

C. Membrane transport : passive transport, active transport and vesicular transport

I. Passive and active transport

I.1. Membrane transport

Membrane transport is the passage of a molecule, ion, or particle through the lipid bilayer of the plasma membrane or organelles. As a result, the cell membrane acts as a highly selective barrier. This selectivity allows:

- Essential molecules (amino acids, glucose, etc.) to pass into the cell.
- Intermediate metabolites to remain inside the cell.
- Metabolic waste products to leave the cell.

These exchanges enable the cell to maintain solute concentrations in the cytoplasm that differ from those in the extracellular environment.

I.2. Definition of permeability

Permeability is the property of the cell surface to directly absorb substances from the extracellular environment and eliminate others. It can take two forms.

- Passive permeability or passive transport: This depends exclusively on physicochemical laws and does not require active intervention by the cell. There are two types: simple diffusion and facilitated diffusion.
- Active permeability or active transport: this involves the participation of the cell through the supply of metabolic energy, a mechanism that allows transport against the concentration gradient.

I.2.1. Passive permeability

I.2.1.1. Simple diffusion

Occurs through the lipid portion of the plasma membrane; no involvement of membrane proteins. It is a purely physicochemical phenomenon. This diffusion occurs in the direction of the concentration gradient. It involves fat-soluble molecules. The smaller the molecule, the more easily it passes through (steroids, O₂, CO, etc.).

- **Concentration gradient:** the net flow of a substance occurs from the compartment with high concentration to the compartment with low concentration. Fick's law can be used to calculate the flow.
- **Fick's law:** consider a molecule that diffuses through a membrane with surface area A and thickness X, separating two solutions with concentrations C1 and C2 (C1 > C2).

Fick's First Law

Movement of particles (diffusion flux) from high to low concentration is directly proportional to the particle's concentration gradient

$$J \propto \frac{d\phi}{dx} \quad \text{or} \quad J = -D \frac{d\phi}{dx}$$

J = diffusion flux

D = diffusion coefficient or diffusivity

$d\phi$ = change in concentration of the particle

dx = change in position

$\frac{d\phi}{dx}$ = concentration gradient of the particle

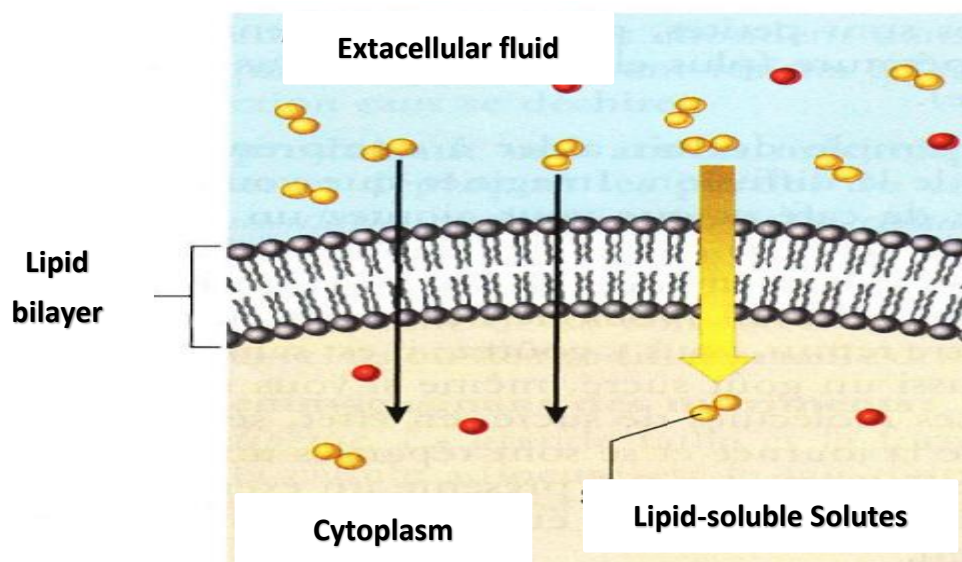
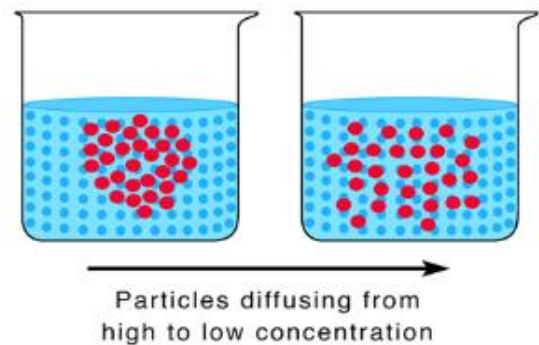


Figure II.10. Simple diffusion through the plasma membrane [12].

