BIOLOGICAL MEMBRANES: FUNCTIONS, STRUCTURES & TRANSPORT

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BMLS II / B Pharm II / BDS II

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What are some of the functions of biological membrane?

- Boundaries around cells (Plasma Membrane),
- Boundaries round distinct sub-cellular compartments (Nucleus, Mitochondria, Lysosomes, Golgi bodies, etc.),
- Compartmentalize and Segregate intracellular events, and Separate cells from one another,
- Membranes mediate regulation of cellular functions by:
  - Acting as selective barriers,
  - Allowing inside environment of cells or organelles to differ from outside

- Membranes are involved in signalling processes:
  - Contain specific receptors for external stimuli
  - Involved in chemical and electrical signal generation
- Specific enzyme systems are localized on membranes,
- Plasma membrane is selectively permeable outer boundary of cell
- Plasma membrane contains:
  - Specific systems; Pumps, Channels, Transporters used for exchange of nutrients and other materials with the environment
- Normal cellular function starts with normal cell membrane:
  - Damage to membrane can affect water balance and ion influx and therefore grossly alter most processes within the cell;

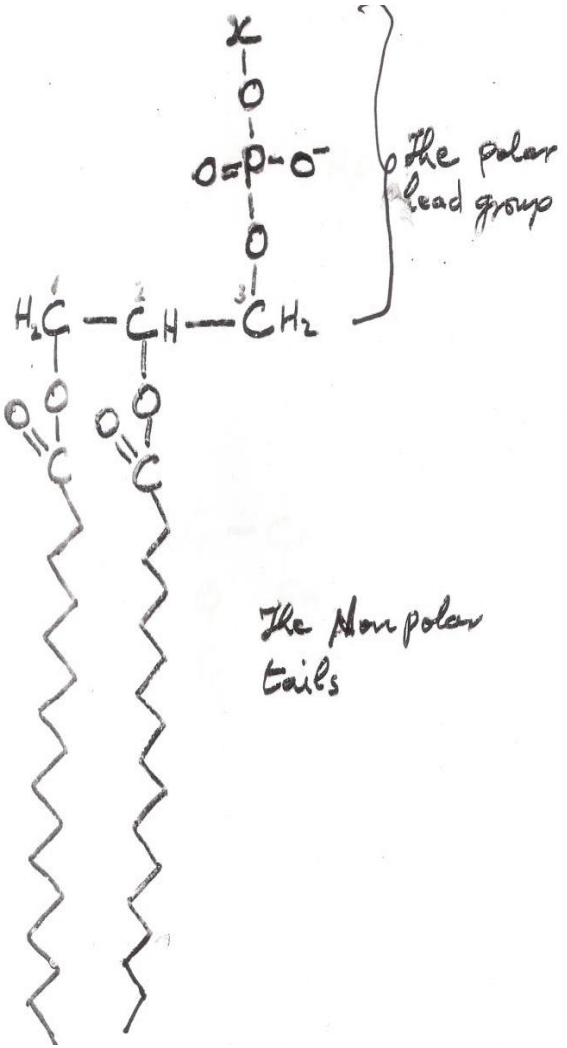
What are the basic components in biological membrane?

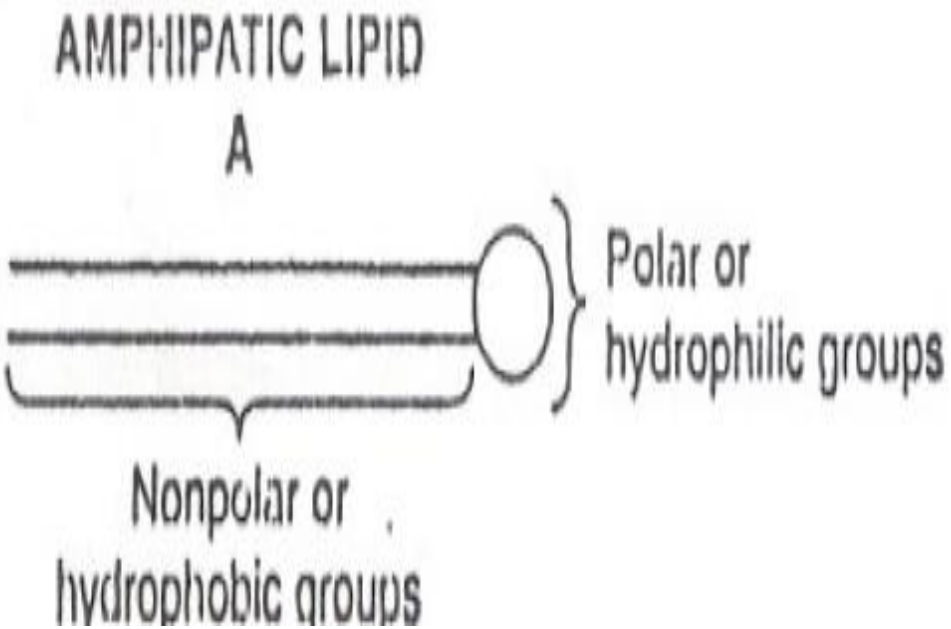
- Two basic components:
  - Lipids
  - Proteins
  - Some membranes also contain carbohydrate
- Composition of lipid, protein and carbohydrate varies from one membrane to another,
- Ratio of Lipid to Protein is not fixed in most membranes,
- Lipid to Protein ratio in membranes varies widely from **4:1 to 1:4**, depending on the specific functions of the membrane,

What are the major lipids in the biological membrane?

- Major lipids in biological membranes are:
  - Phospholipids,
  - Glycolipids, and
  - Cholesterol
- Lipids in membranes are Amphipathic (Amphiphilic),
  - Having both Hydrophobic and Hydrophilic ends
- Orientation of Amphipathic compounds (Lipids) in aqueous solution is to prevent Hydrophobic region coming into contact with water molecules,

