


Physiology---- Introduction

- **Study of the functions** of various systems and different organs of the body .
- **Functions** – provision of Oxygen, removal of metabolites & waste products, BP maintenance, reproduction, locomotion etc.
- In unicellular organisms— all functions are done by single cell
- In multicellular organisms— individual systems develop

Cell membrane

- Cell is the structural and functional unit of living body.
- Each cell has a covering called cell membrane
-  fig of a cell

Cell membrane

- It is protective sheath enveloping the cell body.
- It separates ICF from ECF
- Its thickness is 70 – 100 A (A – angstrom)
- CM is selectively permeable.
- Nutrients are absorbed and waste products are excreted through it.
- It is responsible for the maintenance of size and shape of cell.

Cell membrane-- structure

- **Fluid mosaic model** -proposed by **singer and Nicholson**
- CM consists of a double layer of lipid molecules in which proteins are scattered or embedded.
- Due to the scattering of proteins – it gives the appearance of **mosaic**
- Lipids are **fluid** in nature.

- Proteins = 50 % of dry wt of membrane
- lipids = 45 % “
- Carbohydrate = 5% “

both sides.

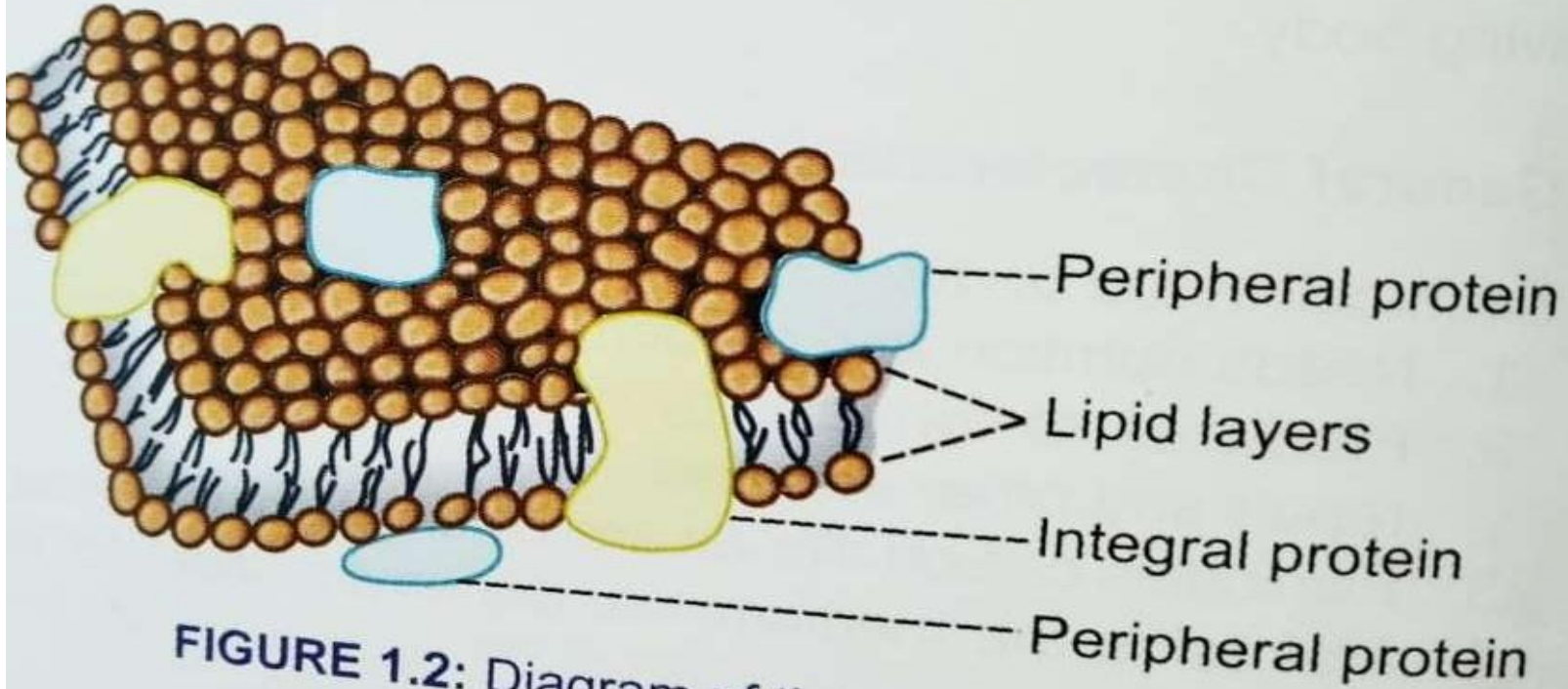


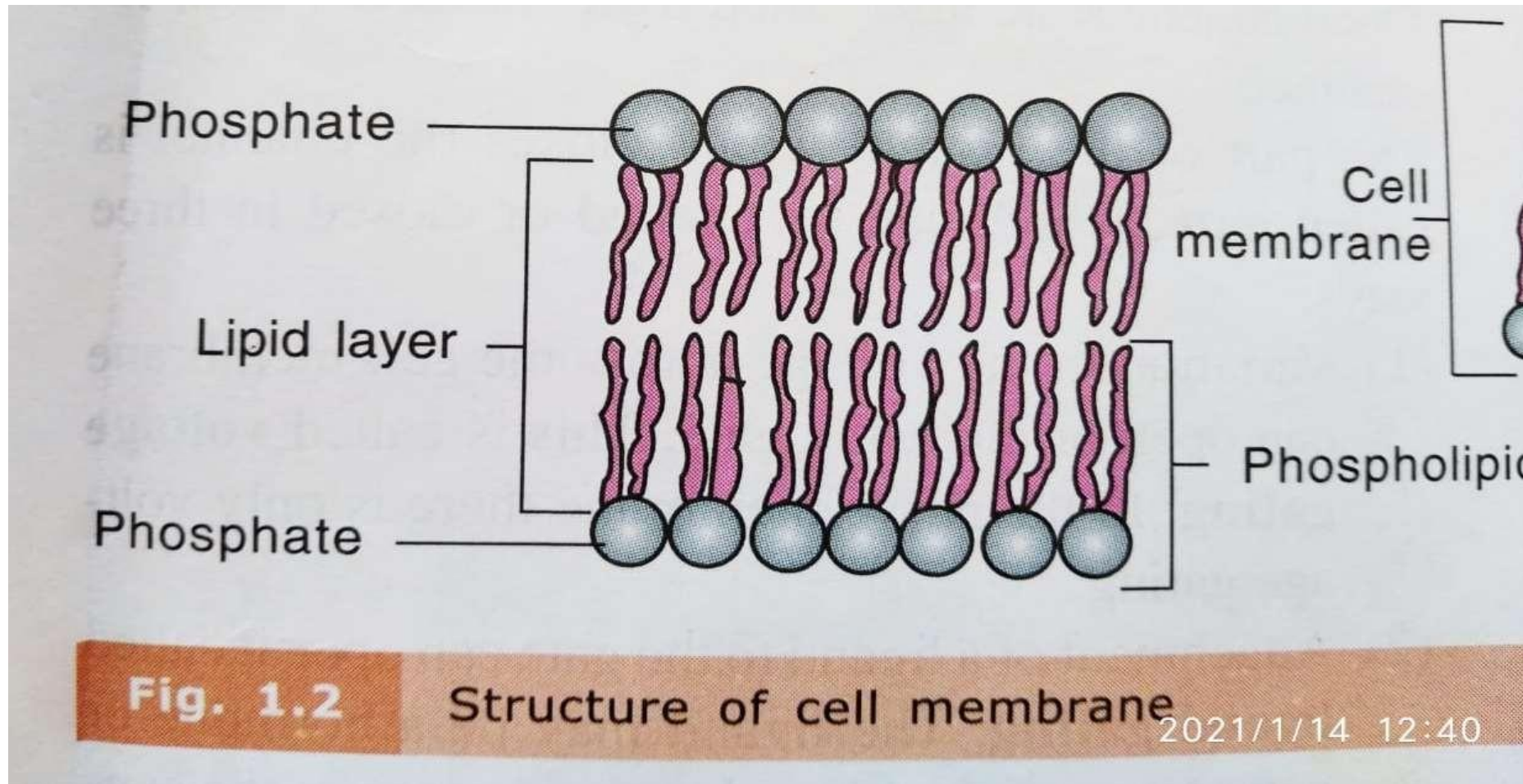
FIGURE 1.2: Diagram of the cell membrane

Lipids

Lipids ---- Phospholipids , cholesterol and glycolipids
--mainly phospholipids

- Phospholipid molecule --shape – clothes pin
- It has head and tail
- **Head** contains PO₄ group, +vely charged, **hydrophilic**
- **Tail** – contains 2 fatty acids chains, and **hydrophobic**

lipid molecules are arranged- tail ends towards centre and head ends directed outwards the cell memb



Protein layer of Cell Membrane

- According to arrangement - 2 type of proteins
- Integral proteins & peripheral proteins
- **Peripheral proteins**- present on **outer surface** of lipid layer
 - - **do not penetrate** the cell memb
- **Integral proteins** - located in the **inner surface** of cell memb
 - -- penetrate the cell memb
- **Transmembrane proteins**- lie throughout the memb

