CELL MEMBRA

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INTRODUCTION

- Every cell, prokaryotic or eukaryotic, is surrounded by a thin layer of outermost boundary called the **plasma membrane or cell membrane or plasma - lemma.**
- It maintains the difference of the internal environment of the cell from its external environment by controlling the entrance and exit of the molecules and ions.
- It checks the loss of metabolically useful substances and encourages the release of toxic metabolic byproducts of the cell. Thus, it functions as **semi-permeable or selectively permeable membrane.**
- **It is** about 70-100A in thickness.
- It is an important cell organelle composed of lipids and proteins.

History

- It had been shown by **Karl W. Nageli (1817-1891) that the cell membrane is semi-permeable** and is responsible for the osmotic and other related phenomena exhibited by living cells.
- Before 1855, he used the term zellen membrane in his early papers.
- The term plasma membrane was used in 1855 by him to describe the membrane as a firm protective film that is formed by out flowing cytoplasm of an injured cell when protein rich cell sap came in contact with water.

Lipid nature of cell membrane

Overton 1895

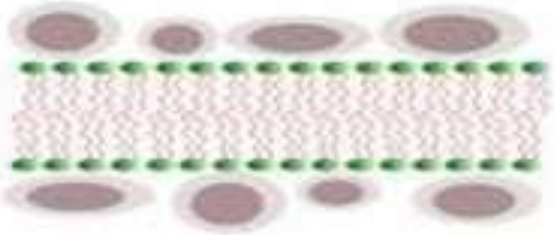
Orientation of polar molecules

Langmuir 1917

Amphipathic lipids form a lipid bilayer

Gorter and Grendel 1925

Proteins are associated to the cell membrane

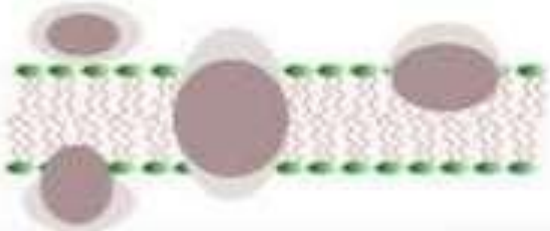


Davson and Danielli 1935

The pattern dark-clear-dark is universal for cell membranes.
It is called unit membrane

Robertson 1960

There are transmembrane proteins. Molecules can move laterally.



Singer and Nicolson 1973

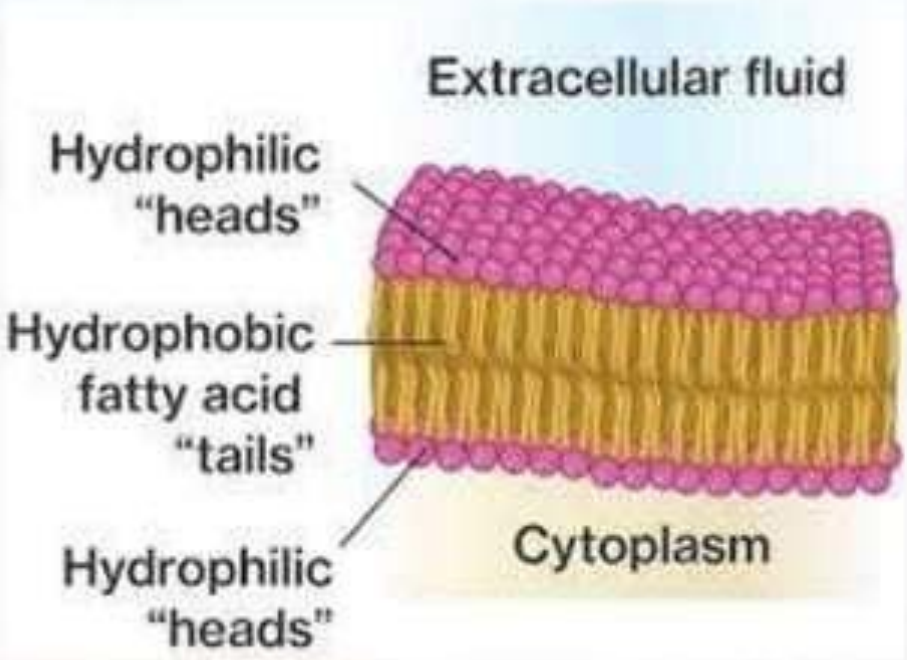
MODELS OF CELL MEMBRANE

MODELS OF CELL MEMBRANE

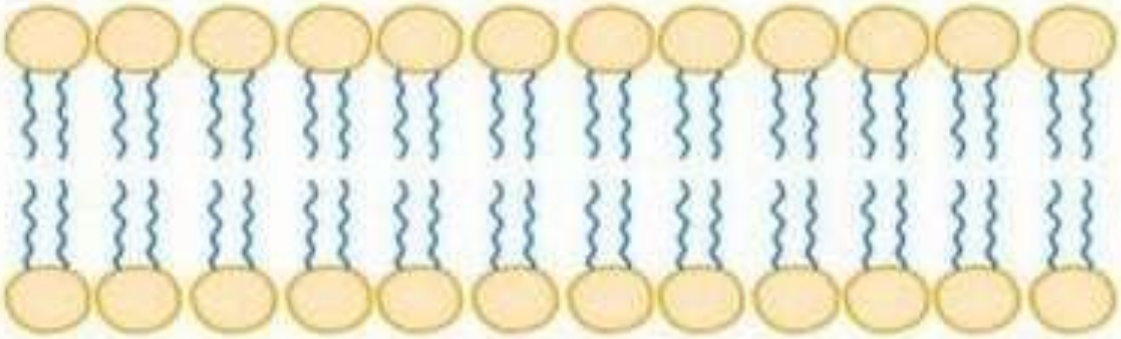
1. • Lipid and Lipid Bilayer Model
2. • Protein-Lipid –Protein hypothesis
   - Sandwich Model
   - Unit membrane model
3. • Fluid mosaic Model

Lipid and Lipid Bilayer Model:

- This model explain the structure of plasma membrane given by Overton, Gorter and Grendel.
- Previously only indirect information was available to explain the structure of plasma membrane.
- In 1902, Overton observed that substances soluble in lipid could selectively pass through the membranes. On this basis he stated that plasma membrane is composed of a **thin layer of lipid**.
- Subsequently, Gorter and Grendel in 1926 observed that the extracted from erythrocyte membranes was twice the amount expected if a single layer was present throughout the surface area of these cells. On this basis they stated that plasma membrane is made up of **double layer of lipid** molecules.
- These models of Gorter and Grendel could not explain the proper structure of plasma membrane but they put the foundation of future models of membrane structure.



The phospholipid bilayer



Hydrophilic Phosphate heads

Hydrophobic Fatty Acid Tails

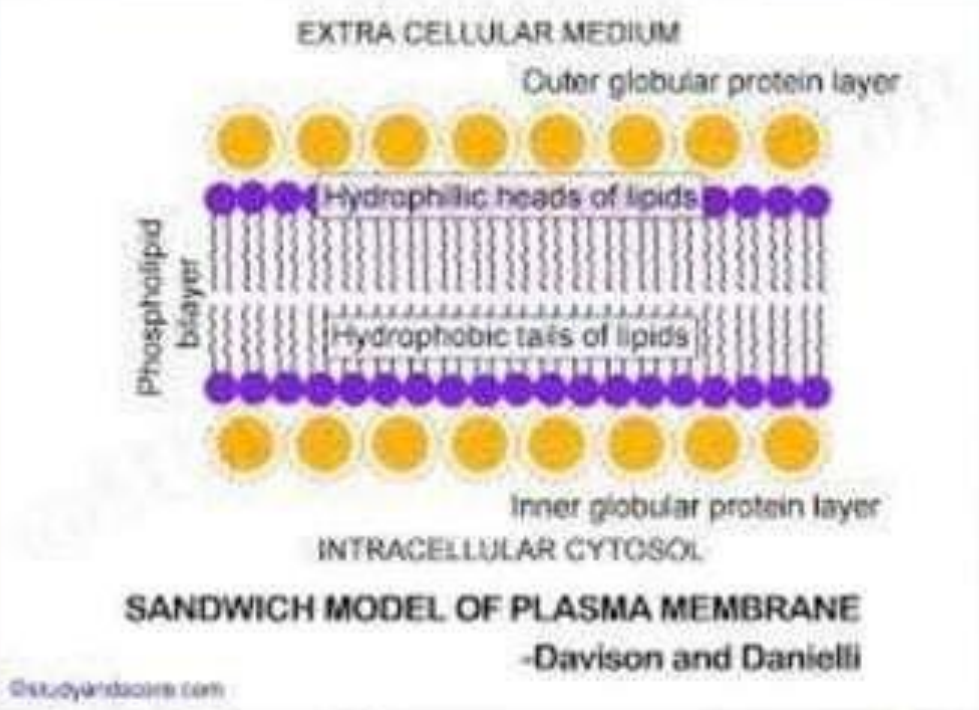
Hydrophilic Phosphate heads

PROTEIN-LIPID –PROTEIN HYPOTHESIS

- This hypothesis was proposed by Davson Daniell and Robertson.
- When surface tension measurements made on the membranes, it suggests the presence of proteins. After the existence of proteins the initial lipid bilayer model proposed by Gorter and Grendel was modified. It was suggested that surface tension of cells is much lower than what one would expect if only lipids were involved.
- It may also be observed that if protein is added to model lipid water system, surface tension is lowered. This suggested indirectly the presence of proteins. On this basis Davson and Danielli proposed that plasma membrane contained a lipid bilayer with protein on both surfaces.
- Initially they supposed that proteins existed as covalently bonded globular structures bound to the polar ends of lipids. Subsequently they developed the model in which the protein appears to be smeared over the hydrophilic ends of the lipid bilayer. This model makes its popularity for a long time.
- With the availability of electron microscope later, fine structure of plasma membrane could be studied. Definite plasma membrane of 6 nm to 10 nm (10nm = 100 Å; 1 nm = 10_{-6}mm) thickness was observed on surface of all cells, and plasma membranes of two adjacent cells were found to be separated by a space, 1-15nm wide.

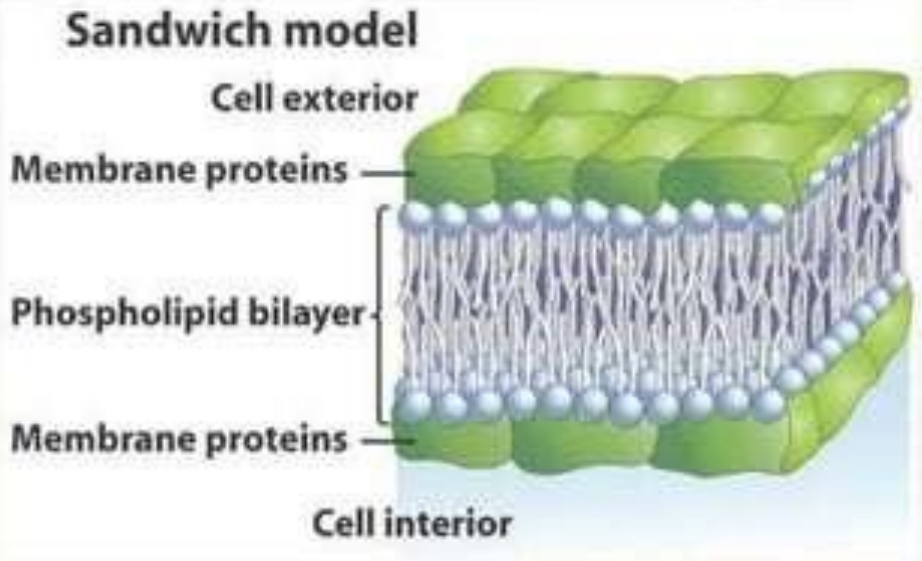
Danielli and Davson Model (Sandwich Model)

- Harvey and Coley (1931) and Danielli and Harvey (1935) studied surface tension of cell membrane and on the basis of their observation they pointed out the existence of protein molecules adsorbed on the surface of lipid droplets which reduce the surface tension of droplets.
- This conclusion led James Danielli and Hugh Davson in 1935 to suggest bimolecular leaflet model of cell membrane. Danielli and Davson model was the first attempt to describe membrane structure in terms of molecules and to relate the structure to biological and chemical properties.
- According to bimolecular model of Danielli and Davson, plasma membrane consists of two layers of phospholipid molecules (a bimolecular leaflet) in which phospholipid molecules are arranged in such a way that hydrophilic heads of the phospholipid molecules face outside and hydrophobic non-polar lipid chains are associated in the inner region of leaflet.
- The hypothesis also suggested that the polar ends of lipid molecules are associated with monomolecular layer of globular proteins.
- The plasma membrane would thus consist of a double layer of phospholipid molecules sandwiched between two essentially continuous layers of protein.



SANDWICH MODEL OF PLASMA MEMBRANE

-Davison and Danielli



Problems with the Davson-Danielli model

By the end of the 1960s, new evidence cast doubts on the viability of the Davson-Daniell model.

- The amount and type of membrane proteins vary greatly between different cells.
- It was unclear hoe the protein in the model would permit the membrane to change the shape without bonds being broken.
- Membrane proteins are largely hydrophobic and therefore should not be found where the model positioned them: in the aqueous cytoplasm and extracellular environment.

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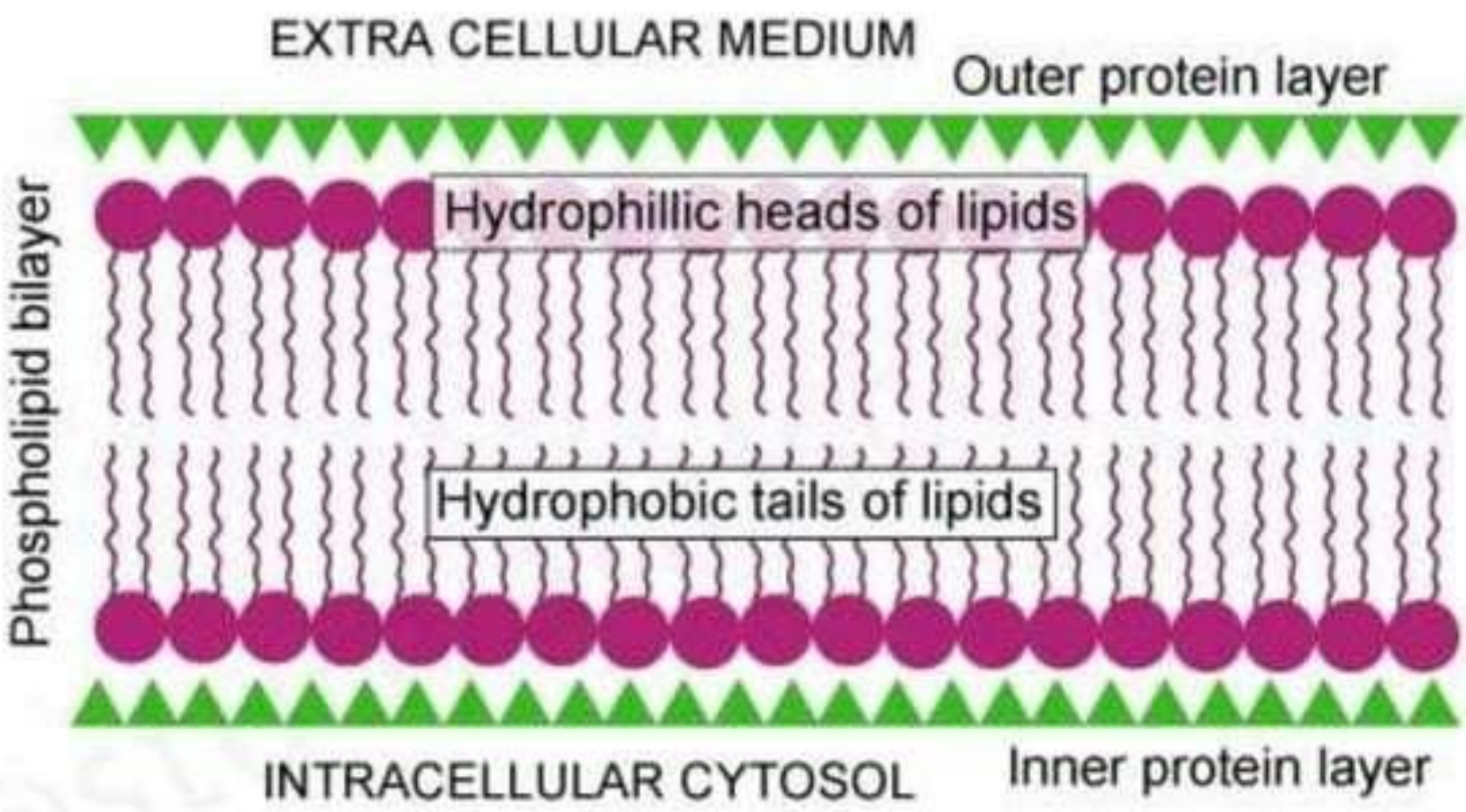
- This basic model has been modified from time to time. Danielli (1938) suggested the presence of two types of proteins; tangentially arranged in contact with the lipid and globular proteins on the outer surface. Again Davson and Danielli (1943) and Danielli (1954) considered proteins to be in the form of a folded P-chain.
- Perhaps, these units form micelles of membranes indicated in recent electron micrographs. Membrane models are usually postulated to contain protein lined polar pores of about 7 Å diameter which probably permit the passage of small ions and water molecules across the membrane.
- In still other variations the proteins are thought to be in coiled or globular form on both sides of lipid layers [Fig. 2.3 (A), (B), (C)] or they are thought to be asymmetrical, with a folded P-chain on one side and globular proteins on the other [Fig. 2.3 (D)]. Models with globular proteins on both the sides or with folded P-proteins on both the surfaces and helical proteins extending into the pores are also suggested.

UNIT MEMBRANE MODEL

- In 1950 J. David Robertson studied the cell membranes from electron micrographs of sectioned material. The preparations involved usual fixing in solutions of osmium tetraoxide and potassium permanganate ($KMnO_4$), and dehydrating in solvents such as acetone before sectioning.
- In late 1950s Robertson summarized a large number of ultra-structural data obtained by him and some other workers and concluded that the plasma membrane and the membranes of all cell organalles were similar in structure. Although the similarity is not resolved by light microscopy, it is clearly seen in electron micrographs.
- This conclusion led Robertson in 1953 to propose unit membrane hypothesis according to which all biological membranes show generalised unit membrane construction.
- The unit membrane model visualises cell membrane as a trilaminar and indicates structure consisting of two dark osmiophilic layers separated by a light osmiophilic layer.

- The physical appearance of this trilaminar model has led to the term unit membrane. The unit membrane concept implies a trilaminar appearance with a bimolecular lipid layer between two protein layers.
- Each dense osmiophilic band is made up of protein (20 Å) and the polar groups of phospholipids (5 Å) and is thus 25 Å thick.
- The clear Osmiophilic zone 35 A in thickness is a bimolecular layer of lipids without the polar groups.
- In other words, the unit membrane is 75 Å thick with a 35 Å thick phospholipid layer between two 20 Å thick protein layers.
- The plasma membrane surrounding the cell is thicker at the free surfaces of the cell than where it is in contact with other cells.
- In unit membrane model the protein layers are assymetrical. On the outer surface it is mucoprotein while on the inner surface it is non-mucoid protein.



UNIT MEMBRANE MODEL OF PLASMA MEMBRANE

-Robertson

Fluid Mosaic Model:

- The fluid mosaic model of cell membrane was proposed in 1972 by S.J. Singer and G.L. Nicolson.
- According to this model, the cell membranes have been visualised as mosaics of lipids and proteins. The lipids are thought to be arranged primarily in a bilayer in which peripheral and integral proteins are embedded.
- Membrane proteins are not fixed within the lipid layer but are free to move laterally like icebergs floating in a sea of lipids. This picture has inspired Singer and Nicolson to coin fluid mosaic model.
- Singer and Nicolson considered the lipoprotein association to be hydrophobic and fluidity of the membrane results due to hydrophobic interaction. It should be noted that phospholipids and many intrinsic proteins are amphipatic molecules, i.e., both hydrophilic and hydrophobic groups occur within the same molecule.

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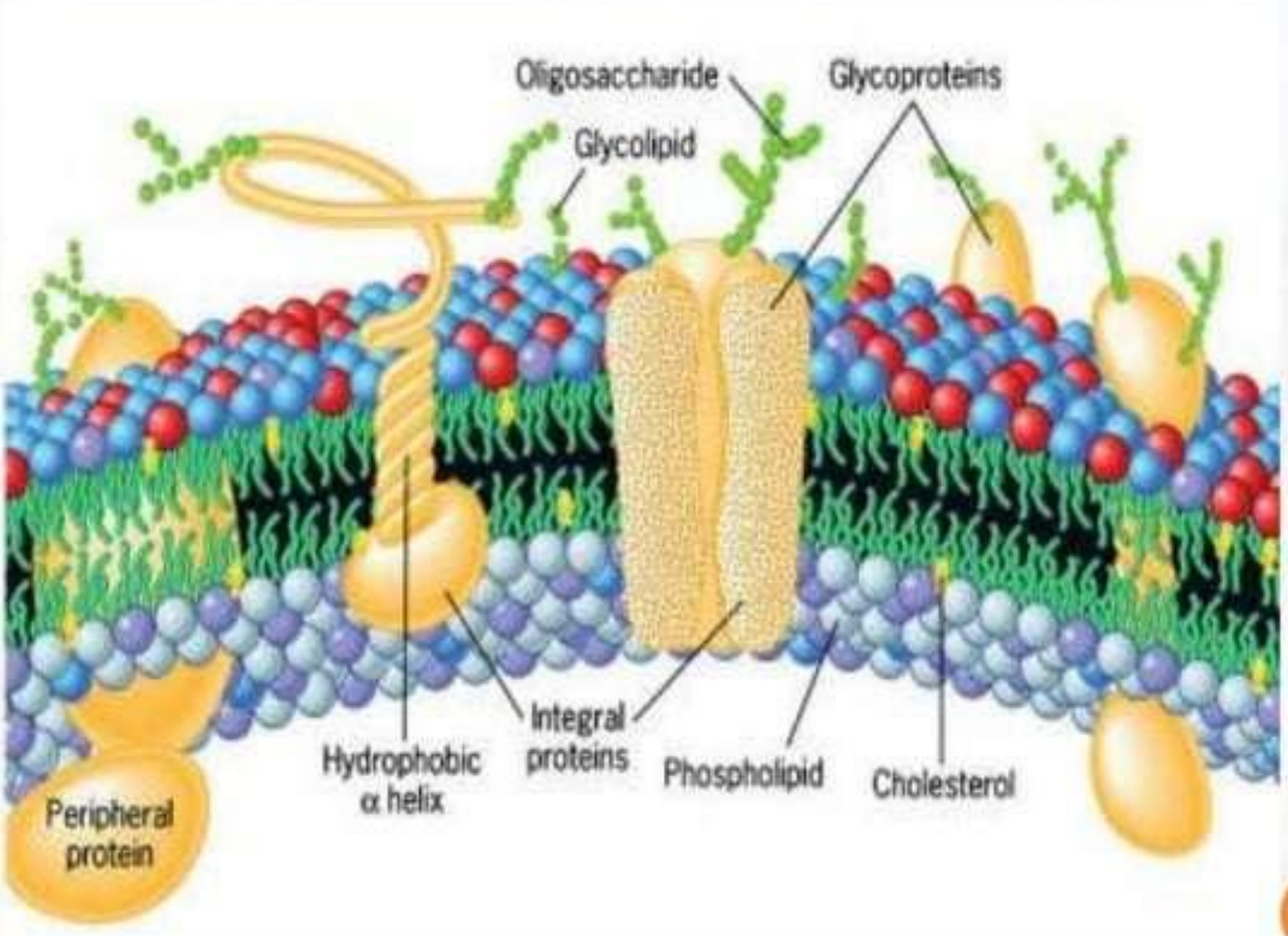
- The globular proteins of the membrane are of two different types: extrinsic (peripheral protein) and intrinsic (integral proteins).
- Because of rapid movement of lipid and protein molecules, the fluid mosaic model is different from the static picture of the membrane in Danielli and Davson model. The proteins of the membrane are concerned with the enzymatic activities, transport of molecules and with receptor function. The lipid bilayer acts as the permeability barrier.
- The fluidity of lipid is supported by many indirect studies based on x-ray diffraction, differential thermal analysis and electron spin resonance (ESR) techniques.


