Contents

1- How membranes are organized .Fluid -Mosaic theory. Bilayer mobility (fluidity)-Three components of Biological membrane:

a- Membrane Lipids : Three types of lipid Phospholipids were identified phospholipids,glycolipids and Cholesterol.

b-Membrane proteins :

Peripheral protein — Integral proteins (Transmembrane - Channel protein – Transmembrane carrier protein)

C-Carbohydrates

Glycoprotein (Glycocalyx in epithelium of small intestine)-

Glycolipid .

2- How membranes are made . New membranes from old - Membrane lipids -Membrane proteins

4- How small molecules cross membranes .(osmosis –diffusion-facilitated diffusion –Active transport)

5- How large particles cross membranes. Giving out and taking in Exocytosis –Endocytosis -Receptor-mediated endocytosis .Membrane fusion: key to exocytosis and endocytosis .

6- How messages cross membranes. (Nerve impulses).What happens at the synapse .

1-How membranes are organized

- To stay alive, all living things needmembranes.
- Membranes are **barriers** which give cells their **outer boundaries (plasma membranes) and their inner compartments (organelles).**
- **Being selectively permeable .**
- Membranes control the **movement of substances into and out of cells.**

-Membranes control the **flow of information between cells either by recognizing** signal molecules received from other cells, or by sending chemical or electrical signals to other cells.

- Membranes are involved in the **capture and release of energy ,Compartementalization , Cell recognition .**

-Three membrane components

Biological membranes are made of three major components: **lipids,proteins and sugars.**

I-Three types of lipid

Lipids are biologically important substances that are insoluble in water but soluble in organic solvents such as propanone (acetone), ethanol,trichloromethane (chloroform), ethoxyethane (diethyl ether) and light petroleum (b.p. 40–60 °C).

-There are **three** major types of lipid found in biological membranes: **phospholipids, glycolipids and cholesterol. They** each play different roles in the membrane.

***Phospholipids contain phosphate**

-The most common type of phospholipid consists of **glycerol** (propan1,2,3-triol) linked to two **fatty acid chains**, **phosphate** and **choline**. The fatty acid chains usually contain between 14 and 24 carbon atoms.

-.

One chain is **usually unsaturated**, containing from one to four ***cis*** double bonds. Each double bond puts a bend in the fatty acid chain .

Glycolipids contain sugars:

-Glycolipids are found on the outer surface of the plasma membrane with their sugars exposed at the cell surface.

Cholesterol: in a class of its own

-The third type of membrane lipid is cholesterol, a molecule that is **structurally** quite different from the phospholipids and glycolipids. Cholesterol contains a four-ring steroid structure together with a short hydrocarbon side-chain and a hydroxy group.

Two-faced membrane lipids

-A common feature of membrane lipids is that they are **amphipathic.**This means that they have a hydrophilic (water-loving, or polar) region and a hydrophobic (water-fearing, or non-polar) region.

-Bilayers form because the hydrocarbon tails have a strong tendency to stay away from water, and are '**squeezed** together' by water molecules. Such bilayers will close on themselves to form **sealed** compartments, called **liposomes,** to eliminate the edges where the tails would be in contact with water .

-Liposomes are useful model membranes for research, and may also be used to deliver drugs to particular organs of the body. Liposomes are absorbed by many cells by fusion with the cell plasma membrane. If methods can be developed for targeting liposomes to particular tissues, **drugs could be carried in liposomes to these tissues**.

- **Cholesterol**, too, is amphipathic due to its hydrophobic rings and side-chain, and its hydrophilic hydroxy group. It can be incorporated into phospholipid bilayers , **but cannot form a bilayer on its own.**

II-Membrane proteins

-Many of the specific functions of membranes are carried out by proteins.

-There are several different ways in which proteins are associated with lipid bilayers to form functional membranes.

(i) Many membrane proteins extend across the lipid bilayer. Such **transmembrane proteins have hydrophobic regions that are embedded** within the bilayer and interact with the hydrophobic tails of the phospholipids. These regions are often helical, forming rigid 'tubes'.

(ii) Some intracellular proteins do not span the membrane but are covalently attached to the inner surface, by either a fatty acid chain or a phospholipid . Such proteins are sometimes termed **anchored proteins; they are firmly attached to the membrane and can only be** removed by treatments (e.g. using detergents or organic solvents) which disrupt the membrane. The proteins are, therefore, called **integral membrane proteins**. Examples are the enzyme **cholinesterase** which is found in synapses, and the **G-proteins** involved in sending messages across membranes.

(iii) Many proteins are weakly bound to one or other surface of the membrane by non-covalent interactions with other membrane proteins. They can be removed by mild treatments (such as altering the pH or ionic strength) which leave the membrane intact. Such proteins are called **peripheral membrane proteins. An example is** cytochrome *c of the inner mitochondrial membrane.*

Getting things across cell membranes :(glucose –amino acids-K+,Na)

-There are two types of **transport** protein: **channels and carriers.**

-Some **carrier** proteins transport only one solute across the membrane. These are called **uniports, and an example is the glucose** transporter in red blood cell membranes.

- Others transport two solutes at the same time so they are called **co-transporters.**

If the two solutes are transported in the same direction, it is called **symport; if they are transported** in opposite directions, this is known as **antiport.** An example of symport is the co-transport of amino acids and Na +into the cells of the gut. An example of antiport is the Na+/K +pump which pumps Na out of cells and K +into cells.

-Glycoproteins contain sugars

-Most of the proteins of the plasma membrane that are exposed to the cell surface have covalently linked **sugars (Glycocalx).**

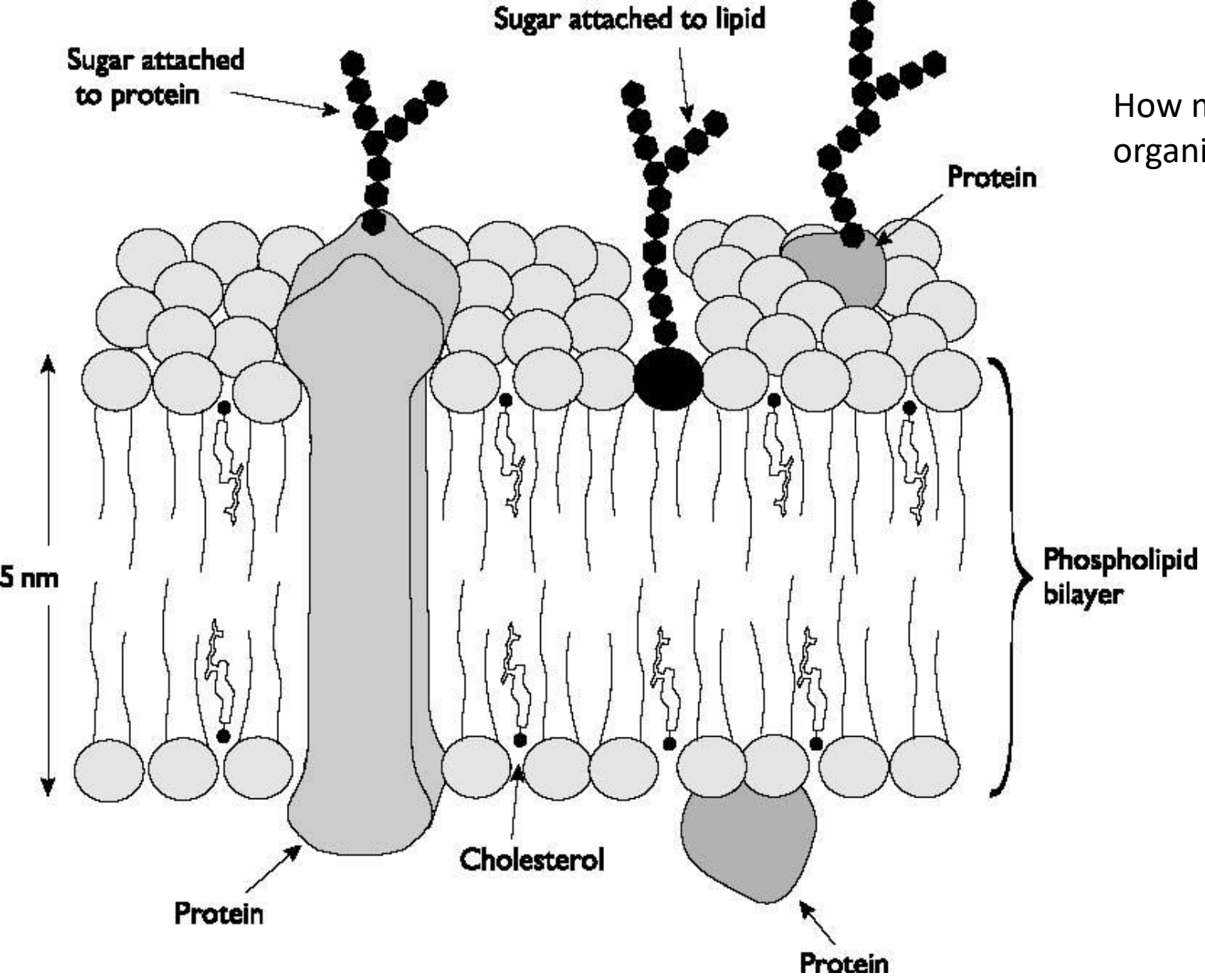
Membrane structure summarized

The **fluid mosaic model of membrane structure, proposed by S.J. Singer.** Biological membranes are thus lipid–protein–sugar 'sheets', in which the permeability barrier and structural integrity are provided by the lipids; specific functions are carried out by the proteins; and the distinctive 'appearance' is provided by the sugars.