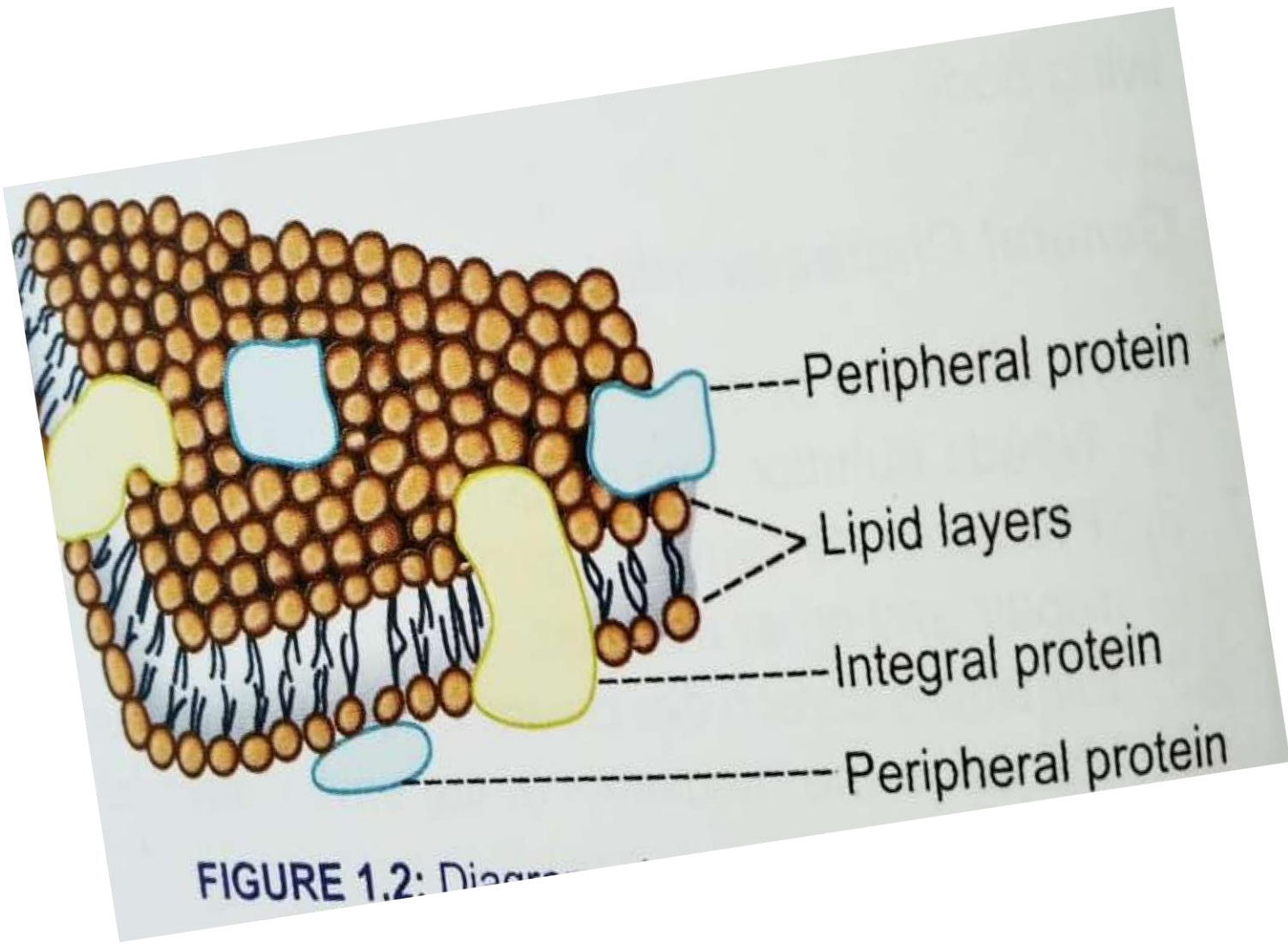
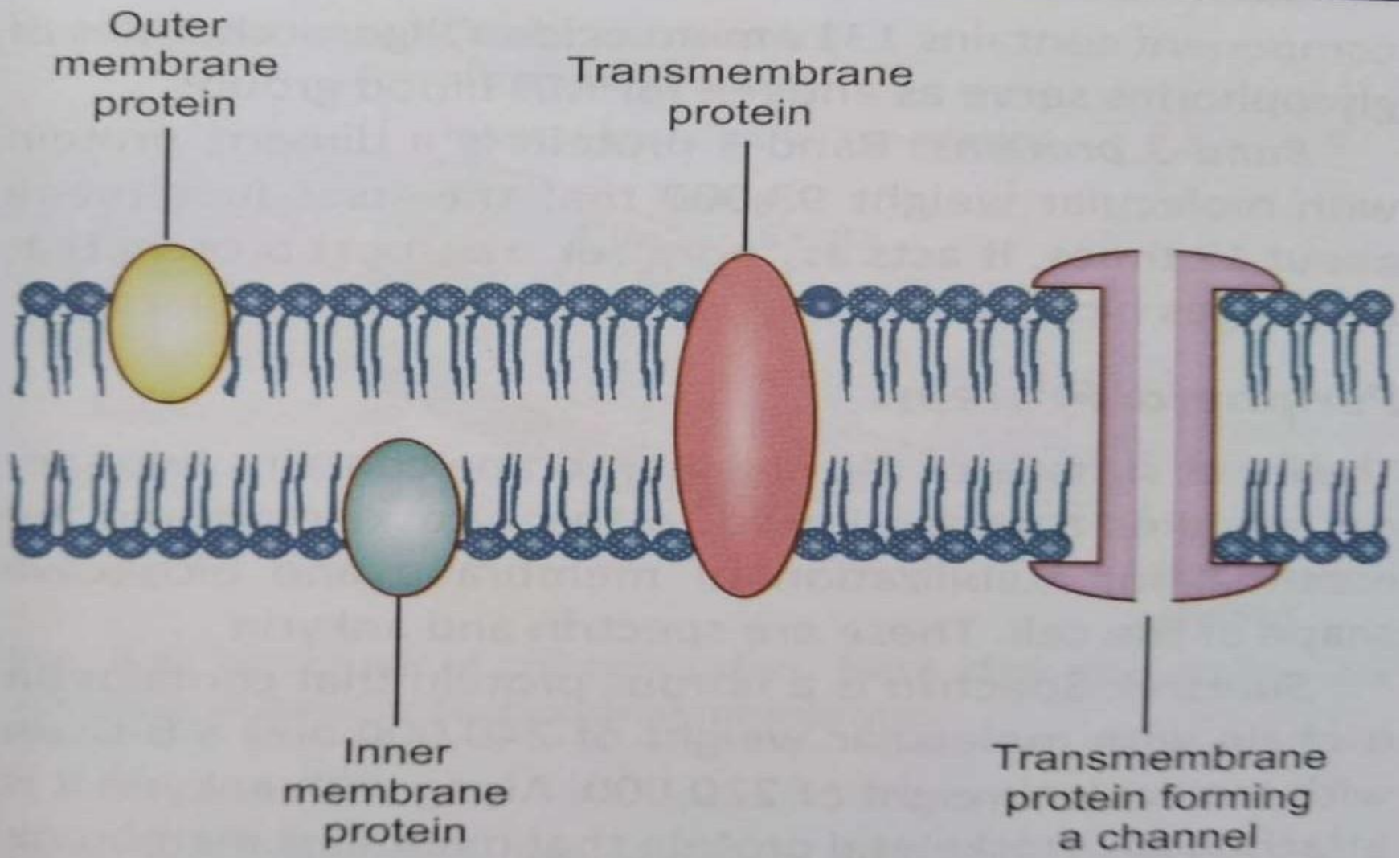


FIGURE 1.2: Diagram of a cell membrane



Functions of proteins

- Structural components of membrane
- Protein pumps
- Carrier proteins
- Ion channels
- Enzymes
- Antigens
- Receptors
- Cell adhesion molecules

Transport across cell memb

1 **Passive transport**

simple diffusion

facilitated diffusion

osmosis

2 **Active transport**

primary active transport

secondary active transport

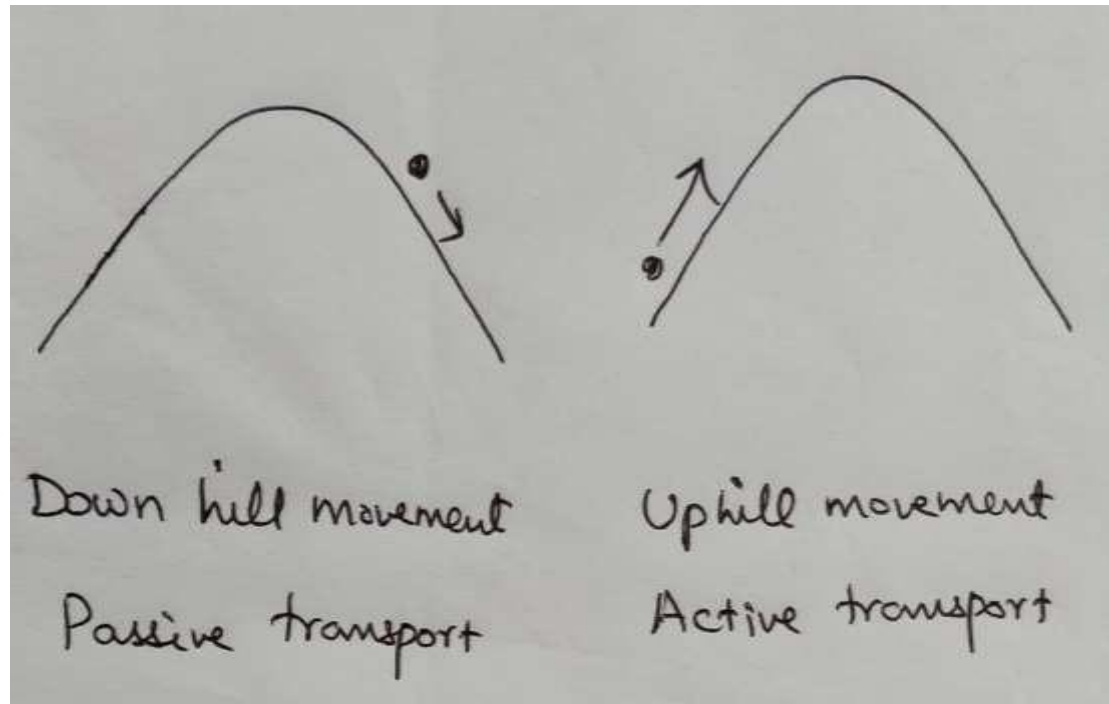
3 **vesicular transport**

endocytosis – phagocytosis and pinocytosis

exocytosis

Passive transport

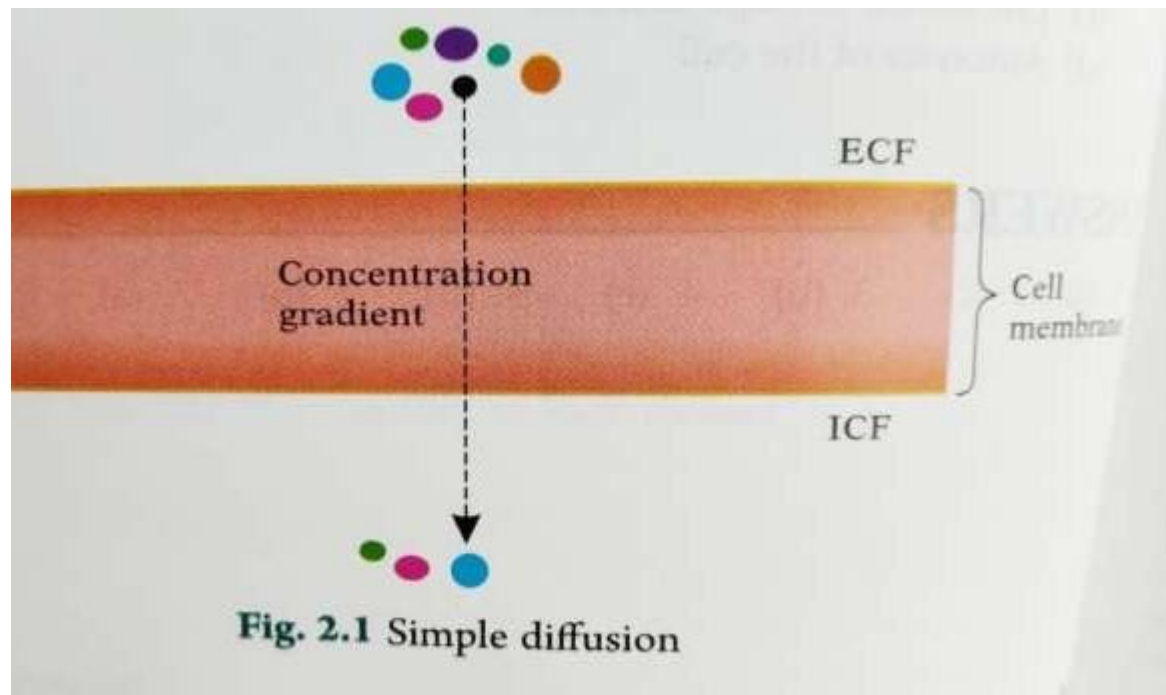
- Here substances move across cell memb **without any expenditure of energy**
- -- transport **from high conc to low conc** ie, along the gradient
- ---**Down hill movement**



