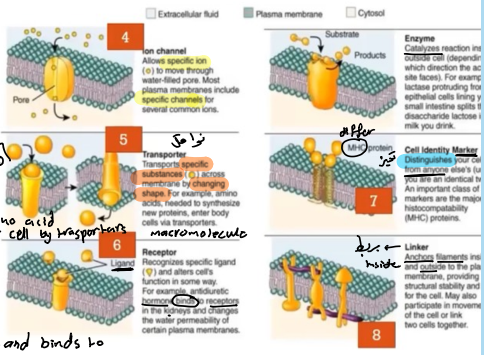
cell membrane

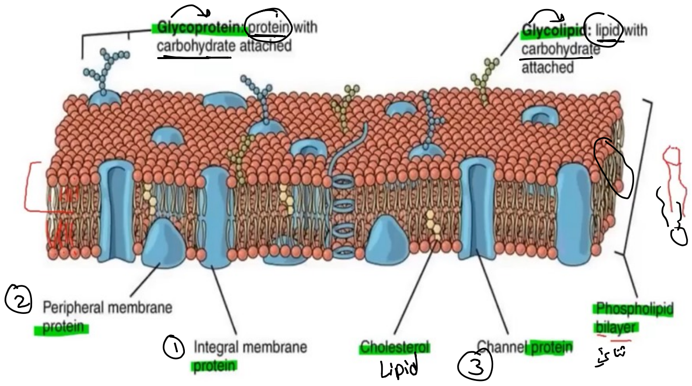
Topics

1- Introduction: cellular membrane is composed of :

2- Lipids: There are many types, most important is phospholipid
→ Lipids maintain fluidity

3- Proteins

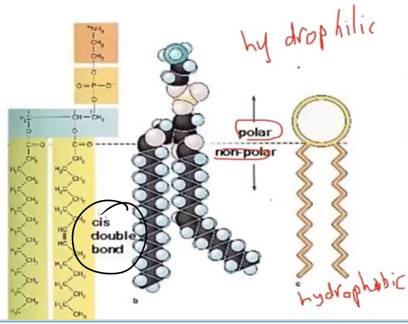




1- INTRODUCTION

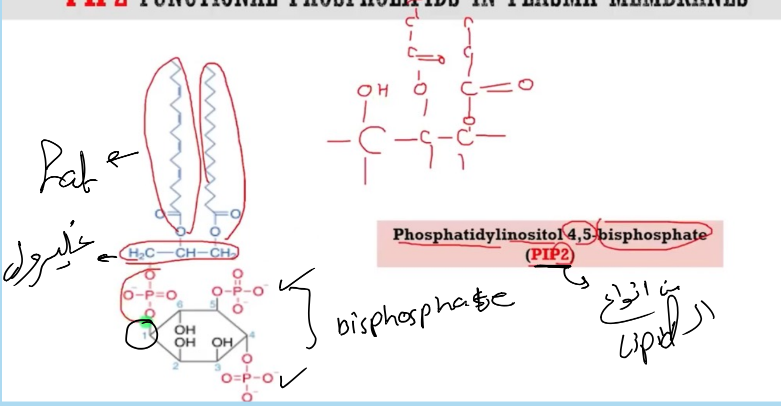
- In general, cellular membrane is a lipid bilayer
- Cellular membrane is composed of:
  1) Lipids: For example, we have glycolipids, phospholipids, cholesterol … etc
  2) Proteins: These proteins achieve several functions, we will see them in this lecture
  3) Carbohydrates

2- LIPIDS



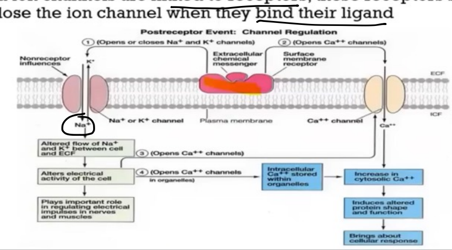
- You can notice here that some carbon chains are unsaturated, and this is important for fluidity
- Best fluidity for membrane is 37C

PIP2 FUNCTIONAL PHOSPHOLIPIDS IN PLASMA MEMBRANES



4- CHANNELS

- Function: transporting things from one side of the membrane to another
- Very specific, so they can pass definite things such as sodium channels, potassium channels, calcium channels, water channels (Aquaporines) …. Etc.
- The activity of these channels are highly controlled, can be controlled by chemical ligands, voltage … etc.
- Ligand gated ion channels are linked to receptors, these receptors send messages to open or close the ion channel when they bind their ligand



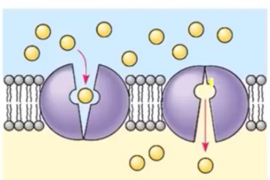
* sodium potassium channels يفتحو لما توصل الخلية ل volte معينة -55

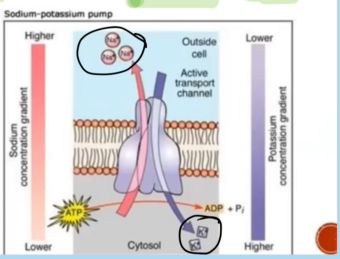
* Some receptors send massage for channel to open OR close when some chemical ligand bind in