-Membrane fluidity : The fluidity of a lipid bilayer is affected by **temperature, fatty acid composition and cholesterol content.**

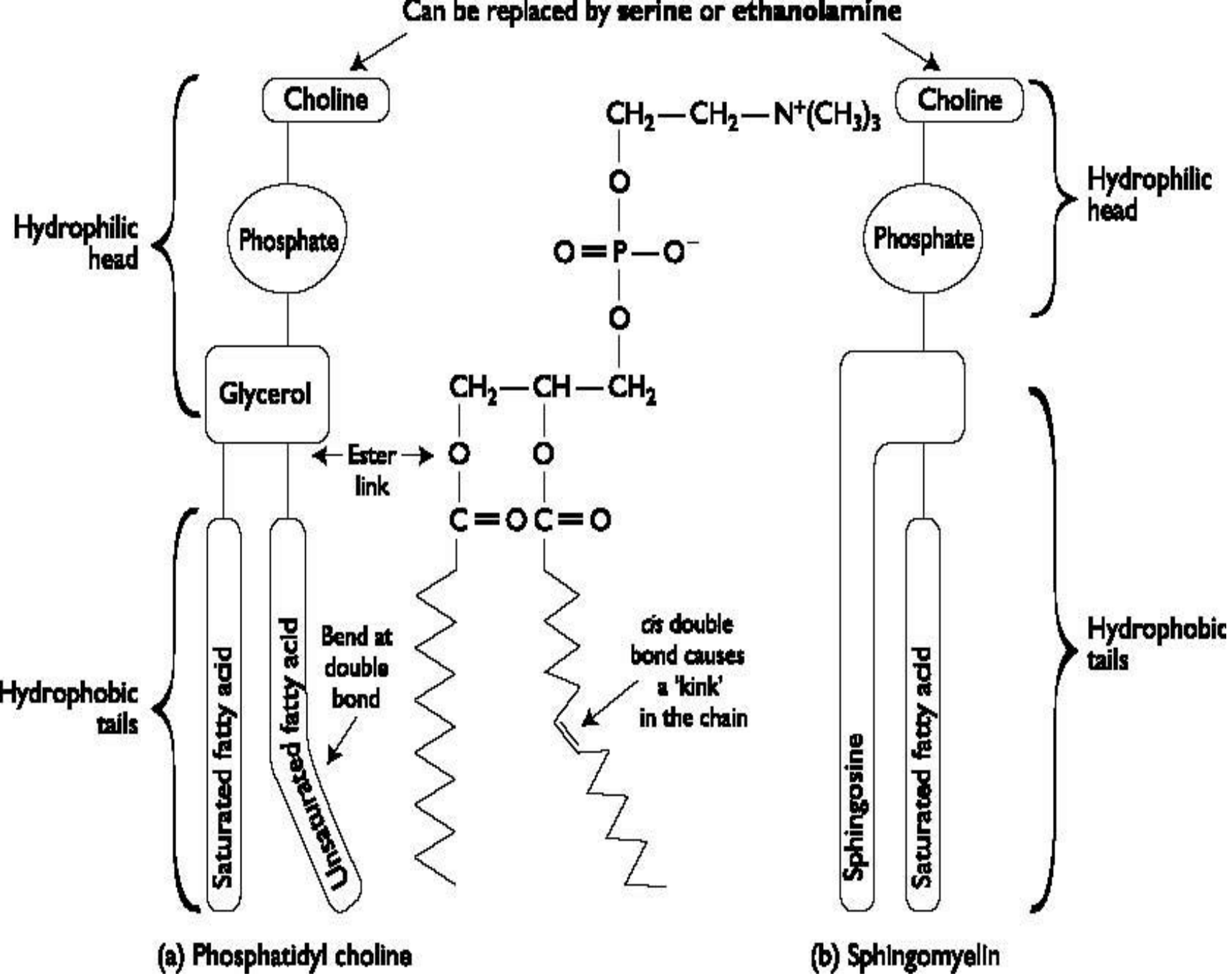
-Movements :Lateral diffusion-flexion –rotation-Flip-flop.

-flip-flop: in membranes of the endoplasmic reticulum, where phospholipids are synthesized, there is a rapid flip-flop of particular lipids across the bilayer.This is achieved by proteins called **phospholipid translocators** (or **flippases).**

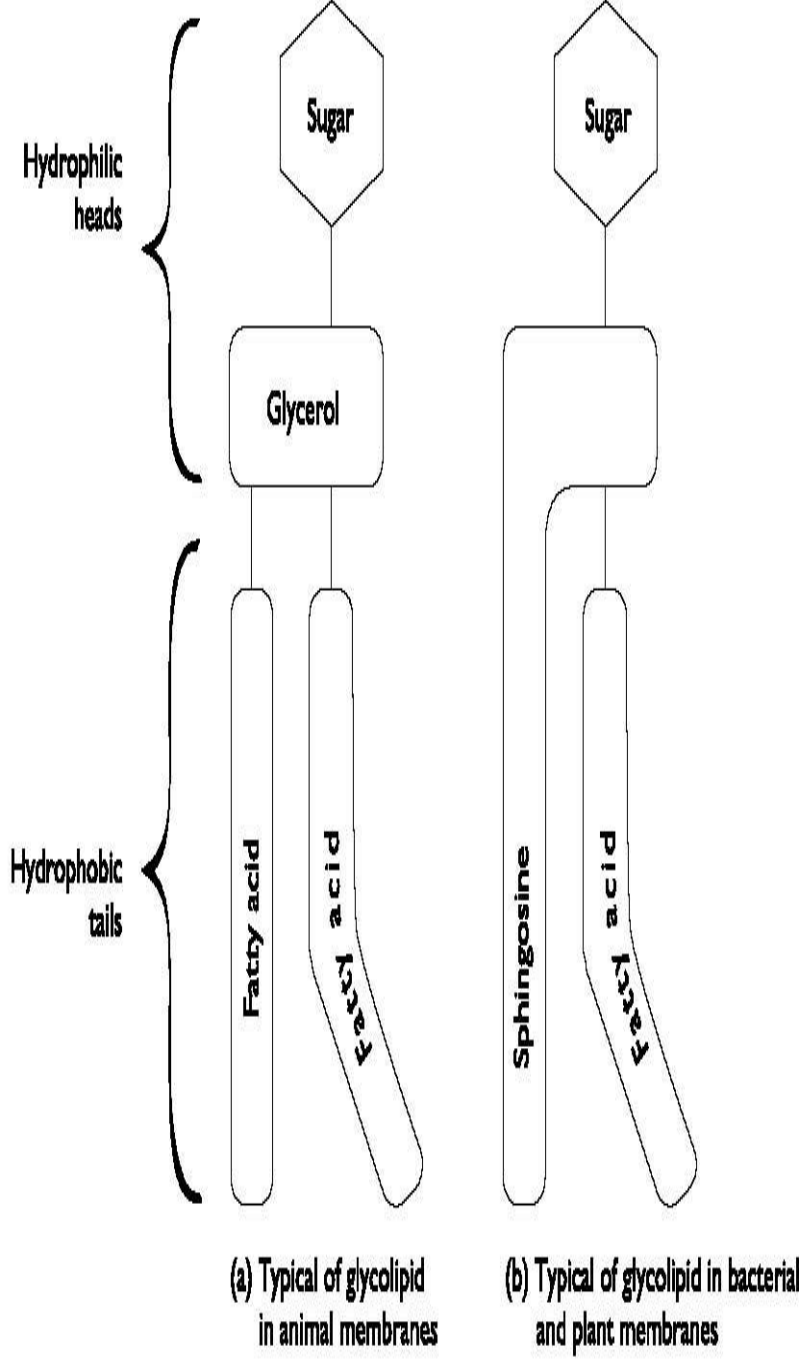


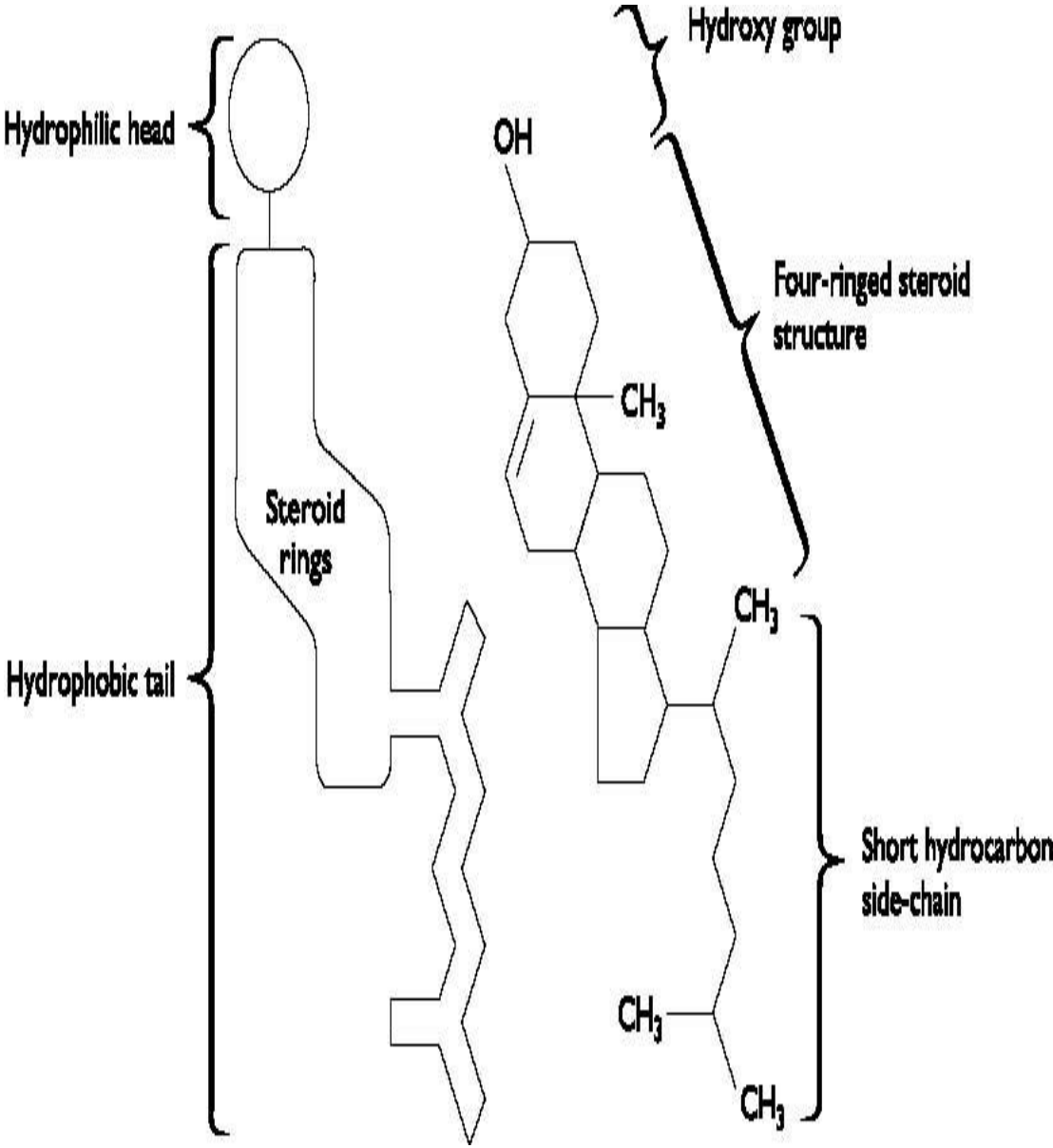
How membranes are organized

Diagrammatic representation of a biological membrane.
membrane only: for example, on the outer surface of the plasma membrane



