CELL MEMBRANE

Molecular organization and functional role

- **A** plasma membrane encloses every type of cell, both prokaryotic and eukaryotic cells.
- It physically separates the cytoplasm from the surrounding cellular environment.
- Plasma membrane is a ultrathin, elastic, living, dynamic and selective transport-barrier.
- It is a fluid-mosaic assembly of molecules of lipids (phospholipids and cholesterol), proteins
- and carbohydrates.
- Plasma membrane controls the entry of nutrientes and exit of waste products, and generates differences in ion concentration between the interior and exterior of the cell.
- It also acts as a sensor of external signals (for example, hormonal, immunological, etc.) and allows the cell to react or change in response to environmental signals.
- The cells of bacteria and plants have the plasma membrane between the cell wall and the
- cytoplasm.
- For cells without cell walls (*e.g.*, mycoplasma and animal cells), plasma membrane forms the cell surface..
- The plasma membrane is also called **cytoplasmic membrane**, c**ell membrane,** or **plasmalemma**

CHEMICAL COMPOSITION

- Chemically, plasma membrane are found to contain proteins, lipids and carbohydrates, but in different ratios
- . For example, in the plasma membrane of human red blood cells proteins represent 52 per cent, lipids 40 per cent and carbohydrates 8 per cent.

1.LIPIDS:

Four major classes of lipids are commonly present in the plasma membrane and other membranes : **phospholipids** (most abundant), **sphingolipids**, **glycolipids** and **sterols** (*e.g.*, **cholesterol**)

2. Proteins

- The amount and types of proteins in the membranes are highly variable :
- in the myelin membranes which serve mainly to insulate nerve cell axons, less than 25 per cent of the membrane mass is protein, whereas, in the membranes involved in energy transduction (such as internal membranes of mitochondria and chloroplasts), approximately 75 per cent is protein. Plasma membrane contains about 50 per cent protein.
- According to their position in the plasma membrane, the proteins fall into two main types :
- **integral** or **intrinsic proteins** and **peripheral** or **extrinsic proteins**, both of which may be either **ectoproteins**, lying or exposing to external or extracytoplasmic surface of the plasma membrane or **endoproteins**, lying or sticking out at the inner or cytoplasmic surface of the plasma membrane.
- The intrinsic proteins tend to associate firmly with the membrane, while the extrinsic proteins have a weaker association and are bound to lipids of membrane by electrostatic interaction.
- On the basis of their functions, proteins of plasma membrane can also be classified into three main types : structural proteins, enzymes and transport proteins (permeases or carriers).
- Some of them may act as **antigens**, **receptor molecules** (*e.g.*, insulinbinding sites of liver plasma membrane), **regulatory molecules** and so on.
- **Structural proteins** are extremely lipophilic and form themain bulk (*i.e.*, backbone) of the plasma membrane.
- **Enzymes** of plasma membrane are either **ectoenzymes** or **endoenzymes** and are of about 30 types.
- **Transport proteins** transport specific substances across the plasma membrane and other
- cellular membranes.

3. Carbohydrates

- Carbohydrates are present only in the plasma mambrane.
- They are present as short, unbranched or branched chains of sugars (**oligosaccharides**) attached either to exterior ectoproteins (forming **glycoproteins**) or to the polar ends of phospholipids at the external surface of the plasma membrane (forming **glycolipids**).
- No carbohydrate is located at the cytoplasmic or inner surface of the plasma membrane.
- All types of oligosaccharides of the plasma membrane are formed by various combinations
- of six principal sugars (all of which are glucose-derivatives) : **D-galactose**, **D-mannose**, **L-fucose**, **Nacetylneuraminic acid** (also called **sialic acid**), **N-acetyl-D-glucosamine** and **N-acetyl-D-galactosamine**.

STRUCTURE OF PLASMA MEMBRANE

1. Evolution of Fluid Mosaic Model of Membrane

- The existence of the plasma membrane of the cell was difficult to prove by direct examination before 1930's (when electron microscopy was invented) because of technological limitations.
- The membrane is beyond the resolution of the light microscope, rendering a morphological approach of its study quite unfeasible with this instrument.
- Thus, most of the experimental approaches have been provided by only indirect evidences of the existence of such a membrane around the cells.

