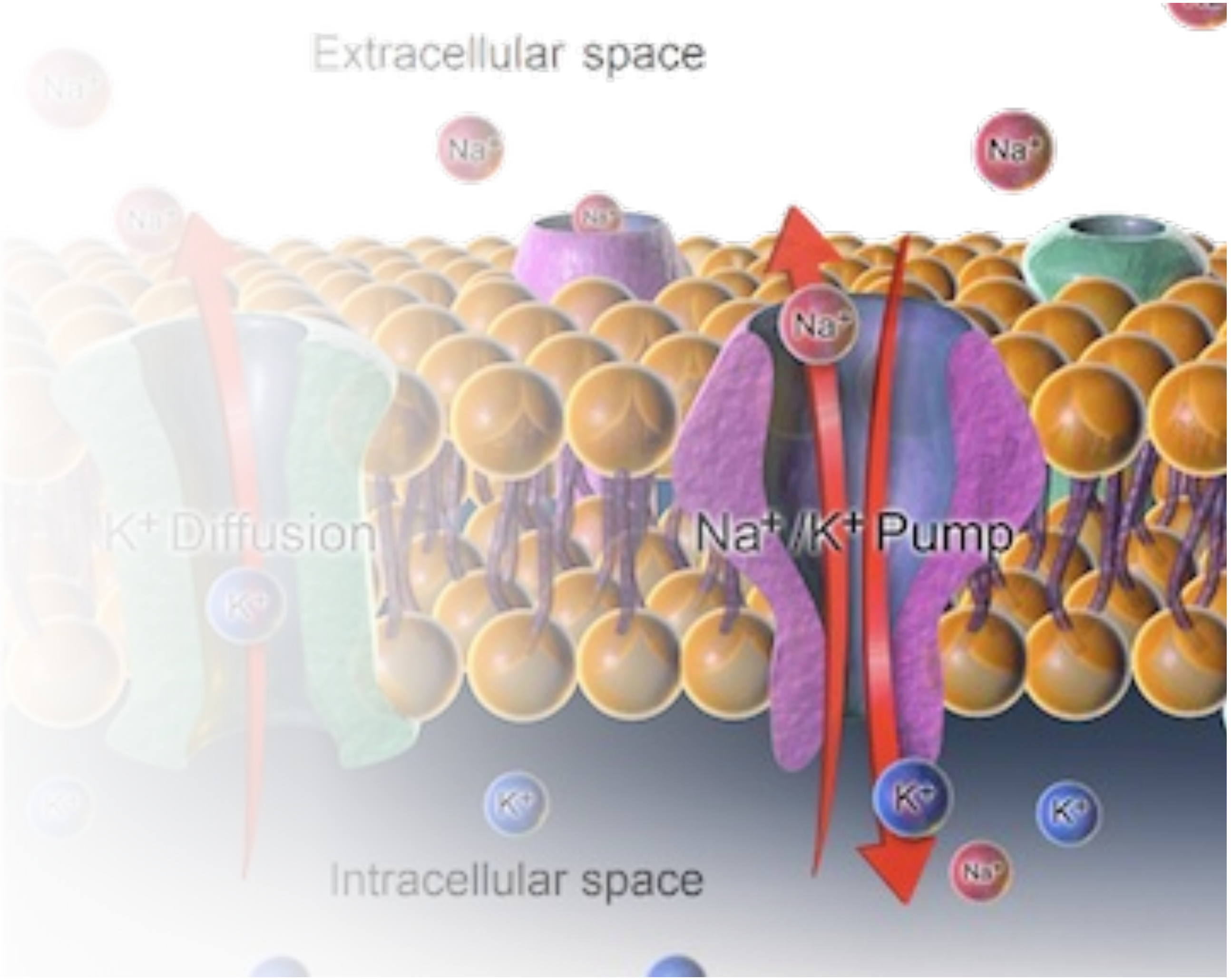
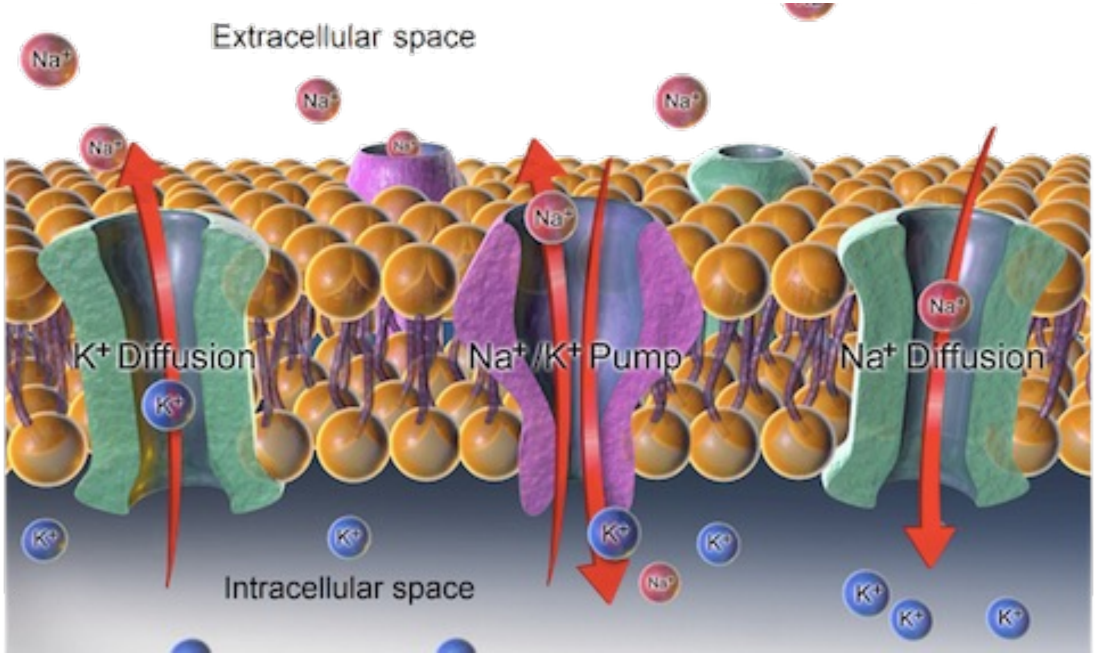
The transport across the plasma membrane



The transport across membranes

Cells must face two main issues in order to regulate transport of solutes (molecules and ions) across membrane.



1. Permeability: the lipid bilayer is semi-permeable (only hydrophobic molecules can pass through)
2. Direction: the direction of movements is driven by two main natural forces (or gradients): chemical and electrical gradients.