Diffusion

– Passage of ions or molecules from a region of higher conc to a region of lower conc without expenditure of energy

- Simple diffusion
- Facilitated diffusion



- **Simple diffusion**
- It occurs either through lipid bilayer or protein layer of cell memb

- **Diffusion through lipid bilayer.—**
- Depends on lipid solubility
- **Lipid soluble** substances – O₂, N₂, CO₂, alcohol, steroid hormone etc

- **Simple diffusion through protein layer (protein channels)**
- **Lipid insoluble** substances pass through protein channels present in CM ---- eg ions

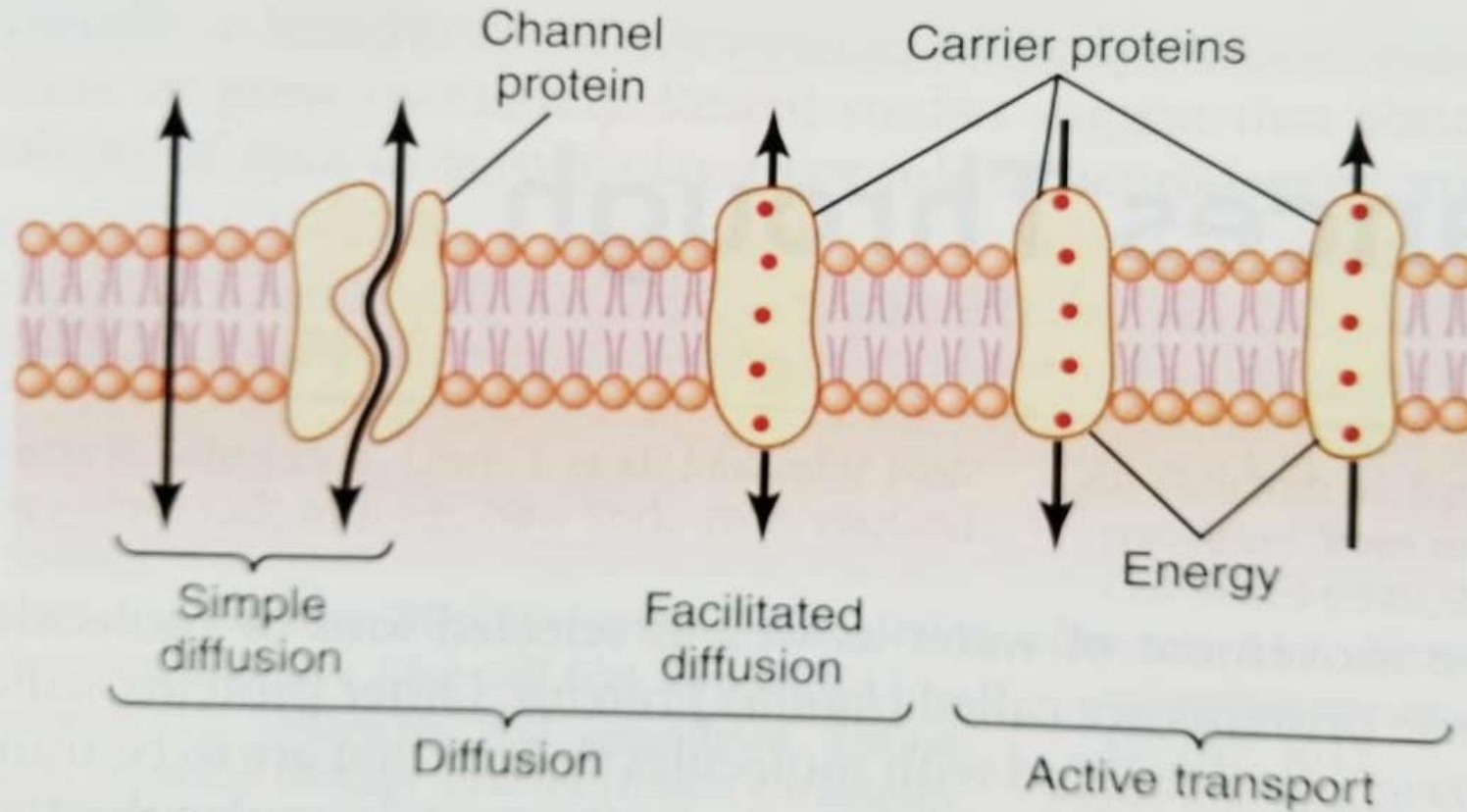


Figure 4.2

- Protein channels

- tube shaped channels or hydrophilic pores which extend in CM from ICF to ECF

- Protein channels = ion channels

- **specificity**

- Eg Na channels - allow only Na

- K+ “ - K+

- Ca Ca

Factors affecting diffusion

- Thickness of membrane ---inversely proportional
- Size of molecule- “
- Lipid solubility - directly proportional
- Surface area of membrane “
- Temperature “
- Conc gradient “
- Distribution of protein channels in cell memb “

Regulation or gating of channels

- Channels - opened
- - closed

- Opened channels
- they are always open , known as leaky channels (ungated channels)
- Eg K⁺ channel

- Closed channels = gated channels
- Gates are present

Gated channels

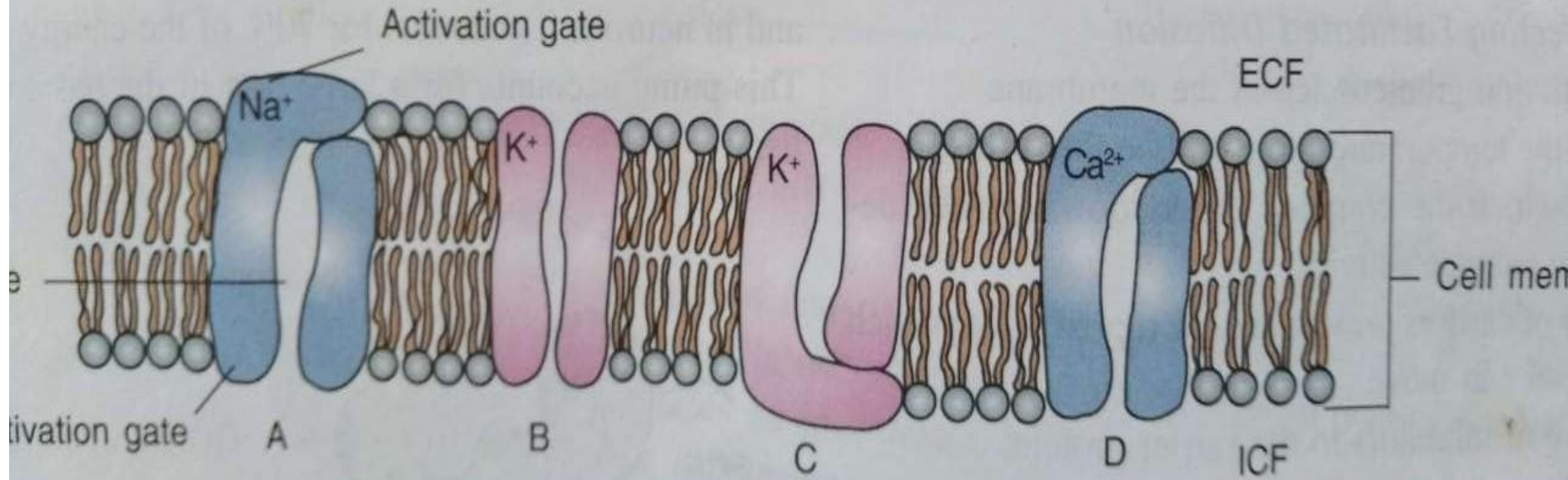
- Gated channels -3 types
- Voltage gated channel
- Ligand gated channel
- Mechanical gated channel
- **Voltage gated channel** – they open or close only if there is any change in pot difference across the C M

- **Ligand gated channel**

- these channel open when some chemical molecules (ligands) bind with the gate

- **Mechanical gated channels**

- they open by some mechanical factors like stretch, sound , touch etc



1.3 Transmembrane protein channels. A, Sodium channel; B, Potassium leak channel; C, Gated K⁺ channel; D, Calcium channel

Sodium Channel

Sodium channels are also tetrameric in structure.

...ries the substance to the interior of the cell.

Na channel

- It is a tetramer (has 4 sub units)
- Subunits surround a central pore
- Channel diameter= .5 nm
- Hydrated ion diameter = .36 nm
- Na channel is closed from outside in resting state
- No of channels in unmyelinated nerve = 110 / squm of cell memb
- in myelinated nerve, at node of ranvier= 2000 / squm
- Na channel blockers- tetrodotoxin (TTX), Saxitoxin

- K⁺ channels

- tetramer

- Channel diameter= .3nm

- Hydrated ion diameter= .24nm

- K⁺ channel blockers- tetraethyl ammonium, 4-aminopyridine

leaky channel

closed channel

- Ca channel
- closed from outside in resting condition
- Blockers– verapamil, nifedepine

- **Facilitated diffusion**

(or **carrier mediated diffusion**)

- If size of substances or ions $>$ that of channel ,

they cannot easily diffuse through channel, they can pass with the help of some carrier proteins - facilitated diffusion .

