8

Cytology

Doctor 2019 | Medicine | JU

◉ Sheet ○ Slides

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8.10 Diffusion through the lipid bilayer

The plasma membrane is selectively permeably, allowing small inorganic molecules like CO2, O2 and H2O to cross the lipid bilayer, as well as solutes with high lipid solubility, while ions and polar organic solutes, such as sugars and amino acids, need special transporters to cross.

Diffusion of substances through membranes

For a substance to diffuse passively across a membrane:

1. <u>The substance must be at a higher concentration on one side</u>

There is free energy stored in the electrochemical gradient, which is dissipated when the substance diffuses.

2. <u>The membrane must be permeable to the substance.</u>

Either because:

a) The solute can dissolve and pass directly through the lipid bilayer, like CO_2

b) The solute can travel across a pore in the membrane, like H_2O

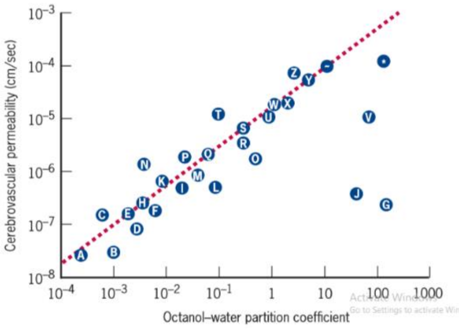
Both Polarity and particle size affect the how permeable a membrane is to the substance.

Polarity:

A quantitative measure of the polarity of a substance in its **Partition coefficient**, which is the ratio of its solubility in an organic (non-polar) solvent to its solubility in water. The more polar a substance, the less its partition coefficient.

For example, water and octanol(non-polar) are mixed and substance X is added. The concentration of X in octanol is 12 times greater than its concentration of water (X is more soluble in octanol). The partition coefficient for X is 12.

This graph shows plots the permeability of substances against their partition coefficients. The greater the partition coefficient(lipid solubility) of a substance, the higher its permeability across a membrane.



Molecular size:

If two molecules have approximately equal partition coefficients, the smaller molecule usually diffuses across the plasma membrane more rapidly.

Very small, uncharged molecules like CO_2, H_2O, NO and O_2 penetrate very rapidly through cellular membranes.

Larger polar molecules like sugars and amino acids barely penetrate cellular membranes. Therefore, the plasma membrane keeps essential metabolites from diffusing out of the cell.

The cell uses carrier proteins to get these molecules from the bloodstream, as they are essential for the cell. We will look at this later in more detail.

The diffusion of water through membranes

Cellular membranes are said to be semipermeable because water penetrates them much more readily than do solutes like ions.

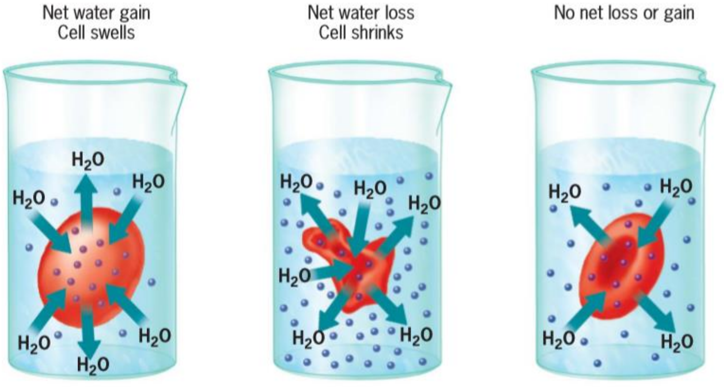
Osmosis is the diffusion of water through a semipermeable membrane.

Water moves from the region with high water potential (low solute concentration) to the region with low water potential (high solute concentration).

We can demonstrate osmosis by placing a cell in a solution that contains a nonpenetrating solute.

An Isotonic solution is one where the concentration of solutes is equal inside and outside of the cell and no net movement of water occurs. This is the normal state for animal cells.

A Hypotonic solution is a solution that has a lower solute concentration than that the inside cell.