The electro-chemical gradient is the sum of two components:

1. **The chemical gradient**: The difference in magnitude of molecules concentration from one point to the other is called chemical gradient.

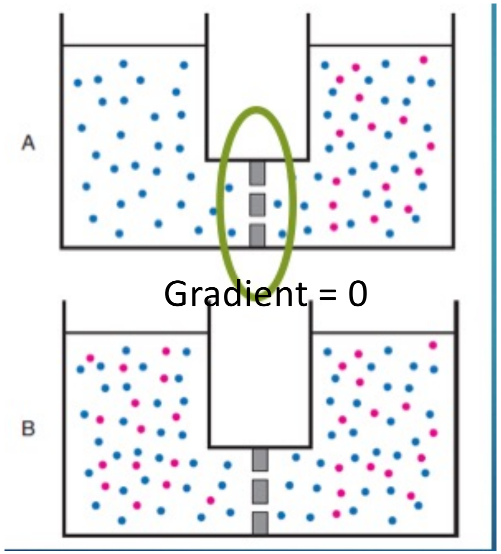
Molecules move generally from a region of higher [concentration]() to a region of lower concentration. This movement is called diffusion

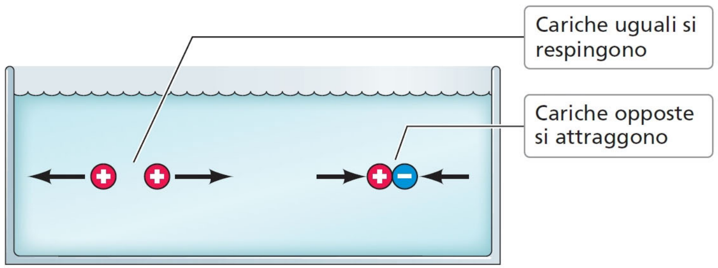
2. Electrical gradient):

The difference in magnitude of electric charge from one point to the other is called electrical gradient.

Charged (or polar) molecules move toward molecules with opposite charge and viceversa.

Gradient >0





(C) Forze elettrostatiche

What strategies does the cell adopt to transport molecules across the membrane?

Cells need to transport molecules, often membrane-impermeable, also in opposite direction with respect to the directions the electrochemical gradient would naturally move them.

Transport across membrane

3 main strategies

Passive Transport

- In favor of the electrochemical gradient.
- No need for energy

Active transport

- Against the electrochemical gradient.
- Energy required

Vescicular transport

- Highly regulated mechanism
- Gradient-independent
- A lot of energy required

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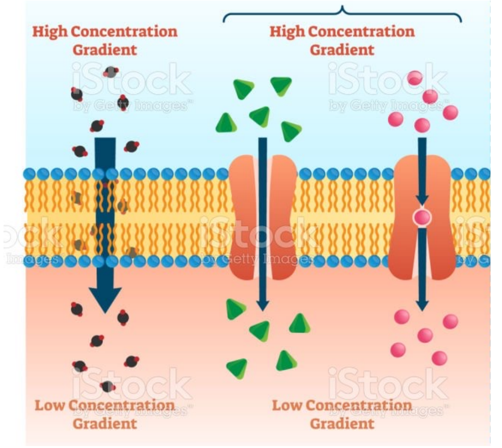
Transport across membrane

3 main strategies

Passive Transport

DIFFUSION FACILITATED DIFFUSION



Active transport

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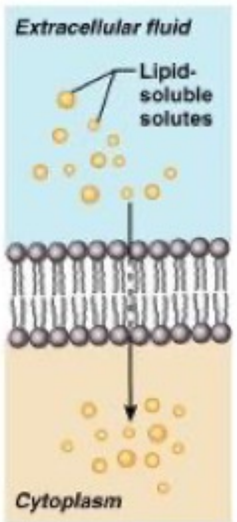
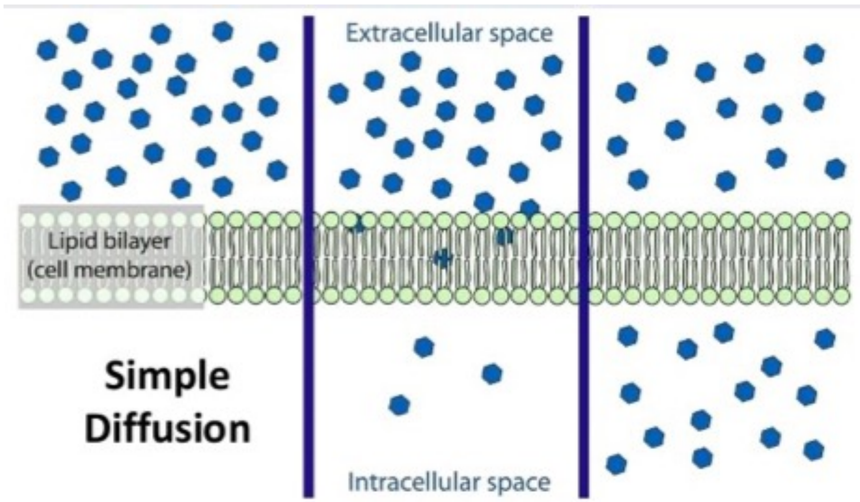
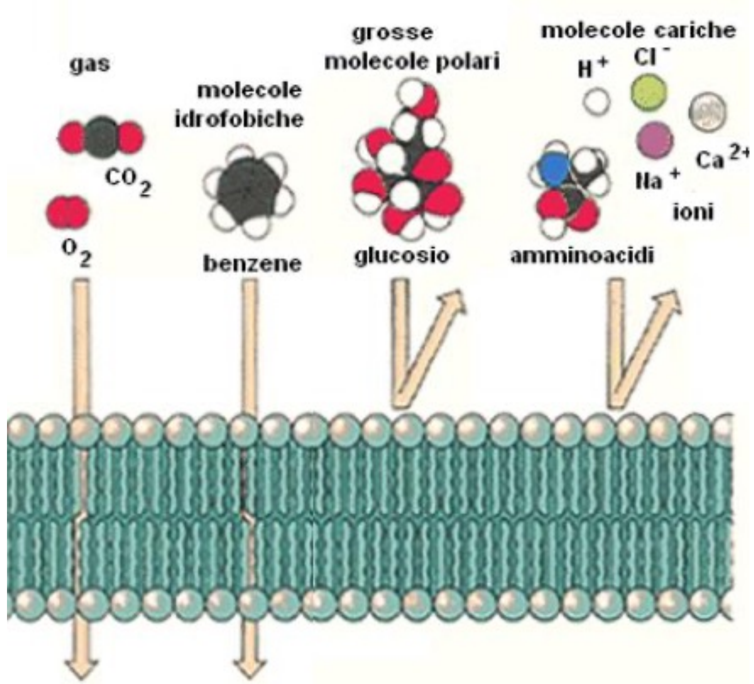


