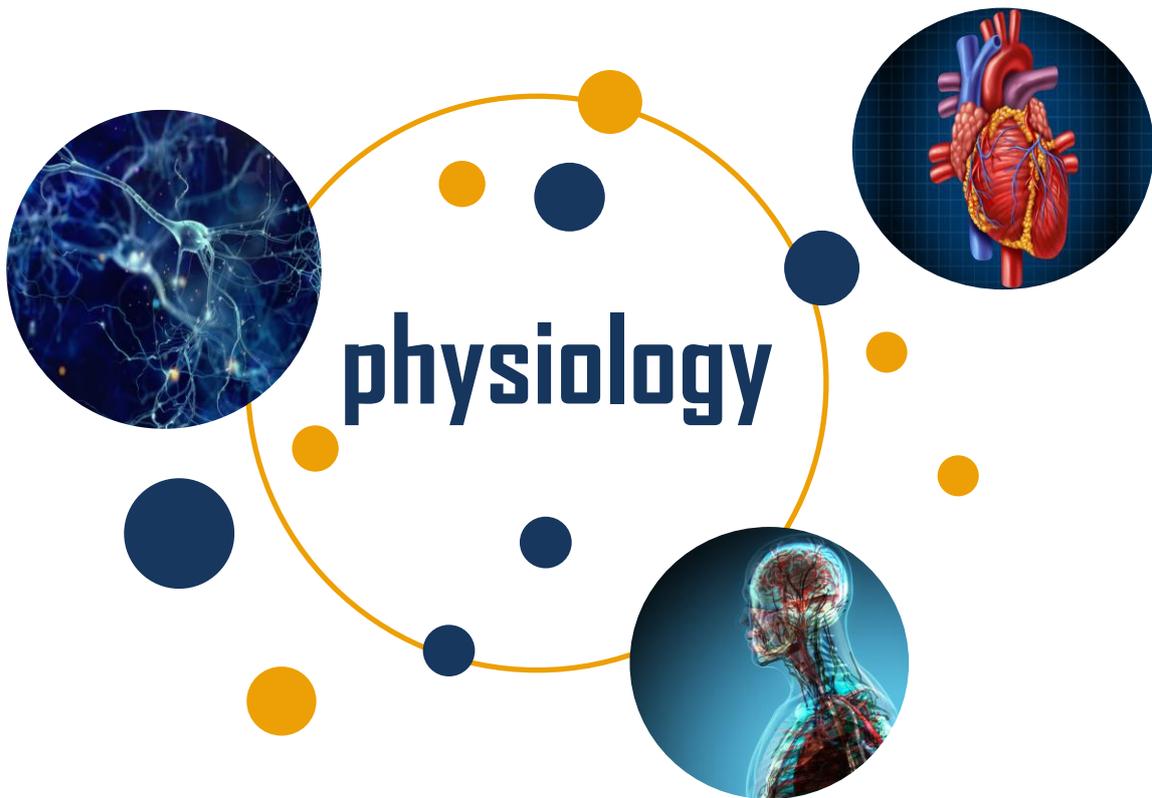


Excellence

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The syllabus

- Homeostasis, control systems, negative & positive feedback mechanism
- Cell Membrane.
- Units: moles, osmoles and equivalent. Osmosis and osmotic pressure
- Transport-I (Passive / Simple Diffusion, Facilitated Diffusion, Osmosis)
- Transport-II (Active / Primary Active, Secondary Active: Co-and Counter-Transport, Vesicular transport)
- Excitable Membranes: Resting Membrane Potential: Origin and Determinants. Distribution Of Different Ions Across Cell Membranes
- Electrochemical Equilibrium (Nernst Equation) As a Predictor For RMP
(E_{Na^+} , E_{K^+} , $E_{Ca^{++}}$, E_{Cl^-} / Other Equations Which Predict RMP: Goldman-Hodgkin-Katz Equation And Chord Conductance Equation)
- Autonomic Nervous System (I) Organization: Sympathetic and Parasympathetic.
- Autonomic Nervous System (II)
- Body Water: Distribution & Measurements
- Abnormalities of body fluid volume regulation Hypo-osmotic dehydration & overhydration. Hyper-osmotic dehydration & overhydration. Edema (definition, types, difference between IC & EC edema).

- All or none versus graded potential
- Excitatory Post Synaptic Potential EPSP And Inhibitory Post Synaptic Potential IPS
- Action Potential: Cardiac Action Potential (Fast Response AP) Vs Slow Response AP (The Pacemaker Concept)
- Basic neuronal circuits: Synapses: types, transmission of AP, neurotransmitters, facilitation, inhibition, summation, electrical events, processing, fatigue...etc.
 - Excitatory and Inhibitory postsynaptic potential
- - Neurotransmitters, types, synthesis, location (pre-and postganglionic)
 - Receptors: types and location.
 - Adrenal medulla.
- Neurons: Types and classifications
- Microcirculation: Capillary Structure; Fluid Filtration (Forces) & Reabsorption, (Starling Law of Capillary Exchange / Lymphatic System)
- Receptors: types and adaptation
- Signal Transduction (Regulation of cellular machinery)
 - Extracellular regulators: nervous, endocrine, paracrine and autocrine
- Steroids: Their Signal Transduction and Mechanism of Action.

First of all, what is **Physiology**?!

- The science that is concerned with the **function** of the living organism and its parts, and of the physical and chemical processes involved.
- The science of **body functions**

Systems emerge to meet the needs of the body such as the need for supplying the cells with nutrients and to get rid of the wastes

❖ **System level**

- **A system consists of related organs with a common function**
- Explanatory example of the Organ-system level → Digestive system breaks down and absorbs food, also it includes organs such as the mouth, small and large intestines, liver, gallbladder and pancreas
- Each system works for a certain function, but all of them work for a general function which is keeping the internal environment almost constant, that is known as **Homeostatic function**

So, what is homeostasis?!

- It is a condition of **equilibrium** (balance) in the internal environment of the body, where it is maintained at an almost **constant** level
- Homeostasis is **dynamic** not static, that means that the body has a **normal range** of values for each variable (with narrow variation)

Wait a minute.... What is a variable?? 

A variable is a condition in the internal environment of the body, such as blood pressure (BP), blood glucose level (BGL), body temperature, PH of blood, concentration of {CO₂, O₂, Na⁺, K⁺, Ca⁺²}

الخلاصة



- Homeostasis هي حالة من الاتزان الداخلي للجسم و تكون هذه الحالة ثابتة إلى حد كبير
- طيب شو قصدك بكلمة إلى حد كبير!!!
- لأنه المتغيرات والظروف بالجسم ثابتة بشكل حركي (غير جامد) و بالتالي لا يكون هناك قيمة واحدة ثابتة وطبيعية لهذه الظروف ولكن يجب أن تبقى القيمة في مدى محدد (مثلا: عشان تجيب بالمادة A لازم علامتك تكون بين 92 و 100 وما بتحكي لازم علامتك تكون فقط 100) تمام؟! 😊

If there is a disturbance (abnormal changes) in the homeostasis → Feedback system works to restore the homeostasis (balance)

Feedback System

- It keeps the internal environment constant.

Feedback system has three Basic components:

1.Receptors:

- Body structures that monitor changes in a controlled condition.
- Sends input to the control center.
- Example: Nerve ending of the skin in response to temperature change.