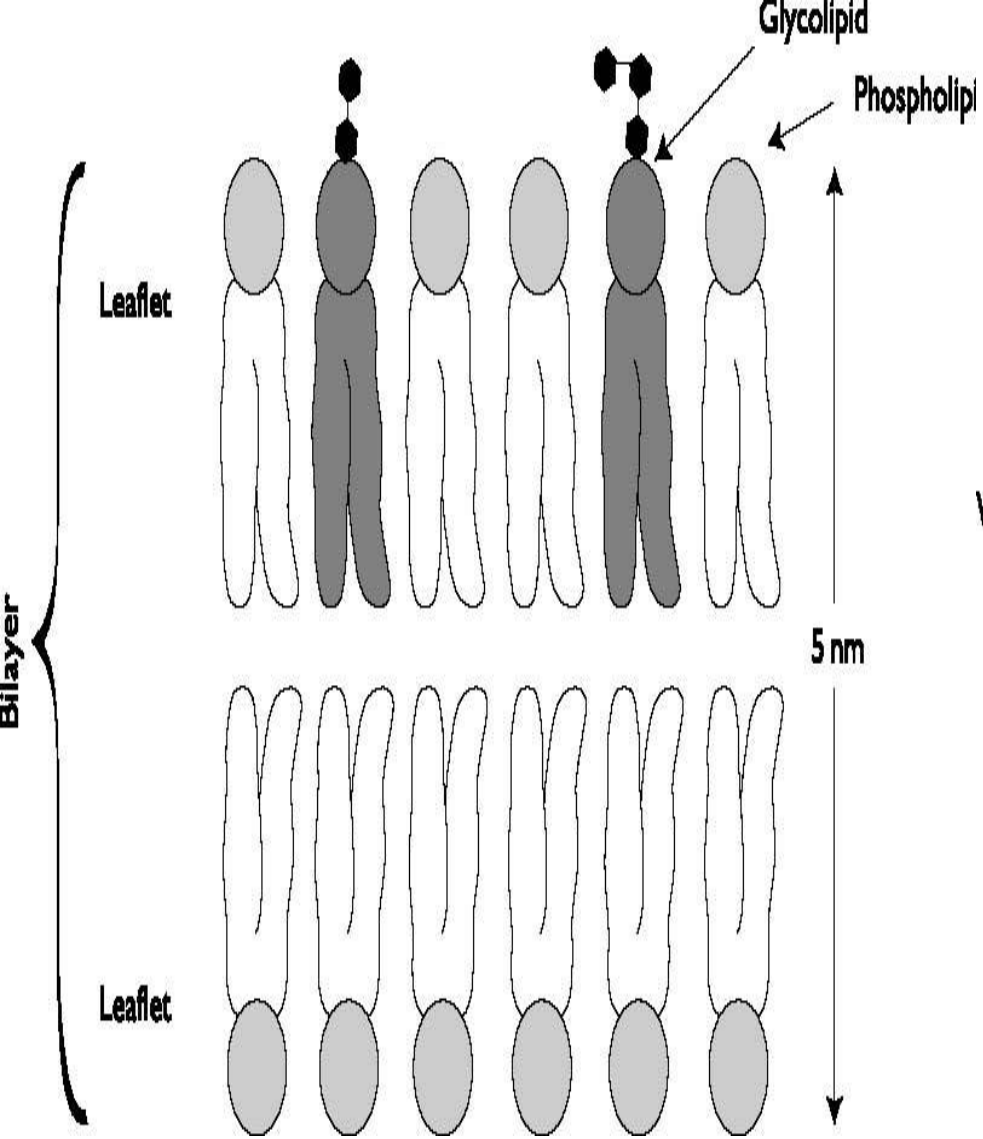
(a) Phosphatidyl choline, a glycerophospholipid; (b) sphingomyelin, a sphingophospholipid.



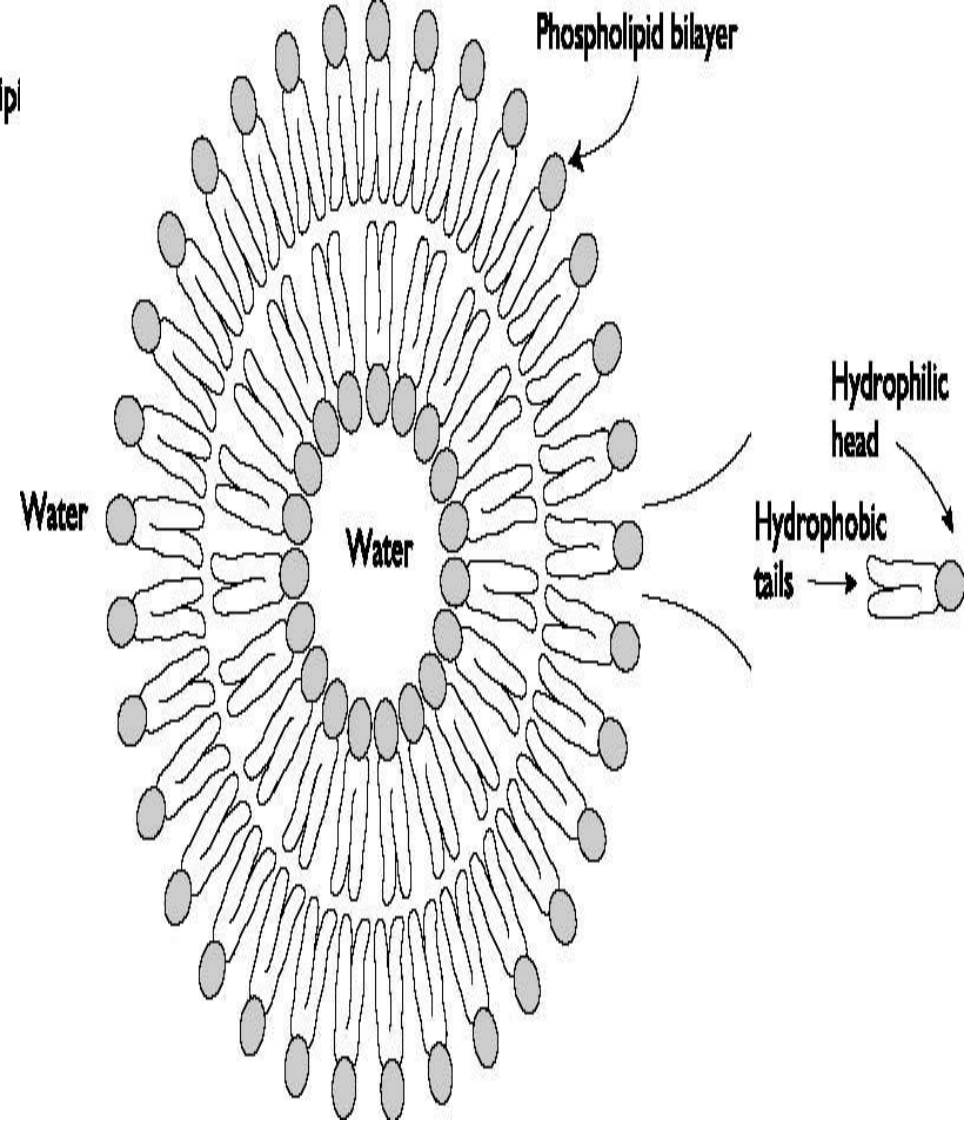


Cholesterol

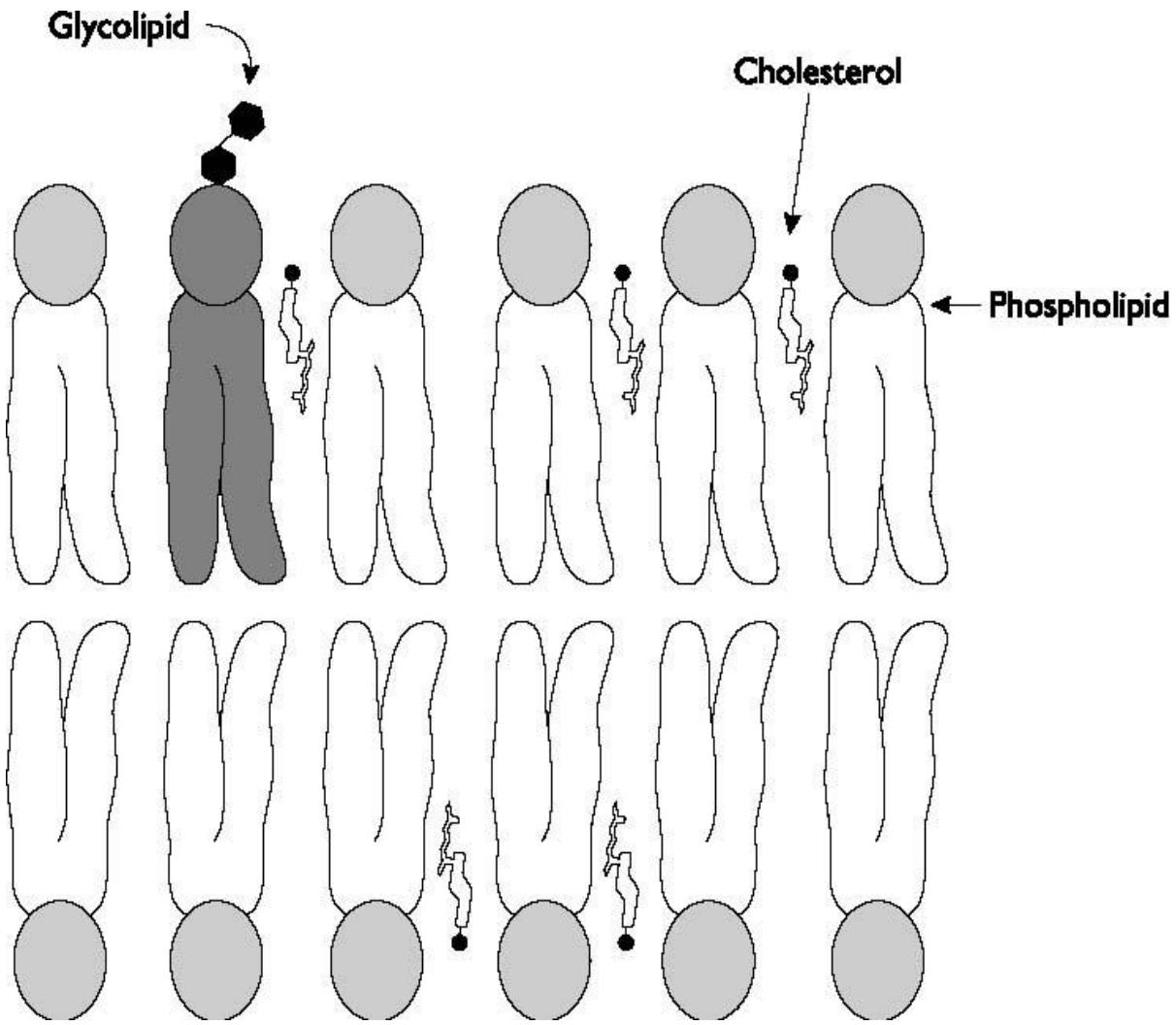
Figure 3. Glycolipid structures.