Let us narrate in brief the saga of evolution of presently well accepted fluid-mosaic model of structure of the plasma membrane :

1. The plasmolysis of plant cells in hypertonic solutions suggests the existence of the plasma membrane in the plants.

2. The very fact that a cell, especially an animal cell which has no cell wall, can exist as a physically defined entity suggests that it must have some sort of boundary around it.

3. The presence of plasma membrane can be inferred because protoplasm leaks out of animal cells when cell surface is punctured.

4. In 1899 **Overton found that** because of an outer lipoid layer in which hydrophobic compounds were more soluble. He correctly speculated that this layer might contain cholesterol, lecithin and fatty oils.

5. **Hober** (1910) and **Fricke** (1925) found that the intact cell had low electrical conductivity, indicating the presence of a lipid layer around it.

6. If a lipid containing **hydrophilic groups** (such as the carboxyl groups of fatty acids or the phosphate groups of phospholipids) is dissolved in a highly volatile solvent (*e.g.*, benzene) and several drops of it are then carefully applied to the surface of the water, the lipid spreads out to form a thin, onemolecule- thick or **monomolecular film**.

In this film, it is found that the hydrophilic parts of each molecule project into the water surface and the hydrophobic parts are directed up, away from the water.

7. In 1917, **Langmuir** (Nobel Laureate of 1932 in chemistry) fabricated a **trough** or **film balance** (Fig. 5.1) for measuring the specific minimum surface area occupied by a monomolecular film of lipid and the force necessary to compress all the lipid molecules into this area. Langmuir trough consists of a shallow trough filled with water on which lipid substance can be spread to make a monomolecular film. A barrier can be pushed across the trough to compress the film.

8. In 1925, **Gorter** and **Grendel** discovered that the area covered by the lipid monomolecular layer film was twice than what was needed to cover the surface of the cells from which the lipid was extracted.

9. By studying the surface tension of cells (**Harvey** and **Cole**, 1931, **Danielle** and **Harvey**, 1935) suggested the presence of proteins in the plasma membrane, in addition to the lipids.

10. In 1935, **Danielli** and **Davson**, proposed a model, called **sandwich model**, for membrane structure in which a lipid bilayer was coated on its either side with hydrated proteins (globular proteins).

11. Using evidence from various electron micrographs, **Robertson** in 1960, proposed the **unit**

memb-rane hypothesis. This hypothesis states that all cellular membranes have an identical **trilaminar** structure (or dark-light- dark or railway track patteren)

12. **S.J.Singer** and **G.L.Nicolson** (1972) suggested the widely accepted **fluid mosaic model** of biological membranes.

- According to this model (Fig.), the plasma membrane contains a bimolecular lipid layer, both surfaces of which are interrupted by protein molecules.
- Proteins occur in the form of globular molecules and they are dotted about here and there in a mosaic pattern.
- Some proteins are attached at the polar surface of the lipid (*i.e*., the extrinsic proteins); while others (*i.e.*, integral proteins) either partially penetrate the bilayer or span the membrane entirely to stick out on both sides (called **transmembrane proteins**).
- Further, the peripheral proteins and those parts of the integral proteins that stick on the outer surface (*i.e*., ectoproteins) frequently contain chains of sugar or oligosaccharides (*i.e*., they are glycoproteins).
- Likewise, some lipids of outer surface are glycolipids.
- The fluid-mosaic membrane is thought to be a far less rigid than was originally supposed.
- In fact, experiments on its viscosity suggest that it is of a fluid consistency rather like the oil, and that there is a considerable sideways movement of the lipid and protein molecules within it.
- On account of its fluidity and the mosaic arrangement of protein molecules, this model of
- membrane structure is known as the "fluid mosaic model" (*i.e*., it describes both properties and organization of the membrane).
- The fluid mosaic model is found to be applied to all biological membranes in general, and it is seen as a
- dynamic, ever-changing structure.
- The proteins are present not to give it strength, but to serve as enzymes catalysing chemical reactions