I.2.1.2. Facilitated diffusion

This concerns the permeability of various polar molecules (sugars, ions, amino acids) that pass through the plasma membrane under the effect of the concentration gradient. It does not require energy, as it follows the concentration gradient. Facilitated diffusion is faster and more efficient than simple diffusion. It necessarily involves transmembrane proteins (transporters), therefore:

- Specificity of transport proteins/substrate;
- Possibility of competitive inhibition;
- Possibility of chemical inactivation;
- Saturable phenomenon.

Facilitated diffusion via permeases or transporters

These are transmembrane proteins that specifically bind to the molecule to be transported, “permease,” which changes conformation and releases the molecule to be transported to the other side of the membrane

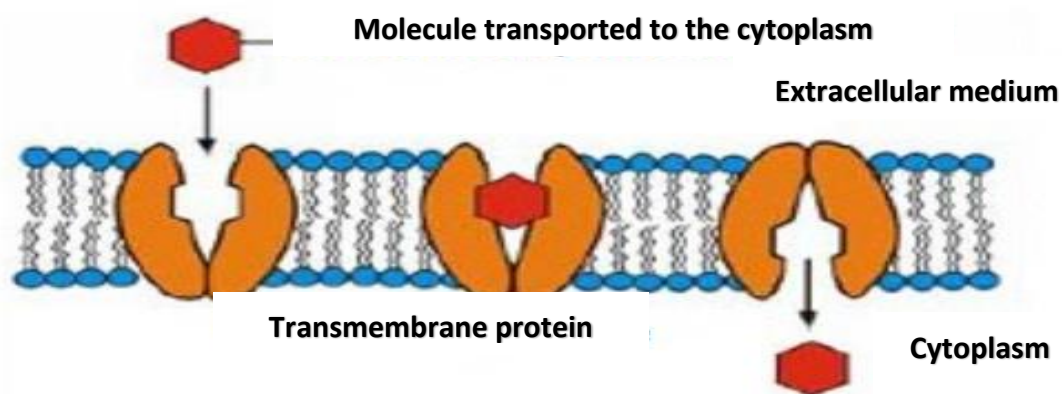


Figure II.11. Diffusion through permeases [13].

In addition, the transporter or transmembrane channel can ensure passage:

Uniport: transports only one molecule in a given direction.

Symport: transports two molecules simultaneously in the same direction (cotransport).

Antiport: transports two molecules simultaneously in opposite directions (cotransport).

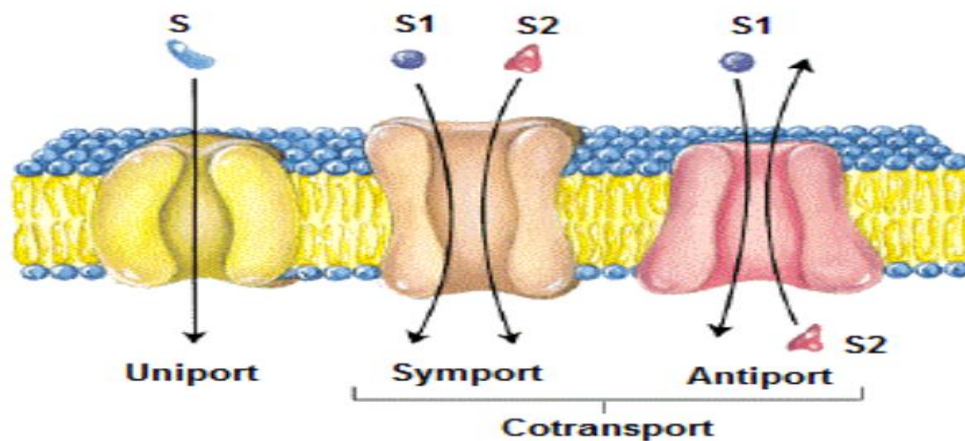


Figure II. 12. Types of transporters [13].