(a) Simple diffusion directly through the phospholipid bilayer





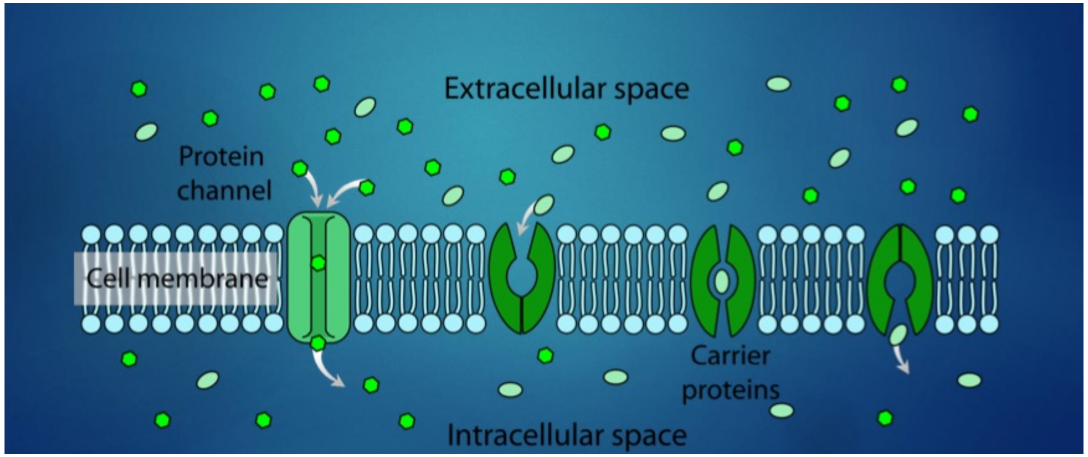
Simple diffusion:

for permeable molecules

- Modality of transport of exclusively permeable molecules. Quite rare in nature.
- Molecules that are cell membrane permeable are non-polar, of small dimension, like gases
- The speed rate depends on concentration gradient and degree of solubility

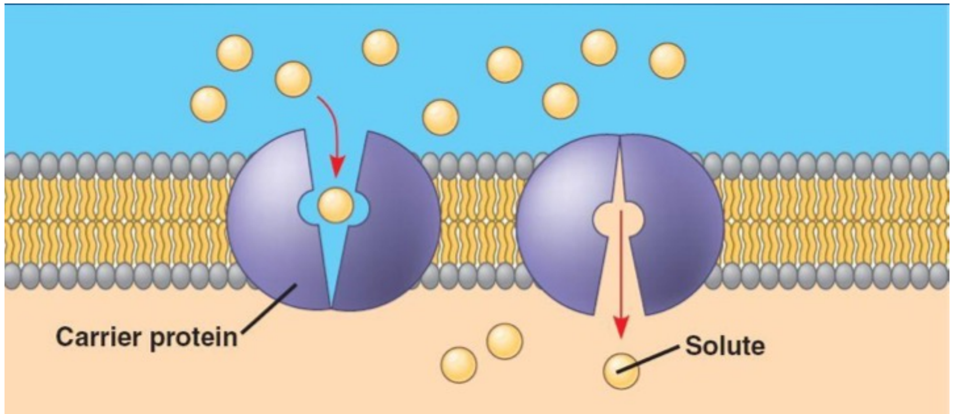
Facilitated diffusion

- Solutes are membrane non-permeable (usually hydrophilic, or big molecules), including sugars, amino acids, nucleosides, ions
- Most common modality for solute transfer
- Requires the presence of specific transmembrane proteins: **carrier protein** (or transporters) or **protein channels**



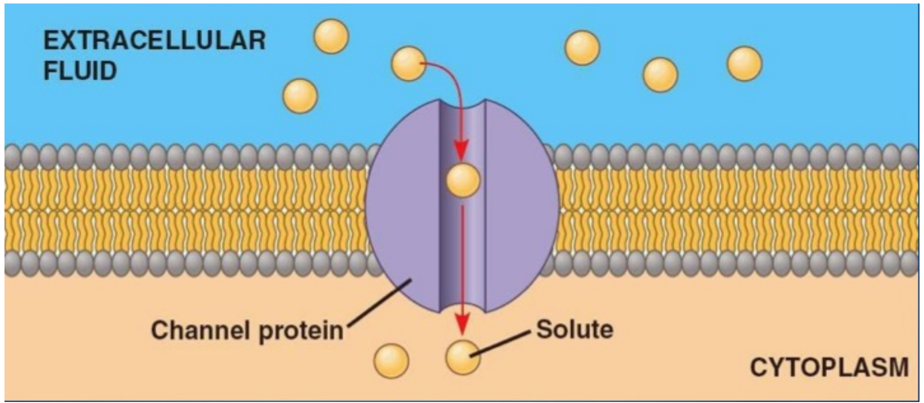
Facilitated diffusion

Carrier proteins



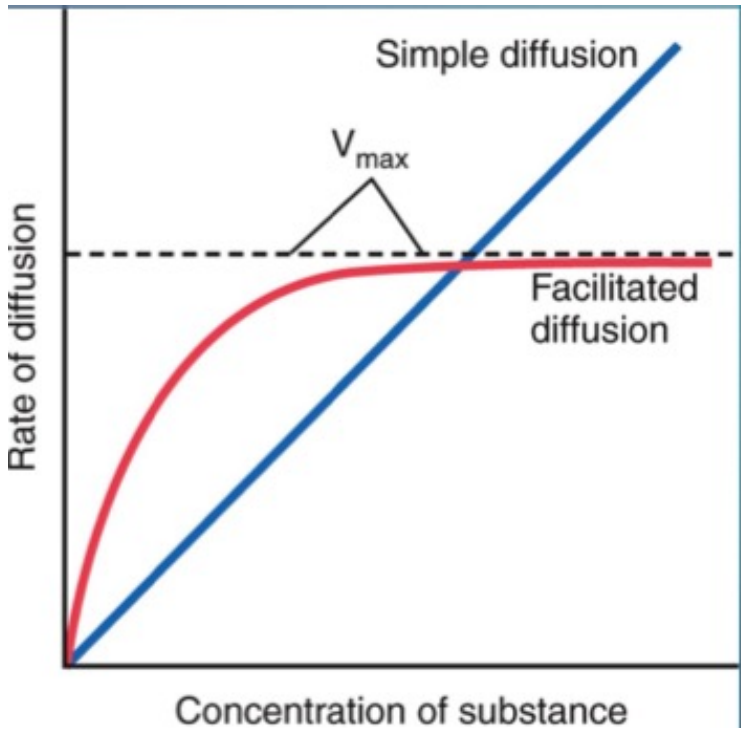
- The binding of the solute leads to a conformation change in the protein, that allows the release of the solute on opposite side
- Regulated by the solutes
- High selectivity (for specific solutes)