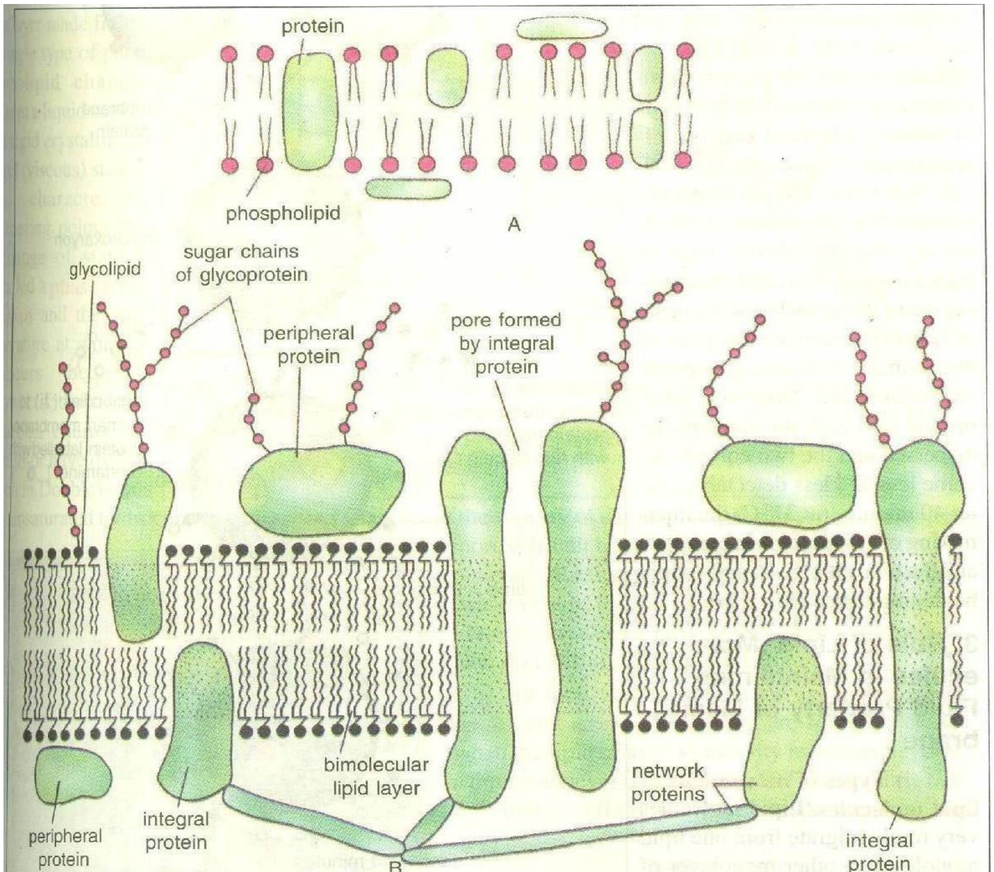


Fig. 5.5. Fluid mosaic model of the plasma membrane. A — Simplistic view; B— Complex view (after Berns, 1983; Sheeler and Bianchi, 1987).

FUNCTIONS OF PLASMA MEMBRANE

- The plasma membrane acts as a thin barrier which separates the intra-cellular fluid or the
- cytoplasm from the extra-cellular fluid in which the cell lives.
- In case of unicellular organisms (Protophyta and Protozoa) the extra-cellular fluid may be fresh or marine water, while in multicellular organisms the extra-cellular fluid may be blood, lymph or interstitial fluid.
- Though the plasma membrane is a limiting barrier around the cell but it performs various important physiological functions which are as follows :

1. Permeability. The plasma membrane is a thin, elastic membrane around the cell which usually allows the movement of small ions and molecules of various substances through it. This nature of plasma membrane is termed as permeability. According to permeability following types of the plasma membranes have been recognised :

(i) Impermeable plasma membranes. The plasma membrane of the unfertilized eggs of certain fishes allows nothing to pass through it except the gases. Such plasma membranes can be termed as impermeable plasma membranes.

(ii) Semi-permeable plasma membranes. The membranes which allow only water but no solute particle to pass through them are known as semi-permeable membranes. Such membranes have not so far been recognised in animal cells.

(iii) Selective permeable plasma membranes. The plasma membrane and other intra-cellular membrane are very selective in nature. Such membranes allow only certain selected ions and small molecules to pass through them.

(iv) Dialysing plasma membranes. The plasma membranes of certain cells have certain extraneous coats around them. The basement membranes of endothelial cells are the best examples of extraneous coats. This type of plasma membrane having extraneous coats around it, acts as a dialyzer. In these membranes the water molecules and crystalloids are forced through them by the hydrostatic pressure forces.