Oligosaccharide
Glycoproteins
Glycolipid
Hydrophobic
α helix
Integral
proteins
Phospholipid
Cholesterol
Peripheral
protein

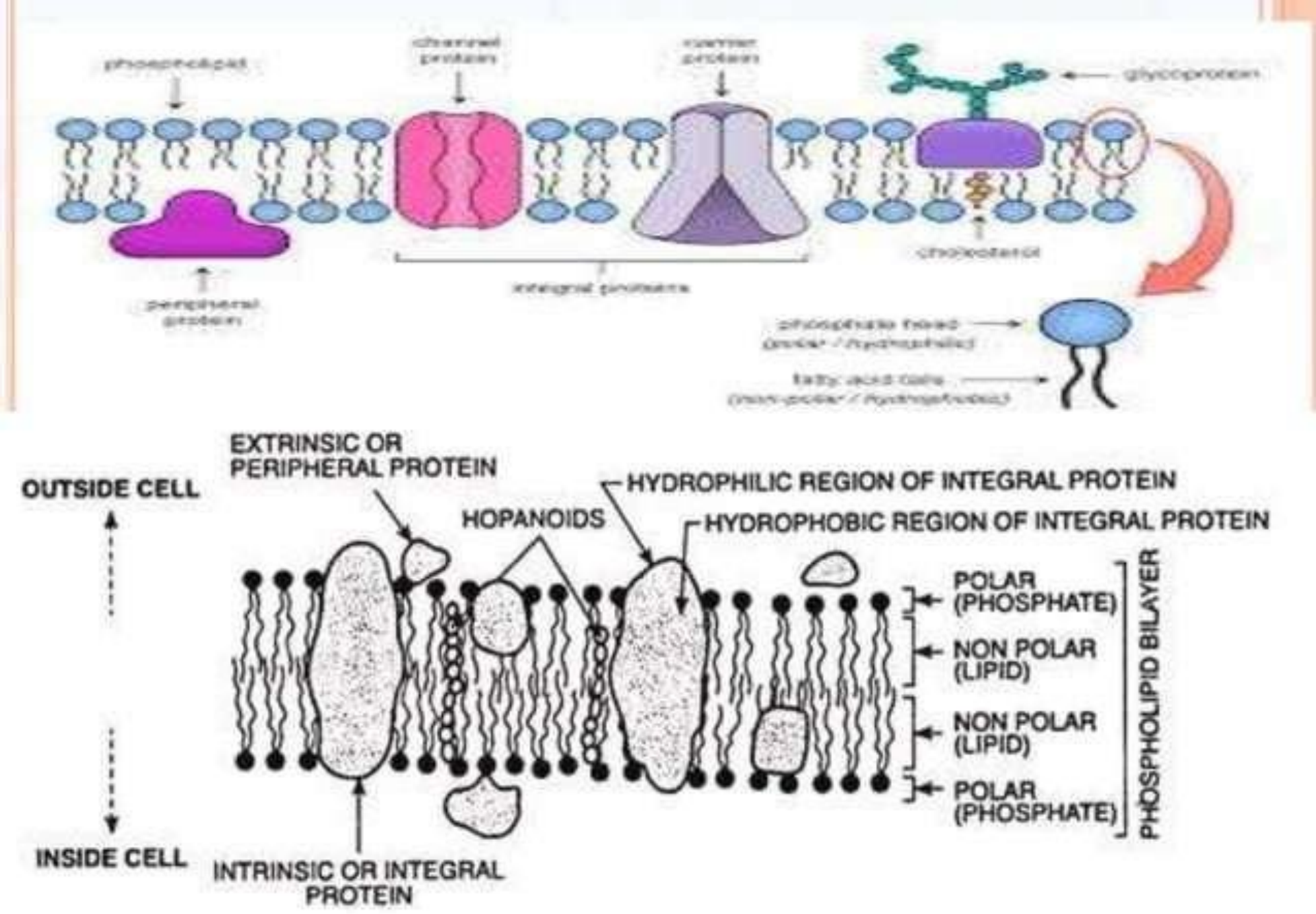
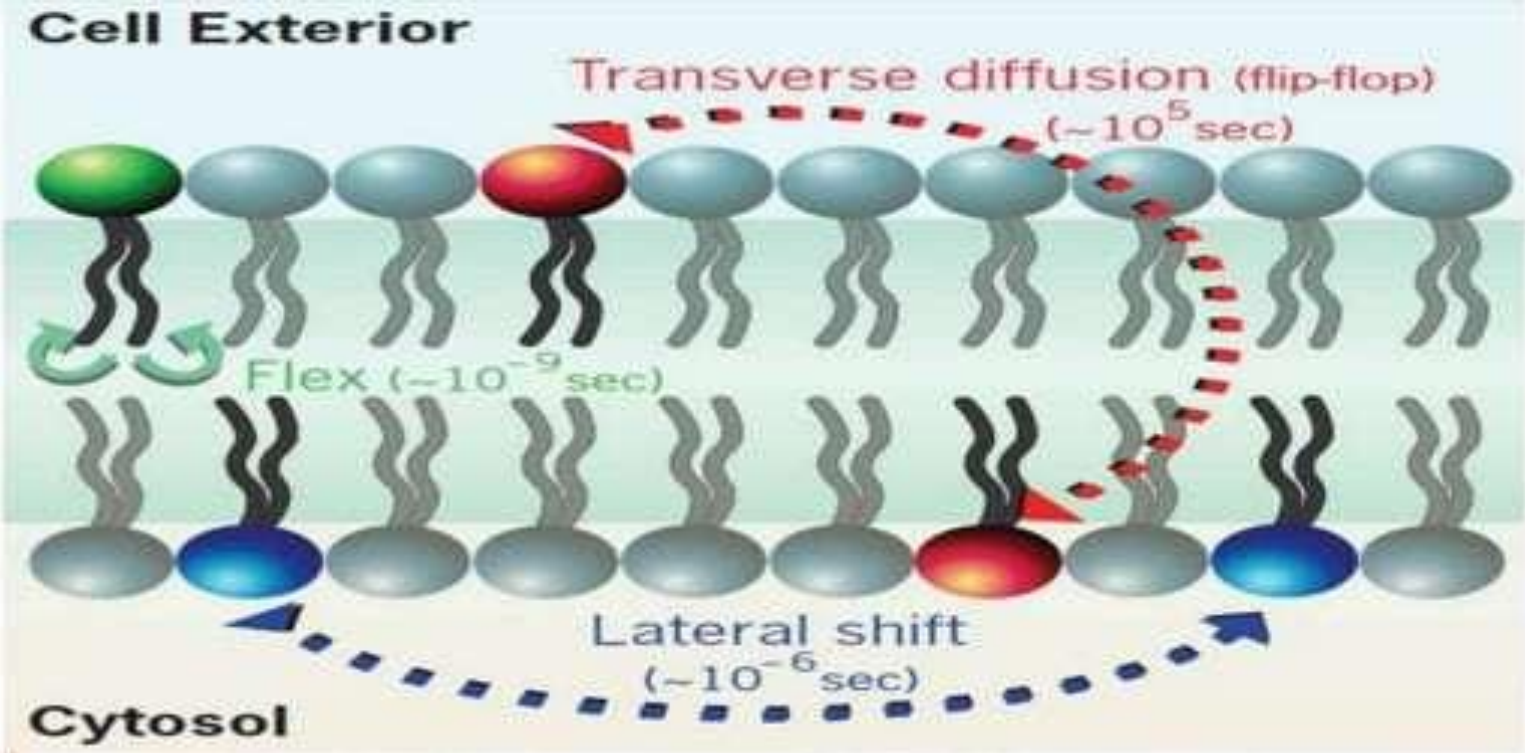


FIG. 5.15. Diagrammatic representation of the fluid mosaic model of plasma membrane.

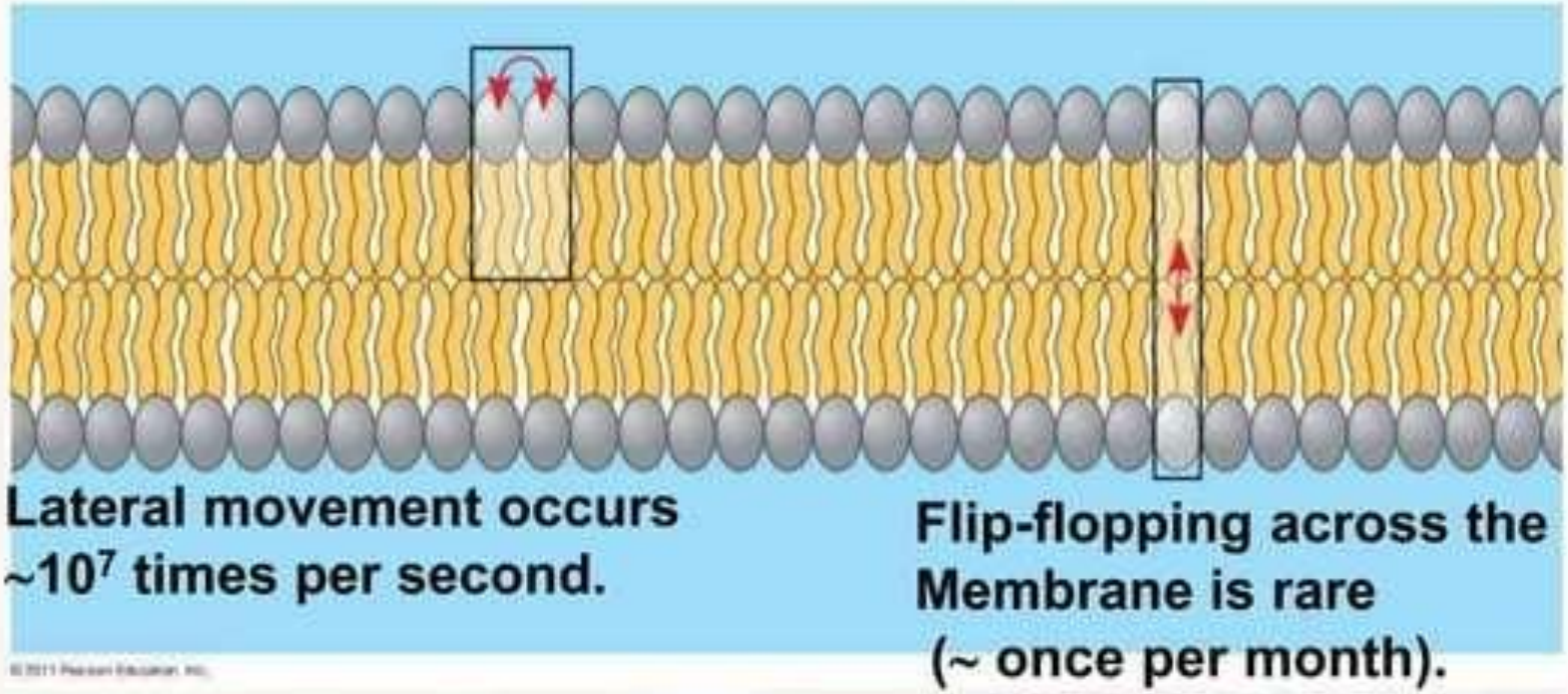
DYNAMIC PROPERTIES OF LIPID BILAYER

1. The rapid motion involving flexing within each lipid molecule is possible.
2. A rapid lateral diffusion of lipid is possible.
3. Slow motion of lipid molecule from one side of the bilayer to the other is also possible.
4. The lipid molecules might rotate about their axis.
5. The fluid mosaic model of cell membrane is now widely accepted as it is presumed to apply to membranes of all types regardless of their varying characteristics and differences in lipids protein ratio.
6. In fact this model can account for the molecular organisation and ultrastructure of membranes in-terms of their chemical composition.



The possible movements of phospholipids in a membrane. The types of movements in which membrane

- phospholipids can engage and the approximate time scales over which they occur.
- Whereas phospholipids move from one leaflet to another at a very slow rate, they diffuse laterally within a leaflet rapidly.
- Lipids lacking polar groups, such as cholesterol, can move across the bilayer quite rapidly.


Lateral movement occurs
~10^7 times per second.
Flip-flopping across the
Membrane is rare
(~ once per month).

ULTRA-STRUCTURE OF CELL MEMBRANE

Composition of cell membrane

Biological membrane / Plasma membrane

Chemical composition of membranes:

Membranes are composed of

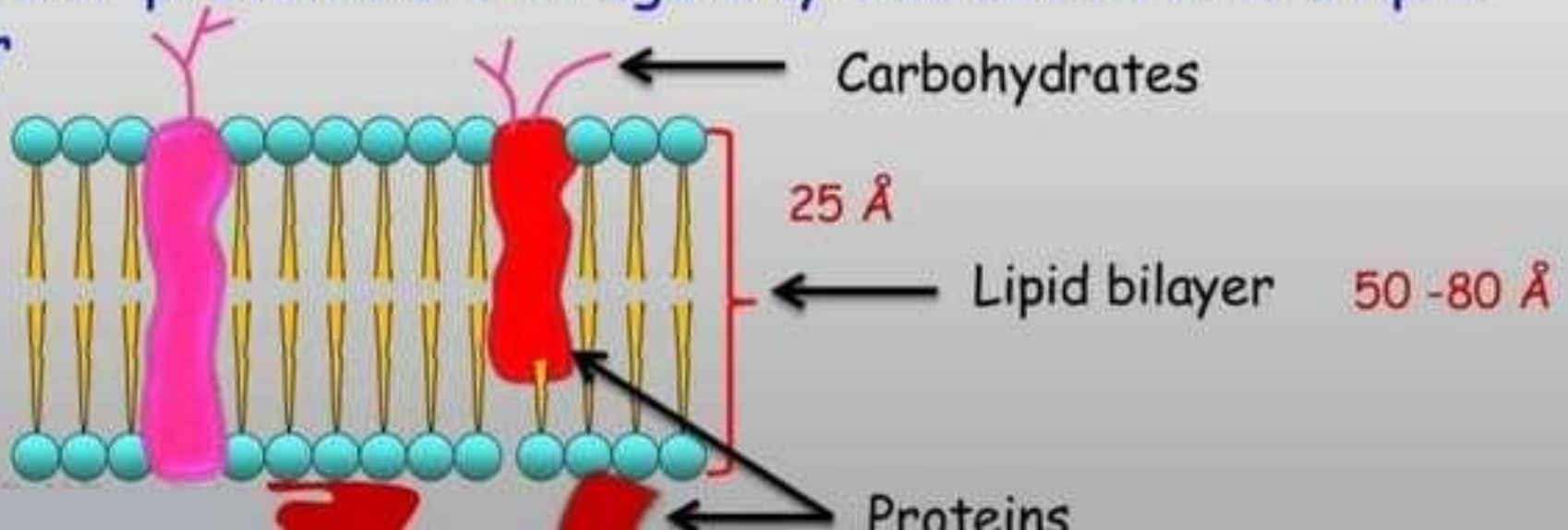
- Lipids
- Proteins
- Carbohydrates -do not exist free form in membrane

luid mosaic model of plasma membrane

- A lipid bilayer model – originally proposed Davson and Danielle
- Modified by Singer and Nicholson - is a more recent and acceptable model for membrane structure.

- Membrane essentially composed of a lipid bilayer.

- Globular proteins are irregularly embedded in the lipid bilayer



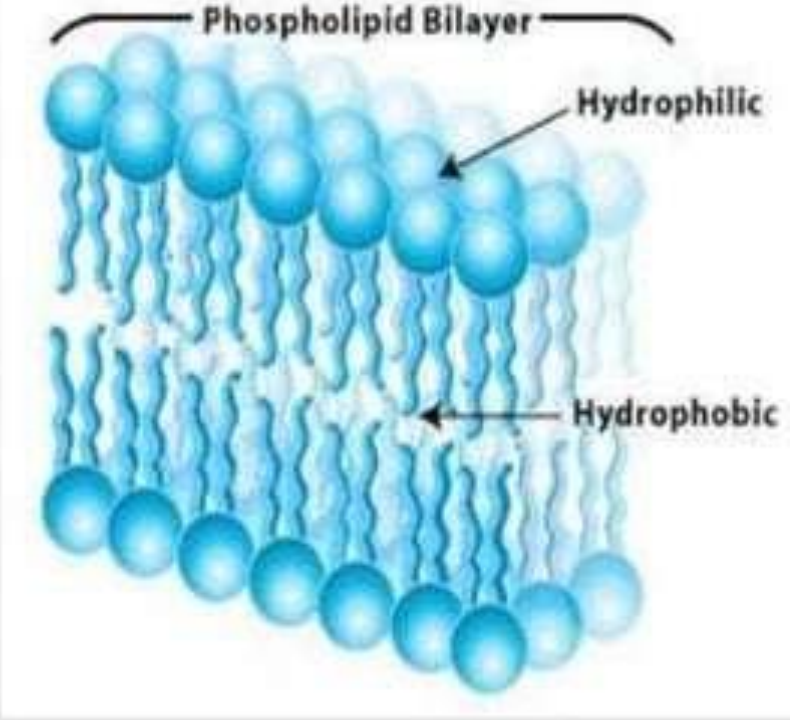
Membrane Lipids

- They are the basic structural components of cell membranes.

- Amphipathic lipids (containing hydrophobic & hydrophilic groups) namely Phospholipids, Cholesterol and Glycolipids

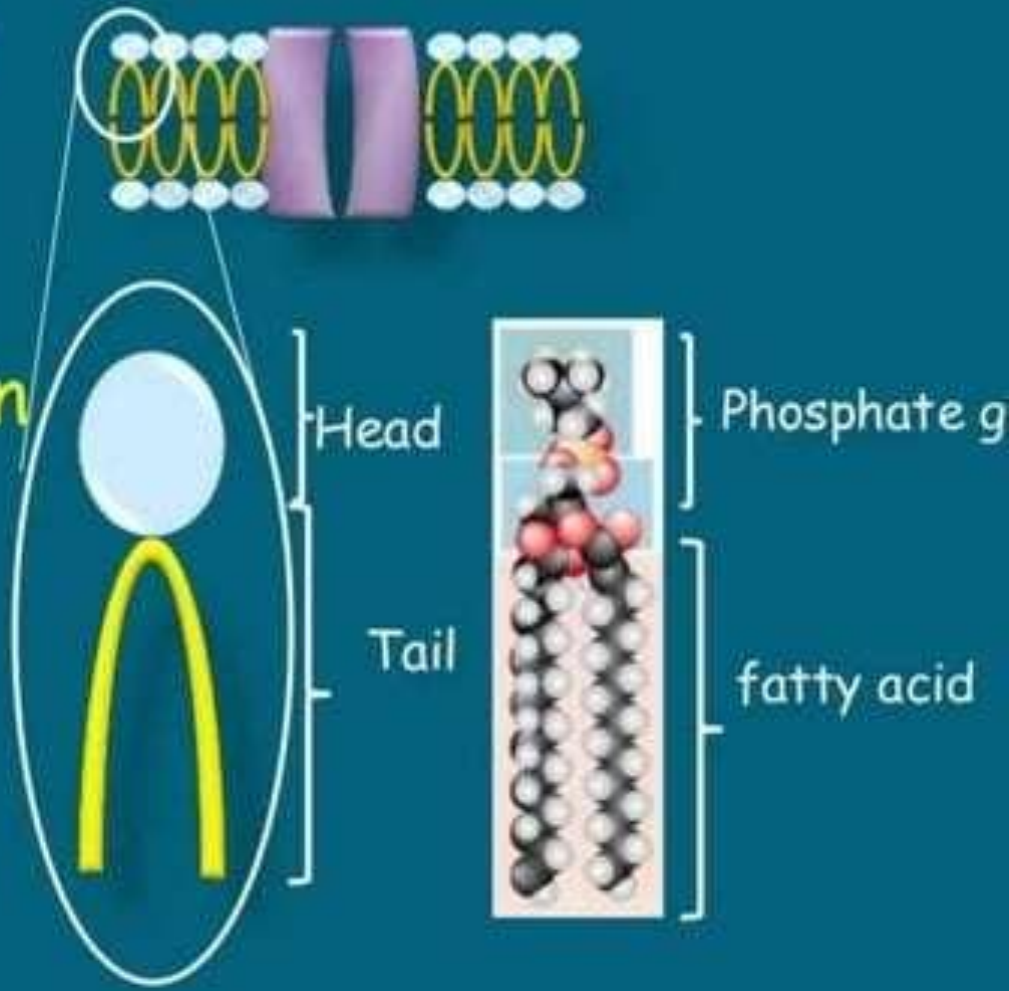
Membrane Lipids

- 75% - Phospholipids
- 20% - Cholesterol
- 5% - Glycolipids

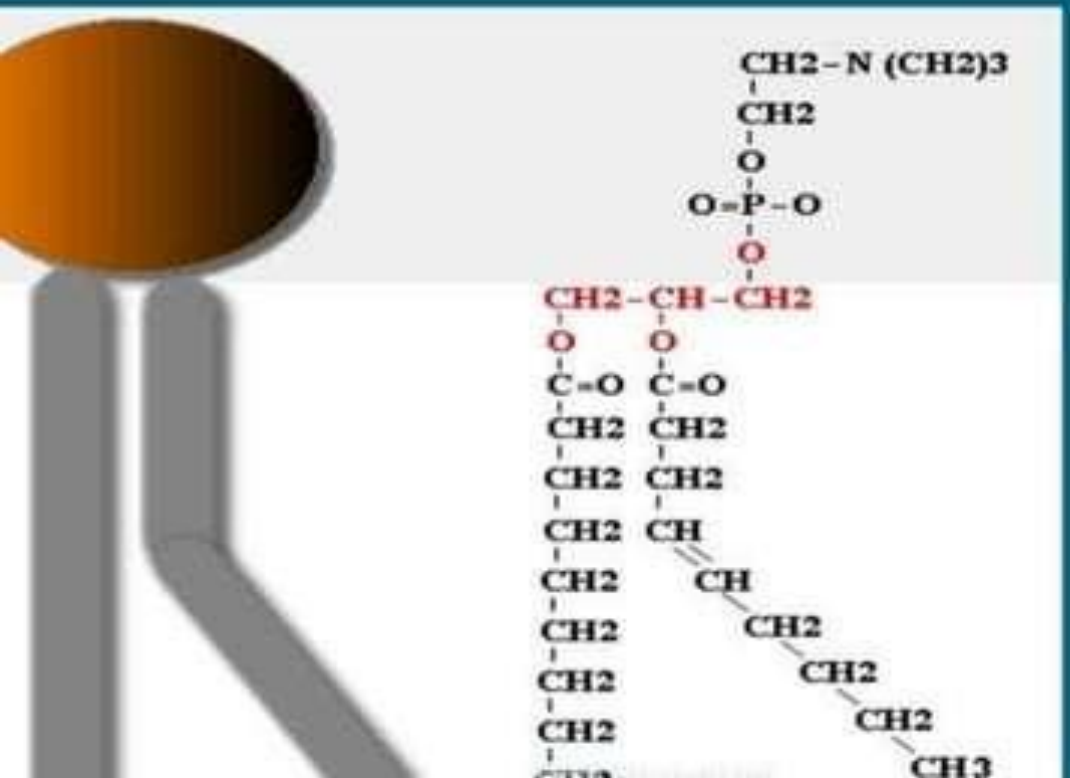


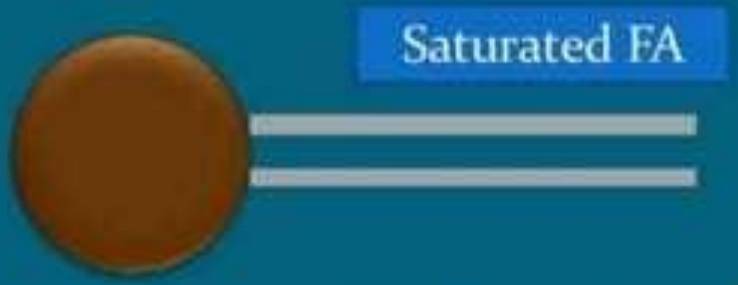
Phospholipids

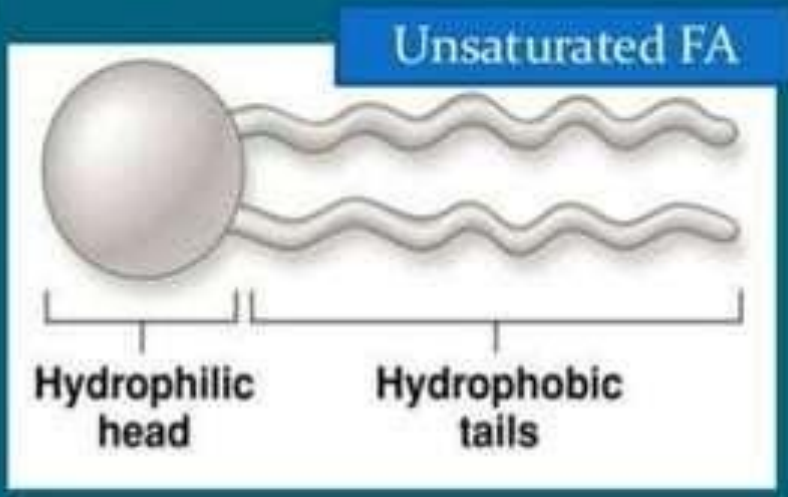
- "Head" - Polar part (Hydrophilic) - phosphate group
- "Tail" - Non polar part (Hydrophobic) -
  - long chain fatty acids
    - ✓ Even-numbered carbon
    - ✓ 16 or 18 carbons
    - ✓ Unbranched
    - ✓ can be saturated or unsaturated



- Saturated fatty acids -- straight tails
- unsaturated fatty acids - exist in the cis form in membranes, make kinked tails.
- Kink - Membrane becomes less tightly packed and therefore more fluid.