(a) Hypotonic solution (b) Hypertonic solution (c) Isotonic solution

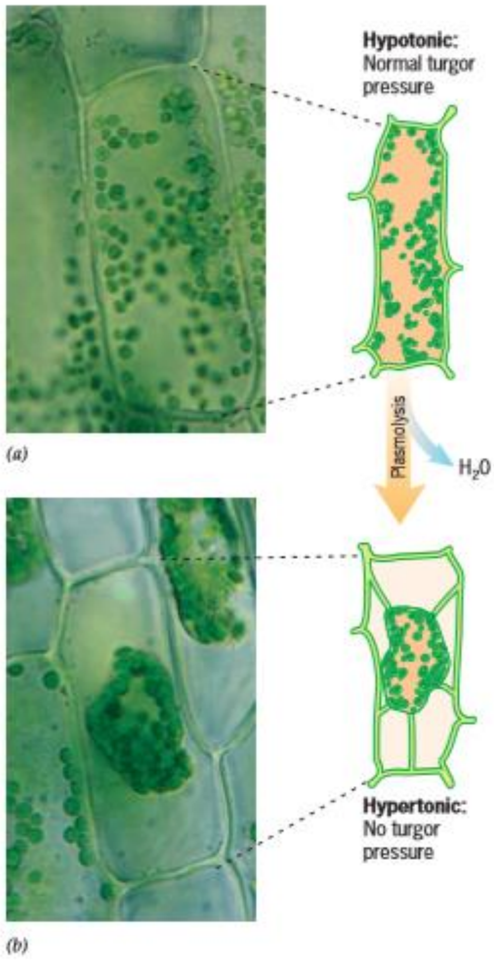
→ Water moves into the cell and the cell swells. The cell loses ions to reduce its internal osmotic pressure (make the solute concentration inside equal to that outside). If the cell fails to equalize the solute concentration inside and out, the cell will burst.

A Hypertonic solution is one that has a higher solute concentration than that inside the cell.

→ Water moves out of the cell, so the cell shrinks. The cell recovers by gaining ions from the solution.

Your digestive tract secretes several liters of water daily, which is reabsorbed by osmosis by the cells that line your intestine. If this water was not reabsorbed, you would be severely dehydrated.

Plants, on the other hand, prefer to be hypertonic compared to their surroundings (in a hypotonic solution). They achieve this by having a central vacuole that has a high salt concentration, which draws water from the cytoplasm by osmosis, which draws water from the surroundings.



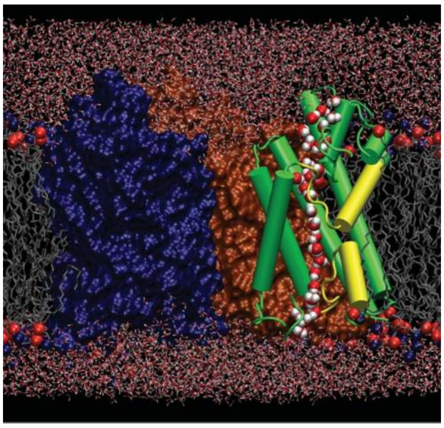
The cell does not burst when this water enters as it has a cell wall, instead, the cell develops an internal pressure called **Turgor pressure.** We can see the green chloroplasts distributed throughout the cell under the microscope (as in (a)).

Turgor pressure provides support for some part of the plant like the leaves.

When plant cells are in a hypertonic solution, they lose water and the plasma membrane separates from the cell wall in what is called **Plasmolysis.** The green chloroplasts can be seen concentrated in a circle in the center of the cell. This occurs to a lesser extent in isotonic solutions as well.

Some cells are more permeable to water than others. Many cells have a high permeability to water than cannot be explained by simple diffusion alone.

Aquaporins are a family of integral proteins that allow the passive movement of water through the plasma membrane. Their central channels are lined primarily with hydrophobic amino acids that prevent ions from diffusing into the cells. Water, however, can still cross aquaporins despite the hydrophobic amino acids.



8.11: The diffusion of ions through membranes

Ions can only diffuse through ion channels in the plasma membrane. Ions diffuse according to their electrochemical gradient, which is a combination of chemical (concentration) gradient and electrical gradient (due to charge difference).