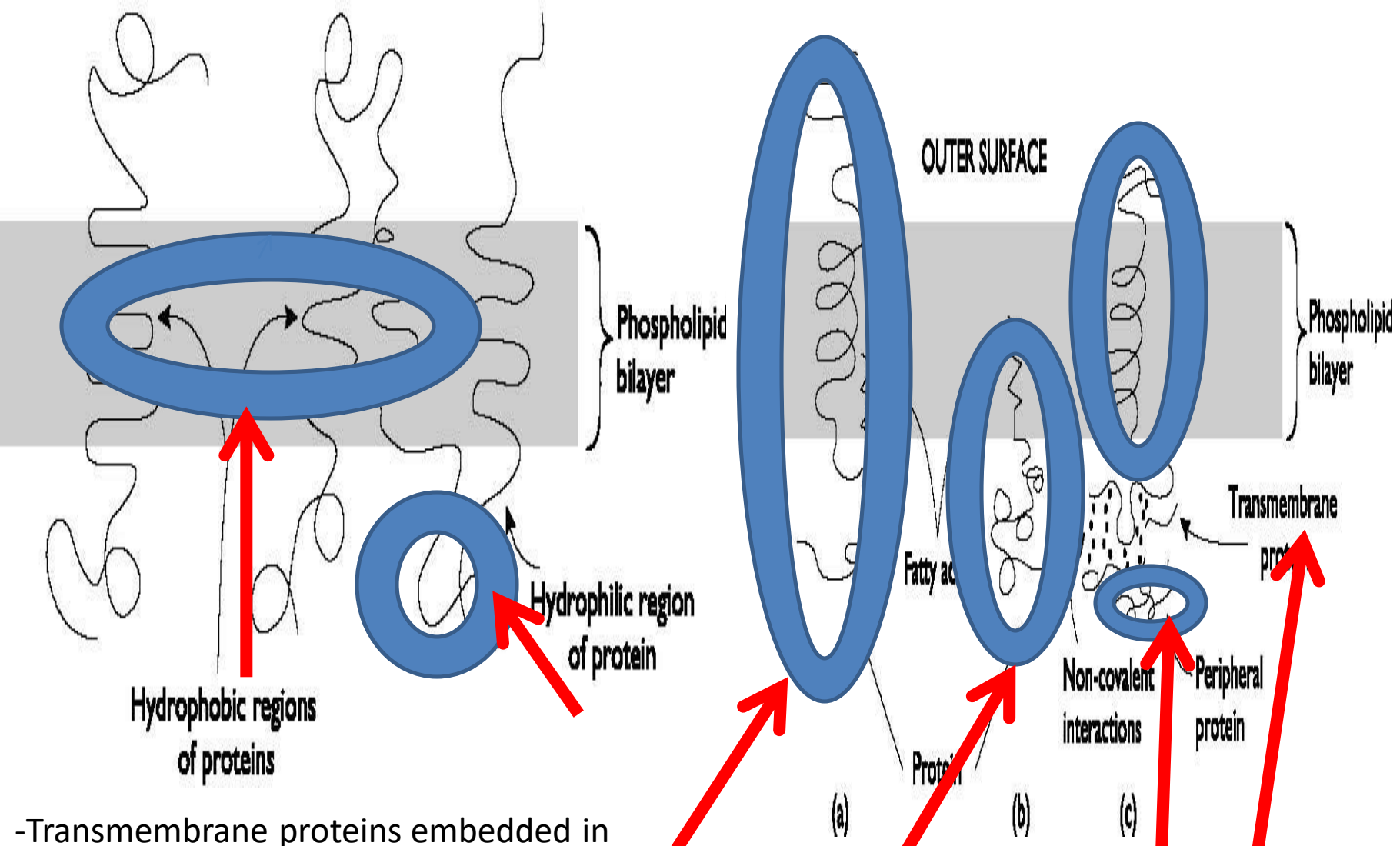
A membrane bilayer.



Section through a **liposome**



Cholesterol incorporated into a membrane bilayer.



-Transmembrane proteins embedded in the bilayer.

(a) Transmembrane protein attached to bilayer by fatty acid chain; (b) integral membrane protein (e.g. cholinesterase) attached by fatty acid chain; (c) peripheral membrane protein (e.g. cytochrome *c*) attached to a transmembrane protein.

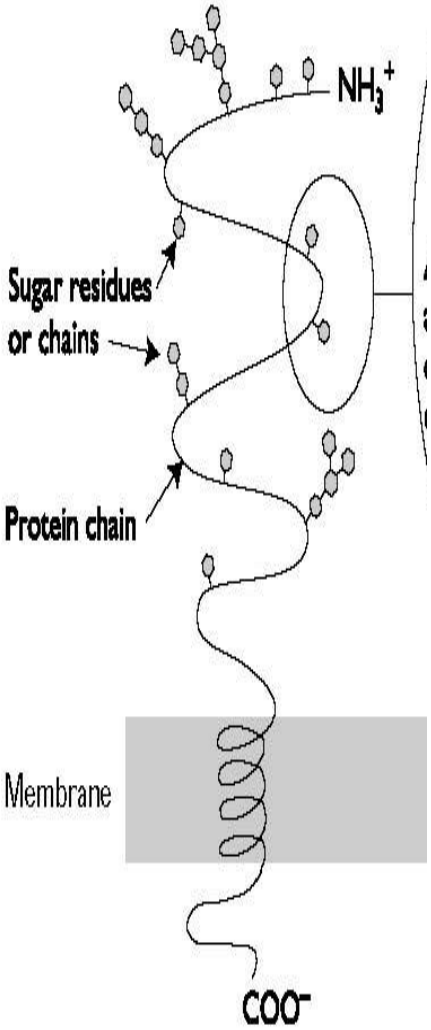


Figure 10. Diagrammatic representation of a glycoprotein embedded in a membrane bilayer (e.g. glycophorin A, a glycoprotein found in red cell membranes).

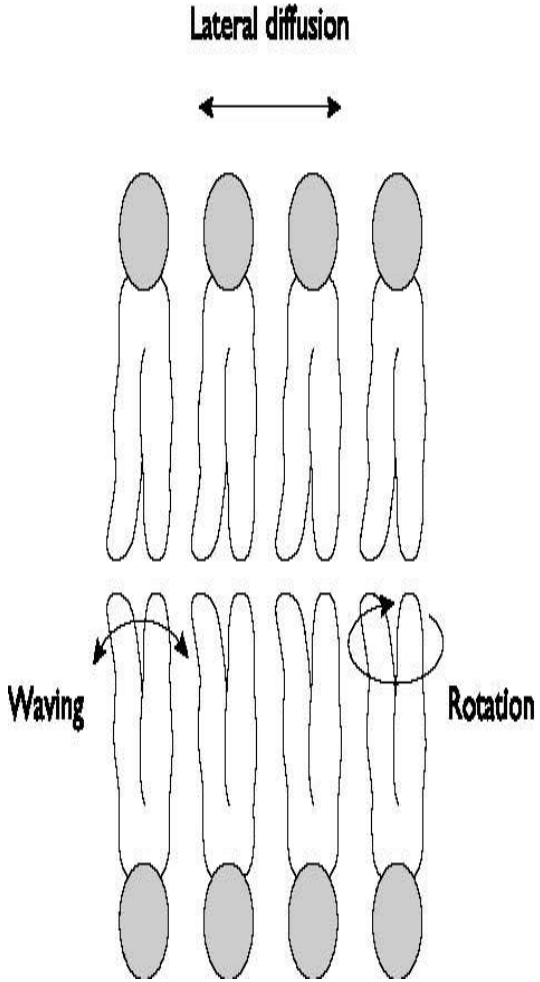


Figure 11. Movements of phospholipids in bilayers.

. Flip-flop movements of phospholipids within bilayers are very rare.

