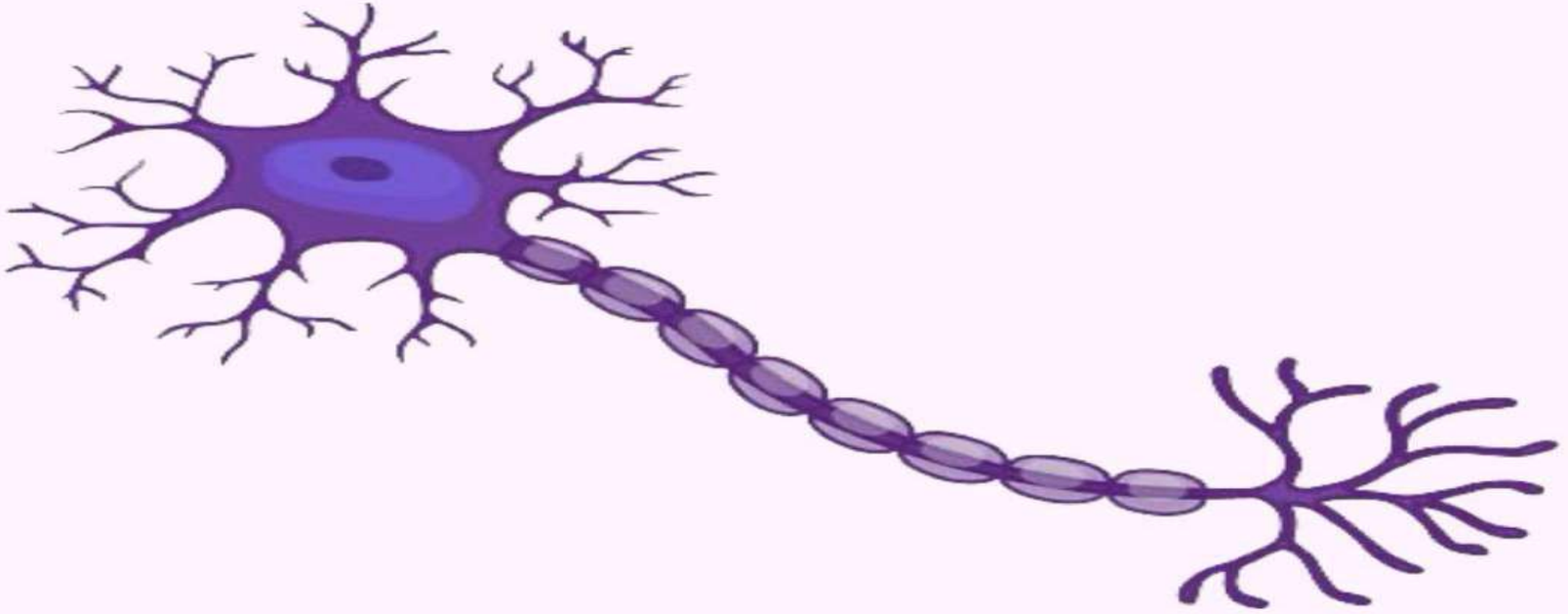
PHYSIOLOGY



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وَقُل رَّبِّ زِدْنِي عِلْمًا

Introduction to Celluar Physiology

Course: Destistry
Hashemite University

Lecture No. 1

1. **Levels of organization in the body**
2. **Levels of Homeostasis and body fluids**

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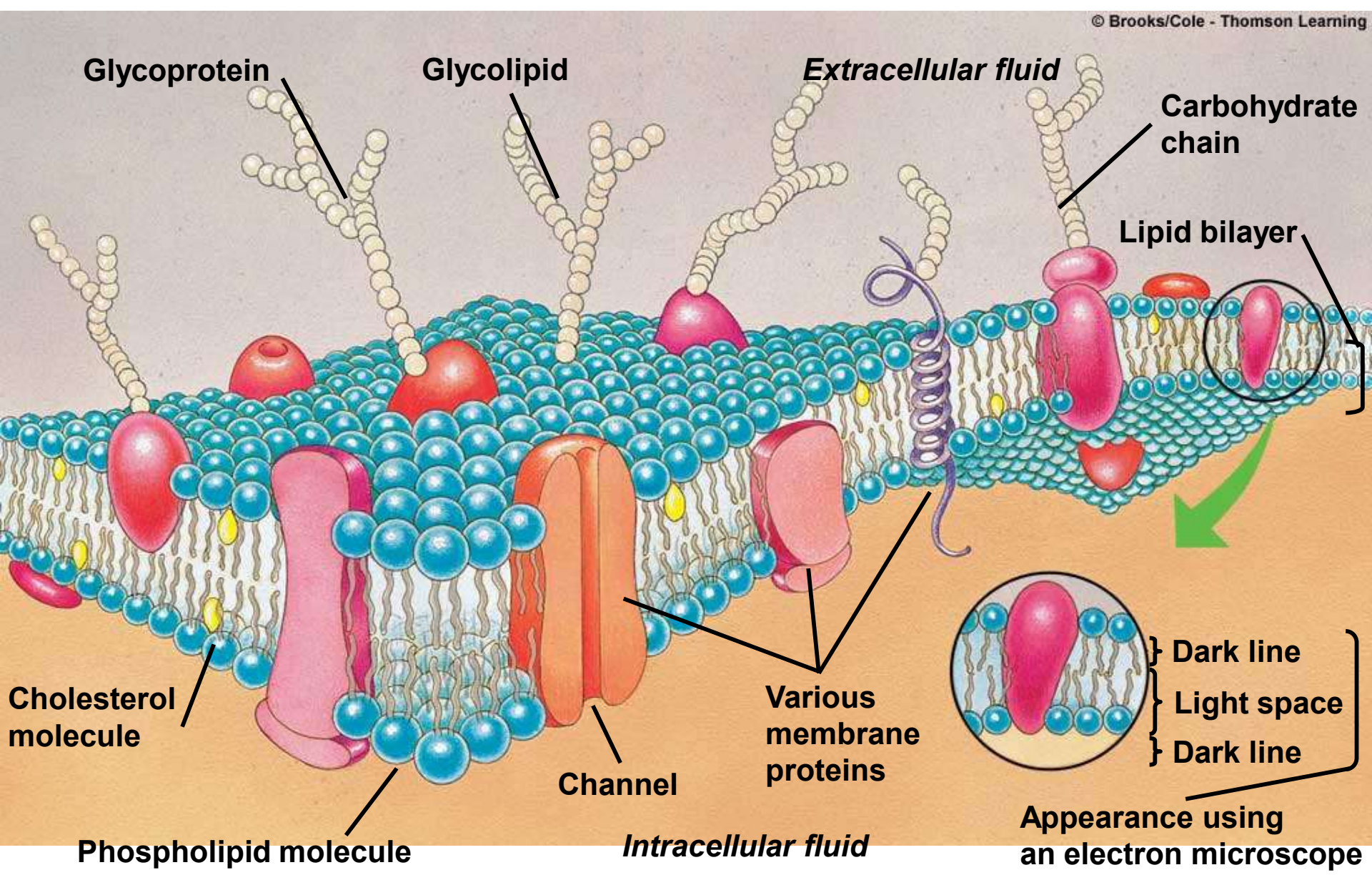


- Composition
  - Proteins 55%
  - Lipids 42%
  - carbohydrates 3%

Fig. 3-3, p. 45

The structure of the membrane is a bilayer of lipids (fatty acids) the tail inside the membrane and the head outside.
We have so many structures which are embedded in the membrane, some look to the outside, some have access to the inside, and some can be through outside and inside
All of them have functions.