Phospholipid

Most predominant molecular component of all membrane

Principal Phospholipid – phosphatidylcholine (Lecithin) –50%
phosphatidylethanolamine (Cephaline)
phosphatidylserine
diphospatidyl glycerol (cardiolipin)
phosphatidylinositol
Sphingomyelin - prominent in myelin sheaths

Composition of lipids in membrane depends on the physiological role played by the cell or organelle.

IMM – rich in cardiolipin and phosphatidyl ethanolamine.

Phosphatidylcholine and Sphingomyelin – outer leaflet of the bilayer

Phosphatidylserine and Phosphatidylethanolamine – inner leaflet.

Function of membrane lipids :

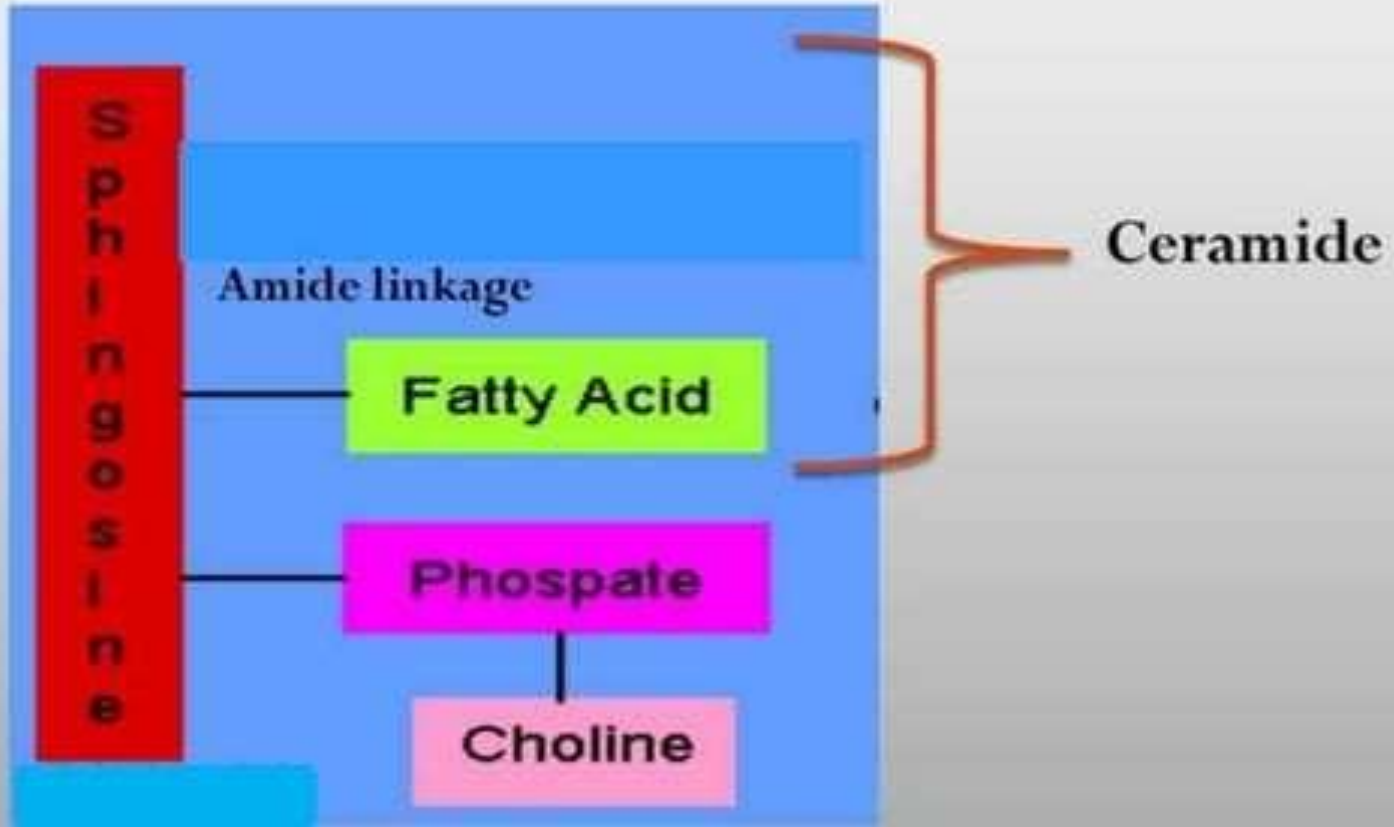
Acts as Permeability barriers.

Essential for the maintenance of fluidity of membranes.

Sphingolipids:

Sphingomyelin

hey are found specially in the tissues of nervous system.



Cholesterol –

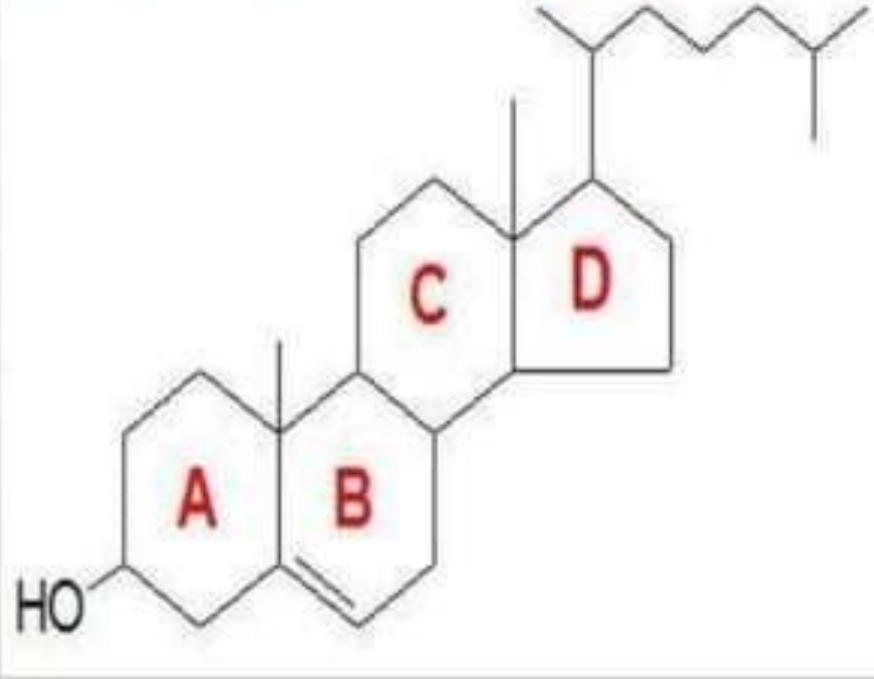
weakly amphipathic

abundant in mammalian cells, absent in prokaryotic cell

OH gr – faces exterior
cyclopentanophenanthrene ring – hydrophobic lipid phase.

Stability to membrane

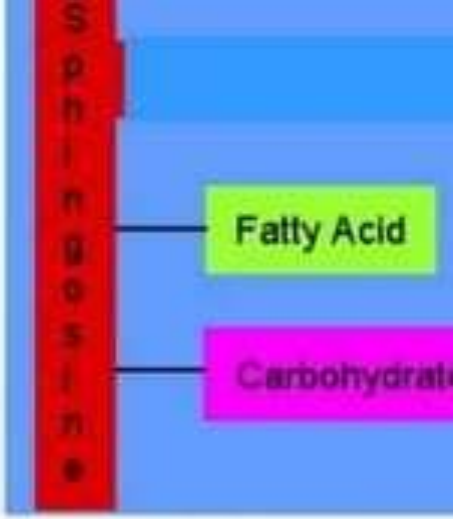
Alters Fluidity of membrane

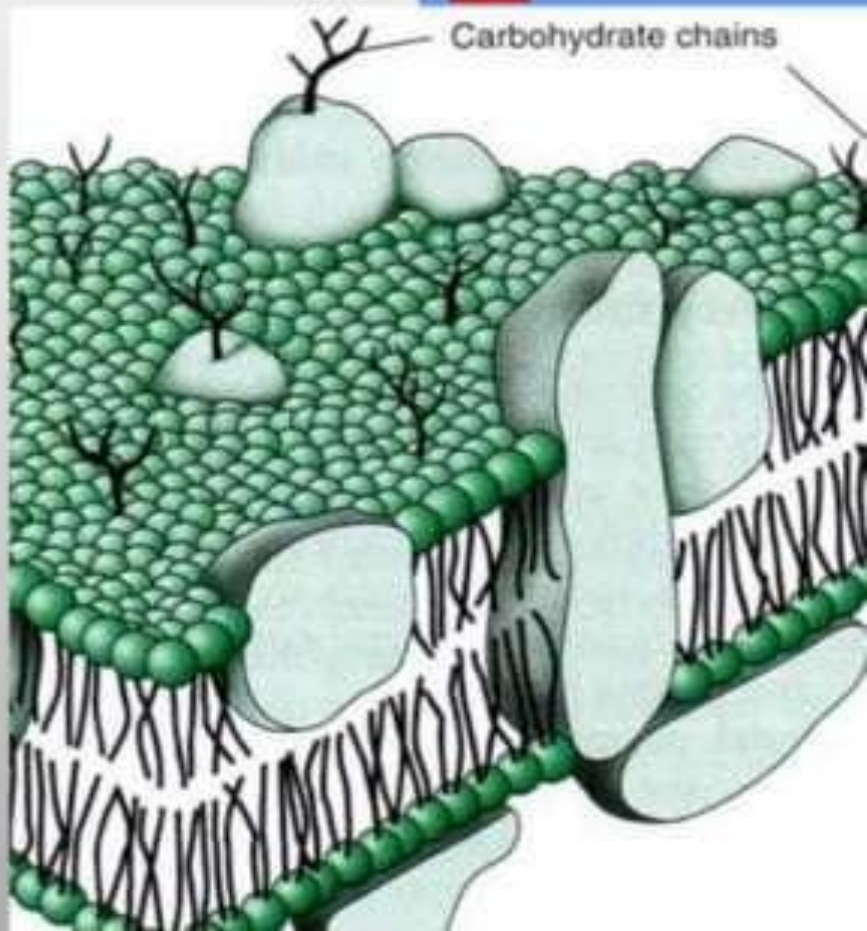


Glycolipids - 2-10%

- present only on the outer surface of membrane.

- Single sugar or branched oligosaccharide attached to sphingosine backbone of lipids.

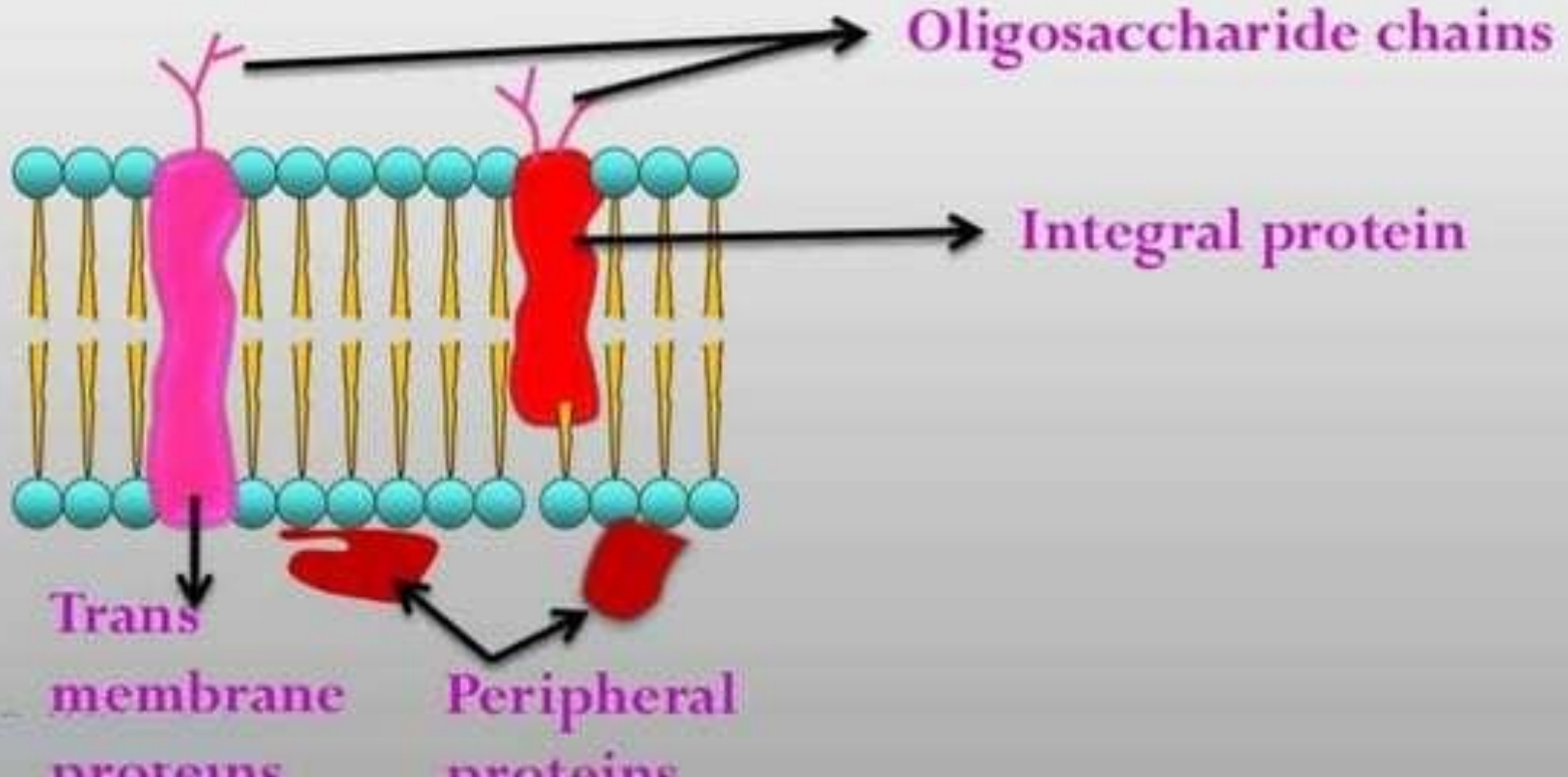




Membrane Proteins

The main types of membrane proteins are

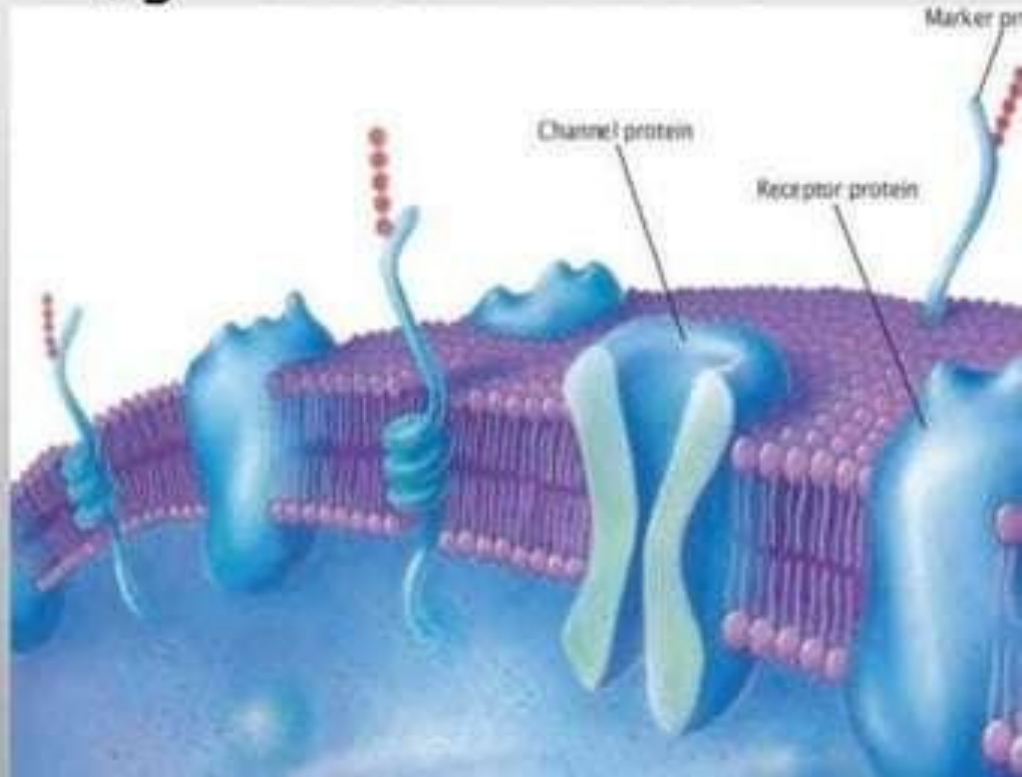
1. Integral membrane protein (intrinsic)
2. Peripheral membrane protein (extrinsic)
3. Trans membrane protein



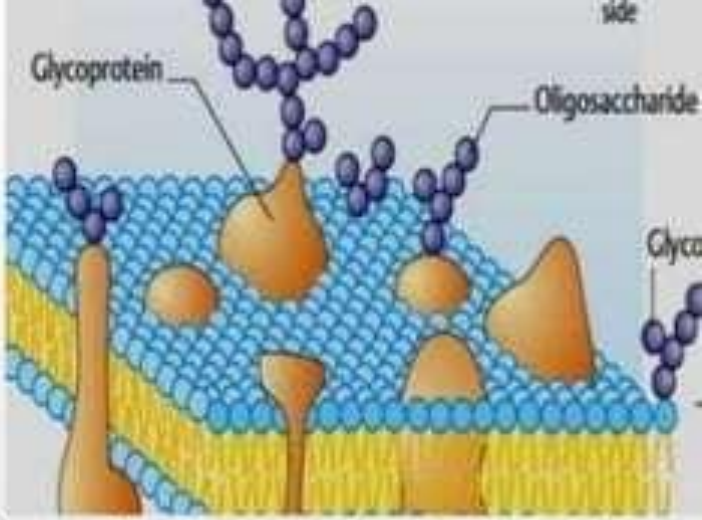
Integral proteins / intrinsic proteins	Peripheral proteins / extrinsic proteins
Embedded deeply in the bilayer	Bound to external face of membrane
Amphipathic -two hydrophilic ends separated by an intervening hydrophobic region that traverses the hydrophobic core of the bilayer	Bound to the hydrophilic regions of specific integral proteins and head groups of phospholipids
Hydrophobic /van der waals force	Electrostatic & H bonds
Removed by detergents /organic solvents.	No detergents Salt solutions of different ionic strength /pH is enough to remove
Spans the whole layer - Transmembrane protein	Usually poses enzymatic activity
Ion channels Carriers (transporters)	Receptors Enzymes

Functions of membrane proteins

- Ion channels Carriers (transporters) ,pumps
- Structural component
- Receptors -These proteins can serve as receptors for hormones, neuro transmitters, growth factors etc.
- Membrane based Enzyme
- Tissue specific antigen



Membrane Carbohydrates



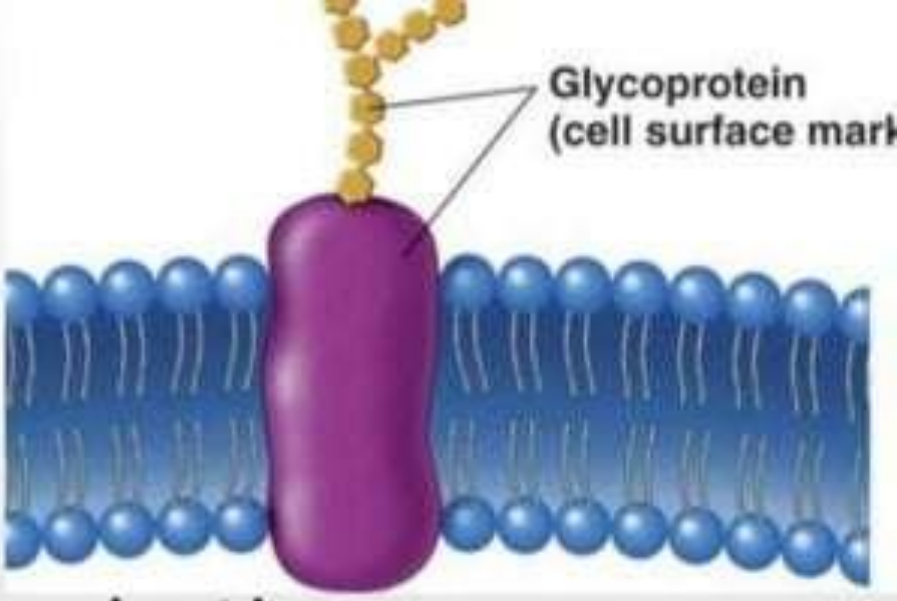
Minor component 5-8%

Occur as oligosaccharide that is Covalently bound to lipids and proteins to form glycolipids and glycoproteins.