5- CARRIERS OR Transportars

يغير التركيب

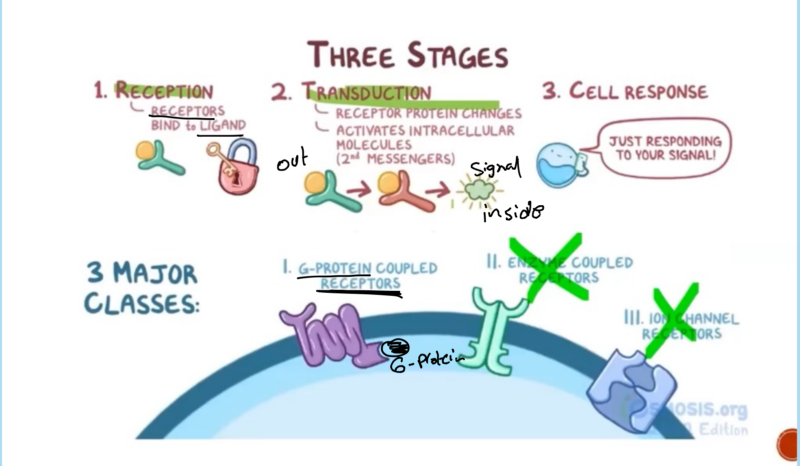
- These proteins induce a conformational change in their structure to move particles from one side to another (of proteins)
- If it moves particles from the high concentration gradient to the low concentration gradient, it's ATP independent
- If it moves particles from the low concentration gradient to the high concentration gradient, it's ATP dependent (Famous example is sodium potassium pump, where it moves 3 sodium ions outside and 2 potassium ions inside)





3 Na^+ out: high ← ATP — low

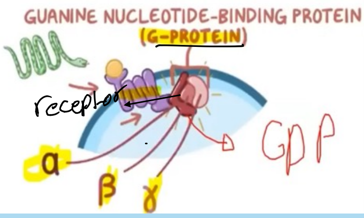
low — ATP → high: 2 K^+ inside

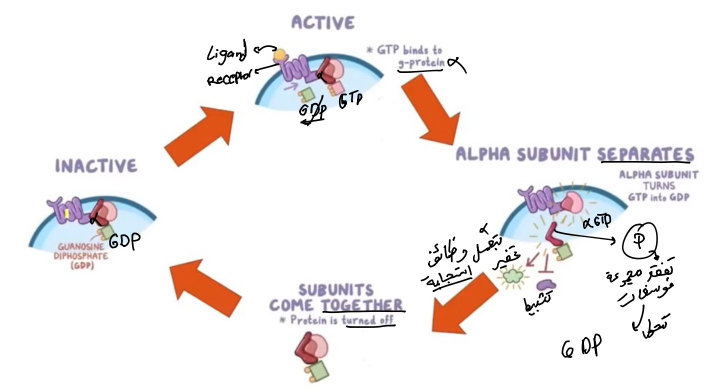


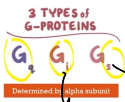
6- RECEPTORS

- Structures that bind to ligands to response in some way for the cell
- ligands could be hormones ,neurotransmitters,, drugs .... etc.
- Receptors are specific: every receptor binds to one specific ligand (There are some exceptions such as adrenergic receptors in autonomic nervous system, as they can bind to epinephrine (hormone) and norepinephrine (neurotransmitter)
- Note: Sometimes the same particle can bind to different receptors with different affinities
- How receptors transmit signals?
  There are many ways one of the most famous ways is by G protein (Guanine nucleotide binding protein)

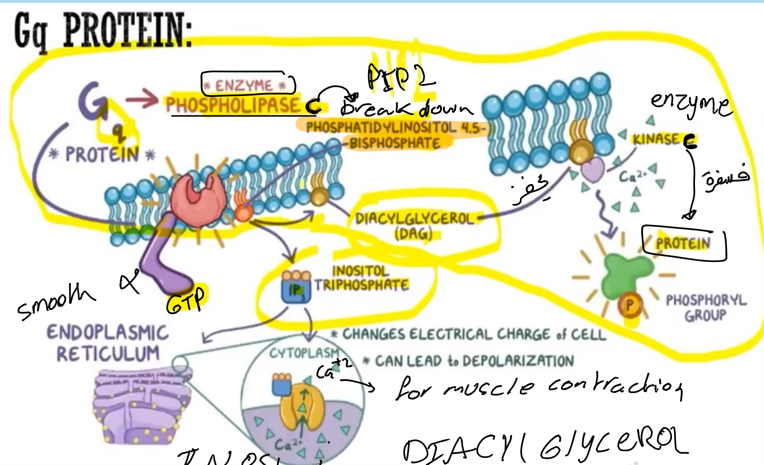
- G protein coupled receptors: receptors that transduce signals through membranes to a protein that is called G Protein
- G protein is composed of three subunits: alpha, beta & gamma
- Alpha subunit is bound to GDP in normal conditions