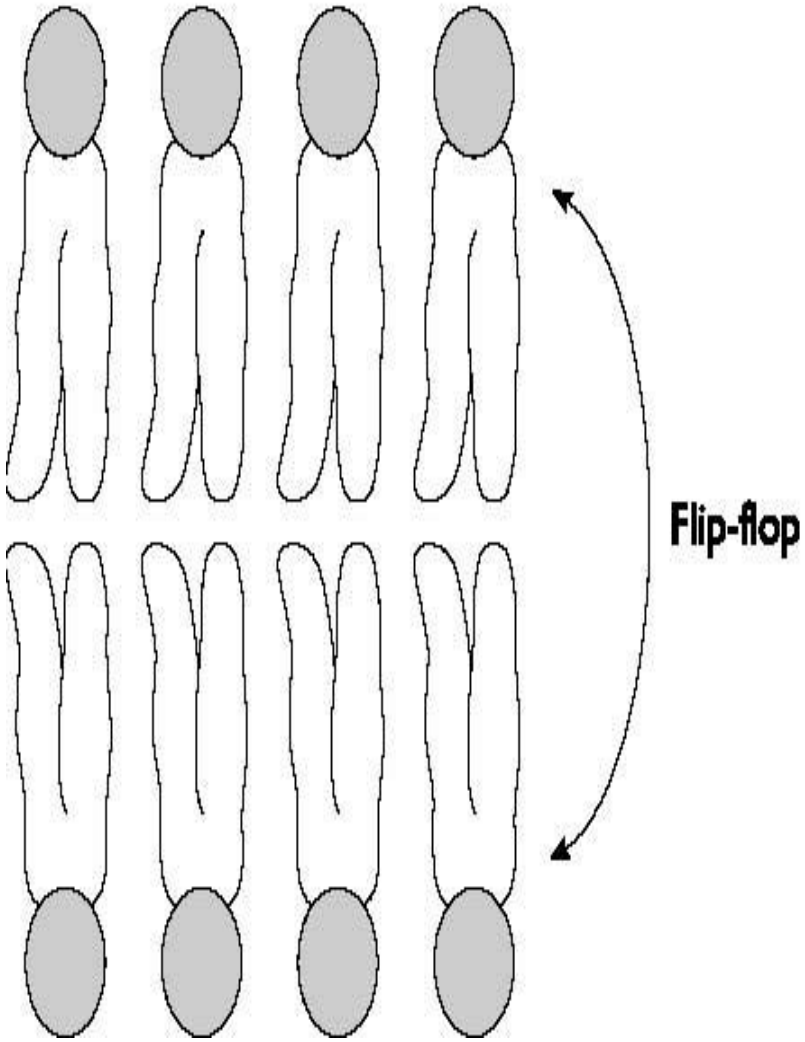
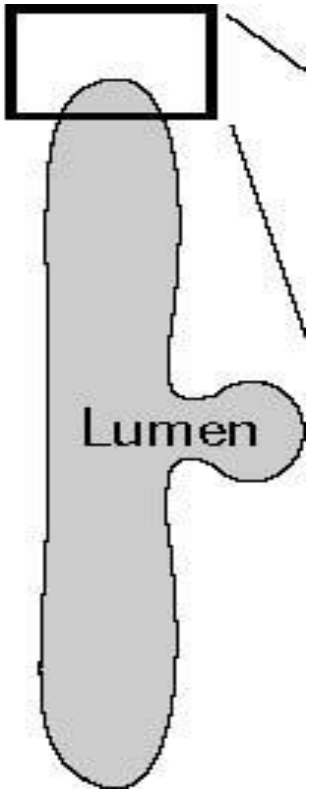
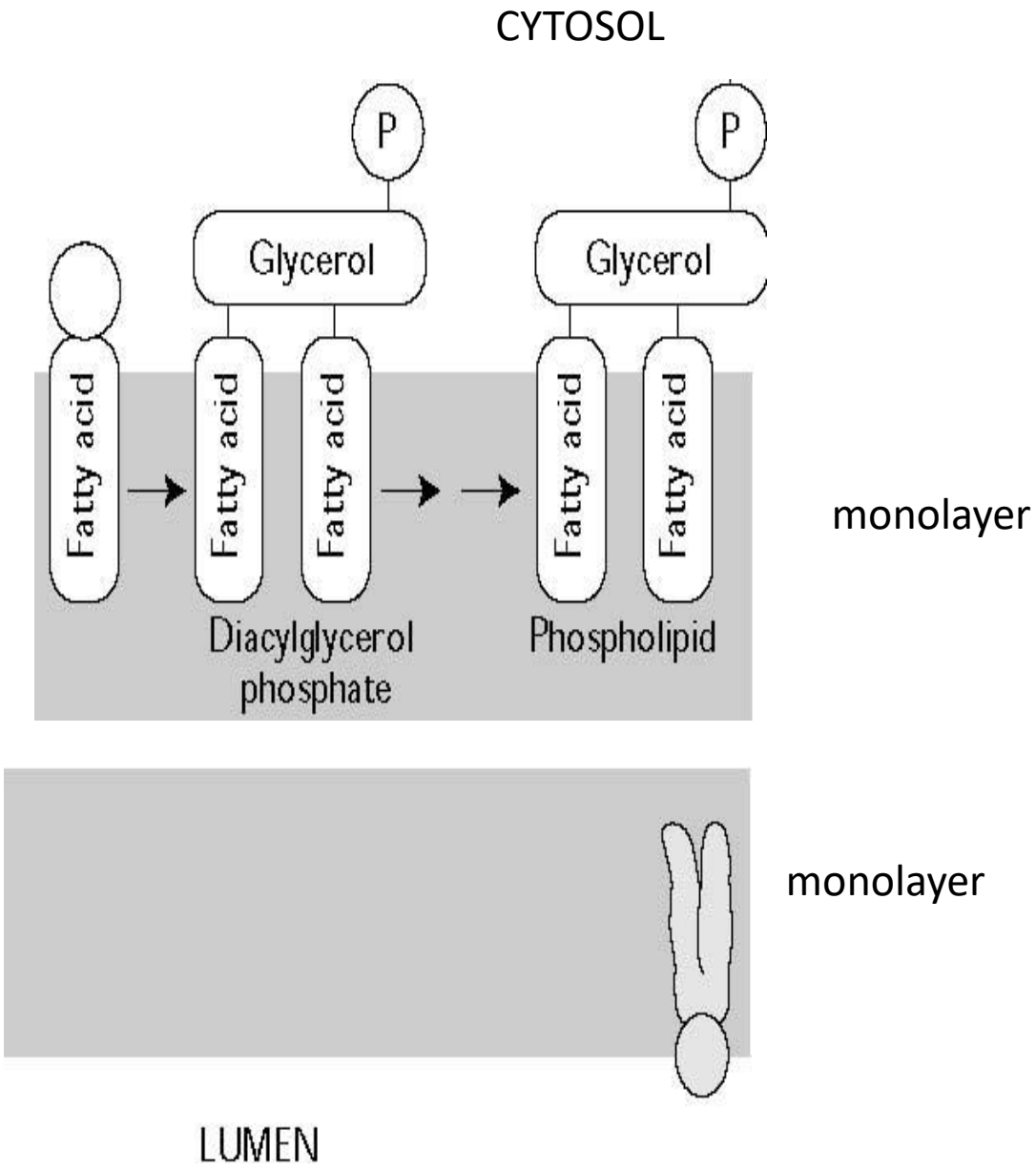


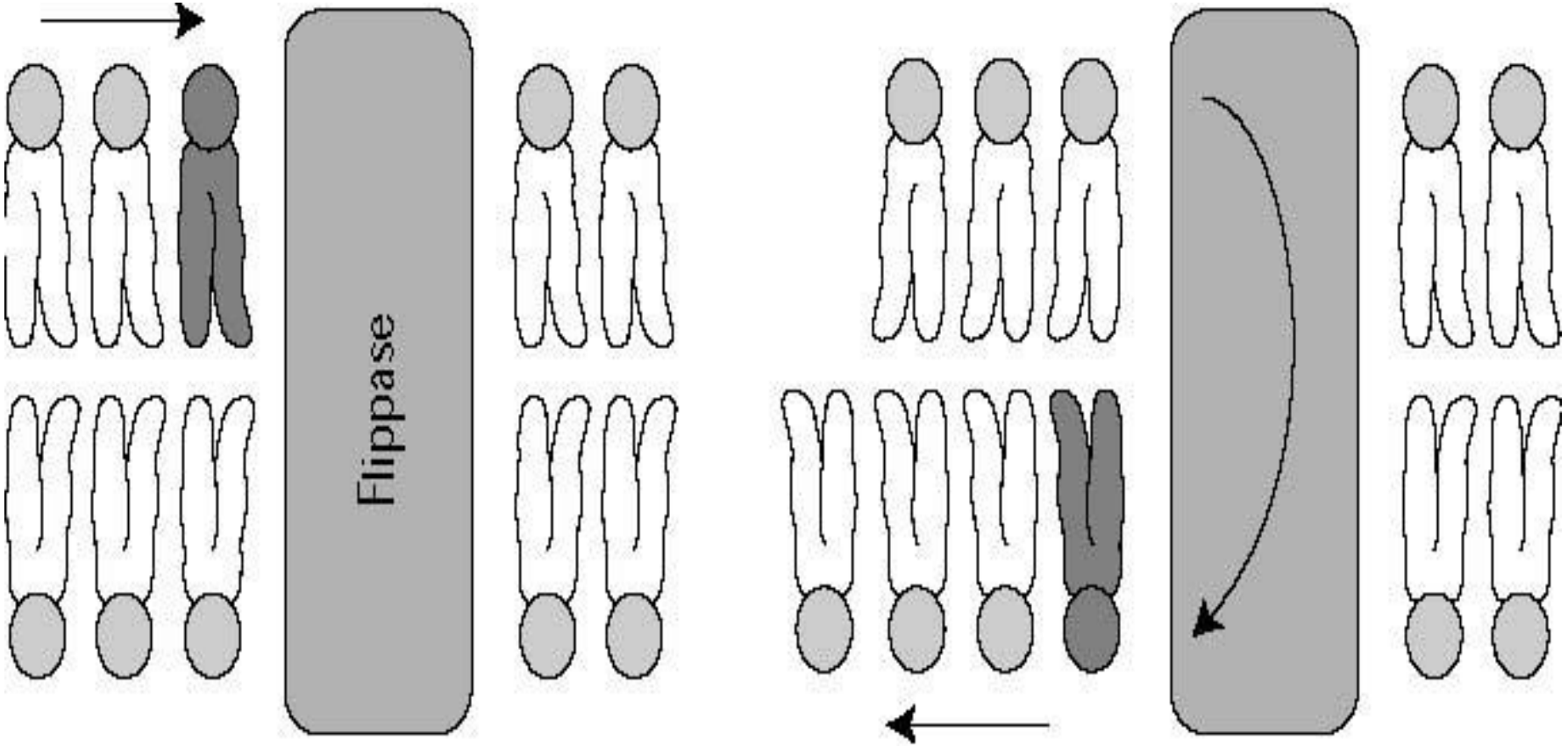
Figure 12. Flip-flop movements of phospholipids within bilayers are very rare.