Channel proteins



- Typically for ions (**Ion channels**).
- Include a hydrophilic pore through which the ion passes
- Opening/closing highly regulated with a variety of mechanisms
- Weak selectivity

Saturability characterizes the facilitated diffusion



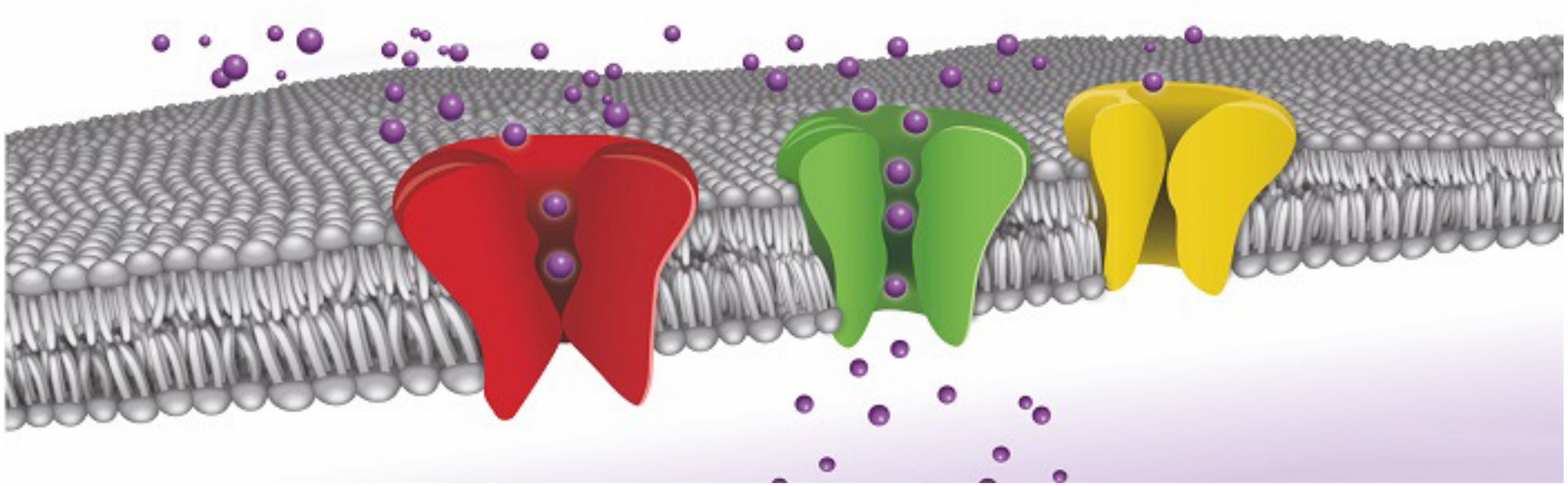
While in simple diffusion the speed (for a given substance) is directly proportional to the concentration gradient, in facilitated diffusion after initial increase the rate of diffusion reaches a plateau.

SIMPLE DIFFUSION

FACILITATED DIFFUSION

Ion channels:
the most frequent channel proteins in the brain, the mediators of neuronal transmission

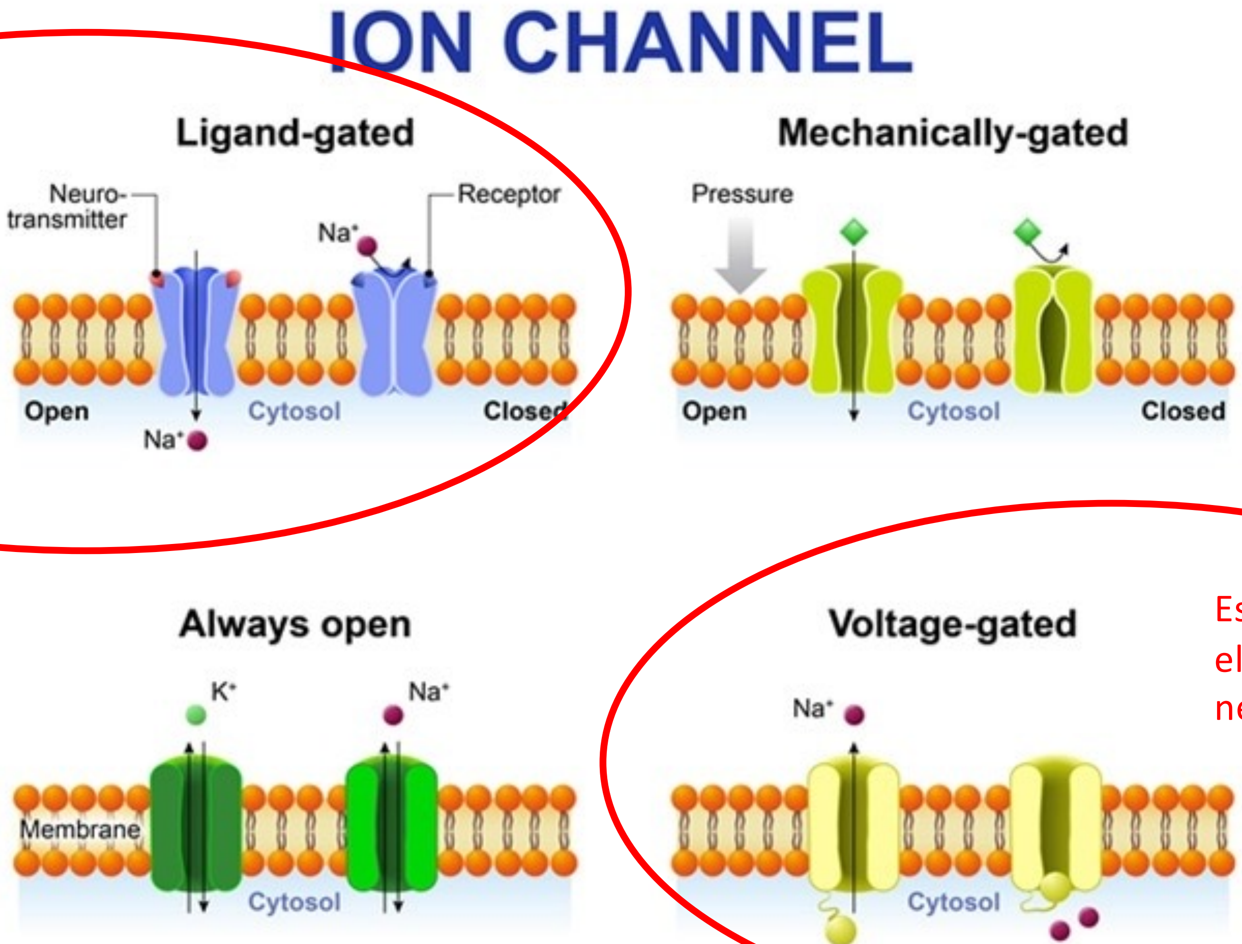
Ion channels are pore-forming membrane proteins that allow ions to pass through the channel pore.