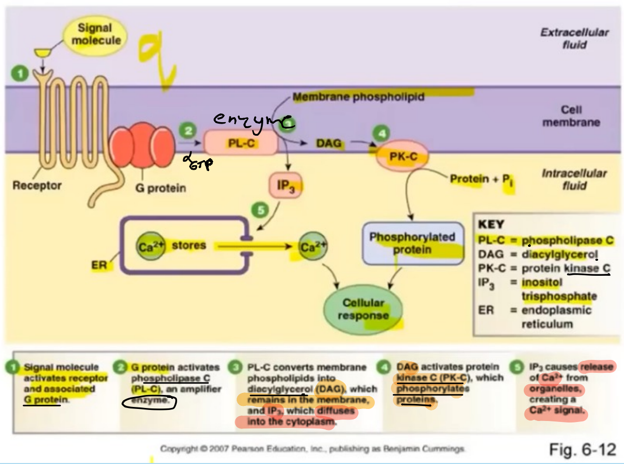


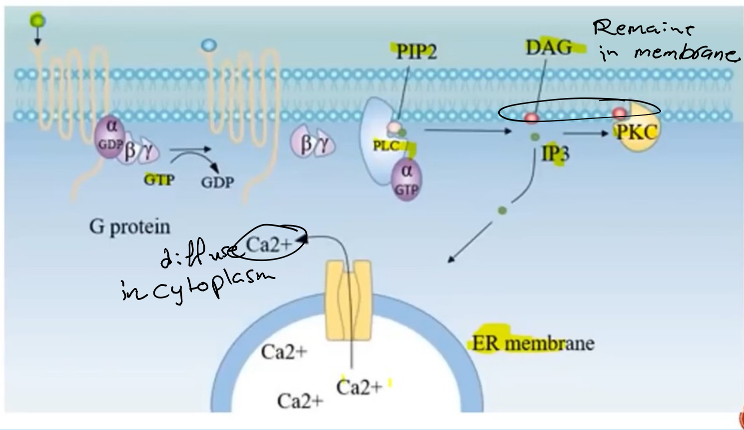




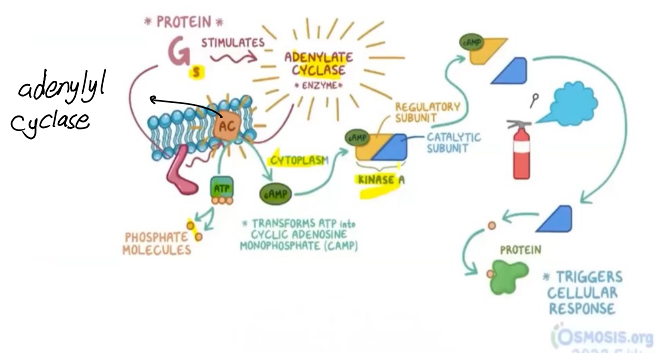
- Steps of activation of G protein
  1) Ligand binds to the receptor
  2) Receptor sends signal to the G protein
  3) Alpha subunit in G protein binds to GTP instead of GDP
  4) Alpha subunit separates from beta and gamma subunits and go to achieve it's function
  5) It achieves it's function by dephosphorylation of GTP so it converts into GDP
  6) Alpha subunit binds again to beta and gamma and the receptor so the receptor return back to it's shape
- What are functions that it can achieve?
  This depends on the type of alpha subunit
  there are 3 types: s, i and q

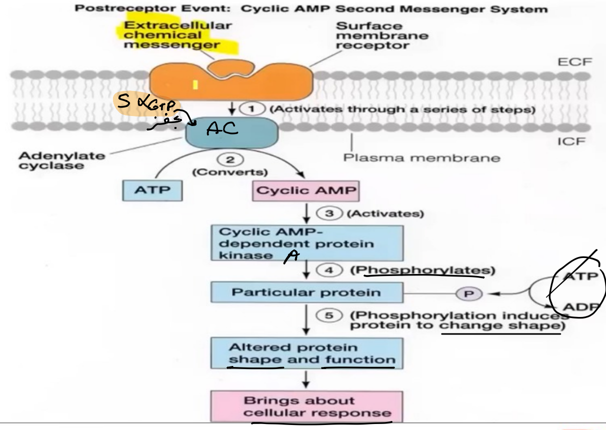


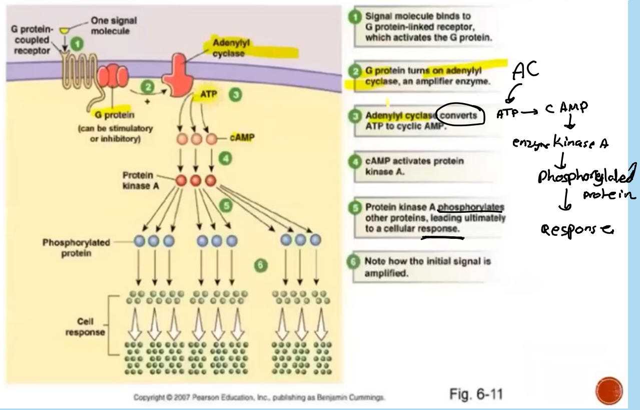




GS PROTEIN:







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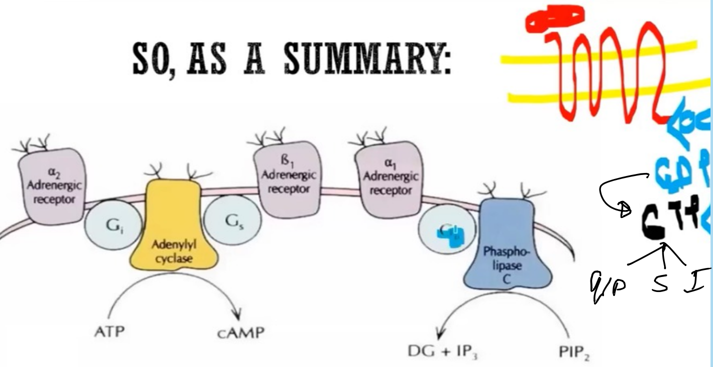
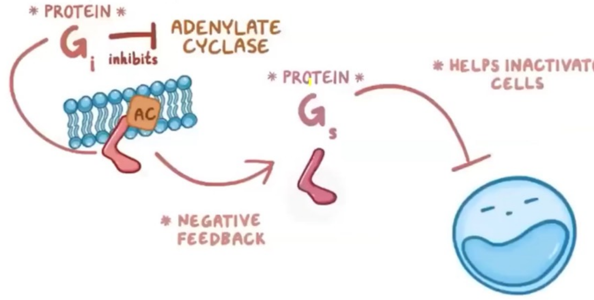