Never as free form

These are mostly - Glucose , Galactose , Mannose
N-acetyl glucosamine , fucose, sialic acid.

Glycocalyx – loose Carbohydrate layer on outer surface of cell

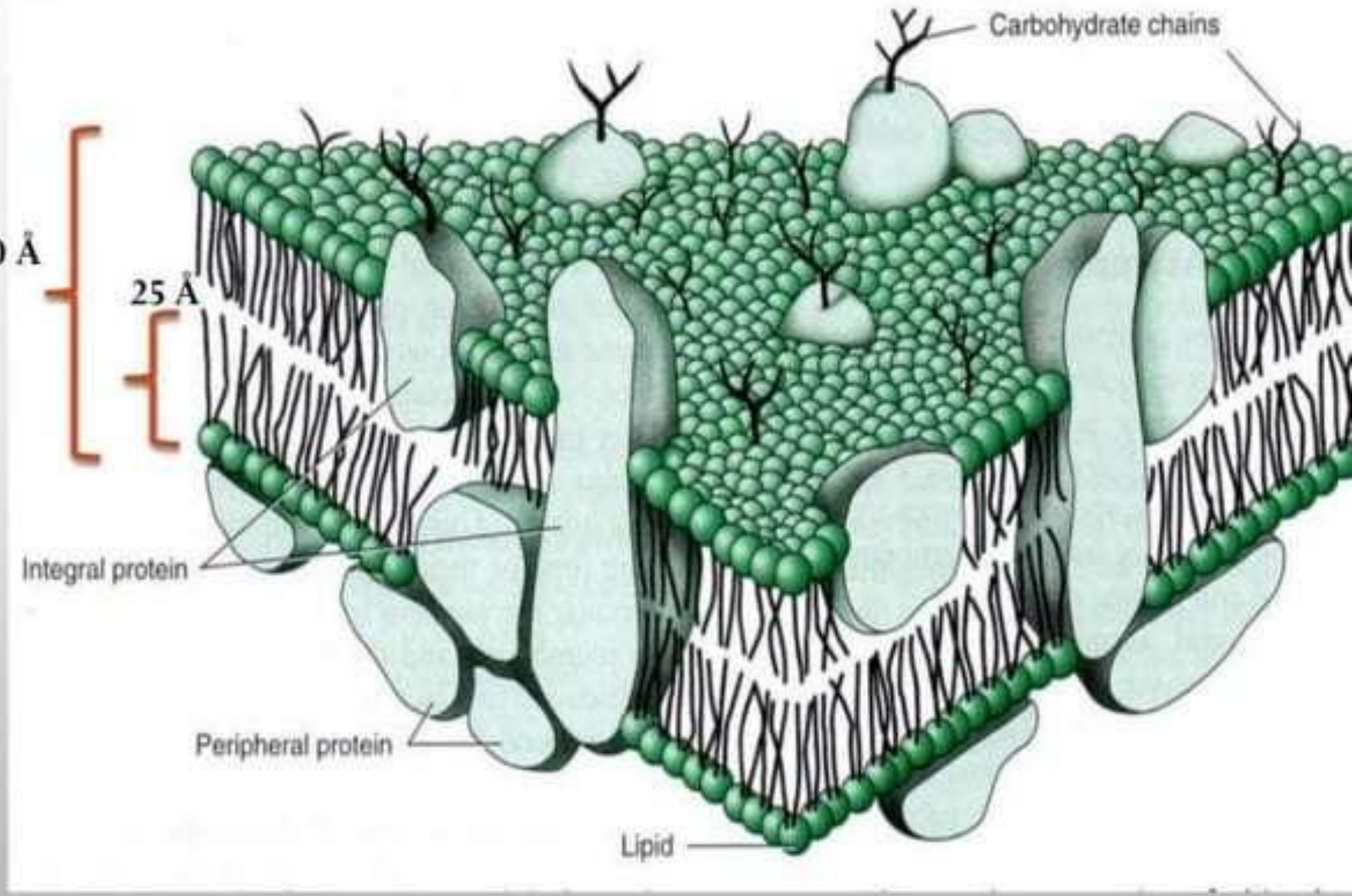


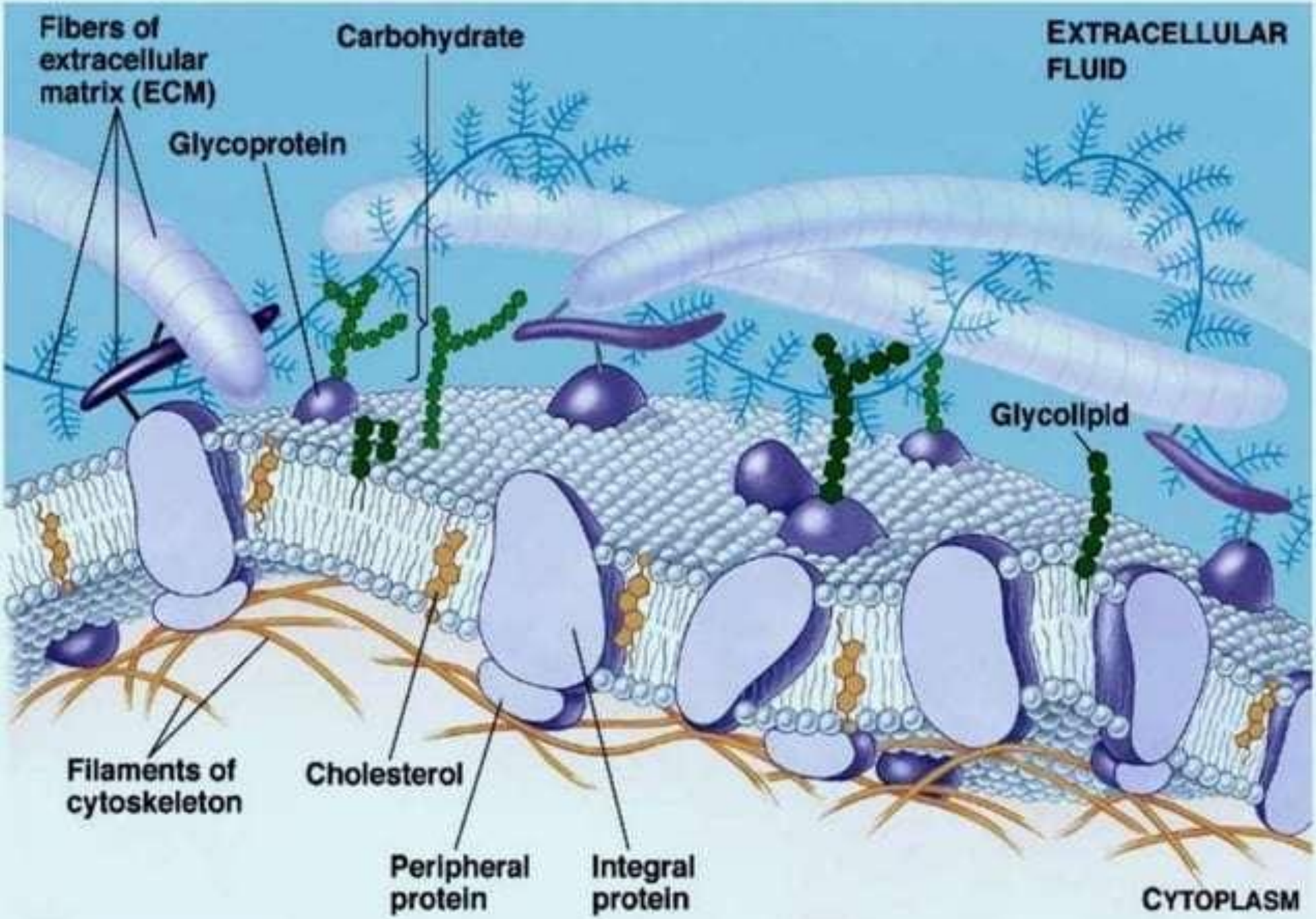
Functions –

- Cell recognition and communication
- Impart –ve charge to cell- repels other particles.
- helps in inter-cellular attachment / adhesion.
- act as receptors
- Cell identity markers (glycoproteins & glycolipids) , antibody processing.

Membrane asymmetry

- Mainly by protein – inserted in asymmetric fashion
- Different Lipids composition in two leaflets
- Oligosaccharide always project towards the exterior


Carbohydrate chains
50-80 Å
25 Å
Integral protein
Peripheral protein
Lipid

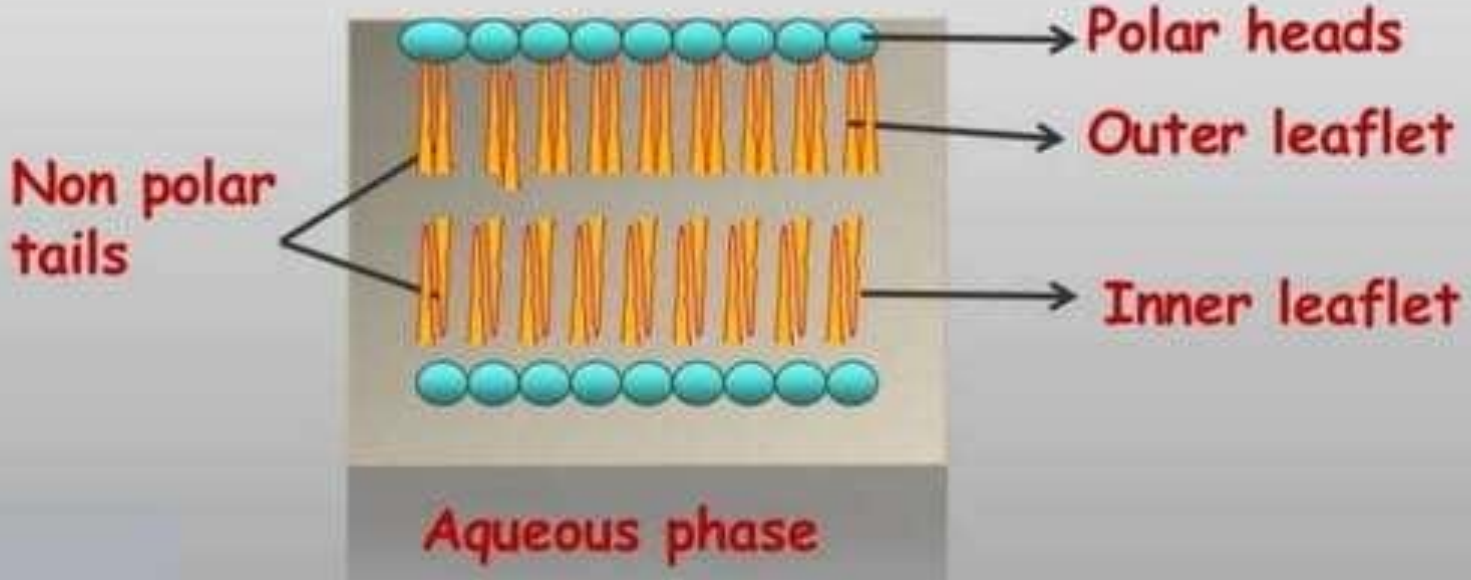

Fibers of extracellular matrix (ECM)
Carbohydrate
EXTRACELLULAR FLUID
Glycoprotein
Glycolipid
Filaments of cytoskeleton
Cholesterol
Peripheral protein
Integral protein
CYTOPLASM

Polar head – external surface of the membrane

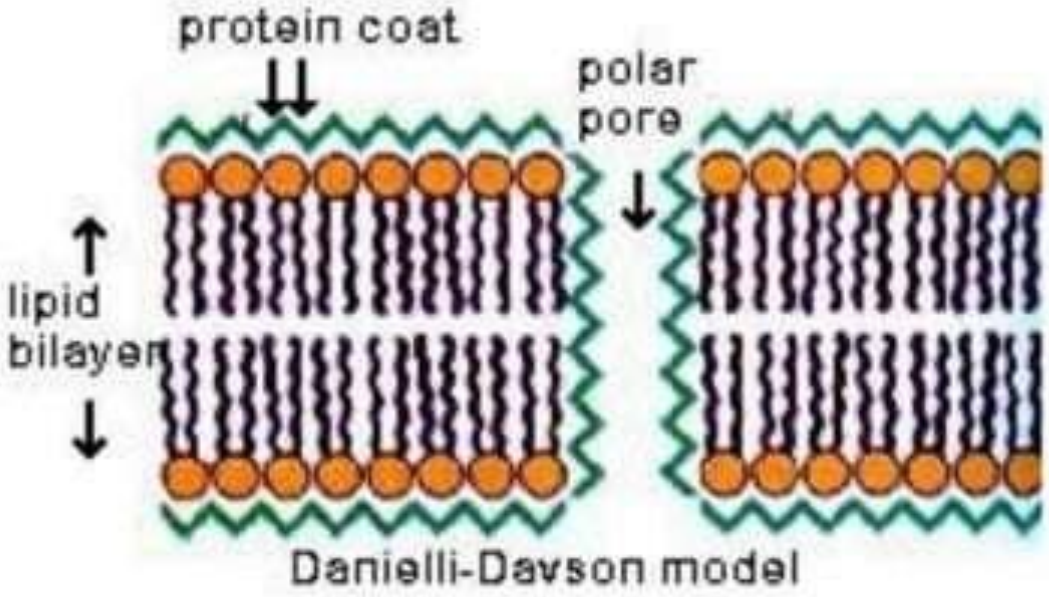
Non polar tail – inside the membrane

Lateral movement - Interior of membrane is fluid in nature

Flip flop movement – restricted



DANIELLI AND DAVSON MODEL



Danielli-Davson model

Membrane Fluidity

Influences its physiological function

Influenced by two major factors : Temperature and lipid composition of the membrane

At Low temperature – fluidity is less

As the temperature increases - the hydrophobic side chains undergo a transition from the ordered state to a disordered one – increase in fluidity

The temperature at which the structure undergoes the transition from ordered to disordered state is called the **"transition temperature"** (T_m).

Fluidity of membrane maintained by :

length of hydrocarbon chain

degree of unsaturation

Short chain FA – increase the fluidity

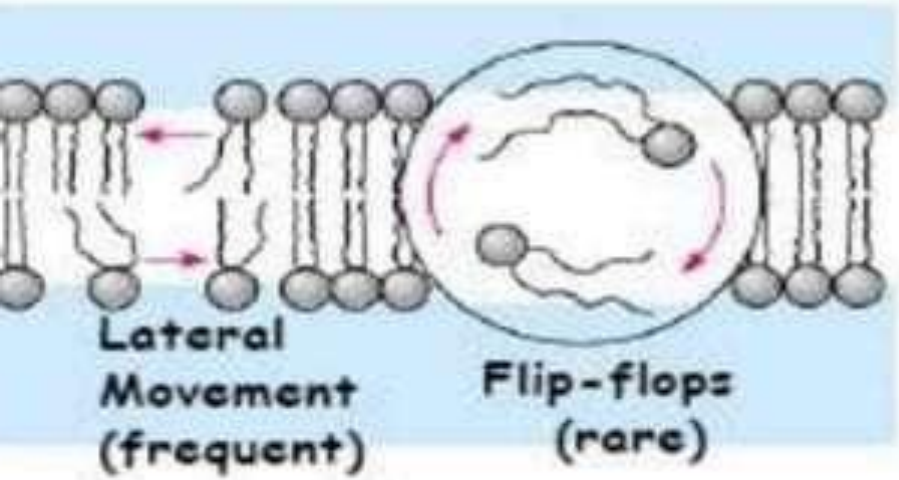
Long chain FA– decrease the fluidity

Unsaturated FA that exist in the *cis* configuration – increase the fluidity

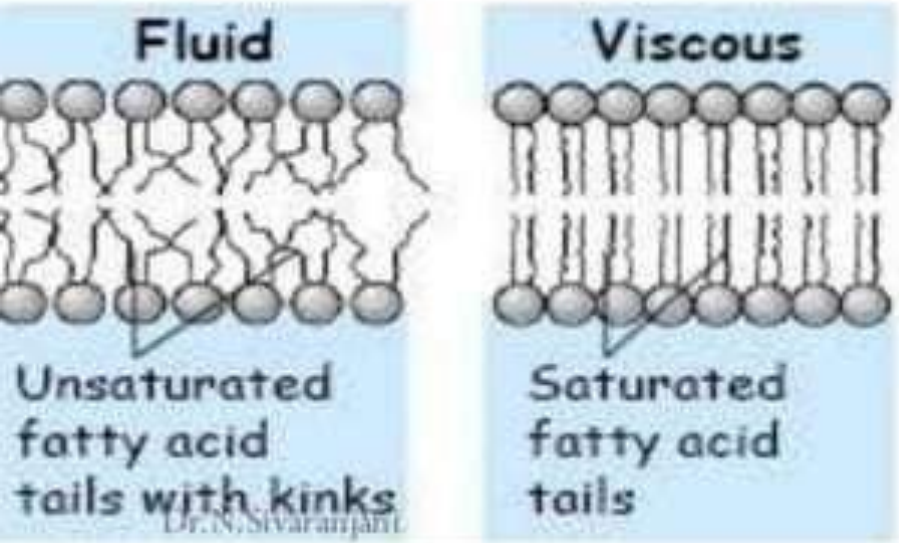
More the number of double bonds – greater is the fluidity.

Trans FA- decrease the fluidity of membrane

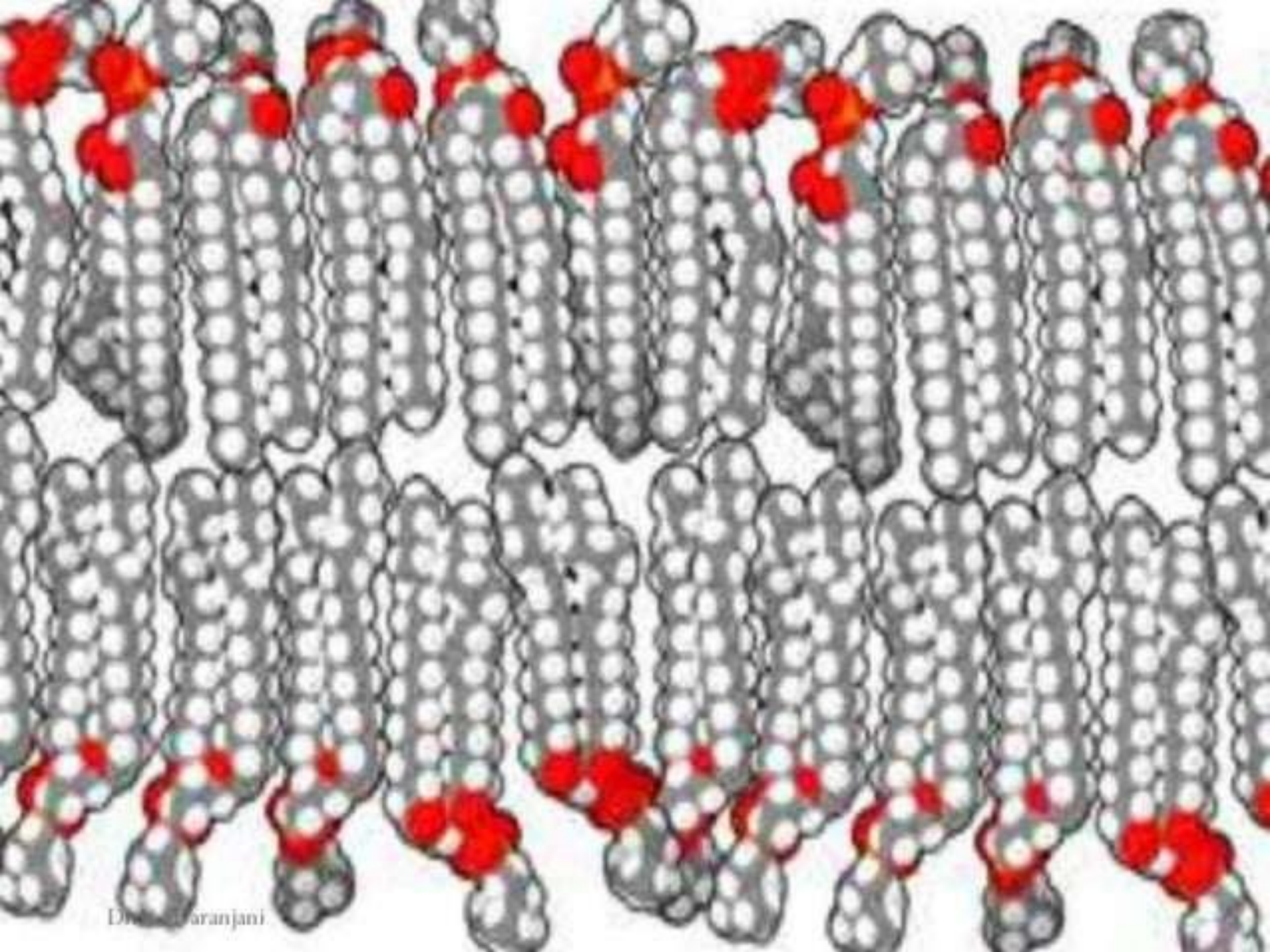
Fluidity of membranes



Frequent lateral movement of lipids; infrequent flip-flops across membrane leaflets.



Degree of unsaturated/saturated fatty acid tails (hydrocarbon) determines membrane fluidity.



Cholesterol

- Increase in cholesterol conc. – less fluid on outer surface, more fluid on inner surface

- Effect of cholesterol on fluidity is different with different temperature.

