CELL BIOLOGY
PLASMA MEMBRANE

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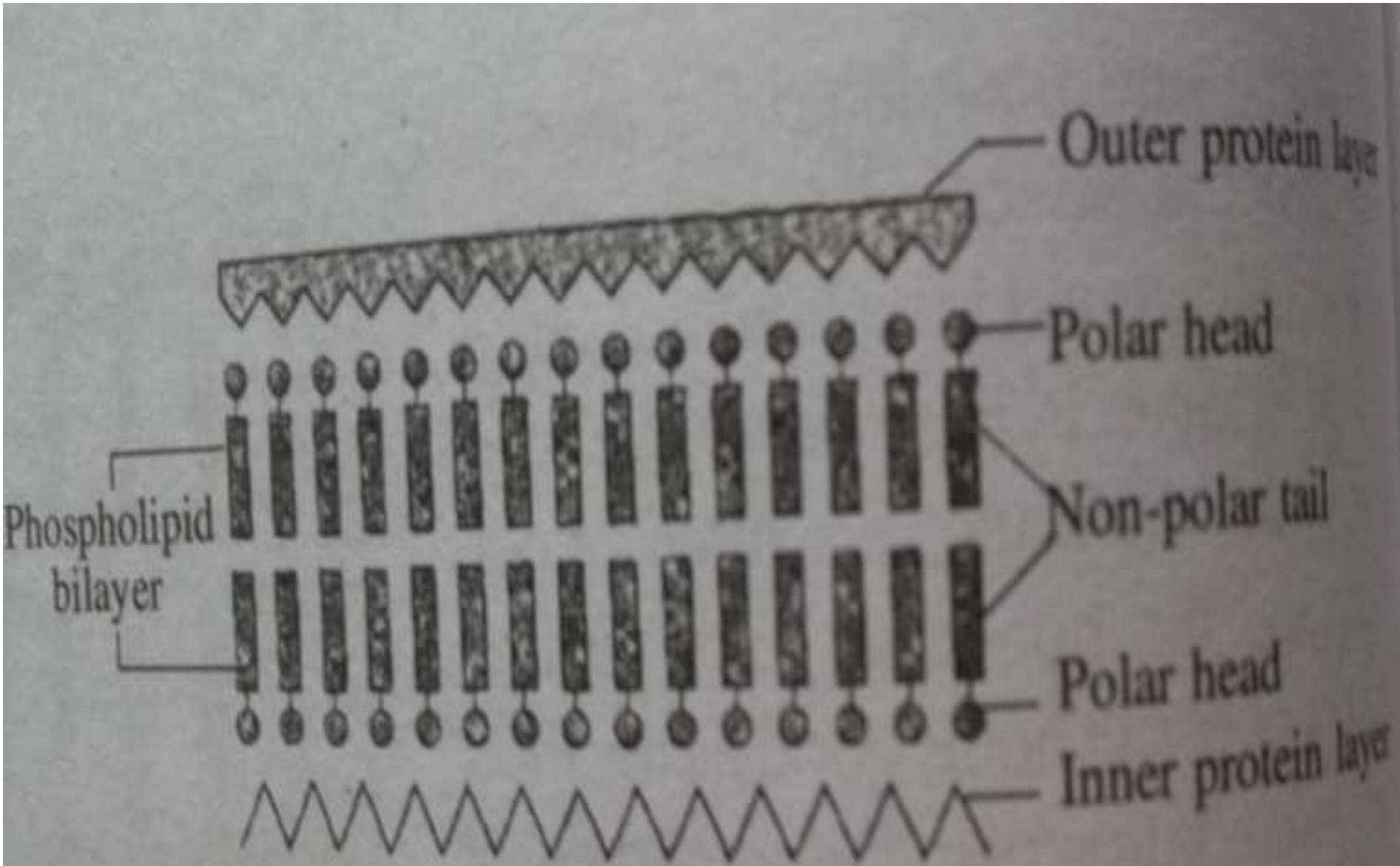
Plasma membrane- Chemical organization

- Plasma membrane is highly organized biologically active molecular assembly formed of 25-80% lipids,20-70% proteins, 1-10% carbohydrates and 20% water
- Components
- Membrane lipids- Mainly phospholipids
- Membrane proteins- structural and functional proteins
- Membrane carbohydrates
- Water

Robertson's Unit membrane concept

- David Robertson (1959) based on the previous model proposed by Danielli –Devson
- According to the unit membrane concept all the biological membranes have the same trilaminar structure with approximately 75 A° thickness. He named Unit membrane b's of this universal nature
- The central zone (bimolecular lipid layer) 25-35 A° in between two marginal zones (thin and flat protein monolayers) of 20-25 A°



Robertson's unit membrane model

Unit membrane model continued--

- The membrane comes from a pre-existing membrane
- ER are extensions of plasma membrane
- Short comings
- 1. Oversimplified
- 2. Does not explain the permeability, dynamic nature as well as transport ability of the membrane

Fluid mosaic model of Plasma membrane

- Proposed by Singer and Nicolson in 1972
- P.m is a 2 dimensional quasifluid solution of organized lipids and globular proteins
- Mosaic molecular arrangement and free molecular movement
- Fluidity is directly proportional to the chain length and un saturation of the fatty acids
- Components have a covalent interaction

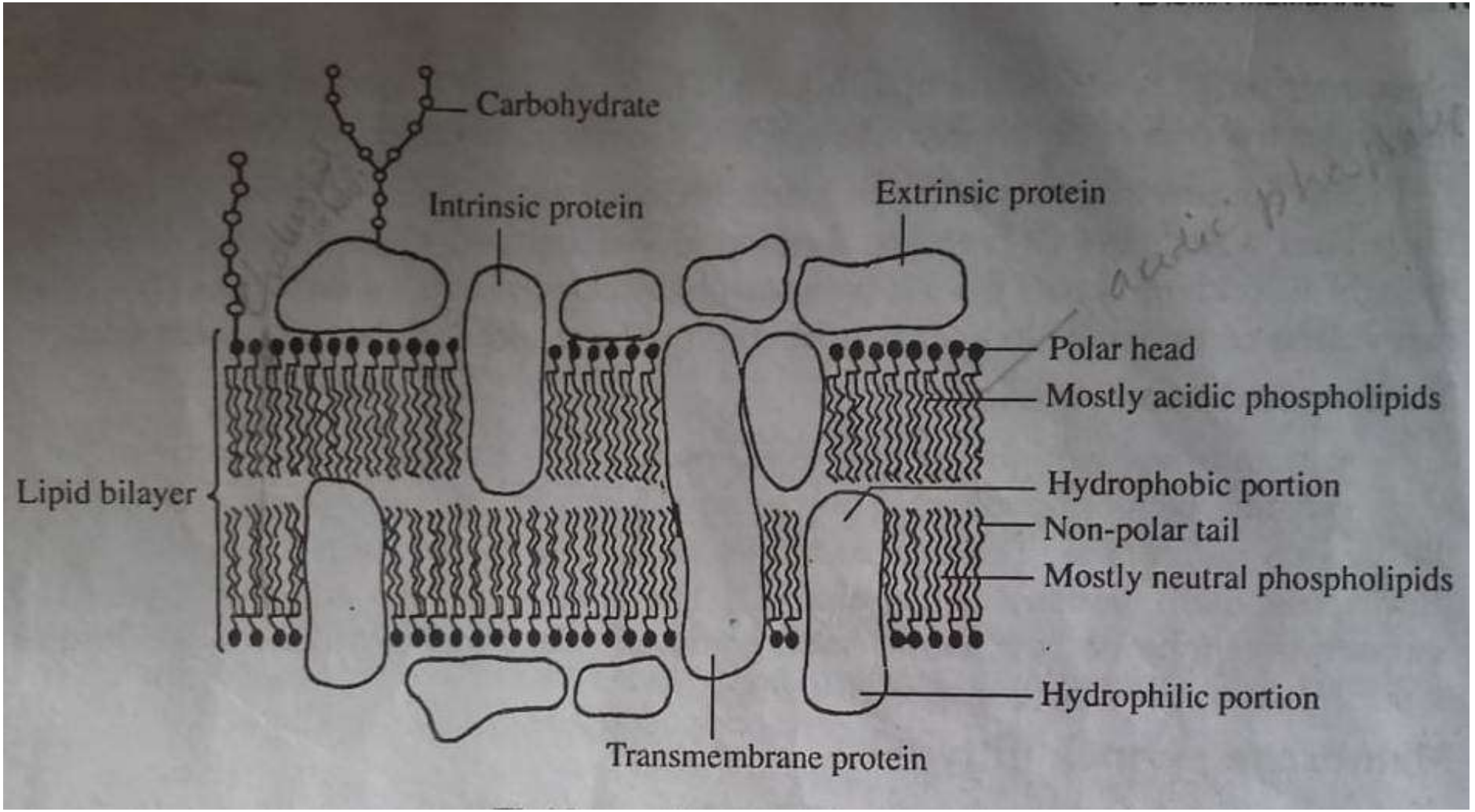
- Fluid mosaic model was proposed based on thermodynamic principles of organization of membrane lipids and proteins and available evidence of asymmetry and lateral mobility within the membrane matrix [S. J. Singer and G. L. Nicolson, Science 175 (1972) 720–731]. After over 40 years, this basic model of the cell membrane remains relevant.