Ion channels are:

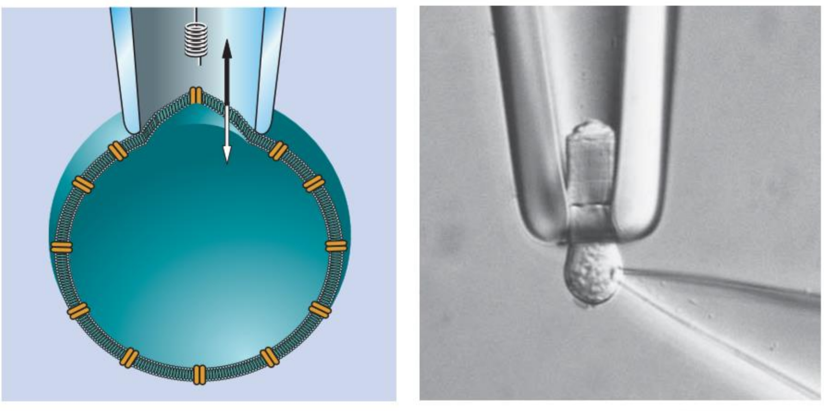
1- Selective

Each type of channel only allows one particular type of ion to pass through it.

2- Bidirectional

They allow ions to move into and out of the cell.

The technique used to study ion channels in cell membranes is called **patch-clamping**.



(a) (b) 35 µm

Some ion channels are said to be **gated**, meaning that they have a closed and an open conformation.

There are 3 types of gated channels:

1- Voltage-gated channels:

Their state depends on the voltage across the membrane (difference in ionic charge across the membrane).

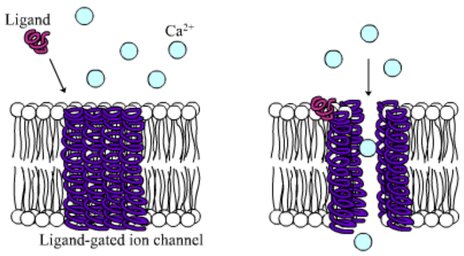
Example: Voltage-gated potassium channels in Eukaryotes.

2- Ligand-gated channels:

A specific molecule (ligand) binds, either to the outer surface or to the inner surface of the channel, and this opens or closes the gated channel.

The ligand that binds to the channel is usually not the solute that passes through the channel.

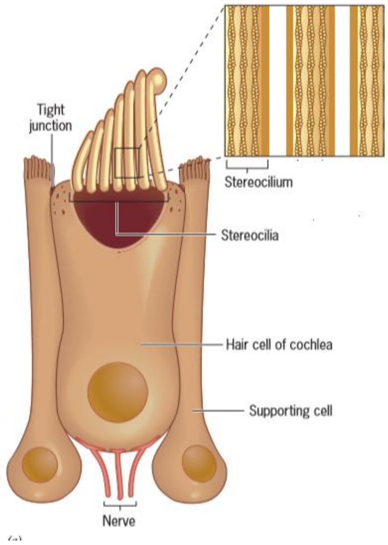
Example: Ligand-gated channels in nerve cells that open when a neurotransmitter binds to them.



3- Mechano-gated channels:

Their state depends on mechanical forces, like stretch-tension, that are applied to the membrane.

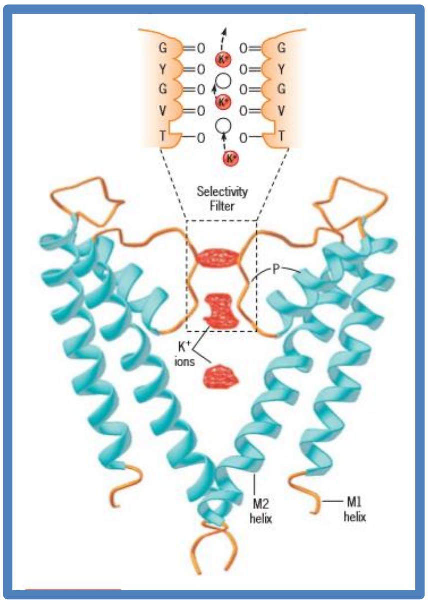
Example: Cation channels that are opened when sound or motion moves stereocilia on hair cells in the inner ear.