Facilitated diffusion through protein channels with controlled opening

There are protein channels that are normally closed. They only open temporarily under specific conditions. When they open, they allow a particular ion or group of ions to pass through (specificity). There are two types :

- Ion channels with ligand-gated opening that only allow ions to pass in the direction of the concentration gradient after the ligand has bound.
- Ion channels with voltage-gated opening that only allow ions to pass in the direction of the concentration gradient after a small change in the membrane potential.

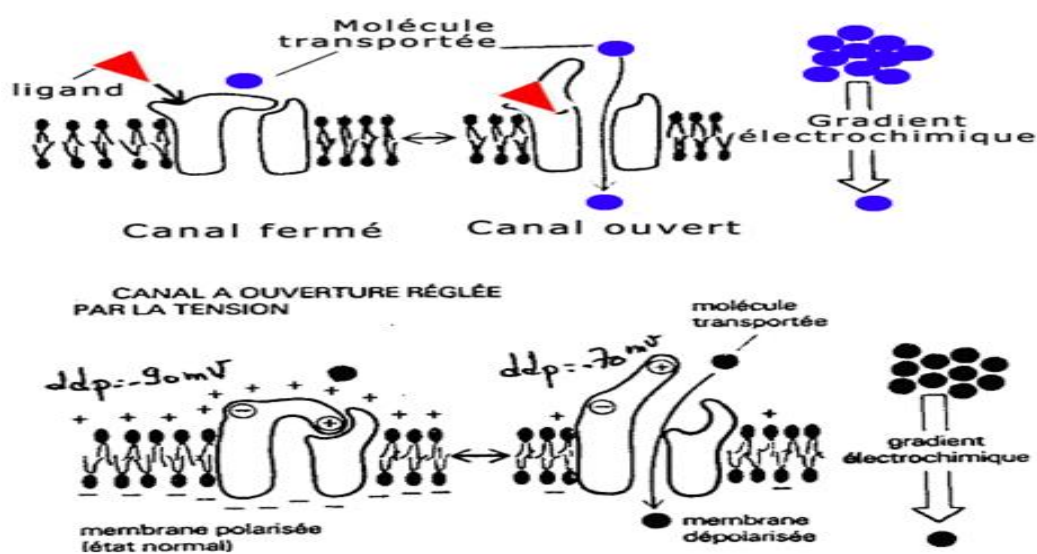


Figure II. 13. Facilitated diffusion through protein channels with controlled opening [14].

I.2.2. Special case of water: the phenomenon of osmosis

During osmosis, water selectively passes through a semi-permeable membrane (plasma membrane) from the hypotonic medium (the least concentrated or most diluted) to the hypertonic medium (the most concentrated and therefore least diluted). In effect, water works to dilute the hypertonic environment until equilibrium is reached on both sides of the membrane. Osmosis requires no energy and involves only the movement of water. There are two types of diffusion: through the lipid bilayer or through water channels (aquaporin proteins).