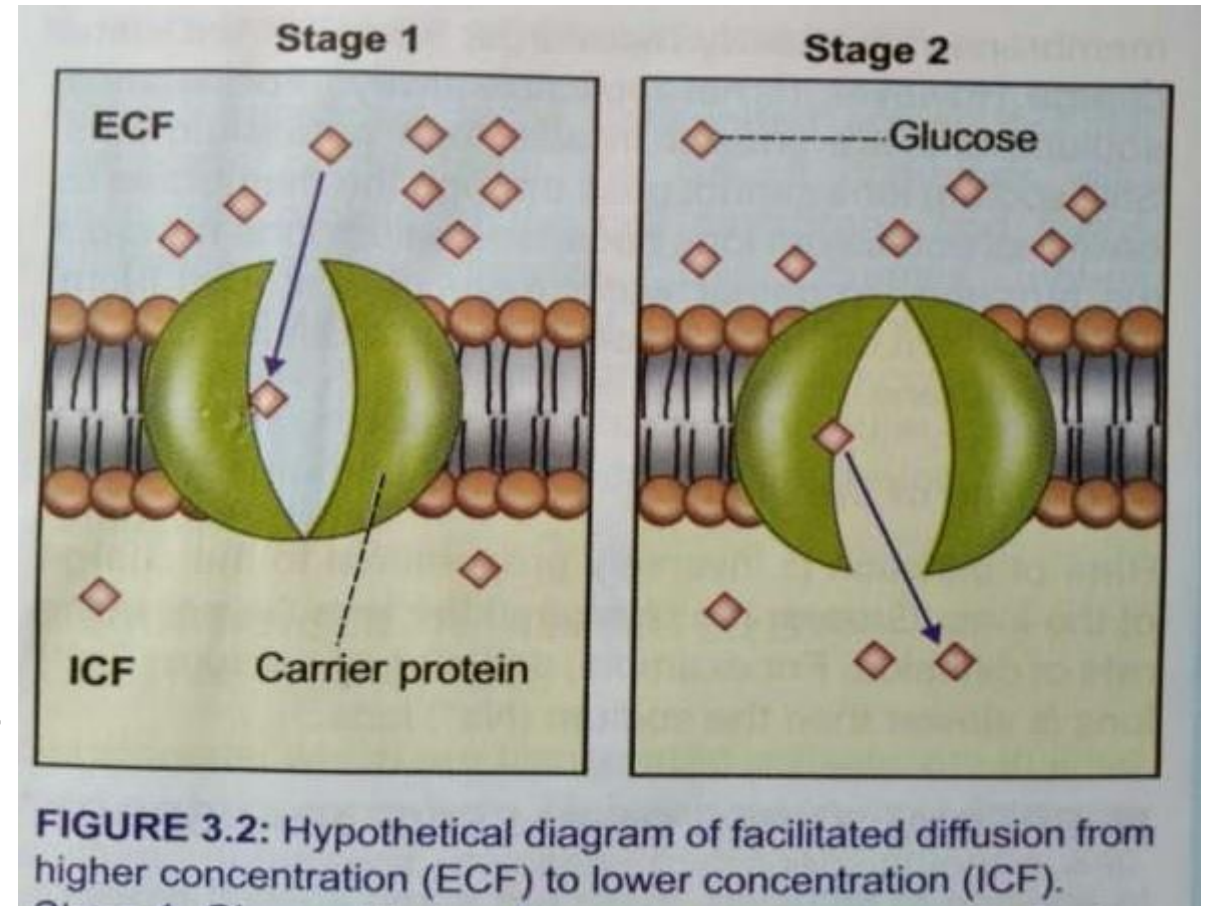
Carriers have binding sites and specificity

Eg FD of glucose

-

FD of glucose by GLUT across intestinal epithelium

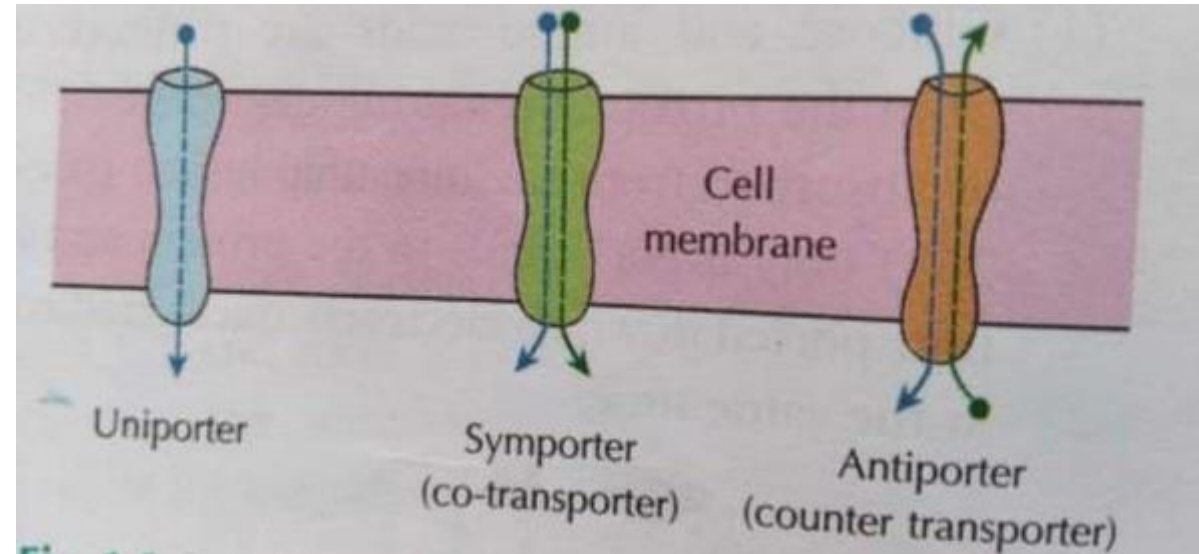
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- Glucose bind with GLUT
- Conformational change of carrier
- Glucose releases from GLUT



- Eg substances transported by FD include –fructose, galactose, vitamin

Carrier proteins

- 3 types

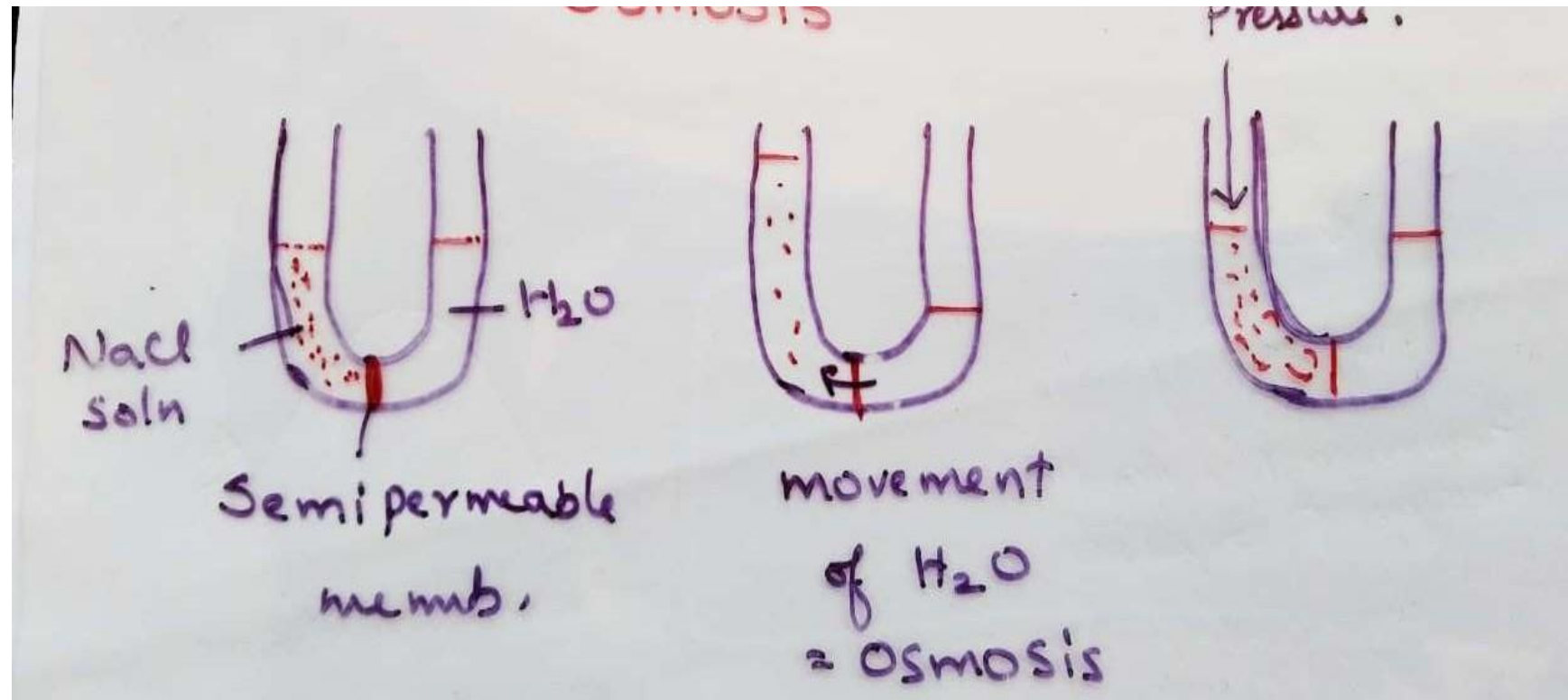


- **Uniport**-transports only 1 type of molecule in 1 direction
Eg F D of glucose
- **Symport** – transports 2 substances in same direction
---Secondary active transport of glucose
- **Antiport** – transports 2 substances in opposite directions.
---Na+K+ pump

osmosis

- it is defined as the movement of water or any other solvent from an area of lower solute concentration to an area of higher solute concentration across a semipermeable membrane

- fig



- Osmotic pressure

- the osmosis can be prevented by applying pressure to the more concentrated soln.
- The amount of pressure required to prevent osmosis is called osmotic pressure

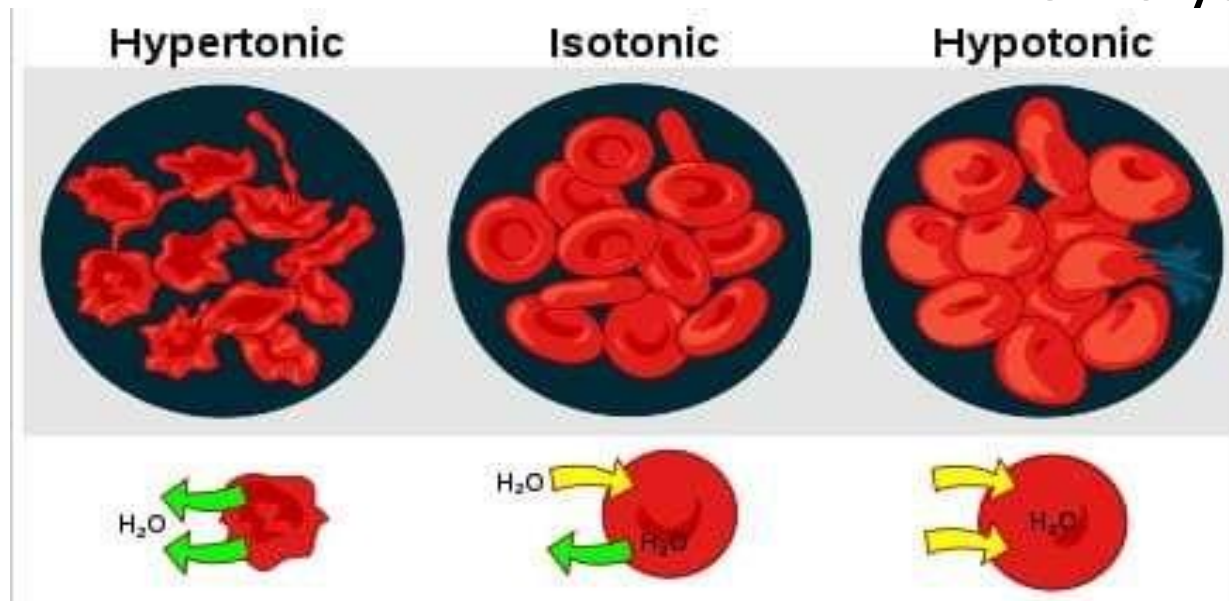
- **Osmole** – the conc of osmotically active particles is expressed in osmoles
- **Osmolarity** – no of osmoles per litre of soln
- **Osmolality** – no of osmoles per kg of solvent