Diagram of the structure of membrane lipid

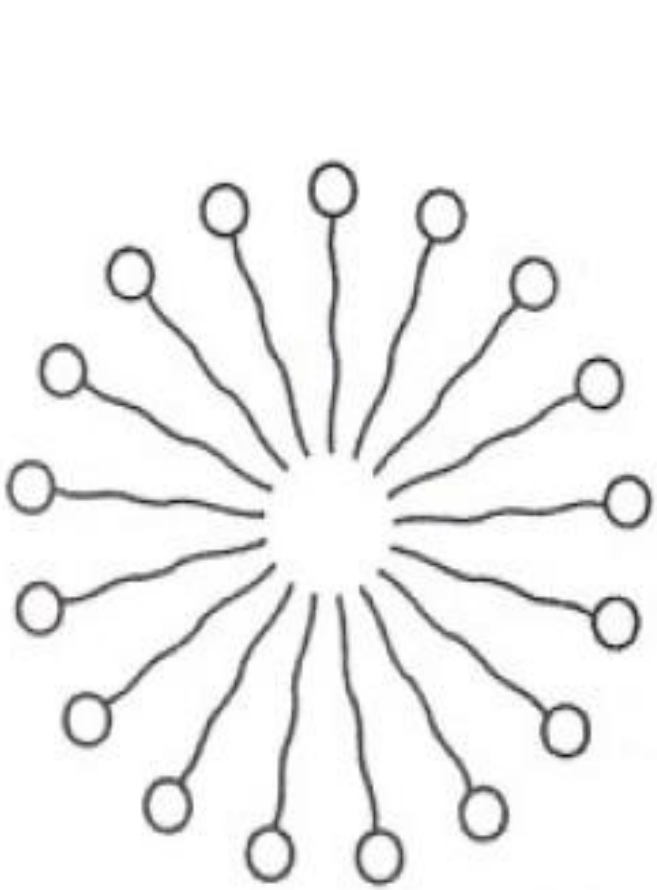


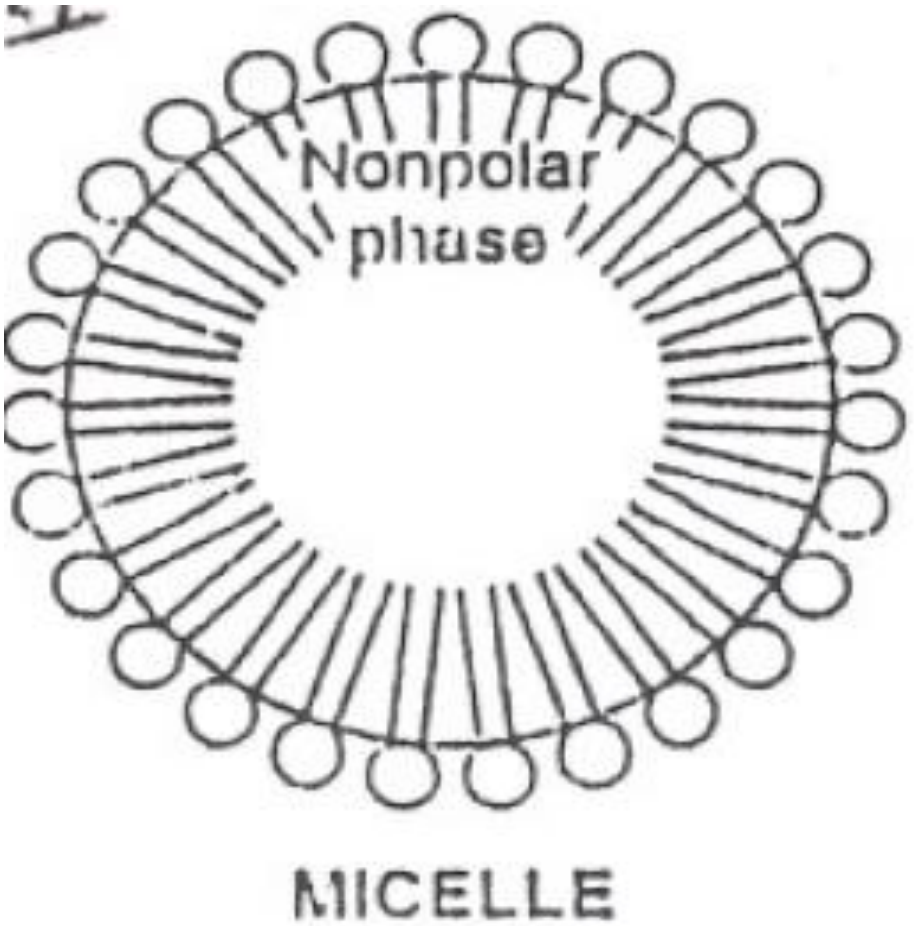


What is the structure of the Micelle?

- Interaction of fatty acid and alkaline forms fatty acid salt (eg. Sodium Palmitate, a constituent of soap),
- Molecules of Sodium Palmitate in water forms a spherical Micelle structure,
- Orientation of molecule is such that the Hydrophobic Fatty Acid chains are hidden inside the Micelle and the Hydrophilic Head-groups interact with the surrounding water molecules, (See diagram)

Diagram of the structure of Micelles

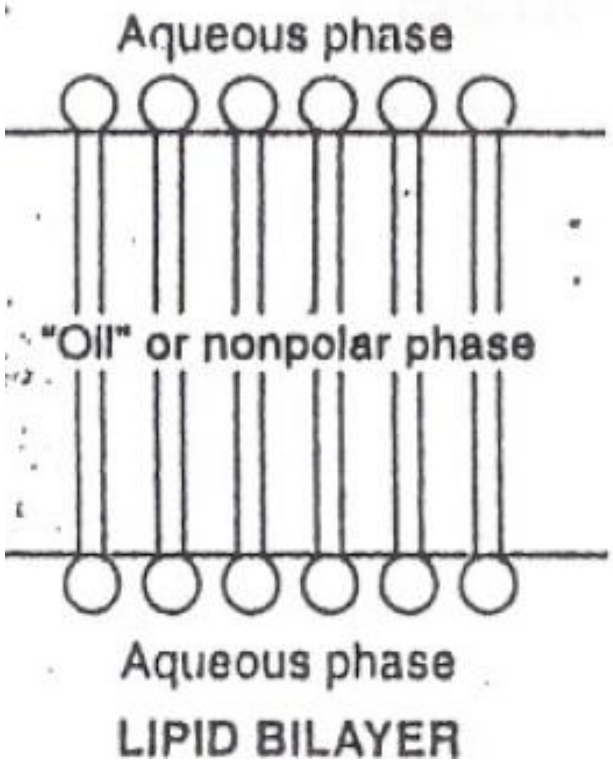


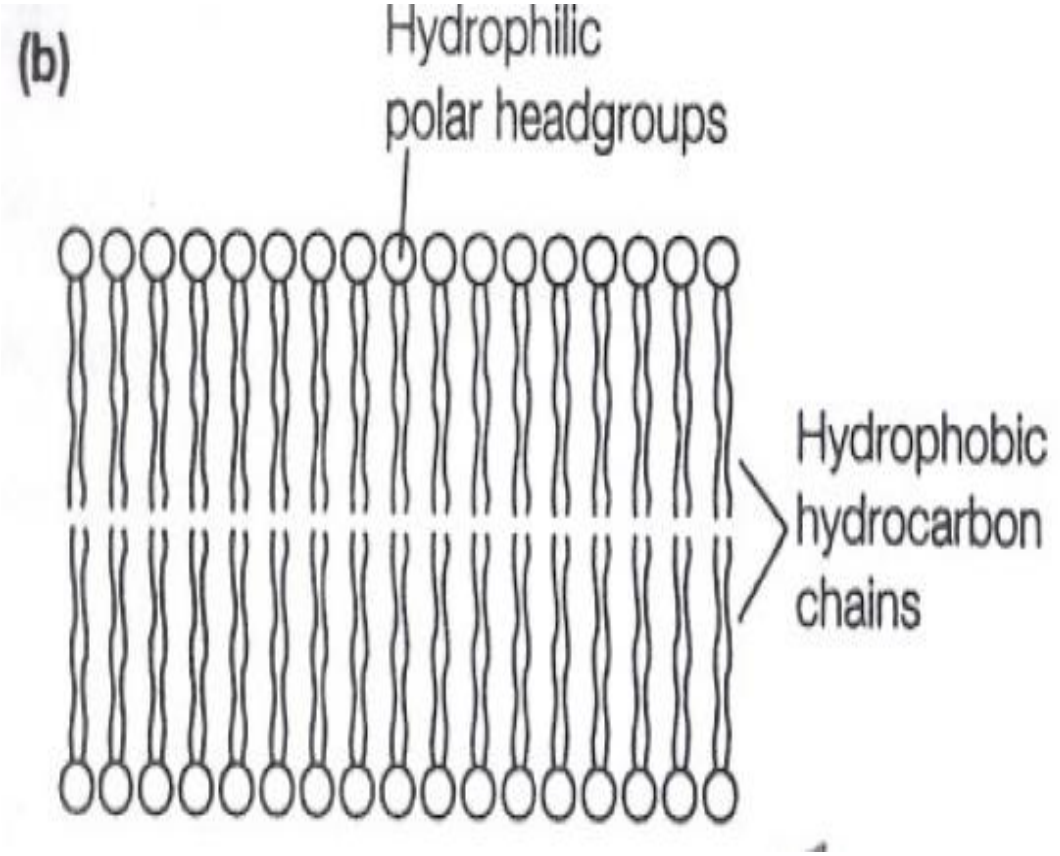


How is the Lipid Bi-layer formed?