These structures could be receptors for hormones, chemicals, glucose and so on, also they can be channels for k,Na,Ca.

Remember that fat doesn't need a transport system because the fat can dissolve in fat.
When we come to glucose, it has a charge so it needs a transport system also amino acids + ions

ممكن يخطر ببالنا سؤال، الماء كيف بنتقل؟ طبعًا لا تحتاج لأي شيء لينقلها، تنتقل لوحدها.
في عنا special structure فقط لنقل الماء، و حتّى بيدخلوا أي خلية بالجسم وصولًا للدماغ.

مش سهل لأي مادة تدخل للbrain، ف هو impermeable to almost substances except 2 types يلي هما
1-glucose: because the metabolic activity of the brain depends on it.
ك شرح لالها: لما بنصوم، شو بيعمل الجسم؟ الcontrol system بيعمل shut all the metabolic activity، عشان توفّر الغلوكوز يلي بجسمنا للدماغ، حتى خلال عمل التمارين، لازم نحافظ على معدّل الغلوكوز في الدماغ.
2-chiton bodies are acidic, when their production is increased as what happens in diabetes.
عشان هيك الناس المُصابين بالسكري لازم دائمًا يحافظوا على أكلهم و مستوى السكر.
3- urea : which is produced by the metabolic activity of proteins
طبعًا هي زي الماء بتقدر تدخل اي مكان بدون ناقل، لهيك عنا نظام قوي جدًا في الكلية يتخلص من وجودها في الدم، لانها لو وصلت للدماغ رح تعمل damage لهيك مهم جدًا نحافظ على عدم وصولها للدماغ.

باقي الخلايا لا تسمح بمرور المواد الا عن طريق
channels for each substance

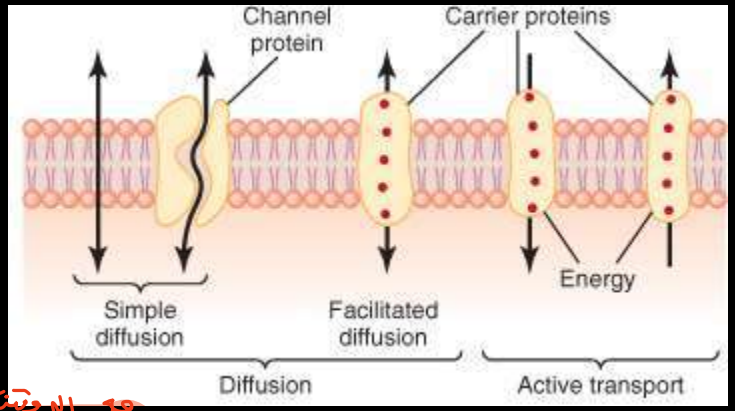
Cont. cell membrane composition →

- Proteins

Actions:

- Integral; penetrate cell membrane. (اختراق مشترك)
- peripheral; attached to integral protein, don't penetrate the cell M. (خارجي)

a) Forming channels (pores)
b) Carrier proteins. as receptor
c) enzymes.



- Carbohydrates

Actions:

— can be part of:
- With proteins (glycoproteins) (مع البروتينات)
- With lipids (glycolipids) (مع الدهون)

→ Glycocalyx

a) receptors.
b) Share in immune reaction.
c) Help in attachment of one cell to another. ← اتصالات الخلايا ببعض خاصة بالدفاع
d) Provide negative charge to the cell. ← عشان تنبذ المواد اللي أصلها negative إنها تدخل الـ membrane.

Responsible for antigenic properties of the cells

ليش لازم نحافظ على membrane عشان نحافظ عليها.

Why do we care about cell membranes?

لأنه هو يلي بتحكم بدخول المواد وخروجها من الخلية

- If the cell membrane breaks, the cell dies.!
- Cell membrane creates and maintains concentration differences between the intracellular and extracellular solutions.
- Contrast concentration and conditions

Inside and outside the cell..:

1- much higher K+ conc. Inside than outside.

2- much higher Na+ conc. outside than Inside.

3- much higher Cl- conc. outside than Inside.

4- much higher Ca++ conc. outside than inside.

5- higher protein conc. inside than outside.

6- outside is slightly alkaline (PH=7.4) while inside is neutral (PH=7).

7- osmolarity of solutions inside and outside is similar

	EXTRACELLULAR FLUID	INTRACELLULAR FLUID
Na^+	142 mEq/L	10 mEq/L
K^+	4 mEq/L	140 mEq/L
Ca^{++}	2.4 mEq/L	0.0001 mEq/L
Mg^{++}	1.2 mEq/L	58 mEq/L
Cl^-	103 mEq/L	4 mEq/L
HCO_3^-	28 mEq/L	10 mEq/L
Phosphates	4 mEq/L	75 mEq/L
SO_4^-	1 mEq/L	2 mEq/L
Glucose	90 mg/dl	0 to 20 mg/dl
Amino acids	30 mg/dl	200 mg/dl ?
Cholesterol, Phospholipids, Neutral fat	0.5 g/dl	2 to 95 g/dl
PO_2	35 mm Hg	20 mm Hg ?
PCO_2	46 mm Hg	50 mm Hg ?
pH	7.4	7.0
Proteins	2 g/dl (5 mEq/L)	16 g/dl (40 mEq/L)

→ Na^+, K^+, Ca^{+2} They are the main 3 ions which have effect on the phesyology of the body, They control the osmilarity, in particular Na^+, K^+

هدول همّ الأيونات يلي بدي أعرف تركيزهم

→ Ca has an important effect on the central nervous system and its stability
↳ if Ca goes below the normal concentration (2.4 mEq/L), the central nervous system will become unstable.
→ If the concentration goes up 2.5 > 0.5 5%, it could stabilize, or could supress in the CNS.

* أهمية الكالسيوم لاتكمن فقط في osmolarity وإنما لتأثيره في CNS.

→ The aim of this processes is to maintain constant environment for the cells to be able for living

How do substances (particles) cross cell membranes?

كيف تنتقل المواد عن طريق الأغشية ؟ (Between inside and outside the cell)

→ Note: most of the carriers are proteins

1. Diffusion (الانتشار)
   - Simple → بسيط → high concentration to low. like water.
   - Facilitated → يعني في channel → it means that there is a compound which transfer substances.

2. Osmosis (خاصية الأسموزية) → usually The movement of water from high (H_2O) con to low (H_2O) cont or low solute con → high solute con

3. Active transport (The most important transport system in our body) — it consumes energy
   - Primary (K/Na pump) — ATP directly needed — يلي هي شغلها تطلع صوديوم برا مقابل بوتاسيوم لجوا
   - Secondary — Don't need ATP directly, it is needed to do something else.

   usually from low to high concentration.

   مثل امتصاص الغلوكوز ب gi system ، يلي بنقله الغلوكوز من الامعاد للدم هو compound و هذا يحتاج للصوديوم، الفرق في التركيز هو القوة الدافعة، و كأنه الغلوكوز يتطفّل على ناقل الصوديوم عشان ينتقل.

4. In vesicles
   - Endocytosis
   - Exocytosis.

Endocytosis is uesd to absorb lrg molecules like what happens in infants
ف الطفل حديث الولادة ما بيقدر يكوّن immune globulins عشان immune system ف هو

Exocytosis it is the release of the substance from inside the cell to the outside
كمثال بسيط بنقدر نحكي عن neuromuscular transmission
يلي هي ال joint between neuron and muscle ف هاي
ال junction فيه gab و يحتوي على fluid
اللي بهمني كيف ال action potential رح ينتقل من ال neuron
to muscle ؟ عن طريق افراز acetilcolina هاد الافراز رح

The driving force for the movement of the particles is the concentration difference.