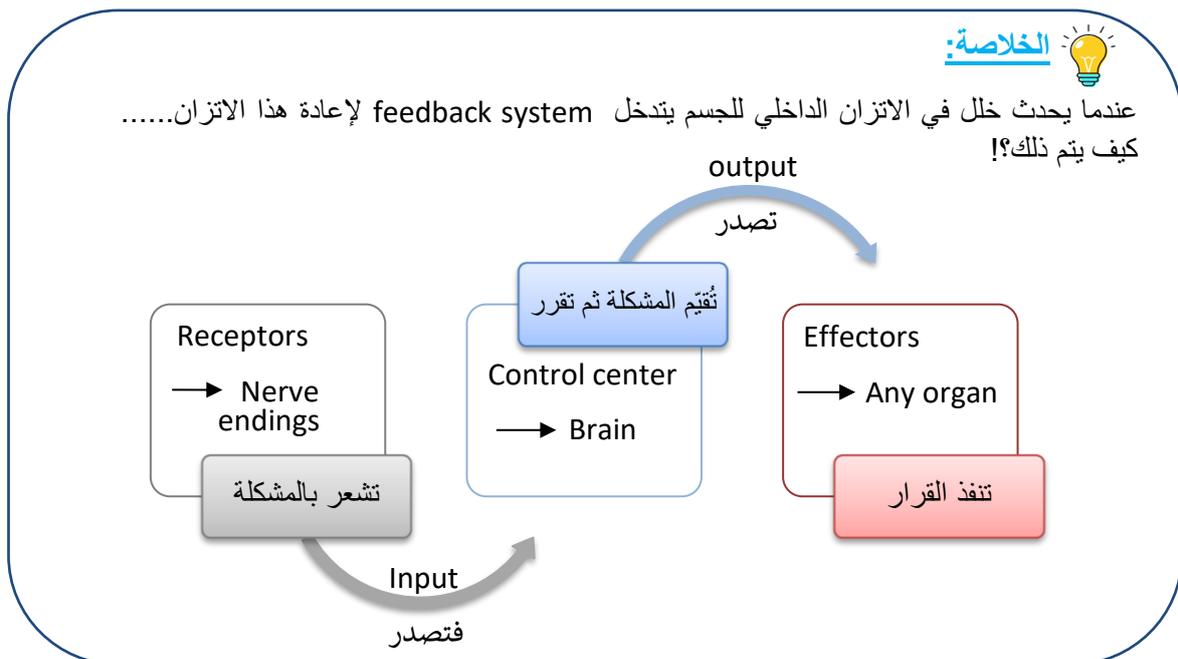
2.Control center:

- Brain
- Sets the range of values to be maintained.
- Evaluates input received from receptors and generates output command.
- Example: Brain acts as a control center by receiving nerve impulses from skin temperature receptors.

Note: The input and output signals could be either nerve impulses (nervous system) or hormones (endocrine system)

3.Effectors:

- Receives output from the control center.
- Produces a response or effect that changes the controlled condition.
- Found in nearly every organ or tissue.
- Example: Body temperature drops skin receptors sense drop the brain sends impulse to effector (skeletal muscles) muscles contract rapidly causing shivering which generates heat



Negative and Positive Feedback systems

❖ Positive Feedback systems

- **Strengthen or reinforce** a change in a controlled condition
- Examples:

➤ Normal childbirth:

During this process the uterus start contract slowly and infrequently, and these contractions increases until the delivery of a baby takes place.

*Notice that the response (increase in contractions) is in the **same direction** as the stimulus (which is the beginning of the contractions)

➤ Blood Loss:

- Normally the heart pumps the blood to body cells (for nutrients and oxygen)
- **BUT** when there is a severe loss of blood so the **blood pressure will drop** then cells won't take sufficient nutrient and oxygen, if the loss continues → heart cells become weaker → doesn't pump blood → **blood pressure (BP) continues to fall**

❖ Negative Feedback systems

- **Reverses** a change in a controlled condition
- stimulus and response **opposite** each other (if one of them increases the other one decreases)

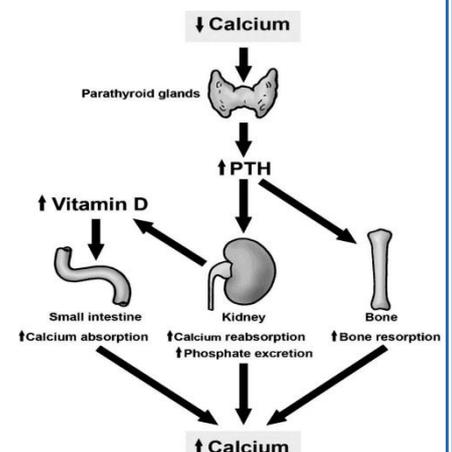
Examples:

➤ PH changes

- When it decreases this system increase it to the normal level

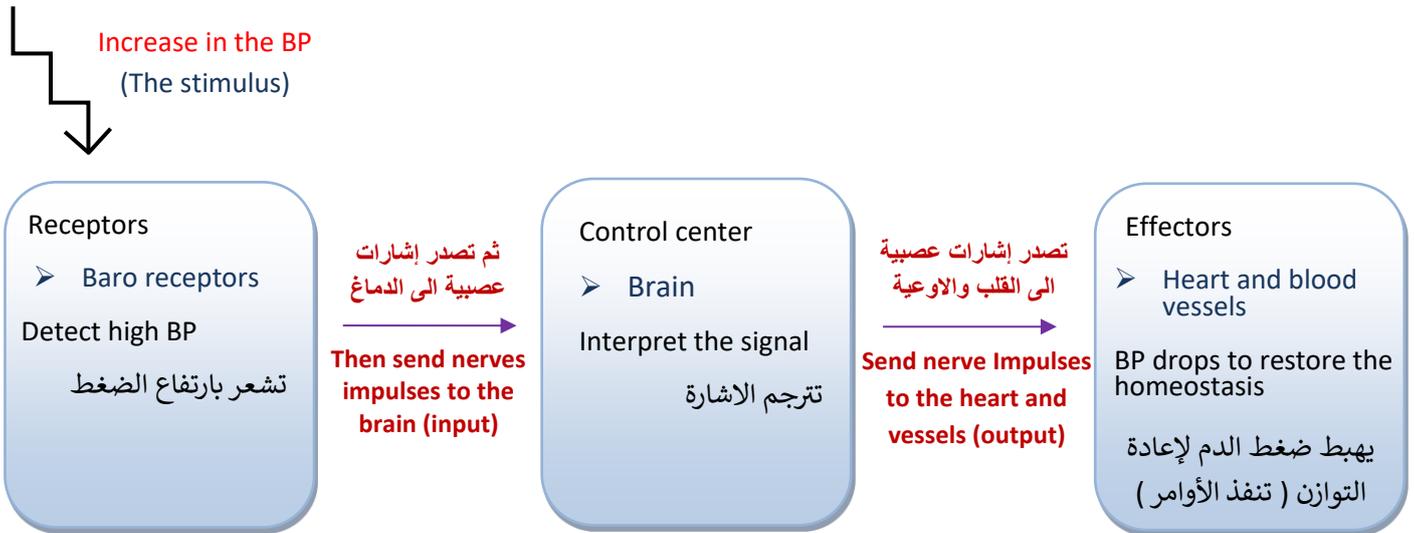
➤ Regulation of calcium levels

- Decrease in Ca^{+2} levels → receptors sense this decrease → send inputs to the control system (brain) → Brain analyzes this signal then → sends outputs to the effector (parathyroid gland)
- This gland will try to restore the homeostasis in several ways



➤ Regulation of blood pressure

So how blood pressure is regulated by negative feedback system?



