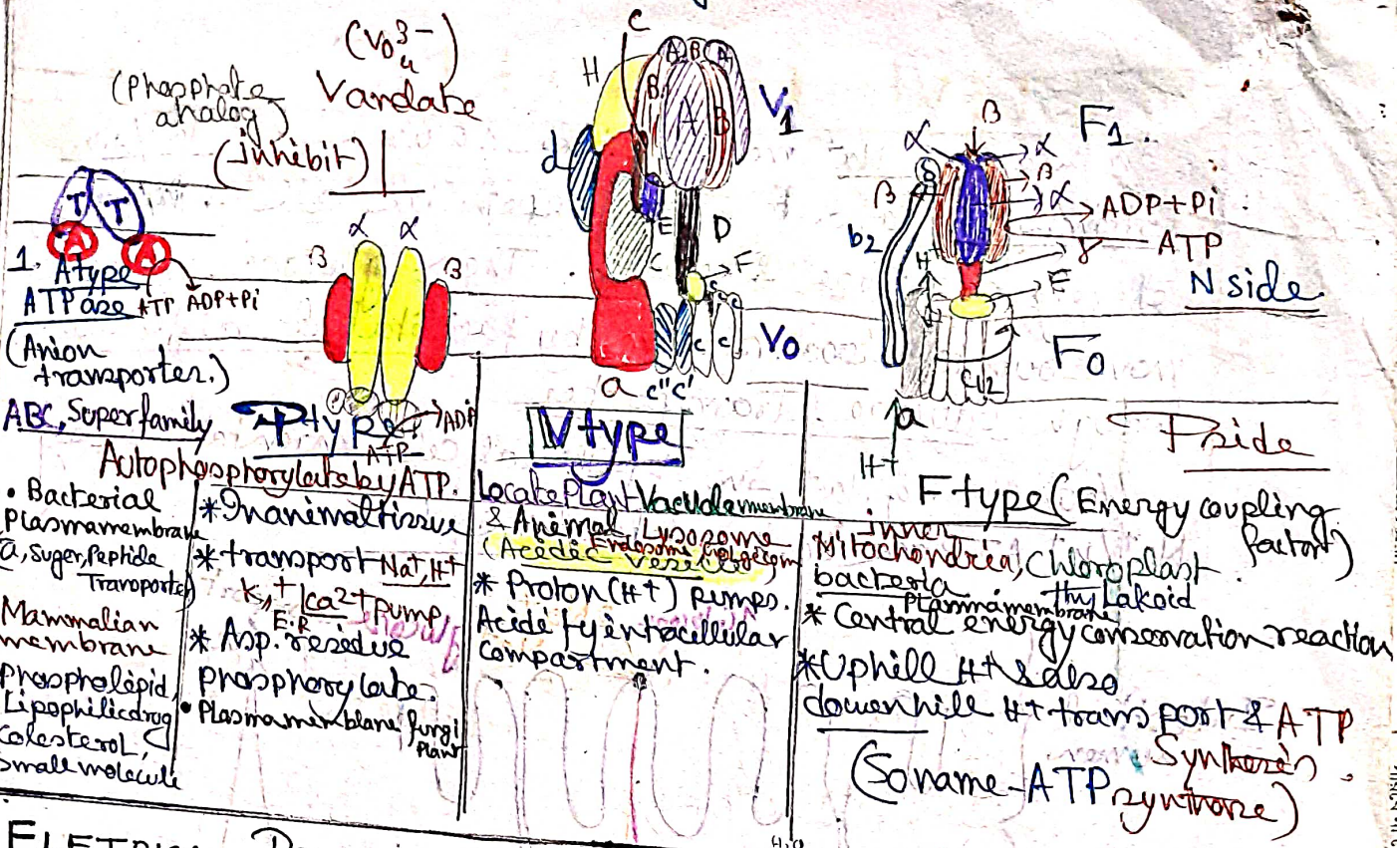
* Using light energy:-

By Halobacterium salinarium

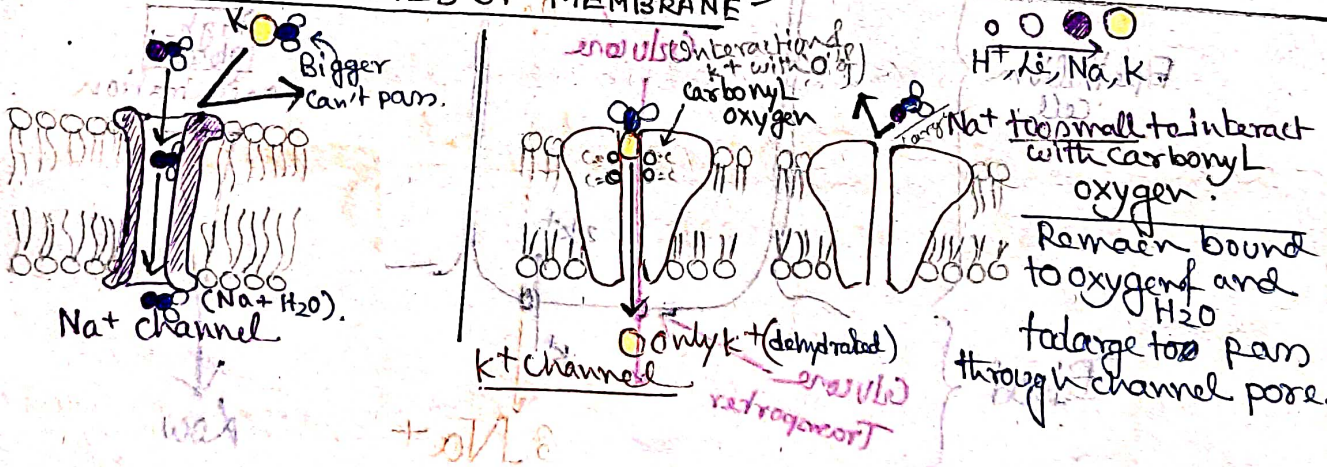


* HCO_3^- is much more soluble in blood than CO_2 in blood plasma.

Ion Transporting ATPases.



Eletrical Properties Of Membrane –



Ionophores –

carry

1) Valinomycin (cyclic peptide surround K+)
O_2 atoms binds to K+ → K^+
External polypeptides hydrophobic.

2) Monensin – → Na^+