Potassium (K+) channels:

1- In bacteria:

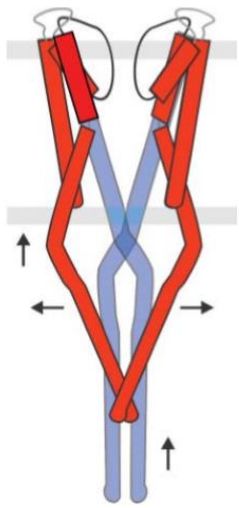
The potassium channels in bacteria are called **KcsA** channels and are made up of 4 identical subunits that span the membrane, each subunit containing 2 helices (M1 and M2), as well as a pore region (P) at the extracellular end of the channel. In this picture, two of the four subunits are shown, the other two are into and out of the page.



The four P regions form the *borders* of the *selectivity filter,* which only allows K+ ions to pass through and blocks other ions like Na+. (The K+ ions do NOT flow through the pore regions but through the selectivity filter).

Although there are 4 places for K+ ions in the selectivity filter, only 2 ions pass at a time due to their repulsion.

The picture above (with blue border) of the 2 subunits was their closed confirmation, as the M2 helices are straight and cross over one another to seal the cytoplasmic side of the pore.



The channel opens when the M2 helices bend at a point where the amino acid Glycine is located, opening this seal and allowing 10 million K+ ions to pass through each second.

In the photo to the side, the blue shows when the channel is closed, and the red is when it is open.

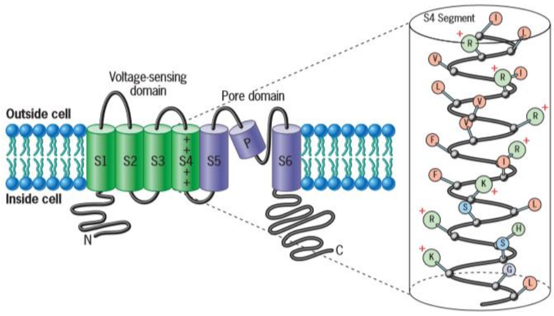
2- In Eukaryotes:

In eukaryotes, the voltage gated K+ channel (**Kv** channels) is a little more complicated, as we will see.

The Kv channels in plants play an important role in the salt and water balance of the cell and so regulating its volume.

Like the KcsA channel, a single eukaryotic Kv channel consists of four homologous subunits arranged symmetrically around the central ion-conducting pore.

The four subunits of the eukaryotic Kv channels each contain 6 helices which are embedded into the membrane, and the are called S1 to S6 (compared to only M1 and M2 in bacteria).



The picture to the side shows ONE OF THE FOUR SUBUNITs of Kv channels, containing S1-S6.

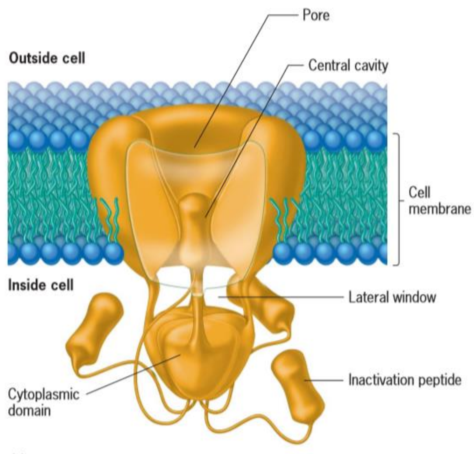
These 6 helices are grouped into 2 groups according to their function:

1- Pore domain (S5, S6, P-segment):

This is the part that acts as the selectivity filter (only allows K+). It is virtually identical to the entire KcsA channel in bacteria (M1=S5, M2=S6).

2- Voltage-sensing domain (S1-S4):

The part that senses the voltage across the plasma membrane. The S4 helix acts as the key element of the voltage sensor.



This is the 3D model for the structure of the Kv channel. As you can see, it is made of 4 identical subunits, with a pore in the middle.

Our plasma membranes normally have a potential difference (voltage) across them where the inside of the cell is more negative. Under resting conditions, this negative potential across the membrane keeps the gate closed. If this potential changes to a more positive value, an electric force is exerted on S4 which causes the protein to change shape, opening the gate at the cytoplasmic end of the channel and allowing K+ to pass through.

Because the channel allows K+ ions to diffuse so rapidly, after it has been open for a few milliseconds, it is automatically closed as a small *inactivation peptide* moves and blocks the cytoplasmic mouth of the pore in a process called **Inactivation.** Later in the cycle, the inactivation peptide is released, and the gate to the channel is closed.

The channel can exist in three different states:

1- Open
2- Closed
3- Inactivated