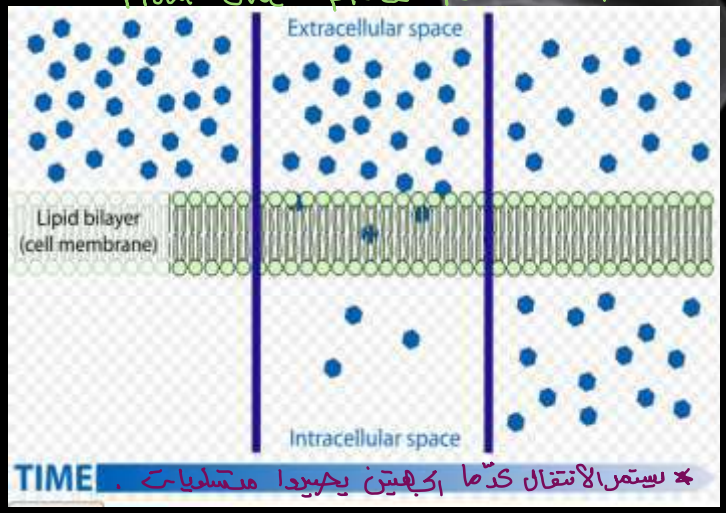
simple → no carriers

facilitated → we need a carrier

Diffusion

→ The passage (movement) of the substance from one place to another.

- Is the random movement of particles in a solution. This movement depends on the temperature. * تتحسن بكرة
- The process of diffusion causes particles to move from an area of high concentration to an are of low concentration. Finally the concentration of particles becomes equal through out the solution.
- The net diffusion is always from high Conc. to low. دائماً من التركيز الأعلى للتركيز الأقل



* يستمر الانتقال كدّما اكبهيتن يحيدا متساويات

Diffusion tries to reach equilibrium Where the conc. are the same everywhere. No energy source is needed, the random movement of the particles is all what is needed.

→ any fat substances + any substance that can dissolve in fat can pass across the cell membrane passively without the need of a carrier

→ For example :-
vitamin (A, K, E, D) , They can cross the membrane passively because they are fat soluble.

Cont. simple diffusion →

- Two types of simple diffusion

simple

a) Through intermolecular spaces of the membrane

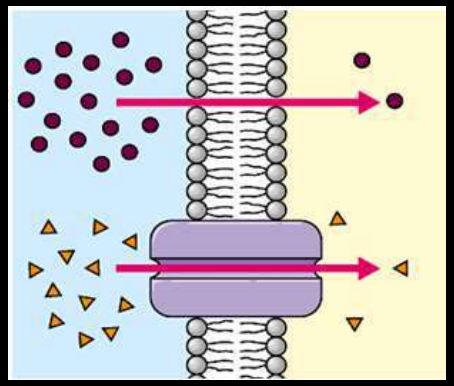
"lipid soluble substances"

(A, K, E, P)

b) Through membrane channels → facilitated.

غالباً بيكون بروتين Carrier

"water and lipid insoluble molecules"

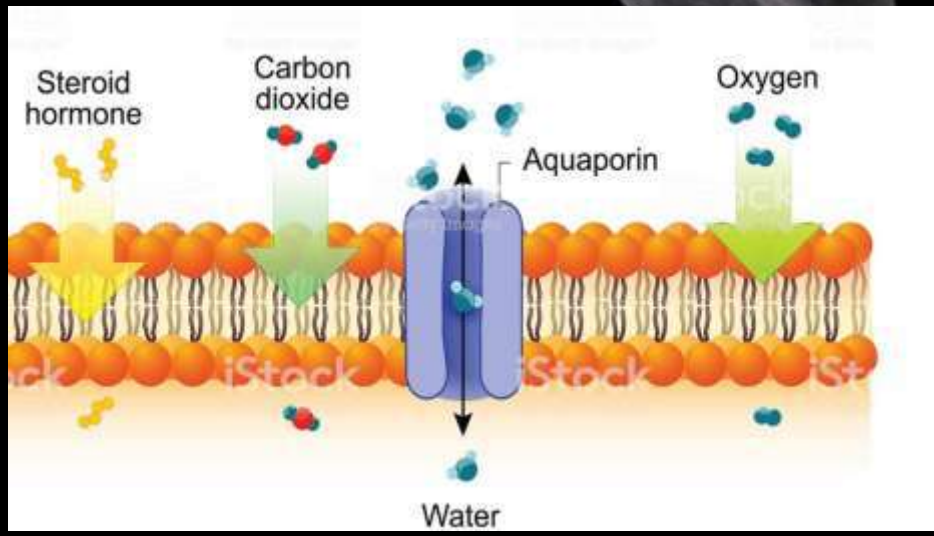


Carrier ي. تحتاج & -

Gases + H2O

Simple diffusion (Cont.)

- **Lipid-soluble molecules like oxygen and CO2 cross the cell membrane by simple diffusion. The degree of diffusion of these substances is determined mostly by their lipid solubility.** ذائبيتهم في الدهون



→ example :-
urea can enter the cell with water without the need of a carrier.

يذوبي في الدهون لا يذوبي في الماء

- **Hydrophobic, lipophilic substances like fatty acids, fat-soluble vitamins and drugs can dissolve in the lipid bilayer of the cell membrane and diffuse across the membrane.**

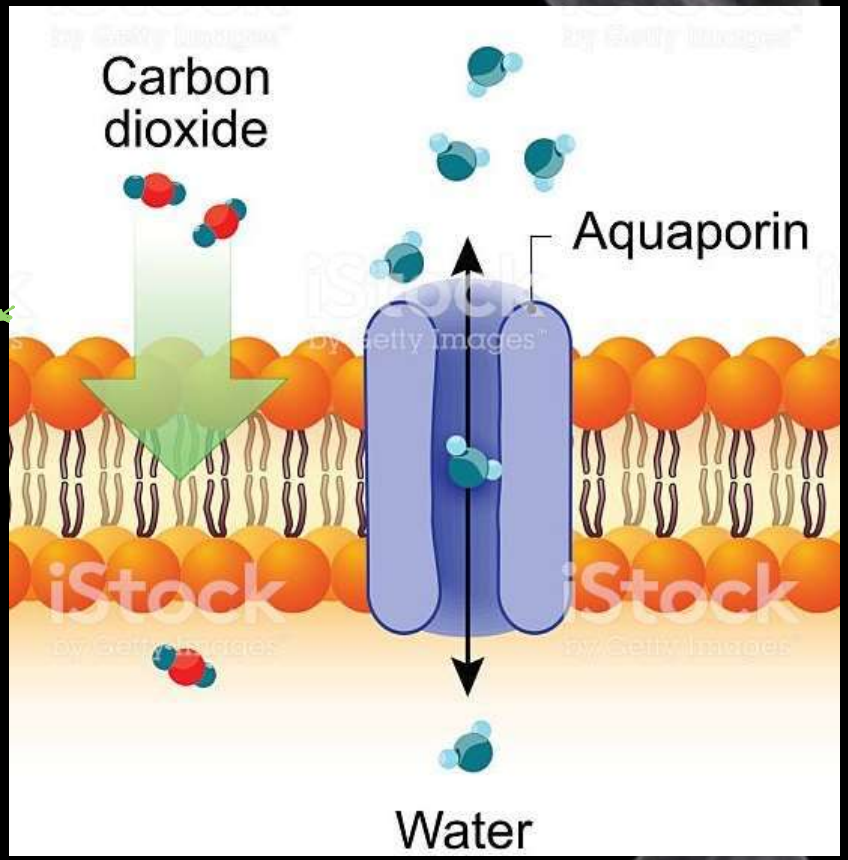
Simple diffusion (Cont.)