- **Tonicity** - osmolality of a soln relative to plasma
- **Isotonic solns** – the solns that have same osmolality as plasma eg .9% NaCl soln. Or 5% glucose soln.
- **Hypertonic soln** – soln whose osmolality > plasma
conc > .9% NaCl
- **hypotonic soln** – soln whose osmolality < plasma
eg -- pure water

- RBC in different solns

- In isotonic soln – no change for RBC
- In hypertonic soln.—RBC will shrink---crenation
- In hypotonic soln - RBC will swell and rupture

---hemolysis



Active transport

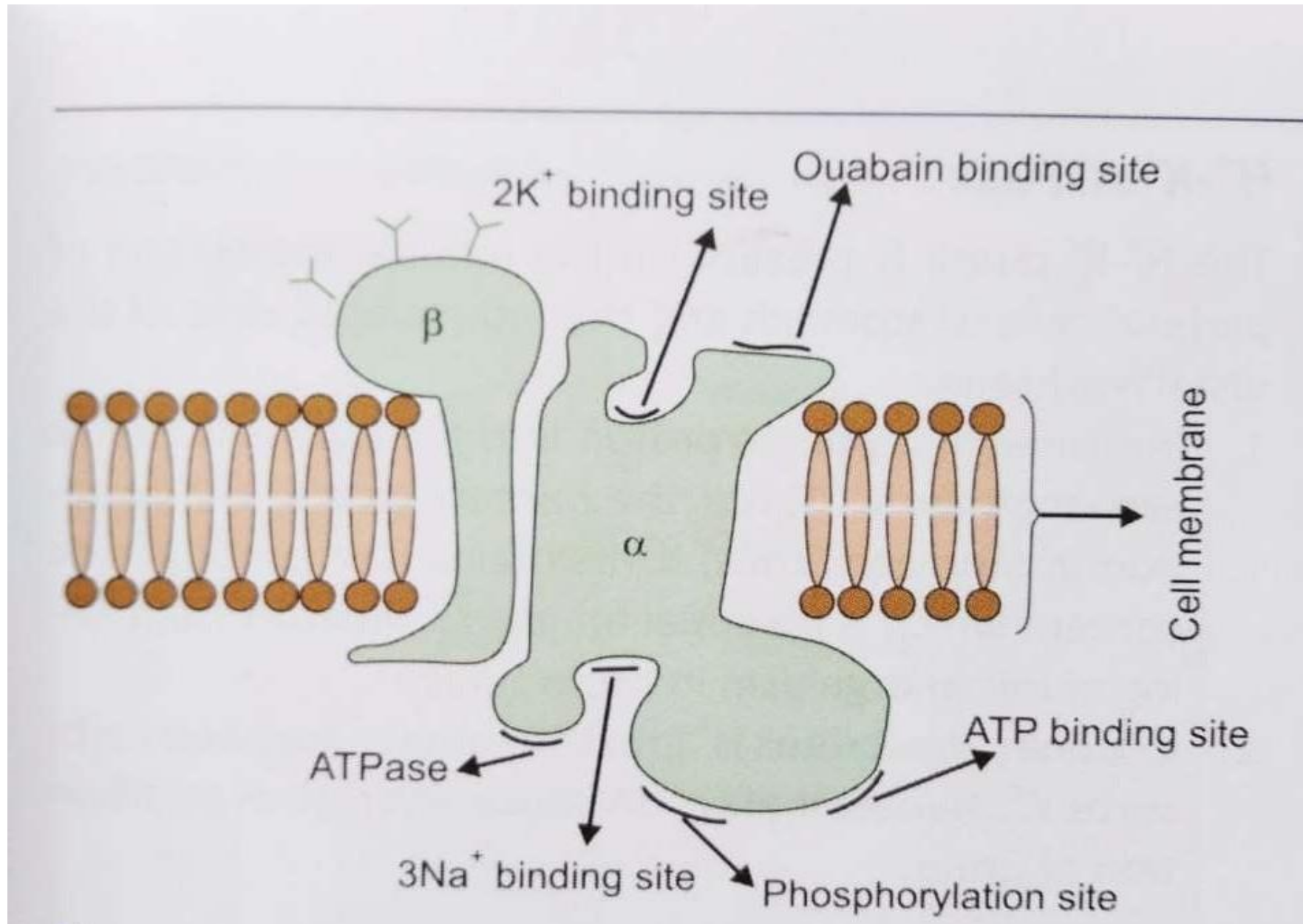
- Transport of substances against their electrical and chemical gradients at the expenditure of energy
- The energy is provided by hydrolysis of ATP
- Transport against gradient -- uphill movement

- 2 types – primary active transport
- -- secondary active transport

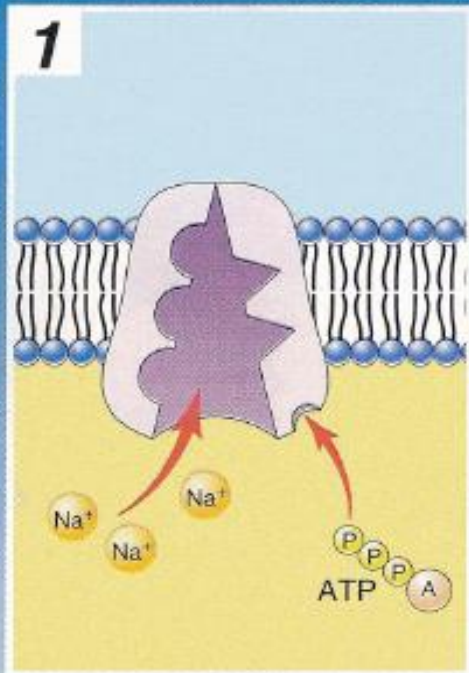
- **Primary active transport** – energy is derived directly from hydrolysis of ATP
- eg , Na⁺K pump , K⁺H⁺ pump

Sodium potassium pump---Na⁺K⁺ pump

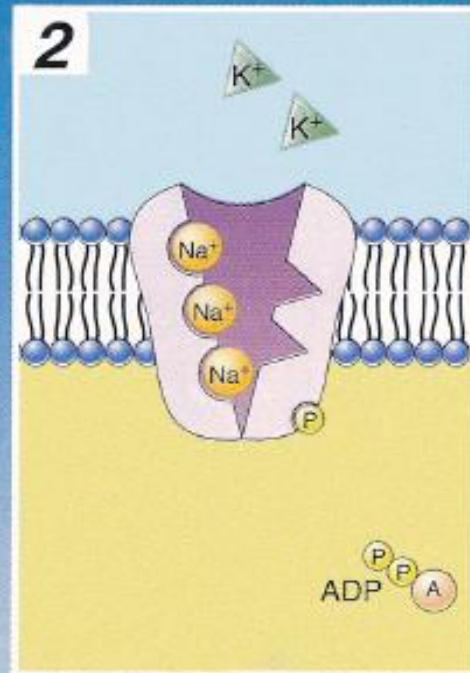
- Present in all the cells of body
- ATPase as carrier molecule - Na⁺K⁺ ATPase = Na⁺K⁺ pump
- **Structure**
 - 2 separate proteins – **alpha and beta**
 - Alpha subunit has
 - **in the inner surface**
 - 3Na⁺ binding site
 - ATP binding site
 - phosphorylation site
 - **in outer surface**
 - 2 K⁺ binding site
 - ouabain binding site



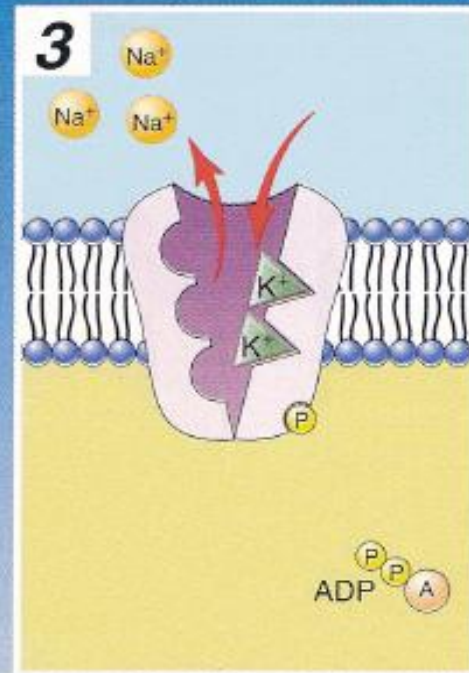
SODIUM-POTASSIUM PUMP



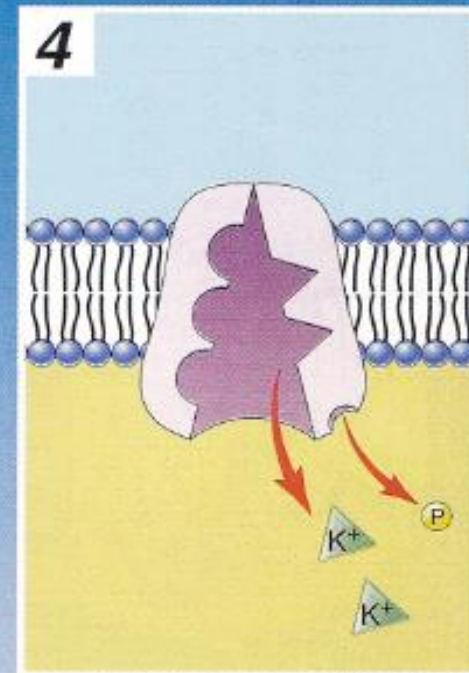
The sodium-potassium pump binds three sodium ions and a molecule of ATP.



The splitting of ATP provides energy to change the shape of the channel. The sodium ions are driven through the channel.



The sodium ions are released to the outside of the membrane, and the new shape of the channel allows two potassium ions to bind.



Release of the phosphate allows the channel to revert to its original form, releasing the potassium ions on the inside of the membrane.

