Physiology | Lecture 3

Transport across the plasma membrane

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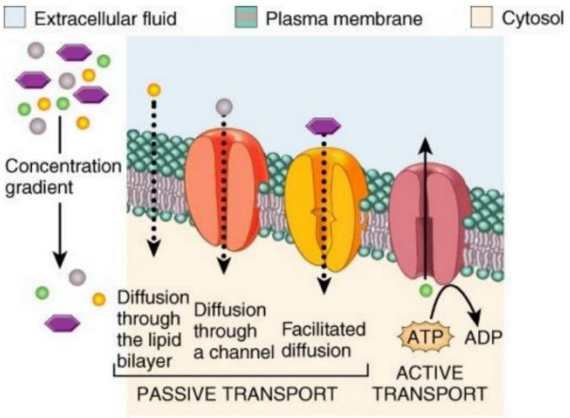
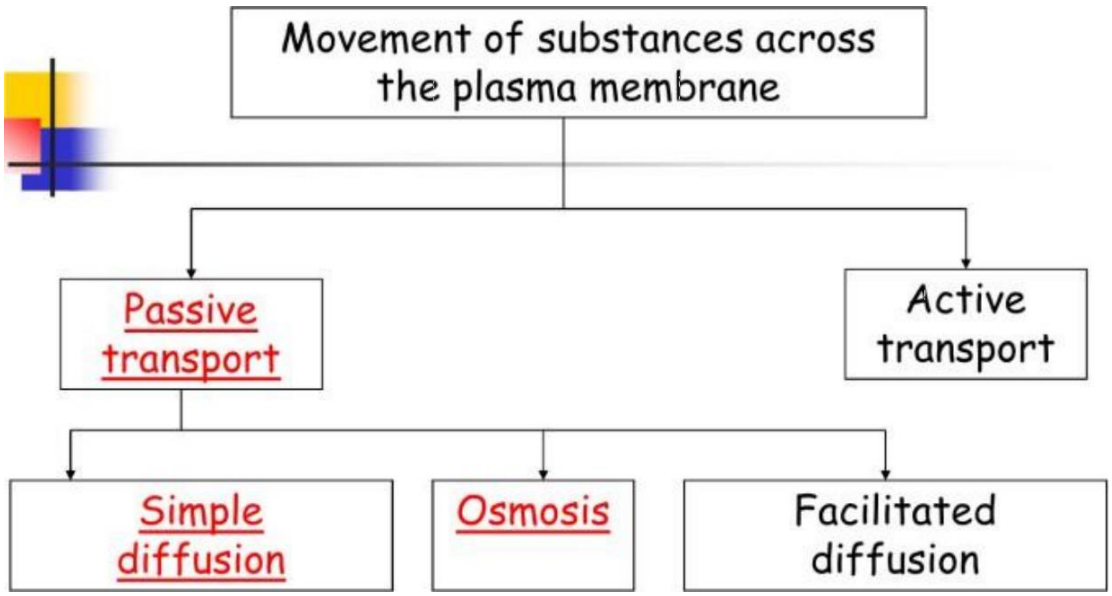
Transport across Plasma Membrane

In this lecture we will talk about transport modalities across the plasma membranes.
To understand the general idea of the transportation, you can follow the link below:



https://www.youtube.com/watch?v=A9ihz5gYxU4

We talked previously about the plasma membranes , and that we have proteins impeded in them . These proteins help with transportation across the membrane ,for example using carriers or channels.
But besides that, we can have some particles passing through the Lipid bilayer structure(its simply transported that way) .
Also ,we have some carriers that consumes energy to transport particles from low to high concentration (we call it active transport modalities) .
Passive = without consuming macro-energetic molecules (ATP).
*Active= there is consumption of macro-energetic molecules (ATP).



Diffusion :

Generally, dissolved particles found in solution are in
Constant movement. This random motion is due to thermal energy
In particles that found themselves at a temperature above the
Absolute zero (in living systems about 310 degrees K). The random
Motion in liquids and gases will result in a random collision of
Particles with each other and with the wall. These haphazard
Collisions will cause a transfer of kinetic energy from one particle
To another and change in the direction of motion. This continuous
Movement in liquids and gases is known as **diffusion.**

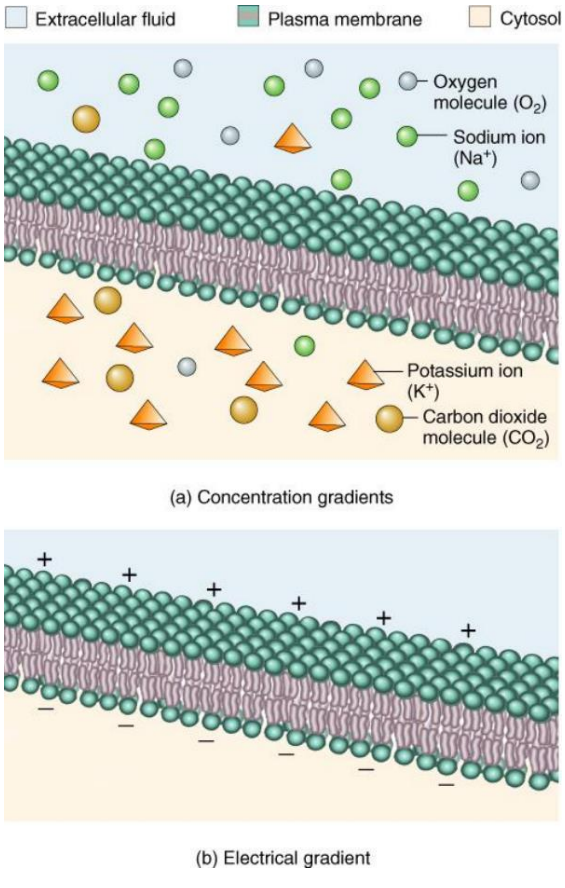
- Random motion: Each molecule moves in unpredictable directions due to collisions, but without a specific purpose. This motion never stops as long as the temperature is above absolute zero

- Diffusion: the overall movement of molecules from a high concentration area to a low concentration area. It results from many random movement but only happens when there is a concentration difference
- Reminder: More kinetic energy means higher concentration.For example,If you have high concentration in a compartment, you have high kinetic energy in that compartment, and so on.
- The reason why diffusion doesn't need to consume macro-energetic