- Phospholipid is made up of:
  - Two Non-polar (Hydrophobic) fatty acid chains: Tails
  - One polar (Hydrophilic) group: Head
- When in contact with water, the two non-polar chains are too bulky to fit into the interior of a micelle,
- Stable structure for Phospholipids in water is a two-dimensional bimolecular sheet or lipid bilayer (see diagram),
- Lipid bilayer: Phospholipid molecules are orientated with
  - Hydrophobic chains in the interior of the structure and
  - Hydrophilic head groups on the surface
- Each layer in the lipid bilayer is referred to as Inner and outer leaflets

Diagram of Lipid Bilayer: showing Inner and Outer leaflets





What types of Phospholipids are in the biological membrane?

- Biological membranes contain different types of lipids asymmetrically distributed between two leaflets
- Plasma membrane of Erythrocytes contains:
  - Sphingomyelin and Phosphatidyl-Choline are preferentially located in the **Outer leaflet**,
  - Phosphatidyl-Ethanolamine and Phosphatidyl-Serine are mainly in the **Inner leaflet**,

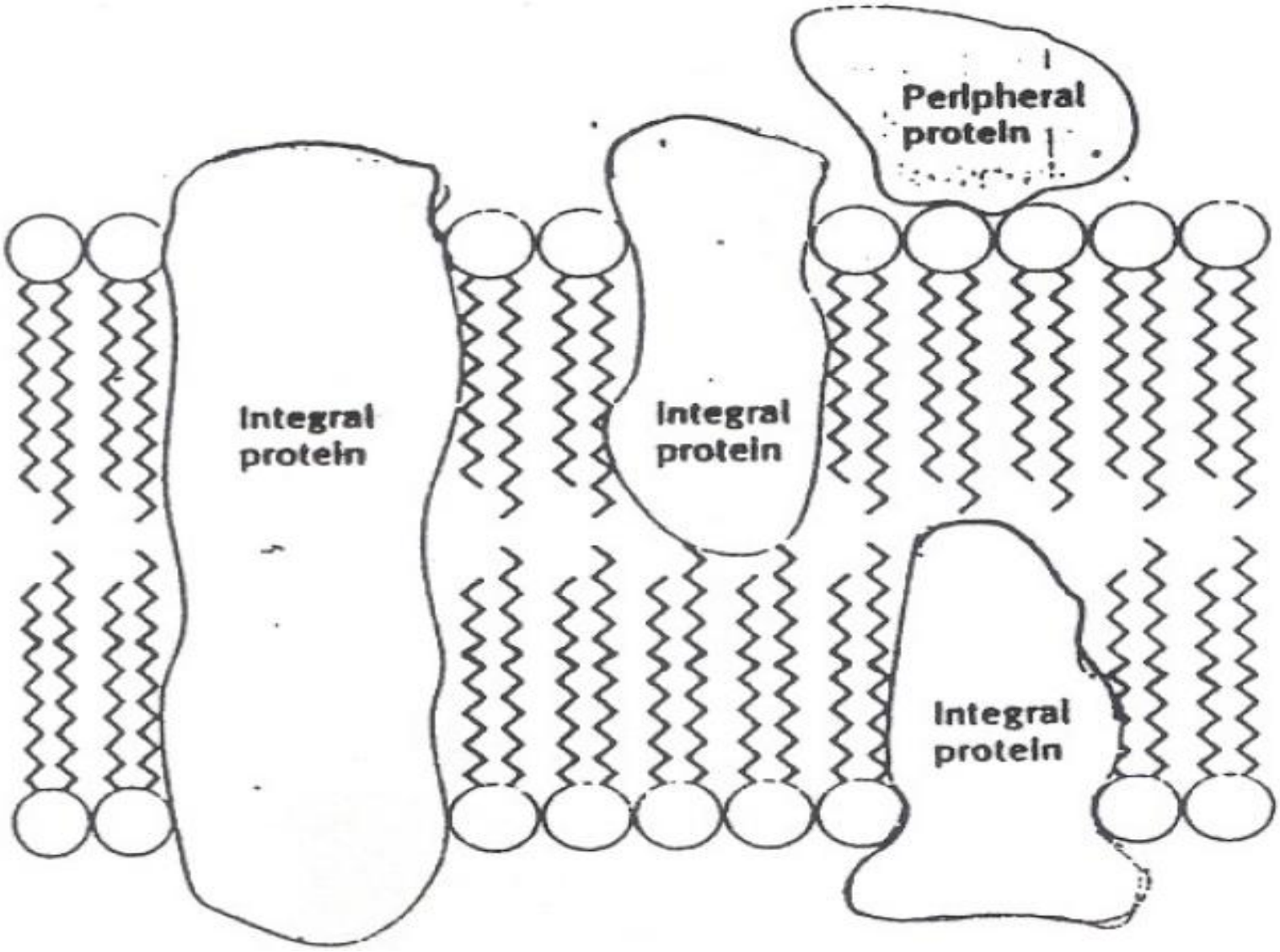
What forces maintain the structural integrity of biological membranes?

- Hydrophobic effect is the major driving force for formation of lipid bilayer,
- Hydrophobic fatty acid chains avoid contact with water,
- Lipid bilayer structure is maintained by multiple non-covalent interactions:
  - Hydrophobic interactions,
  - Van Der Waals forces between the hydrocarbon chains
- Charge interactions and Hydrogen bonding between Polar Head-groups, and
- Hydrogen bonding between Head-groups and surrounding water molecules,

What are the different types of proteins in biological membrane?