Na⁺ K⁺ pump - mechanism of operation

- It is activated when intracellular Na⁺ conc increases
- When 3Na⁺ and ATP bind with their binding sites , ATPase is activated and ATP is hydrolysed.
 - $ATP \rightarrow ADP + P_i + \text{energy}$
- Alpha unit is phosphorylated and causes conformational change in pump and extrudes 3Na⁺ to ECF
- Then 2K⁺ bind extra cellularly to its binding site – dephosphorylation occurs
- Pump returns to its previous conformation and releases 2K⁺ to ICF

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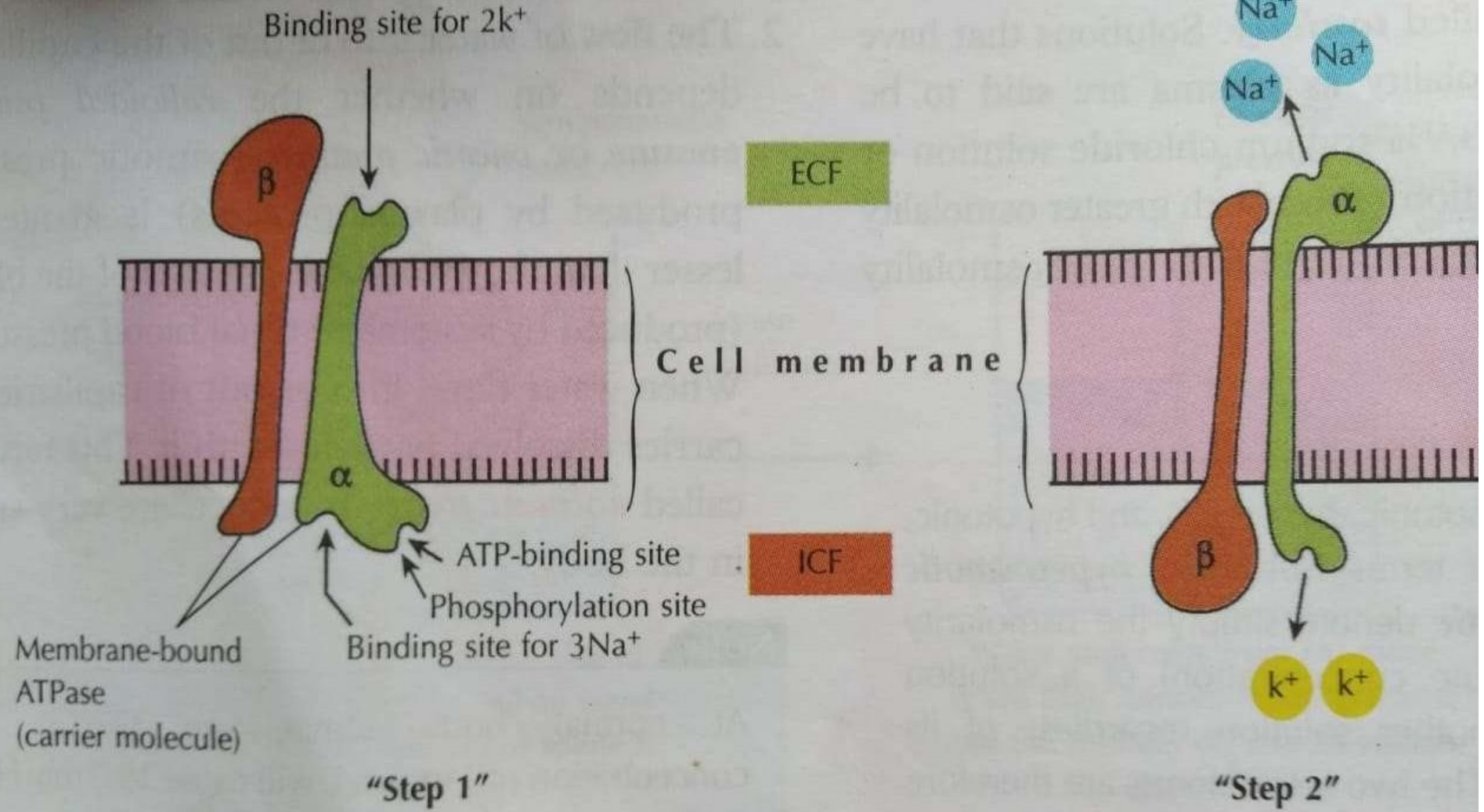


Fig. 1.2.4 Mechanism of operation of Na⁺ - K⁺ pump

Functions of Na⁺K⁺ pump

- 1 electrogenic activity

- it pumps 3Na⁺ outward and 2K⁺ inwards—coupling ratio = 3:2

Net loss of 1 +ve charge inside, continuous activity creates -vity insid

- 2 responsible for distribution of Na⁺ and K⁺ across cell memb

- 3 controlling cell volume

it maintains normal tonicity across cell memb. If pump is not working, inside the cell Na⁺ conc increases,(Na is osmotically active particle) it leads endosmosis of water -- cell will swell-- hemolysis

Regulation of sodium pot pump

The activity of sod pot pump is **increased** by

- cAMP
- thyroid hormone
- aldosterone
- insulin
- G actin

The activity of sod pot pump is **decreased** by

- low temperature
- Oxygen lack
- dopamine
- Ouabain
- digitalis

NaK pump----applied aspect

When blood is cooled at 4 degree celcius

—Na K pump becomes inactive,

so that plasma contains **excess K⁺** and
interior of RBC contains **excess Na**

This is a dangerous situation

---during blood transfusion – it may lead

hyperkalaemia

Secondary active transport..

It occurs in some tissues,

when Na pumps out of cell due to by Pr A T - **Na K pump** , a large **conc gradient** of sodium develops with high conc outside than inside.

This gradient represents a **store house of energy** ,
because the excess Na outside the membrane is always attempting to diffuse to the interior.

Under appropriate conditions, this diffusion energy of Na can pull other substances along with Na through cell memb.----this is **co-transport**

If substance moves in opposite to Na ---**counter transport**

The energy is not directly due to hydrolysis of ATP, but stored energy due to primary active transport.

ie, **energy is derived from the ionic conc gradient ,that have been created by Pr A T**

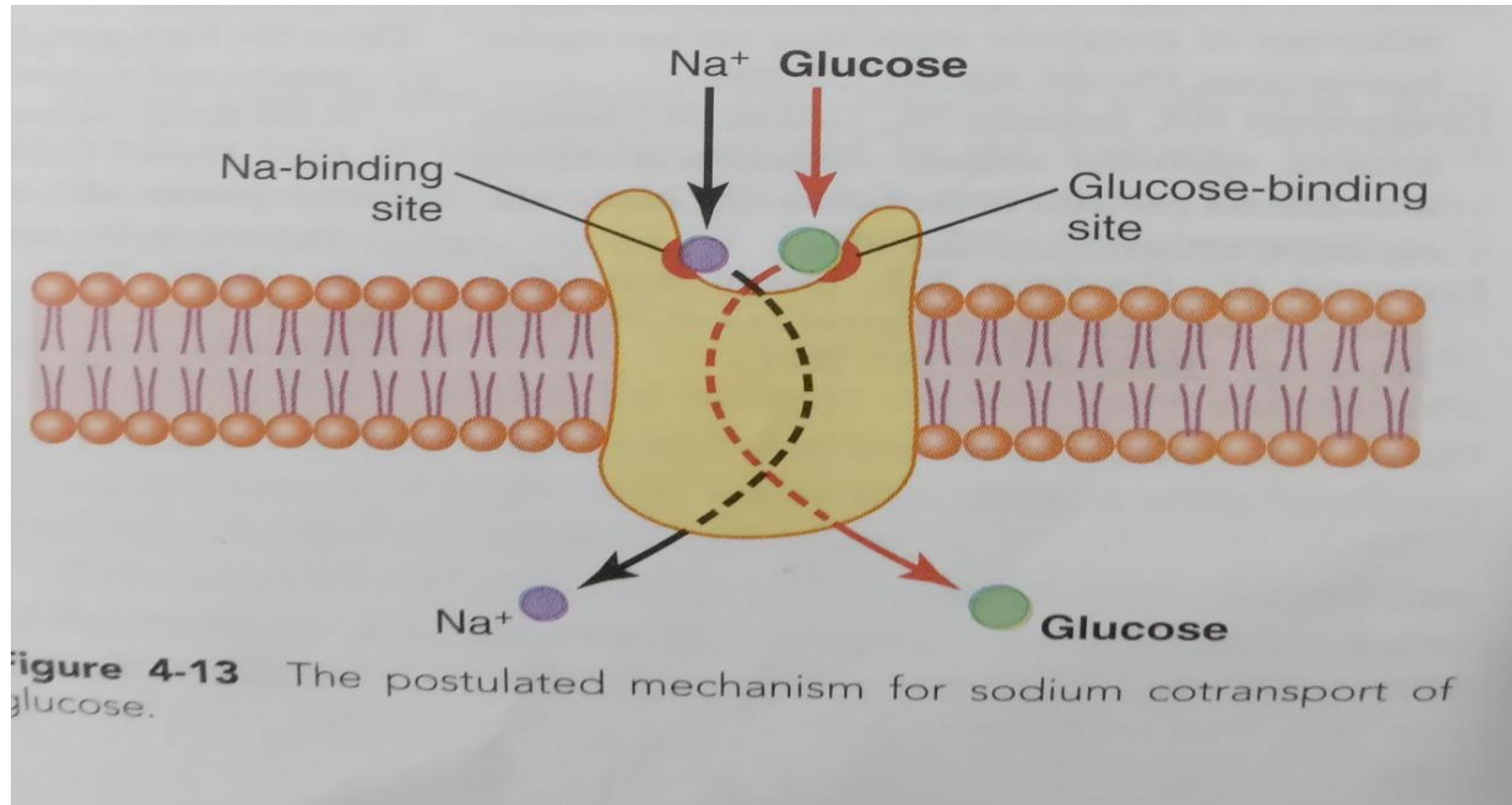
Co transport----symport

Eg---Na co transport of **glucose**

---Na Co transport of **amino acids**

-----occurs through epithelial cells of intestinal tract and renal tubules of kidney.