Particles can move across membrane by diffusion. This type of transport does not need consumption of energetic compounds ATP(Passive)

Diffusion through lipid Bilayer

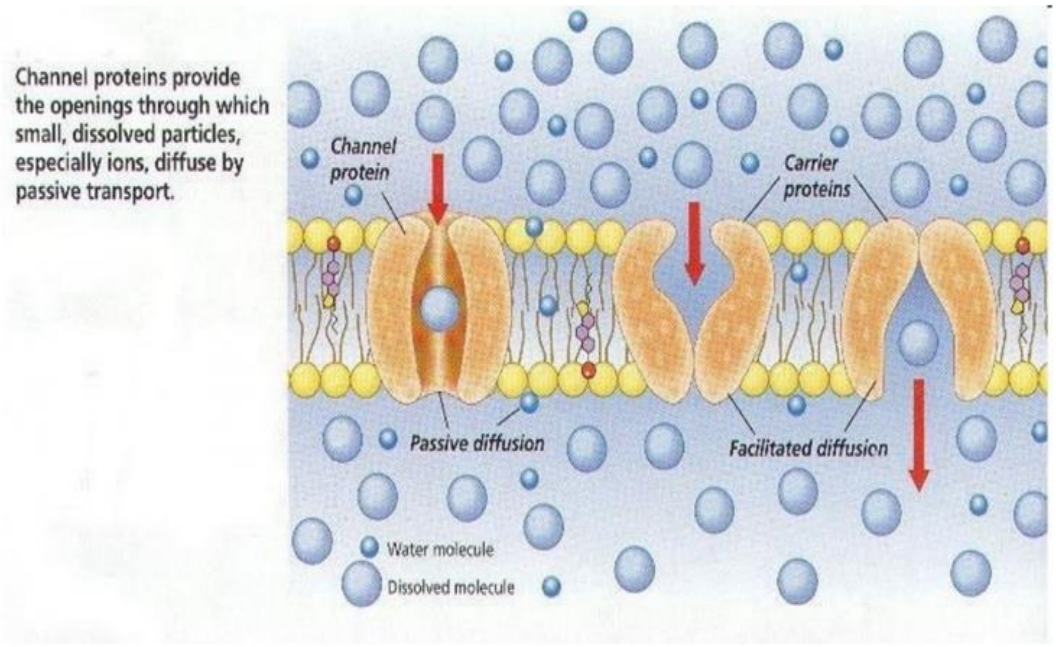
● We have <u>some particles</u>
(lipid soluble substances):
•*CO2*
• *O2*
• *NO*
• *Steroid Hormones*
• *Monoglycerides*
These can move through the Lipid bilayer structure (Their diffusion depends on the **<u>solubility of particles in the lipid bilayer.)</u>**



The higher the liposolubility → the more molecules can pass through the membrane.

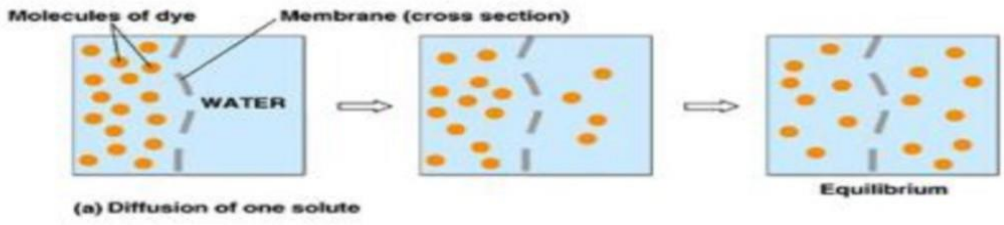
Diffusion through channels

Other particles (charged particles for example or bigger particles) , we need protein structures that can help them to move across the membrane.



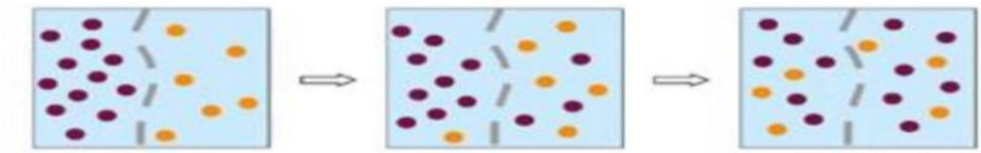
The Concept of Simple Diffusion

In this example, we have a membrane that separate two compartments, one contains number of dies and the other is empty. The dies start to move (**downhill**) from the higher concentration to the lower concentration until it reaches a state of **Equilibrium** where the **net diffusion is zero**. Equilibrium doesn't mean that there are no diffusion between the two compartments, it means that **the rate of diffusion to the right is the same rate of diffusion to the left**.(net diffusion=zero



(a) Diffusion of one solute

This example is the same as above, but notice that there are **two different dies** (**red** and yellow), the movement of each particle depends on it **its own concentration** gradient throw the membrane,not the number of all particles in each compartment.(the yellow dies move according to the number of only yellow dies in each section, not the number of red and yellow dies).



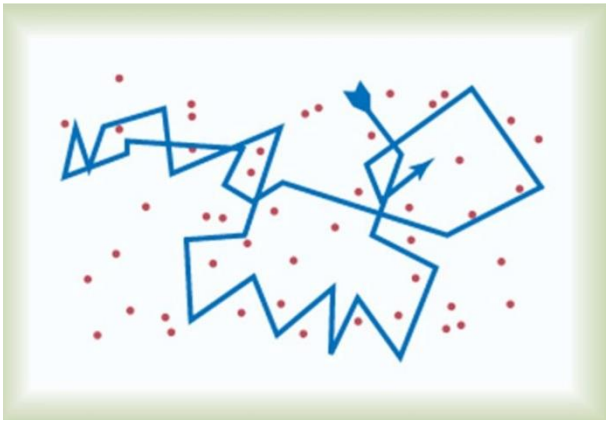
(b) Diffusion of two solutes

Note that simple diffusion doesn't consume ATP as a source of energy, but what is moving these particles is the kinetic energy.