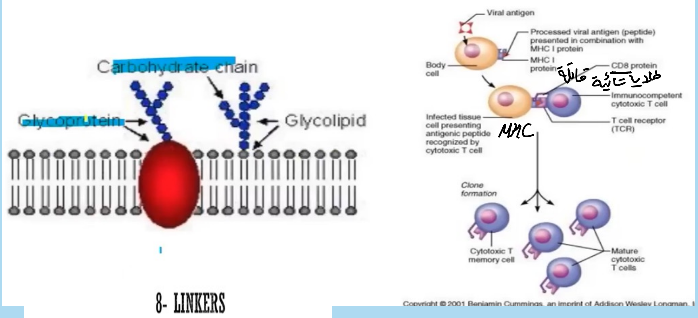
GI PROTEIN:



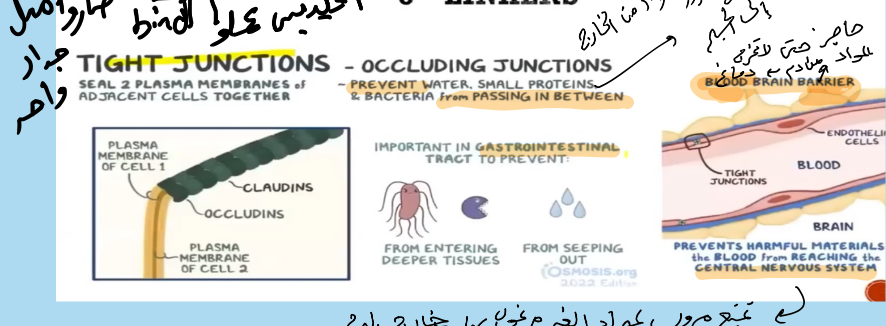
7- CELLS IDENTITY MARKERS

- Glycoproteins that identify the cell
- They are different among people
- Important example is MHC molecule that is used to differentiate between self and non-self antigens, this is important in immune response of the body

7- CELLS IDENTITY MARKERS



8- LINKERS

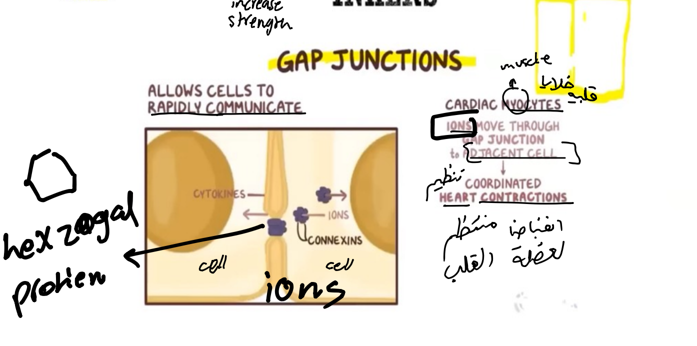


تمنع مرور المواد الغير مرغوب بها خارج الدم

8- LINKERS

- connection between cells used for communication
- There are many types:
  1) Gaps junction: pores between cells that helps in keeping the internal environment similar between adjacent cell
  Important example are cardiac muscle cells: when action potential starts in one of them, the signal reach nearby cells fast and the heart cells contract with each other
  2) Desmosomes: adherent junctions, it adhere cells by connecting cytoskeleton of adjacent cells
  3) Tight junctions

8- LINKERS



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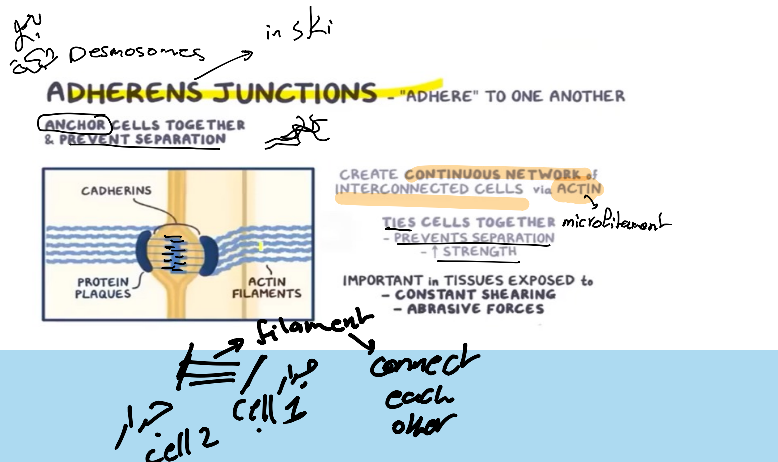
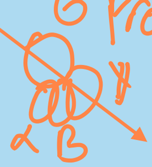


Function of proteins in cell membrane

* structural protein
* 55% of cell membrane

* integral protein.

- channels
  - ↳ not gated → nerve (K^+ channel)
  - gated (بوابة تفتح)
    1. voltage
    2. Ligand bind to receptor
       - G protein
       - ext → int



- carrier
  - facillated diffusion
    - No ATPase
    - No ATP
    - with gradiant
  - active
    - ATPase
    - ATP
    - Against gradiant
    - Na^+ glu → symport
    - Na^+ K^+ pump → anti
    - → uni: Ca pump

* Perpheral protein.