- Two basic types of membrane proteins:
- Integral (Intrinsic) membrane proteins, and
- Peripheral membrane proteins, (see diagram)

Diagram of two types of membrane proteins



What are the differences between Integral and Peripheral proteins

Integral (Intrinsic) membrane proteins:

- Tightly associated with hydrophobic core of lipid bilayer,
- Interact with the Hydrocarbon tails of lipids,
- Transmembrane proteins are Integral proteins that are exposed on both sides of the membrane; they extend across the width of the membrane,
- Integral proteins can be removed from the membrane only with organic solvents or detergents that disrupt the membrane structure,

Peripheral membrane proteins:

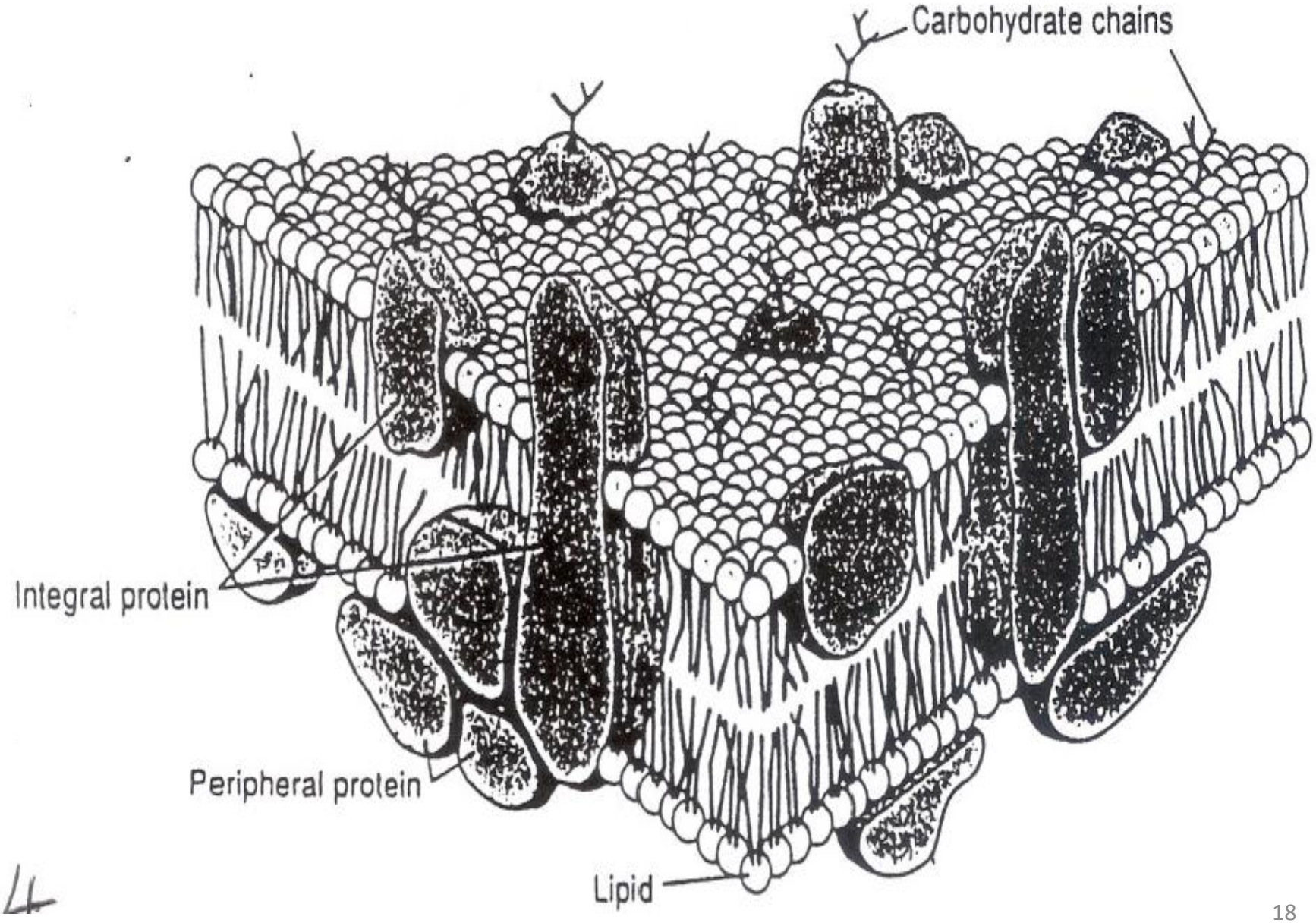
- Loosely bound by Hydrogen bonding or Electrostatic interactions to the exposed surface of integral proteins,
- Readily be removed by washing the membranes with solutions of high ionic strength,
- High ionic strength disrupts the Non-covalent ionic and Hydrogen bonds holding the proteins on the surface of the membrane,

What is the Extracellular matrix

Extracellular matrix:

- Is the flexible and sticky layer of complex Carbohydrates, Proteins and Lipids that covered the surface of cells,
- Is cell-specific,
- Serves in cell-cell recognition and communication,
- Creates cell adhesion,
- Provides a protective outer layer;