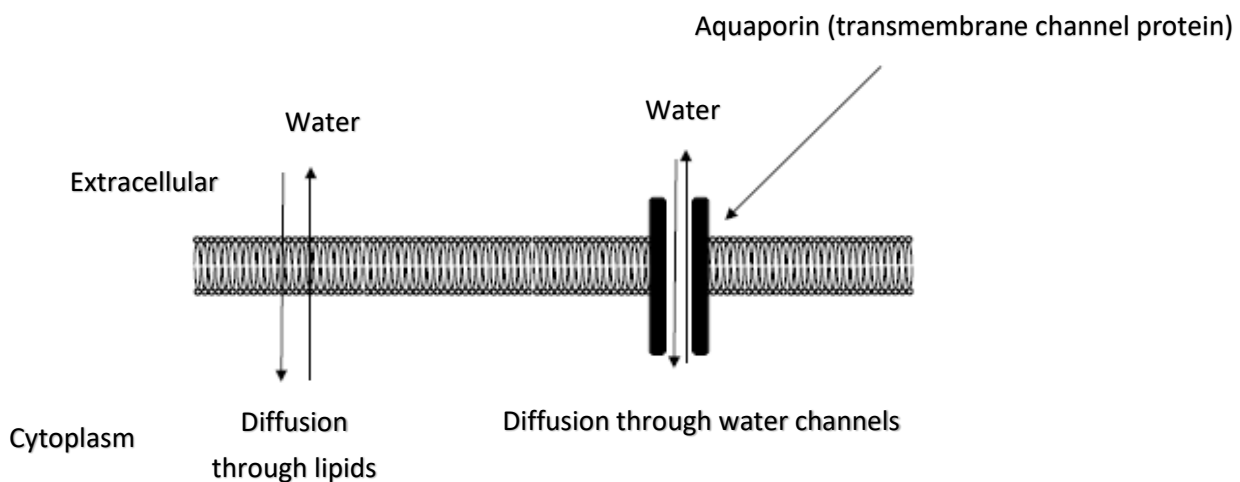


Figure II. 14. Water move across plasma membrane [15].

I.2.3. Active permeability or active transport

This type of transport allows movement against the concentration gradient. It uses transporters whose change in configuration, allowing the substance to pass through, requires energy, mainly provided by the degradation of ATP. The presence of protein means that this phenomenon is saturable.

There are many examples in eukaryotes: the Na^+/K^+ pump, which is involved in the generation of nerve impulses, among other things; the Ca^{++} pump, which enables muscle contraction; and the H^+ pump, which plays an important role in the recovery of energy from respiration.

The Na^+/K^+ ATPase antiport pump

It consists of two subunits:

- A non-glycosylated α subunit of 110 kDa that has ATPase enzymatic activity.
- A glycosylated β subunit of 55 kDa.

This pump brings two K^+ ions into the cell and pumps out three Na^+ ions.

The enzyme therefore has two different conformations:

E1: high affinity for Na^+ oriented towards the inside of the cell.

E2: has a high-affinity binding site for K^+ on the extracellular side.

The different stages of this type of transport:

- E1 binds 3 Na^+ and one ATP to form a ternary complex;
- The complex reacts, producing an energy-rich aspartyl~P intermediate;
- The intermediate takes on a low-energy E2-P conformation and releases Na^+ outside the cell;
- E2-P binds 2 K^+ .
- The phosphate group is hydrolyzed;
- E2 reverts to E1 after releasing K^+ into the cell.