Here when Na and glucose attach with protein , then **conformational change occurs in protein** , and both move in same direction to interior

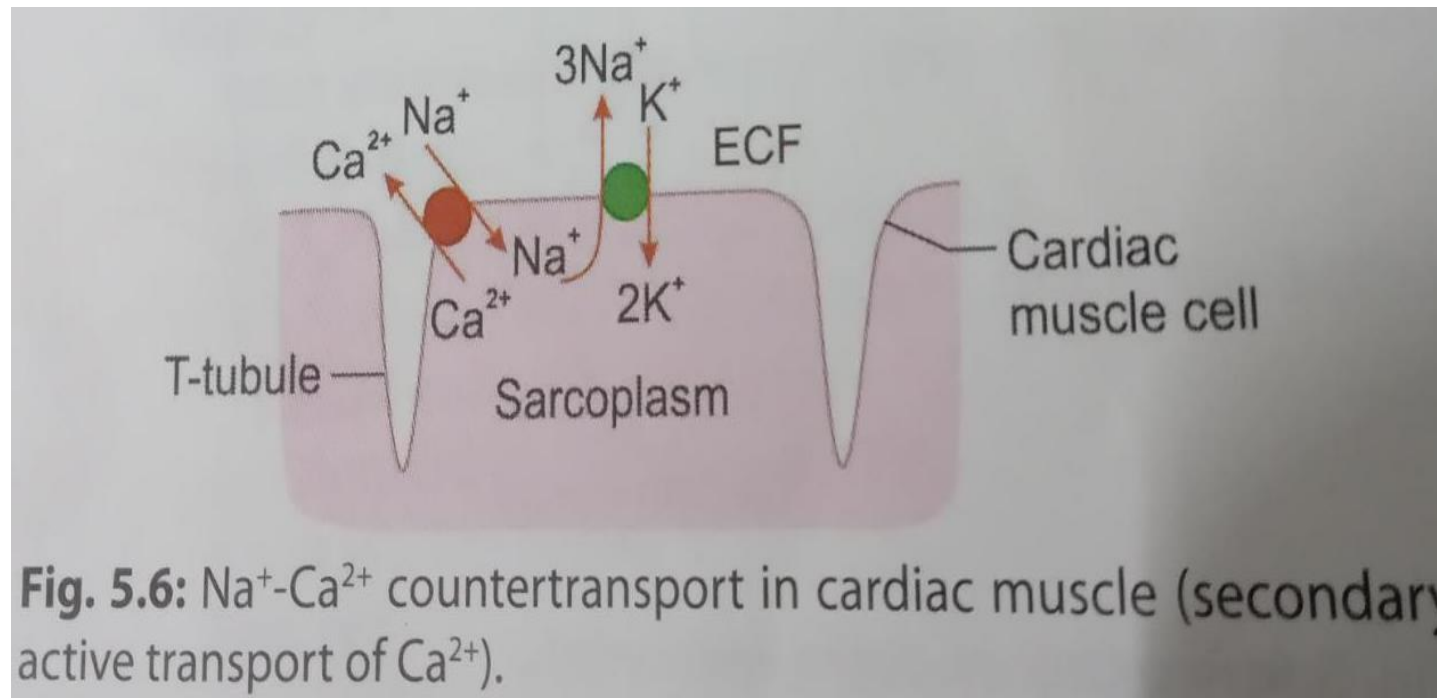


Sodium counter transport

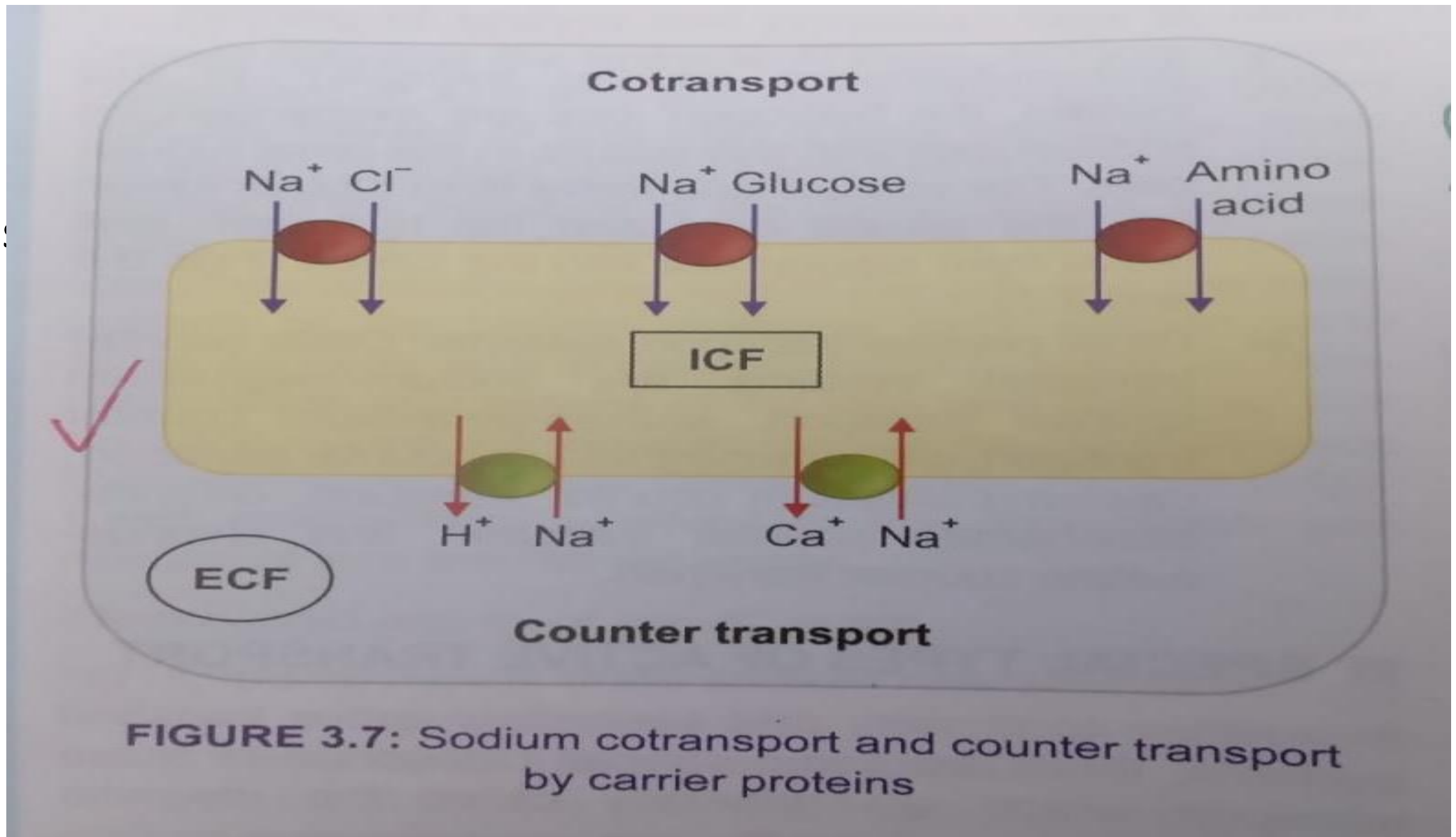
Sodium Ca counter transport ---- in myocardial cells

When Na enters, Ca goes out

Na H counter transport ---present in renal tubular cells.



• Fig of s



Digitalis---drug used in congestive cardiac failure

---causes inhibition of Na K pump

--Na exit is decreased

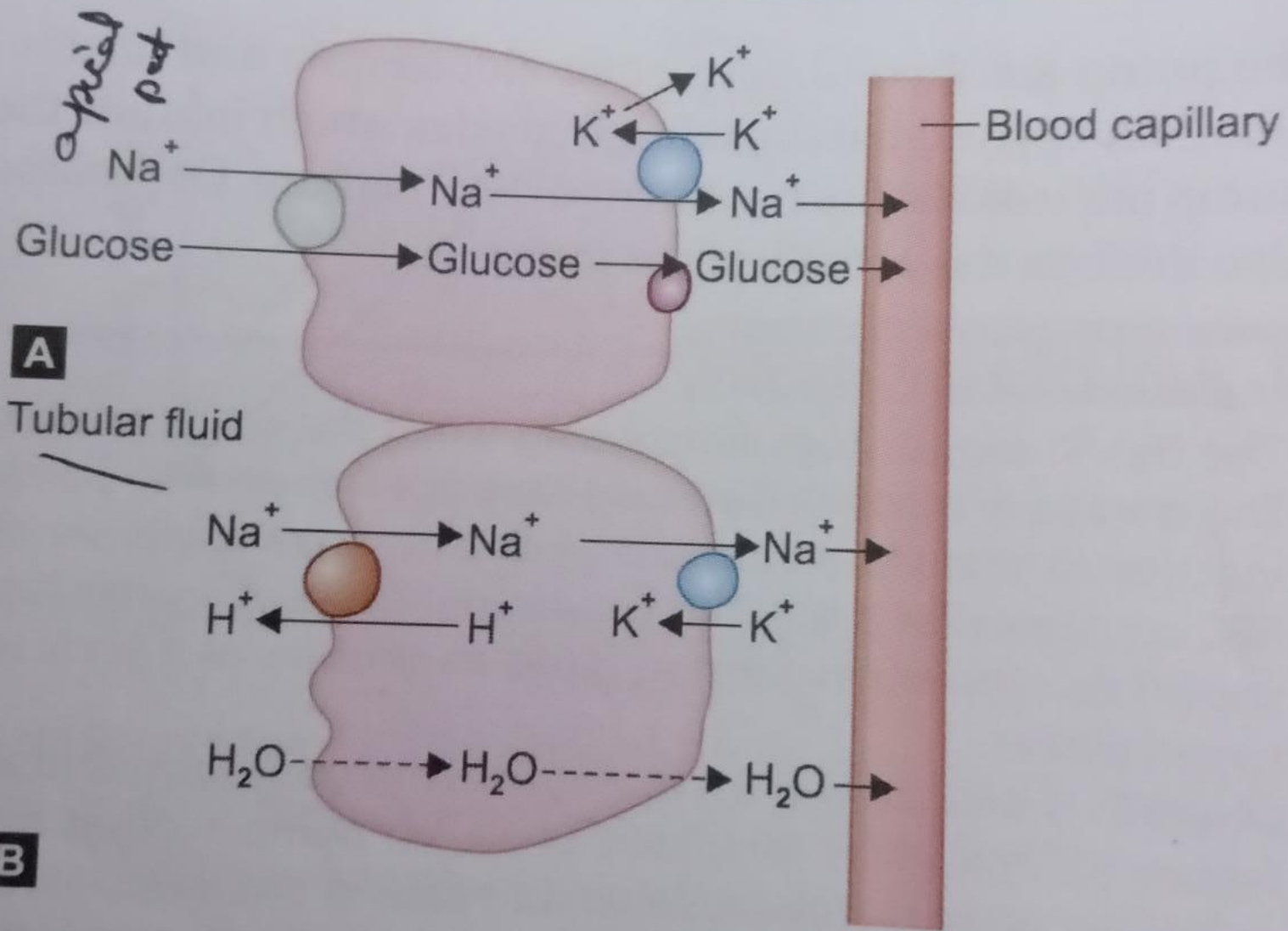
--increase in ICF Na conc & decreasing Na gradient across
the cell memb

--decreases Na influx (due to sec A T)