endoplasmic reticulum



1. Phospholipid diffuses .
2. Flippase transfers phospholipid to flippase to opposite monolayer .



Phospholipid diffuses away from flippase

Action of flippases

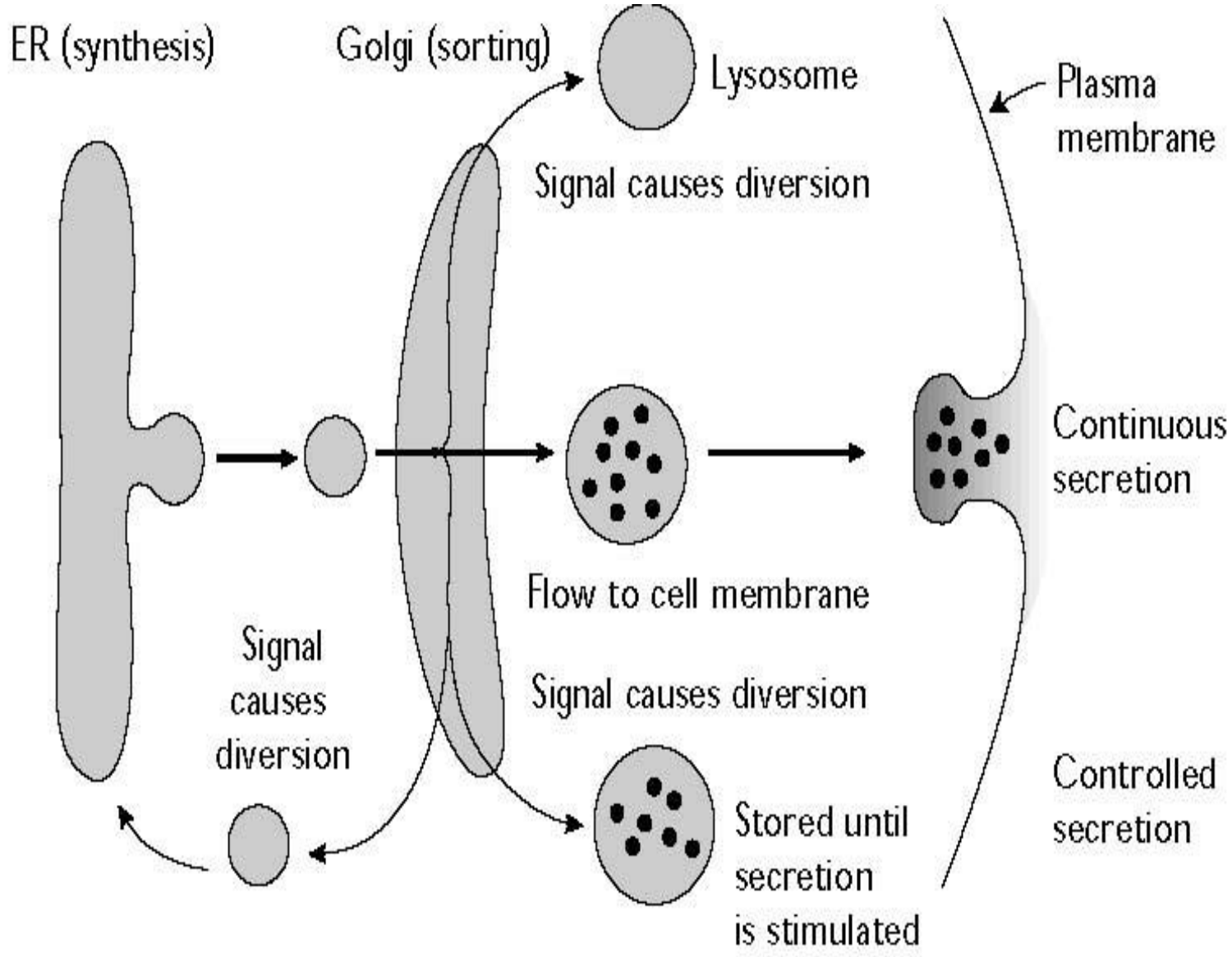


Figure 14. Flow of membranes in eukaryotic cells.

3-How membranes are made New membranes from old ?

- Phospholipid molecules are assembled **step-by-step** .
- First, two fatty acids, which are activated, and embedded by their hydrocarbon chains in the ER membrane, are attached one by one to cytosolic glycerol phosphate.
- The resulting amphipathic molecule (diacylglycerol phosphate) is embedded in the ER membrane by its two hydrocarbon tails.
- Next, the phosphate is replaced by the polar head-group (for example, phosphate-choline) to form a membrane phospholipid.
- The enzymes that catalyse these steps are integral proteins which are embedded in the ER membrane so that their active sites face the cytosol.

- These reactions occur in the outer monolayer of the ER membrane; however, **flippase enzyme**s, present in the ER membrane of eukaryotes and in the plasma membrane of prokaryotes, transfer some of the newly formed phospholipids to the opposite monolayer .

4-How small molecules cross membranes:

A--Small non-polar molecules such as O2 and N, and **uncharged polar molecules** such as ethanol or **urea,** can rapidly cross lipid bilayers;

they cross a **10 nm** bilayer in **seconds** (diffusion).

- The rate of diffusion is described by **Fick's law**. This states that the rate of diffusion (moles per second) across a membrane, is directly proportional to the difference in solute concentration (C-C_i) on each side
- of the membrane, to the area (A) of the membrane and to the permeability coefficient (P), which is itself inversely proportional to membrane thickness (d).

B- Osmosis

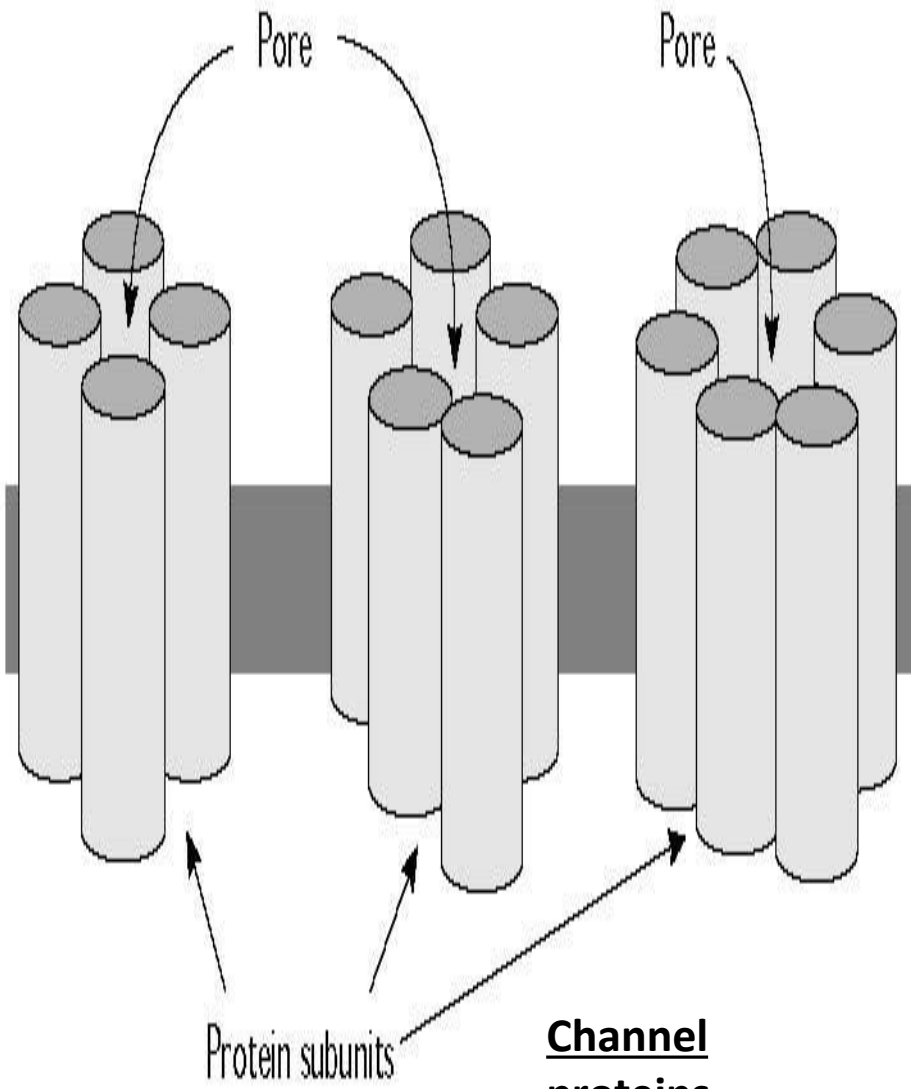
-Water is unusual in that, although it is polar, it can cross lipid bilayers rapidly, passing through a **10 nm bilayer** in about **one millisecond.(osmosis)**

-

3-Passive and active transport

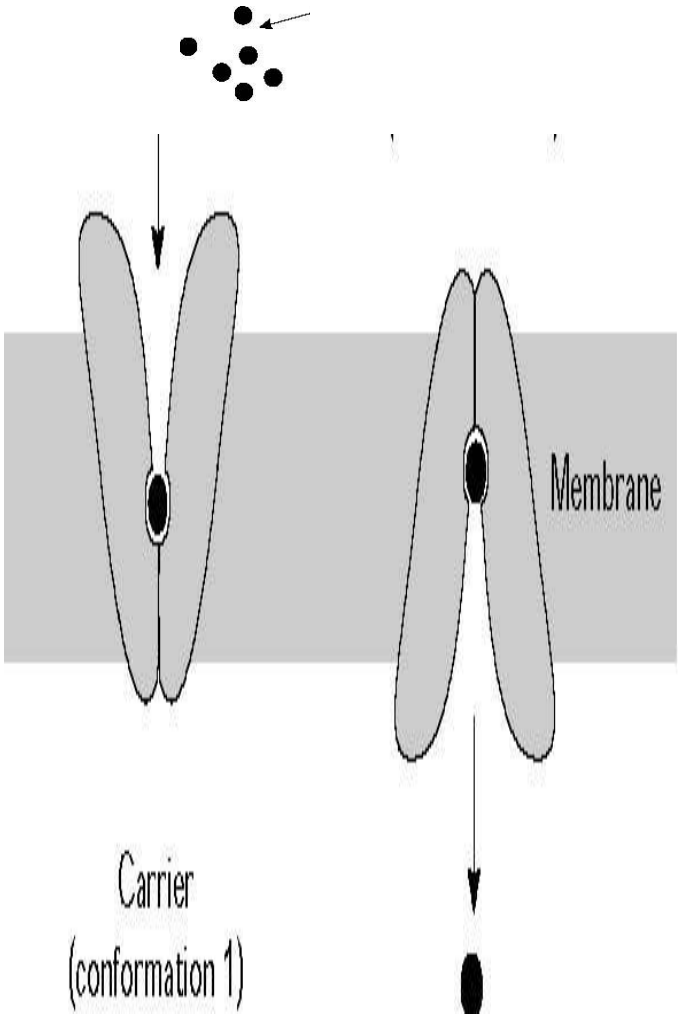
- All **channel** proteins, and many **carrier** proteins, transfer molecules or ions across the membrane downhill.

- This process is called **passive transport** because no input of energy is needed to bring it about . It is also called **facilitated diffusion** because the normal process of diffusion is helped or facilitated by the membrane proteins**.**
- **Facilitated diffusion differs from simple diffusion in that it is selective and saturable (i.e. when all the carriers have bound a solute molecule, the rate of diffusion is not increased by increasing the concentration of solute**
- Cells also have transport proteins that transfer solutes across the membrane uphill, against their electrochemical gradient. This process is called **active transport** because an input of energy is needed to bring it about . It is always done by carrier proteins, not by channels .



Channel proteins

Material to be transported



Carrier (conformation 2)

Carrier proteins

Figure 19. Diagrammatic representation of membrane channels.