Receptor alone (inactive) → (active) Receptor–Ligand complex

G-protein: send sign to enzyme.

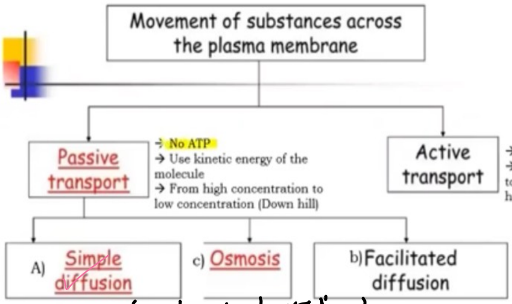
- α
- Gs → stimulation (يحفز الإنزيم)
- Gi → inhibition (يثبط الإنزيم)
- Gq
- AMP → ATP (regulatory protein)

number + sensitivety of Receptor (مستقبل) $\propto \frac{1}{\text{Ligand concent}}$

identity protein (Glycoprotein) → help immune syst to recognize self from other sell

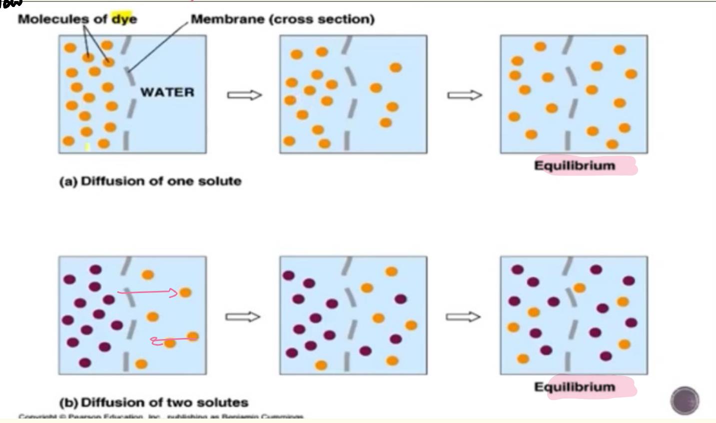
Passive transport

1) Transport across Plasma Membranes



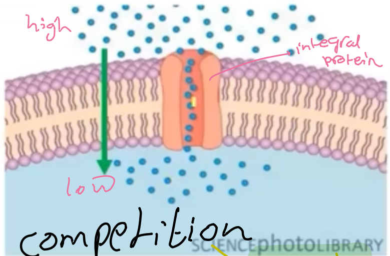
2) Simple diffusion

- The movement of particles without the need of carriers
- Can occur through:
  a- lipid bilayer
  b- channels
- A- Diffusion through lipid bilayer: Occur with molecules that can dissolve in the lipids (hydrophobic/ lipophilic)
  e.g. CO_2, O_2, NO, Steroid Hormones, Monoglycerides … etc.
- Look at the picture in the next page:
  a- we have a membrane that separate between right and left, the left contains a yellow dye while the right is empty. The dies start to move from the higher concentration (left) to the lower concentration (right) until it reaches Equilibrium where the **net diffusion** is zero.
  B- we have a membrane that separate between two solutes, each solute will diffuse to the other side independently on the other solute until the net diffusion is zero for the two solutes
- Extra note: we use in anaesthesia nitrogen gas instead of chemical materials because it is diffuse through the membrane rapidly



2) Simple diffusion

- b- channels: Allow ions and other particles that can't pass through the lipid bilayer to move downhill

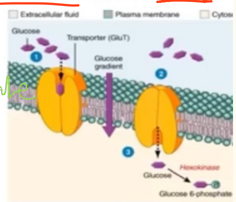


2) Simple diffusion

- The rate of diffusion (J) OR FLUX, depends on 5 factors:
  1) P = Permeability
  2) D = Diffusion Coefficient
  3) A = Surface area
  4) C = Concentration
  5) X = Membrane thickness
- $J = P \times \Delta C$
- But $P = \frac{D \times A}{\Delta X}$
- So $J = \frac{D \times A \times \Delta C}{\Delta X}$ and this is called fick's law

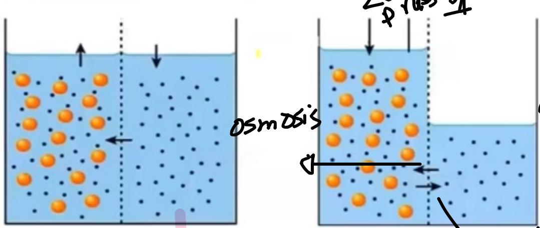
3- Facilitated diffusion

- Also called Carrier mediated diffusion (Carrier is a membrane protein and it is specific like the receptor)
- It achieves conformational change to transport particles from on side to another
- Example of compounds that are transported in this way: Aminoacids, Glucose, Galactose, Fructose … etc.
- This way of diffusion is **saturable** because the binding sites are limited and has transport maximum (T max) or velocity maximum (V max) unlike the simple diffusion that has no limit as long as there is a concentration gradient



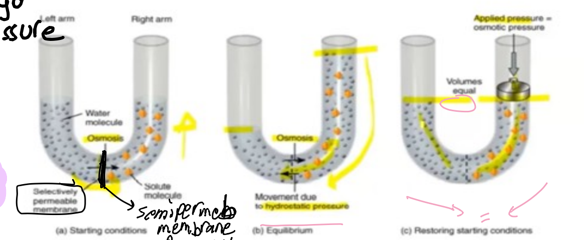
4- Osmosis

- Osmosis: the net movement of water through a selectively semi permeable membrane from an area of high concentration of water (lower concentration of solutes) to one of lower concentration of water (high concentration of solutes)
- Water can pass through plasma membrane in two ways:
  1) Through lipid bilayer by simple diffusion
  2) Through aquaporins, integral membrane proteins.



