# General Physiology
# (Lecture 6)
# Active Transport Through Cell Membrane

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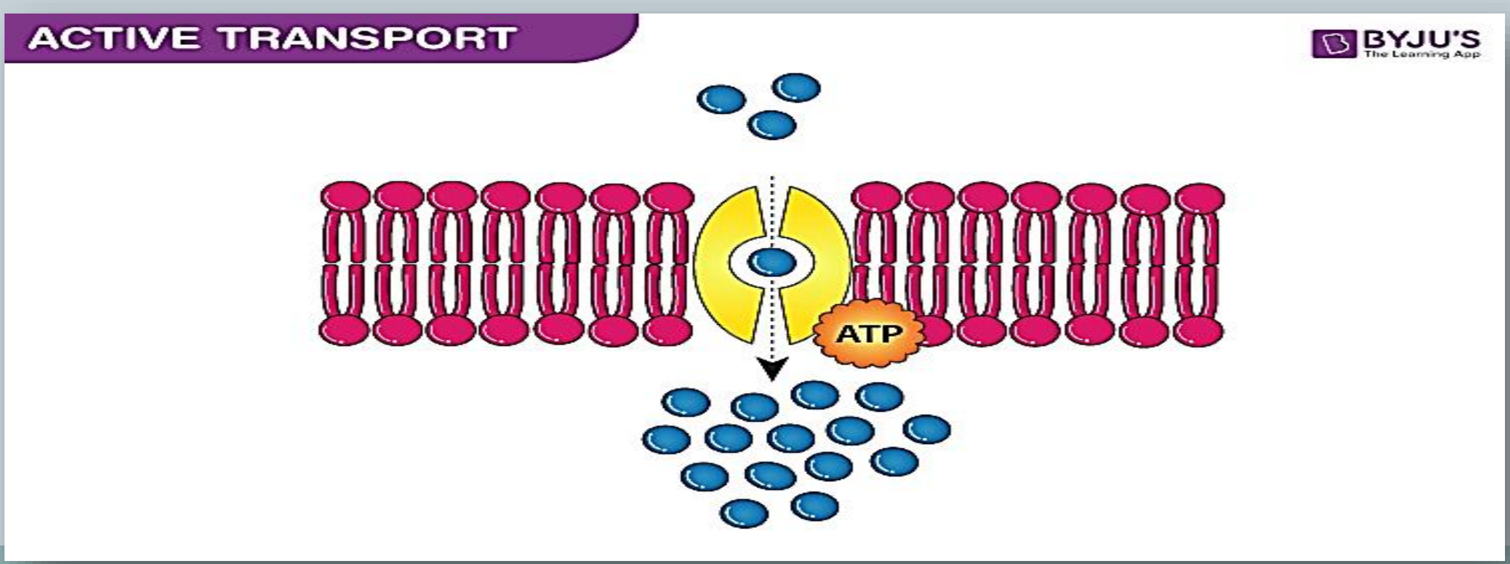


# ACTIVE TRANSPORT

**Characters:**

- This is the **transport of substances through cell membrane against gradient (Uphill)**; **concentration** (i.e. from a lesser to a greater concentration) or **electric gradients or both (physico-chemical or electrochemical gradient)**.
- **It requires energy (ATP)**; **either direct or indirect.**
- **It requires a carrier protein (with ATPase activity)** . Therefore, the carrier molecules are mostly **ATPase enzymes** that catalyze the **hydrolysis of ATP**.
- Active transport has a **saturation property as in facilitated diffusion**, which will be limited by the amount of the **carrier** and amount of **energy available** for the process.

**Types of active transport:**

It includes **2** types according to the source of energy used to cause the transport:

1. **Primary active transport.**
2. **Secondary active transport.**

Both **facilitated diffusion and active transport are carrier-mediated transport** mechanisms.

However, **active transport requires energy and occurs against concentration and electrical gradients (electrochemical gradient)**.

While, **facilitated diffusion does not require energy and occurs only along concentration and electrical gradients**.