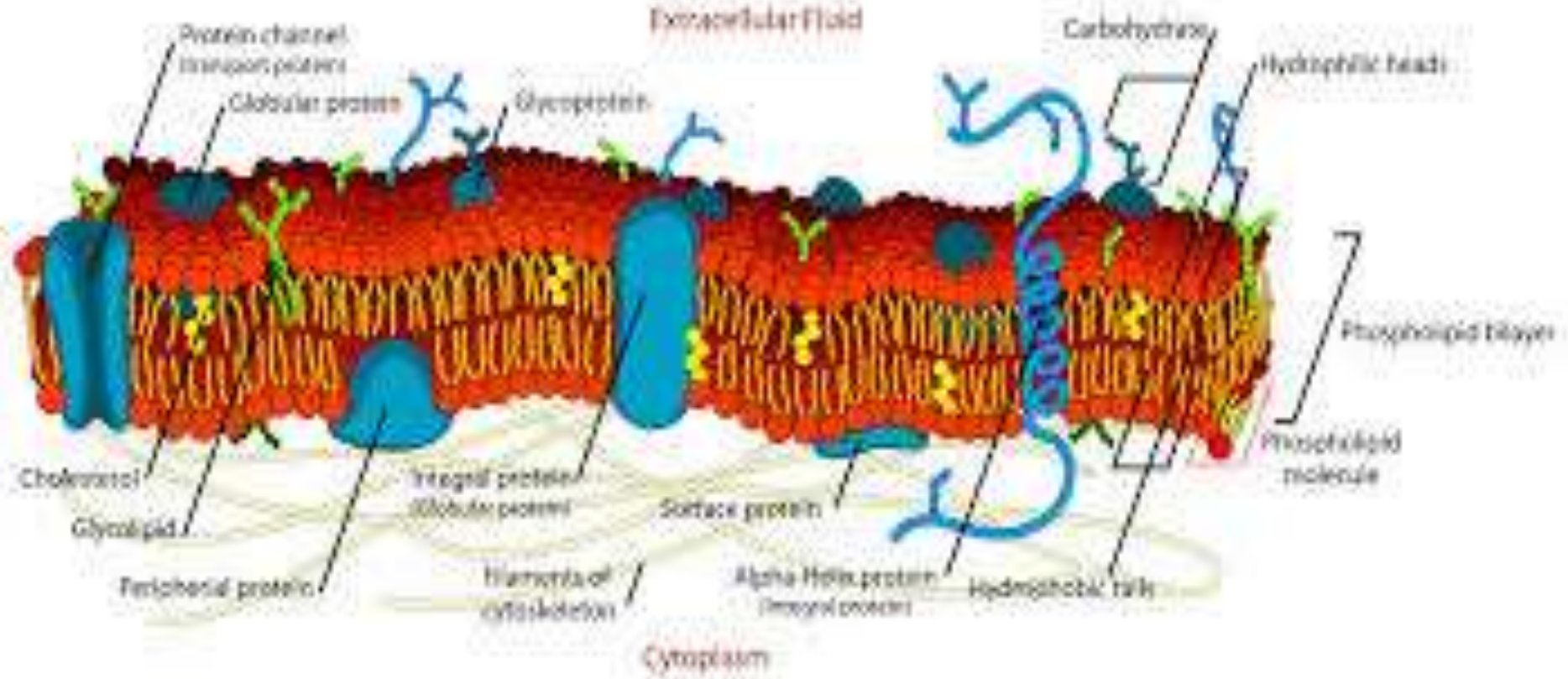
- Free lateral diffusion is possible for the components but no vertical diffusion
- Membrane phospholipids are arranged continuously side to side and back to back in bilayer through hydrophobic interactions contributing to the structural framework
- Polar heads of the lipids are directed towards the aqueous phase
- Non polar fatty acid tails are directed towards the non-aqueous phase

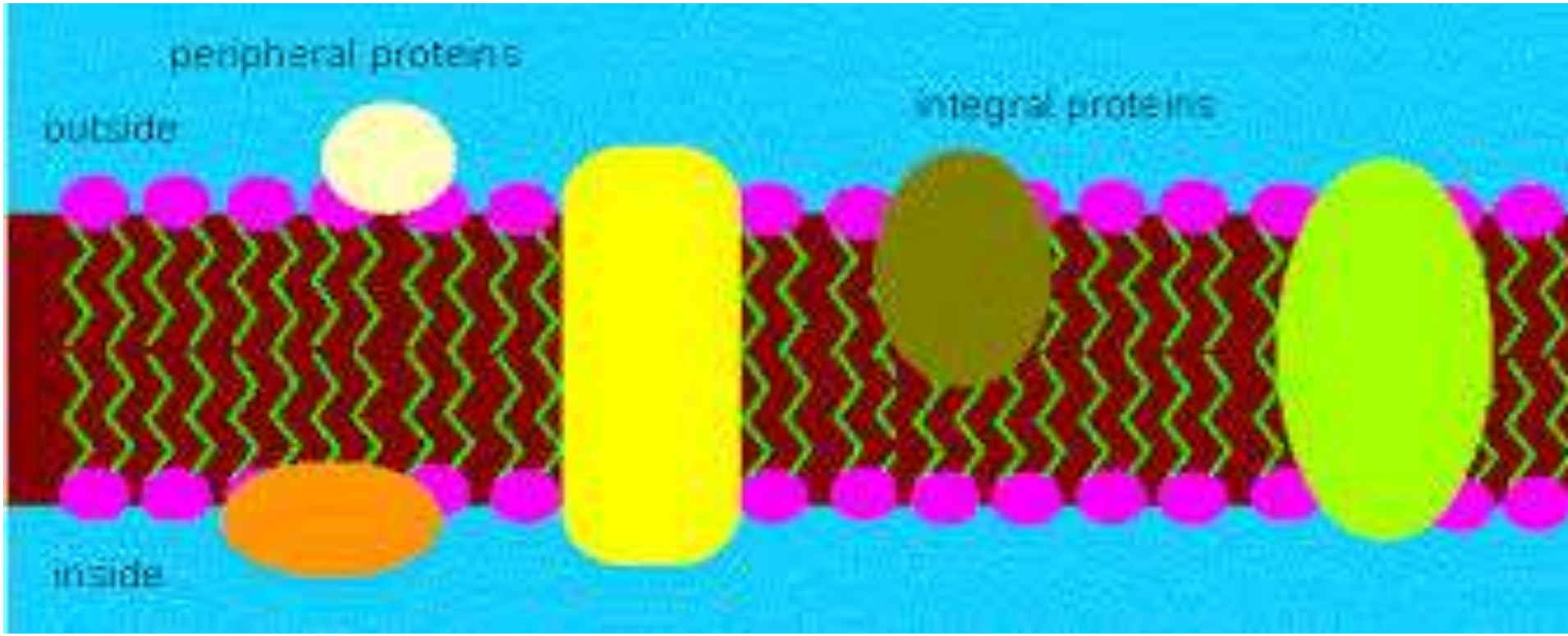
- Proteins have asymmetrical arrangement
- Extrinsic proteins are hydrophilic which bind with the surface by electrostatic interactions and hydrogen bonding.
- Integral proteins – 70-80%. They float like icebergs in the sea. They are amphipathic in nature
- Their lateral movements can bring functional proteins together
- Trans membrane proteins are also called alpha helix proteins
- Transmembrane proteins transmit signals from one surface of the membrane to other surface

- Carbohydrates are of glycolipids and glycoproteins. They undergo cross linking to form a network. They form the cell coat or glycocalyx.
- Cholesterol is seen tightly bound to phospholipids.
- This enhances the stability and reduces the flexibility and permeability and keep the membrane in more gel state
- Keep the lipid bilayer at low temperature

Fluid Mosaic Model




Extracellular Fluid
Protein channel
(transport protein)
Globular protein
Glycoprotein
Carbohydrate
Hydrophilic heads
Phospholipid bilayer
Phospholipid
molecule
Cholesterol
Glycolipid
Integral protein
(Globular protein)
Surface protein
Peripheral protein
Filaments of
cytoskeleton
Alpha Helix protein
(Integral protein)
Hydrophobic tails
Cytoplasm


peripheral proteins
integral proteins
outside
inside

Functions of plasma membrane

- Act as centre of respiration and oxidative phosphorylation in prokaryotes
- Selective gate way
- Maintains the constancy of the intracellular envt
- Transport of materials
- Transmission of impulses
- Recognition of foreign cells,hormones
- Chemoreception in bacteria

Cell Coat or Glycocalyx

- Glycocalyx is the protective coat of 10-20nm thickness formed of glycolipids and glycoproteins seen outer to the plasma membrane In animal cells .
- It undergoes continuous renewal.
- The carbohydrates involved are mainly oligosacharides
- They contain negatively charged sialic acid termini which can bind Ca++ and Na++ ions

Functions of Glycocalyx

1. Protection of cell from chemical and mechanical damages
2. Buffer regulation- It act as a buffer barrier with different ionic and pH from that of extracellular fluid
3. Act as a filter for differently sized molecules

   This is mainly seen in the glomerulus of the nephrons
4. Creates a microenvironment for cells as it serves as a diffusion barrier. For eg. Glycocalyx around the sarcolemma can trap Na++

5. Provides enzymes like alkaline phosphatase etc
6. Act as a biological barrier against bacteria and other antigens
7. It act as exoskeleton of the cell
8. Cell recognition and cellular adhesion it enables the cell to recognize each other and to distinguish between the self and non-self, detection of invaders like microbes and other pathogens as well as tissue grafts etc.