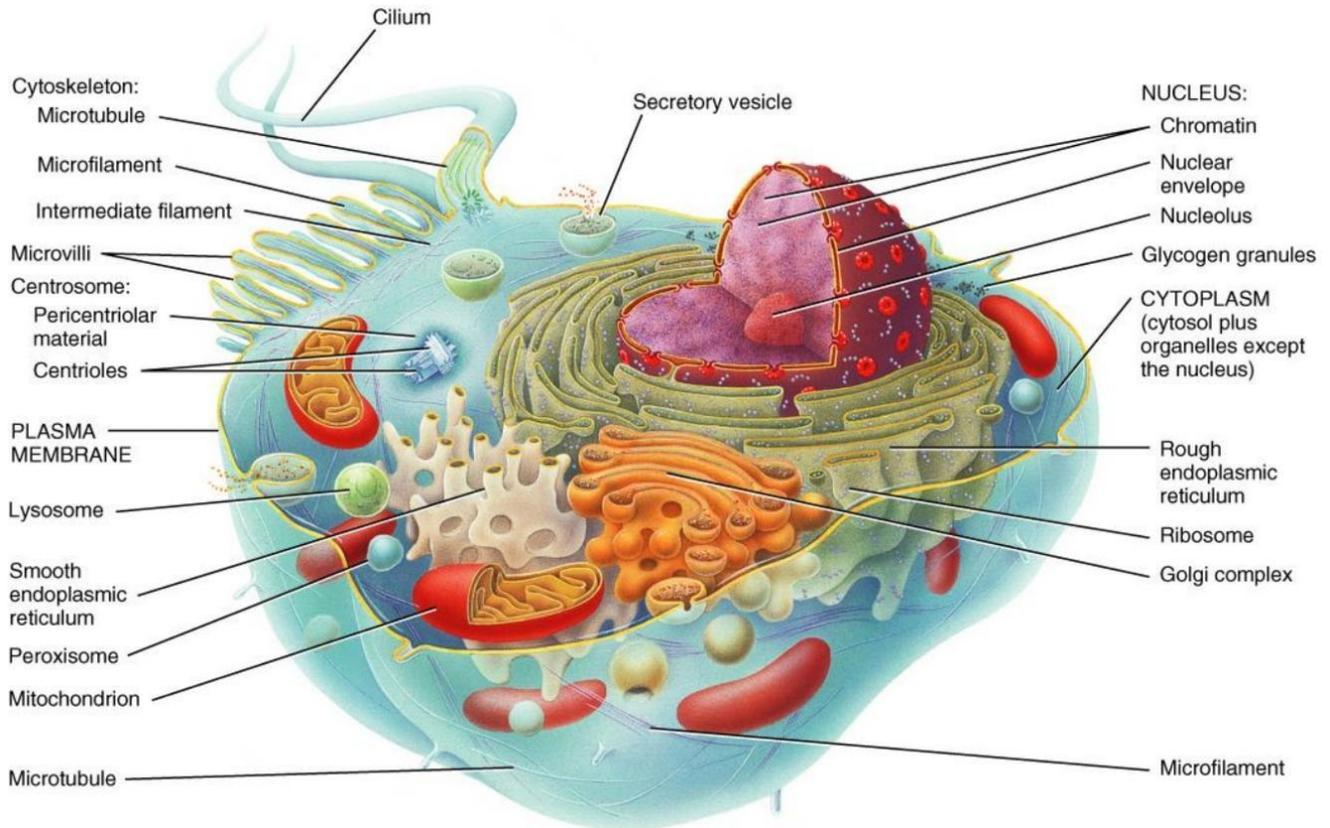
Note: افهم المثال و احفظ الملاحظة

- What is baro receptors? The receptors that is sensitive to pressure
- Notice that the response (decrease in BP) negate the stimulus (increase in BP)
- ❖ **Blood pressure** is the force exerted by blood as it presses against the walls of the blood vessels (*the resistance to blood flow*)
- ❖ **Vasodilation**: decrease in BP (so decrease in the resistance to blood flow)
- ❖ **Vasoconstriction**: increase in BP (so increase in the resistance)

الخلاصة:

- عند حدوث مؤثر في الاتزان الداخلي يتدخل Feedback system، فإذا كان هذا التدخل:
- بنفس اتجاه ونمط المؤثر يكون positive feedback
 - بعكس اتجاه ونمط المؤثر يكون negative feedback
- اما الأمثلة فهم وليس حفظ بصم

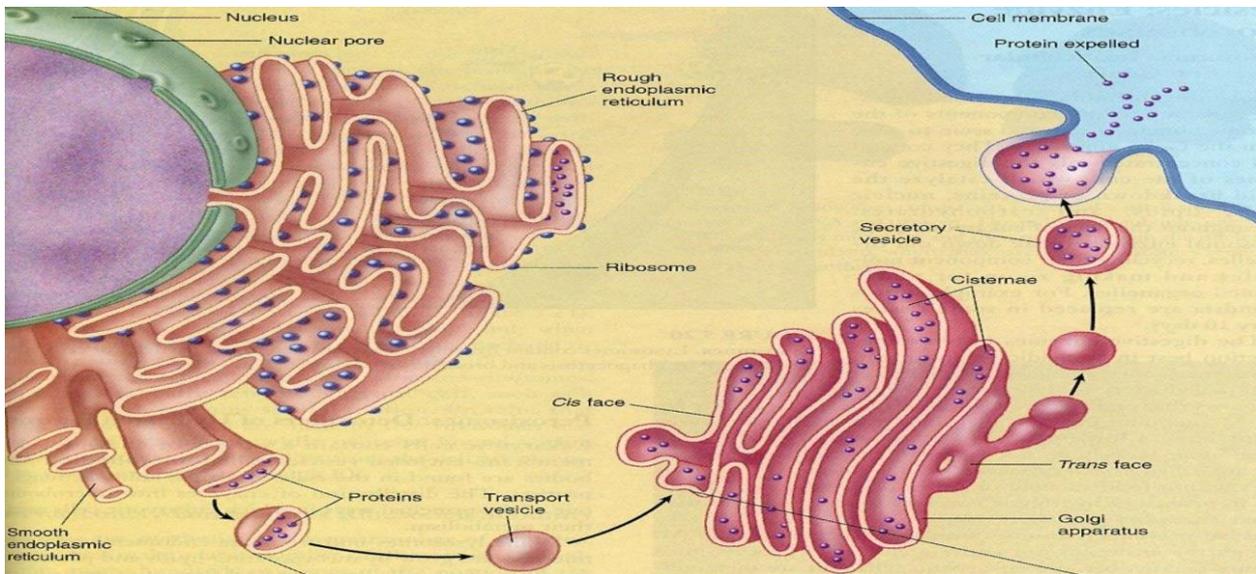
Generalized Body Cell:



- ✓ The outer boundary of the cell → **Plasma membrane**
- ✓ The plasma membrane separates the internal environment of the cell from the external environment
- ✓ It is a selective barrier
- ✓ Membranes are made from a lipid bilayer that contains proteins
- ✓ Cells have also membranes in the cytosol, these membranes:
 - Surround the organelles
 - Lead to compartmentalization and separate each organelle from the others and this help in controlling cell functions

❖ Endoplasmic Reticulum:

- It is a membrane bound organelle
- It is divided into rough endoplasmic reticulum (RER) and smooth endoplasmic reticulum (SER)
- RER has Ribosome on its surface



❖ Ribosomes:

- It is the apparatus responsible for **protein synthesis**

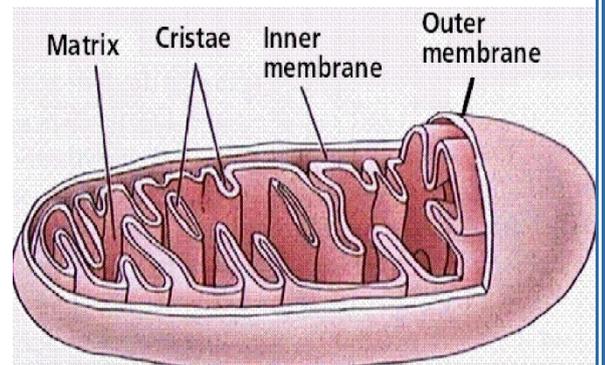
❖ Lysosomes:

- Membrane bound organelles
- They contain digestive enzymes to break materials

❖ Mitochondria:

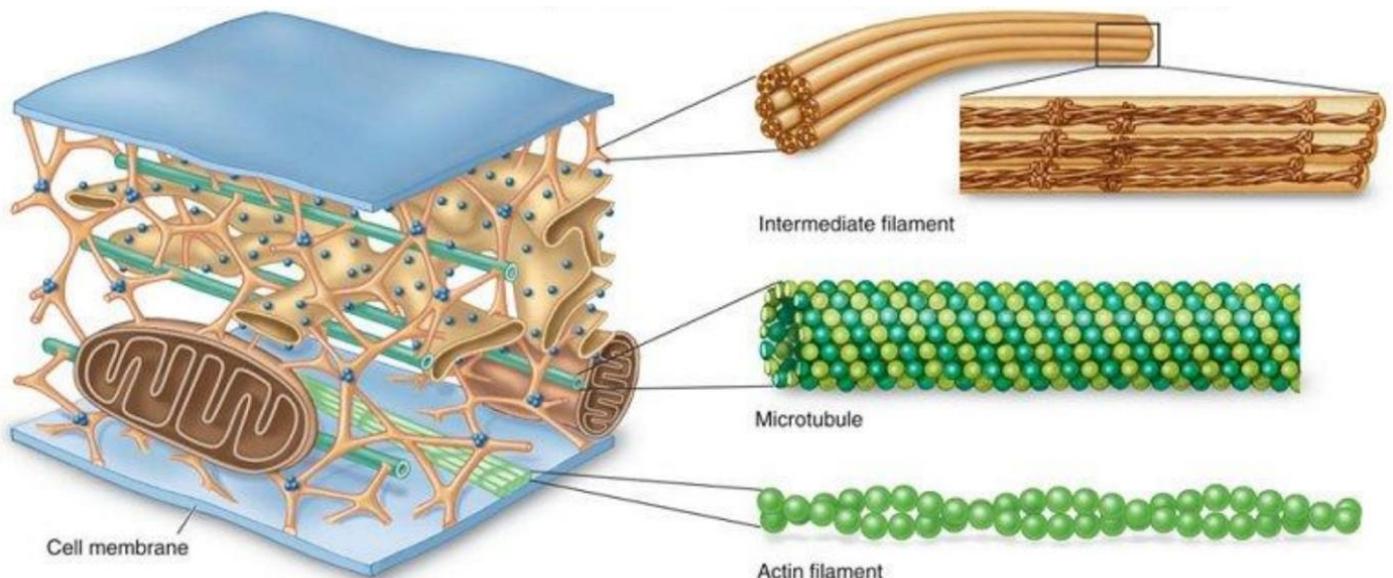
- It is double membranous → 2 membranes (inner and outer membranes)
- Contain high concentration of protons (H^+) in the intramembranous space → due to the presence of ETC (electron transport chain)

- In the ETC → electrons move through ETC complexes from a high energy state into a lower energy state
- The energy difference is used to pump protons from the matrix into the intramembranous space
- The last complex (5th) is ATP synthase → use the concentration gradient of protons to produce ATP



❖ Cytoskeleton:

- They are composed of proteins → examples are microtubules, actin filaments and intermediate filaments
- They **determine the shape of the cell** (shape serves the function)
 - Muscle cells are elongated → increase the efficiency of contraction
 - Red blood cells are biconcave disks → to bind oxygen and diffuse more efficiently
 - In neurons we have dendrites which increase surface area to receive more signals
- Help in **transporting material and vesicles** inside the cells (mainly microtubules)
- Microtubules make the **mitotic spindles** which help in cell division



- **Microtubules make Cilia** which project from the surface of the cell and cilia are responsible for moving mucus
- **Actin filaments form pseudopods** → help in moving the cell
- Actin filaments participate in **muscles contraction**

Structure of the Membrane:

- **It is composed from a lipid bilayer** → made up of phospholipids, cholesterol and glycolipids
 - Phospholipids have a **polar head (hydrophilic)** and **2 hydrocarbon (hydrophobic) tails**
 - Cholesterol → decrease membrane fluidity (decrease the movement of the membrane and increase its stability)
- The membrane is not static (**Dynamic**) and it is constantly moving

- It contains many proteins:

1. Integral proteins:

- Extend through the lipid bilayer
- Usually act as channels and carriers

2. Peripheral proteins:

- attached to the inner or outer surface of the membrane, do not extend through it
- Involved in maintaining cell shape, cell motility and can be enzymes

Glycoproteins:

- Membrane proteins with a carbohydrate group
- This carbohydrate group protrudes to the ECF

Membrane proteins:

They can act as channels, carriers, linkers, enzymes and cell identity markers:

1) Channels:

- They can act as channels to move ions across the membrane **down their concentration gradient**
- These channels can be linked to receptors
- **Aquaporins:** They are channels that move water across a membrane

2) Carriers:

- They are proteins that transport molecules across the membrane by having **conformational changes** in the protein structure
- They can transport molecules **down** their concentration gradient (facilitated diffusion) or **against** concentration gradient (active transport)

3) Linkers:

- They are the junction between cells that connect them together and allow them to communicate

- There are 3 types of linkers:

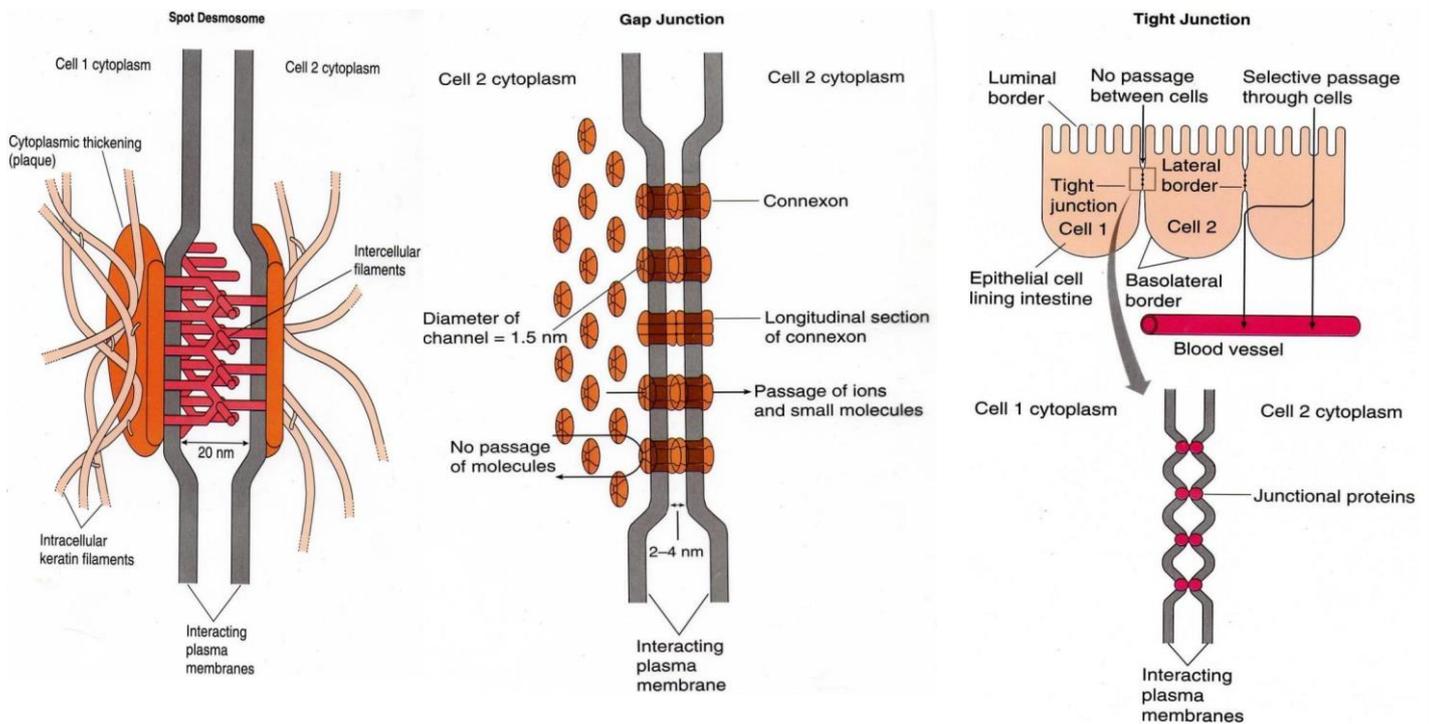
- **Tight junctions**

- **Gap junctions**

- ✓ They are pores between cells, allow them to exchange materials and communicate

- **Desmosomes (Adhering junctions)**

- ✓ They help cells to keep in contact next to each other and they are attached to cytoskeleton



4) Cell identity markers:

Each cell has unique glycoproteins, which help in identifying the cell

Membrane Permeability

Plasma membrane is selective, what does it mean?!

- That means that it is either permeable to certain molecule or impermeable
 - It is amenable (permeable) to **lipid soluble substances** (such as O₂, CO₂, water and steroids), because it is a phospholipid bilayer
 - Other molecules that are impermeable (such as ions and glucose) are transported across the membrane by transmembrane proteins (**channels and transporters**)

There are 2 types of transporting the molecules across a membrane:

1) Passive transport

2) Active transport

First, Passive transport:

- ❖ Substances move across cell membranes without the input of **any energy** {from **higher concentration to lower concentration**, we call it downhill}
- ❖ Does it need input of energy? **NOOO**
So, what drives it to move across the membrane? The kinetic energy of the molecules

The movement of molecules from the higher concentration to the lower concentration is called diffusion (which is a passive transport)

Let's talk about **diffusion rate (J)** ...

There are 5 factors on which diffusion depends:

- **Directly proportional:** Concentration Gradient, surface area, solubility in lipid .
- **inversely proportional:** square root of molar mass, thickness of membrane .

Also, diffusion depends on temperature

Note:

We can call Diffusion using **Channels** either Facilitated or simple diffusion by channels

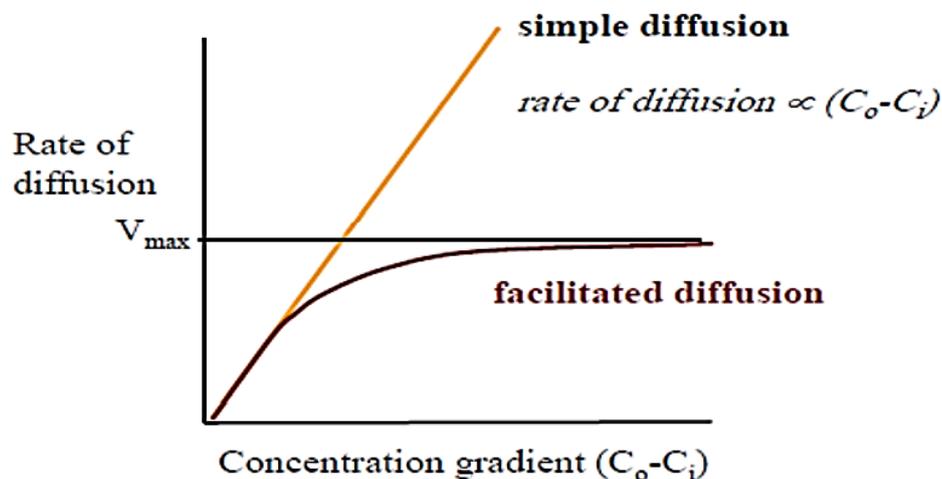
- Some channels have a **gate**... How these gates are opened and closed??

By:

- Change in voltage (**Voltage-gated**)
- Change in the concentration of a particular Substance (**Chemically-gated**)

❖ Facilitated diffusion (by carriers) has a **limit** and a **maximum** of diffusion rate (this maximum is called T max or V max) ... So, it is called **saturable**, **Why??**

- Because it depends on the **number of available carriers** and binding sites
- In the diffusion by channels there is no limit of the rate (no Vmax)



❖ Osmosis

- The net movement of **water** through a **selectively permeable** membrane
- It moves from **High concentration of water to low concentration of water** (or low concentration of solutes to high concentration of solutes)

Water can pass through plasma membrane in 2 ways:

- Through **lipid bilayer** (so we can consider it as Simple diffusion)
- Through **aquaporins**, which are channels specific to water (so we can consider it as Facilitated diffusion)

Before we proceed to the next concept, you should know 2 definitions:

➔ Osmolarity: Number of molecules / Liter water

➔ Osmolality: Number of molecules / Kg water

These 2 definitions are equal (يعني بس اختلاف أسماء)

Osmotic pressure:

Is the pressure needed to be applied to prevent movement of water molecules (also called applied pressure)