So , For simple diffusion we need :

- A selectively permeable membrane for the substance/both substances.
- To have low concentration in one compartment and high concentration in the other one .
- We don’t need to consume Macro-energetic molecules (ATP)

❖ <u>The energy is held in the particle, its called ***KINETIC ENERGY***</u>

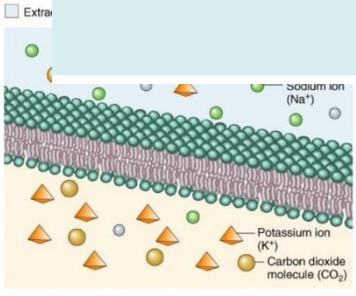


(If you have high concentration in a compartment, you have high kinetic energy in that compartment, and so on).

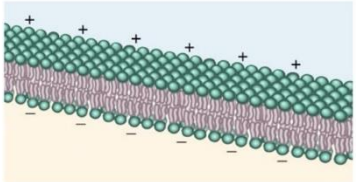
Simple diffusion

Diffusion through lipid bilayer

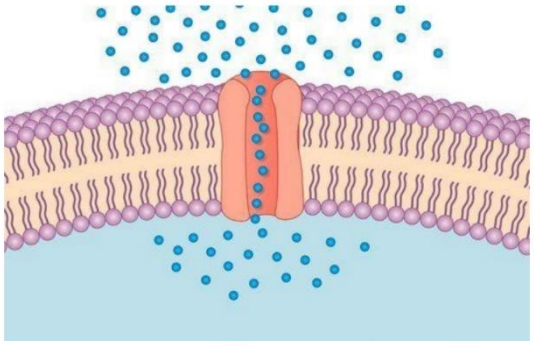
- CO2
- O2
- NO
- Steroid Hormones
- Monoglycerides

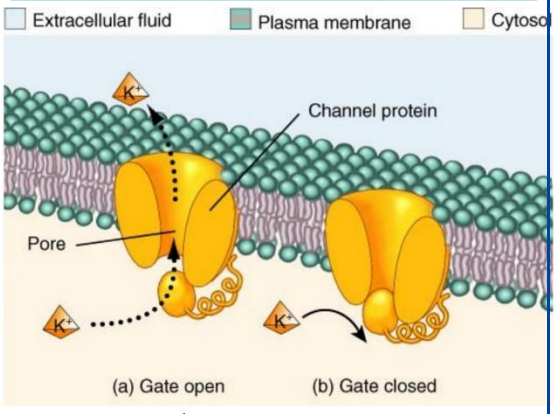


(a) Concentration gradients



Diffusion through Channels





* changing the permeablity *

■As we said , diffusion depends on the permeability of the membrane and the concentration gradient.

Fick's Law

- $J = P.\Delta C$
- $P = D.A/\Delta X$
- $J = D.A.\Delta C/\Delta X$

J = Flux (Rate of diffusion)
P = Permeability
D = Diffusion Coefficient
A = Surface area
C = Concentration
X = Membrane thickness

This law combines these parameters to **calculate the rate of diffusion.**

■ Diffusion net rate:

the number of particles that moves from one side to another (more precisely : [from **high** to **low** - from **low** to **high**])

▪ One of the **factors** that influence the Rate of net diffusion is **concentration gradient** (ΔC= CA-CB), which represents the Chemical Potential for movement of particles across membranes.

▪ In addition to concentration gradient, net rate of diffusion (Q)
Depends also on:

- ❖ **Permeability** of the membrane to a given substance (P): the

Higher the permeability for a substance the greater the diffusion rate is
Through membrane.

- ❖ **Surface area** of transport (A): diffusion increases by increasing (A).

The increase in surface area in biological membranes will result in
More protein channels that can be used for diffusion from one
Compartment to another.

- ❖ **Molecular weight** (MW): lighter molecules move more quickly

Than heavier.

- ❖ **Membrane thickness** (X) (distance of movement): the greater the

Distance the slower the rate of diffusion.

All these **factors** form the Ficks' law of diffusion:

- J = P.ΔC.....(J = Flux, P=Permeability, ΔC = Concentration gradient)

- P = D.A/ΔX ..... (, A: surface Area, ΔX = membrane Thickness)

- J = D.A.ΔC/ΔX..... (D=Diffusion Coefficient)

For each molecule we have a diffusion coefficient that depends on the size for this molecule

In addition to all these factors, diffusion can also be *influenced* by:

- Effect of membrane electrical potential: mainly influences

Electrically charged particles.
The presence of a negative potential inside the cell prevents movement of negative (-) charged particles from the extracellular
Compartment to the intracellular compartment and the positive charged particles from the intracellular to the extracellular compartment.

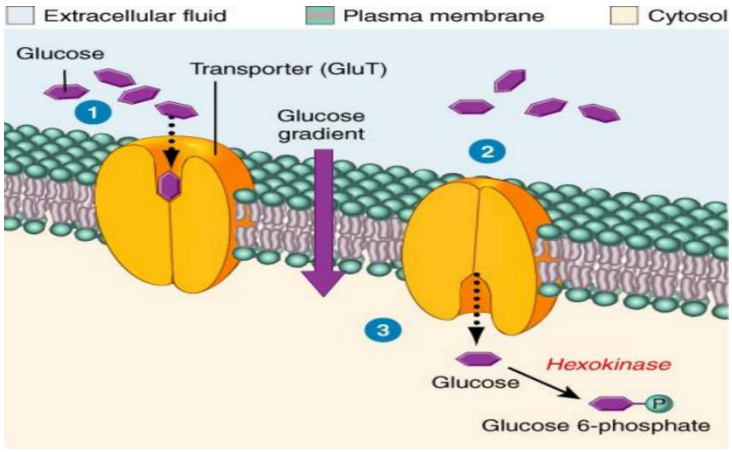
So, movement of charged particles is governed by an electrochemical
Potential. This will be discussed in more details later.

- Effect of pressure:

The presence of pressure difference between two compartments
will cause more kinetic energy in particles in the compartment with
Higher pressure. This will cause movement of more particles from the High pressure side to the low pressure side.