(the lectins (a family of extrinsic proteins) can recognize the oligosacharides of cell coats. glycoproteins of cell coat can act as recognition molecules as well as receptor molecules of hormones and neurotransmitters also)

Transmembrane Transport

- The materials transported into the cell are water, sugar, amino acids, fatty acids, steroids

  Inorganic ions etc.

1. passive Transport
2. Active Transport
3. Vesicular transport

PASSIVE TRANSPORT

- It is the spontaneous, energy independent, downhill flow of substances in a concentration gradient or electrochemical gradient.
- 3 driving forces like concentration gradient, potential gradient and the force of the solvent drag operate
- It occur under the action of osmotic forces
- Concentration gradient is maintained by differential osmotic and ionic concentrations on the two sides of the membrane.

- Potential gradient is resulted due to differential distribution of ions inside and outside the membrane
- The force of solvent drag occurs when the solution flows through the pores of the membrane

Types of Passive Transport

1. Osmosis
2. Simple diffusion
3. Facilitated diffusion

Osmosis

- Net movement of water and other solvent molecules from a hypotonic solution to a hypertonic solution through a semi permeable membrane in response to a concentration gradient or potential gradient in order to equalize the concentrations in both sides
- Endosmosis- Inflow of water into the cell- takes place when intracellular fluid is hypertonic awhen compared to the external medium
- Exosmosis- Outflow of water from the cell

- Osmotic flow always occur from lower to higher osmotic potential or tonicity.
- Tonicity is the solute concentration
- Osmotic potential is directly proportional to tonicity
- Tonicity and osmotic potential are high in hypertonic solutions and low in hypotonic solution

Passive diffusion

- Spontaneous flow of low molecular weight metabolites in a concentration gradient without energy utilization or a carrier molecule
- Rate of flow is directly proportional to the concentration gradient an lipid solubility
- It is a slow process, less selective and non-steriospecific

Facilitated diffusion

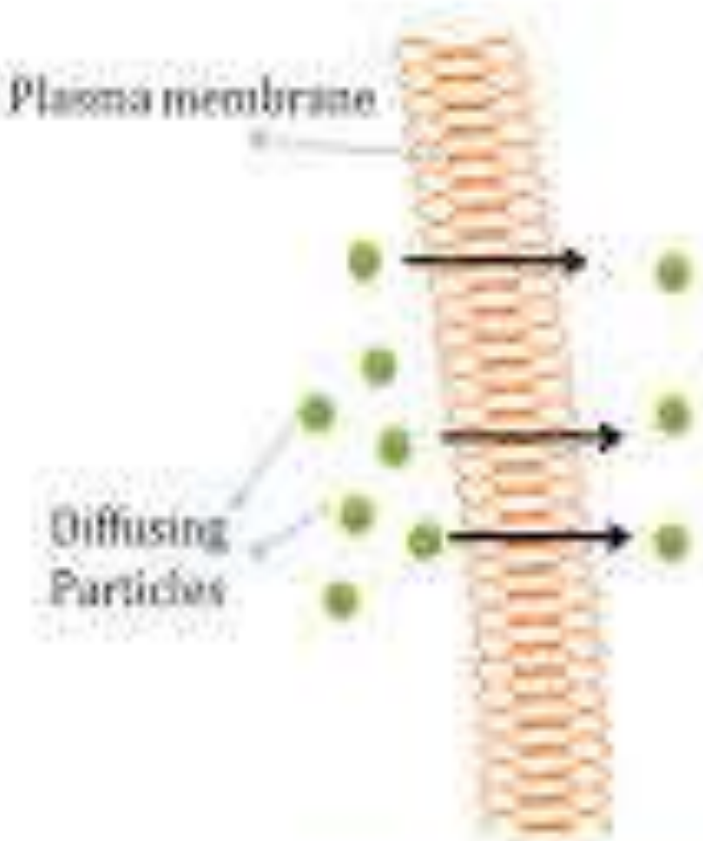
- (Carrier mediated diffusion)
- Transmembrane transport of metabolites in a concentration gradient with the help of a mobile carrier called permease or translocase without energy utilization

Facilitated Diffusion continued--

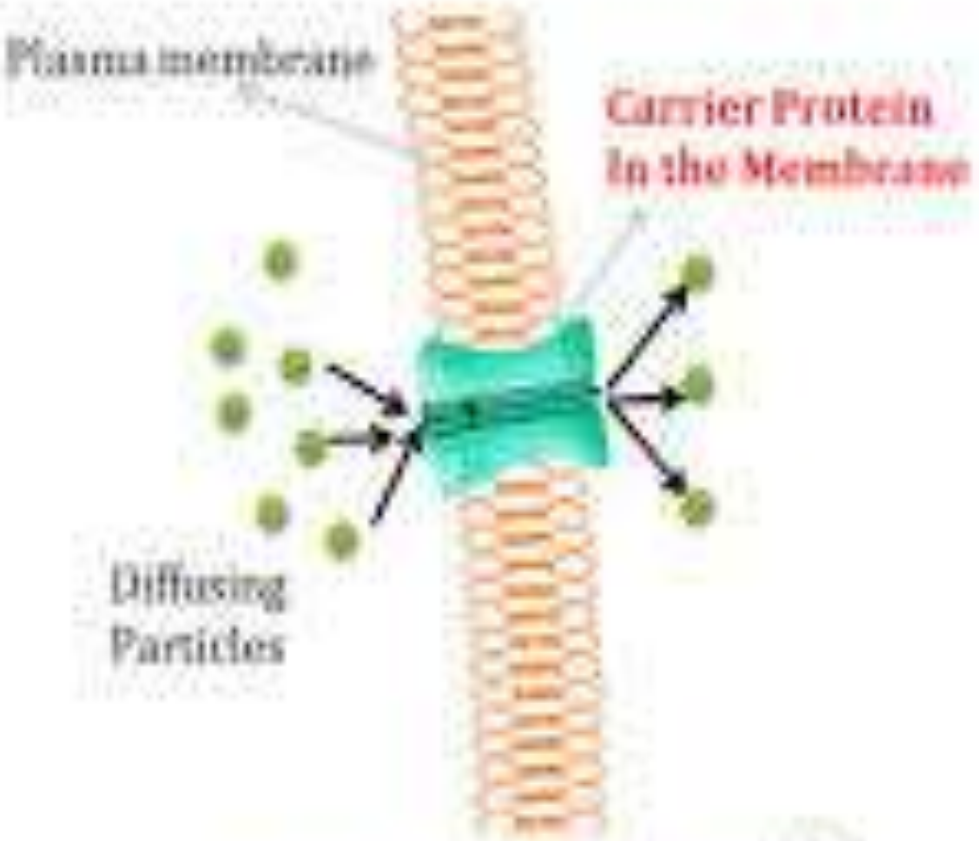
- The metabolite binds with the Permease to form Metabolite permease complex
- This complex undergoes conformational and positional changes in the permease
- The complex moves to interior of the cell by thermal diffusion,rotation,oscillationetc
- In the interior dissociation of the complex takes place and releases the metabolite in the cell
- Permease is now free to bind with another metabolite

- The transport of fat soluble vitamins, steroid hormones, hexose sugars undergo facilitated diffusion
- Permease has high specificity for the metabolites

Simple Diffusion vs Facilitated Diffusion



Simple Diffusion



Facilitated Diffusion

Assignment - Comparison

Facilitated diffusion

1.Stereo specific

2.It shows saturation kinetics

3. Faster

4.Rate limited- (depends on the availability of permease than the concentration gradient)