# 1. Primary active transport

**Characters:**

**Energy is derived directly from breakdown of ATP (or other high energy phosphate compounds):**

ATP → ADP + Pi + energy

**Examples:**

**1. Sodium-Potassium pump ($Na^+$-$K^+$ pump):**

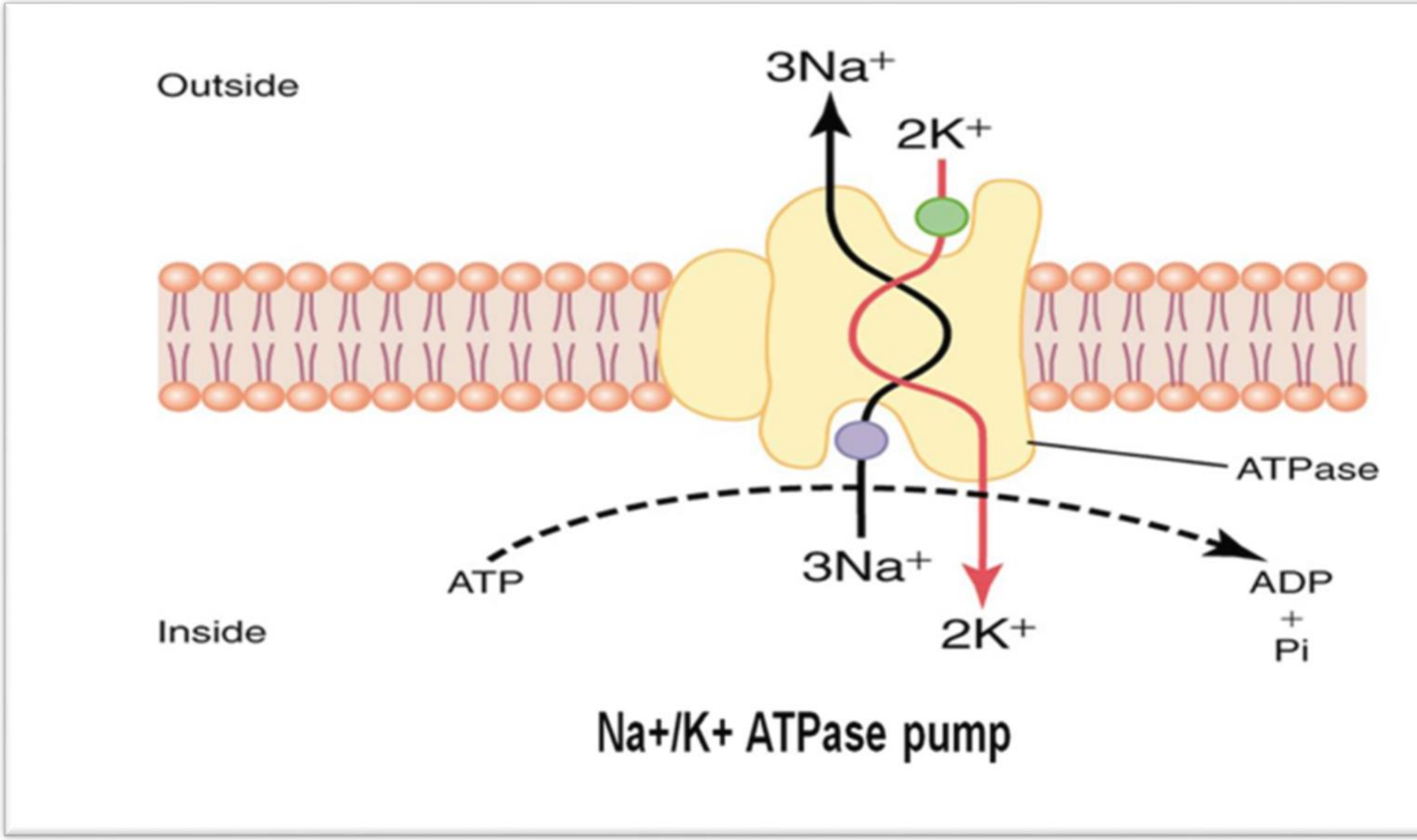
- It is **present in all cell membranes**.
- It **transports 3 $Na^+$ out (efflux) and 2$K^+$ in (influx)**.
- It is an **electrogenic pump**. Because it creates an electrical potential across the cell membrane. This electrical potential is a basic requirement in nerve and muscle fibers for transmitting nerve and muscle signals.

## $Na^+$-$K^+$ pump:

- The **carrier protein** is a complex of two separate globular proteins:
- **A larger one called the α subunit**, with a molecular weight of about 100,000, and **a smaller one called the β subunit**, with a molecular weight of about 55,000. Although the function of the smaller protein is not known (except that it might anchor the protein complex in the lipid membrane).
- **The larger protein has three specific features** that are important for the functioning of the pump:

1. It has **three receptor sites for binding sodium ions** on the portion of the protein that protrudes to the **inside of the cell**.
2. It has **two receptor sites** for **potassium ions on the outside**.
3. The **inside portion of this protein** near the sodium binding sites has **ATPase activity**.

- **When two potassium ions bind on the outside of the carrier protein and three sodium ions bind on the inside, the ATPase function of the protein becomes activated**. This then **cleaves one molecule of ATP**, splitting it to adenosine diphosphate (ADP) and liberating a high-energy phosphate bond of energy. This liberated energy is then believed to cause **a chemical and conformational change** in the **protein carrier molecule**, **extruding the three sodium ions to the outside and the two potassium ions to the inside**.