Facilitated Diffusion

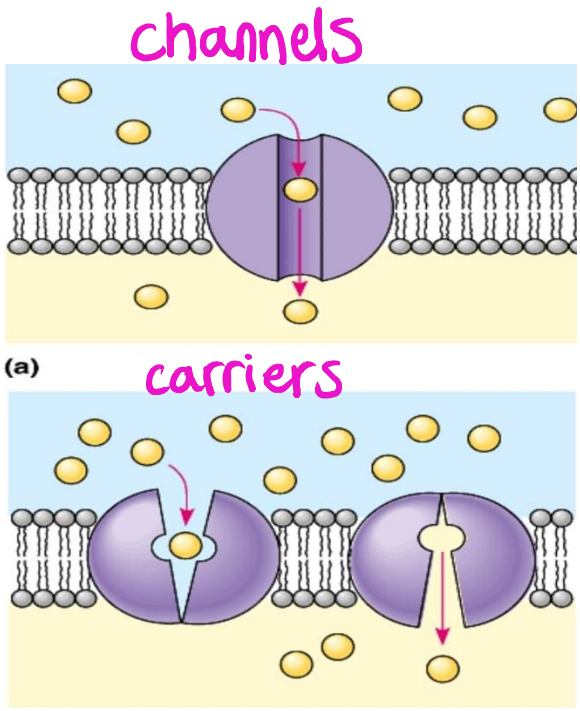
Sometimes, we need to transport bigger molecules. For these particles, we don't have channels, instead we have carriers that can help these particles to transport across the plasma membrane.

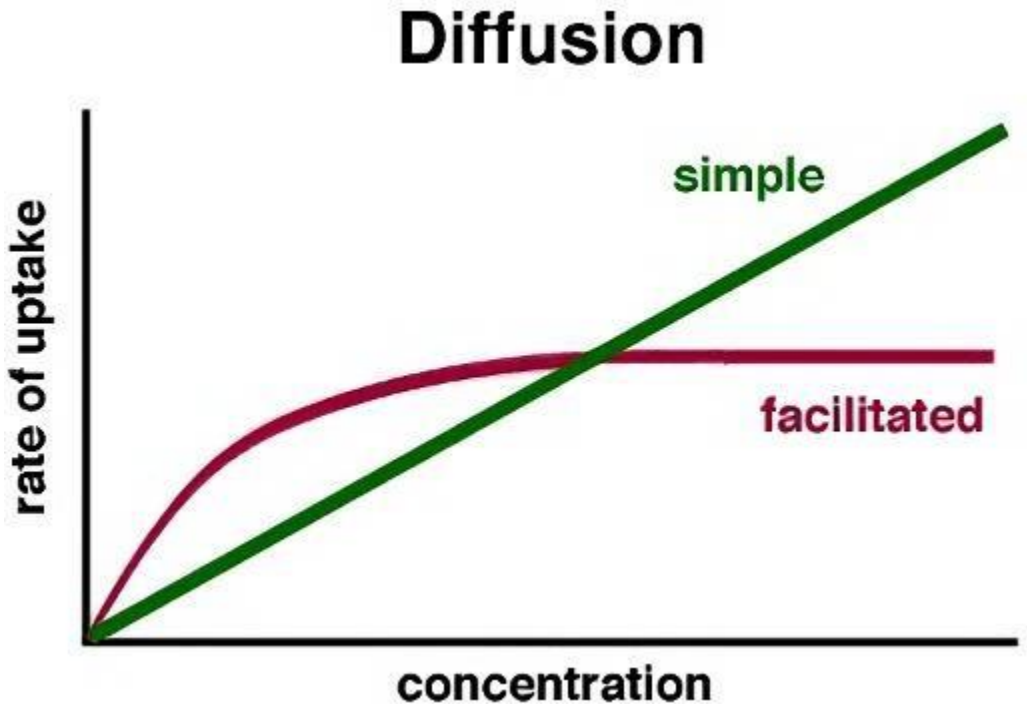


These carriers are specific,
(for example, we have specific carriers for glucose different from the carriers of galactose, and so on).
These carriers have binding sites for these particles, it can get some changes in the protein structure so it can move the particles **from high concentration to low concentration without the consuming of ATP**.

▪ Examples on **big molecules that need carriers:**

- Aminoacids
- Glucose
- Galactose
- Fructose





As you can see, the simple diffusion curve is linear and always **increasing**, but the facilitated one is increasing at the beginning, and after one point it will stop increasing, this is the **limitation point** and at this point it have the maximum velocity of transport (Vmax), why does this happen? Because we have a **limited number of carriers**, when all these carriers are busy in transporting (they are all under use) even if we increase the concentration of specific particle on one side, these carriers won't be able to transport these particles to the other side, **so the curve will stop increasing**.
Now we should go back to the channels, channels follow simple diffusion curve, so at this point they are considered as simple diffusion, but as we mentioned before, channels are protein structures, and for that they should be considered as facilitated diffusion, from our doctor perspective they are just "**diffusion**", neither simple nor facilitated.

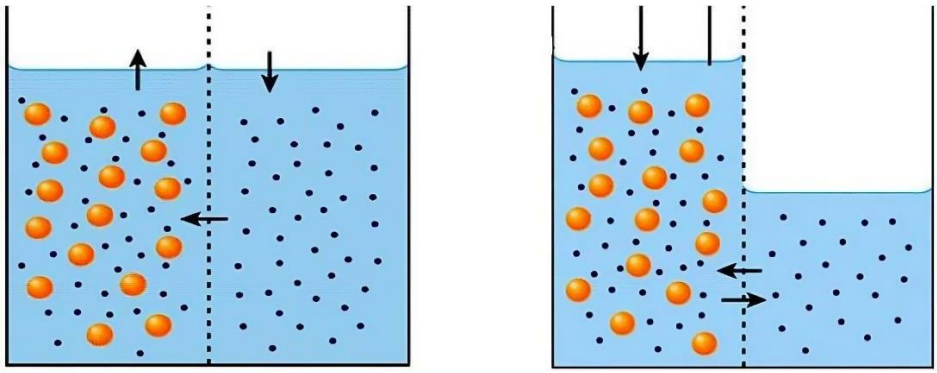
At this point you should ask: The number of carriers is limited, and the channels number too, so why there is limitation point in the curve of facilitated diffusion (carriers) and not in channels (as we mentioned above, they follow simple diffusion curve)?

They don't have limitations because their rate of transport is so high while in carrier proteins their rate of diffusion is way slower because everytime they transport a molecule they change their shapes which takes time and it could reach a limit where all the proteins are occupied

Osmosis

If we assume that there is a membrane that it's not permeable for particles, and permeable for water, what will happen? The water will move from the compartment that has a **high** concentration of **water** to the **low** one, in other words: from **low** concentration of **particles** to **high** concentration of **particles**, this is **Osmosis**.