Simple diffusion

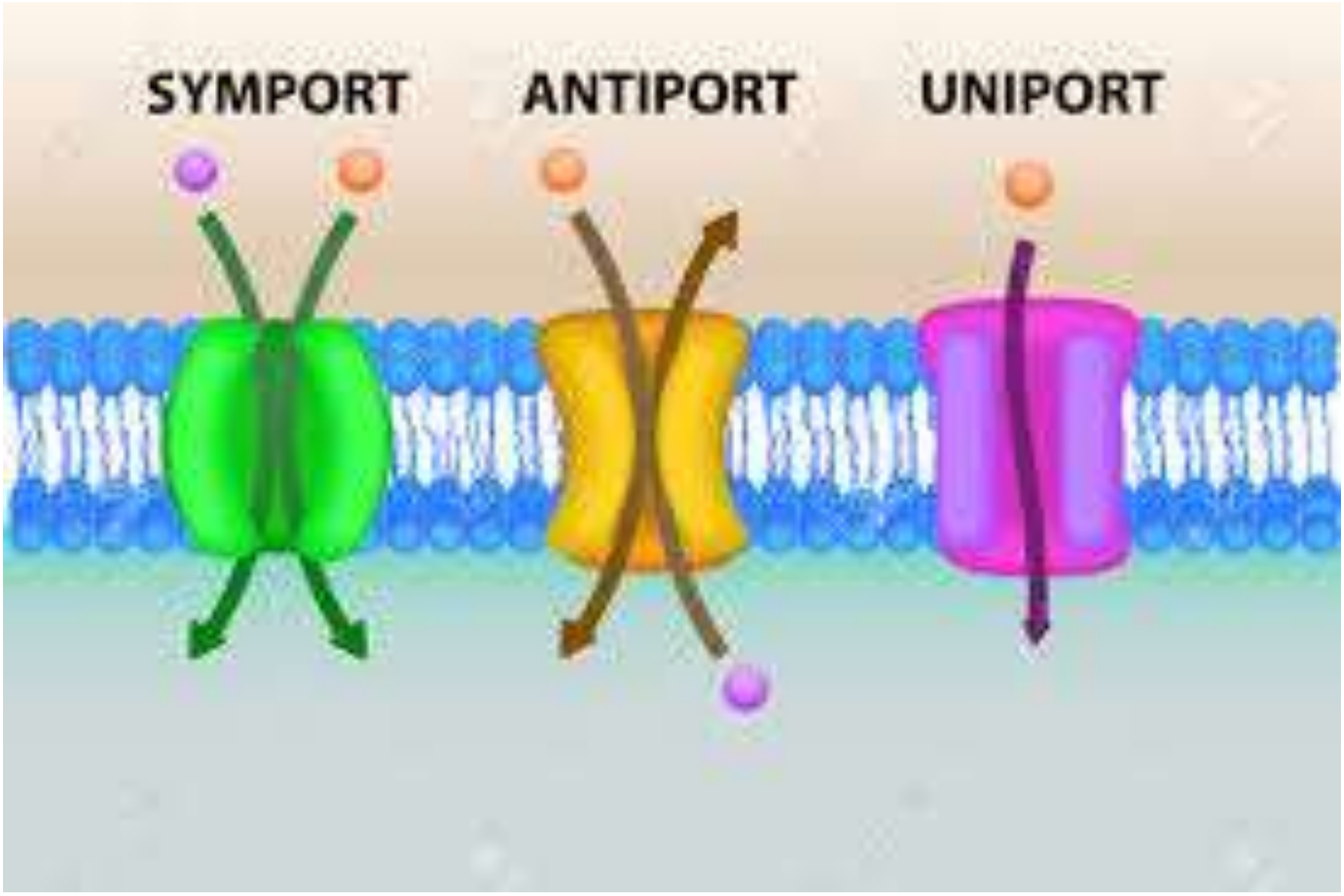
Active Transport

- Energy dependent and carrier mediated uphill flow of metabolites against concentration or electrochemical gradients and osmotic forces
- Active transport always coupled with ATP hydrolysis
- Energy is also used by the electrochemical potential produced by Hydrogen or sodium ions etc.
- This enables the cell to acquire specific ions and molecules

- It resemble facilitated diffusion in many respects and differs from facilitated diffusion it operates against concentration and potential gradients and osmotic processes utilizing energy

3 Types

- Uniport
- Symport
- Antiport


SYMPORT
ANTIPORT
UNIPORT

- It involves 3 stages
- Recognition of the metabolite by the permease and subsequent complexing
- Conformational changes and inward movement of the complex
- Dissociation of the complex and the release of the metabolite

Mechanism of Active transport

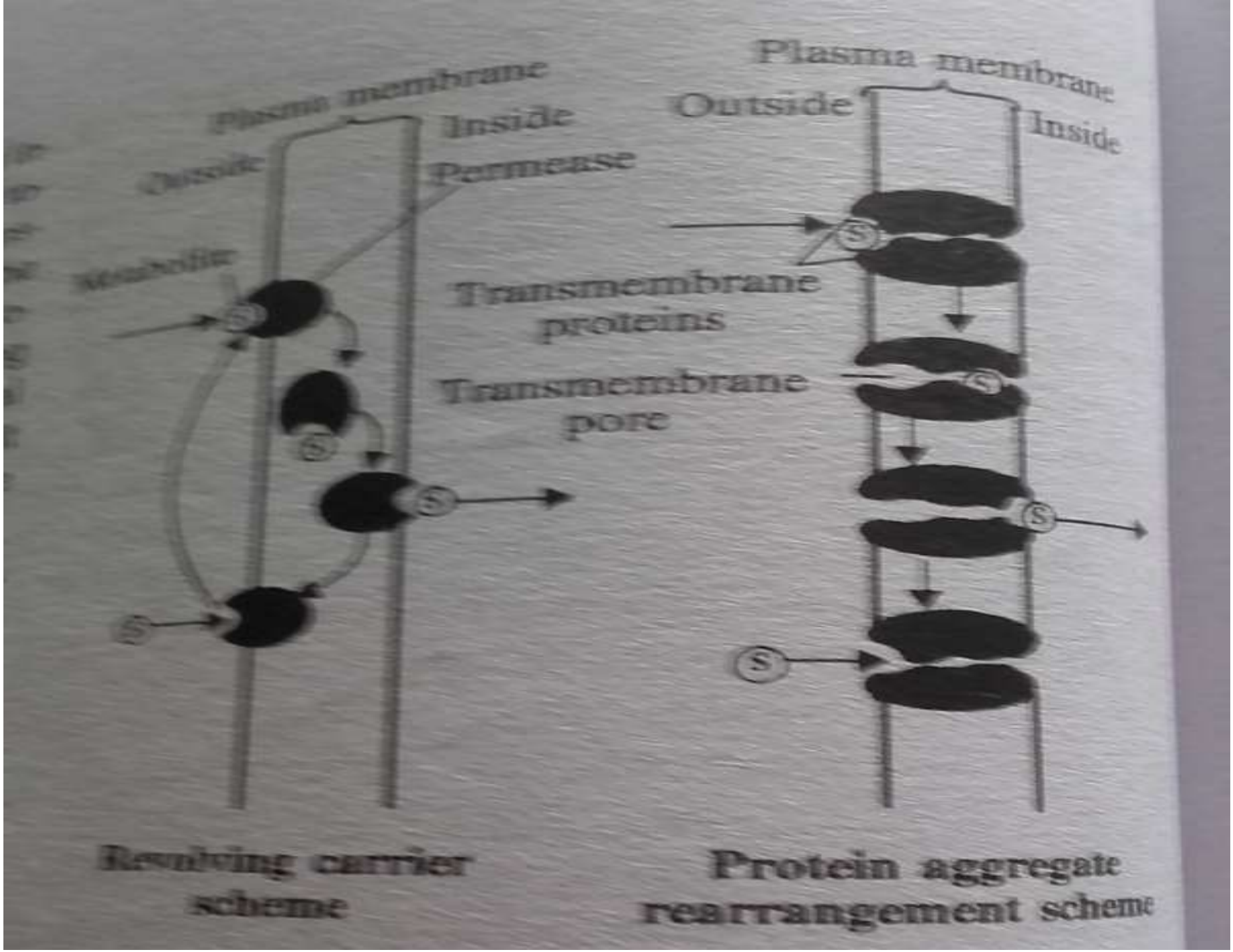
1. Rotating/revolving carrier scheme
2. Protein aggregate re-arrangement scheme

Rotating/revolving carrier scheme

Permease is visualised as a rotating door in the membrane with an outward facing slot to which metabolite can bind to. Then it rotates in such a way so as to bring the slot (where metabolite is attached) to the interior. The conformational changes takes place in the permease as well as its rotational movement require energy .

2.Protein aggregate re-arrangement scheme

- This is also known as fixed pore mechanism
- This visualises a transport site where integral proteins cluster together to form a continuous transmembrane protein or channel or pore. Once the metabolite bind with the site conformational changes occur in the binding site and thus brings the metabolite to the interior of the cell


Plasma membrane
Inside
Outside
Permease
Revolving carrier scheme
Plasma membrane
Outside
Inside
Transmembrane proteins
Transmembrane pore
Protein aggregate rearrangement scheme

Vesicular transport (Bulk Transport)