Outside
3Na+
2K+
ATPase
ATP
3Na+
ADP
+
Pi
2K+
Inside
Na+/K+ ATPase pump


Na$^{+}$-K$^{+}$ Pump

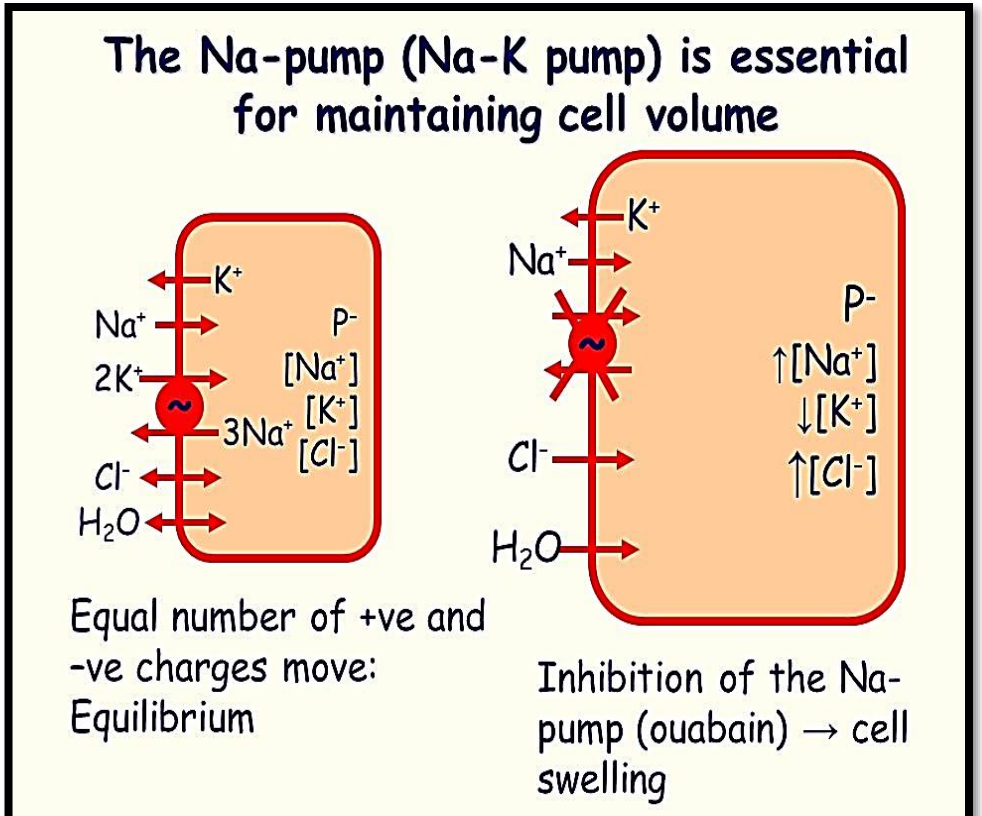
# Importance of $Na^+$-$K^+$ Pump

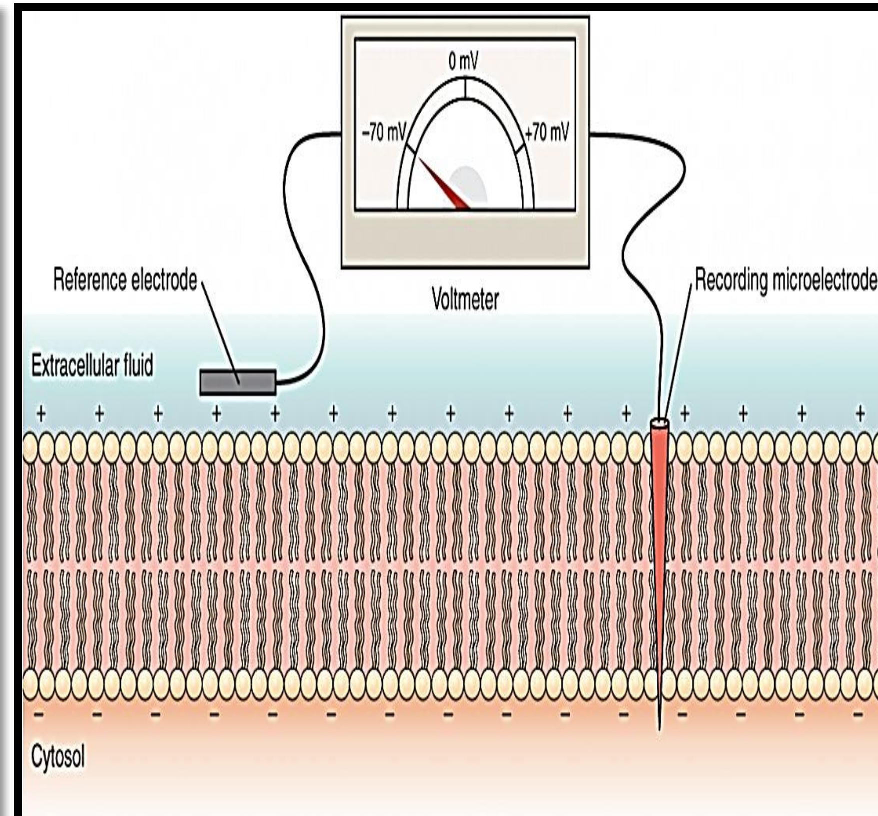
**Importance of $Na^+$-$K^+$ pump:**

1- **Development of resting membrane potential (RMP)**:This pump is responsible for maintaining the sodium and potassium concentration differences across the cell membrane, as well as for establishing a negative electrical voltage inside the cells.

2- **Help in maintenance of the normal cell volume**.

3- Sodium gradient established by this pump **energizes the secondary active transport processes** as for calcium and glucose.


The Na-pump (Na-K pump) is essential for maintaining cell volume
K+
Na+
2K+
3Na+
Cl-
H2O
P-
[Na+]
[K+]
[Cl-]
Equal number of +ve and -ve charges move: Equilibrium
K+
Na+
Cl-
H2O
P-
↑[Na+]
↓[K+]
↑[Cl-]
Inhibition of the Na-pump (ouabain) → cell swelling

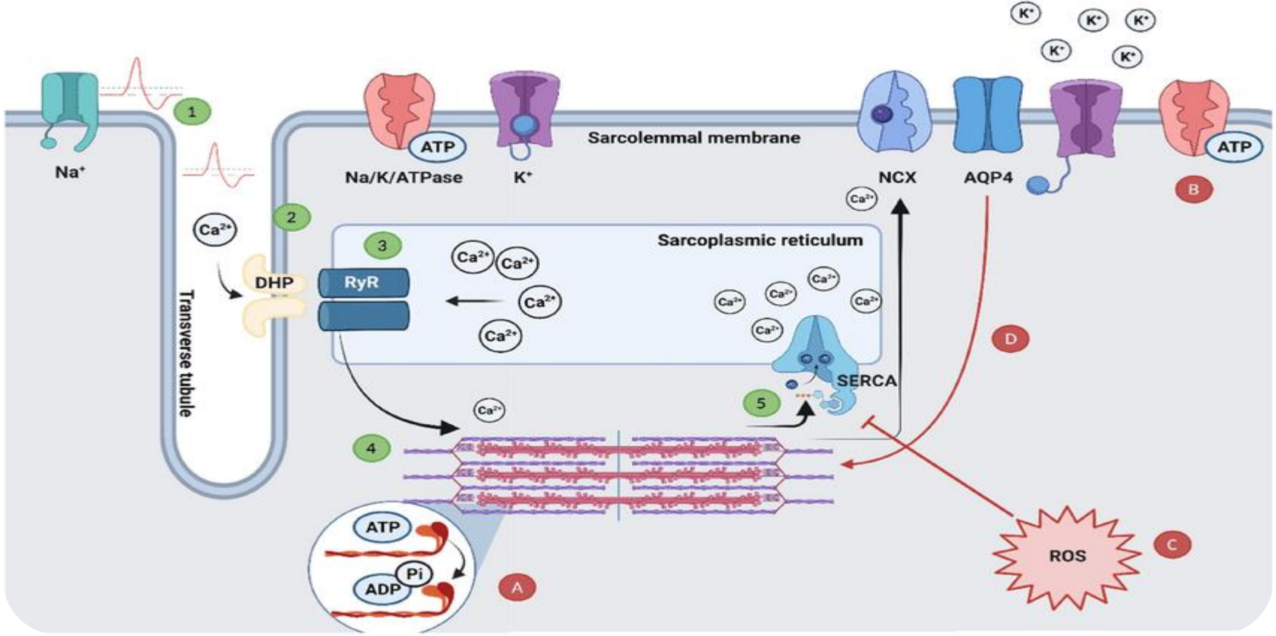

0 mV
-70 mV
+70 mV
Voltmeter
Reference electrode
Recording microelectrode
Extracellular fluid
Cytosol