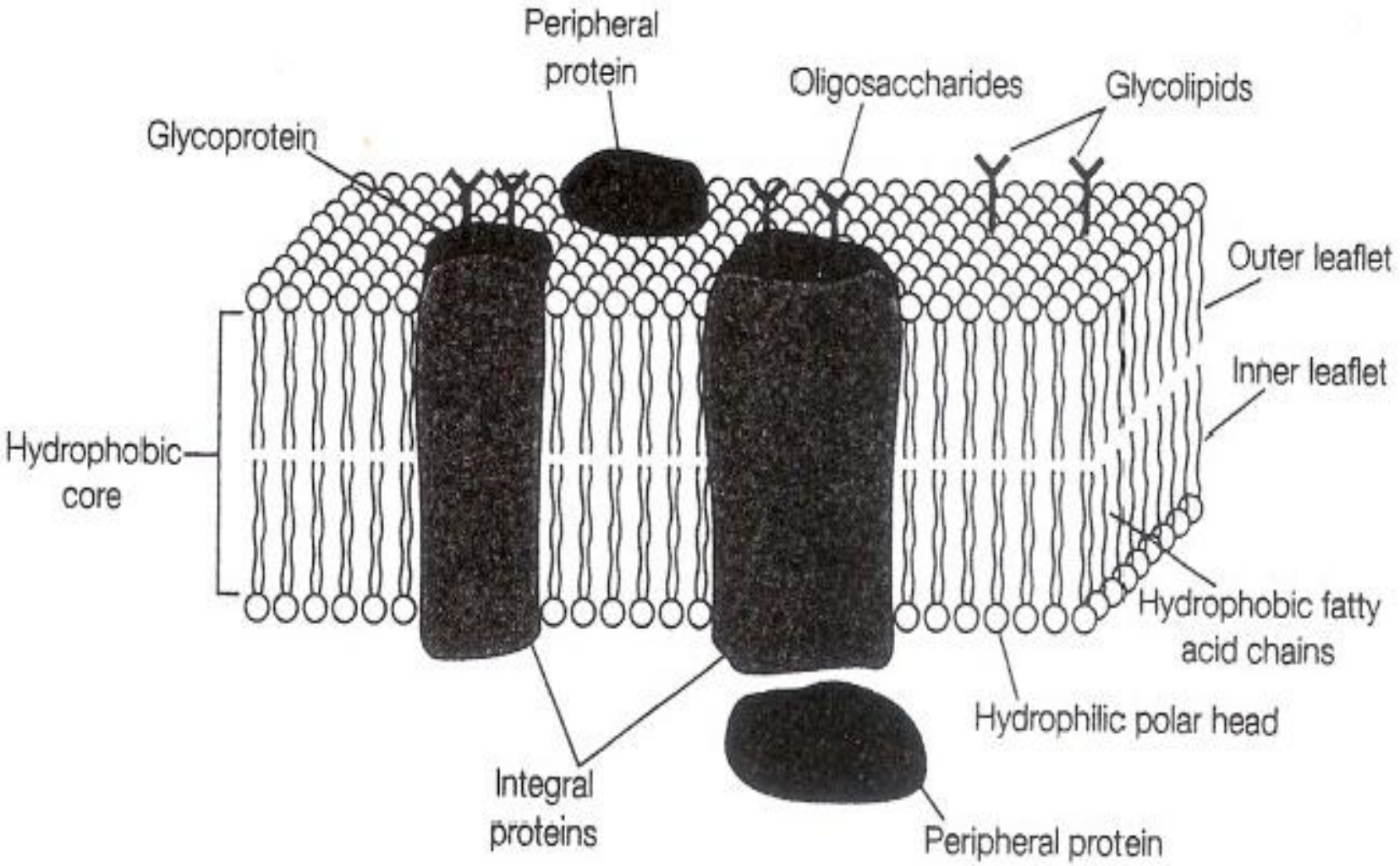
Diagram of Extracellular Matrix



Briefly describe the Fluid Mosaic model of bio-membranes

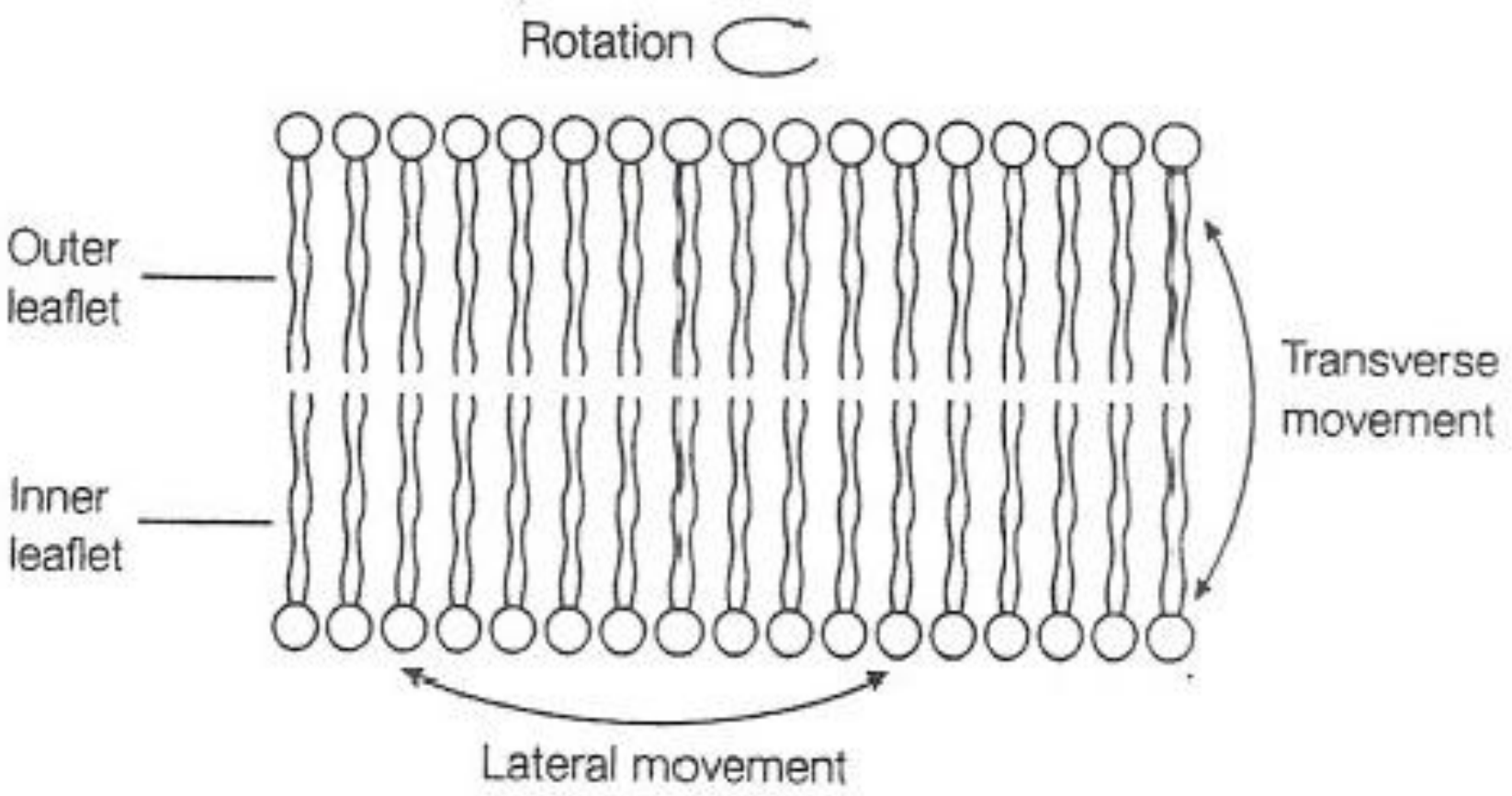
- Jonathan Singer and Garth Nicholson proposed the Fluid Mosaic Model of Biological membranes,
  - Biological membrane can be viewed as Two-dimensional solutions of oriented Lipids and Globular proteins,
  - Integral membrane proteins can be considered as “Icebags” floating in a two-dimensional lipid “Sea”,

Diagram of Fluid Mosaic Model



- They proposed the following:
  - Lipid bilayer act both as a solvent for the Amphipathic integral membrane proteins and as a permeability barrier,
  - Some lipids may interact with certain membrane proteins; these interactions are essential for the normal functioning of the proteins,
  - Free lateral movement of proteins occur in the plane of the lipid bilayer,
  - Proteins cannot flip from one side of bilayer to the other side