- **Diffusion of water is through membrane channels. Water penetrates very rapidly the cell membrane through protein channels (aquaporins).**

المسؤولة عن هَل الماء في الجسم

- **Urea can cross the cell membrane by simple diffusion through protein channels. Urea molecule is 20% larger than water molecule and thus → its rate of diffusion is less than water.**

وهاد طبعًا شيء مفيد ، لأنها لو انتقلت بنفس سهولة انتقال الـ H2O رح تسبب تلف وأمراض في أجهزة جسم الإنسان .



معناها إنه ماعدها طاقة .

Simple diffusion (Cont.)

- **Transport of ions (Na+ and K+) is by simple diffusion through protein channels.**

? passively يكون ions هل انتقال هذه
التركيز بالخارج يكون ← Na^+ 140 في الداخل 10
← K^+ في الداخل 140 في الخارج 5

>> these channels are:

not simple diffusion ← can cross the membrane

a) **Selectively permeable to certain substance.**

b) **Opened or closed by gates.**

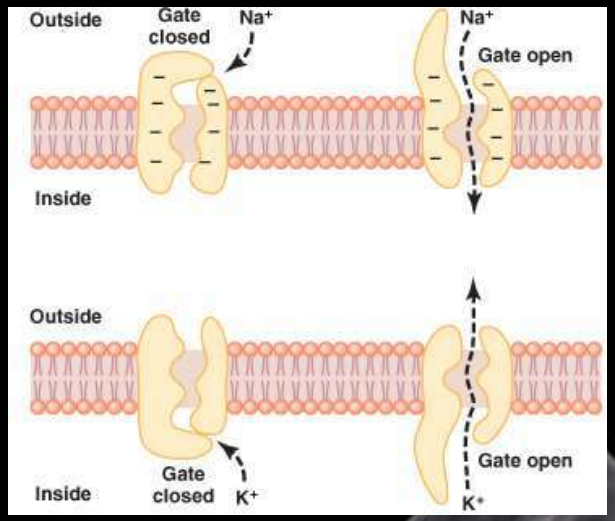
- **The presence of gates in these channels controls the movement of ions through these channels.**
- **The opening and closing of these gates are controlled by:**

* طيب إيش هو اللي يتحكم بانتقال هاي الأيونات ؟

a. Changing the potential of the cell "voltage gating". resting membrane potential

b. Binding chemical substances To the gate "chemical or ligand gating".

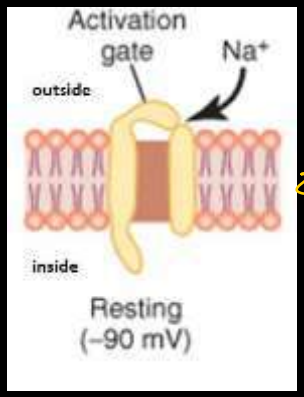
→ you can force the Na^+ channels to open so that Na^+ can cross the membrane



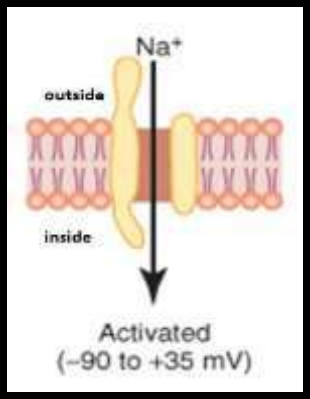
← رح ينشرح بالتفصيل بالمحاضرة الجاي .

Voltage-gated channels

Closed Na+ channel



open Na+ channel



Less negative

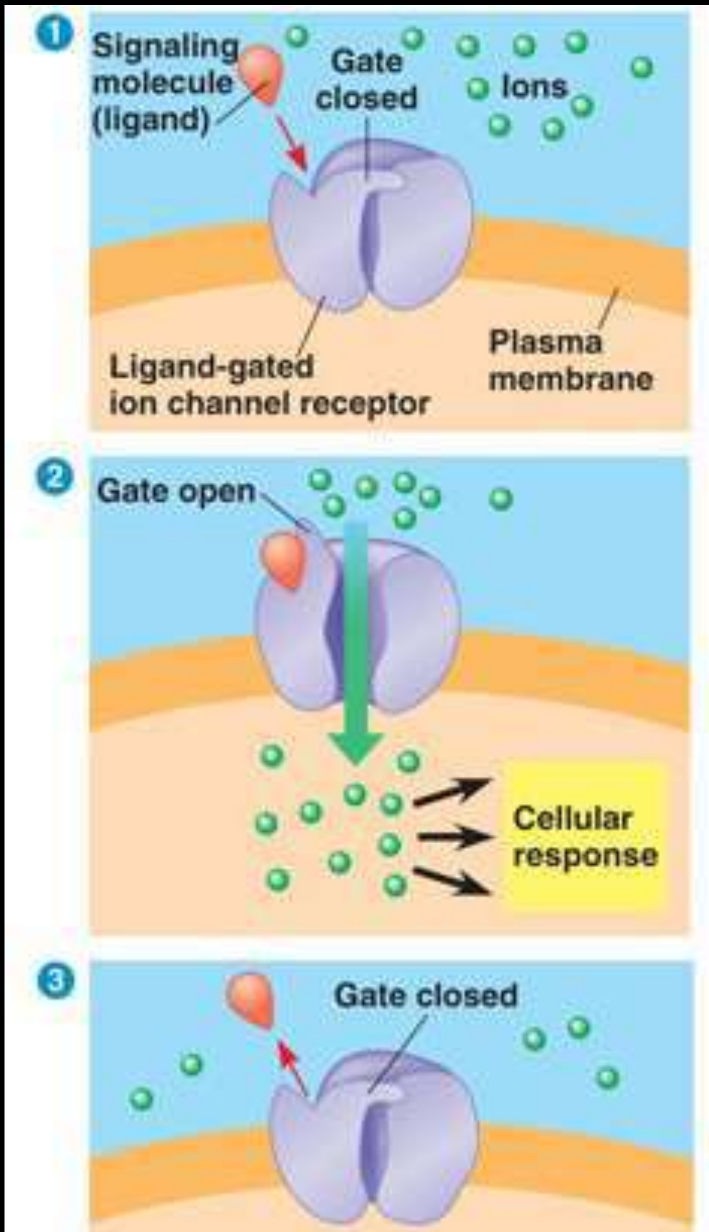
- Na+ voltage gated channels are open when the inside of the membrane becomes less negative, allowing Na+ to pass from outside to inside the cells.
- Conversely, these Na+ channels are closed when inside of the membrane is highly negative

- K+ voltage gated channels are open when inside the membrane becomes positively charged.

→ once the cell loses the ability to maintain the voltage, will die

Ligand (chemical) gated

→ where the channels will open by a ligand (chemical compound)



- Example:

(موجودة بالمساحة بين العصب والعضلة (موجود فوق)

- Acetylcholine chanels (they open when Ach binds with its receptor. These channels are 0.65 nm in diameter and negatively charged.)