It is attributed to the osmolarity of the solution

+ Van't Hoffs equation:

$$\pi = inRT$$

π = Osmotic Pressure

i = number of ions and active molecules

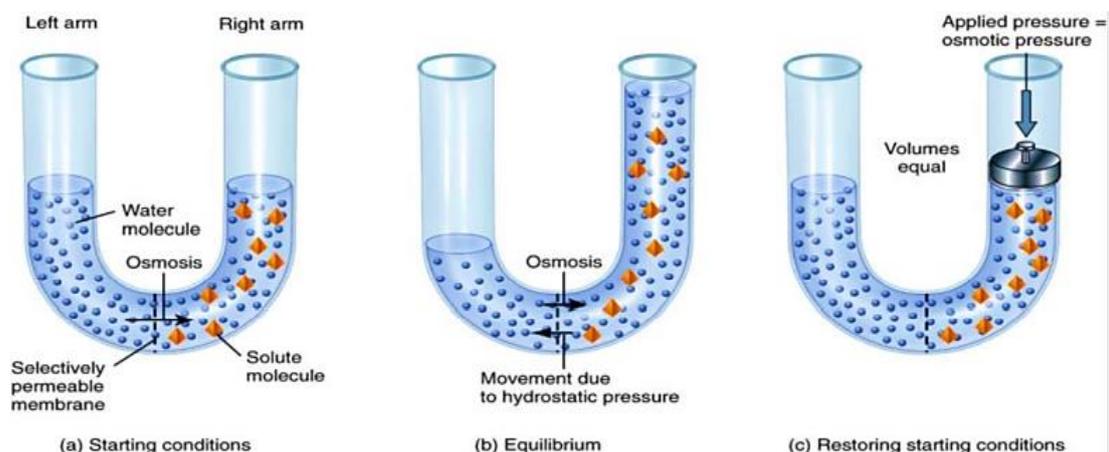
n = Molarity of the solution

R = the universal gas constant

T = Temperature in Kelvin

Note :

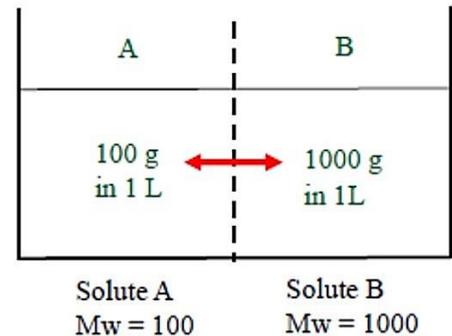
- The higher the molar concentration (n), the higher osmotic pressure is (it is the main factor)
 - The greater the number of osmotically active ions/molecules, the greater the osmotic pressure is سيتم شرح المقصود بها في الفقرات القادمة
 - Osmotic pressure is a colligative property meaning that it depends on the concentration of the solutes not their identity
 - ➔ The osmolarity of 23 g of Na^+ ($M_w = 23$) is equal to osmolarity of 39 g of K^+ ($M_w = 39$) because both has the same number of active particles (ions) which is 1 mole, despite they are different substances
- M_w is the Molecular weight ($\text{Moles} = \text{Mass} / M_w$)



In A: The Molarity is 1 mole/liter (Moles = Mass / Mw = 100 / 100 = 1)

Also in B the Molarity is 1 mole/liter

- So no net movement of water because molarity the same
- Which solution has the greatest osmolarity?
The same
- Which has the greatest molar concentration?
The same
- Which has the greatest number of molecules?
The same



Solution pressures:

❖ Osmotic pressure:

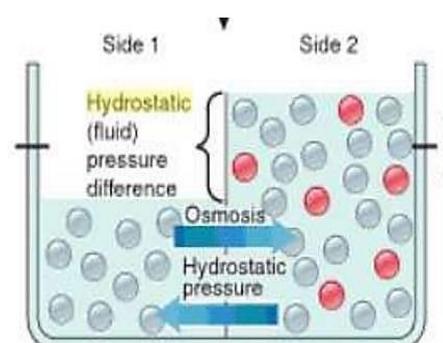
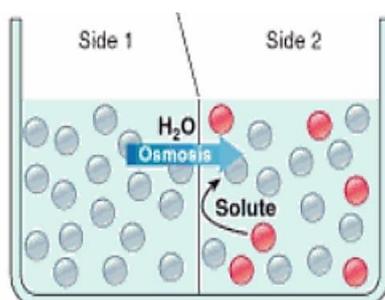
- As we said before but in other way, it is a pulling pressure that measures the tendency of a solution to pull the water into it, because the concentration of non-penetrating solutes (water move toward the higher conc. of solution)

❖ Hydrostatic pressure:

- Is the pressure exerted by a stationary fluidic part of the solution on an object (semi permeable membrane in case of Osmosis)
- Net hydrostatic pressure of a solution = hydrostatic pressure – osmotic pressure and it equals zero at **equilibrium**

❖ What is equilibrium?!

It is a state when the movement of water under osmotic pressure (the tendency to move toward high solute concentration) equals the movement of water under hydrostatic pressure (the tendency of pushing water back through the membrane), so the 2 tendencies are equal as in the picture on the right.



Relation between osmolarity and molarity

- Osmolarity or mOsm/L = The concentration of **particles** per liter solution
 - Molarity or mM/L = index of concentration of **molecules** per liter solution
- 150 mM NaCl = 300 mOsm... Why?

Because osmolarity is the concentration of particles so we have 150mM of Na⁺ and 150 mM of Cl⁻

يعني باختصار عند حساب الاوزمولارية، إذا كان الجزيء قابل للتفكك نفككه ثم نحسب لكن في المولارية لا نفكك الجزيء (نحسبه كما هو)

What is Osmol? Osmolarity caused by a Mole of osmotically **active substances**

300 mM glucose = 300 mOSM (الجلوكوز لا يتفكك بالتالي المولارية تساوي الاوزمولارية)

100 mM CaCl₂=300 mOSM

هذا المركب يتأين ويتفكك إلى أيونين من الكلور وايون كالسيوم وبالتالي الاوزمولارية ٣ أضعاف المولارية فنضربها (٣ب)

- ✓ To make it easier if the Molarity equals (n) the osmolarity equals (i × n)

الخلاصة :



- معدل الانتشار diffusion rate يعتمد على عدة عوامل هي: الفرق في التركيز، مساحة سطح الانتشار، الذائبية في الدهون (طردية)، الجذر الربيعي للكتلة المولية، سماكة الغشاء (عكسي)
- الضغط الاسموزي هو الضغط اللازم تطبيقه على المحلول لإعادته إلى المستوى الطبيعي (ويساوي الضغط الذي تبذله الجزيئات التي لا تخترق الغشاء (All non-penetrable solutes exert osmotic pressure
- الاوزمولارية تمثل تركيز **الدقائق النشطة** (الايونات/يعني بعد تفكك وتأين المركب) في المحلول، بينما المولارية هي تركيز **الجزيئات** في المحلول
- لتسهيل الفكرة ← إذا كانت المولارية = n بالتالي الاوزمولارية = i × n (حيث أن i هي عدد الجزيئات النشطة)

❖ Content of the body fluids:

- In the normal body the ECF & ICF have **the same** osmolarity
- The Osmolarity of Body-fluids (Plasma of blood) is approximately 300 mOsm

NOTE:

If a solution has osmolarity :

- a) Equal 300 mOsm → it is called Isotonic (Isosmolar)
- b) Larger than 300 mOsm → Hypertonic (Hyperosmolar)
- c) Smaller than 300 mOsm → Hypotonic (Hyposmolar)