Ion channels may be classified by gating, i.e. what opens and closes the channels.
Major categories are:

- **voltage-gated** ion channels: open or close depending on the voltage gradient across the plasma membrane
- **ligand-gated** ion channels: open or close depending on binding of ligands to the channel.

Es. Many Neurotransmitters receptors

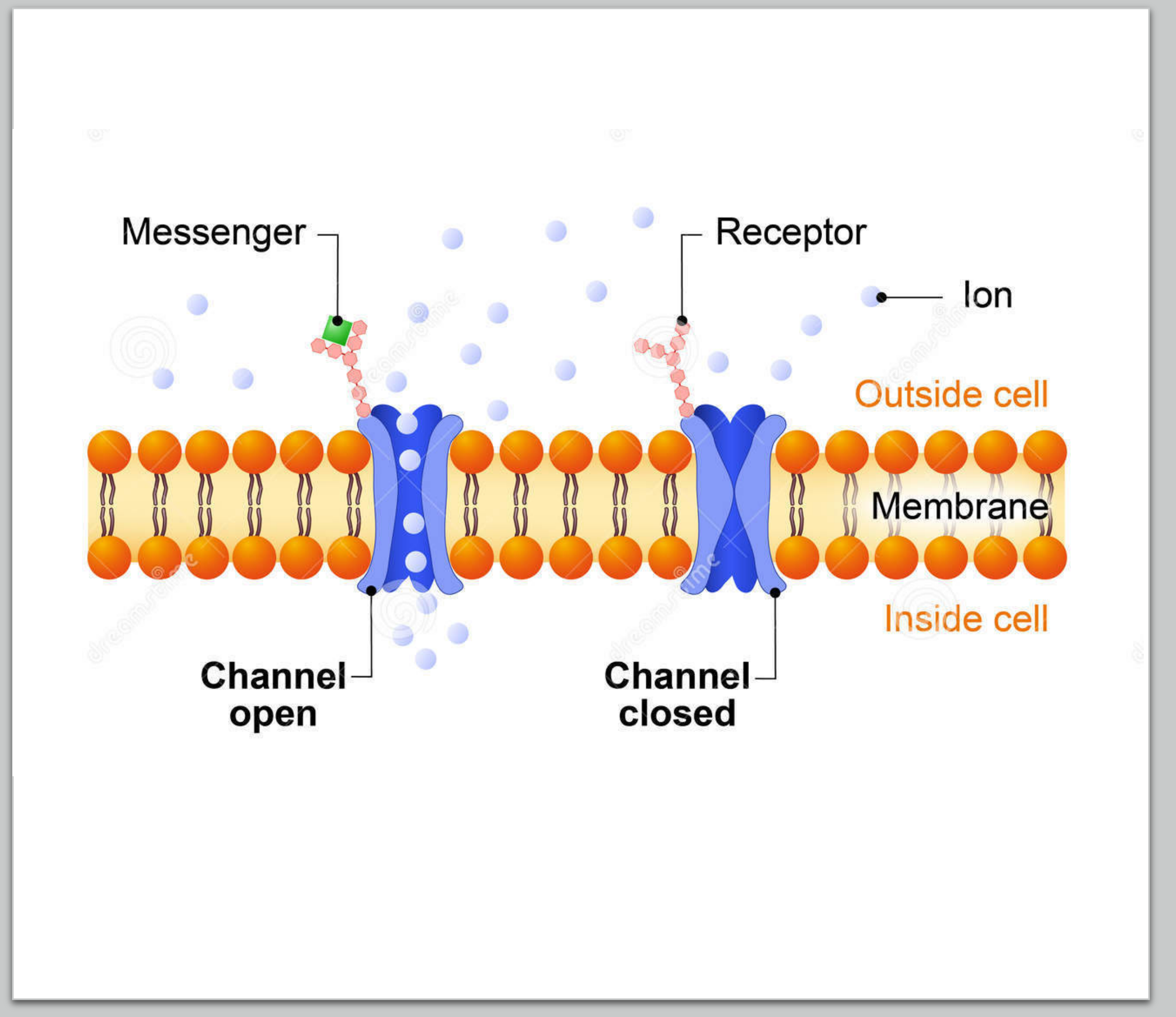


Es. Channels for electrical neurotransmission

Ligand-gated ion channel or ionotropic receptors

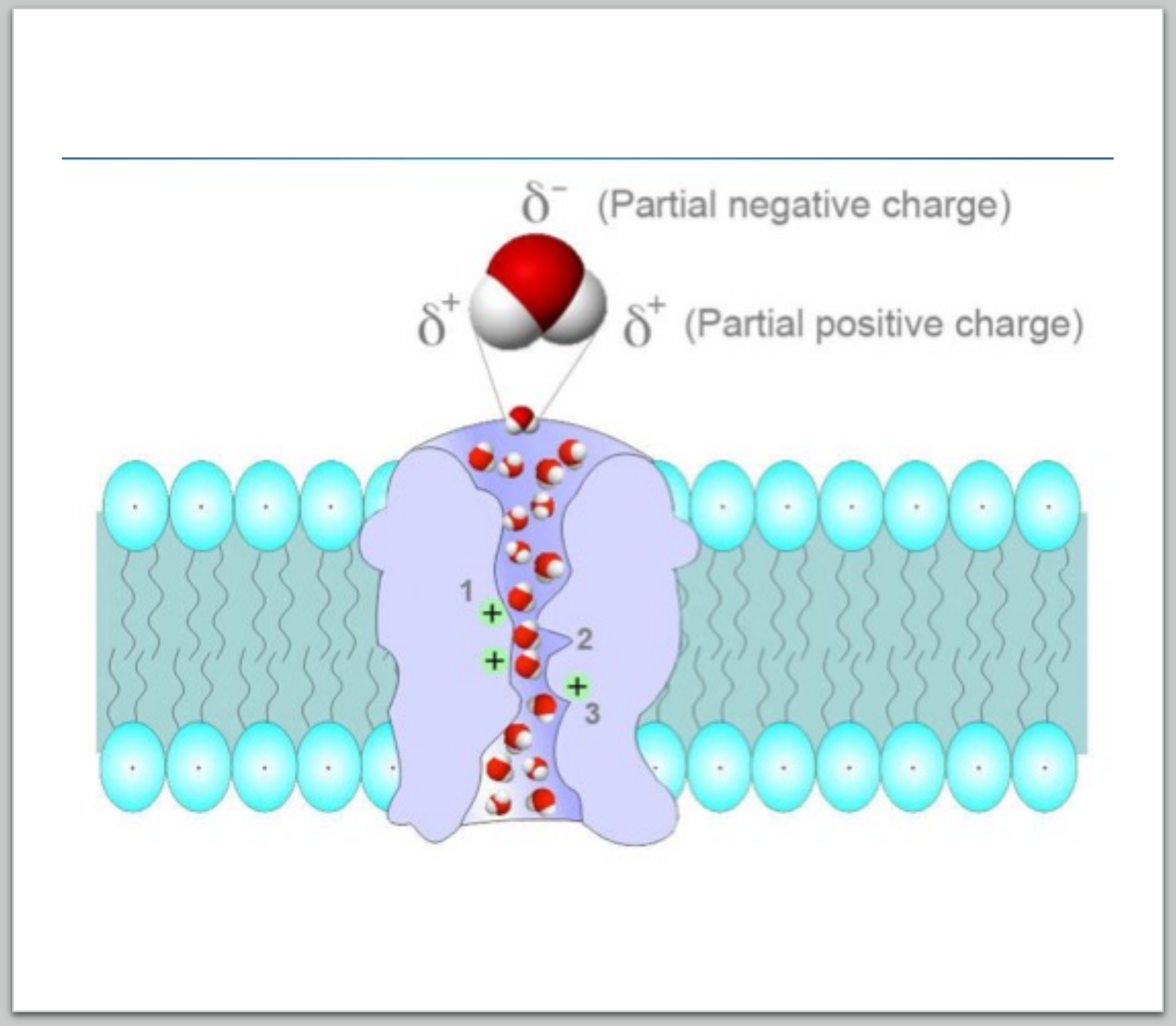
Ion channels that are gated by the binding of a specific ligand

- The probability of the ligand binding to the receptor increases with the ligand concentration
- The ligand-receptor binding is **reversible**.
- Similar molecules, other than ligands can bind to the receptor (agonist or antagonists). Agonists mimic the ligand effect, antagonists block the channel activation in a reversible or irreversible fashion.
- Some channels are provided with an extra site for allosteric modulation. Allosteric modulators increase or decrease the affinity of the channels for the ligand and/or its efficacy