- At temperature below Tm – cholesterol increases fluidity
- At temperature above Tm – cholesterol decreases fluidity

Functions of plasma membrane :

Transport of molecules – channels, pumps

Phagocytosis , pinocytosis – engulfing particles

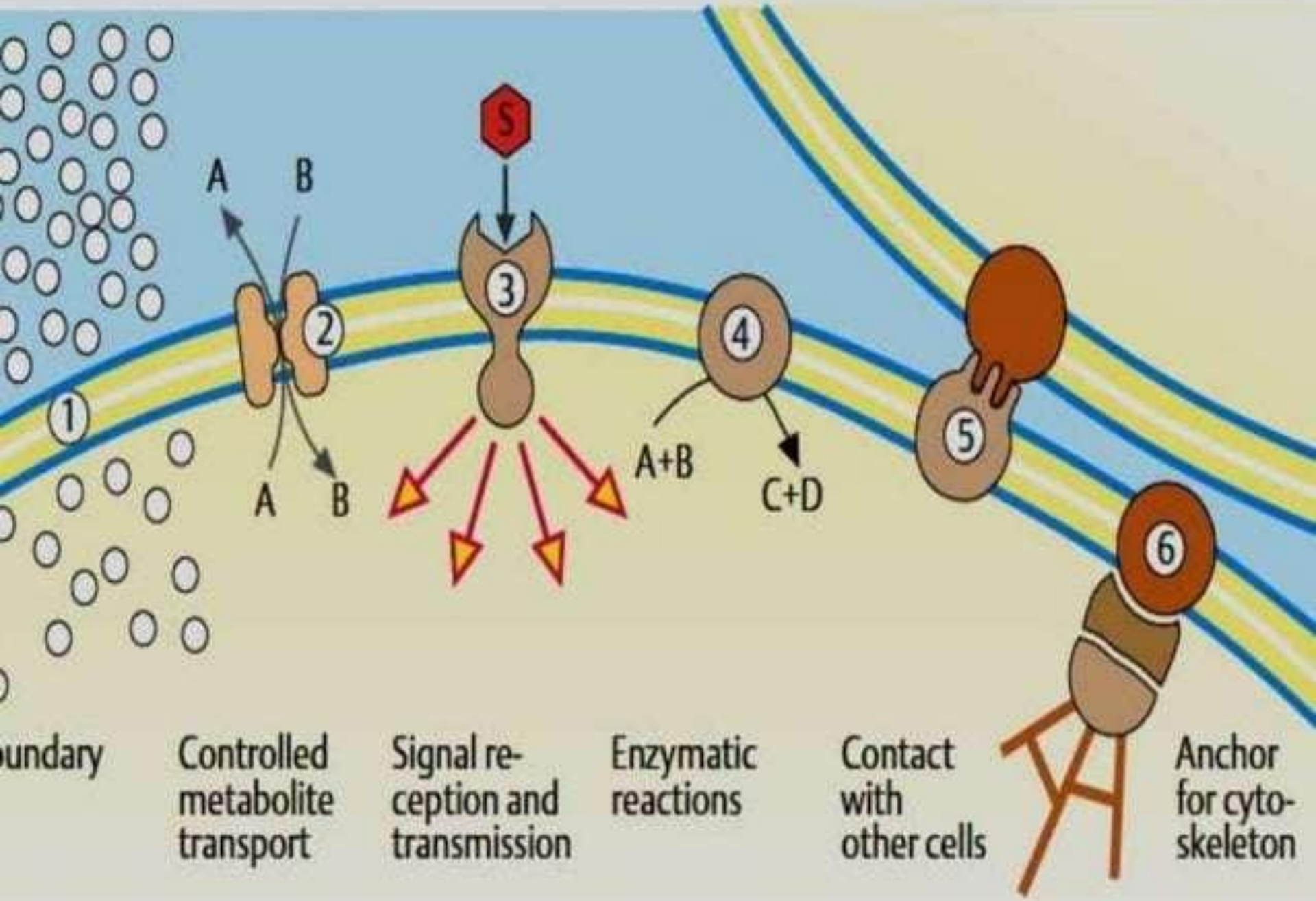
Cell –cell communication – due to presence of carbohydrates

Cell signaling – cell membrane bound receptors, enzymes and proteins

Protects the cellular organelles

Compartmentalization – segregates one part of the cell from other

Membrane modifications for specialized functions – myelin sheath of neurons, microvilli in intestine.


S
A
B
A
B
A+B
C+D
1
2
3
4
5
6
oundary
Controlled metabolite transport
Signal re-ception and transmission
Enzymatic reactions
Contact with other cells
Anchor for cyto-skeleton

Artificial Membranes Model

Phospholipids of natural or synthetic origin that can be treated (eg, by using mild sonication) to form spherical vesicles in which the lipids form a bilayer.

Liposomes

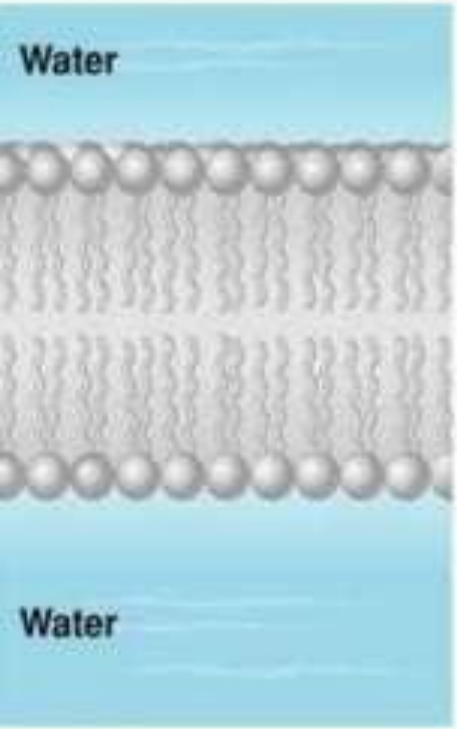
Artificial membrane systems is used to study membrane function

Liposomes can be made to entrap certain compounds inside them

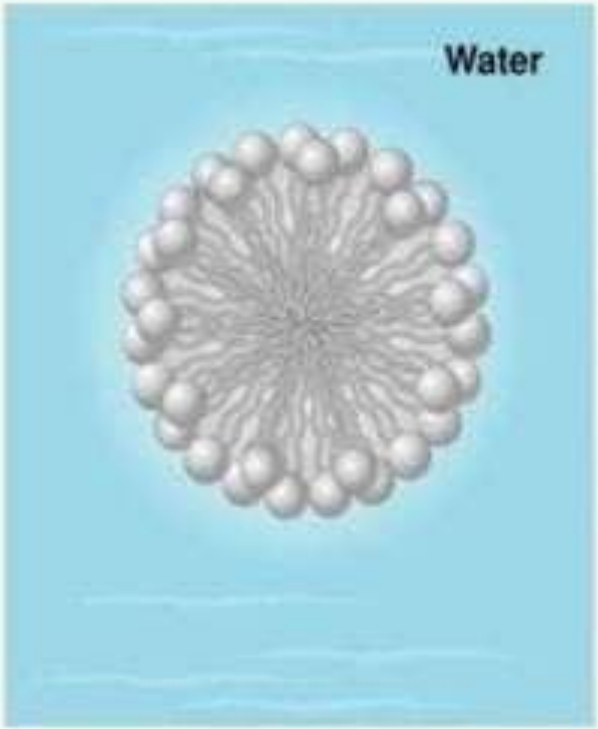
eg, drugs and isolated genes.

liposomes can be targeted to specific tissues or tumors

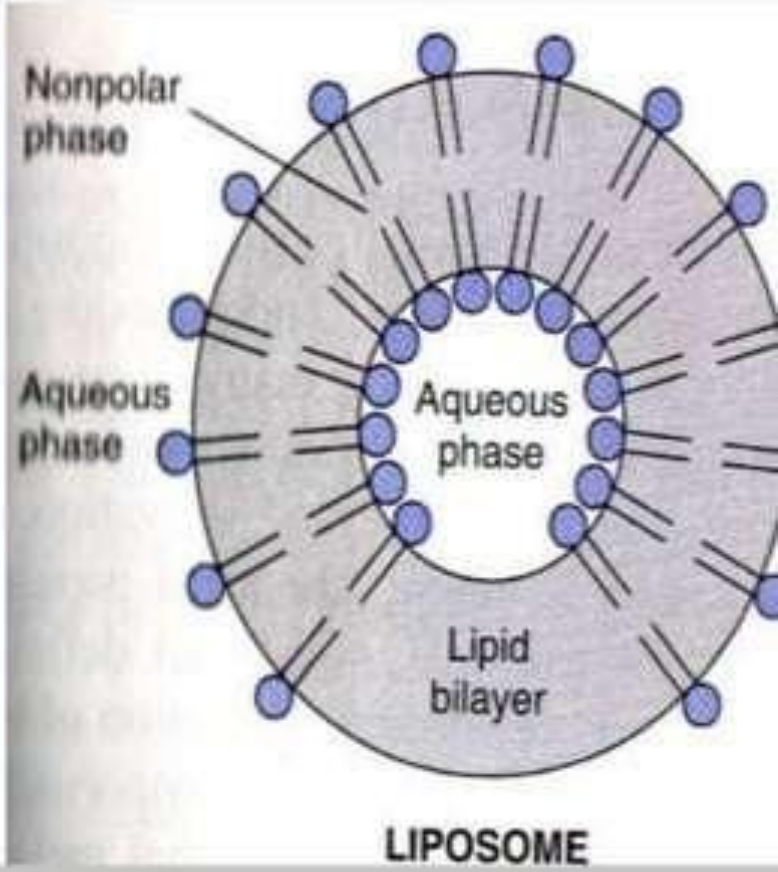
DNA entrapped inside liposomes appears to be less sensitive to attack by nucleases - useful in **gene therapy**.



a) Phospholipid bilayer



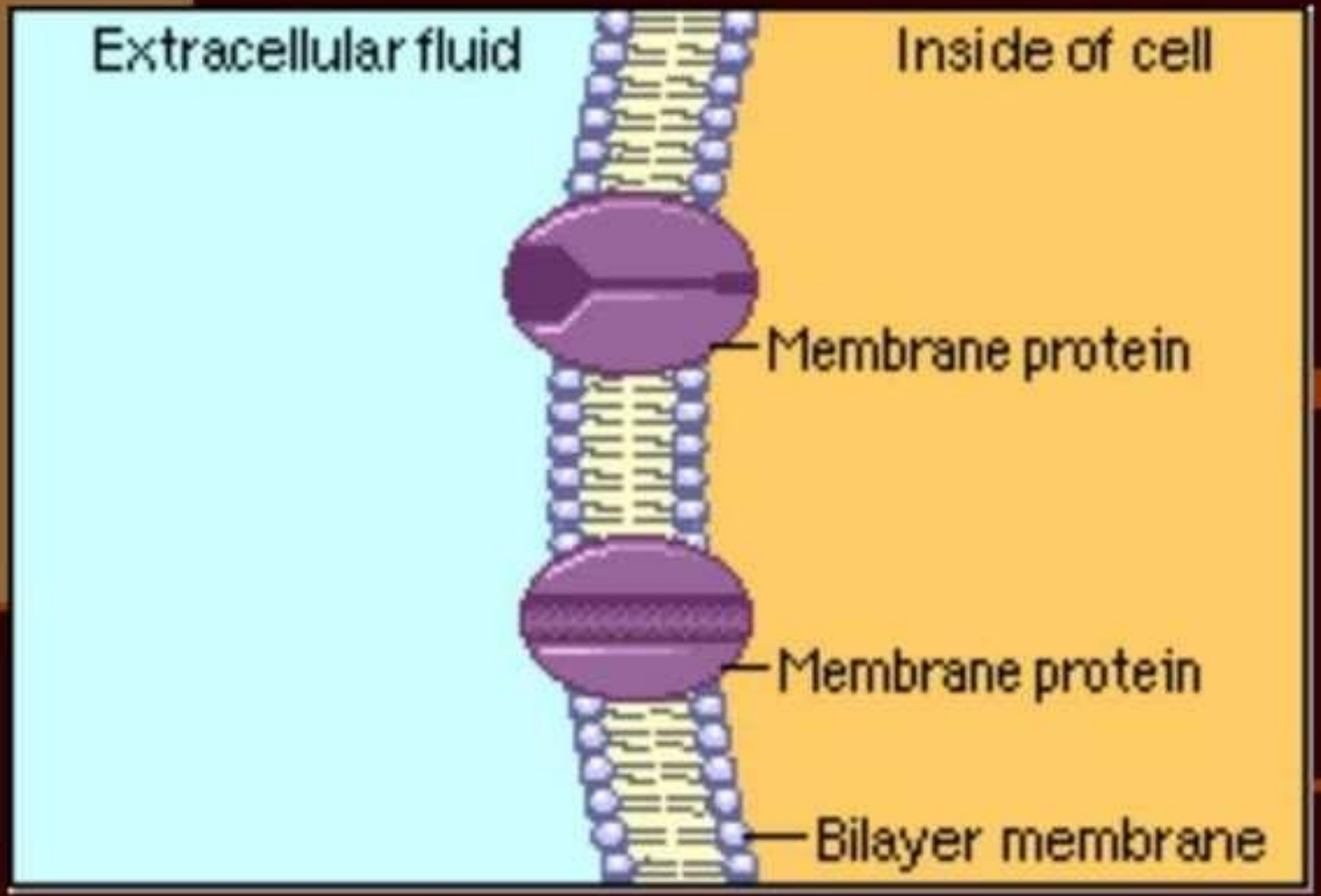
(b) Micelle



LIPOSOME

Vesicles surrounded by a lipid bilayer with an aqueous interior are termed Liposomes.

Transport system



Transport across Cell membrane

- Essential to maintain equilibrium of cell
- Certain substances must move into the cell to support metabolic reactions.
- Other substances produced by the cell for export or as cellular waste products must move out of the cell.

Types of Transport Mechanisms

- Transport of Small molecules
  - Passive transport
    - ✓ Simple diffusion
    - ✓ Facilitated diffusion – Cotransport, Uniport
  - Active transport
    - ✓ Primary Active Transport
    - ✓ Secondary Active Transport

- Transport of Large molecules
  - ✓ Exocytosis
  - ✓ Endocytosis

Types of transport mechanisms

Passive or simple diffusion

Carrier mediated :

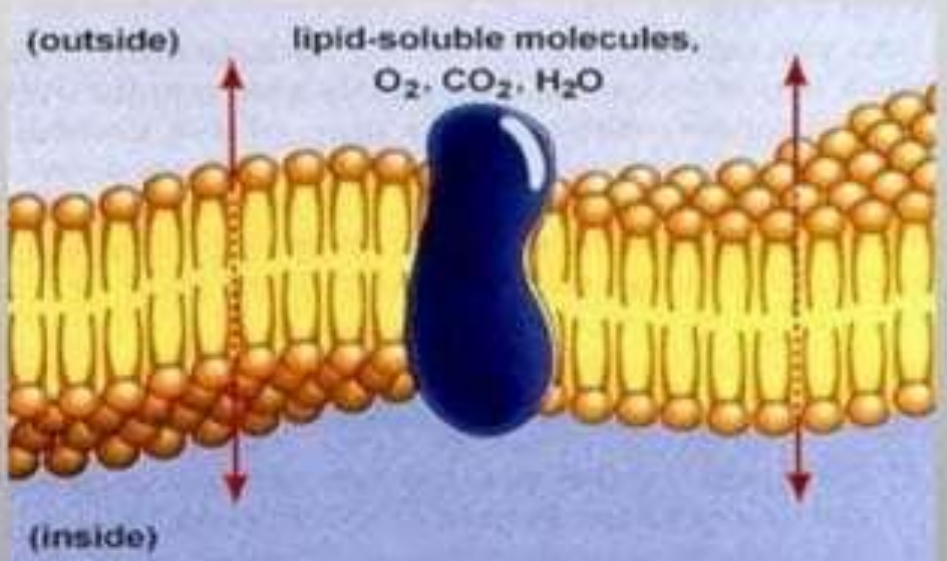
2a. Facilitated diffusion

2b. Active transport

Highly permeable to gases – CO_2,NO,O_2 (small , nonpolar)

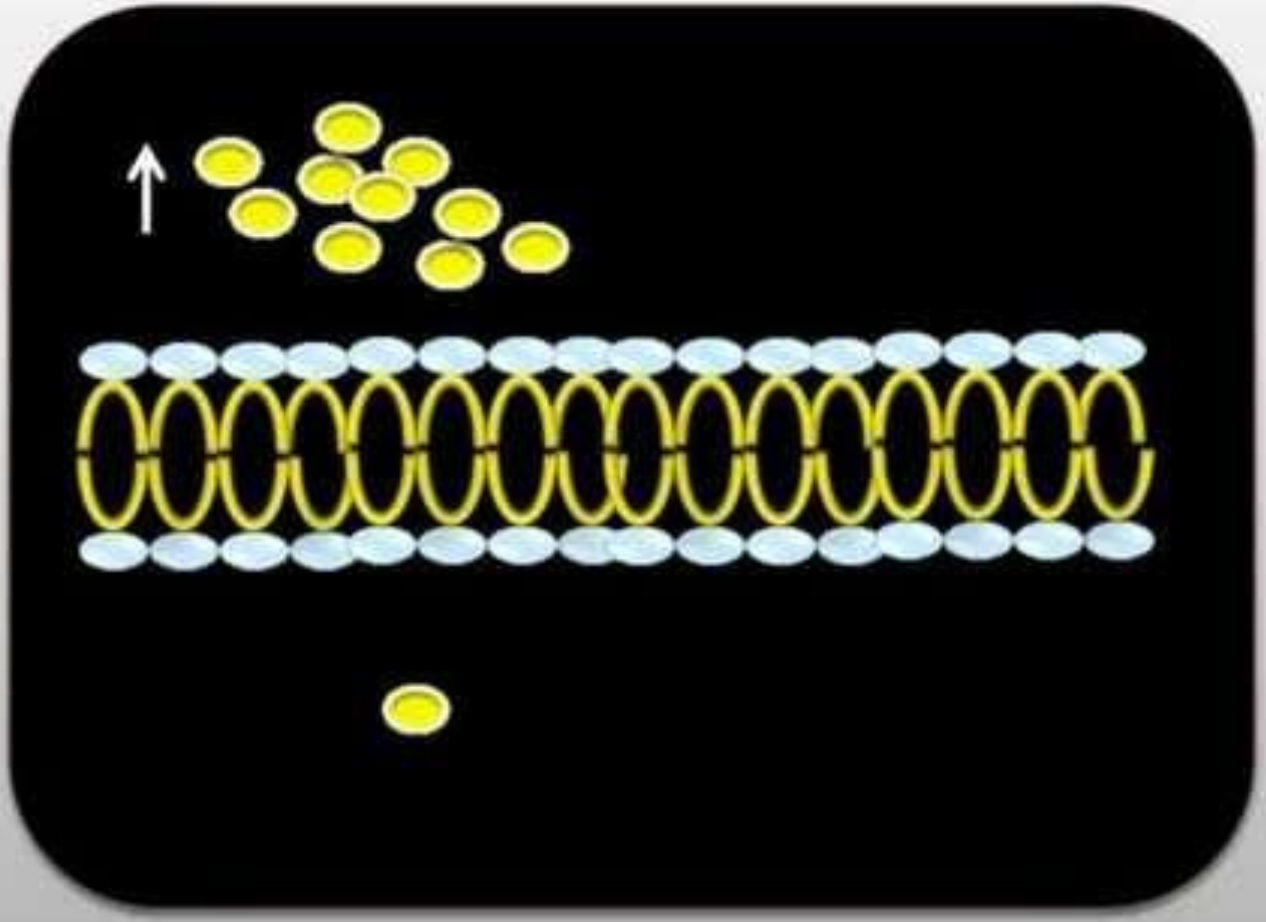
Small uncharged molecule – ethanol , urea.

Moderately permeable to water



Passive Transport

Simple Diffusion :-



2. Carrier mediated system

Mediated by integral protein / Permeases/ porters/translocases.

Proteins are highly specific

Eg: in RBC – GLUT has high affinity for D-glucose but low affinity for related sugars.

Specific for solute transport

Inhibited by structural analogues

b. Facilitated diffusion.

- resembles simple diffusion –
  down the conc. Gradient,
  does not require energy

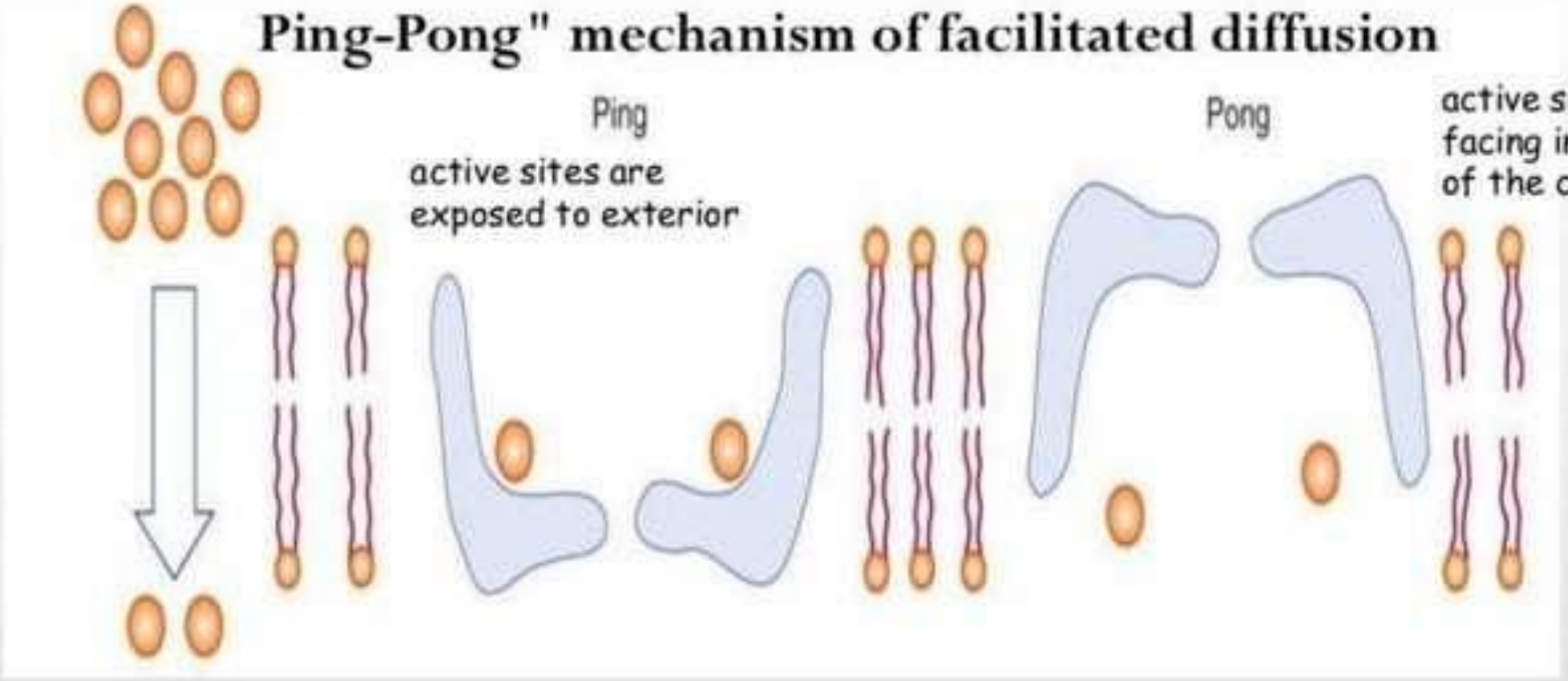
- requires a carrier transport protein.