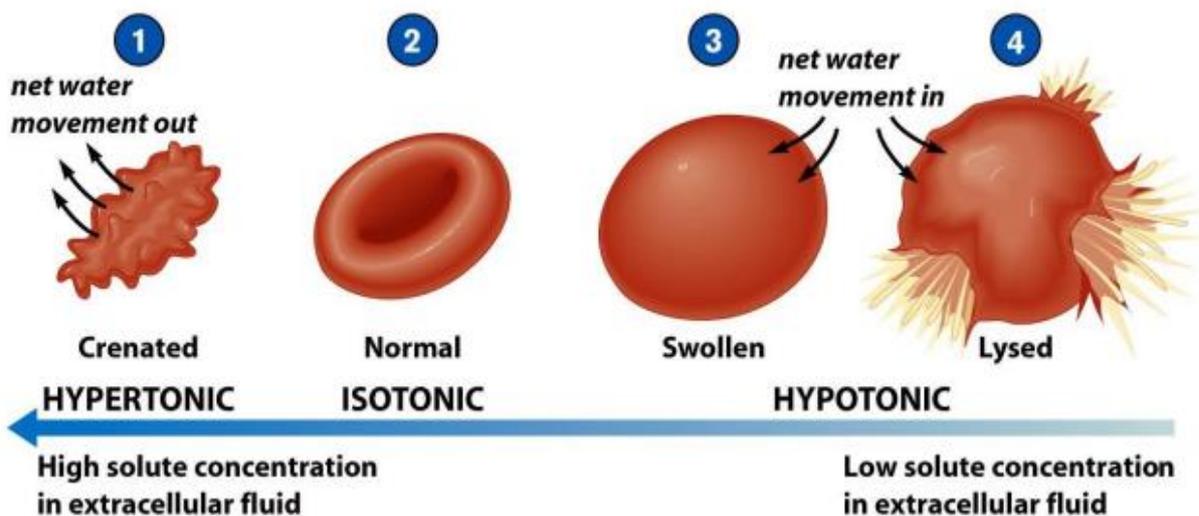
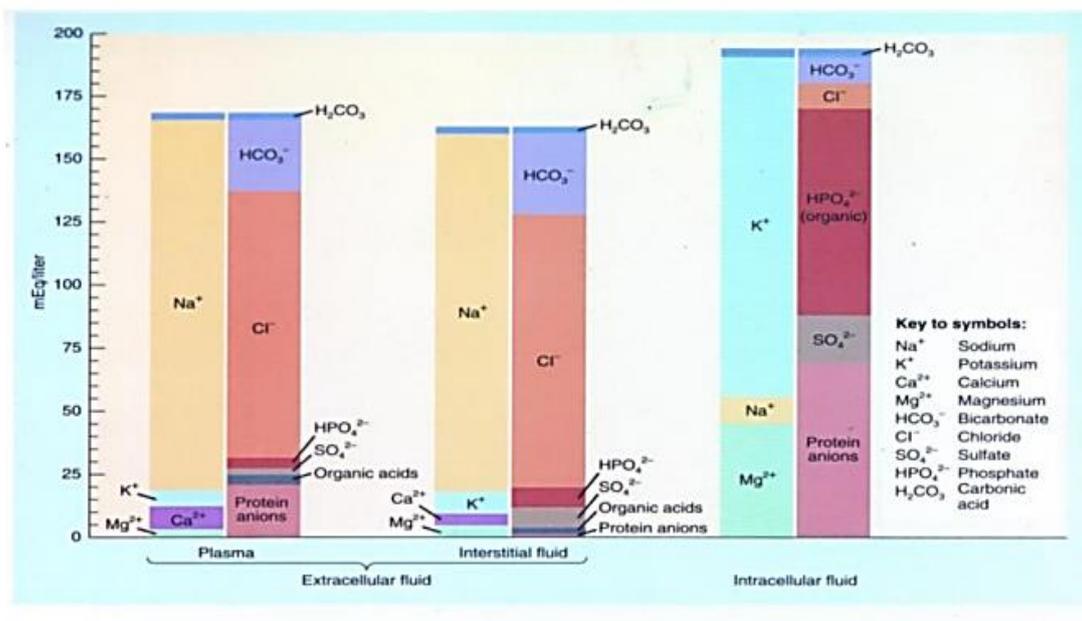
➤ **The ECF:**

- In the blood plasma and the interstitial fluid (both) the **main cation** is sodium ion (Na^+) and the **main anion** is chloride ion (Cl^-) then HCO_3^-
- That means that the osmolarity of the plasma and interstitial mainly depends on the concentration of **sodium and chloride** because they are the main particles.
- The difference between plasma and interstitial is the fact that **proteins anions are present in the plasma more than the interstitial fluid**, Why?

Because the capillaries are impermeable to this proteins so they stay in the plasma (they don't move to the interstitial fluid)

➤ **The ICF:**

- The **main cation** is potassium (K^+) and then magnesium (Mg^{+2}) and the **main anions** are **protein anions** and HPO_4^{-2}



What happens a red blood cell when putting it in:

1. **Isotonic solution:** It **remains normal** (the net movement of water is zero)
 2. **Hypotonic solution:** The water will move toward the higher osmolarity (high solute concentration), so it will enter the cell → causing **hemolysis** → which cause **death**
 3. **Hypertonic solution:** The water will get out from the cells → causing **crenation (Shrinking)**
- ✓ **To make it easier:** Water **always** moves toward the higher osmolarity (higher solute concentration)

Second, Active transport :

- ❖ It requires input of **energy** (uses energy)
- ❖ Solutes are transported **against the concentration gradient** (from the lower conc. to the higher conc.)
- ❖ Such as: Sodium-potassium pump

The Sodium-Potassium pump is called an electrogenic pump?!

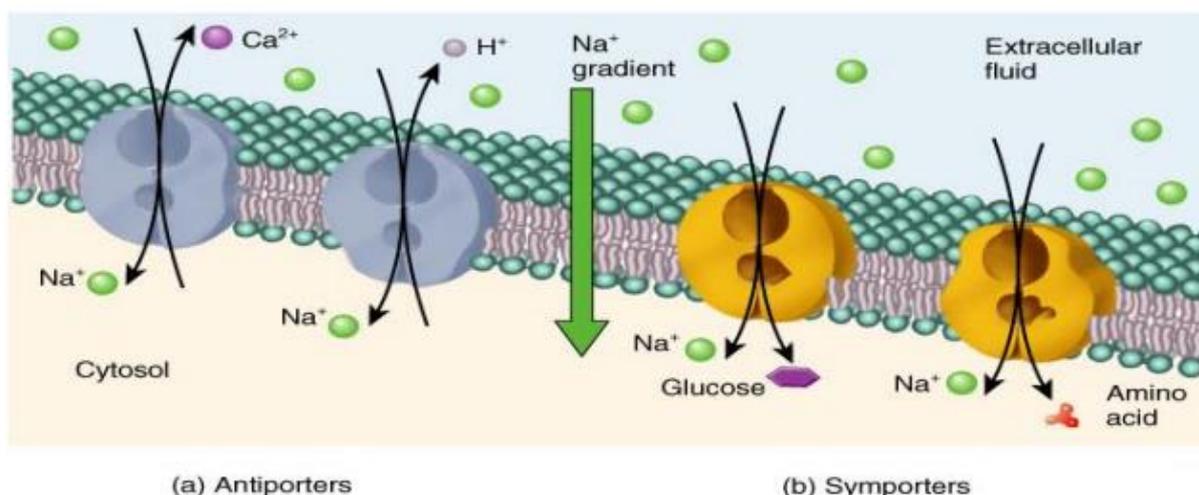
⇒ because it causes a **separation of charges** (Difference in charges inside and outside the cell → **voltage** across the membrane)