4- Osmosis

- Osmotic pressure (the pulling pressure) of a solution is the measure of tendency of a solution to pull water into it by osmosis because of the relative concentration of non penetrating solute and water.
- When water passes from the left side to the right side, a pressure is exerted (hydrostatic pressure) which prevents more water from passing from left to right.
- Hydrostatic pressure of a solution 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
- Equilibrium is achieved when tendency to pull water to side 1 and to push water into side 2 balances out (hydrostatic=osmotic)



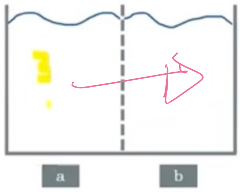
Osmosis: $\pi = CRT = \frac{mRT}{Mr \cdot V}$ (Van't Hoffs)

4- Osmosis

- Osmotic Pressure depends on many factors, they are summaries in Van't Hoffs Equation
- $\pi = CRT$ where
  → π is the Osmotic pressure
  → R is the gas constant
  → C is the concentration (Remember that $C = \frac{n\ of\ Mole}{Volume\ in\ Liter}$ & n of Moles $= \frac{Mass\ (g)}{Molecular\ weight}$)
  → T is the temperature in kelvin
  - Note: All mentioned factors have direct proportion with the osmotic pressure except molecular weight and volume of solution in calculating concentration
- Osmotic pressure depends mainly on the molar concentration or molarity of a solution.

4- Osmosis

- Example: If domain "a" contains 3 moles of a big molecule (glucose), while domain "b" contains 4 moles of a small molecule (sodium), if you know that the volume & temperature for both domains are equal, determine the net direction of movement of water?
- Answer: The direction of the movement of water is toward the domain that have the higher π where π = CRT
- $\pi(a) = CRT = \frac{3}{V} RT$
- $\pi(b) = \frac{4}{V} RT$
- $\frac{4}{V} RT > \frac{3}{V} RT \rightarrow \pi(b) > \pi(a)$
- So water will move toward domain b

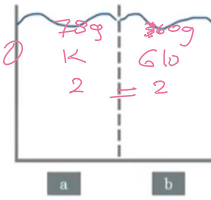


4- Osmosis

- Example 2: If domain "a" contains 78 gram of potassium, and domain b contains 360 gram of glucose, if you know that the volume & temperature for both domains are equal, determine the net direction of movement of water?
(Note: Mw of glucose = 180 & Mw of potassium = 39)

$\pi_a = \frac{m}{Mr} \frac{RT}{V} = \frac{78}{39} \frac{RT}{V} = \frac{2RT}{V}$ $\pi_b = \frac{360}{180} \frac{RT}{V}$ $\pi_b = \frac{2RT}{V}$ equally

No net movement = 0



4- Osmosis

- Example 3: Which of the following have the least π?
- Answer: A

$\pi = \frac{Mass}{Mw \times V} \times T \times R$

Particle/ Info	M. Weight	Volume of solution	Temperature
A	↑	↑	↓
B	↑	↓	↓
C	↑	↑	↑
D	↓	↓	↑

4- Osmosis

- The osmotic pressure of an ionic solution is π = iCRT where "i" is the number of ions formed by dissociation per molecule
- For example: The π of NaCl = 2CRT not 1CRT because NaCl will disassociate in the solution into Na+ & Cl-
- Question: Arrange these solutions based on their π

KCl > $Na_3(PO_3)$ > NaCl > Glu

$CaCl_2 \rightarrow Ca^{2+} + 2Cl^-$ = 3 CRT

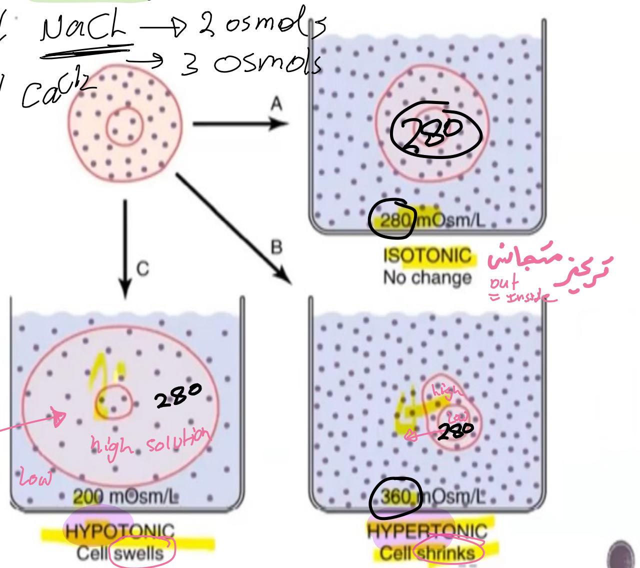
Particle	Concentration
Glucose	300
NaCl	150
Na3(PO3)	100
KCl	300