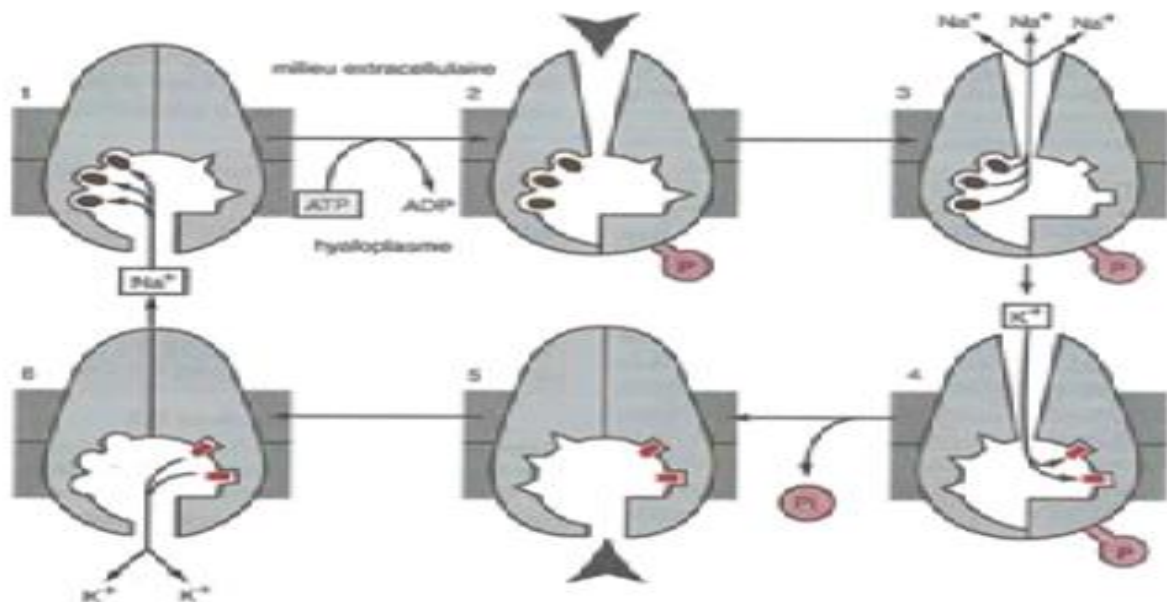


Figure II. 15. The Na^+/K^+ ATPase antiport pump [14].

• **Effect of ouabain**

Ouabain is an alkaloid with the following properties:

- Ouabain inhibits the Na^+/K^+ pump when applied to the outside of the cell.
- Ouabain competes with K^+ .
- Ouabain inhibits an enzyme responsible for the degradation of ATP (ATPase).

II. The transport of macromolecules (vesicular transport)

Cells have also developed methods for transporting material such as proteins or phospholipids that are too large to pass through the membrane via channels or pumps. This transport can occur either between the external environment and the cell, or between different organelles within the same cell.

II.1. Endocytosis

It allows large compounds to enter the cell. This involves invagination of the membrane and pinching, leading to the formation of an endocytosis vesicle. Different types of endocytosis can be distinguished depending on the size of the vesicle formed.

- **Pinocytosis:** the vesicles formed are small (between 50 and 120 nm in diameter). This is a non-specific phenomenon. The cell engulfs part of the extracellular fluid.
- **Receptor-mediated endocytosis:** this is a specific type of endocytosis, in which the particles to be ingested are recognized by membrane receptors. Example: LDL (a form of blood cholesterol). Plasma membrane receptors recognize the Apo-B protein on LDL. Apo-B binds to the receptor at a clathrin-coated pit, allowing the vesicle to form. These vesicles have a diameter of between 100 and 150 nm. Once the vesicle has formed, the clathrin detaches and is recycled back to the membrane. The smooth vesicle fuses with a lysosome.
- **Phagocytosis:** this involves large particles (greater than 1 μ m). It is an immune defense mechanism. Macrophages phagocytose cellular debris and pathogenic microorganisms.