Diagram showing lateral movement of membrane proteins

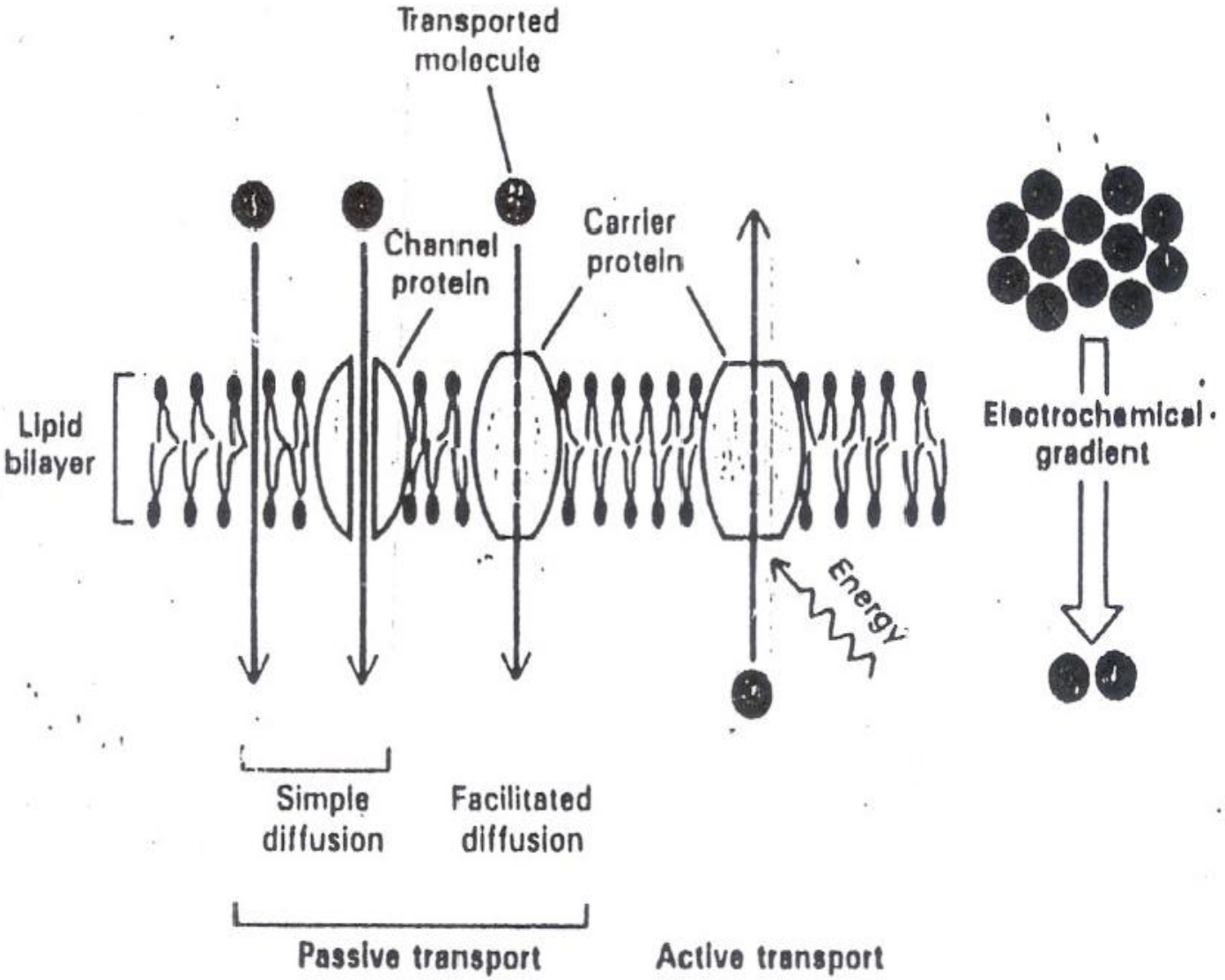


Movement of lipids in membranes.

MEMBRANE TRANSPORT

- Plasma membrane is a selectively permeable barrier,
- Movement across bilayer can be:
  - Unmediated or Carrier-Free Transport: e.g. Water, Gases, Urea
  - Carrier Mediated Transport: Require presence of integral membrane transport proteins (eg. sugars, amino acids, ions)
- Passive transport of molecules across membrane does not require metabolic energy,
- Rate of transport is proportional to Concentration Gradient of the molecules across the membrane,

Different transport systems in biological membranes



What are the types of passive transport?

- Two types of passive transport:
  - Simple Diffusion
  - Facilitated Diffusion

What is simple diffusion?

- Simple Diffusion (unmediated, Carrier-free):
- Small uncharged or hydrophobic molecules (H_2O, O_2, CO_2, other gases, urea, ethanol, esters, ethers, etc.) cross the lipid bilayer by simple diffusion,
- No membrane proteins are involved, so there is no specificity,
- Unmediated (Carrier-free) transport proceeds always in the direction of the concentration gradient
  - High to Low concentration

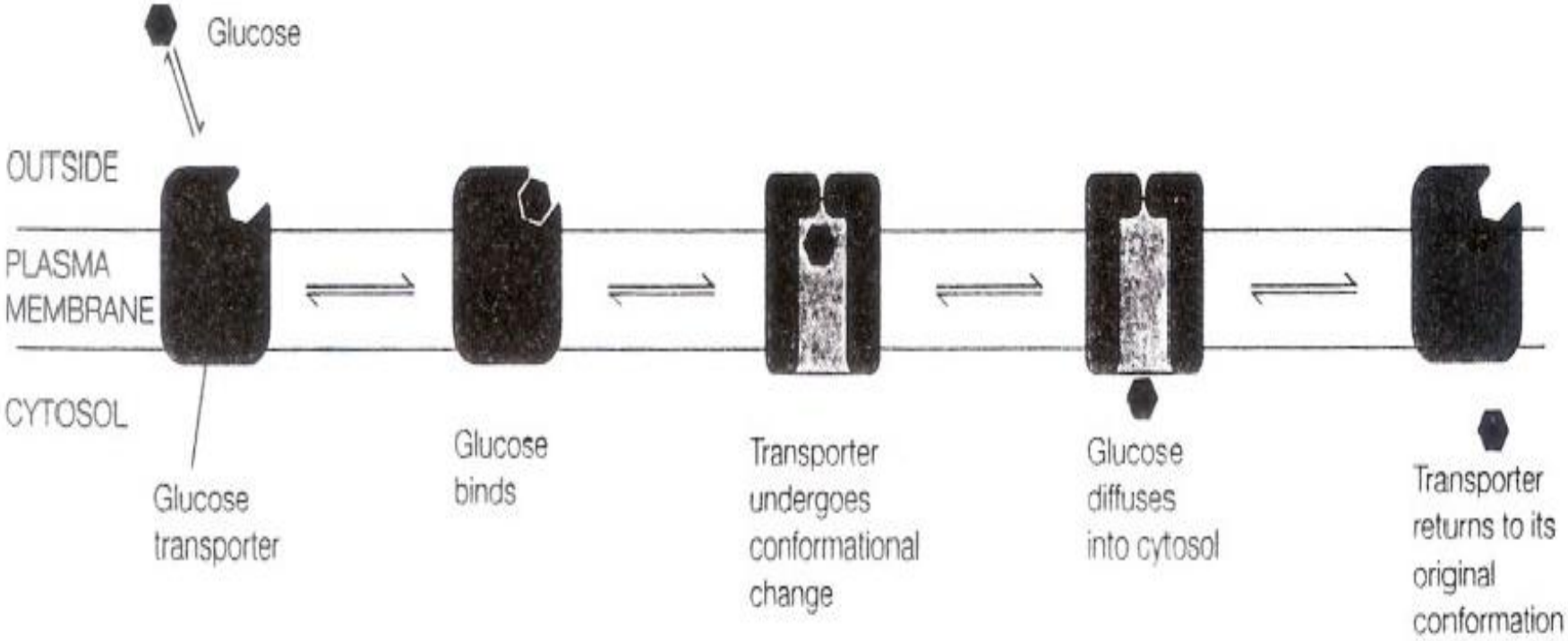
- Rate of diffusion is directly proportional to:
  - Concentration gradient of the molecule across the membrane,
  - Diffusion constant,
  - Temperature,
  - Magnitude of Partition Coefficient,
- Simple diffusion cannot be saturated;

What is Facilitated (Mediated) diffusion?

- Facilitated (carrier-mediated) diffusion of a molecule across biological membrane is dependent on specific Integral Membrane Proteins called **Uni-porters;**
- Uni-porter facilitates translocation of molecules across membrane in the direction of the concentration gradient without any supply of energy;
- Molecule binds to protein on one side of the membrane, the protein then undergoes a conformational change, transports the molecule across the membrane and releases it on the other side,
- Molecules transported in this way include: Hydrophilic molecules such as Glucose, Sugars, Amino Acids;

- Uni-porters are specific for one particular molecule or a group of structurally similar molecules,
- Transport proteins can be saturated,
- Transport protein can be affected by:
  - Temperature,
  - pH,
  - Inhibitor molecules;
- When the transport protein is used for the translocation of one molecule in one direction and another molecule in the other direction without energy supply, the process is called **Exchange diffusion**;

Diagram of Facilitated (Mediated) diffusion of Glucose



Facilitated diffusion of glucose into erythrocytes.

What is active transport?