**2. $Ca^{++}$ ATPase pump:**

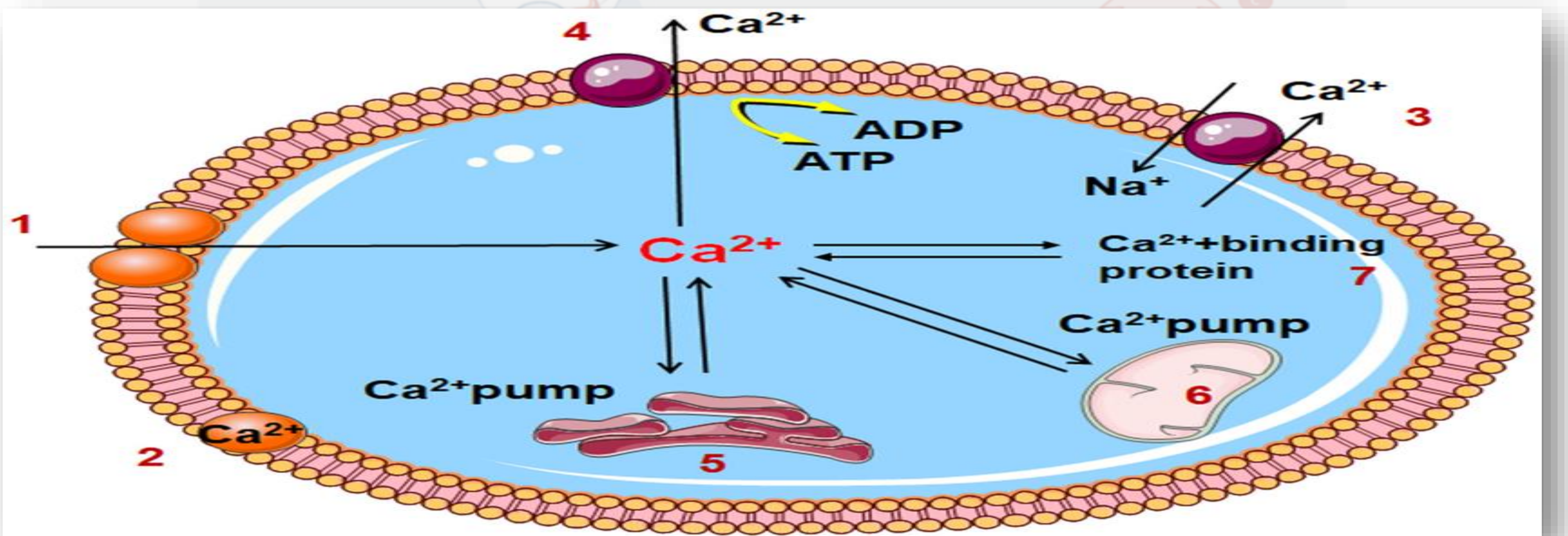
It keeps intracellular calcium at very low level.

**2 types of $Ca^{++}$ pump:**

- One is in the **cell membrane** and **pumps calcium to the outside of the cell**.
- The other **pumps calcium ions into one or more of the intracellular organelles of the cell**, such as the **sarcoplasmic reticulum of muscle cells** and the **mitochondria in all cells**.
- In each of these instances, **the carrier protein penetrates the membrane and functions as an enzyme ATPase**, having the same capability to cleave ATP as the ATPase of the sodium carrier protein.



Na⁺
1
2
Ca²⁺
DHP
Transverse tubule
ATP
Na/K/ATPase
K⁺
Sarcolemmal membrane
NCX
AQP4
ATP
B
Ca²⁺
3
Sarcoplasmic reticulum
RyR
Ca²⁺
SERCA
D
5
4
ATP
Pi
ADP
A
ROS
C

4
Ca²⁺
Ca²⁺
3
ADP
ATP
Na⁺
1
Ca²⁺
Ca²⁺+binding protein
7
Ca²⁺pump
Ca²⁺pump
6
Ca²⁺
2
5

### 3. $H^+$ ATPase pump:

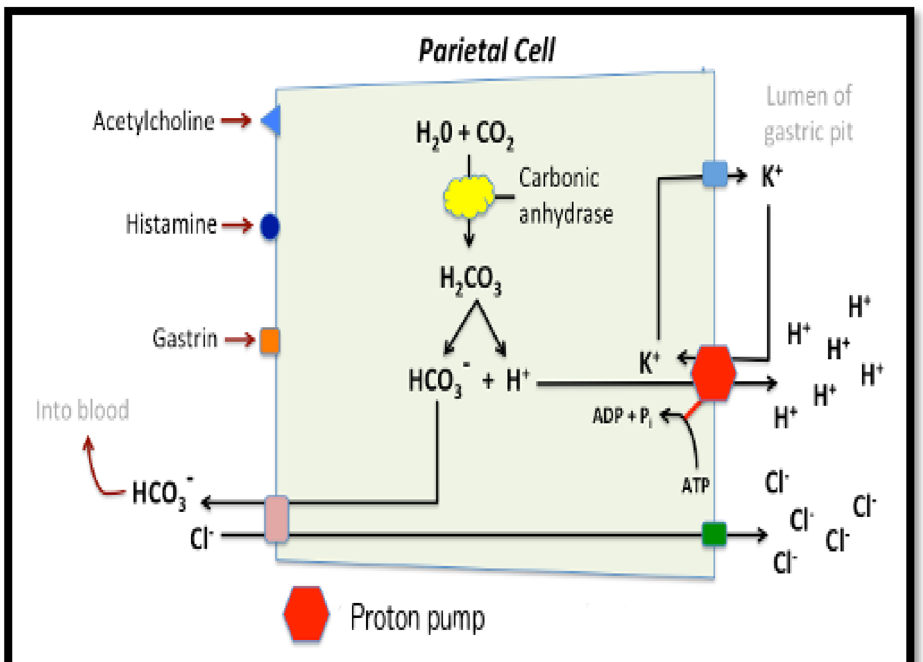
At two places in the body, primary active transport of hydrogen ions is very important:

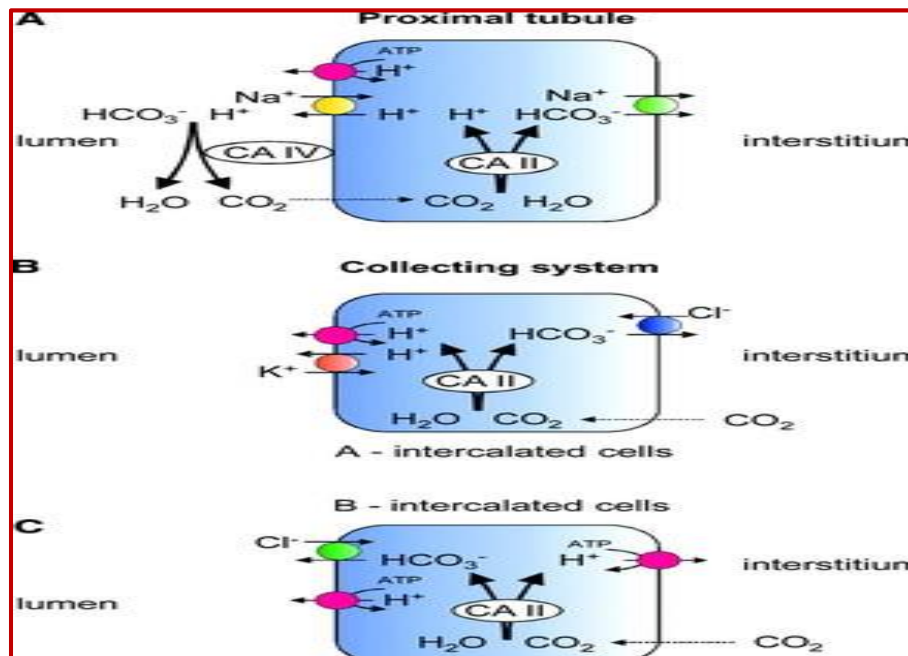
(1) in the gastric glands of the **stomach**: In parietal cells for **HCl secretion**.

(2) in the **late distal tubules and cortical collecting ducts of the kidneys**:

In special **intercalated cells**, large amounts of hydrogen ions are secreted from the blood into the urine for the purpose of eliminating excess hydrogen ions from the body fluids (**to keep acid-base balance**).

(3) In **lysosomes** for acidification to maintain optimal pH (= 5) for **hydrolytic enzymes**.



# 2. Secondary active transport

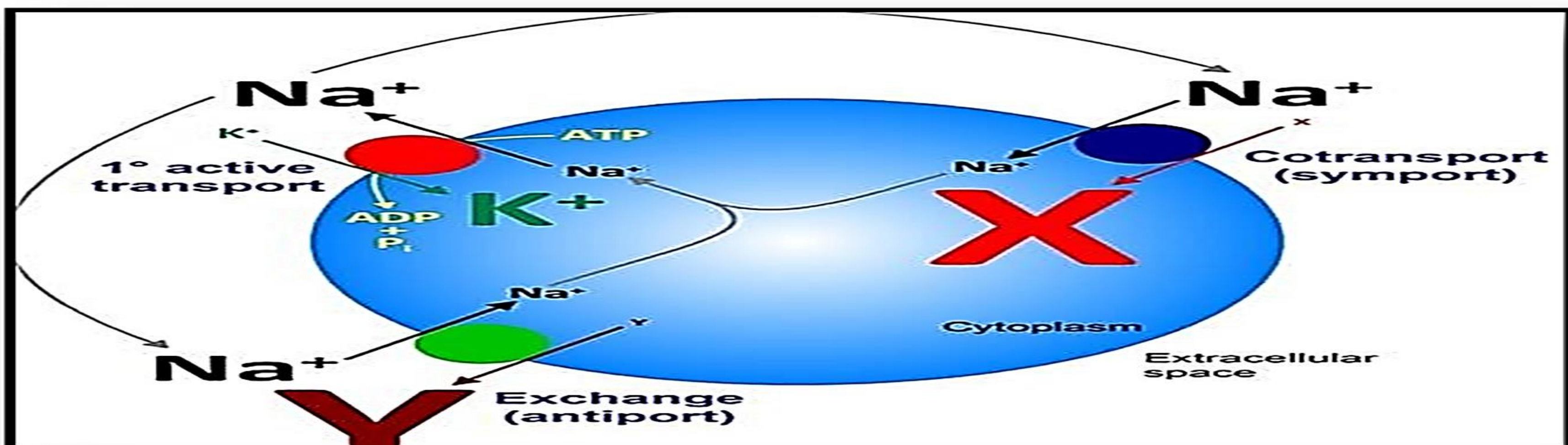
- It is a transport of one or more solutes **against an electrochemical gradient**, **coupled to the transport of another solute down an electrochemical gradient**.
- **“downhill” solute; with electrochemical gradient; is $Na^+$**.
- **Energy is derived indirectly from primary active transport**.
- **Types:**

**A. Co-transport.**

**B. Counter - transport.**

• $Na^+$ is actively pumped out of the cell by $Na^+$-$K^+$ pump creating a concentration gradient for $Na^+$ (high outside and low inside the cell).

• A cotransport (or antiport) carrier binds both $Na^+$ and substance X or substance Y. $Na^+$ moves from outside to inside according to its concentration gradient, while both of substance X and substance Y move against their concentration gradient ( from outside to inside for substance X and from inside to outside for substance Y). The transport of both X and Y is called secondary active transport because it occurs against concentration gradient making use of the energy derived from the concentration gradient of Na+ that is created by the active $Na^+$-$K^+$ pump