We can reach equilibrium in osmosis.

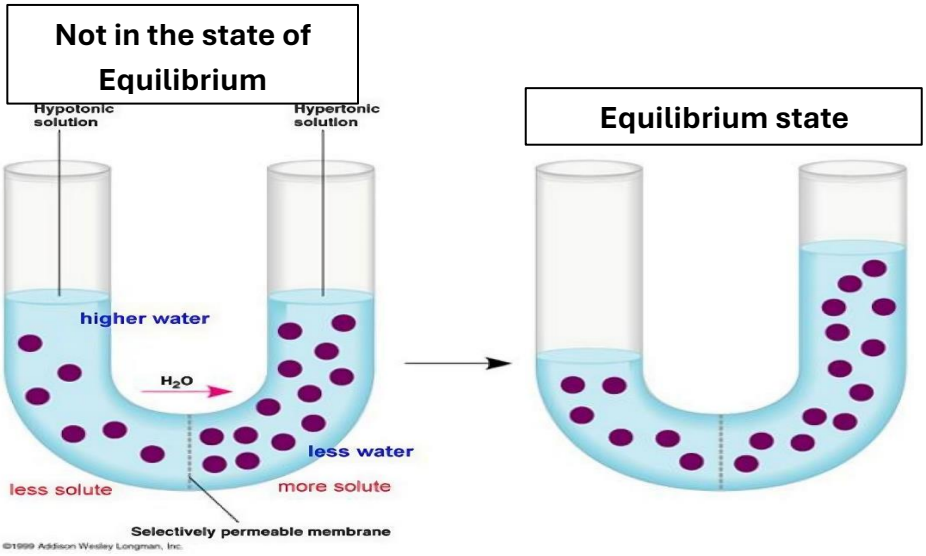


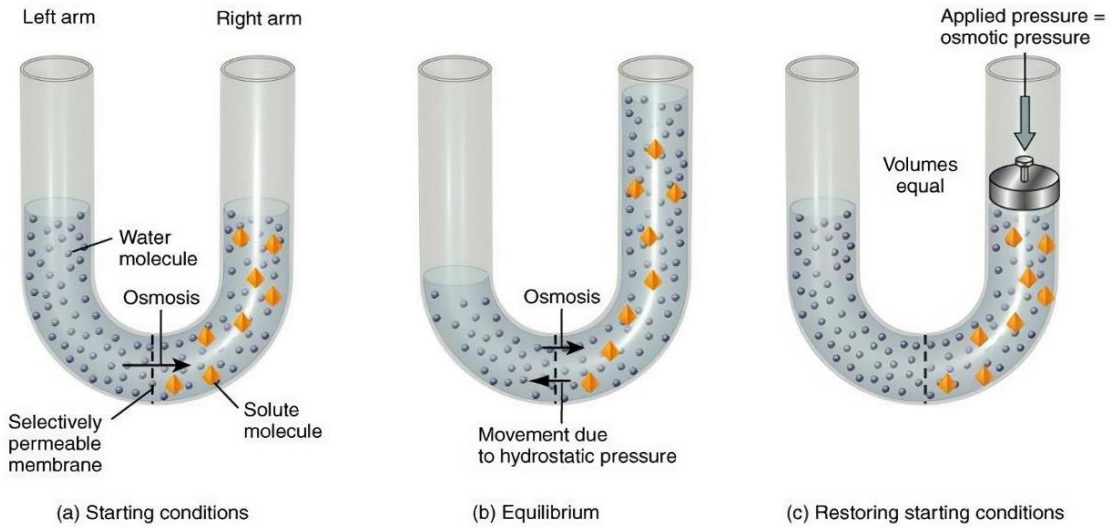
In osmosis, at equilibrium, the number of water molecules entering one side is equal to the number leaving the other side**, so there is no net movement**. So how can equilibrium be reached even though solute concentrations remain different on both sides? **Simply because hydrostatic pressure is created.**

1) Osmotic pull happens (because of the solute gradient) to reach equilibrium
2) As water enters, the volume is increased
3) Hydrostatic pressure acts as a counter force that opposes the movement of osmosis and eventually reaching equilibrium

Hydrostatic pressure opposing more movement of the water is called **the osmotic pressure of that solution**, here is another example:

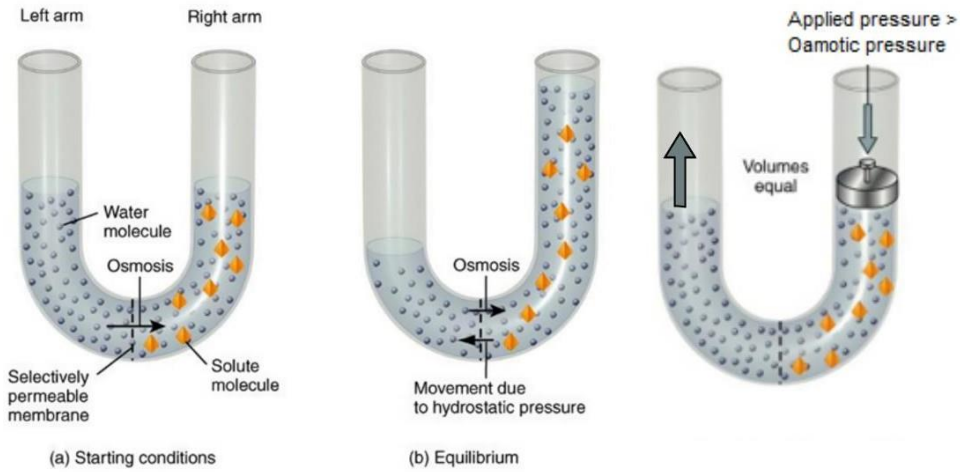
What if we applied external pressure that is opposite to osmotic pressure and equal to it? Look at the next page.





Simply, if we applied an external pressure that is opposite and equal to the osmotic pressure, we will go back to the starting condition.

Did you think about applying an external pressure that is more than the osmotic pressure and opposite to it? The water will move from the lower to the higher concentration of it, this is called **filtration (reverse osmosis)**.