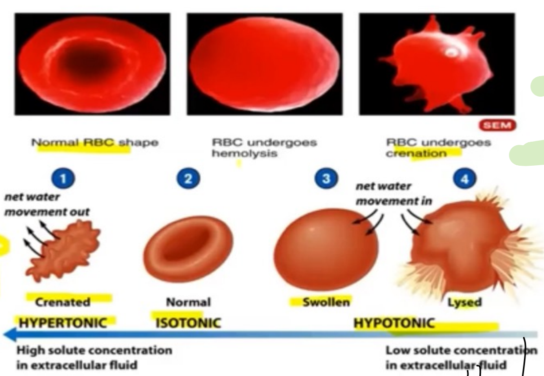
Glucose: not dissociate. NaCl: 2×150 = 300 CRT. Na3(PO3): $3Na^+ + PO_4^{-3}$, 4×100 CRT = 400. KCl: $K^+ + Cl^-$, 2×300 = 600 CRT. non ionized salt

4- Osmosis

- Osmolarity: A term used to describe the total number of osmotically active particles (not permeable solutes) per liter of solution → number of moles
- EXAMPLE :If 39 g of potassium are dissolved in water, we say: the osmolarity of the solution is 1 OsM.
- Two solutions can have the same molarity but may have different osmolarities.
-EXAMPLE:
- OsM of 1 M glucose solution =1 OsM
AND
- OsM of 1 M NaCl solution = 2 OsM
(1 mole of NaCl is dissolved completely, the Na osmolarity is 1, the Cl osmolarity is 1, so the total is 2)
- So we can use Osmolarity instead of concentration to find π
- New law: Water moves from low osmolarity to high osmolarity → movement of solution
- Note: do not be confused with osmolality, where osmolality: A term used to describe the total number of osmotically active particles per kilogram of water
- Another note: mOsm = millisomolar

Osmol concen: 1 mol NaCl → 2 osmols; 1 mol $CaCl_2$ → 3 osmols





Past paper question!

1 mOsmo = 19.3 mmHg
1 L plasma osmo concentration = 290 mOsmol/L = 5000 mmHg = 7 atm

A blood sample is taken from an individual whose blood osmolarity is 300 mOsm/kg H2O. 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)	osmo
1. Na Cl	150	2 × → 300
2. Fructose	300	300
3. Na HCO3	150	2 × → 300
4. Ca Cl2	150	3 × → 450
5. K Cl	100	2 × → 200

1L = 1000 cm
10 × 1000 cm → L
5 × 200 cm → L

osmolarity: osmols / Litre
osmolality: osmols / kg

Patch clamp method

Active transport

Against gradient
need ATP → carrier protein + ATPase

+ Active transport also uses a carrier protein to transfer a specific substance across the membrane, but in this case the carrier transports the substance against its concentration gradient. low → high

primary active transport, in which energy (in the form of ATP) is directly required to power the transport process

All primary-active transport carriers (known as **pumps**) act as enzymes that have ATPase activity, which means they split the terminal phosphate from an ATP molecule to yield adenosine diphosphate (ADP) and inorganic phosphate (Pi) plus free energy. The most important pump is the Na+-K+ pump. Other examples include H+ pump, and Ca+2 pump.

① ② ③

ATP → ADP + P_i

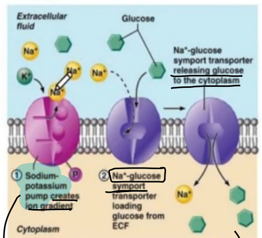
secondary active transport, in which energy is required in the entire process, but it is not directly used to produce uphill movement. That is, the carrier does not split ATP; instead, it moves a molecule uphill by using energy stored in the form of another ion concentration gradient (most commonly a Na+ gradient). This ion gradient is built up by primary active transport -which requires direct supply of energy-

Secondary active transport occurs by two mechanisms—**symport** and **antiport**—depending on the direction the transported solute moves in relation to Na+ movement.

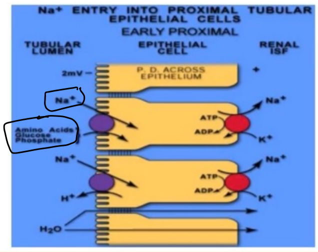
In symport (also called **cotransport**), the solute and Na+ move through the membrane in the same direction—that is, into the cell. Glucose and amino acids are examples of molecules transported by symport in intestinal and kidney cells.

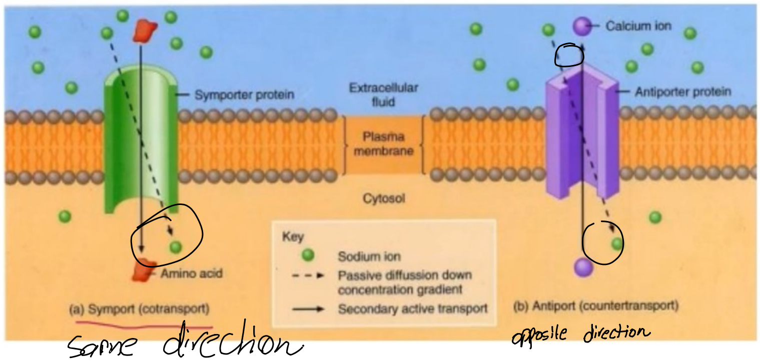
Two substance in two direction

In antiport (also known as **countertransport** or **exchange**), the solute and Na+ move through the membrane in opposite directions—that is, Na+ into and the solute out of the cell. For example, cells exchange Na+ and H+ by means of antiport.