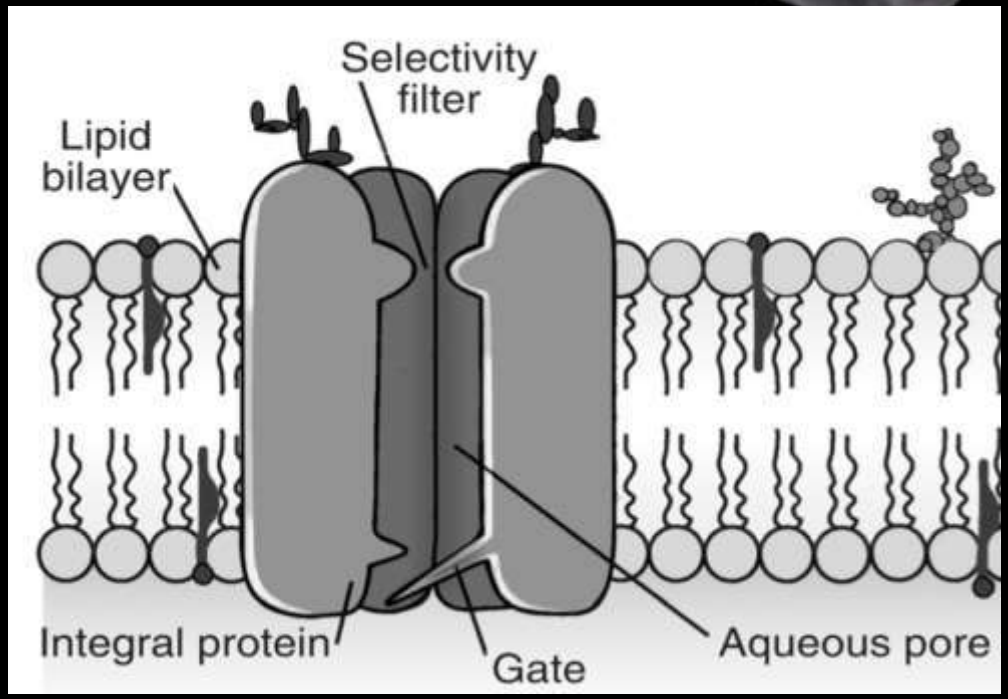
→ The channels can be open by a chemical compound or voltage change.

طيب ممكن تخطر ببالنا سؤال، كيف ممكن نغير voltage ؟ ←
أي signal ع أي مكان في الجسم رح يكون عبارة عن
شيء تحفز الخلايا ويتغير من voltage لإلها.

اختيارية / انتقائية

Selectivity of protein channels

- These channels are selective for transport of one or more specific ions.
- The selectivity depends on:
  1) Shape of the channel.
  2) Size of the channel.
  3) Nature of the electrical charges of the channel.

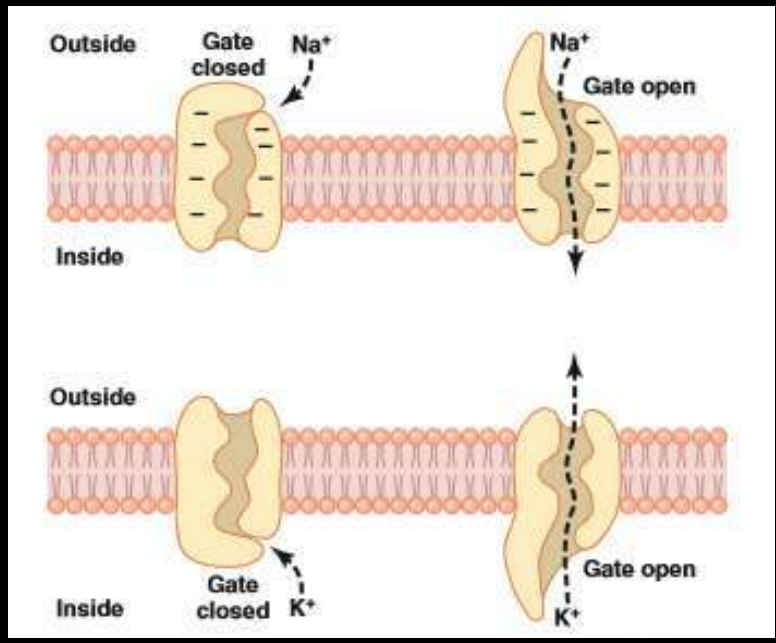


→ in our gi systeum, usually it prefers to absorb glucose, when all of it absorbed the galactose will be absorbed
لكن دائماً الأفضلية للجلوكوز .

→ eg:
Na^+ chanels can't allow the $C_{12}H_{12}O_6$ to pass

Gated sodium and potassium channels

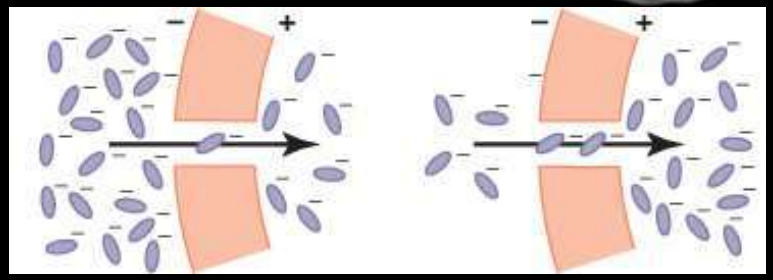
- Sodium channels:
- Negatively charged → pull sodium ion from its water.
- Diameter 0.3 X 0.5 nm.
- Gate is found at the extracellular end of the channel.
- Potassium channels:
- Smaller than sodium channels (0.3 X 0.3 nm).
- Are not charged.
- Gate is found at intracellular end of the channel.



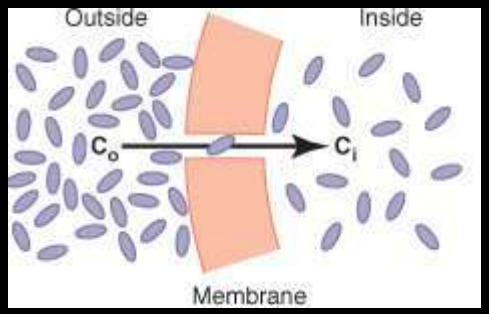
Other Factors affecting the net rate of diffusion:

العوامل اللي تأثر على الانتشار بشكل عام

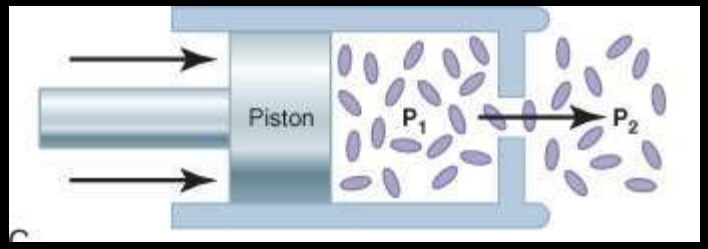
a) **Effect of concentration difference.** كل ما زاد ← كل ما زادت الحركة .
b) **Effect of electrical difference.** مثل كل الخلايا لها نفس الشحنة
c) **Effect of pressure difference.** كل ما زاد الضغط زادت الحركة
d) Tempreture → كل ما زادت الحرارة رح تزيد الحركة .



Effect of electrical difference



Effect of concentration difference

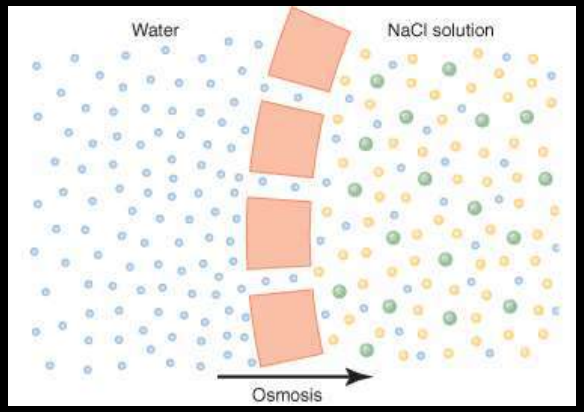


Effect of pressure difference.

Osmosis → movement of water

- Osmosis is the flow of water across a semipermeable membrane cased by a difference in the concentration of the solutions on either side of the membrane.