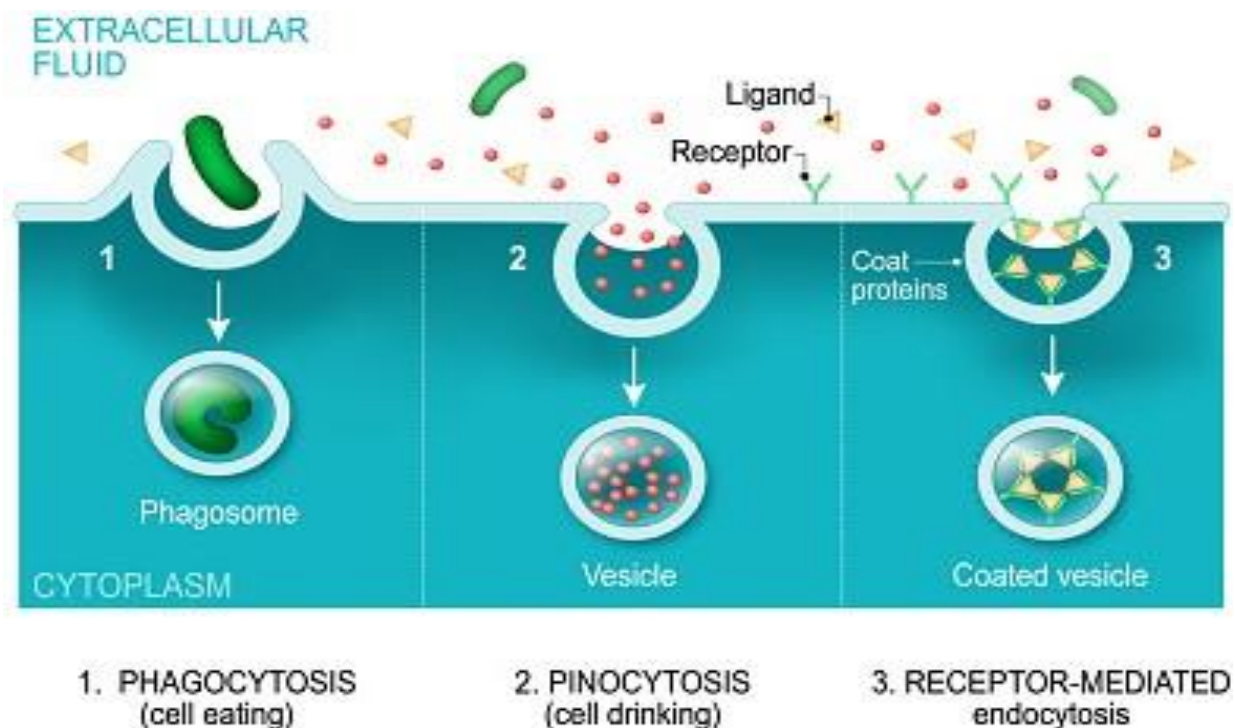


Figure II. 16. The different pathways of endocytosis [16].

II.2. Exocytosis

Exocytosis is a mechanism that allows certain substances to pass from inside the cell to the extracellular environment. Before being expelled, these substances are enclosed in a membrane-bound

sac called a vesicle. The next step is the migration of this vesicle towards the PM and its fusion with it. Finally, the contents of the vesicle are released into the extracellular environment.

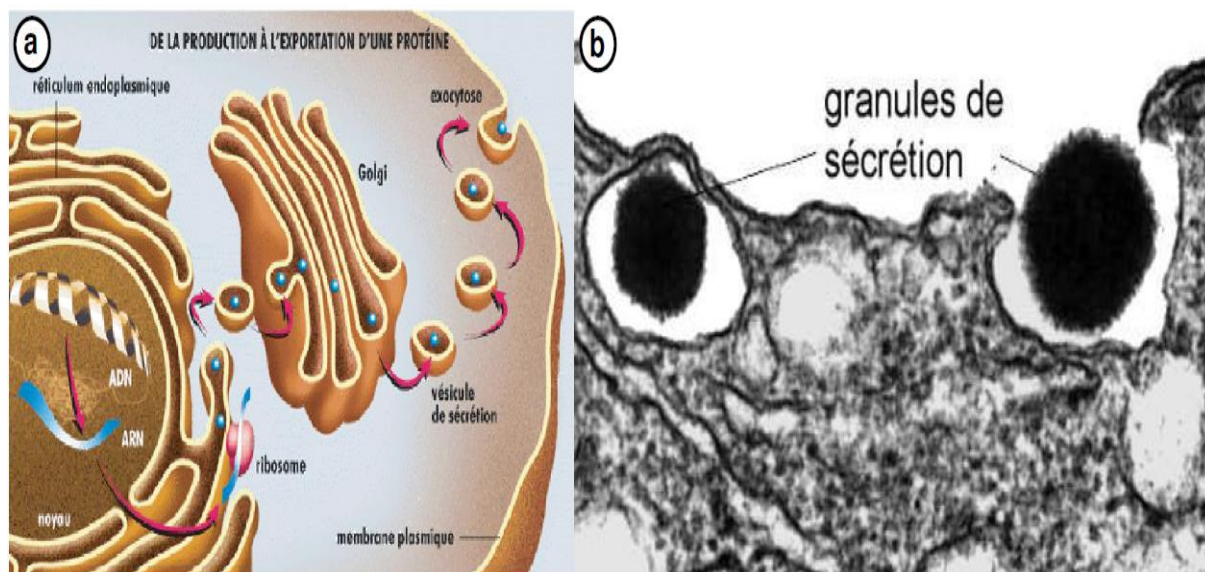


Figure II. 17. Main pathways of intracellular traffic. (a) Secretion and exocytosis pathways involve the endoplasmic reticulum and Golgi apparatus. (b) Exocytosis of secretory vacuoles observed under electron microscopy[17].