electrogenic transport
Anti port 2K↓ 3Na↑ in out
Na–Glu Sym





same direction
opposite direction

Vesicular transport

+ Large particles (such as hormones) are transferred between the ICF and the ECF not by crossing the membrane but by being wrapped in a membrane-enclosed vesicle
+ Vesicular transport requires energy expenditure by the cell, so this is an active method of membrane transport. Energy is needed to accomplish vesicle formation and vesicle movement within the cell.
+ Transport into the cell in this manner is termed **endocytosis**, whereas transport out of the cell is called **exocytosis**.

decrease the plasma membrane
increase the plasma membrane

+ Exocytosis increases the plasma membrane area, while endocytosis decreases it. Thus, the rates of endocytosis and exocytosis must be kept in balance to maintain a constant membrane surface area.
+ There are three forms of endocytosis, depending on the material internalized: (1) **pinocytosis** (nonselective uptake of a sample of ECF), (2) **receptor-mediated endocytosis** (selective uptake of a large molecule), and (3) **phagocytosis** (selective uptake of a multimolecular particle).

carrier protein

prime active
secondary active

*If primary stop secondary will stop because it depend on concentration gradiant of primary

need ATP but by ATPase activity

antiport countertransport opposite side

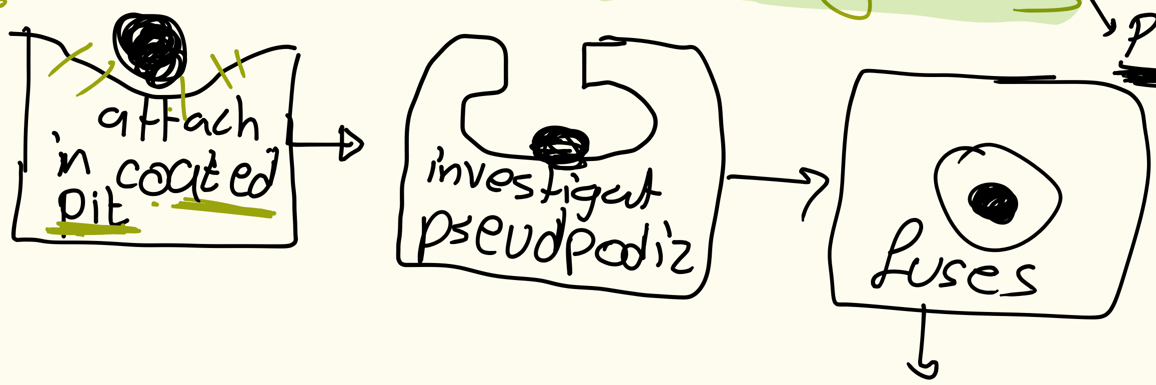
sameside symport cotransport

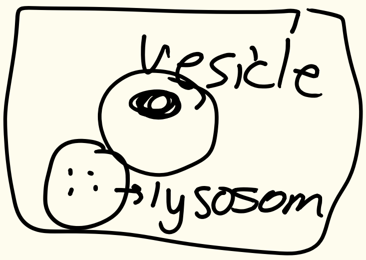
Vessicular Transport: Active

↓ need ATP

→ Trans MACRO molecules

mechanism → endocytosis → Pinocytosis
→ phagocytosis





← Exocytosis

EX:
→ secretion of protein hormone by endocryinal gland

→ constitutive → If coated pit don't have receptor.

Key
→ Receptor mediated → Rapid, specific

Pinocytosis	Phago
cell drinking	cell eating
macro molecules جزئ * protein molecule → soluble in water can't seen in micro * B_{12} + Glycoprotein	Large particles جزء كبير not soluble → seen in microscope * bacteria dead tissue
All cells proteins لان كل خلايا تحتاج RBCs كرات الدم	Phagocytic cells الاكولة WBCs خلايا الدم البيضاء

MSQ:

MCQs Introduction 2

One answer is correct:

1. Facilitated diffusion differs from simple diffusion in:
   - a FD needs ATP.
   - b FD is sensitive to temp changes.
   - (c) FD has a maximum rate.
   - d FD occurs against gradient.
2. Solution with highest OP:
   - a 2 moles $CaCl_2$ in 500 ml.
   - b 3 moles NaCl in one litre.
   - c 3 moles Glucose in 200 ml
   - (d) 3 moles KCl in 250 ml
3. Secondary active transport of glucose: → same side
   - a Stops if prim. active transport of Na is stopped. ✓
   - b needs symport carrier.
   - c occurs against conc. gradient.
   - (d) all of the above.

Q.2 Osmopressure → (1) osmol 1×1000 (2) mosmol 1×19.3 mmHg

a. $2 \times 3 = 6 \times 2$ → osmo = 12 osmol

b. $3 \times 2 = 6$ osmol

c. $3 \times 5 = 15$ osmol

d. $3 \times 2 = 6 \times 4 = 24$ osmol

OP (a) = 12000 mosmol
OP = 12000×19.3
(b) = 6000×19.3
(c) 15000×19.3
(d) 24000×19.3

4 Regarding vesicular transport all are correct except:

a ptn hormones are secreted by exocytosis.

b phagocytosis occurs by all body cells → phagocells WBC

c it is an active process.

d In pinocytosis, the substance is not seen by microscope.

5 Regarding intercellular communication, ch. messenger

a has only cell mem. receptors. → receptor موجود cell membran cytoplasm nucleus

b ↑↑ concent. leads to ++ number of receptors. X

c may act via cAMP.

d cann't affect the cell which secretes it. → autocrine اعتقد ممكن ترجع أثر على الخلية

Answer

c d d b c