Acquaporines: the case of the water transport

- A particular case of facilitated diffusion is the transport of water (solvent, not solute).
- Water is electrically polarized, thus by definition cell membrane impermeable
- Water can pass through protein channels called acquaporines
- The frequency of acquaporines on the membrane is very high



What strategies does the cell adopt to transport molecules across the membrane?

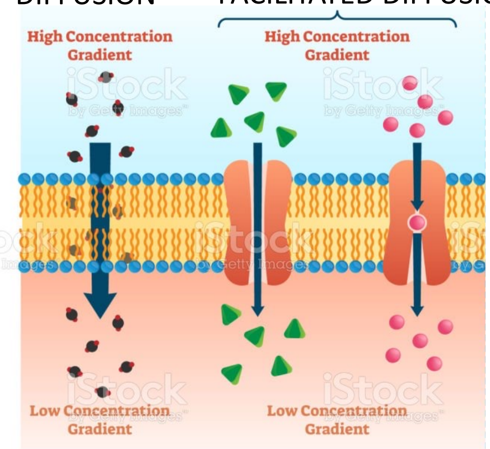
Cells need to transport molecules, often membrane-impermeable, also in opposite direction with respect to the directions the electrochemical gradient would naturally move them.

Transport across membrane

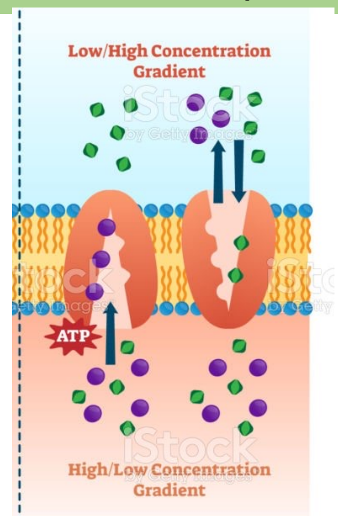
3 main strategies

Passive Transport

DIFFUSION FACILITATED DIFFUSION



Active transport



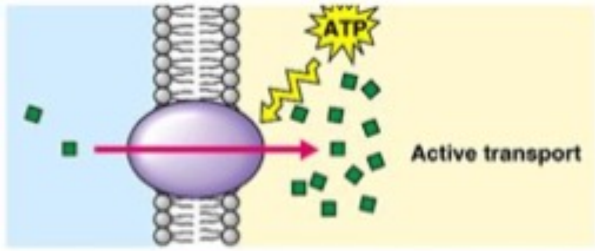
Vescicular transport

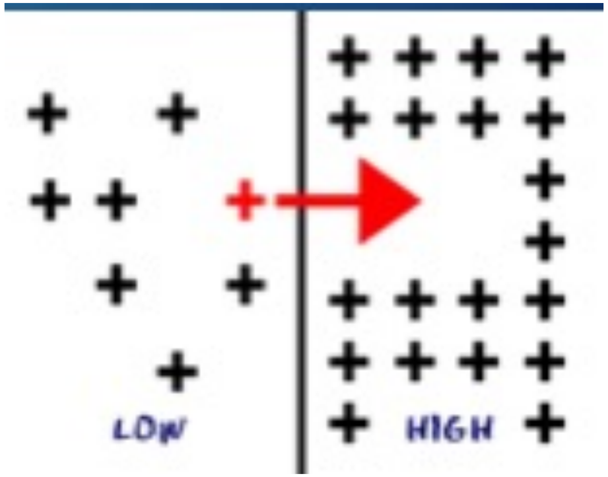
- Highly regulated mechanism
- Gradient-independent
- A lot of energy required