Active transport:

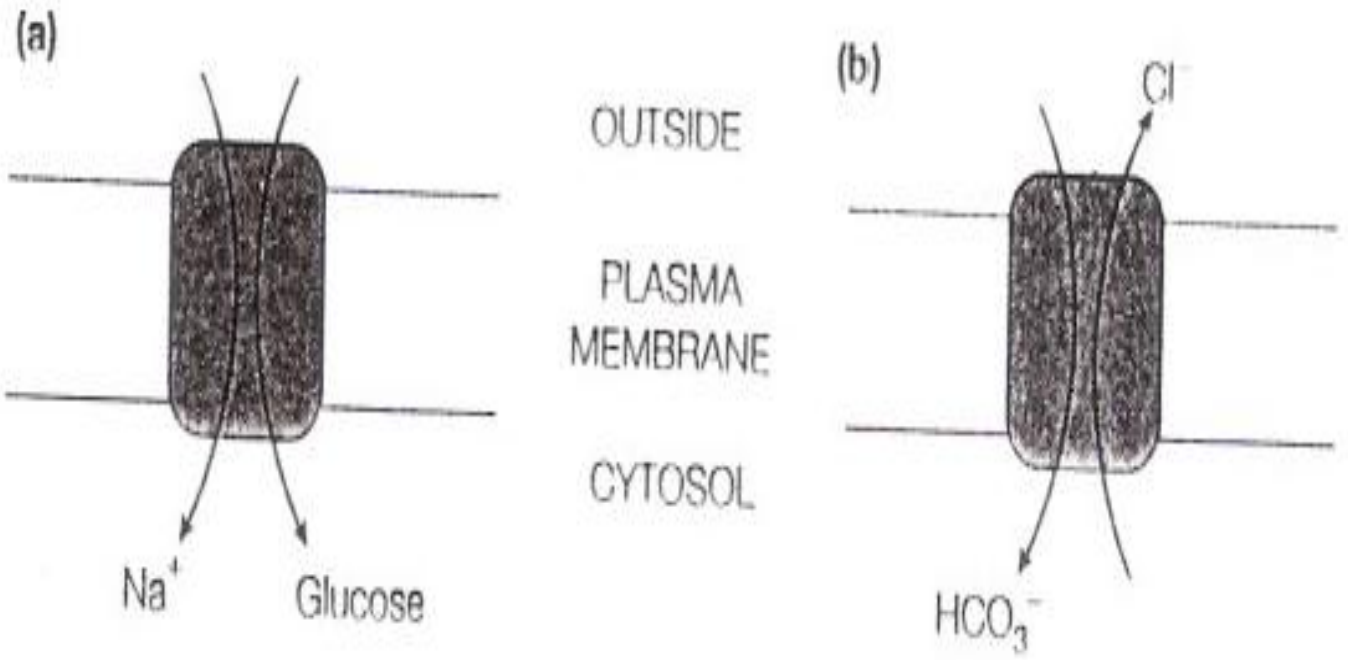
- It is movement of molecules across bio-membrane from site of low to higher concentration,
- It requires both a Carrier-Protein and metabolic energy,
- Energy for active transport can be derived either from direct coupling to hydrolysis of ATP or by coupling to the movement of an ion down its concentration gradient,

Active transport may involve:

- Translocation of a single molecule in one direction (**Uni-port**),
- Translocation of two molecules in opposite directions (**Anti-port**),
- Translocation of two molecules in the same directions (**Symport),**

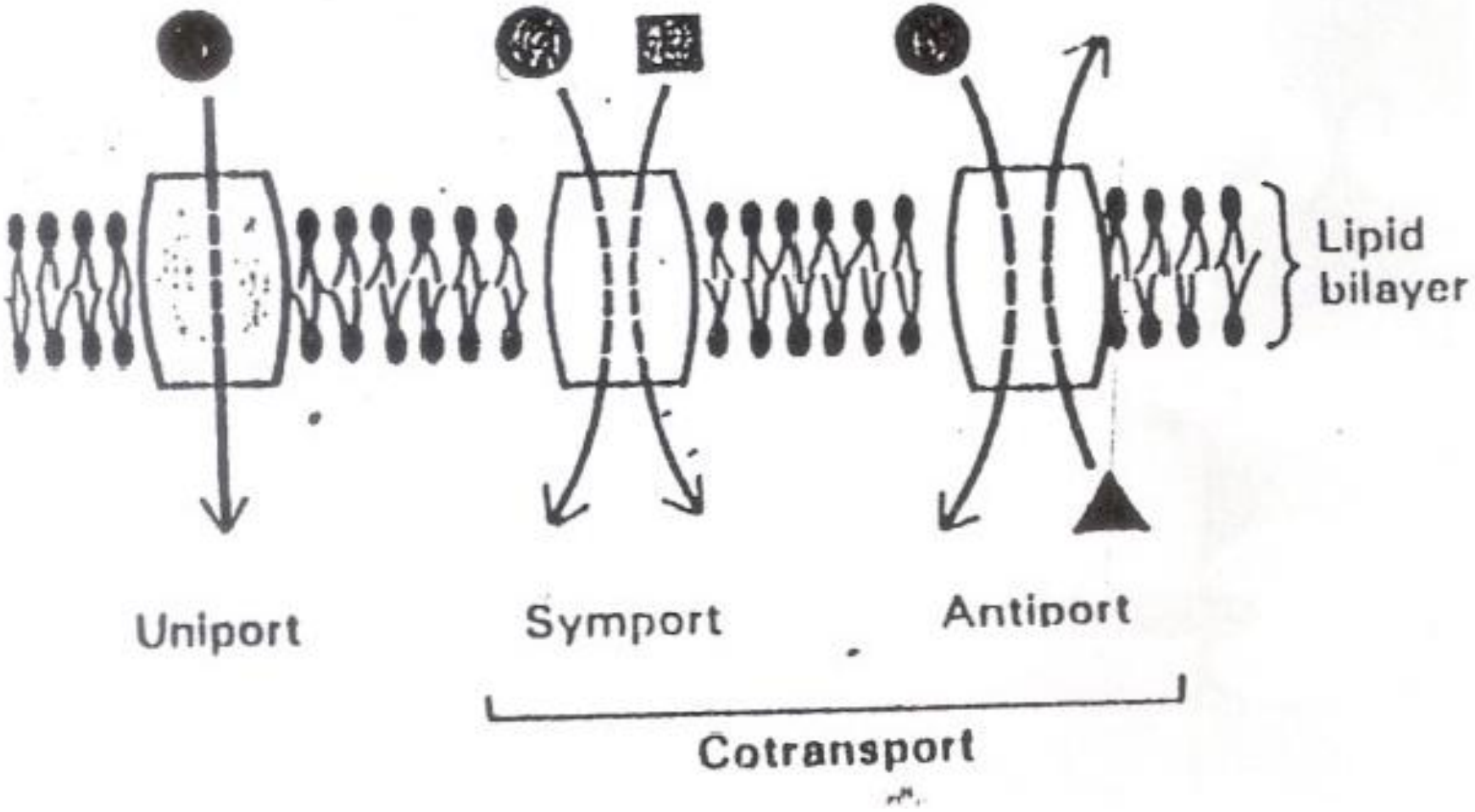
- These processes are also known as **COUPLED ACTIVE TRANSPORT**