Mode of Transport Across Plasma Membrane

- The plasma membrane acts as a semipermeable barrier between the cell and the extracellular
- environment.
- This permeability must be highly **selective** if it is to ensure that essential molecules such
- as glucose, amino acids and lipids can readily enter the cell, that these molecules and metabolic
- intermediates remain in the cell, and that waste compounds leave the cell.
- In short, the **selective permeability** of the plasma membrane allows the cell to maintain a constant internal environment (**homeostasis**). In consequence, in all types of cells there exists a difference in ionic concentration with the extracellular medium.
- Similarly, the organelles within the cell often have a different internal environment from that of the surrounding cytosol and organelle membranes maintain this difference.
- For example, in lysosomes the concentration of protons (H+) is 100 to 1000 times that of the cytosol.
- This gradient is maintained solely by the lysosomal membrane.
- Transport across the membrane may be passive or active. It may occur via the phospholipid bilayer or by the help of specific integral membrane proteins, called **permeases** or **transport proteins.**

A. <u>Passive transport.</u>

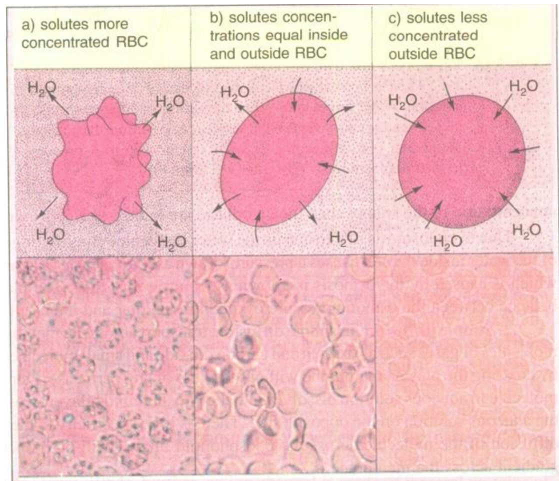
It is a type of **diffusion** in which an ion or molecule crossing a membrane moves down its electrochemical or concentration gradient.

No metabolic energy is consumed in passive transport.

Passive transport is of following three types :

1. **Osmosis.** The plasma membrane is permeable to water molecules.

- The to and fro movement of water molecules through the plasma membrane occurs due to the differences in the concentration of the solute on its either sides.
- The process by which the water molecules pass through a membrane from a region of higher water concentration to the region of lower water concentration is known as **osmosis** (Gr., *osmos*=pushing).
- The process in which the water molecules enter into the cell is known as **endosmosis,** while the reverse process which involves the exit of the water molecules from the cell is known as **exosmosis**.
- In plant cells due to excessive exosmosis the cytoplasm along with the plasma membrane shrinks away from the cell wall.
- This process is known as **plasmolysis** (Gr., *plasma*=molded, *lysis*=loosing) .
- A cell contains variety of solutes in it, for instance, the mammalian erythrocytes contain the ions of potassium (K+), calcium (Ca+), phosphate (PO4 ---), dissolved haemoglobin and many other substances.
- If the erythrocyte is placed in a 0.9% solution of sodium chloride (NaCl), then it neither shrinks nor swells.
- In such case, because the intra-cellular and extra-cellular fluids contain same concentration and no osmosis takes place.
- This type of extra-cellular solution or fluid is known as **isotonic solution** or **fluid.**



Osmosis and the RBC.

- If the concentration of NaCl solution is increased above 0.9% then the erythrocytes are shrinked due to excessive exosmosis.
- The solutions which have higher concentrations of solutes than the intracellular fluids are known as **hypertonic solutions.**
- Further, if the concentration of NaCl solution decreases below 0.9% the erythrocytes will swell up due to endosmosis.
- The extra-cellular solutions having less concentration of the solutes than the cytoplasm are known as **hypotonic solutions.**
- Due to endosmosis or exosmosis the water molecules come in or go out of the cell.
- The amount of the water inside the cell causes a pressure known as **hydrostatic pressure.**
- The hydrostatic pressure which is caused by the osmosis is known as **osmotic pressure.**
- The plasma membrane maintains a balance between the osmotic pressure of the intra-cellular and inter-cellular fluids.