  - **Water flows from the solution containing a low concentration of solute to the solution containing a high concentration of solute.**



Water conc. on this side is higher.
Solute con ↓

Water conc. on this side is lower
Solute con ↑

  - **The water is forced through the membrane by an osmotic pressure difference between the two compartments.**

Measurements of solute concentraion

- Concentration of particles (molecules/ions) is measured in miliosmoles/Litre.
  - 1 molecular weight of undissociated solute like glucose = 1 osmol.
  - 1 molecular weight of dissociated solute:
    - into two ions like NaCl = 2 osmoles.
    - Into three ions like CaCl2 = 3 osmoles.

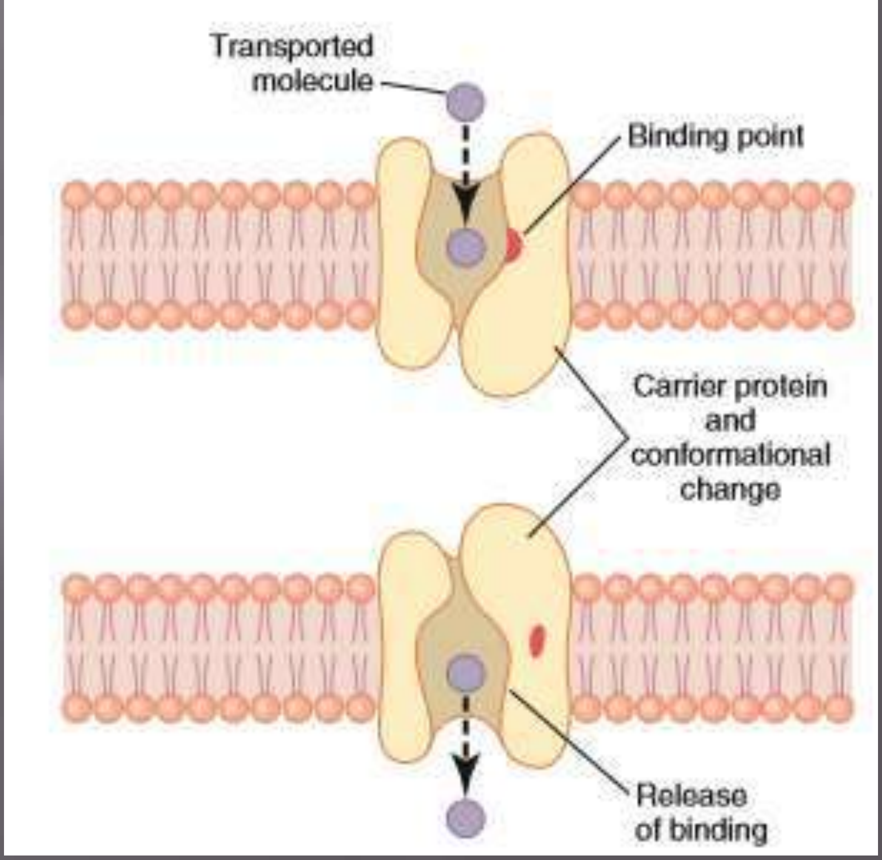
مثال: لو كان عنا 100 carrier و 130 glucose ، 100 رح ترتبط مع 100
رح يضل 30 مخطرين يستنوا ع دور
يعني saturation kinetics

Facilitated diffusion

→ saturation kinetics

** It is passive transport which does not require energy to move the large molecules.

** Used carrier protein to move molecules across the membrane.
Example: transport of glucose and amino acids
into muscle or fat cells. → مكان تخزين الجلوكوز
The hormone "insulin" can increase facilitated diffusion of glucose by 10-20 times.
لأنه الإنسولين هو المسؤول عن تخزين الجلوكوز لما تزيد نسبته بالجسم

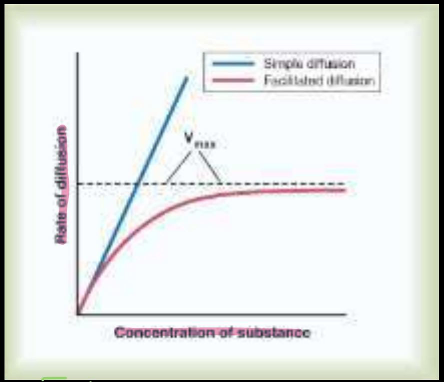


Facilitated Diffusion (carrier mediated diffusion)

- Only one solute is involved by specific carrier. (i.e. it shows specificity)
- The direction of transport is downhill (i.e from high concentration to low concentration).
- The carrier can be saturated. مُشبع

(saturated means: has a capacity, can hold just سعة
A fixed amount of molecules)

- ATP energy is not required.
- They are specific each specific molecule has a certain carrier.

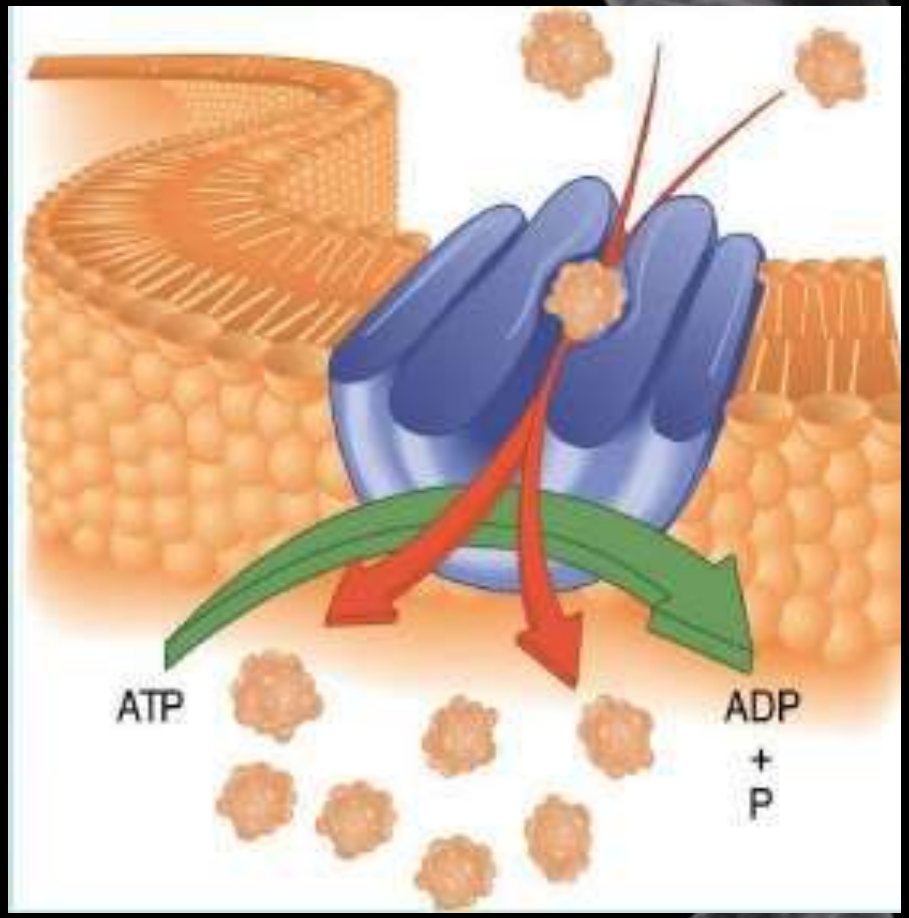


كل ما زادت كمية الكالة رح تزيد نسبة امتصاصها.

→ if the $C_6H_{12}O_6$ concentration below 180, all of them will move
if it goes up 180, 180 inside the body, the rest will be excreted in the urine.