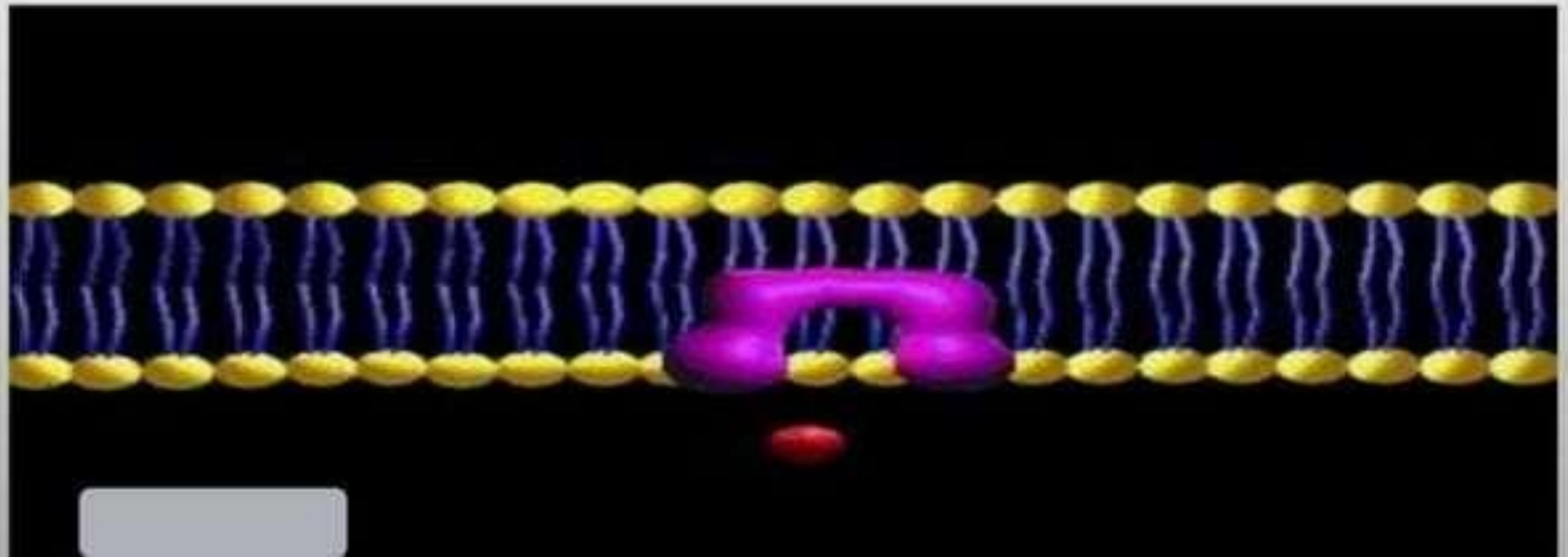
- operates bidirectional.

- More rapid than simple diffusion

- works as ping-pong mechanism.

Ex- Transport of Glucose by GLUT (GLUcose Transporters)
Transport of Amino acids


Ping-Pong" mechanism of facilitated diffusion
Ping
active sites are
exposed to exterior
Pong
active site
facing interio
of the cell

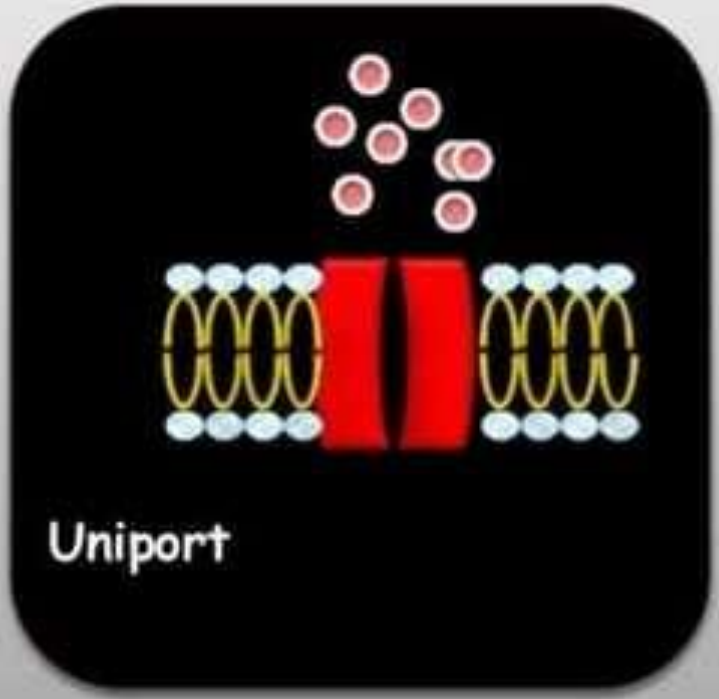


- Uniport
- Cotransport :
  - Symport
  - Antiport

Uniport

Transport of single type of molecule in one direction.

Ex - transport of glucose in RBC by GLUT
Calcium pump.



Active transport

- Primary
- Secondary

rimary Active transport – Requires energy directly

eg: Na^+K^+pump, Ca pump

econdary active transport – Requires energy indirectly

eg: Glucose transport into intestinal mucosal cell

Primary Active transport

- occurs against concentration gradient
- requires specific carrier protein or transport protein
- Energy used directly from hydrolysis of ATP .
- Saturated at higher conc. of solutes
- Susceptible to inhibition by specific organic and inorganic ompounds.

g : - Na-K ATPase / Na Pump
- Ca-ATPase / Ca Pump

Sodium pump :

- Low intracellular conc. of Na and high intracellular conc. of K is maintained by Na-K ATPase / Na Pump

- Made of 2 pairs of unequal subunit $\alpha_2\beta_2$

- ATPase - Integral protein

  binding sites for ATP and Na – located inner side

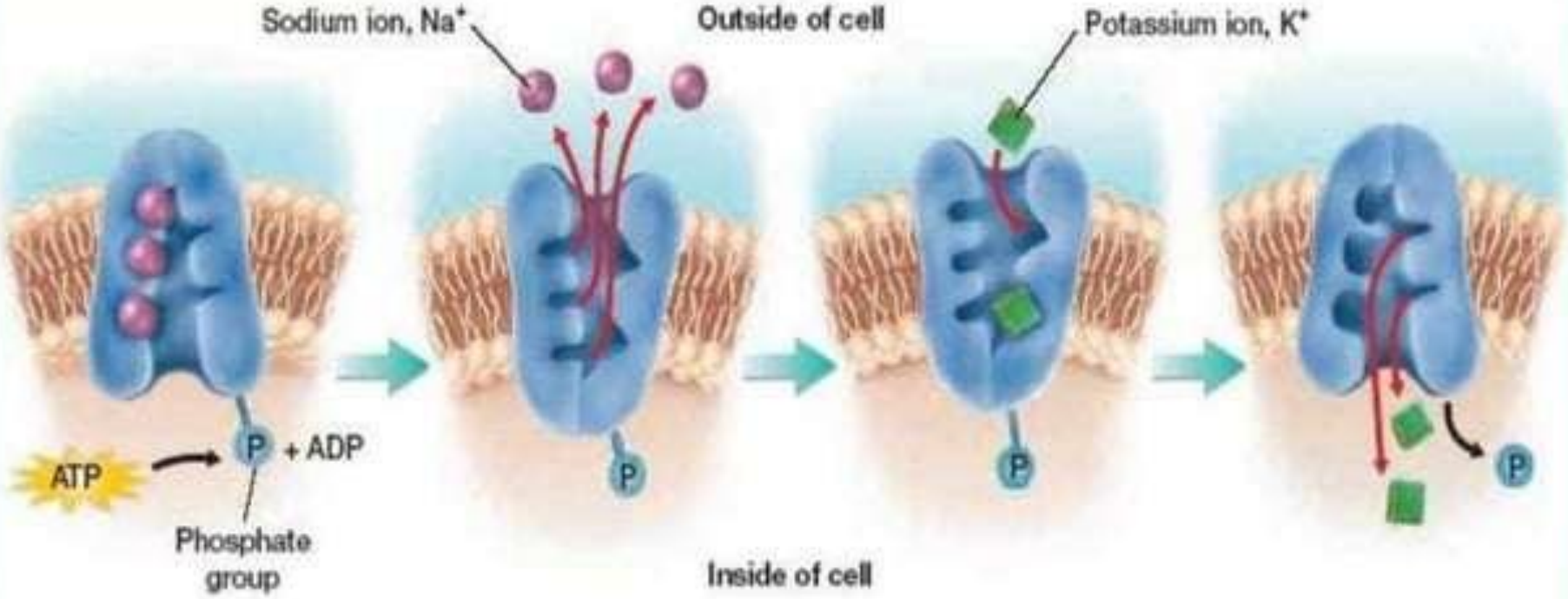
  K binding site – located outside.

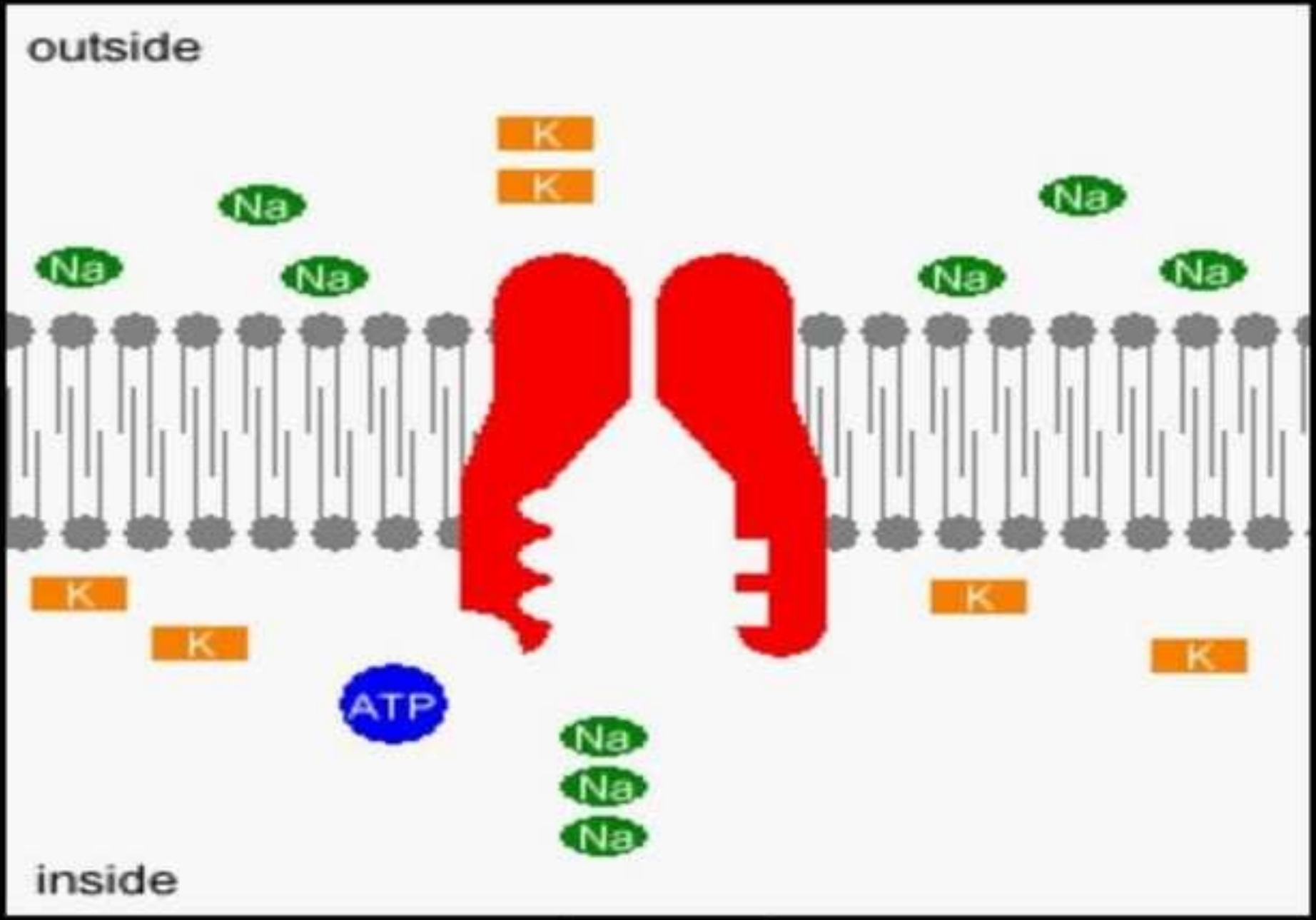
BIO graphic

Sodium-Potassium Pump

The sodium-potassium pump actively transports sodium ions, Na^+, and potassium ions, K^+, against their concentration gradient.

1. Three sodium ions, Na^+ and a phosphate group (P) from ATP bind to the pump.
2. The pump changes shape, transporting the three sodium ions across the cell membrane.
3. Two potassium ions, K^+, bind to the pump and are transported across the cell membrane.
4. The phosphate group and the two potassium ions are released inside the cell.




outside
K
K
Na
Na
Na
Na
Na
Na
K
K
K
K
ATP
Na
Na
Na
inside

Functions of Sodium Potassium Pump

Control cell volume

Renders nerve and muscle cells electrically excitable.

Active transport of amino acids and sugar.

Clinical aspects :

Sodium potassium ATPase is inhibited by digitalis (digoxin) which increases force of contraction of heart muscle by altering the excitability.

Ouabain is another inhibitor

Secondary active transport

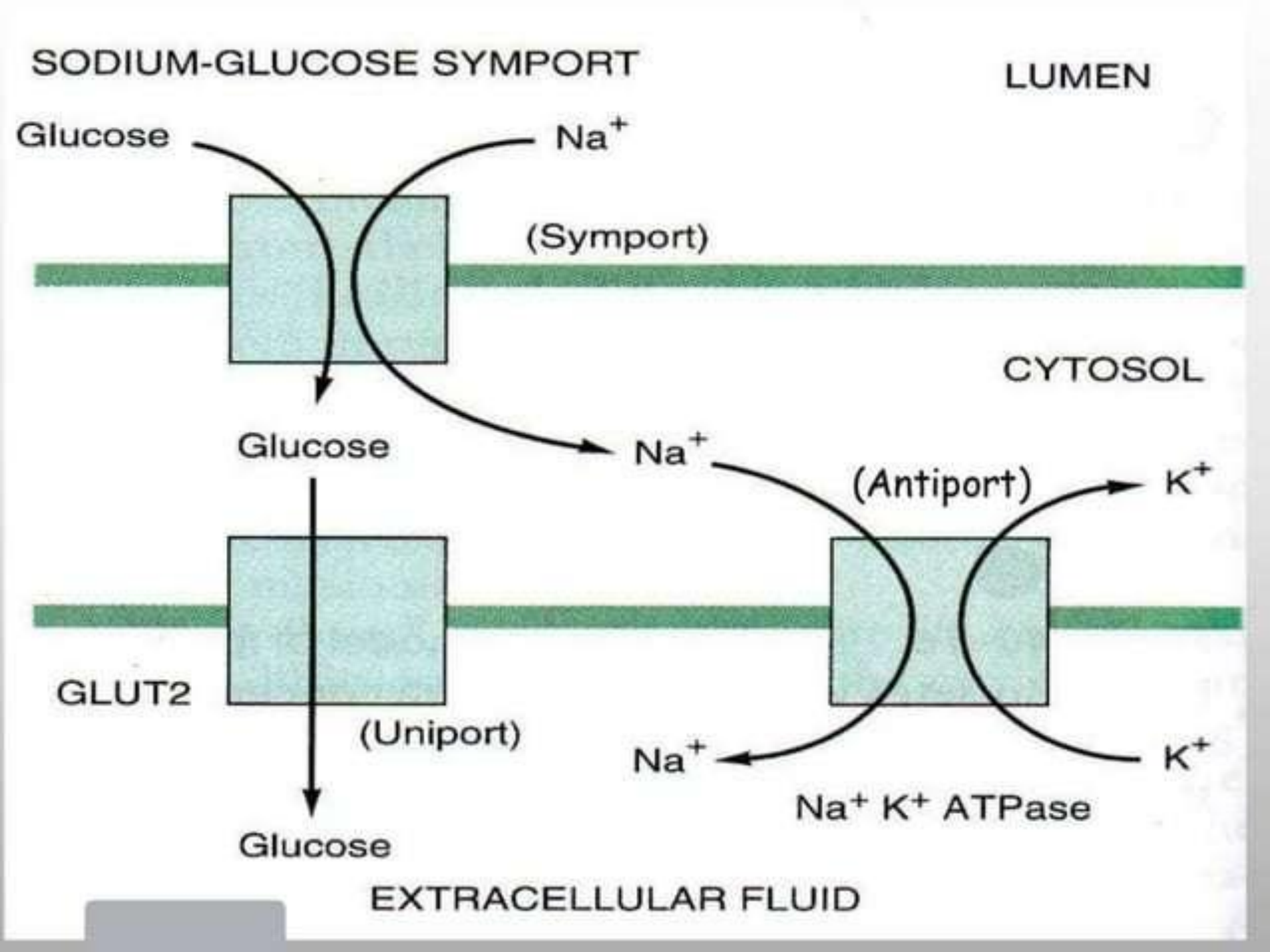
- Movement of a substance down its conc. gradient is coupled to a second substrate against its conc. gradient.
- Eg: **Glucose -Na^+ symport** – movement of Na^+ down its conc. gradient drags glucose against its conc. gradient.
- Energy for the transport comes from a secondary source – stored in electrochemical gradient of Na^+

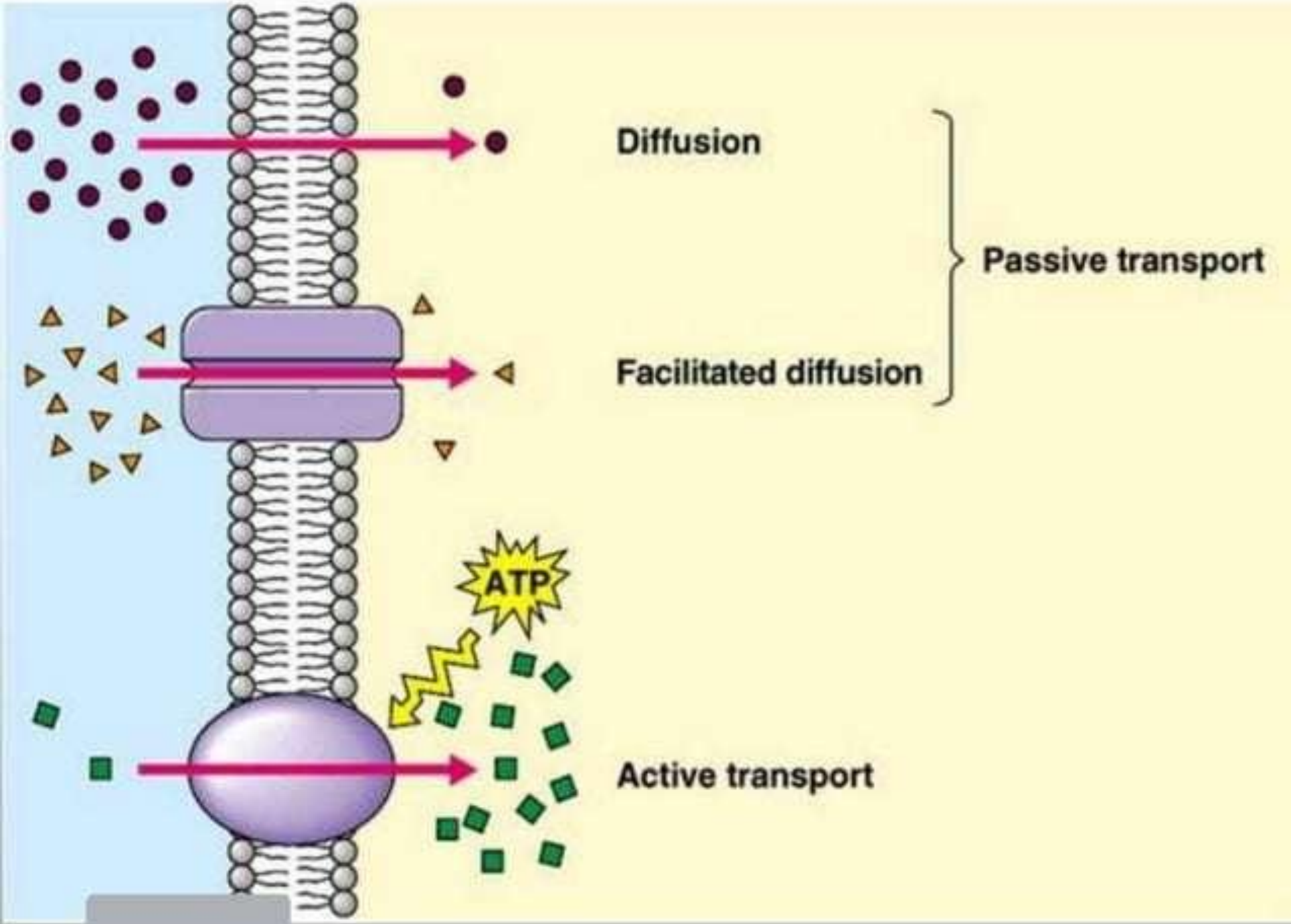
- Absorption of glucose, amino acids in intestinal mucos and also in proximal renal tubule.

- Clinical aspects :

In cholera - severe dehydration occurs.

- **Oral rehydration therapy** - contains NaCl & glucose.
- The transport of glucose and Na^+ across the intestina epithelium forces (via osmosis) movement of water from the lumen of the gut into intestinal cells, resulting in rehydration.
- Glucose alone or NaCl alone would not be effective.


SODIUM-GLUCOSE SYMPORT
LUMEN
Glucose
Na+
(Symport)
CYTOSOL
Glucose
Na+
(Antiport)
K+
GLUT2
(Uniport)
Na+
K+
Na+ K+ ATPase
Glucose
EXTRACELLULAR FLUID


Diffusion
Passive transport
Facilitated diffusion
ATP
Active transport

Transport of macromolecule

Transport of macromolecule like proteins, hormones, nmunoglobulin, LDL and viruses

Transport by formation of membrane bound vesicles
Requires energy -ATP , Ca^{2+} ions.

. Exocytosis

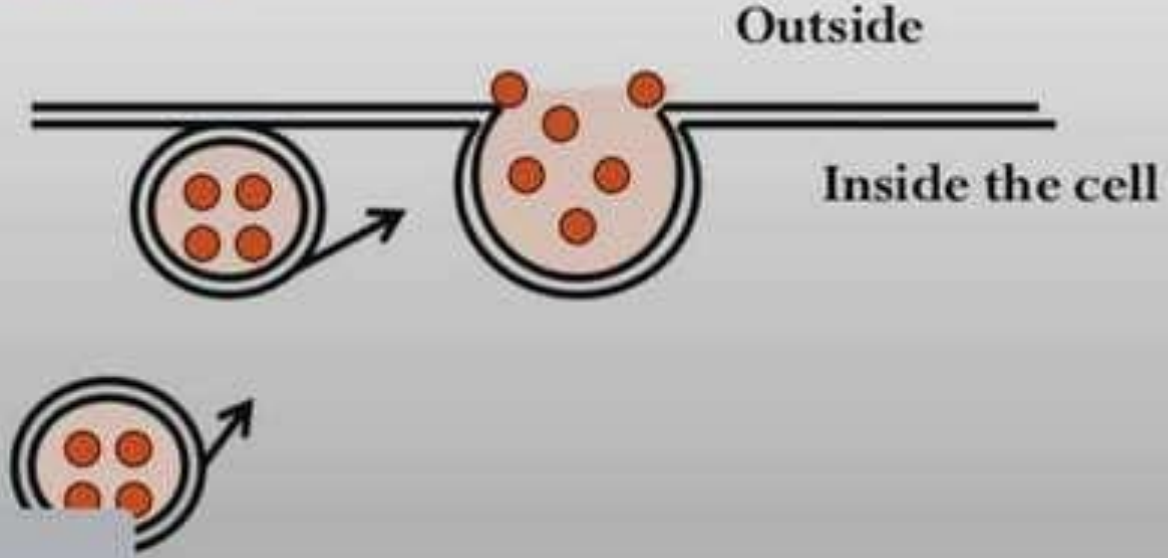
. Endocytosis → Phagocytosis
→ Pinocytosis
→ Receptor mediated endocytosis

Exocytosis

The cells release macromolecules to the exterior by exocytosis.