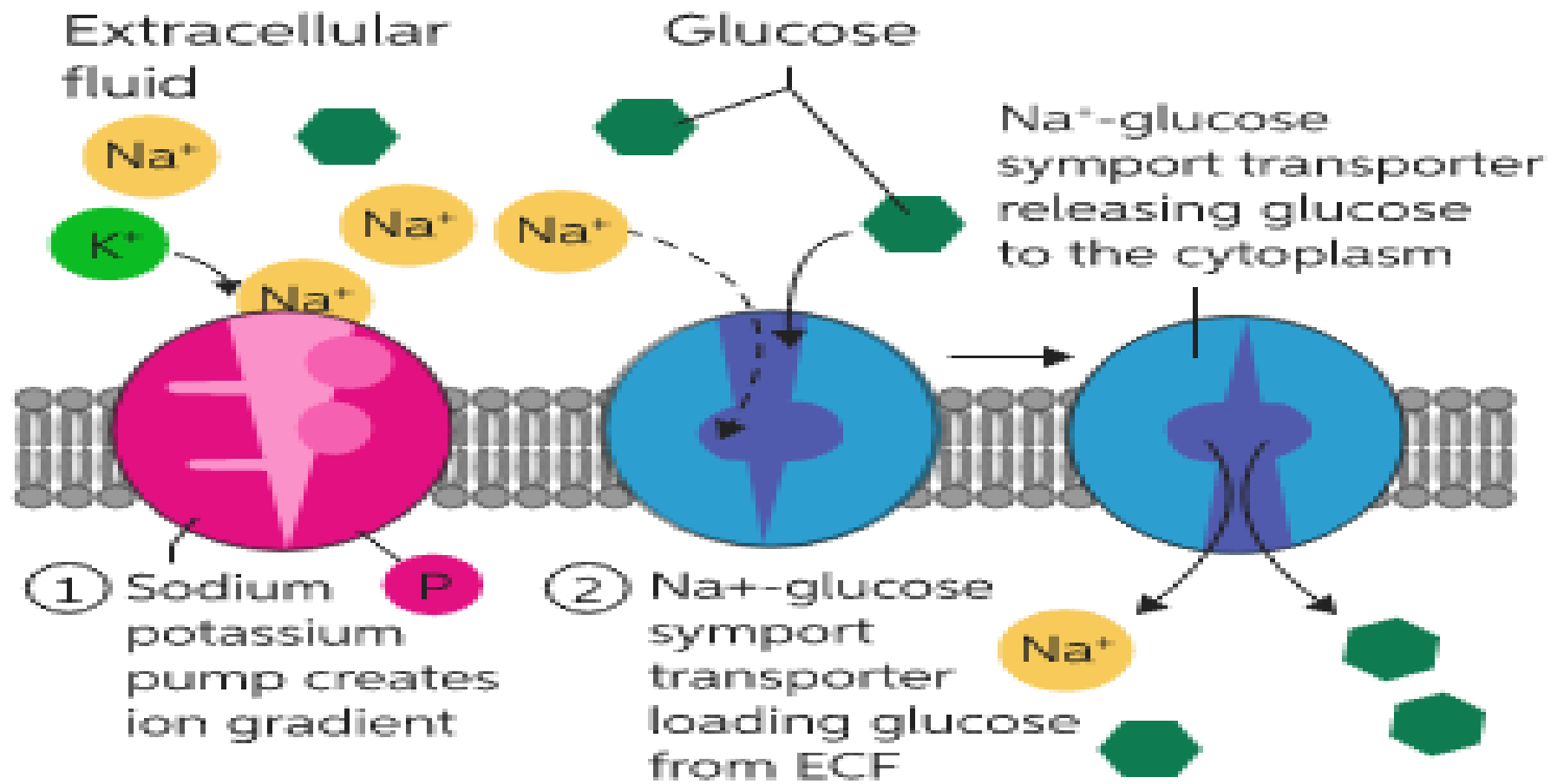
and thus decreases Ca efflux through NaCa exchanger
(2ndary transport)

Increase in Intracellular Ca in myocardial cells

---increase contractility of myocardium.



Figs. 5.7A and B: Secondary active transport in the renal tubular cells: (A) Glucose-sodium symport; (B) Na^+ - H^+ antiport (Glucose and H^+ are transported by secondary active transport).



Vesicular transport

- Bulk transport
- Transport of macromolecules –large protein molecules, hormones etc across cell memb by making vesicles
- 2 types - endocytosis and exocytosis

- Endocytosis
- Here extracellular substances eg bacteria, dead tissue, foreign particles etc are engulfed by the cells
- If the engulfing material is solid that is **phagocytosis** (cell eating) and if it is liquid - it is **pinocytosis** (cell drinking)

- **Phagocytosis** – engulfing - worn out cells, bacteria, viruses, dead tissue etc
- The particle makes contact with the cell memb, which then invaginates.
- The endocytic vesicle pinches off from cell memb and fuses with lysosome and hydrolytic enzymes break down the ingested material
- **Pinocytosis** -- engulf aminoacids, fatty acids, etc

Fig. 1.2.6 Carrier type processes

(cell-drinking).

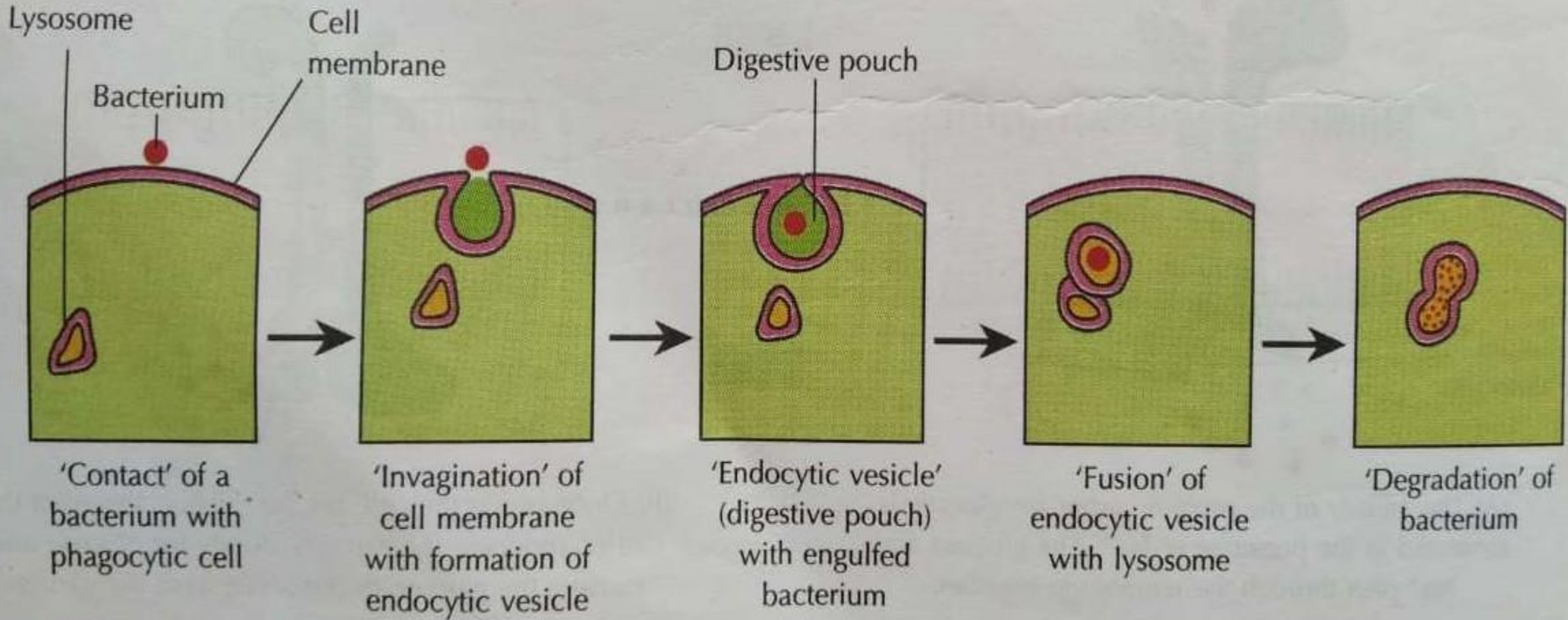


Fig. 1.2.7 Sequence of events in endocytosis

exocytosis

- Here substances synthesized within the secretory cells like digestive enzymes, hormones, mucus , neurotransmitters etc are secreted out of cell etc
- Substance move to cell memb and fuses with it
- The area of fusion breaks down leaving the contents to the outside.

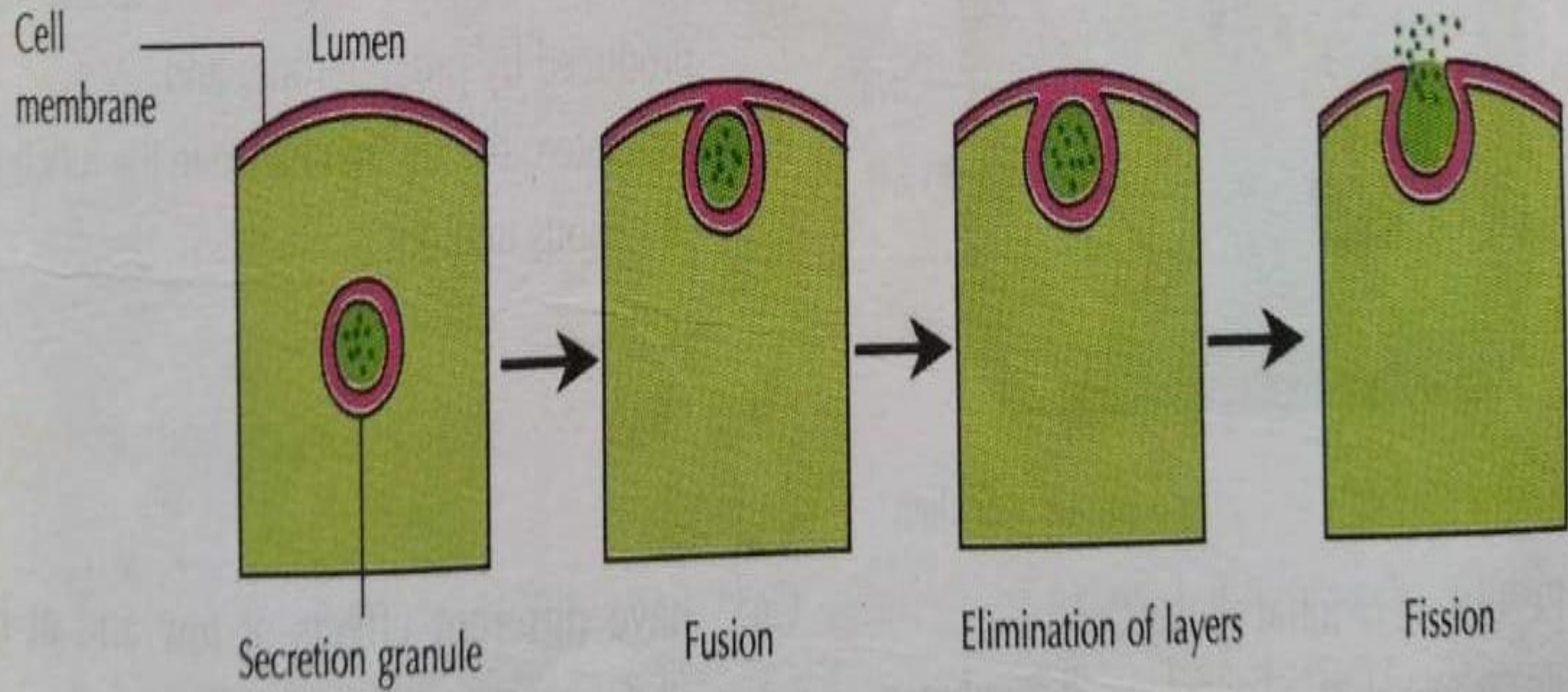


Fig. 1.2.8 Sequence of events in exocytosis

- end end

End end