Active transport

- Transport of ions or molecules **against** their concentration gradient.
- It is **carrier-mediated** (needs carrier).
- **Uses energy.**
- **Examples: transport of; Na+ , K+, Ca++, H+, Cl-, I- Glucose, amino acids.**

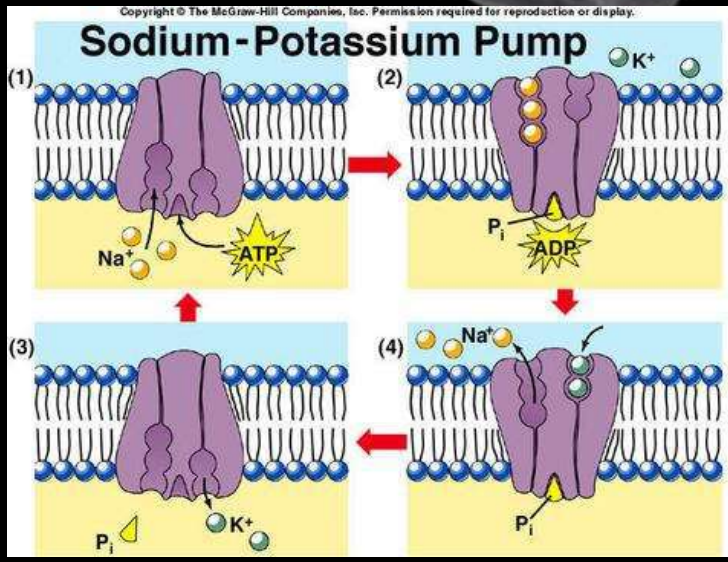


Sodium/Potassium Pump

هاي العضّيّة عبارة عن

**Are proteins which can transport Na+ and K+ from low conc to high conc area, it needs ATP. Transport reaches maximum when all transporters are being used (saturated). Very specific..!

مشبع



جي صوديوم بطلع ، بيدخل جي بوتاسيوم

- 3 Na+ ions are removed from the cell as 2 K+ ions brought into cell, with 1 ATP molecule is used. (it is electrogenic pump).

مضخة كهربائية

- Na/K pump uses large amount of ATP produced by the cell (cells lining renal tubules use 90% of ATP for this pump).

→ related to the kidneys

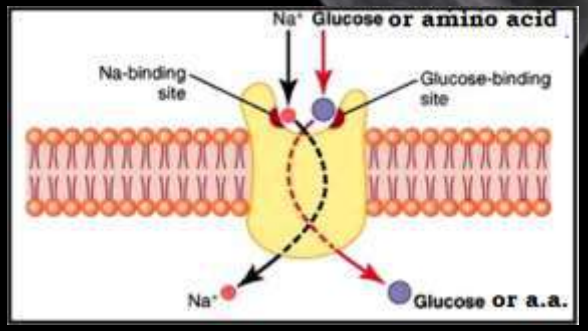
-Importance of Na+ /K+ pump

1. Responsible for creating and maintaining the high K+ and low Na+ in the cytoplasm. These concentrations make cell resting membrane potential and generation of action potential possible.

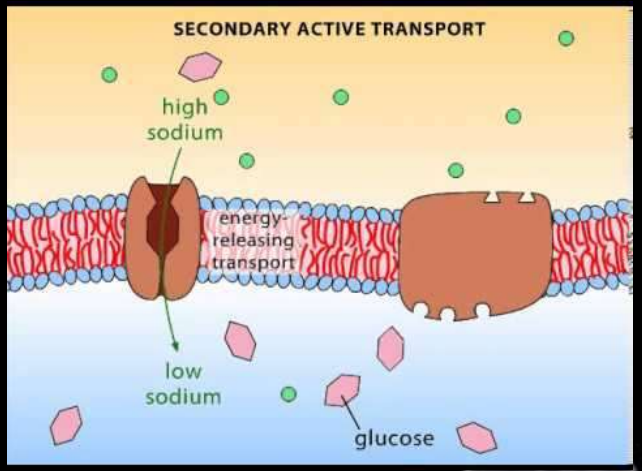
2. The low Na+ conc. inside the cell provides the energy needed for secondary active transport (discussed later). المحاضرة القادمة

3. Prevents cell swelling "i.e. keeps cell volume constant". انتفاخ يحافظ على حجم الخلية و يمنعها من الانكماش

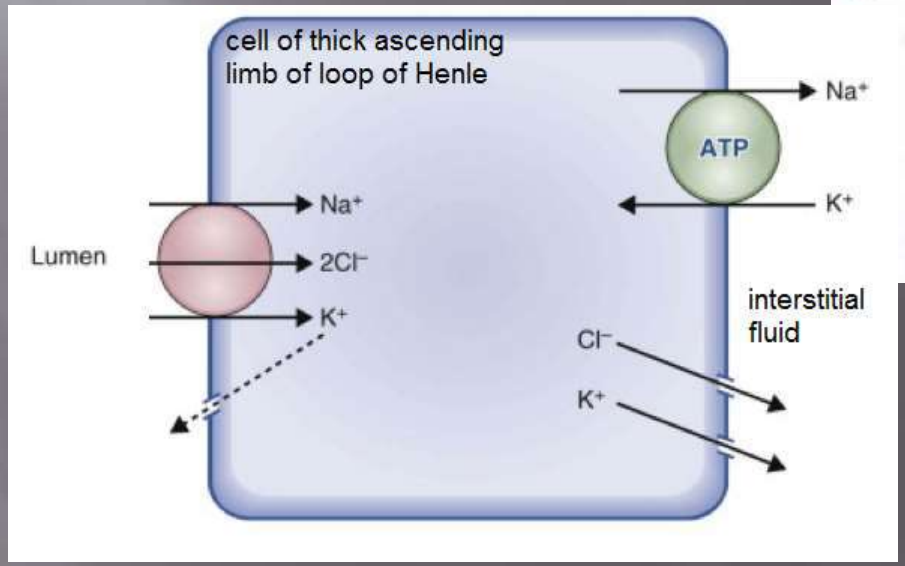
Secondary active co-transport

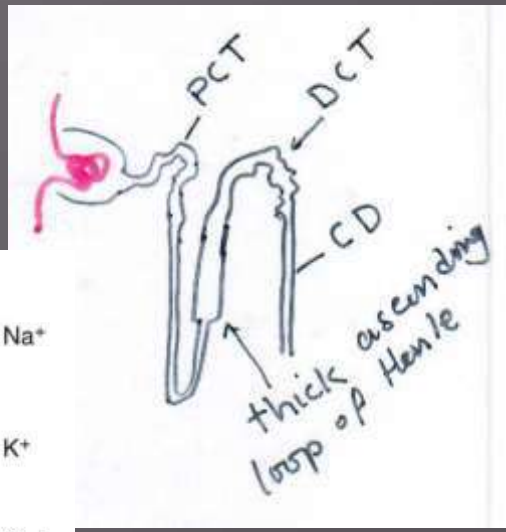


- Na Co-transport of glucose or amino acid:
- **Sometimes called symport.**
- **Both Na+ and Glucose (or amino acid) have to be present.**
- **The energy available from Na+ → gradient is used as an energy source.**
- **Found in the epithelial cells of the intestine.**



** A co-transporter can carry more than 2 ions. For example, a co-transporter in cells of the ascending loop of Henle can carry 1 Na+, 2 Cl- and 1 K+.