Van't Hoff's Law

$$\pi = RTC$$

π = osmotic pressure

R = Gas constant

T = Absolute temperature

C = Concentration of the particles in a solution

-Osmatic pressure depends mainly on the molar concentration (number of particles) in a solution.

-Size doesn't matter. Neither does shape or charge

-**Important note:** the equations are for understanding the correlation between the elements (positive/negative), solving with numbers isn't required.

Osmole, Osmolality and Osmolarity

We know that if we get a specific gram of particle that is equal to its molecular weight, then we have 1-gram molecular weight (1 mole) of it, as an example: glucose molecular weight is 180 grams, so if we have 180 g of glucose, then we have 1 gram molecular weight.

Osmole: An osmole is a unit that measures the number of solute particles in a solution that contributes to its osmotic pressure.

Based on that, if we have 180 grams of glucose, then we have 1 osmole of glucose.

In glucose situation, the glucose doesn't dissociate into ions in water, so we said **1 osmole**, but what if we are dealing with something that dissociates into ions in water?

Let's take sodium chloride as an example, if we have 58.8 grams of it (equal to its molecular weight) then we have 1 gram molecular weight of sodium (1 mole) and 1 gram molecular weight of chlore (1 mole), if we are talking in terms of osmosis, that's **2 osmoles**.

If we take a solution that has 1 osmole of solute dissolved in each kilogram of water is said to have **Osmolality** of 1 osmole per kilogram.

If we take a solution that has 1 osmole of solute dissolved in each liter of water is said to have **Osmolarity** of 1 osmole per liter.

To sum up:

Osmole -> moles * number of dissolved particles

Osmolality -> osmole per kilogram

Osmolarity -> osmole per liter

Glucose ($C_6H_{12}O_6$):
1 mole → 1 particle (no dissociation) → 1 osmole
NaCl:
1 mole → 2 particles → 2 osmoles
$CaCl_2$:
1 mole → 3 particles → 3 osmoles
$AlCl_3$:
1 mole → 4 particles → 4 osmoles

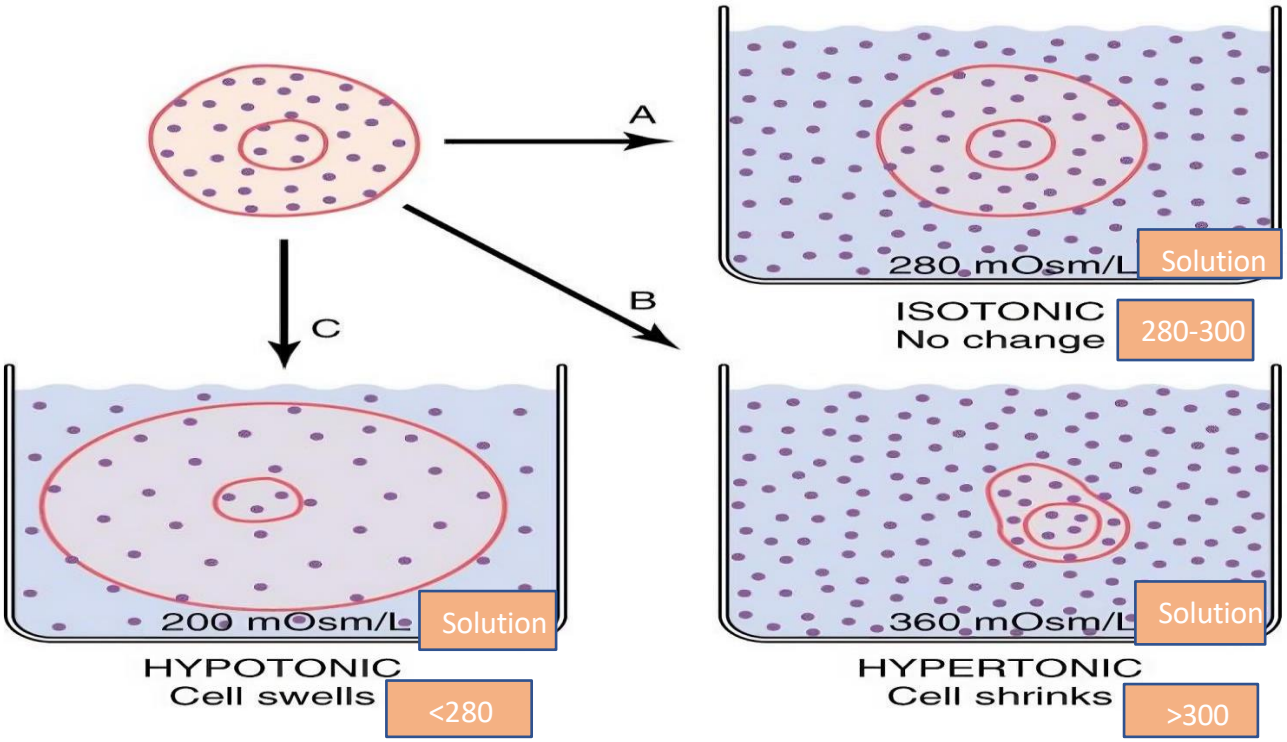
The difference between osmolarity and osmolality is small, but osmolality is considered more accurate when temperature changes, because temperature affects the volume on which osmolarity depends.