The components are carried in the vesicles.

The inner membrane of the vesicle fuses with the outer plasma membrane.



Molecules released by exocytosis have at least **three fates:**

(1) They can attach to the cell surface and become peripheral proteins, eg, antigens.

(2) They can become part of the extracellular matrix eg, collagen and glycosaminoglycans.

(3) They can enter extracellular fluid and signal other cells.

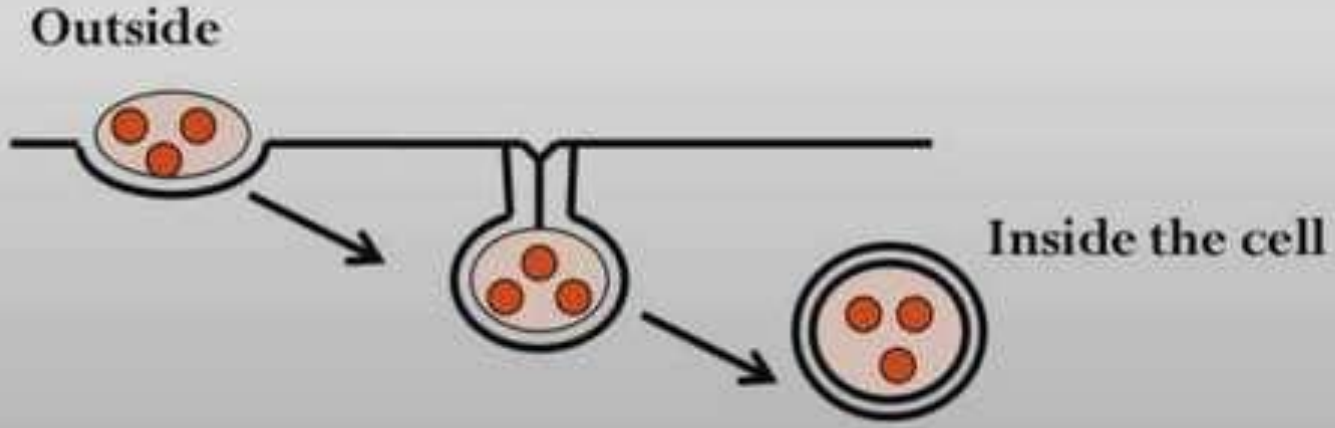
Insulin, parathyroid hormone, and the catecholamines are all packaged in granules and processed within cells, to be released upon appropriate stimulation

- Release of Trypsinogen by pancreatic acinar cell
- Release of Insulin by beta cells of langerhans
- Release of Acetyl choline by presynaptic cholinergic nerves

Endocytosis

Endocytosis vesicles are formed when a segment of plasma membrane invaginates enclosing a minute volume of ECF and its contents.

Then fusion of the plasma membrane and neck sealing of the vesicle occur.

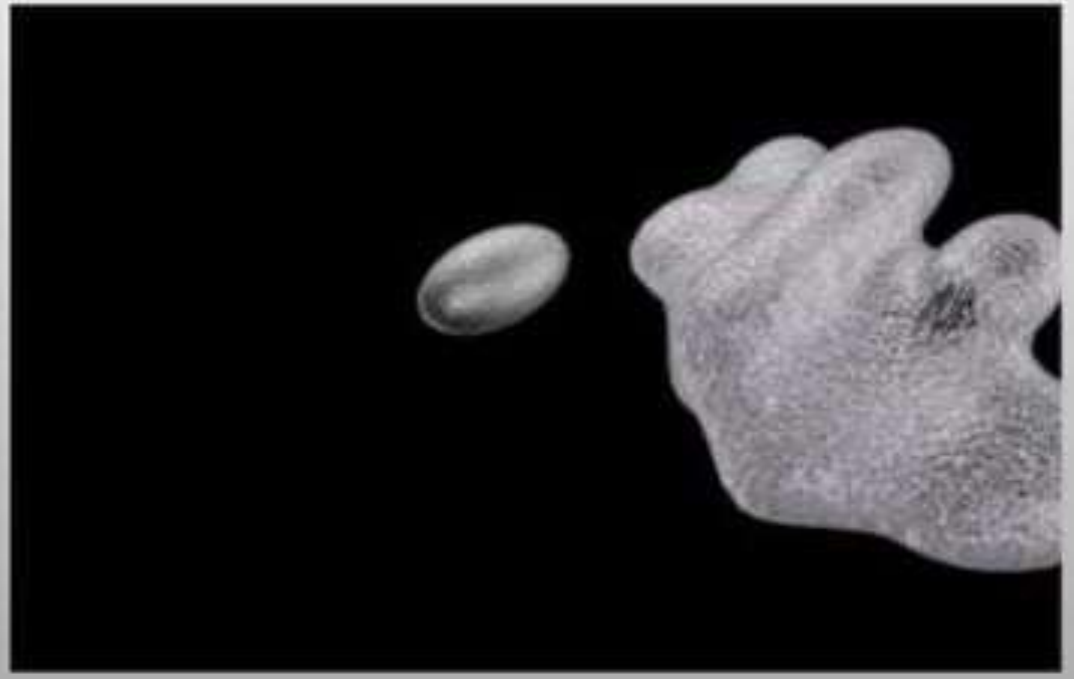


Endocytosis requires

1) Energy, usually from the hydrolysis of ATP;

2) Ca^{2+}; and

3) contractile elements in the cell (probably the microfilament system)

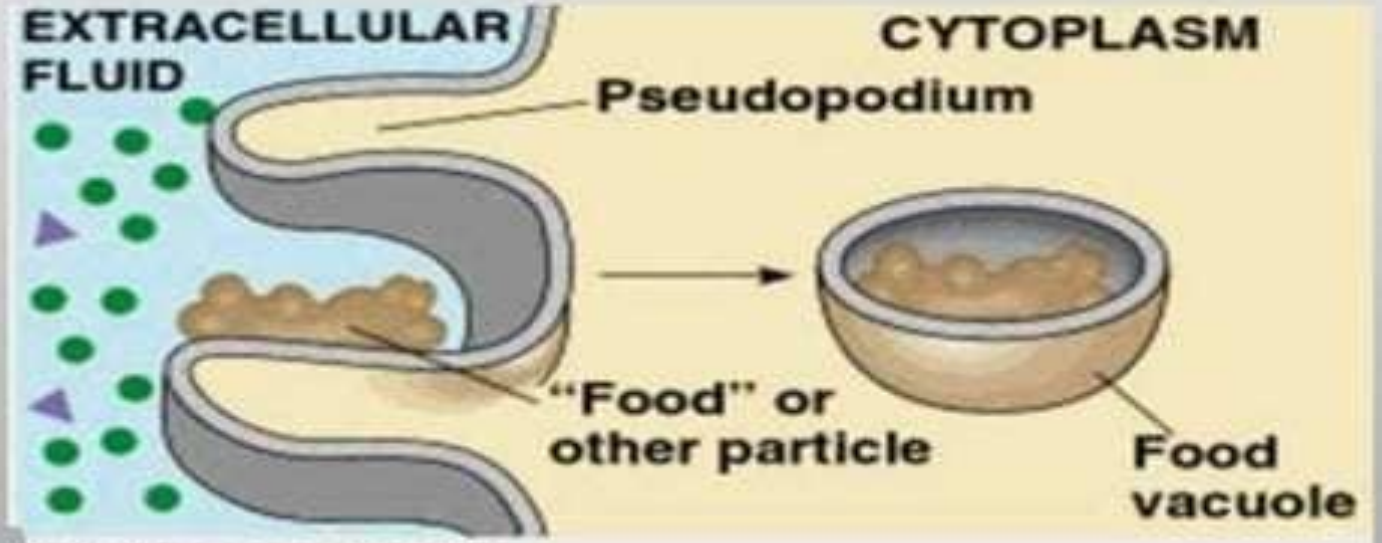


Phagocytosis - cell eating

- Occurs only in **Macrophages and Granulocytes**

- Involves the ingestion of large particles such as **viruses, bacteria, cells, or debris**

- The particles are surrounded by pseudopodia to form phagosomes.



(a) Phagocytosis

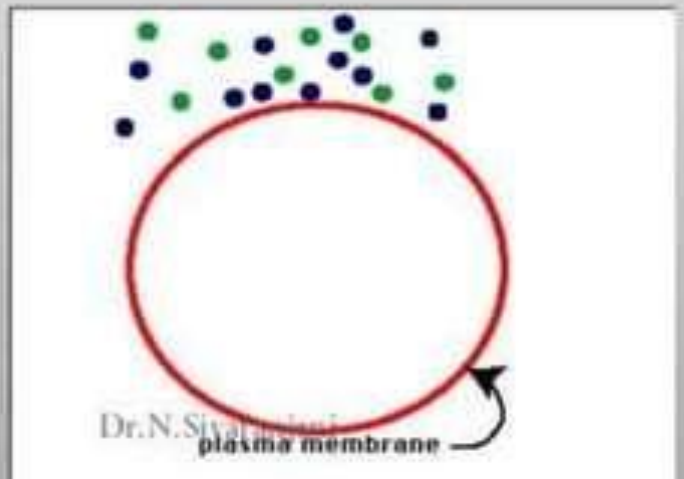
inocytosis – cell drinking

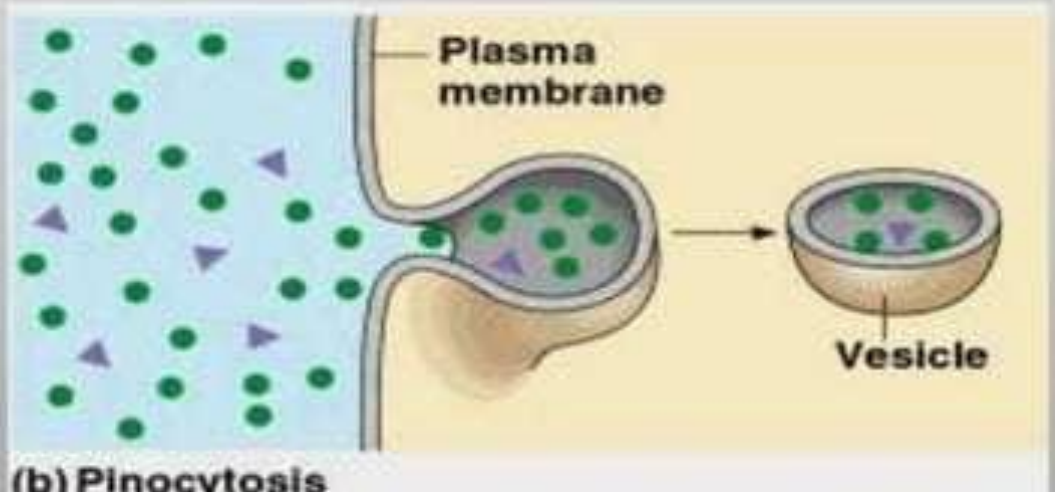
is the property of the cells to uptake fluid and fluid ontents.

Two types :

.) Fluid phase pinocytosis is non selective process of uptake f fluid and its contents.

ormation of small vesicle is an active process.





(b) Pinocytosis

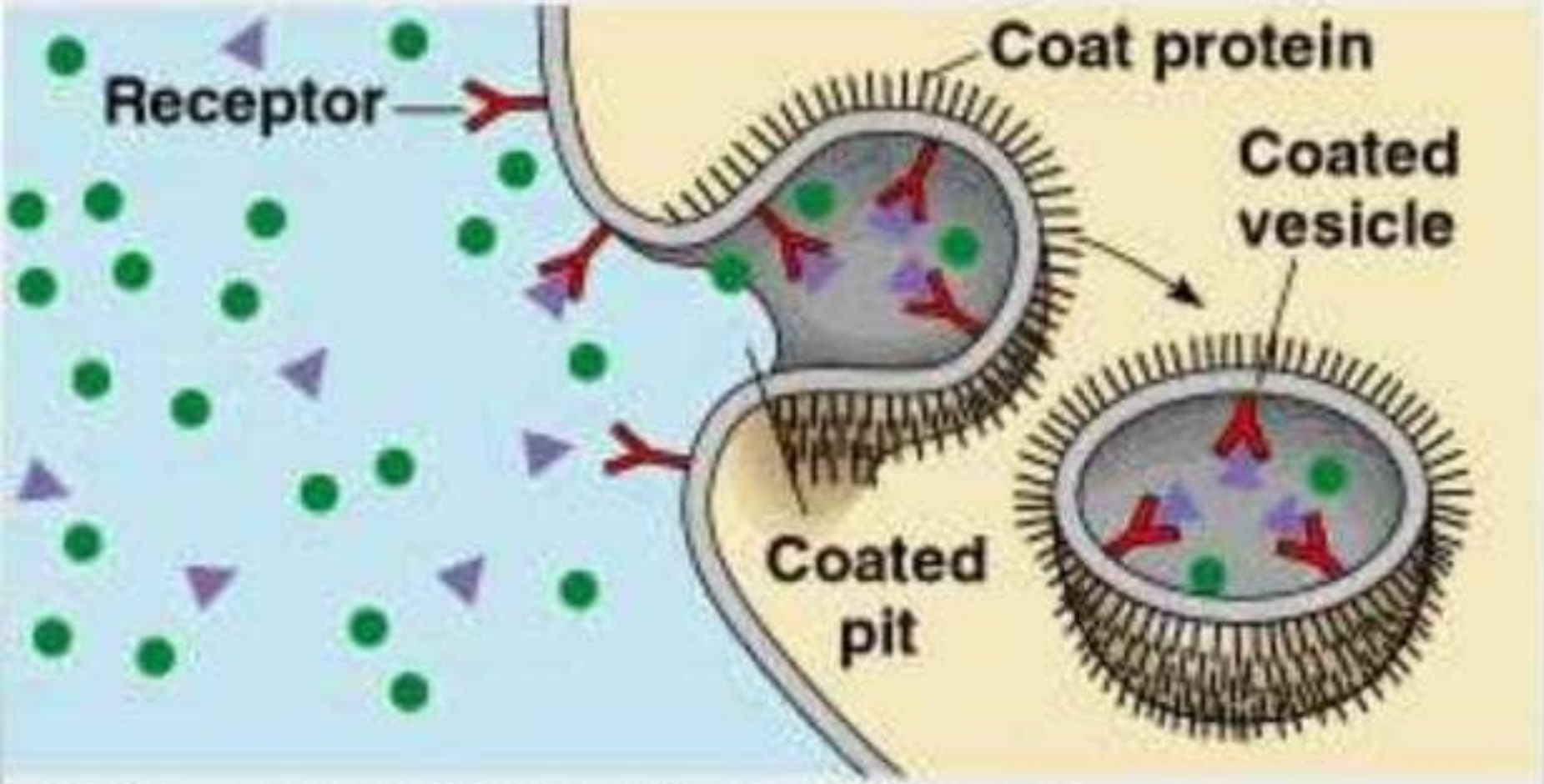
Receptor Mediated Endocytosis / Absorptive Pinocytosis.

- receptor-mediated selective process
- Uptake of macromolecules for which there are a finite number of binding sites on the plasma membrane
- minimize the uptake of fluid or soluble unbound macromolecules
- vesicles formed are coated on the cytoplasmic side with a filamentous material (protein clathrin) - Coated pits
- Clinical importance :-

Some viruses cause diseases by this mechanism

- Hepatitis (affecting liver cells)
- Poliomyelitis (affecting motor neurons)
- AIDS (affecting T cells)

Receptor mediated absorptive pinocytosis



(c) Receptor-mediated endocytosis

Eg: Low-density lipoprotein (LDL-C) and its receptor are internalized by means of coated pits containing the LDL receptor

Absorptive / selective Pinocytosis is receptor mediated.

g : LDL-C binds to LDL receptor

↓

LDL receptor complex is internalized

↓

cytoplasmic side of vesicles coated with Clathrin called c
lathrin Coated pits

↓

Coated vesicles fuse with endosomes

↓

LDL-C is degraded by lysosomal enzymes

↓

receptor molecules are release back to cell surface.

Membrane Channels and Pumps

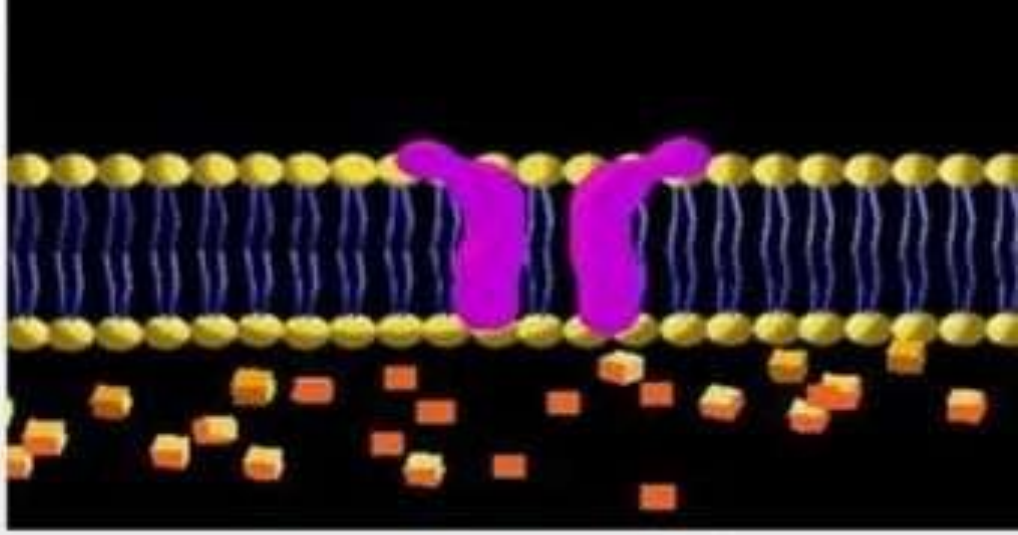
Membrane is intrinsically impermeable to ions and polar molecules

Permeability is conferred by

Channels

Pumps

Ion channels



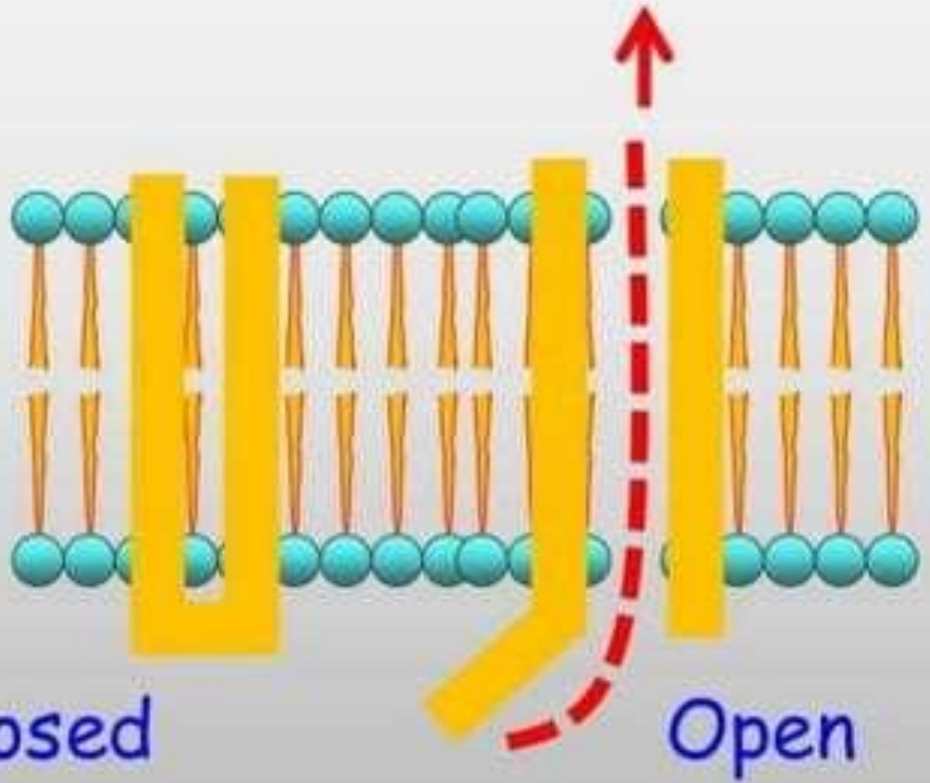
- Transmembrane channels.

- Pore like structures composed of proteins.

- Transport Na^+ K^+ Ca^{++} and Cl^- across the cell membrane.

- Ion channels have gates controlled by opening and closing.

on channel are very **selective**, in most cases permitting
ne passage of only one type of ion



wo types of gated channels :

1. Ligand gated channels – a specific molecule binds to a receptor and opens the channels.
   Eg. Acetyl chlorine receptor
2. Voltage gated channels - These channels open (depolarization)or close (ground state) in response to the changes in membrane potential.

❖Eg:- voltage gated Na+ channel & K+ channel
seen in nerve terminals & helps in nerve conduction .

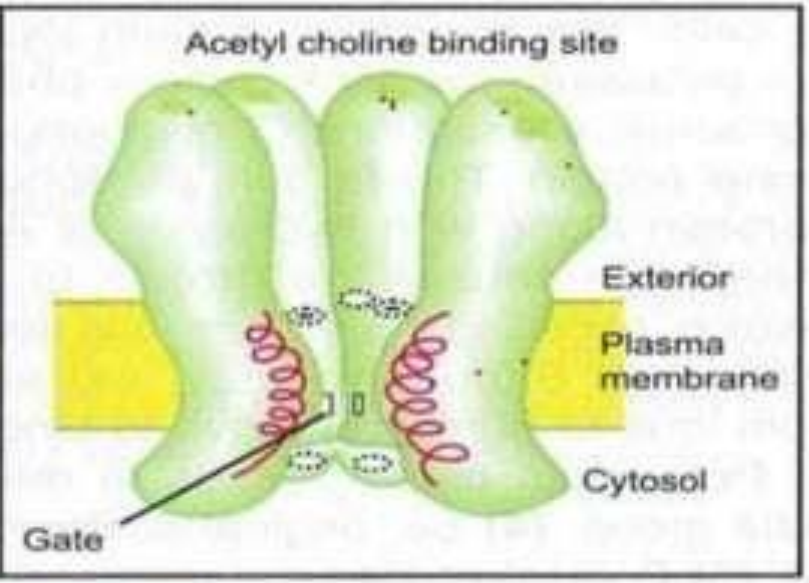
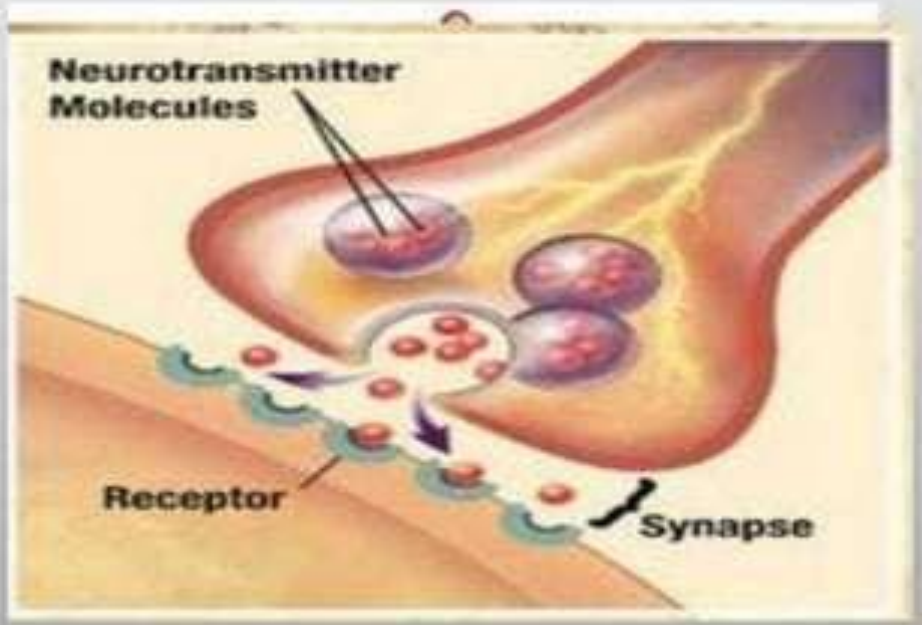


Fig. 2.9 Acetyl choline receptor



Ionophores

- Certain microbes synthesize small cyclic organic molecules called ionophores.