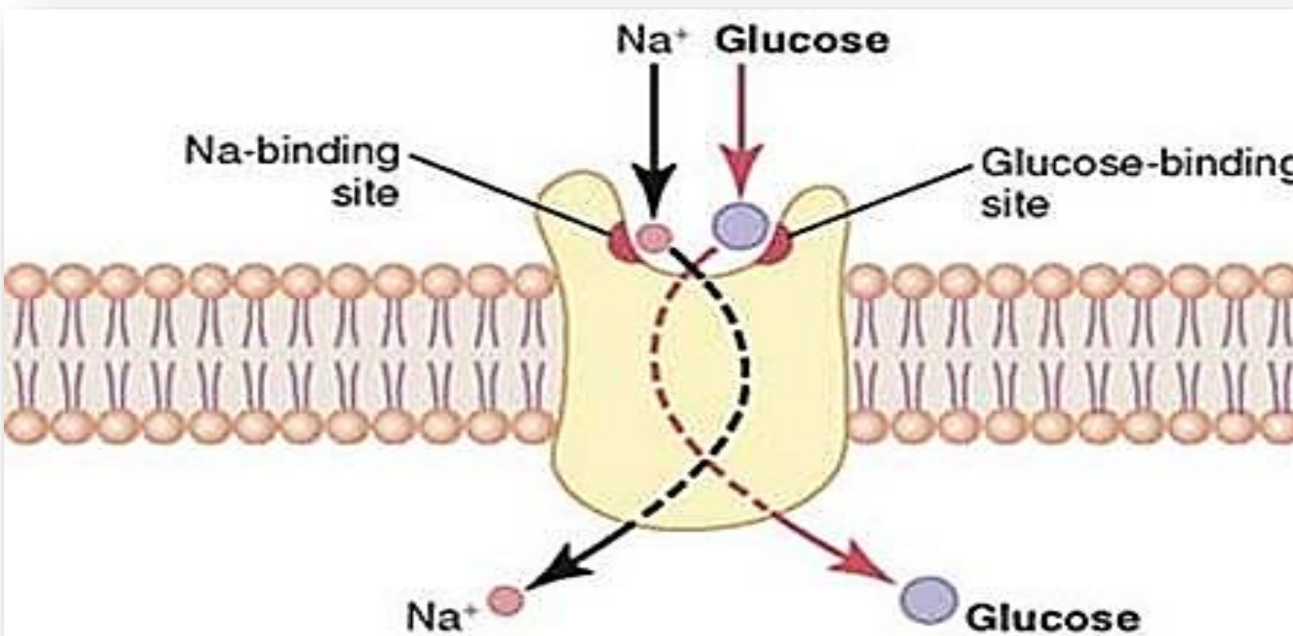
# A. CO-TRANSPORT

- Transport of two substances in the same direction.
- All solutes move in the same direction “inside cell”.
- **Examples:**

• $Na^+$ – glucose Co-transport.

• $Na^+$ – amino acid Co-transport.

(in GIT or renal tubular cell)

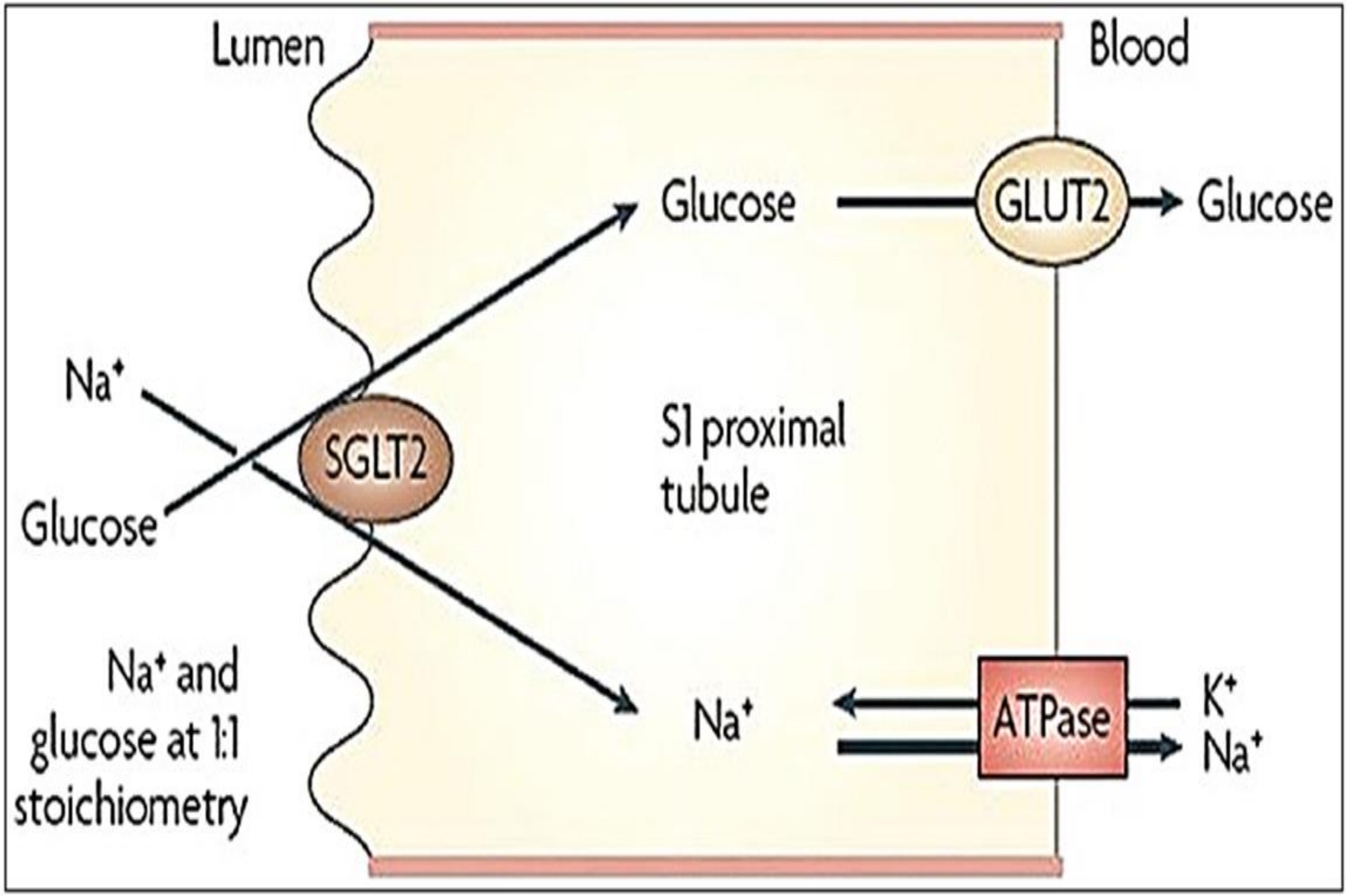


# MECHANISM of CO-TRANSPORT

**Sodium-glucose co-transport mechanism.**

- ✓ The transport carrier protein has two binding sites on its exterior side, one for sodium and one for glucose.
- ✓ Also, the concentration of sodium ions is very high on the outside and very low inside, which provides energy for the transport.
- ✓ A special property of the transport protein is that a conformational change to allow sodium movement to the interior will not occur until a glucose molecule also attaches.
- ✓ When **they both become attached, the conformational change** takes place automatically, and the **sodium and glucose are transported to the inside of the cell at the same time**.