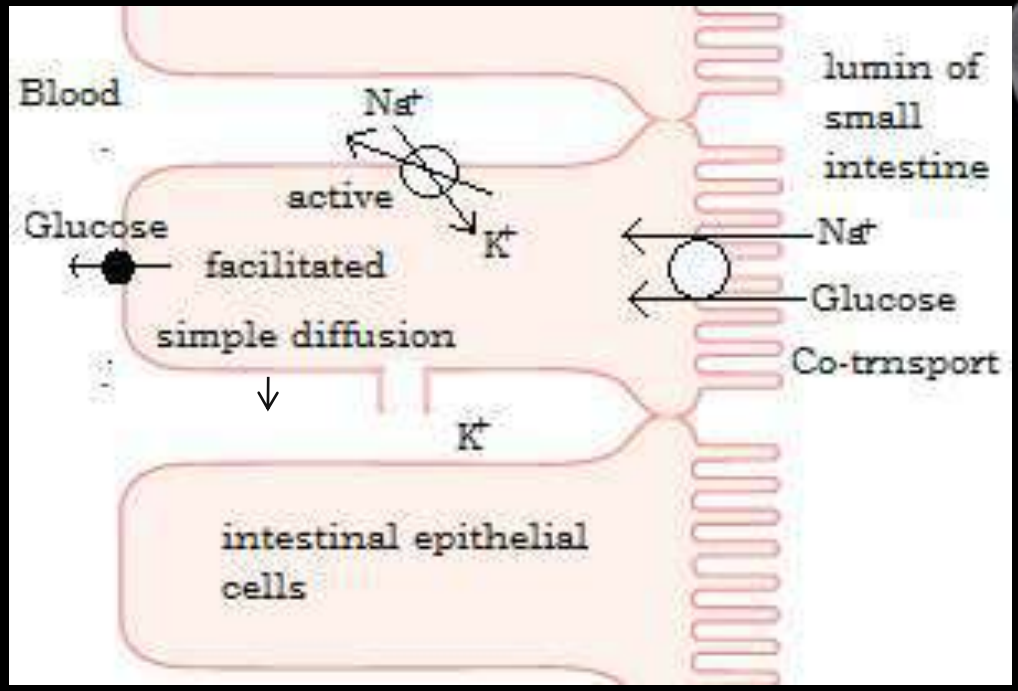




Comparison of simple diffusion, facilitated diffusion and active transport

Active transport	Facilitated diffusion	Simple diffusion	Property
yes	Yes	No	Requires special membrane protein
yes	yes	No	Highly selective
yes	yes	no	Transport saturation
yes	yes	no	Hormonal regulation
yes	no	no	Uphill transport “against concentration gradient”
yes	no	no	Requires ATP energy

Absorption of Glucose from small intestine needs all types of transportation

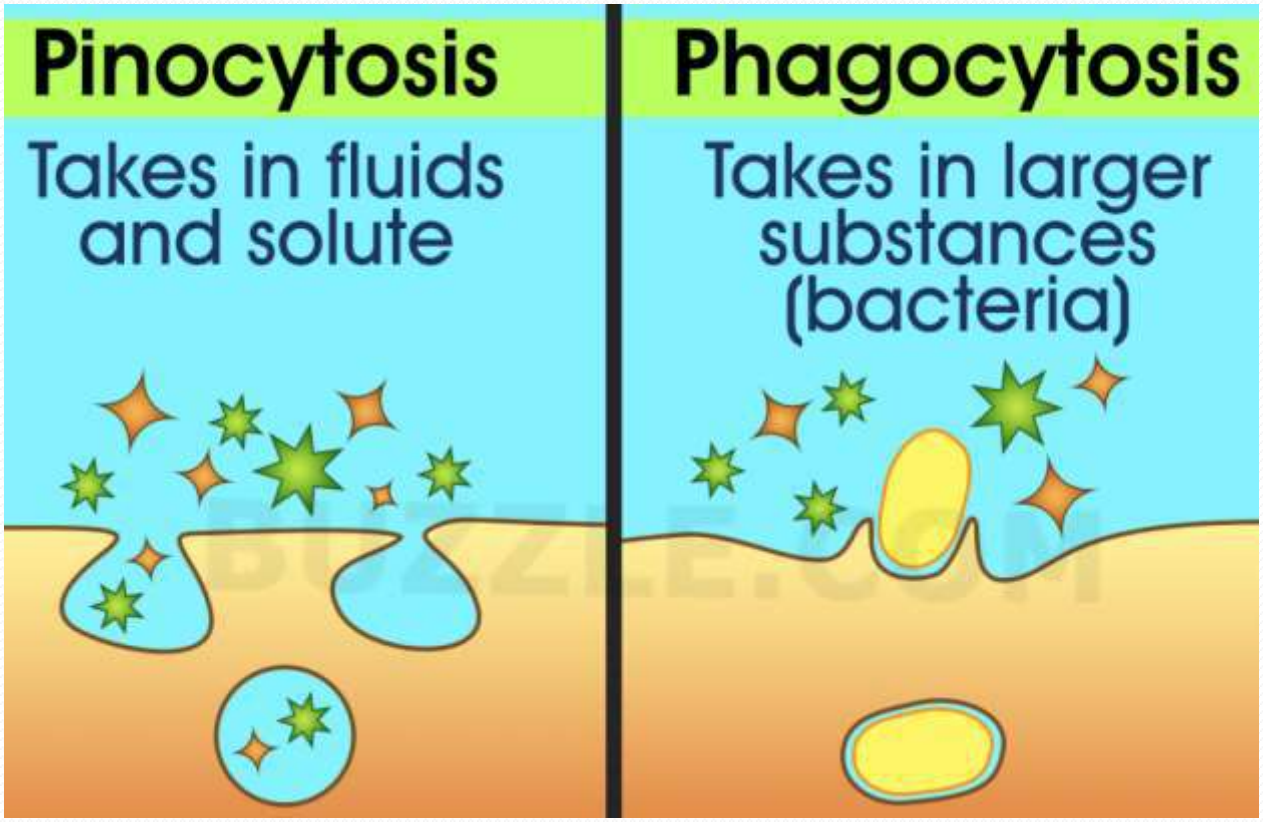


- Glucose transporters:

1- Sodium-Glucose transporter (SGLT) → found in the small intestine and renal tubules.

2- Facilitated diffusion glucose transporter (GLUT)

a. **GLUT 1 Found in RBCs.**
b. **GLUT 2 : transports glucose of intestinal cells.**
c. **GLUT 4 found in muscle and adipose tissue << insulin stimulates this type of transporters.**



Main transport system for immunoglobulins in infants since their immunity system is suppressed when born

Phagocytosis

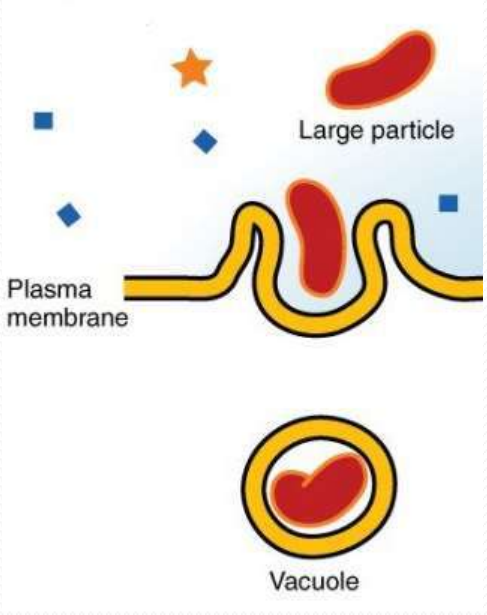
Phagocytosis involves large particles (bacteria, dead cells, or tissue debris) rather than molecules.

Tissue macrophages and some white blood cells have this ability

Bacterium is usually already attached to a specific antibody

Antibody attached to bacteria binds to the phagocyte receptors

The point of attachment invaginates inward forming vesicle inside the cell that contains the engulfed surround the bacteria.



End of lecture