- Two major groups
  - Mobile carriers (Valinomycin)
    readily diffuse in a membrane & can carry an K^+ ion across a membrane
  - Channel formers (Gramicidin)
    create a channel that transverses the membrane & through which ions can diffuse

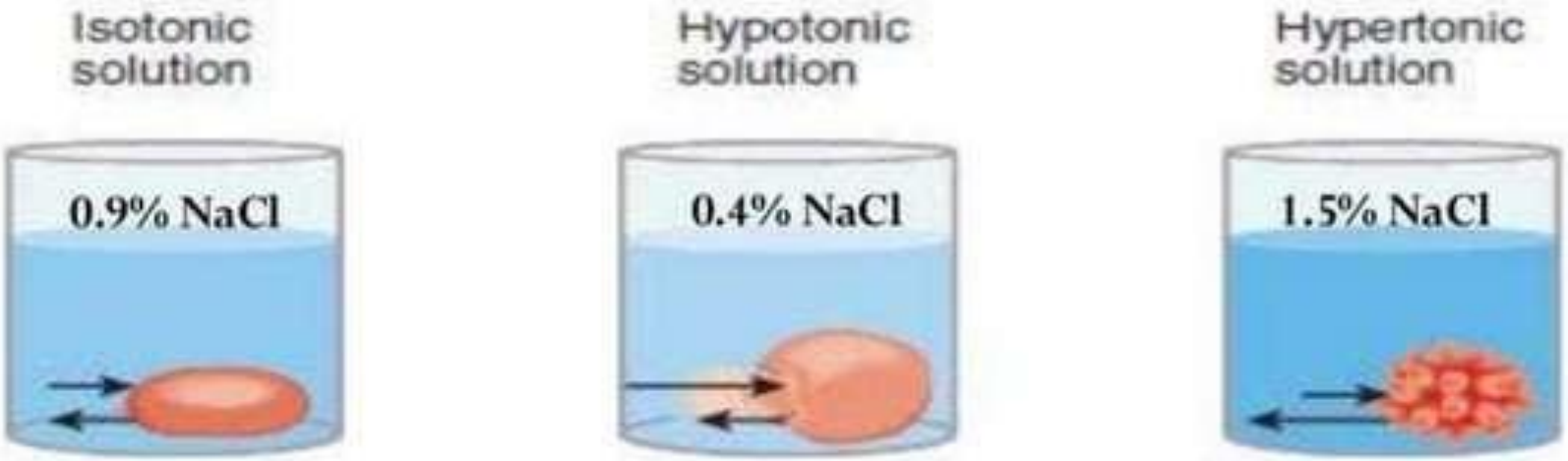
Osmosis

- The diffusion of water through a semi permeable membrane.

- Movement of water molecules occur from an area of lower solute concentration to an area of higher solute concentration.

- Application of osmosis :
  - Fluid balance and blood volume
  - RBC and fragility
  - Diabetes Mellitus – Osmotic diuresis
  - Edema – hypoalbuminemia

Osmotic Fragility Test



(a) Illustrations showing direction of water movement

Normal RBC shape

RBC undergoes hemolysis

RBC undergoes crenation

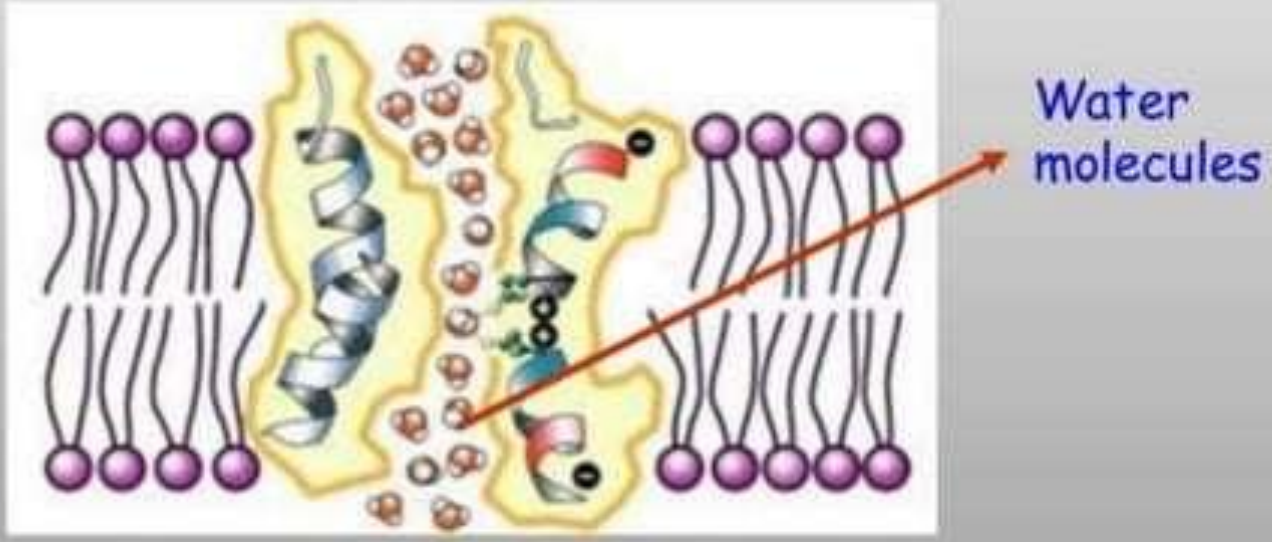
Water channels (Aquaporins)

- Membrane channel proteins that serve as selective pores hrough which water cross the plasma membrane.

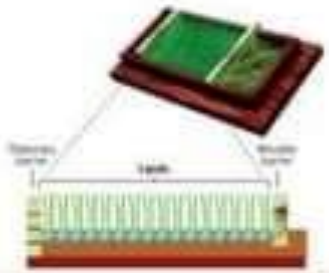
- 10 distinct Aquaporins (AP-1 to AP-10)

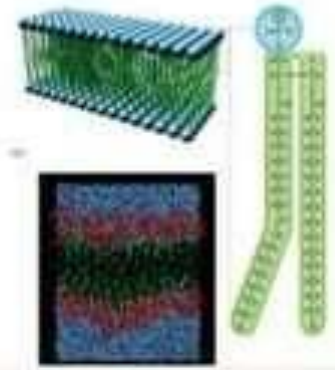
- clinical aspects :

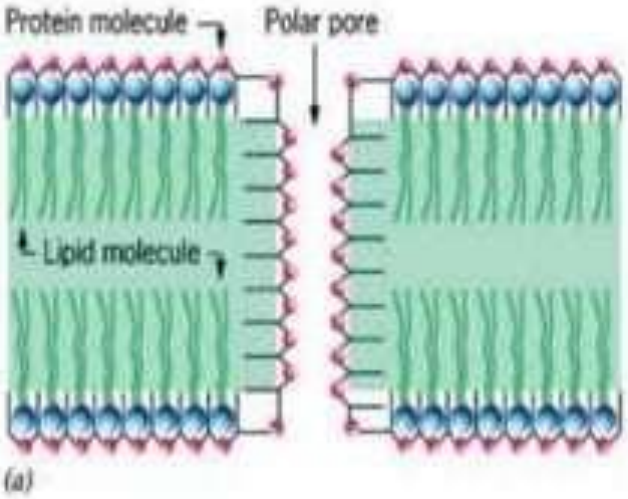
Nephrogenic Diabetes Insipidus - Mutations in the gene ncoding AP-2.

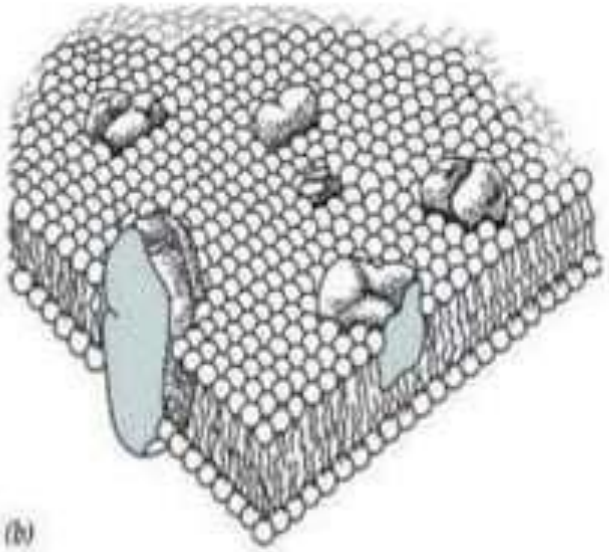


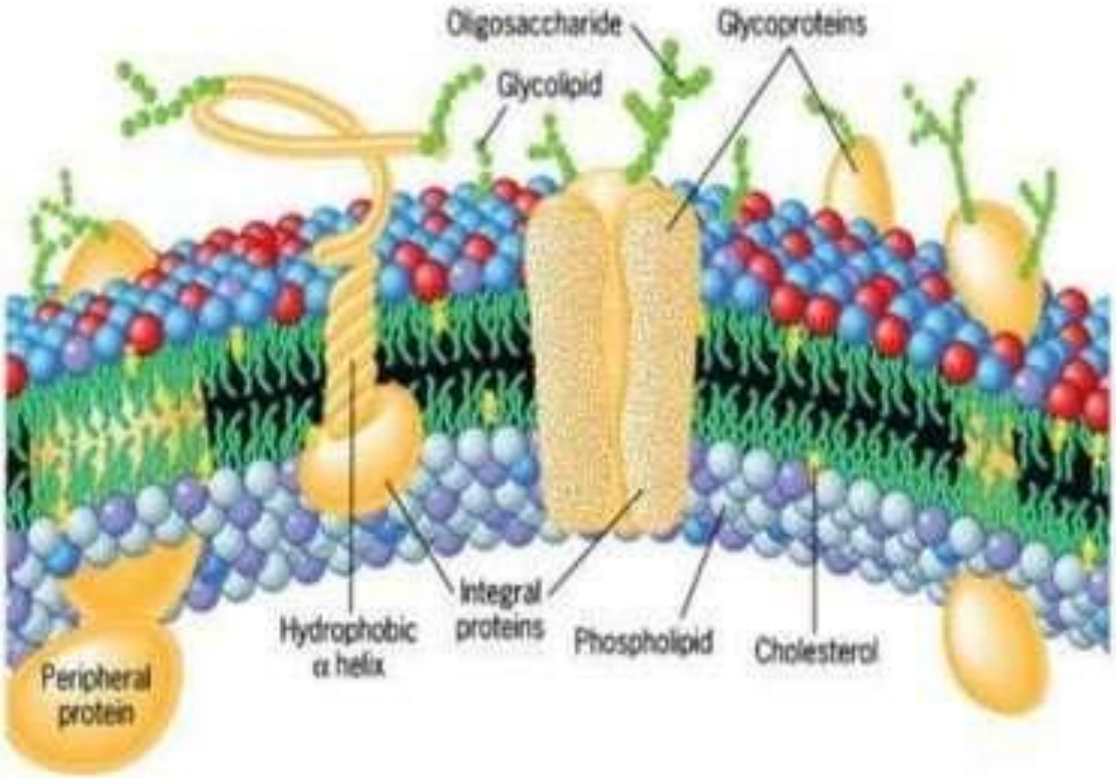
4.2 A Brief History of Studies on Plasma Membrane Structure

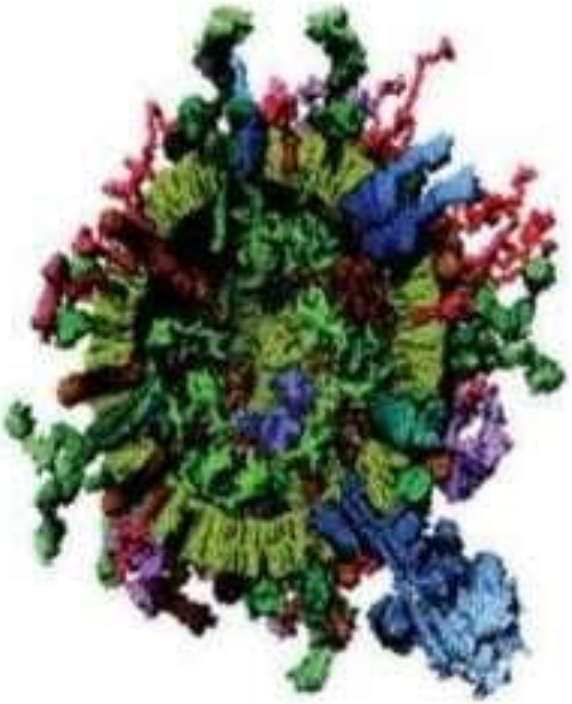


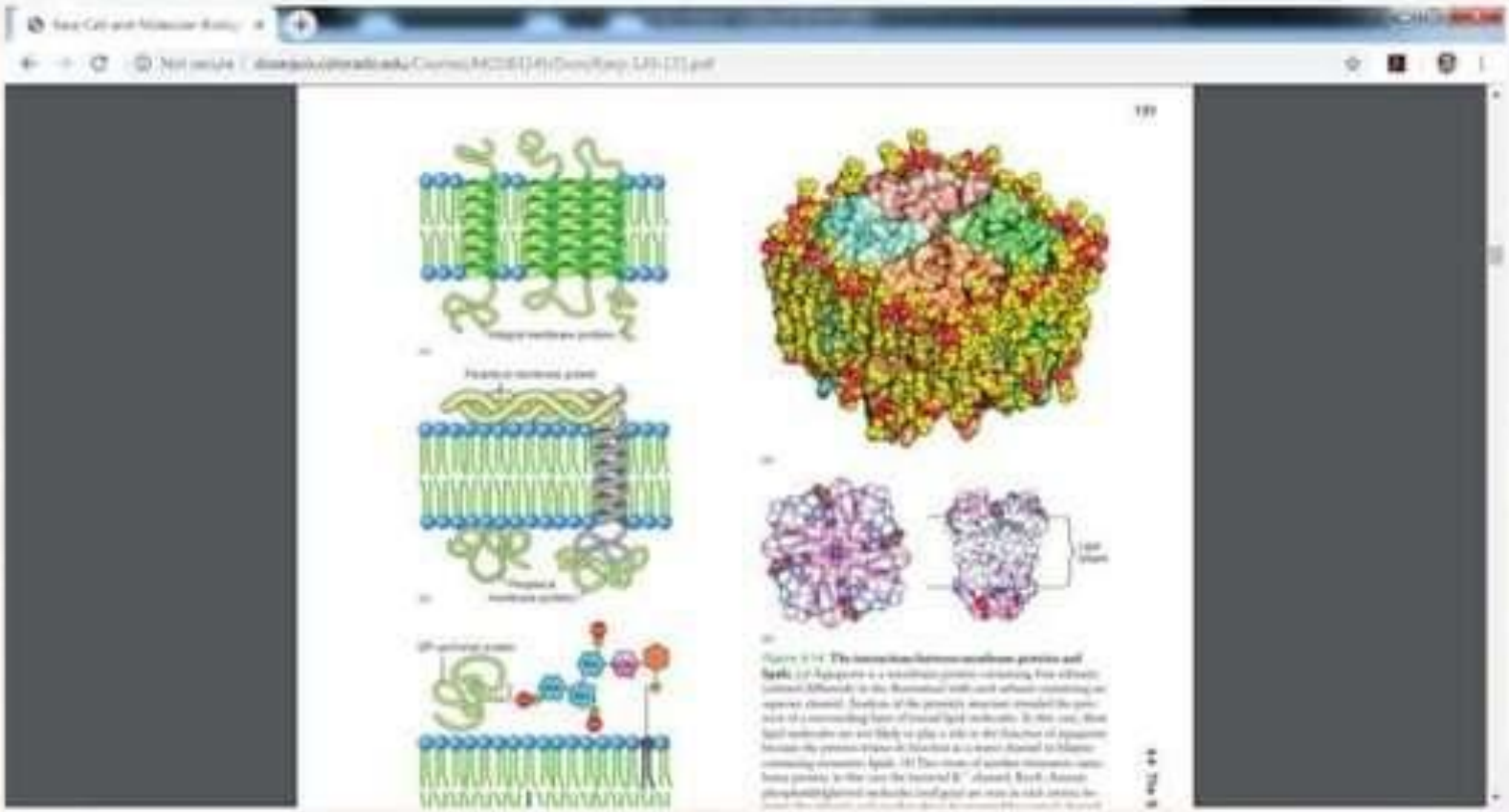



Protein molecule
Polar pore
Lipid molecule
(a)


(b)


Oligosaccharide
Glycoproteins
Glycolipid
Hydrophobic
α helix
Integral
proteins
Phospholipid
Cholesterol
Peripheral
protein



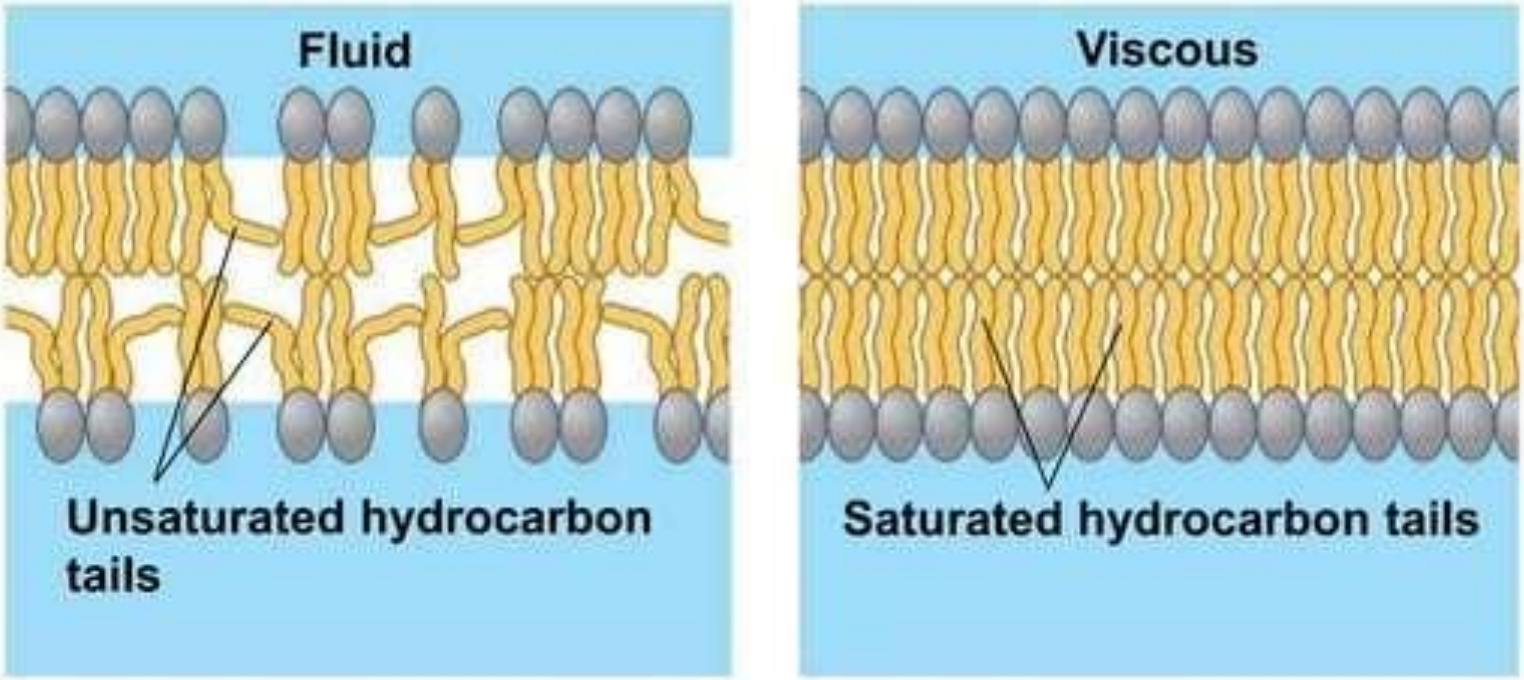


MEMBRANE FLUIDITY

- The structure of the fatty acid tails of the phospholipids is important in determining the properties of the membrane, and in particular, how fluid it is.
- **Saturated** fatty acids have no double bonds (are saturated with hydrogens), so they are relatively straight. **Unsaturated** fatty acids, on the other hand, contain one or more double bonds, often resulting in a bend or kink. (You can see an example of a bent, unsaturated tail in the diagram of phospholipid structure that appears earlier in this article.) The saturated and unsaturated fatty acid tails of phospholipids behave differently as temperature drops:
- At cooler temperatures, the straight tails of saturated fatty acids can pack tightly together, making a dense and fairly rigid membrane.
- Phospholipids with unsaturated fatty acid tails cannot pack together as tightly because of the bent structure of the tails. Because of this, a membrane containing unsaturated phospholipids will stay fluid at lower temperatures than a membrane made of saturated ones.
- Most cell membranes contain a mixture of phospholipids, some with two saturated (straight) tails and others with one saturated and one unsaturated (bent) tail. Many organisms—fish are one example—can adjust physiologically to cold environments by changing the proportion of unsaturated fatty acids in their membranes. For more information about saturated and unsaturated fatty acids, see the article on lipids.
- In addition to phospholipids, animals have an additional membrane component that helps to maintain fluidity. **Cholesterol**, another type of lipid that is embedded among the phospholipids of the membrane, helps to minimize the effects of temperature on fluidity.
- *Image credit: "Cholesterol," by BorisTM (public domain).*
- At low temperatures, cholesterol increases fluidity by keeping phospholipids from packing tightly together, while at high temperatures, it actually reduces fluidity^{3,4}3,4start superscript, 3, comma, 4, end superscript. In this way, cholesterol expands the range of temperatures at which a membrane maintains a functional, healthy fluidity.

- As temperatures cool, membranes switch from a fluid state to a solid state
- The temperature at which a membrane solidifies depends on the types of lipids
- Membranes rich in unsaturated fatty acids are more fluid than those rich in saturated fatty acids
- Membranes must be fluid to work properly; they are usually about as fluid as salad oil
- The steroid cholesterol has different effects on membrane fluidity at different temperatures
- At warm temperatures (such as 37°C), cholesterol restrains movement of phospholipids
- At cool temperatures, it maintains fluidity by preventing tight packing

FIGURE 7.8



(a) Unsaturated versus saturated hydrocarbon tails

(b) Cholesterol within the animal cell membrane