The transport of large molecules across the membrane

The metabolite is taken into a vesicle or pouch of the plasma membrane

3 types-

1. Exocytosis
2. Endocytosis
3. Receptor mediated endocytosis

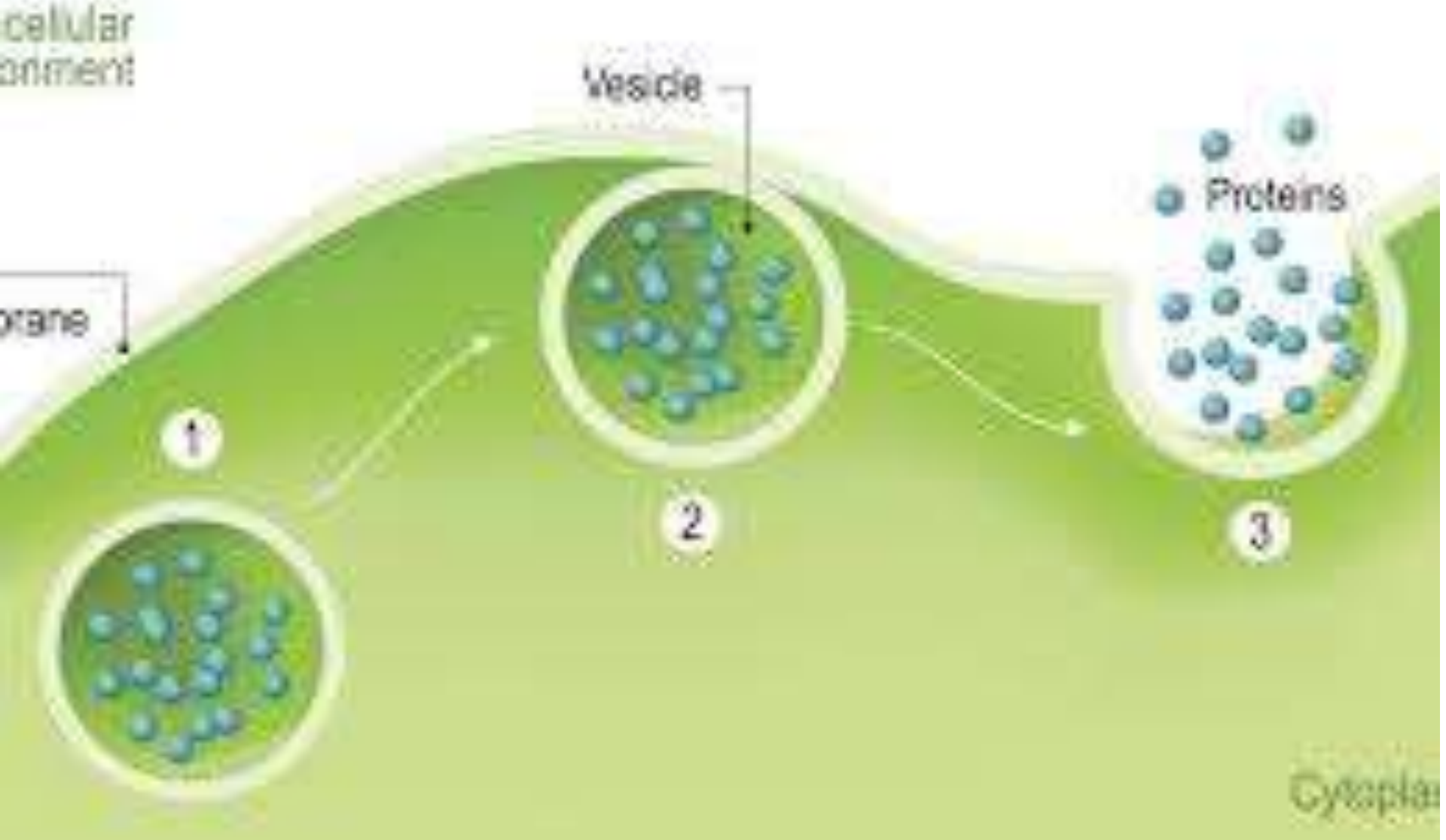
Exocytosis

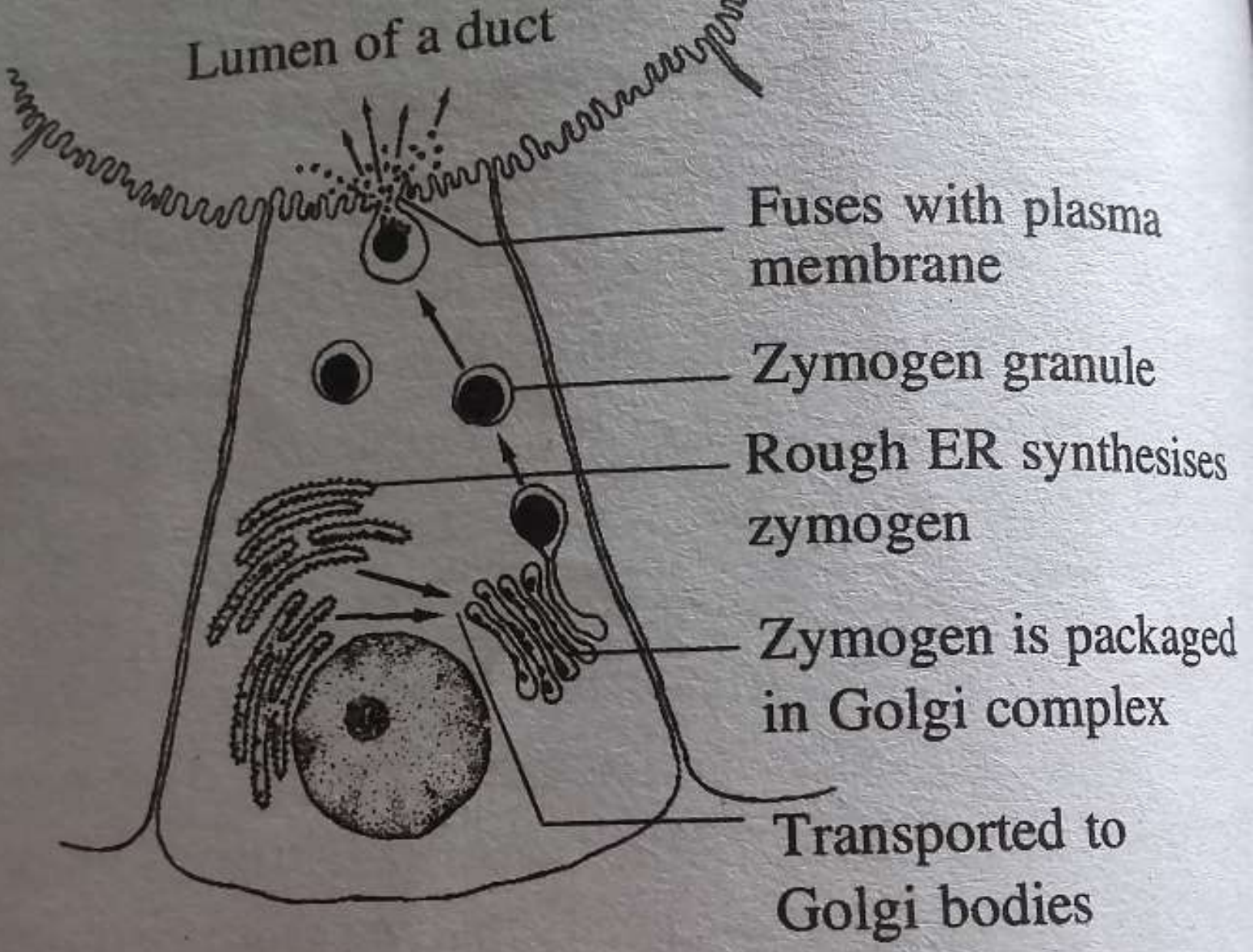
- Expulsion of cellular wastes and the export of some secretion products in large bulk from the cell to the extracellular medium. It is common in secretory cells
- Eg. Excretion of wastes by contractile vauoles, export of extracellular enzymes by digestive glands etc
- Find out other examples of exocytosis

- The substances to be exported is

1. Packed in exocytic vesicles or exosomes with the help of golgi bodies
2. It moves to the plasma membrane
3. It fuses with the membrane and at the point of fusion an opening is produced
4. Through this opening the contents are passed out

EXOCYTOSIS





Exocytosis of zymogen by pancreatic cells

Endocytosis

- Taking in of large amount of useful substances into the cell from the extracellular medium
- When a material come into contact with the plasma membrane

1. the membrane undergoes invagination and forms a pocket known as endocytic vesicles with the help of a glycoprotein called clathrin utilizing energy resulted due to ATP hydrolysis.

- 2.The substance get enclosed within the endocytic vesicles which gets pinched off from the membrane and gets completely internalized forming an endosome
- 3. Endosome fuses with a primary lysosome where the substance gets digested
- It is common in leucocytes,histiocytes,the reticuloendothelial system of bone marrow,liver, spleen etc.