- ✓ Sodium **co-transport of the amino acids** occurs in the same manner as for glucose, except that it uses a **different set of transport proteins**. Five amino acid transport proteins have been identified, each of which is responsible for transporting one subset of amino acids with specific molecular characteristics.

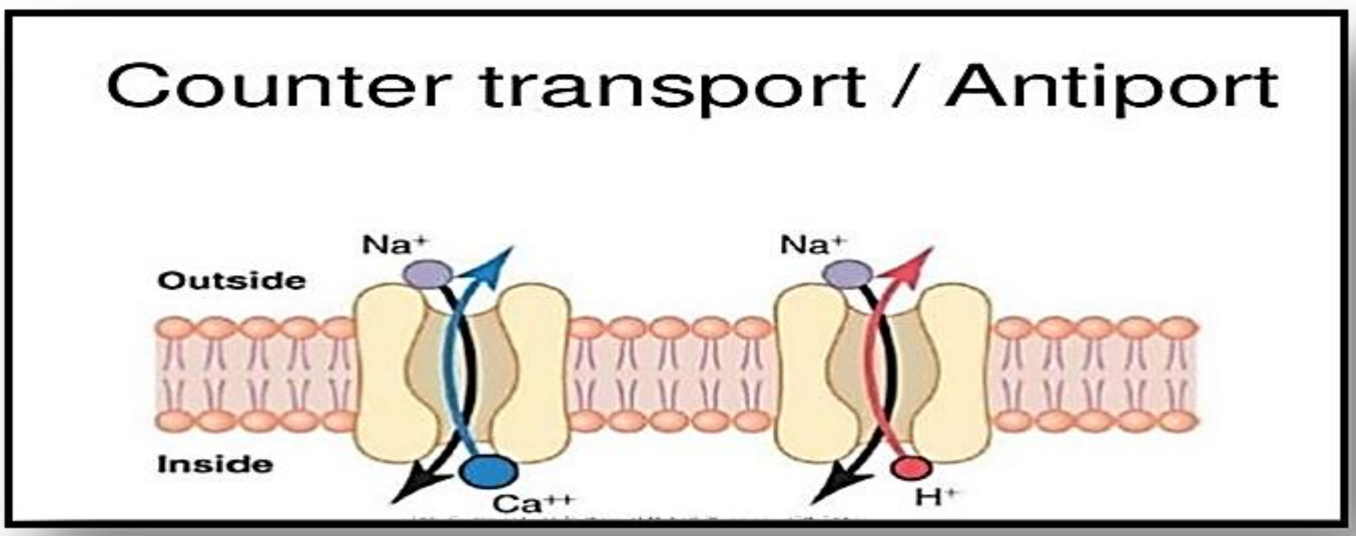

Lumen
Blood
Glucose
GLUT2
Glucose
Na+
SGLT2
Glucose
S1 proximal
tubule
Na+ and
glucose at 1:1
stoichiometry
Na+
ATPase
K+
Na+

# B. COUNTER-TRANSPORT

- Two substances in **opposite direction.**
- **Na+** is moving to the **interior** causing **other substance** to **move out**.
- **Examples:**

• $Na^+ – Ca^{2+}$ counter-transport in the heart.

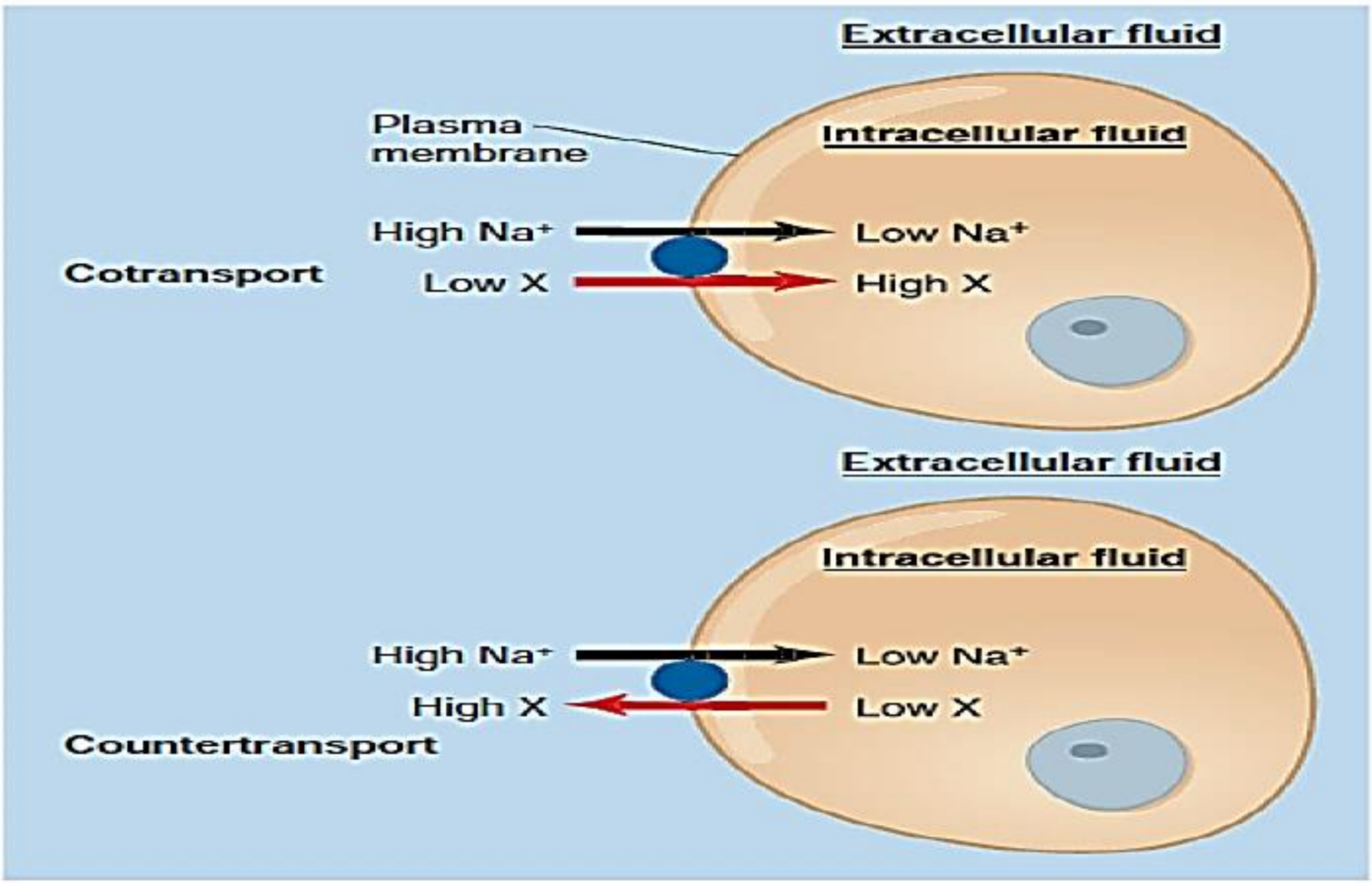
• $Na^+ – H^+$ counter-transport in the kidney (proximal convoluted tubule; PCT).