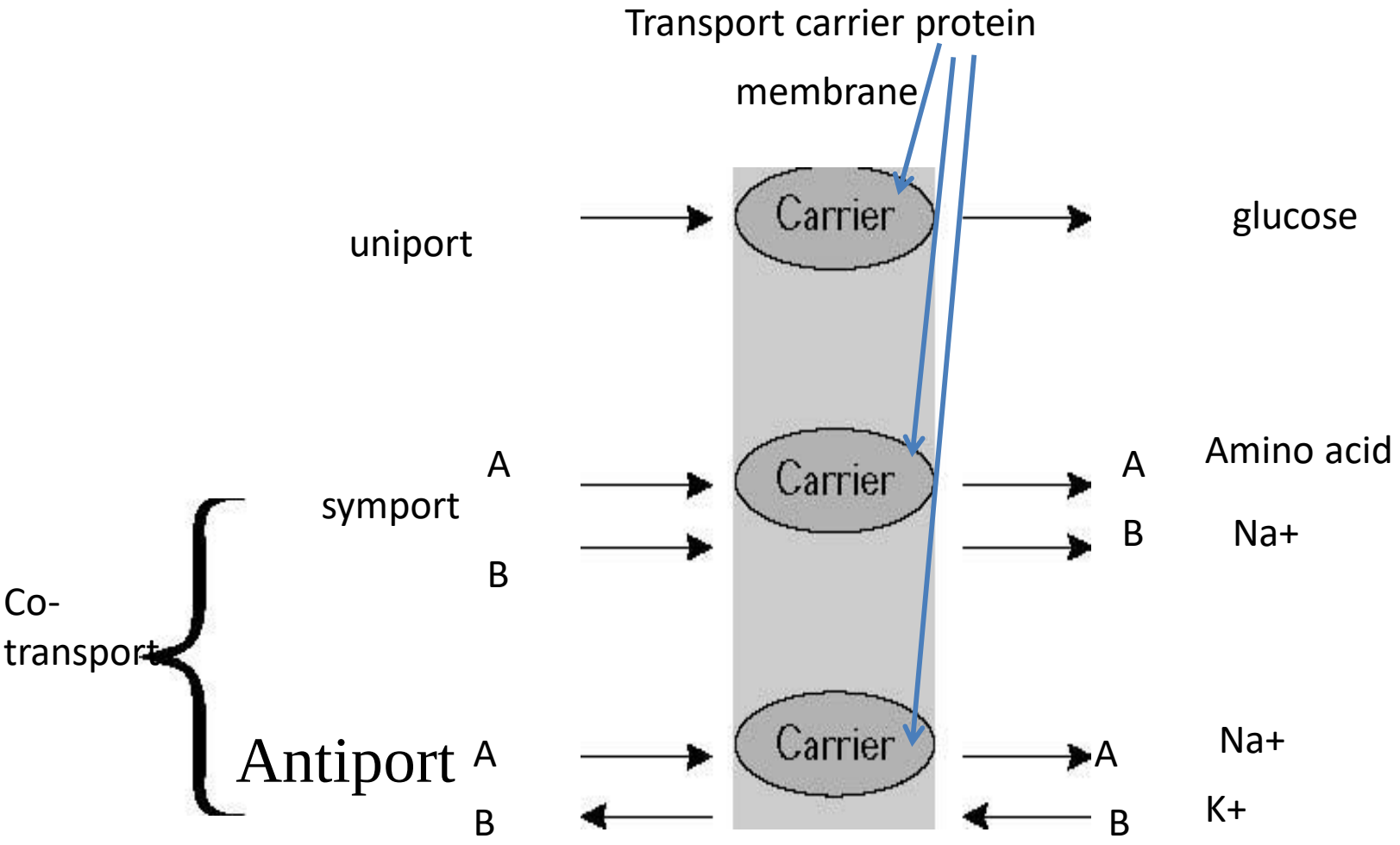
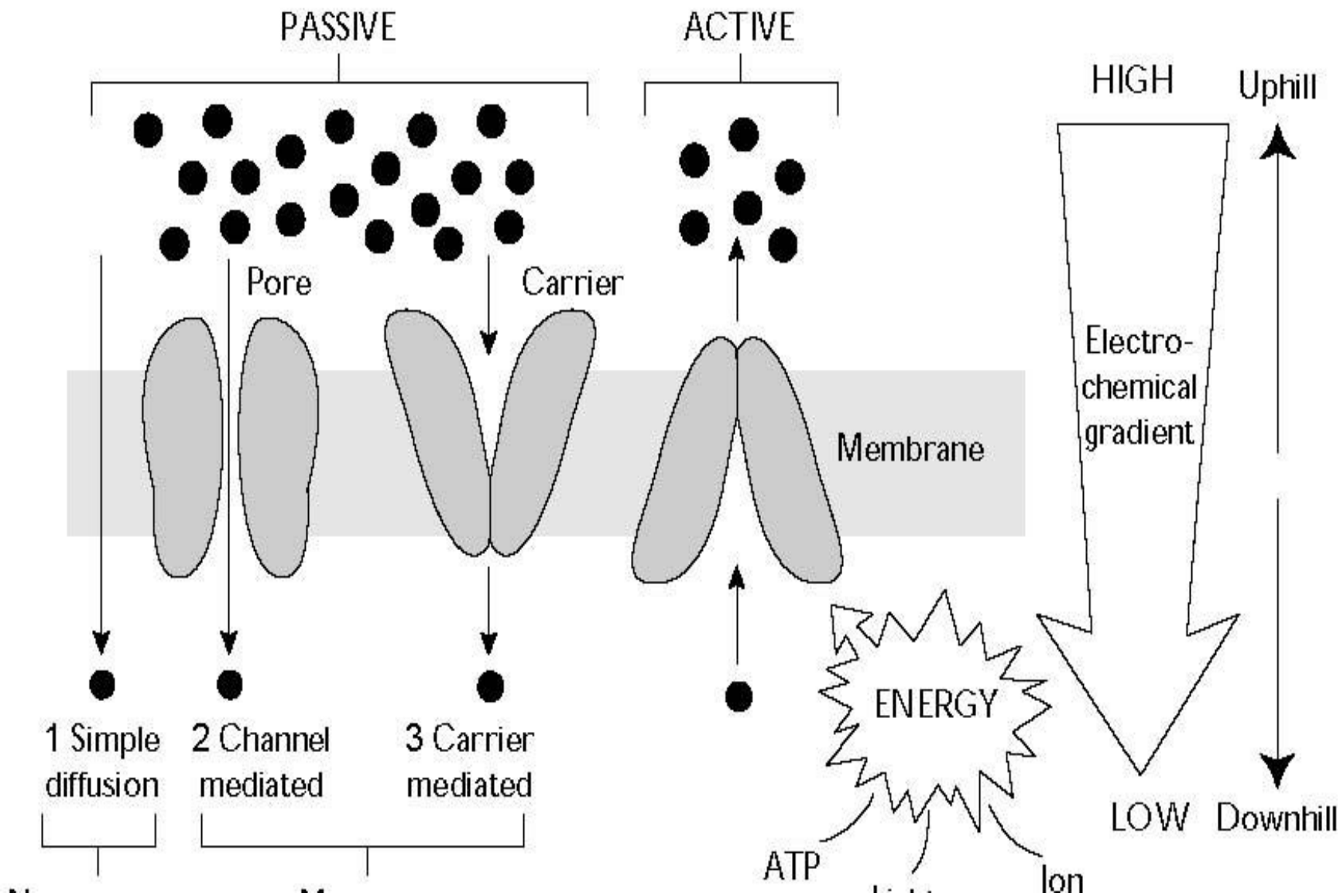
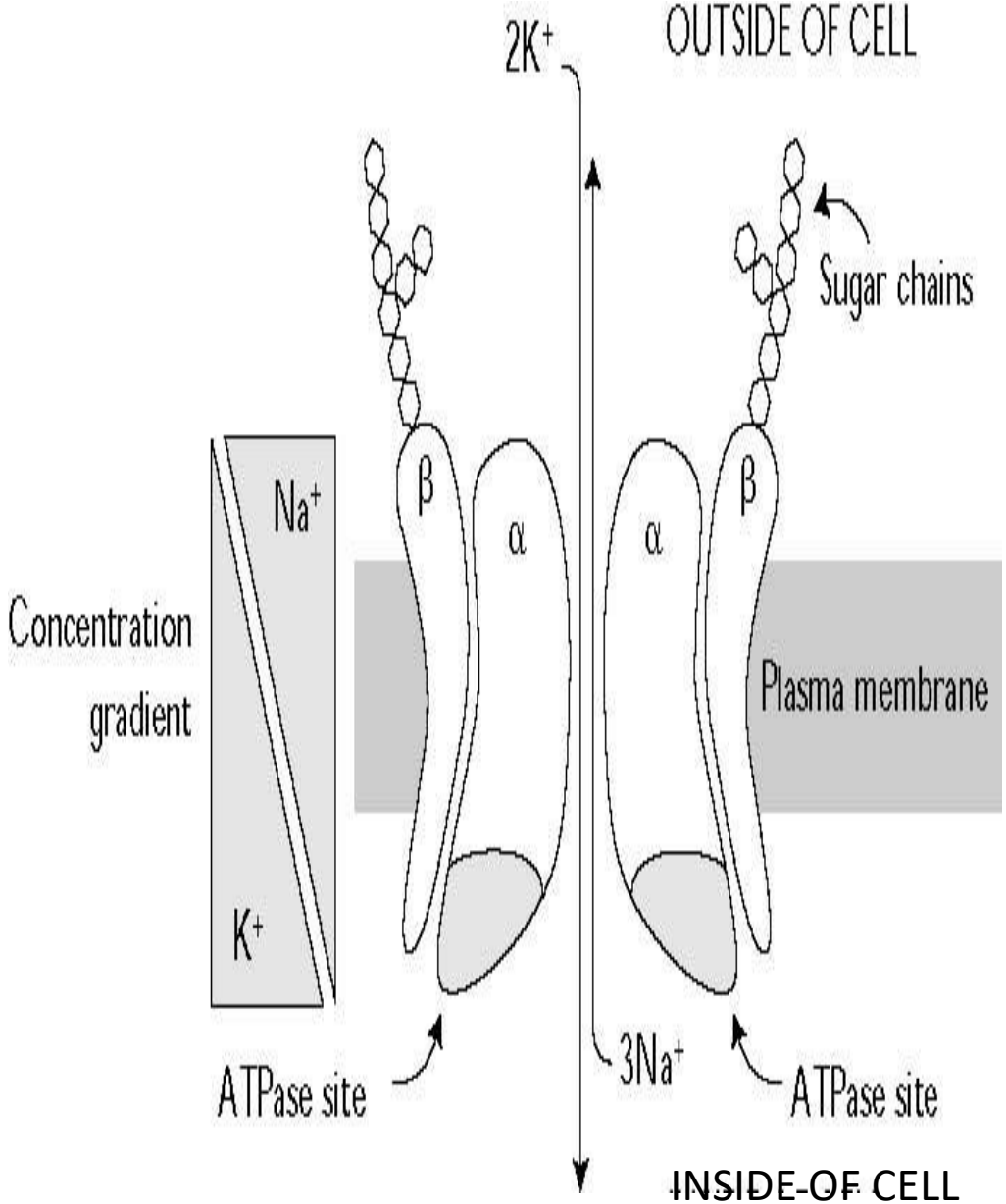

Transport carrier protein
membrane
uniport
Carrier
glucose
symport
A
B
Carrier
A
B
Amino acid
Na+
Co-
transport
Antiport
A
B
Carrier
A
B
Na+
K+

Figure 22. Passive and active transport.