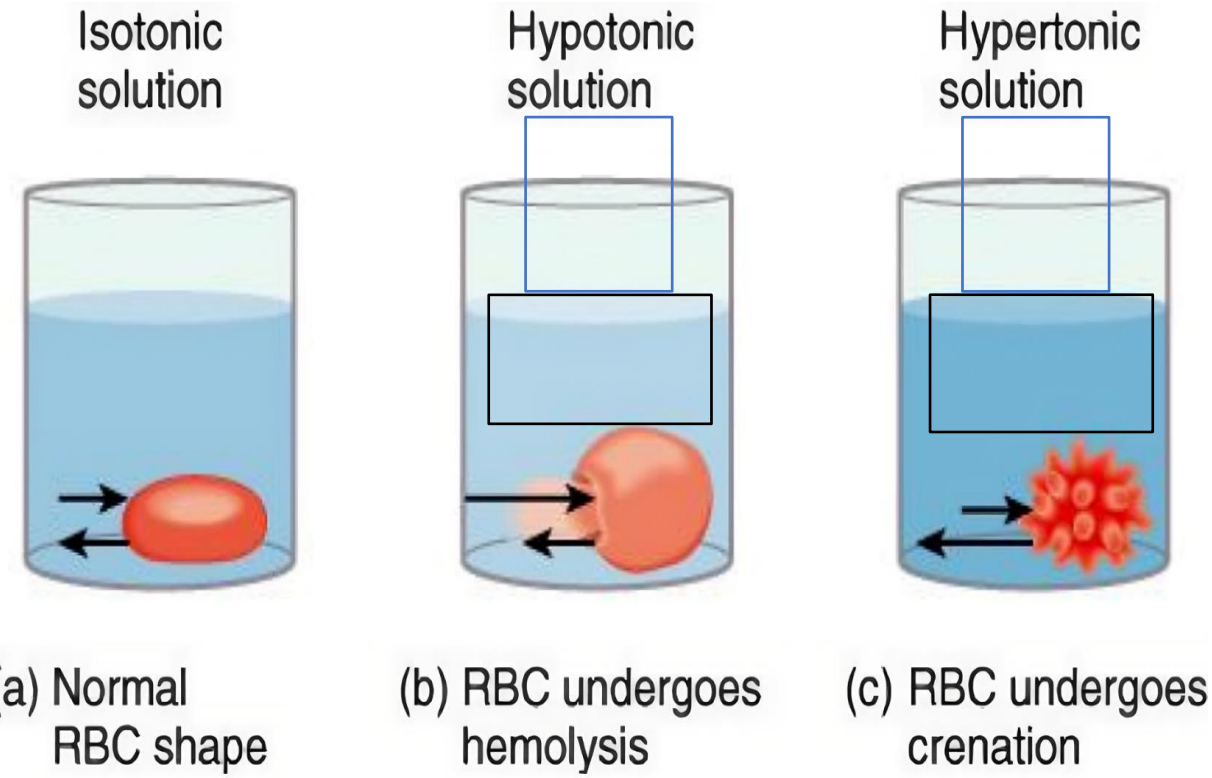
Our cells contain fluid that differs in composition from the extracellular fluid, but they must be similar in osmolarity (~300 mOsm/L).

Why? Because if osmolarity inside and outside the cell were very different, water would move excessively into or out of the cell, causing cell swelling or shrinking, which can damage the cell.

Here comes the definition of tonicity:

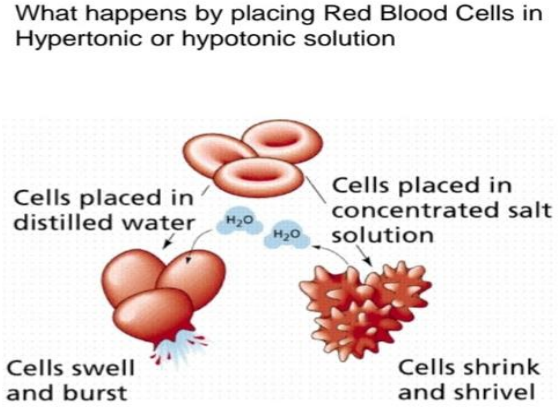
Tonicity of solution: is osmolarity with regard to the osmolarity of plasma (~300 mOsm/L).





QUICK RECAP FOR CLARITY:

- HYPERTONIC SOLUTION → EXTERNAL SOLUTION HIGHER OSMOLARITY THAN INSIDE → WATER LEAVES CELL → CELL SHRINKS
- HYPOTONIC SOLUTION → EXTERNAL SOLUTION LOWER OSMOLARITY THAN INSIDE → WATER ENTERS CELL → CELL SWELLS(BURST)
- ISOTONIC SOLUTION → EXTERNAL SOLUTION SAME OSMOLARITY AS INSIDE → NO NET WATER MOVEMENT → CELL STAYS NORMAL



Question1: Calculate the osmolarity of a 5% glucose solution, assuming a total volume of 1 liter.

5% glucose → 5 g per 100 ml → 50 g per 1 L

Molecular weight of glucose = 180 g/mol

Glucose does not dissociate → 1 mole = 1 osmole

Calculation:

Moles of glucose = 50 ÷ 180 ≈ 0.278 mol/L

Osmolarity = 1 x 0.278 Osm/L ≈ 278 mOsm/L
(we multiply by 1 since glucose does not dissociate)

Question2: How many grams of KCl solution do we need to dissolve in 1 liter to get isotonic solution

Givens:
Isotonic solution = 280 mOsm/L = Osmolarity
liters of solution = 1 liter

Step 1:

Osmolarity = i x M
where i = number of dissociate ions
and M = molarity of the solution

KCl dissociates into 2 ions (K+ and Cl-)

280 mOsm/L = 2 x M
M = 140 mmol/L

Step 2:
Molarity = n / V
where n = number of moles and V = liters of solution

140 mmol/L = n / 1
n = 140 mmol = 0.14 mol

n = m / mm
where m = mass and mm = molar mass

0.14 = m/74.55
m = 10.437 grams of KCl

Membranes and Transport:

Modalities of transport:

DIFFUSION:

Generally, dissolved particles found in solution are in constant movement. This random motion is due to thermal energy in particles that found themselves at a temperature above the absolute zero (in living systems about 310 degrees K). The random motion in liquids and gases will result in a random collision of particles with each other and with the wall. These haphazard collisions will cause a transfer of kinetic energy from one particle to another and change in the direction of motion. This continuous movement in liquids and gases is known as ***diffusion***.

Diffusion through biological membranes:

Particles can move across biological membrane by diffusion. This type of transport does **not** need consumption of energetic compounds (ATP). It is passive. Because of the lipid constituents of the membrane, only lipid soluble substances can diffuse through the lipid structures. Their diffusion depends on the solubility of particles in the lipid bilayer. Example: O2, CO2, NO and lipid particles can diffuse through the lipid structures.

While water soluble particles cannot pass the bilayer. But, they can be transported across membrane through protein channels. This type of transport is can also be characterized as ***simple diffusion (in some literature is considered as FACILITATD DIFFUSION*** by considering have a protein structure (channel) helped these particles to move across membrane. Also, there are some particles can NOT diffuse through membrane only with the help of a protein structures known as **carriers**. This type of diffusion of particles is known as **facilitated diffusion**.