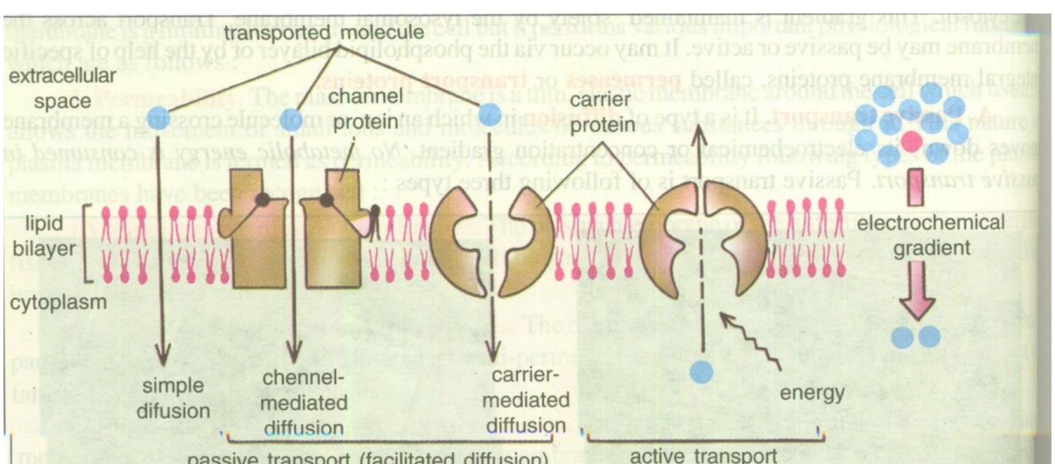


Fig. 5.12. Schematic diagram showing various types of transports across the membrane : simple diffusion passive transport (down an electrochemical gradient) and active transport (against an electrochemical gradient) (after Alberts, *et al.*, 1989).

2. **Simple diffusion.**

- In simple diffusion, transport across the membrane takes place unaided, *i.e.*, molecules of gases such as oxygen and carbon dioxide and small molecules (*e.g.*, ethanol) enter the cell by crossing the plasma membrane without the help of any permease.
- During simple diffusion, a small molecule in aqueous solution dissolves into the phospholipid bilayer, crosses it and then dissolves into the aqueous solution on the opposite side.
- There is little specificity to the process.
- The relative rate of diffusion of the molecule across the phospholipid bilayer will be proportional to the concentration gradient across the membrane.

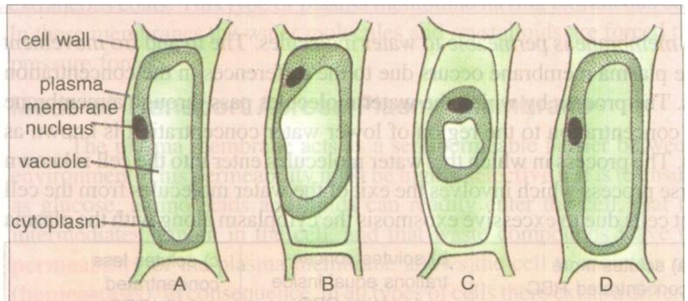


Fig. 5.13. Plasmolysis and deplasmolysis in plant cells. Plasmolysis occurs when a normal plant cell (A) is placed in a hypertonic solution. Water leaves the cell and the plasma membrane shrinks away from the cell wall (B,C). If solutes can penetrate the plasma membrane, the cell will eventually regain water—a process termed **deplasmolysis** (D) (after De Witt, 1977).

3. **Facilitated diffusion.**

- This is a special type of passive transport, in which ions or molecules cross the membrane rapidly because specific permeases in the membrane facilitate their crossing.
- Like the simple diffusion, facilitated diffusion does not require the metabolic energy and it occurs only in the direction of a concentration gradient.
- Facilitated diffusion is characterized by the following special features:
  1)the rate of transport of the molecule across the membrane is far greater than would be expected from a simple diffusion.
  (2) This process is specific; each facilitated diffusion protein (called **protein channel**) transports only a single species of ion or molecule.
  (3) There is a maximum rate of transport, *i.e.*, when the concentration gradient of molecules across the membrane is low, an increase in concentration gradient results in a corresponding increase in the rate of transport.
- Currently, it is believed that transport proteins form the **channels** through the membrane that permit certain ions or molecules to pass across the latter (see **Darnell** *et al*., 1986).