Diagram of Active Transport: Symport and Antiport

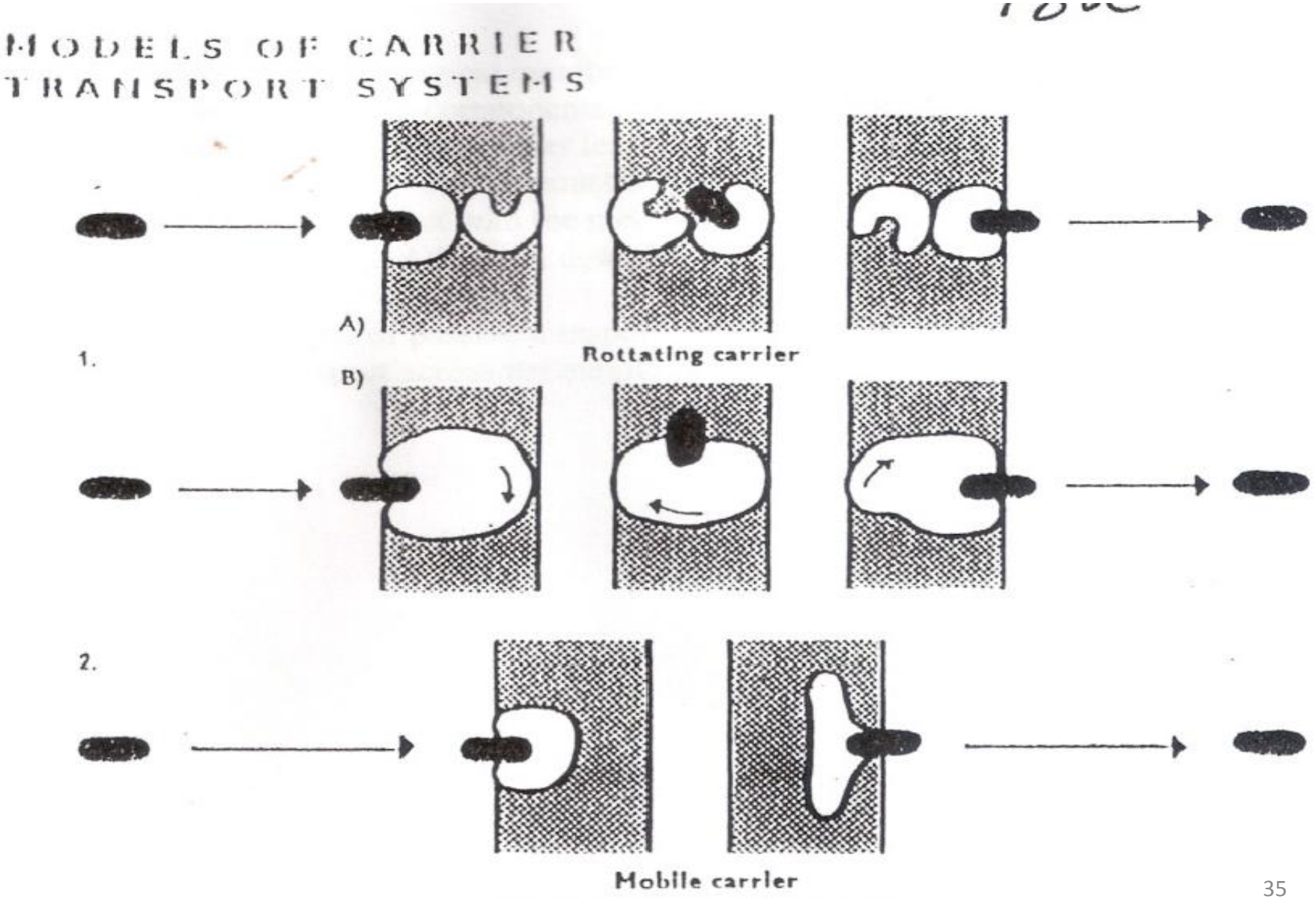


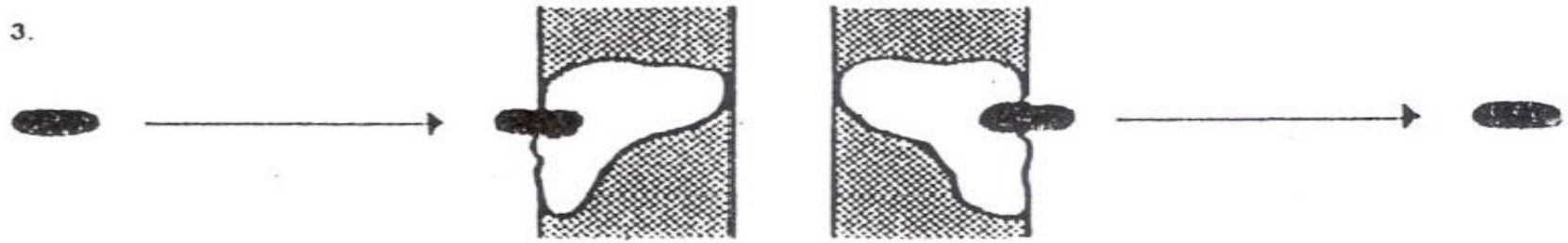
Ion-driven cotransport mechanisms. (a) Symport process involving a symporter (e.g. Na^+/glucose transporter); (b) antiport process involving an antiporter (e.g. erythrocyte band 3 anion transporter).

Diagram of transporters

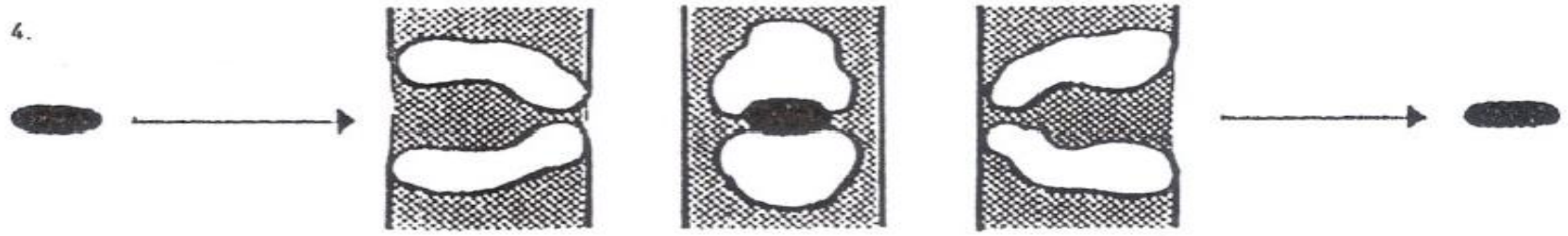


Schematic diagrams of models of carrier transport systems





"Channel"



Assotiation of a rotary carrier and a channel

Assotiation of a mobile carrier and a channel

- Common features of all these models is the sequence of reaction steps:
  - Recognition of Substrate,
  - Binding of Substrate to carrier protein,
  - Translocation,
  - Release,

Study questions

1. What are the functions of the biological membrane?
2. Use a simple diagram to show the components parts of the lipid bilayer.
3. List some of lipids in the outer and inner leaflets of lipid bilayer,
4. List the different types of non-covalent interactions in the lipid bilayer.
5. How do membrane proteins interact with the membranes?
6. With the help of a simple labelled diagram describe the “Fluid mosaic model” of membrane structure.
7. Briefly describe the two types of passive transport across membranes.
8. Briefly describe active transport across the membranes,
9. Draw the general structure of Phospholipid,
10. List the common features of the models of membran transport systems