Factors that influence simple diffusion:

- *Concentration*: More concentration of a substance means more kinetic energy in particles in a given compartment.

Movement of particles across membranes depends on the ***concentration of substances***. Less particles from compartment B where are found in a lower concentration will move to compartment A where are found in a higher concentration.

The Net rate of diffusion (Q) of particles is (diffusion rate from A to B (-) diffusion rate from B to A). One of the factors that influence the rate of net diffusion is *concentration gradient* ($\Delta C = C_A - C_B$), which represents the **Chemical Potential** for movement of particles across membranes.

In addition to concentration gradient, net rate of diffusion (Q) depends also on:

- ***Permeability*** of the membrane to a given substance (P): the higher the permeability for a substance the greater the diffusion rate is through membrane.

- ***Surface area*** of transport (A): diffusion increases by increasing (A). The increase in surface area in biological membranes will result in more protein channels that can be used for diffusion from one compartment to another.

- ***Molecular weight*** (MW): lighter molecules move more quickly than heavier.

-***Membrane thickness*** (X) (distance of movement): the greater the distance the slower the rate of diffusion.

All these factors form the Ficks' law of diffusion:

$J = P.\Delta C$.....(J = Flux, P=Permeability,
ΔC = Concentration gradient)

$P = D.A/\Delta X$.....(, A: surface Area, ΔX = membrane Thickness)

$J = D.A.\Delta C/\Delta X$..... (D=Diffusion Coefficient)

In addition to all these factors, diffusion can also be influenced by:

- ***Effect of membrane electrical potential***: mainly influences electrically charged particles.

The presence of a negative potential inside the cell prevents movement of negative (-) charged particles from the extracellular compartment to the intracellular compartment and the positive charged particles from the intracellular to the extracellular compartment.

So, movement of charged particles is governed by an **electro-chemical potential**. This will be discussed in more details later.

- ***Effect of pressure***:

The presence of pressure difference between two compartments

will cause more kinetic energy in particles in the compartment with higher pressure. This will cause movement of more particles from the high pressure side to the low pressure side.

* Factors that influence facilitated diffusion:

This carrier mediated transport also depends on *concentration gradient* of transported substance, with the difference that the rate of transport approaches a maximum called V_{max} . The increase in the rate of net diffusion in simple diffusion is proportional with the ΔC, while in facilitated diffusion when V_{max} is approached no more increase in diffusion will be by increasing ΔC. The limitation is due to the presence of limited number of *carrier molecules* at the membrane.

OSMOSIS:

Not only the particles of solute are transported across membranes, but also water can move across membranes. Under normal circumstances the **net** movement of water across plasma membrane is zero. This keeps the cell volume constant. Under the condition that membrane is NOT permeable to solute particles and there is a concentration difference of particles between the two sides of a membrane. Water can move from the compartment of higher concentration of water (low solute concentration) to the compartment of lower water concentration (high solute concentration). This movement of water is known as **osmosis**.

If a pressure is applied to the side where the concentration of solute is high, this will reduce, stop movement of water molecules to that side. The amount of pressure needed to stop osmosis is known as **osmotic pressure** of that solution.

The osmotic pressure of a solution depends on the concentration of particles in that solution (osmolar concentration). So, one mole of NaCl solution will dissociate in solution to Na+ and Cl- and will have twice osmotic pressure (2 osmolar concentration) as one mole of glucose (one osmolar concentration).

Osmolality = number of osmoles per kg water

Osmolarity = number of osmoles per liter of solution

Tonicity of solution: is osmolarity with regard to the osmolarity of plasma (300 mosmoles). (hypertonic solution has osmolarity higher than plasma. Hypotonic solution has osmolarity lower than plasma. In Isotonic solution, the osmolarity is equal to that of plasma)

Other Modalities of Transport:

VESICULAR TRANSPORT:

Large particles can NOT pass membranes. But these particles are packaged and enclosed into vesicles by certain organelles, then these vesicles can fuse with the plasma membrane in case of transport from the intracellular to the extracellular compartment or engulfed into vesicles at

plasma membrane, then transported inside. In the second case plasma membrane surround the substance that would be ingested by the cell then pinch off with the engulfed materials and form a vesicle. This mechanism is known as **endocytosis**. Vesicular transport can appear between plasma membrane and the membranes of organelles (such as lysosomes, Endoplasmic reticulum, etc) or between the membranes of organelles. When vesicles are transported through the whole cytoplasm (from one pole to the other pole of plasma membrane) the process is known as (**transcytosis**). If only fluids are transported by vesicular transport from the extracellular compartment, the process is called **pinocytosis.** When large and multimolecular particles are transported by endocytosis, the process is called **phagocytosis**.

The opposite of endocytosis is **exocytosis**. Large synthesized molecules such as enzymes, hormones, neurotransmitters are packaged into vesicles and transported toward plasma membrane. When these vesicles fuse with plasma membrane, their content is released into extracellular fluid. By vesicular transport not only secretory particles are transported toward plasma membrane, but also specific components of the membrane such as channels, receptors, and carriers are added to membrane by fusion of vesicles with plasma membrane.

The release of vesicular content appears to be stimulated event in secretory cells. When the cell is triggered by stimulus, Ca++ increases inside the cytosol, which results in fusion of vesicles and secretion. An example of exocytosis is the release of neurotransmitter at neuromuscular junction. This release of transmitter from the nerve endings appears via Ca++ induced exocytosis.

رسالة من الفريق العلمي:

"اللهم أَنْتَ رَبِّي لَا إِلَهَ إِلَّا أَنْتَ ، خَلَقْتنِي وَأَنَا
عَبْدُك ، وَأَنَا عَلَى عَهْدِكَ وَوَعْدَكَ مَا
اسْتَطَعْت ، أَعُوذُ بك مِنْ شَرِّ مَا صَنَعْت ، أَبُوءُ
لَكَ بِنِعْمَتِكَ عَلَيَّ وَأَبُوءُ لَكَ بِذَنْبِي ، فَاغْفِرْ
لِي فَإِنَّهُ لَا يَغْفِرُ الذُّنُوبَ إِلَّا أَنْتَ " .

دعواتكم الطيبة يا كرام

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Versions	Slide #	Before	After
V0 → V1			
V1 → V2			