B. Active transport.

- Active transport uses specific transport proteins, called **pumps**, which use metabolic energy (ATP) to move ions or molecules against their concentration gradient.
- For example, in both vertebrates and invertebrates, the concentration of sodium ion is about 10 to 20 times higher in the blood than within the cell.
- The concentration of the potassium ion is the reverse, generally 20 to 40 times higher inside the cell. Such a low sodium concentration inside the cell is maintained by the sodium-potassium pump.
- There are different types of pumps for the different types of ions or molecules

C. Bulk transport by the plasma membrane.

Cells routinely import and export large molecules across the plasma membrane.

Macromolecules are secreted out from the cell by **exocytosis** and are ingested into the cell from outside through **phagocytosis** and **endocytosis.**

1. **Exocytosis.**

- It is also called **emeiocytosis** and **cell vomiting**.

- In all eukaryotic cells, **secretory vesicles** are continually carrying new plasma membrane and cellular secretions such as proteins, lipids and carbohydrates (*e.g.*, cellulose) from the Golgi apparatus to the plasma membrane or to cell exterior by the process of exocytosis.
- The proteins to be secreted are synthesized on the rough endoplasmic reticulum (RER).
- They pass into the lumen of the ER, glycosidated and are transported to the Golgi apparatus by ER-derived **transport vesicles**.
- In the Golgi apparatus the proteins are modified, concentrated, further glycosidated, sorted and finally packaged into vesicles that pinch off from trans Golgi tubules and migrate to plasma membrane to fuse with it and release the secretion to cell's exterior.

- In contrast, small molecules to be secreted (*e.g.*, histamine by the mast cells) are actively transported from the cytosol (where they are synthesized on the free ribosomes) into preformed vesicles, where they are complexed to specific macromolecules (*e.g.*, a network of proteoglycans, in case of histamine **Lawson** *et al.*, 1975), so that, they can be stored at high concentration without generating an excessive osmotic gradient.

2. **Phagocytosis.**

- Sometimes the large-sized solid food or foreign particles are taken in by the cell through the plasma membrane.
- The process of ingestion of large-sized solid substances (*e.g.*, bacteria and parts of broken cells) by the cell is known as **phagocytosis** (Gr., *phagein*=to eat, *kytos*=cell or hollow vessel).

Occurrence of phagocytosis. The process of phagocytosis occurs in most protozoans and certain cells of multicellular organisms.

3. Endocytosis. In endocytosis, small regions of the plasma membrane fold inwards or **invaginate**, until it has formed new intracellular membrane limited vesicles.

In eukaryotes, the following two types of endocytosis can occur : pinocytosis and receptor-mediated endocytosis.

(i) Pinocytosis. Pinocytosis (Gr., *pinein* = to drink; 'cell drinkng') is the non-specific uptake of small droplets of extracellular fluid by **endocytic vesicles** or **pinosomes**, having diameter of about 0.1 μm to 0.2 μm.

(ii) Receptor-mediated endocytosis.

- In this type of endocytosis, a specific receptor on the surface of the plasma membrane "recognizes" an extracellular macromolecule and binds with it.
- The substance bound with the receptor is called the **ligand**. Examples of ligands may include viruses, small proteins (*e.g.*, insulin, vitellogenin, immunoglobin, transferrin, etc.), vitamin B12, cholesterol containing LDL or low density lipoprotein, oligosaccharide, etc.

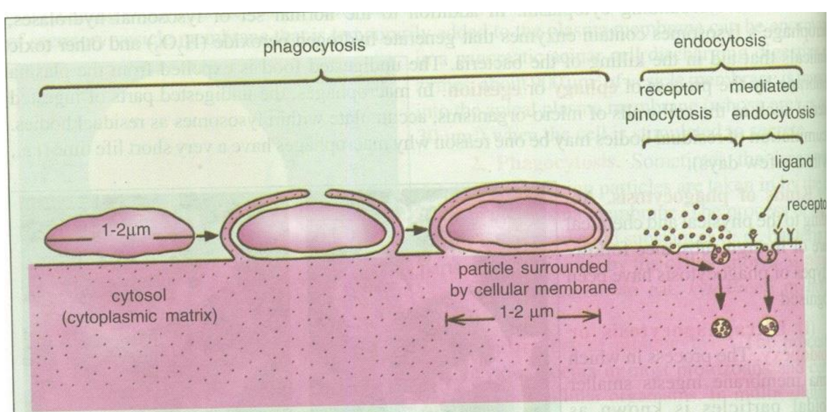


Fig. 5.18. The process of phagocytosis and endocytosis (after Darnell *et al.*, 1986).