3 Types of Endocytosis

1. Phagocytosis
2. Pinocytosis
3. Micropinocytosis

Phagocytosis

- Bulk intake of large sized solid substances

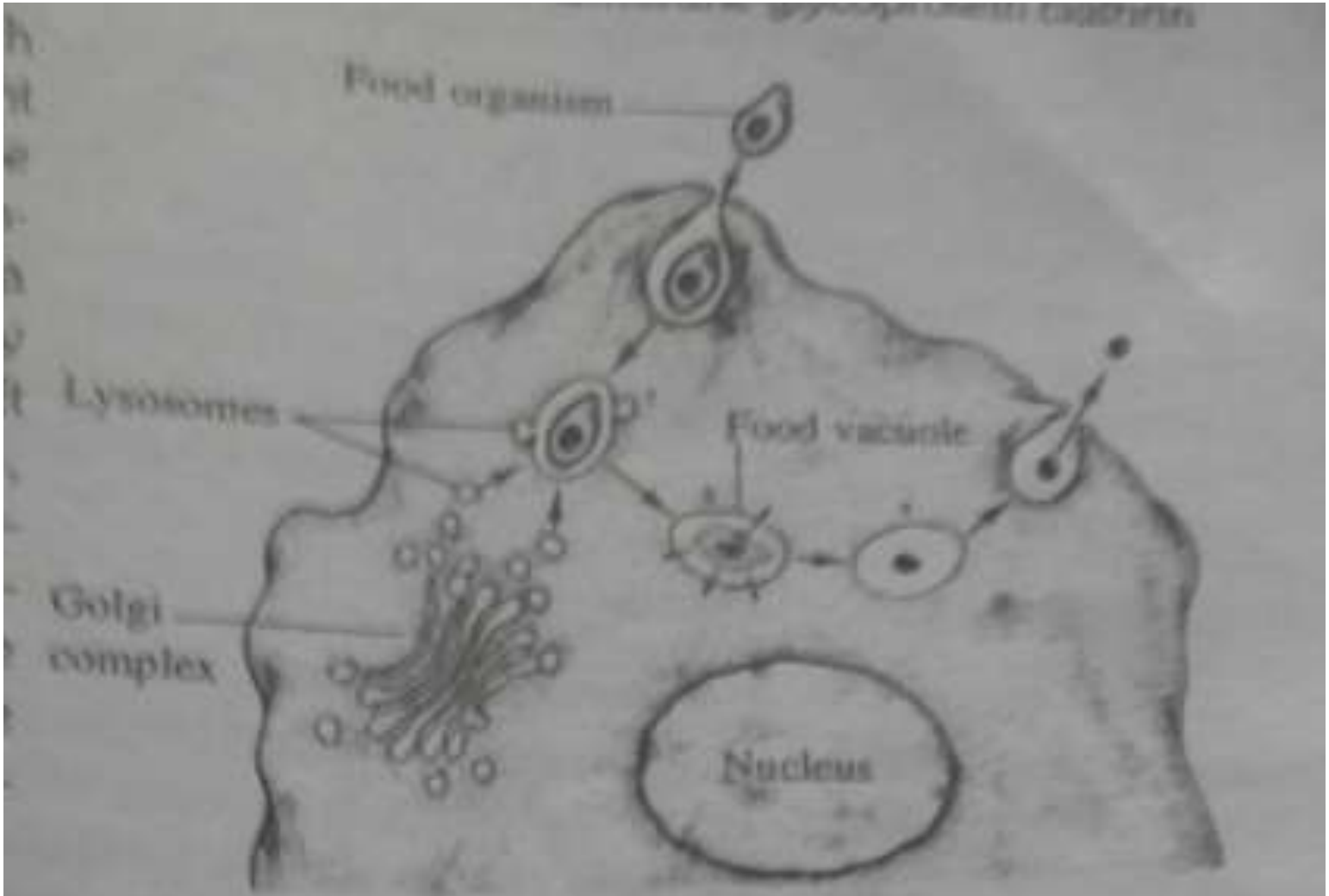
(Ultra phagocytosis also takes place)

3 steps

1.Surface recognition and binding

2.Membrane invagination

3. Vesicle formation



Phagocytosis in Amoeba

Pinocytosis (cell drinking)

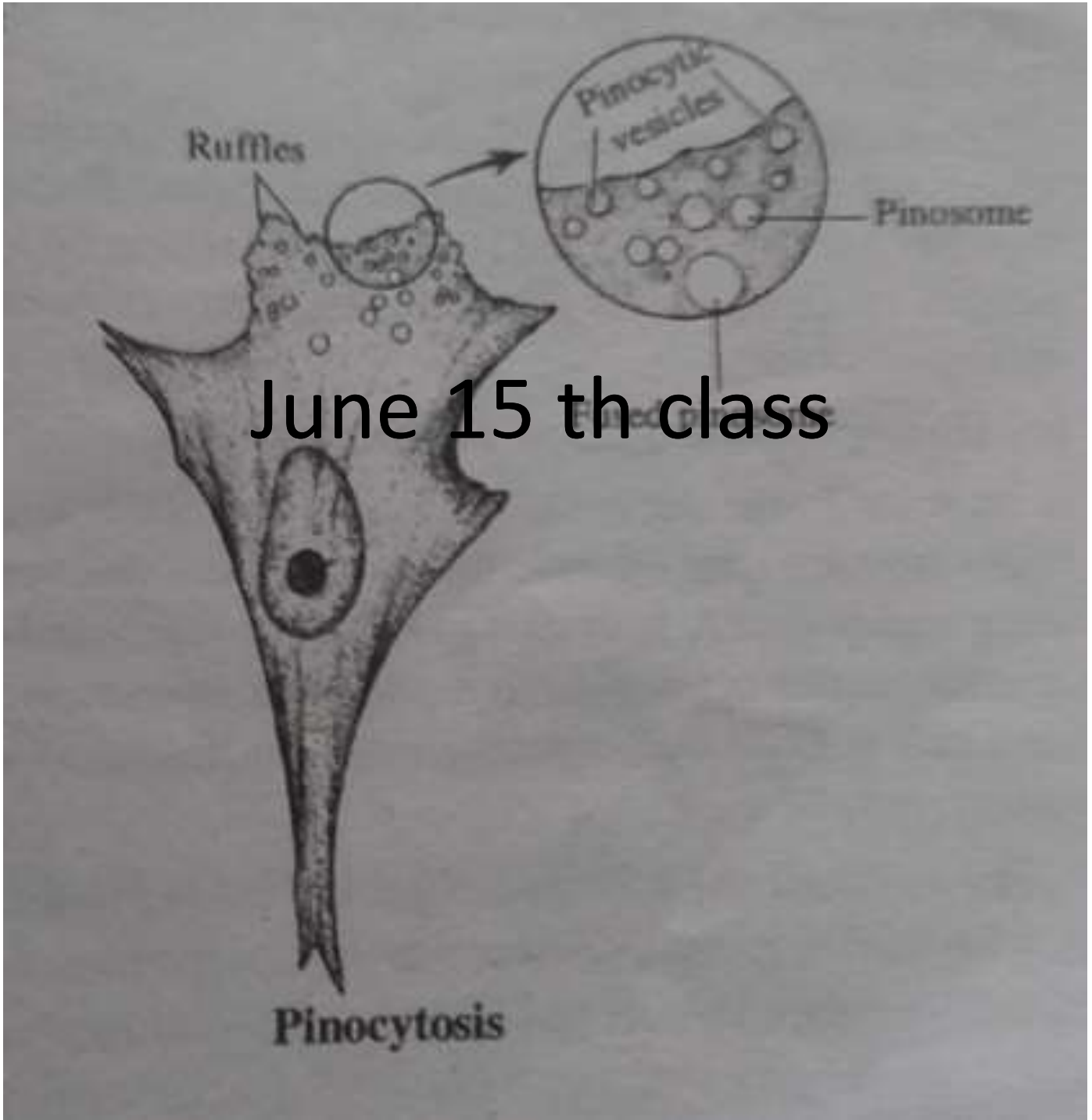
- Bulk intake of liquid or fluid substances and very minute particles
- It is induced by the variety of substances in the extra cellular medium

3 steps

1.Surface recognition and binding

2.Membrane invagination

3. Vesicle formation



June 15 th class

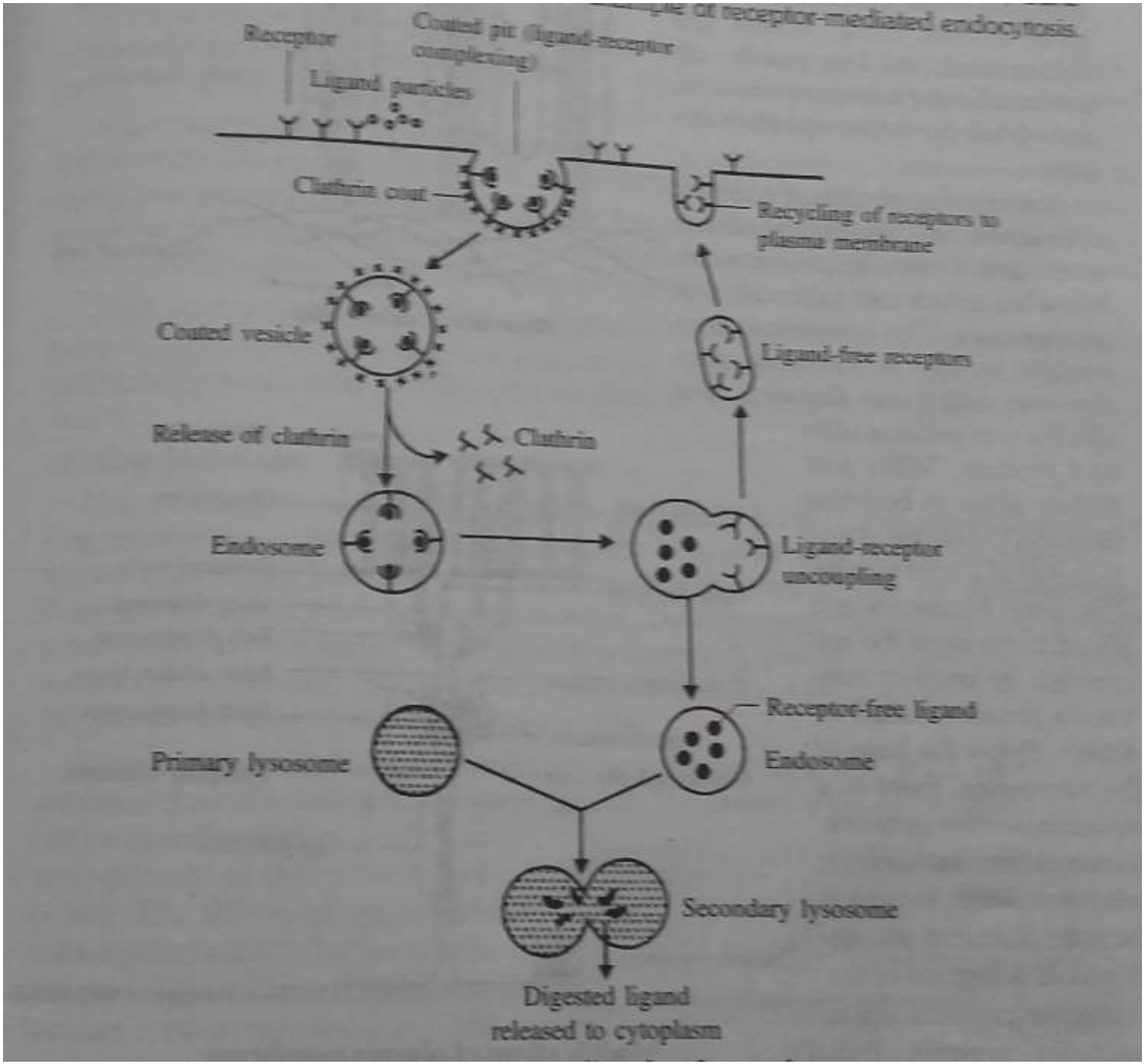
Pinocytosis

Micropinocytosis

- Transcellular transport of fluid substances
- Highly specialised form of pinocytosis
- Micropinosome after internalization move to the opposite end of the cell and fuses with the plasma membrane there and undergo exocytosis
- It is common in the endothelial lining of capillaries