❖ **Primary Active Transport:**

- Molecules are “pumped” against a concentration gradient at the expense of energy
- direct use of energy (**Direct use of ATP**)
- driven by pumps such as: Potassium sodium pumps /calcium pumps/ hydrogen pumps

❖ **Secondary Active Transport:**

- Transport is driven by the **energy stored in the concentration gradient** of another molecule (such as Na^+), **indirect use of energy**
- It has 2 types :
 - **Antiporter (Counter transport):** Transport 2 substances in 2 directions (opposite to each other)
 - **Symporter (Co-transport):** Transport 2 substances in 1 direction (the same direction)



- ✓ The primary & secondary active transport are **saturable**
- ✓ It is rate limited by **V_{max} of the transporters**
- ✓ Up to 90% of the cell energy expended for active transport

Finally, Transport In Vesicles:

What is a vesicle? It is a spherical sac that buds from a membrane

❖ Exocytosis:

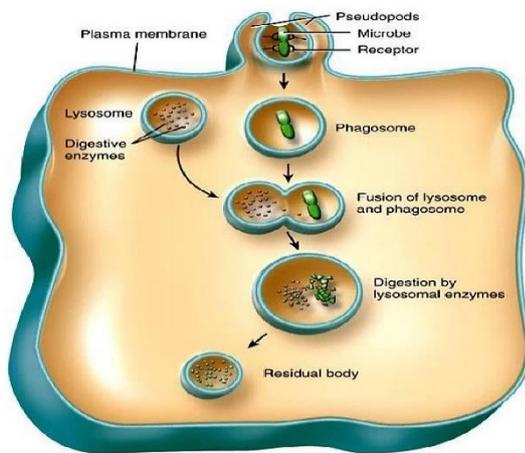
- vesicles fuse with the plasma membrane, releasing their contents into the extracellular fluid

❖ Endocytosis:

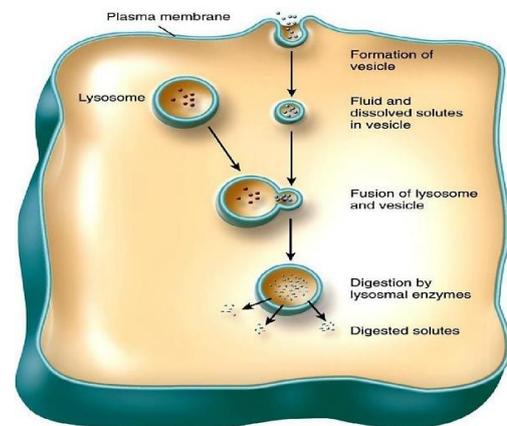
- Materials move into a cell in a vesicle formed from the plasma membrane.
- **There are 3 types of endocytosis :**
 - **Phagocytosis:** cell uses pseudopods to capture the molecules and take it into the cell (to be digested by the Lysosomes)
 - **Pinocytosis (bulk-phase endocytosis):** it is mainly used for fluids, and it may use pseudopods
 - **Receptor mediated endocytosis:** it is almost specific to a certain substance, and it may use pseudopods

❖ Transcytosis:

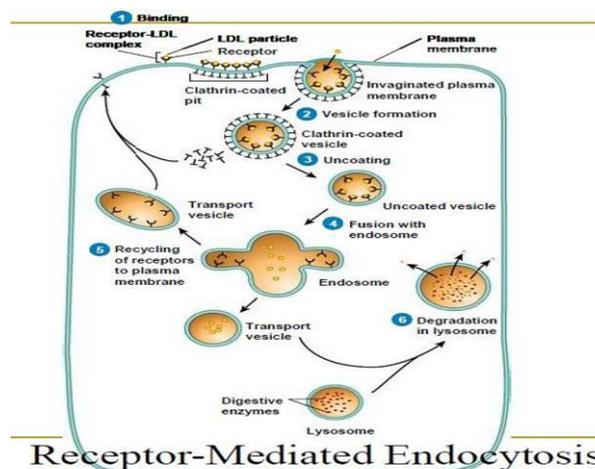
- It is a combination of Endocytosis and Exocytosis at the same time



Phagocytosis



Bulk-phase endocytosis



Receptor-Mediated Endocytosis

Test bank and past papers:

1) An experiment is done to measure the uptake of an amino acid into a cell the above data are obtained. If Na^+ is removed from the extracellular bathing solution, or a drug is added that prevents the cell from making ATP, the uptake of amino acid into the cell is markedly reduced. Based on this information which of the following mechanisms is likely responsible for the transport of the amino acid into the cell?

- A. Uniporter (one molecule unidirectional)
- B. Transport ATPase (pump)
- C. Na^+ symporters (co-transport)
- D. Passive diffusion through the lipid bilayer
- E. Na^+ antiporter (counter transport)

Answer: C

2) Which of the following transport mechanisms is NOT rate limited by an intrinsic transport maximum (V_{max} or T_{max})?

- A. Facilitated diffusion via carrier proteins
- B. Primary active transport via carrier
- C. Secondary counter-transport (antiport)
- D. Secondary co- transport (symport)
- E. Simple diffusion through protein channels

Answer: E

3) Which of the following substances has the highest intracellular fluid to extracellular fluid concentration ratio for most mammalian cells?

- A. Carbon dioxide
- B. Calcium
- C. Proteins
- D. Potassium
- E. Sodium

Answer: D

4) A blood sample is taken from an individual whose blood osmolality is 300 mOsm/kg H_2O , Red blood cells from this sample are then replaced in the following solution, in which solution cells will shrink?

- A. 1
- B. 2
- C. 3
- D. 4
- E. 5

	Molar concentration (mM/liter)
1. Na Cl	150
2. Fructose	300
3. Na HCO ₃	150
4. Ca Cl ₂	150
5. K Cl	100

Answer: D

5) The cell membrane is most permeable to which of the following

- A. Sodium fluoride
- B. Oxygen
- C. Potassium Chloride
- D. Albumin protein
- E. NaCl

Answer: B

6) The forces governing the diffusion of a gas through a biological membrane are listed below. Which of the following changes DECREASE the diffusion of gas through a biological membrane?

- A. A
- B. B
- C. C
- D. D
- E. E

Answer: B

	ΔC	A	S	T	MW
A.	↓	↓	↓	↓	↓
B.	↓	↓	↓	↑	↑
C.	↓	↑	↑	↓	↓
D.	↓	↓	↑	↓	↓
E.	↑	↑	↑	↑	↑

Abbreviations: (ΔC): concentration difference across the membrane; (A): the cross sectional area of the membrane; (S) the solubility of the gas; (T) thickness of the membrane and (MW) the molecular weight of the gas. ↓=decrease, and ↑=increase

7) A cell is equilibrated in an aqueous solution of 300 mOsm/L sodium chloride which of the following best describes what will happen to cell volume when the cell is placed in an aqueous solution of 300 mOsm/L Calcium Chloride?

- A. Decrease and then increase.
- B. Increase and then decrease.
- C. No change
- D. Increase
- E. Decrease

Answer: C



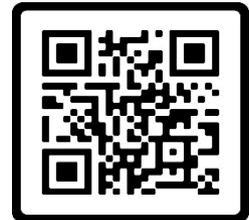
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