Active transport

- Movement of molecules **against** the electrochemical gradient (from the lower to the higher concentration)
- It requires energy consumption
- Always protein-mediated
- Based on the energy source, two modalities can be distinguished:

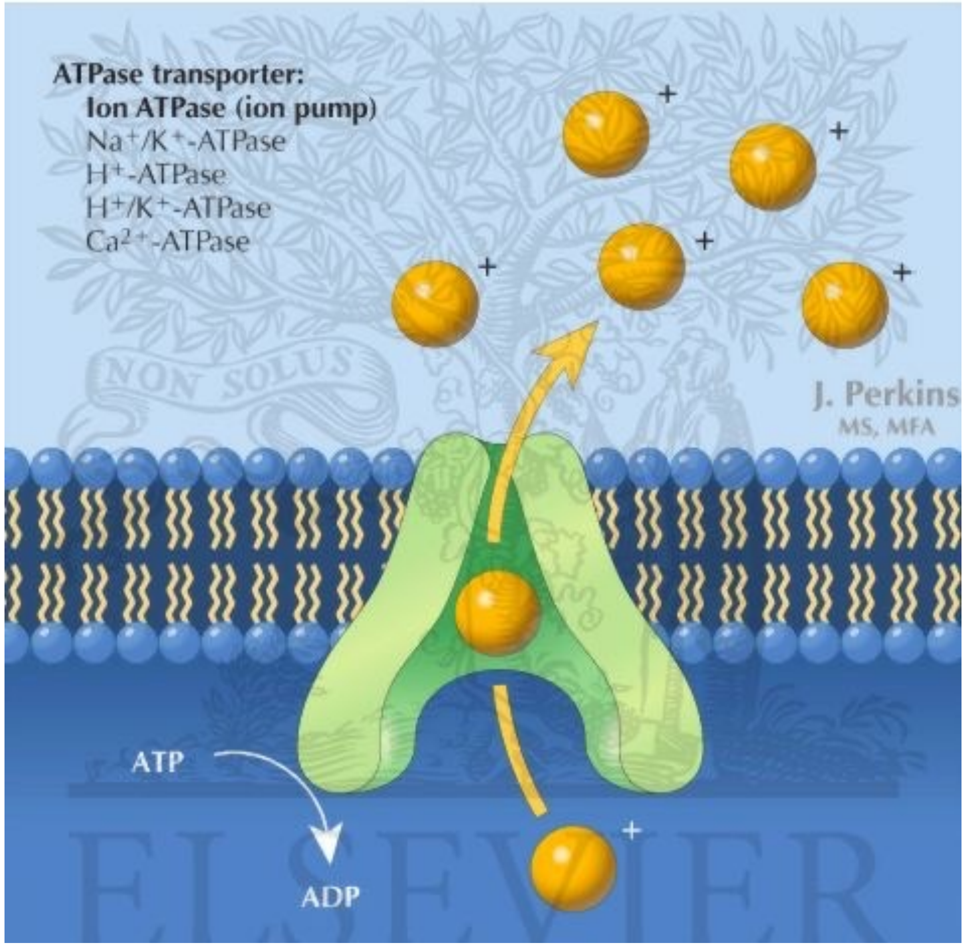
1. **<u>Primary active transport</u>**: directly consuming the energy currency, like ATP
2. **<u>Secondary active transport</u>**: coupled with the energy released from an exoergonic process



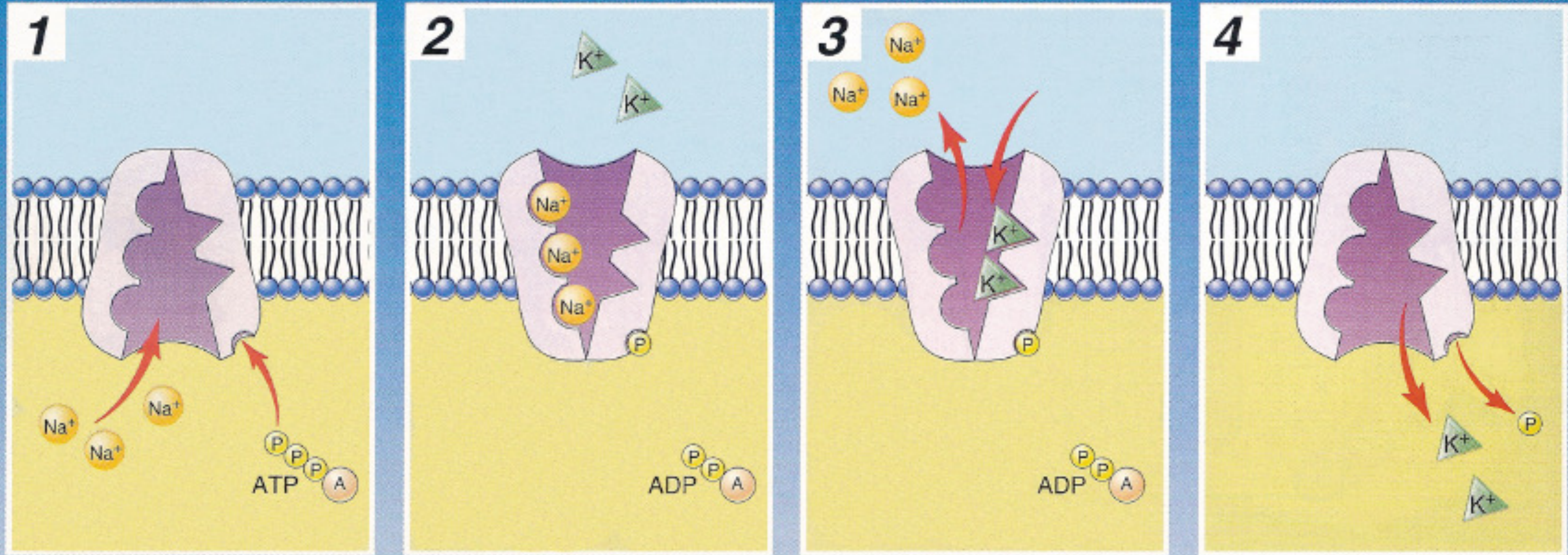


Primary active transport: the ATPase transporters

These special protein transporters carry a specific ATP binding cassette. ATP hydrolysis releases the energy required to open the transporter hole