Receptor mediated endocytosis

- This takes place in shallow depressions of p.m characterized by Clathrin coated pits
- Involves membrane receptors which are glyco proteins
- Ligands (extracellular substances) bind to the receptors to form ligand receptor complex in the coated pits

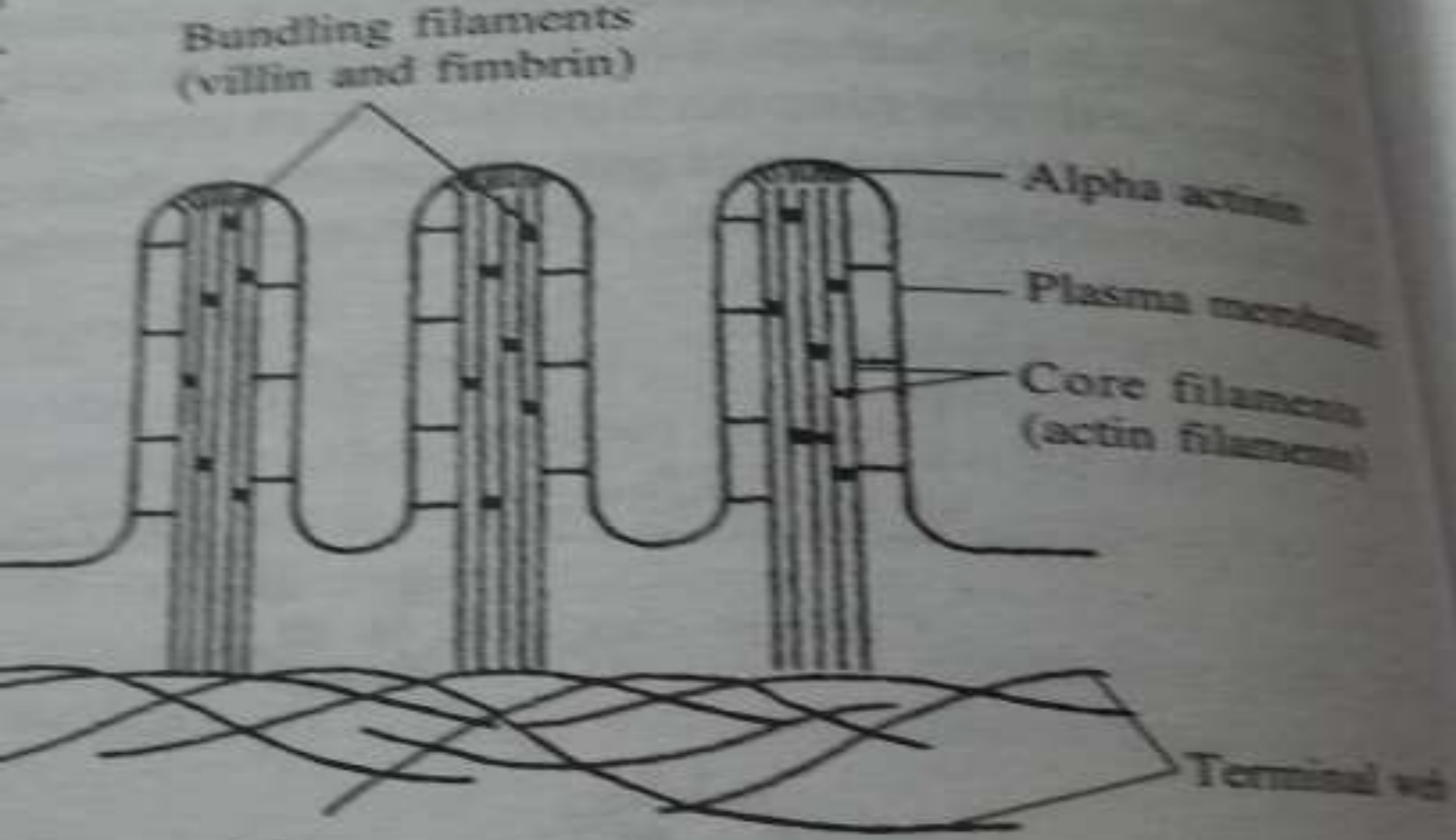

Receptor
Coated pit (ligand-receptor complexing)
Ligand particles
Clathrin coat
Recycling of receptors to plasma membrane
Coated vesicle
Ligand-free receptors
Release of clathrin
Clathrin
Endosome
Ligand-receptor uncoupling
Receptor-free ligand
Primary lysosome
Endosome
Secondary lysosome
Digested ligand released to cytoplasm

Modifications/specializations of plasma membrane

- In many cells plasma membrane is modified to perform many functions like absorption, secretion, cell to cell contact etc.
- Major modifications are
- I. Microvilli
- II. Intercellular junctions
- a. Tight junctions
- b. Gap junctions
- C. Desmosomes
- C.1 Spot Desmosomes
- C.2 Belt Desmosomes
- C.3. Hemidesmosomes

Microvilli

- Found like long and slender projections giving cells striated or a brush border appearance
- Seen on the apical surface of the secretory and absorptive cells (intestinal and respiratory mucosa, kidney tubules,gall baldder, uterus etc)
- They increase the surface area for the transmembrane transport as well as seive as sieve for the absorption, act as pathways for pinocytosis.



Structure of microvillus

- Terminal web is formed of actin, alpha actinin, myosin,tropomyosin and spectrin
- The core filaments bring about the contraction of the microvilli and the Terminal web keeps the stiff and upright position of it.
-

Intercellular junctions

- Adjacent cells are separated form one another by 100-200A° wide gap. At some points they come into close contact through modification of plasma membrane. Intercellular junctions are common in epithelial cells

Tight junctions(Zonula Occludens)

- Abundantly seen in renal epithelial cells
- Adjacent plasma membrane fuse together, leaving no gap in between. They are seen below the apical border as a projecting ridge representing the line of fusion (sealing strand) of the two membranes
- This is formed due to the interactions between lipids, proteins and fibrous cytoplasmic strands.
- The integral proteins Occludin and Claudin of the adjoining cells meet together and form continuous fibrils

Functions of Tight junctions

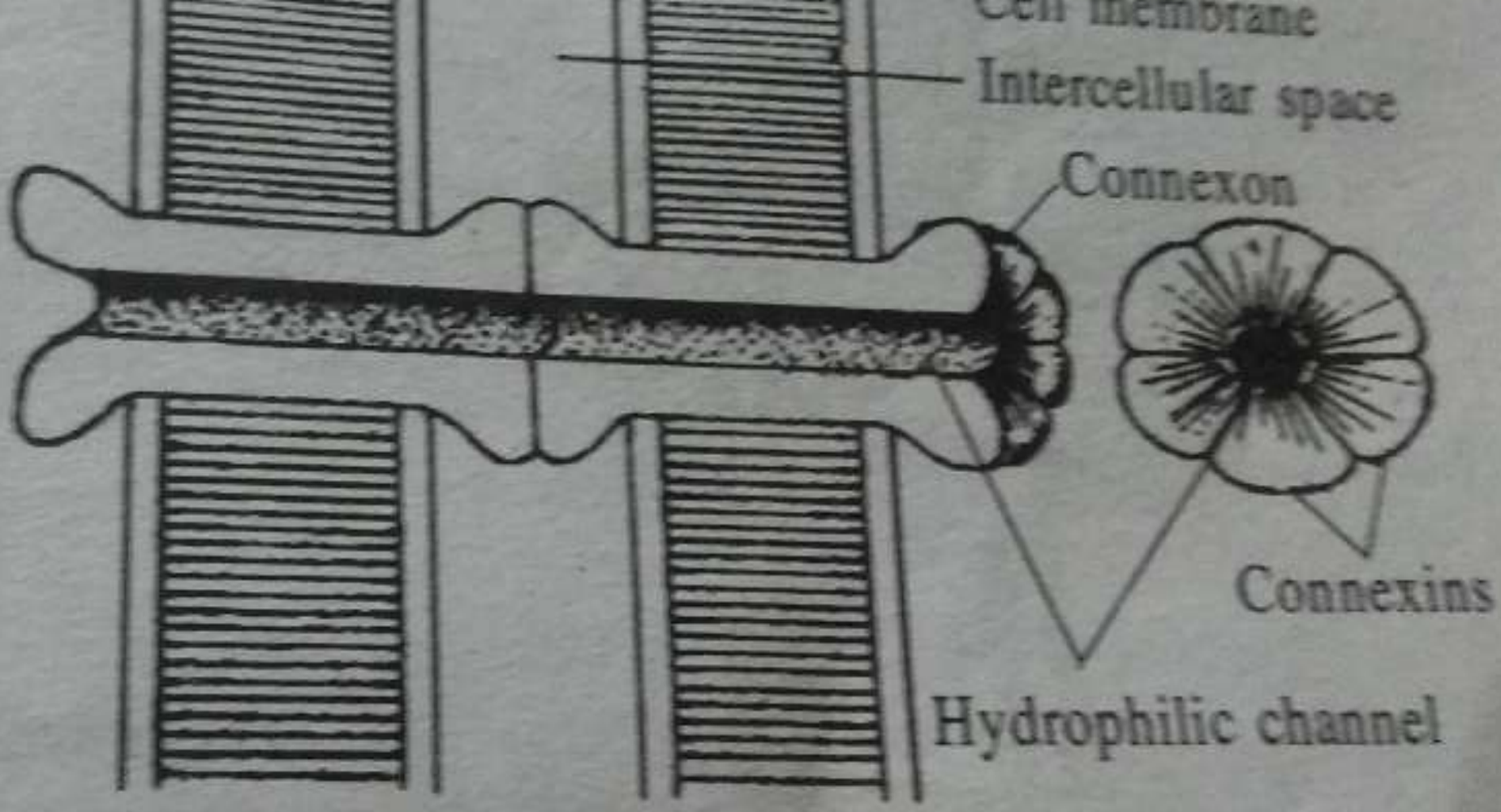
1. To prevent the leakage of ions and molecules between the cells
2. Serve as physical barriers to the diffusion of macromolecules