2K+
OUTSIDE OF CELL
Sugar chains
β
α
α
β
Na+
Concentration
gradient
Plasma membrane
K+
ATPase site
3Na+
ATPase site
INSIDE OF CELL

Exocytosis

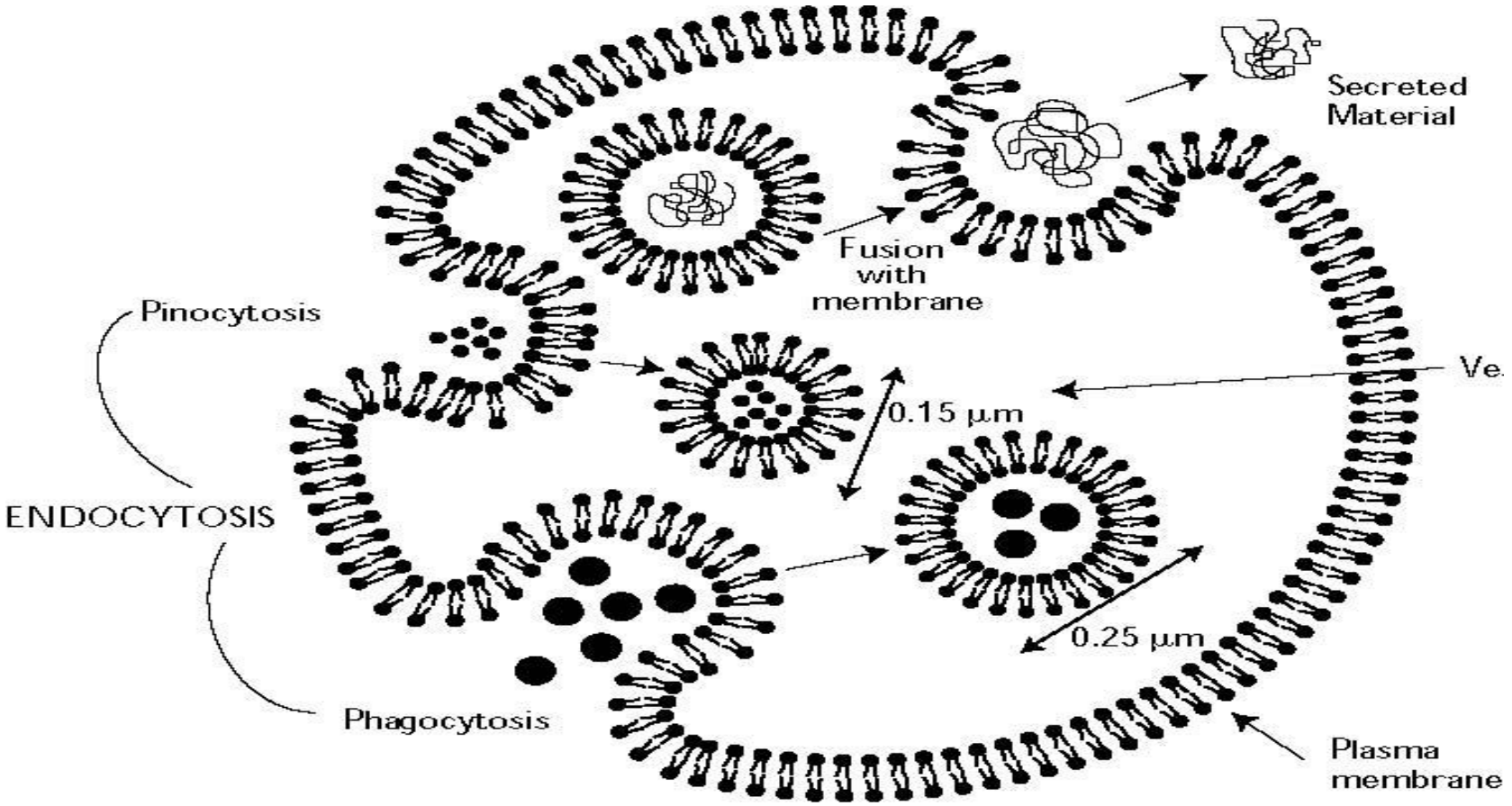


Figure 24. Exocytosis and endocytosis.

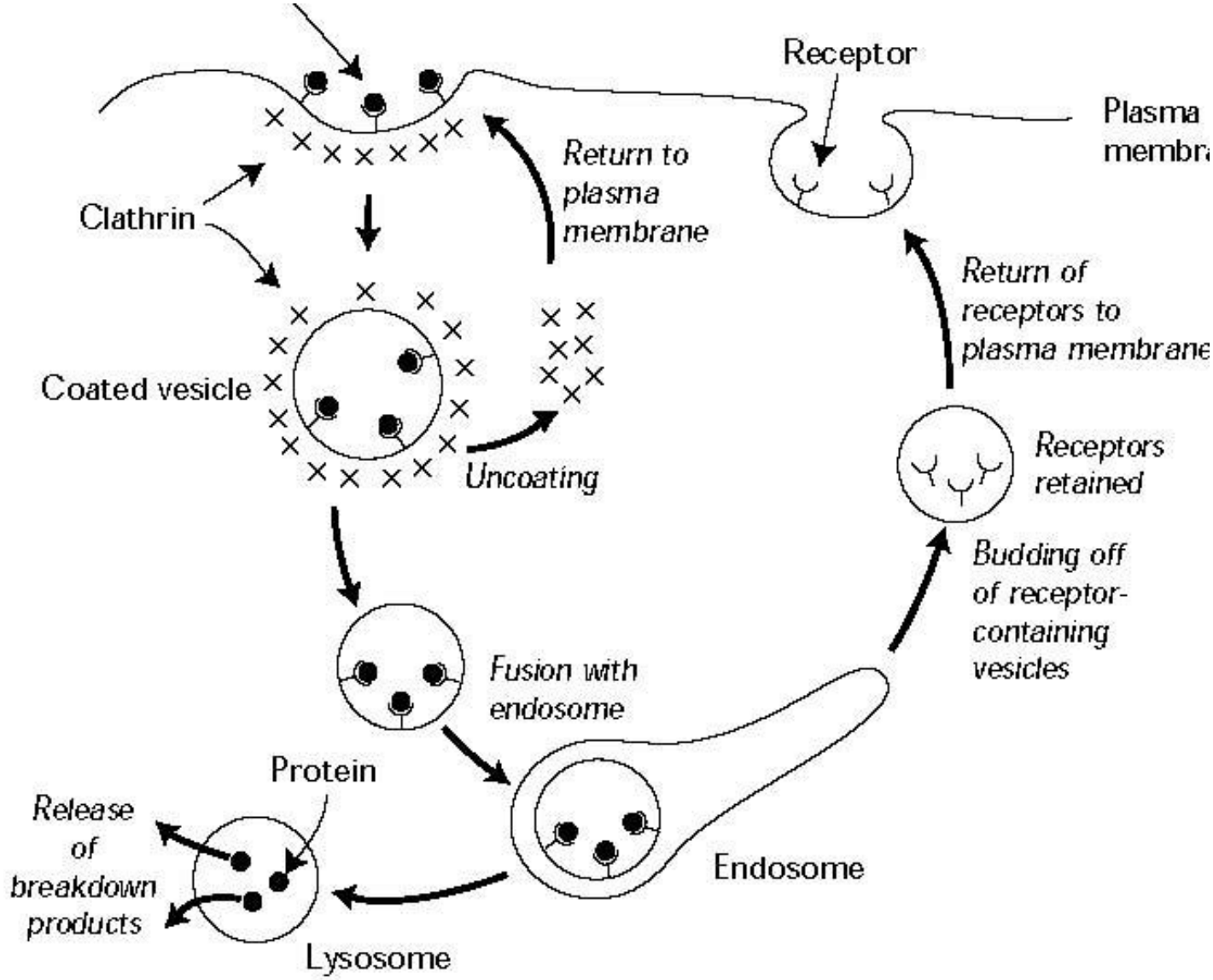


Figure 25. Receptor-mediated endocytosis.

- **Transport driven by ATP**
- All animal cells actively pump Na^+ ions out and pump K^+ ions in. These two transport processes are carried out by the enzyme Na^+/K^+exchanging ATPase, also called the **sodium pump**. The sodium pump is an integral prote in of the plasma membrane. It is a tetramer of two types .(sarcoplasmic reticulum)

- **Transport driven by light**
- Retinal is sensitive to light; the absorption of light will cause its straight hydrocarbon tail to bend (as a *trans* double bond is isomerized to *cis*). As a result, an attached proton-bearing group is moved into a position where it can pass on its proton to an acceptor group, which results ultimately in the transfer of a proton from inside the cell to outside. The retinal then returns to its straight-chain form, ready for the light-driven transport of another proton.

- Cells secrete macromolecules by **exocytosis** and take in macromolecules by **endocytosis**.
- Exocytosis may be **constitutive** or **regulated**. **Constitutive exocytosis** goes on all the time (it is part of the cell's constitution).
- **Endocytosis**
- There are two types of endocytosis, which differ in the size of the vesicles formed. In **pinocytosis** (or cell drinking), fluid or small particles are taken into small vesicles about 150 nm in diameter. In **phagocytosis** (or cell eating), large particles such as micro-organisms and cell debris are taken into large vesicles (or vacuoles) about 250 nm in diameter. Most cells carry out pinocytosis; only specialized phagocytic cells carry out phagocytosis.
- **Receptor-mediated endocytosis**

- Specific macromolecules are taken into cells by receptor-mediated endocytosis (Figure 25). The method is used, for example, on hormones bound to plasma membrane receptors. There, receptor–hormone complexes cluster in special regions of the plasma membrane called **coated pits**. These are dents in the membrane which have on their cytosolic side a coating of a protein called **clathrin**.

What happens at the synapse

- When the nerve impulse reaches the end of the axon, it finds a gap called a **synapse** between it and the next nerve cell (or the muscle cell in the case of a nerve that stimulates a muscle). Another property of membranes — their fluidity — is used to transmit the message across the synapse.
- When the nerve impulse reaches the presynaptic membrane, it brings about the fusion of hundreds of synaptic vesicles with the presynaptic membrane. Each vesicle contains neurotransmitter molecules which are released into the synaptic gap by exocytosis. The molecules diffuse across the 50 nm gap to the next membrane (in nerve or muscle), bind to receptors there and generate a new nerve impulse which travels on.