SODIUM-POTASSIUM PUMP



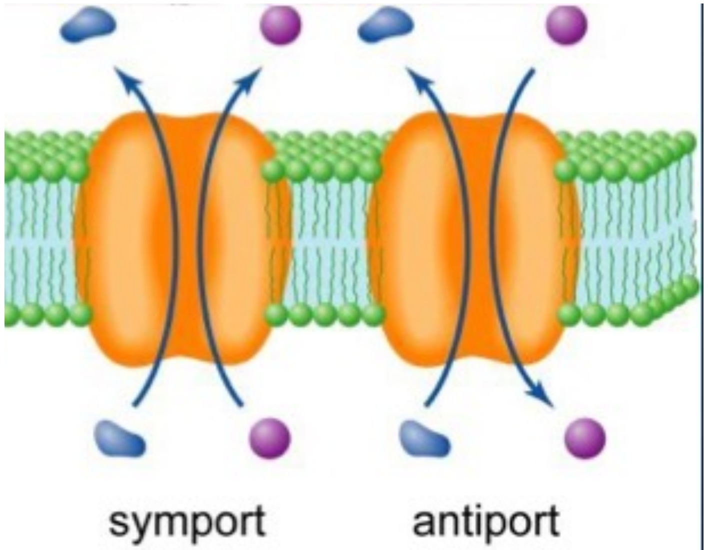
The sodium-potassium pump binds three sodium ions and a molecule of ATP.

The splitting of ATP provides energy to change the shape of the channel. The sodium ions are driven through the channel.

The sodium ions are released to the outside of the membrane, and the new shape of the channel allows two potassium ions to bind.

Release of the phosphate allows the channel to revert to its original form, releasing the potassium ions on the inside of the membrane.

Secondary active transport: the cotransport

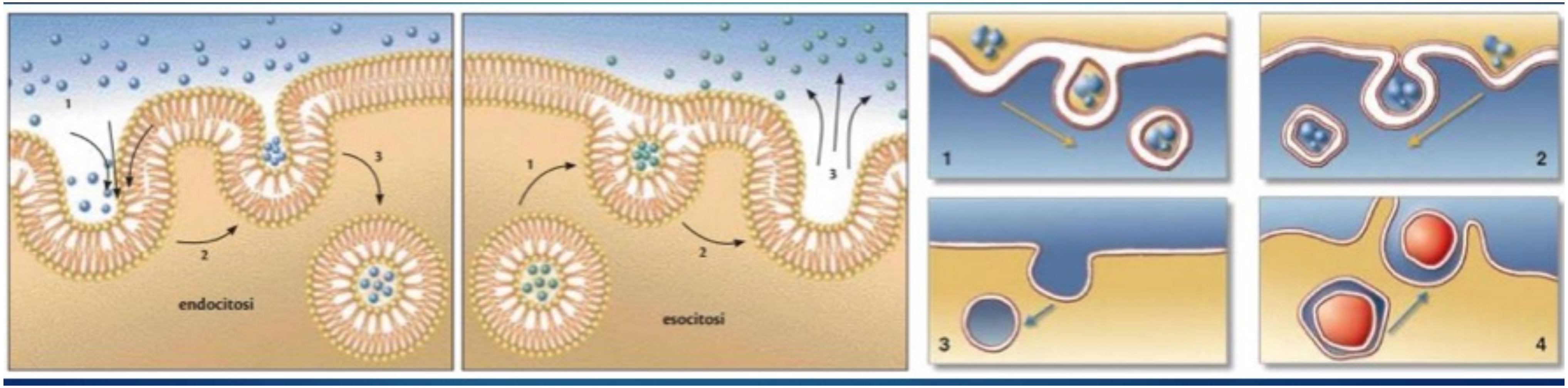


Cotransport

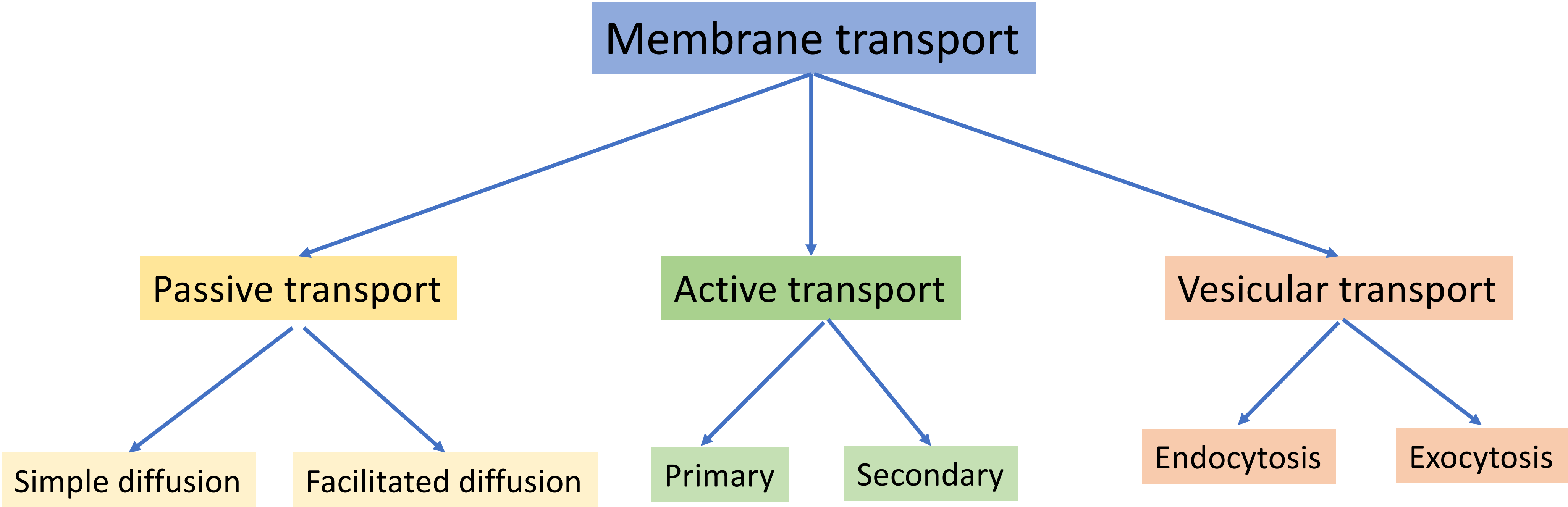
The transfer of the molecule against the energy gradient can occur exploiting the energy released by the simultaneous movement of another molecule in favor of its gradient

Other form of transport: vesicular endocytosis and exocytosis

- This type of transport in or out of the cell can be considered an active transport since it requires lots of energy



To recap:


Membrane transport
Passive transport
Active transport
Vesicular transport
Simple diffusion
Facilitated diffusion
Primary
Secondary
Endocytosis
Exocytosis