Gap Junctions

- Intercellular junctions with very narrow gap in between the adjacent cells
- It consist of a pair of molecular cylinders formed of transmembrane proteins
- The Transmembrane protein from one cell join with the T.M P of the adjacent cell to form a tube called connexon which is open at both ends
- Each TMP is made of a ring of 6 protein subunits arranged around a hydrophilic central channel.
- Each protein subunit is called a connexin
- The rearrangement of the proteins can open or close the connexon. High levels of Calcium ions causes closing of the channel

Functions of Gap junctions

- Enable cellular adhession
- Serve as a permeability pathway for the cell to cell passage of variety of molecules like Cyclic AMP, Nucleotides,aminoacids etc.



Gap junction

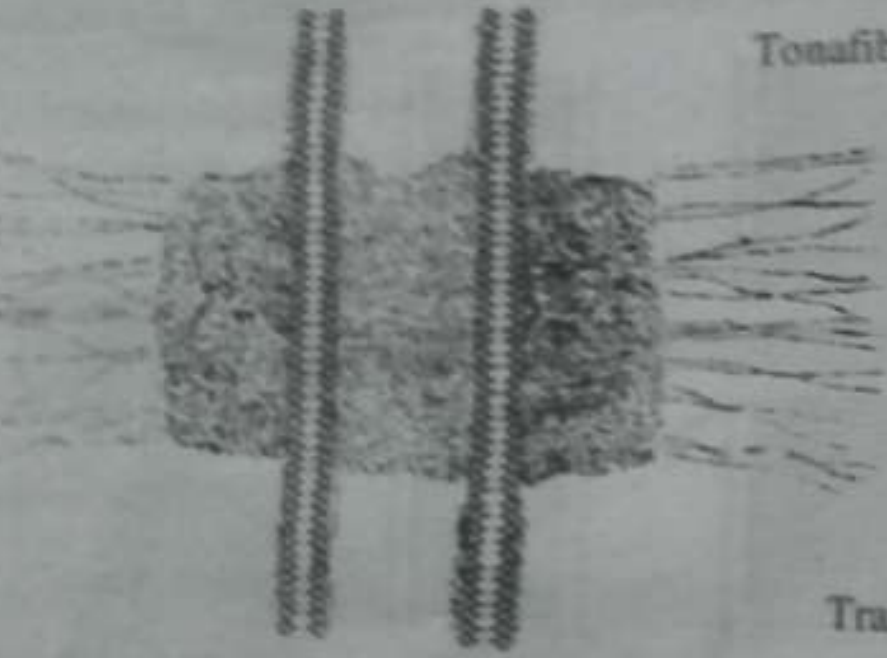
Desmosomes

- These are intercellular junctions where adjacent cells are anchored to each other with the help of intercellular filaments
- Numerous in epithelial cells of skin, Uterus, cervix etc which are regions of mechanical stress.

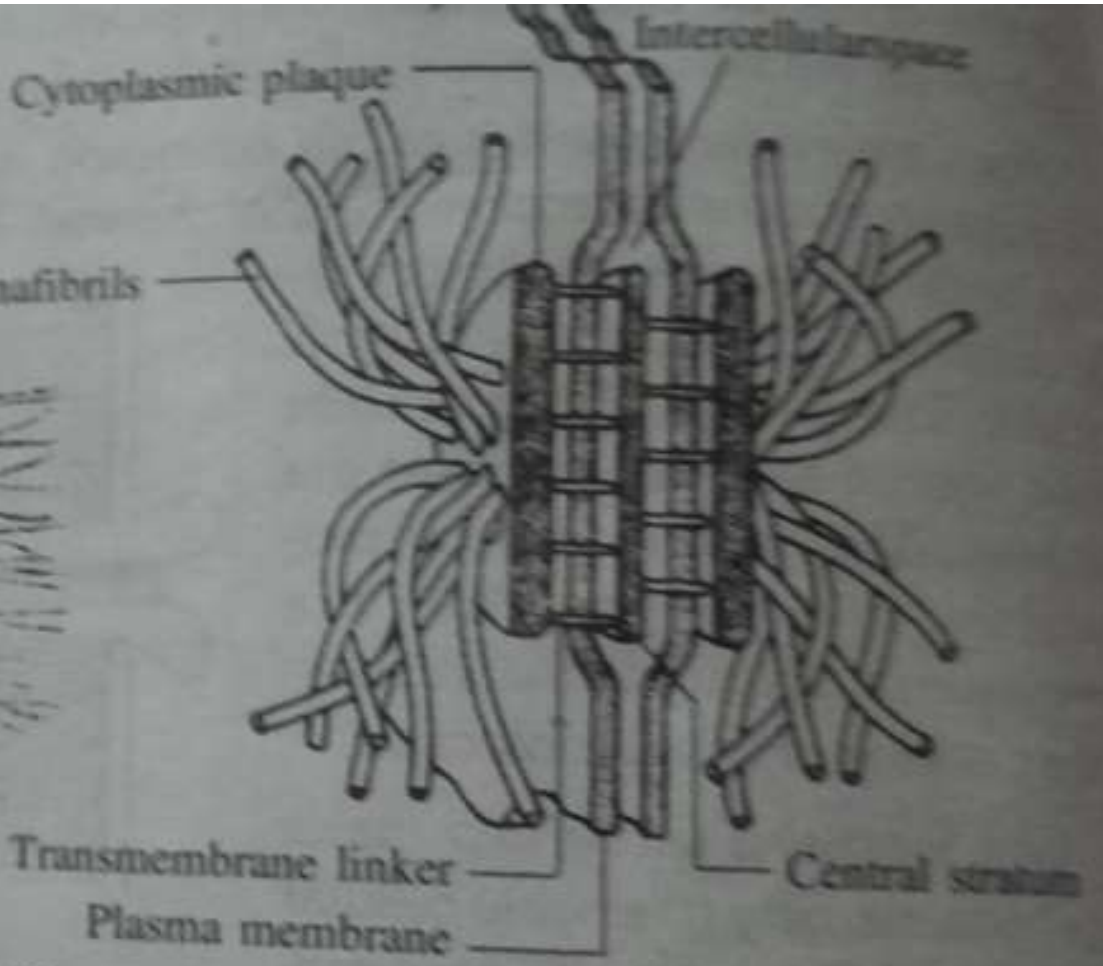
Spot desmosomes (macula adherens)

- Button like desmosome.
- The cytoplasmic surface of each cell has a dense discoidal area called cytoplasmic plaque. It contains numerous protein filaments and non contractile filaments (tono fibrils)
- Bridging filaments are made of keratin anchor the plaques together and some of these form an intercellular network called central stratum

- Another filaments extending across the plaques are transmembrane linkers/filaments made of proteins called cadherins
- The linkers provide mechanical coupling between the plaques
- The whole filaments together known as biological cables



A magnified view of desmosome



Diagrammatic representation of a spot desmosome

Belt desmosomes (Zonula adherens)

- Band like found in columnar epithelium. Seen below the tight junctions
- No plaques, tonofibrils
- Actin present in the intercellular gap

Hemidesmosomes

- Morphologically half desmosomes with different chemical organizations and found at the bases of epithelial cells. They differ from desmosomes in 2 features
- 1. terminal portion of the tonofibrils are deeply anchored in the cytoplasmic plaque
- 2.Transmembrane linker proteins are formed of the protein Integrin