# MECHANISM of COUNTER-TRANSPORT

- In counter-transport, **sodium ions attempt to diffuse to the interior** of the cell because of their large **concentration gradient**. However, this time, **the substance** to be transported is on the inside of the cell and must be **transported to the outside**.
- Therefore, **the sodium ion binds to the carrier protein where it projects to the exterior surface** of the membrane, while the **substance** to be counter-transported **binds to the interior projection of the carrier protein**. **Once both have bound, a conformational change occurs, and energy released by the sodium ion moving to the interior causes the other substance to move to the exterior**.

# Secondary active transport



# Vesicular Transport

**Large molecular sized substances** enter and leave the cells by these mechanisms:

## 1. ENDOCYTOSIS

**Mechanism:**

- Active process requiring energy.
- The material makes contact with the cell membrane.
- The cell extends cytoplasmic processes (i.e. pseudopodia) around the substance which becomes enclosed as a food vacuole within the cytoplasm).

**Endocytosis includes:**

**a. Phagocytosis (cell eating)** is the process by which bacteria and dead tissue, are engulfed by cells such as the polymorphonuclear leukocytes of the blood.

**b. Pinocytosis (cell drinking)** is a similar process with the **vesicles much smaller in size and the substances ingested are in solution**.

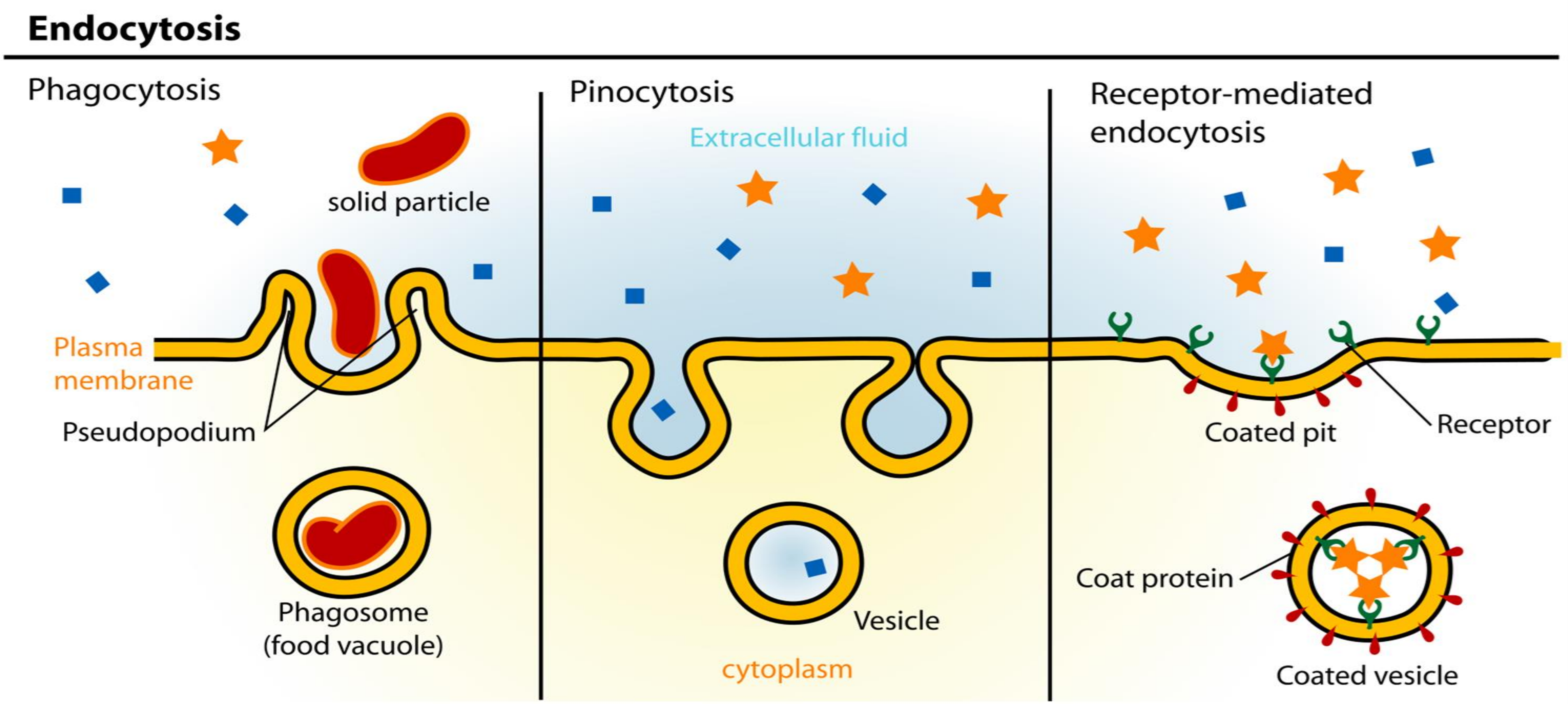
**There are 2 kinds of endocytosis:**

**a. Constitutive endocytosis:**

This is a continuous process that is not induced by signals.

**b. Receptor- mediated endocytosis:**

This is triggered by ligands that bind to receptors on the cell surface, and it occurs via special **coated pits** on the cell membranes.

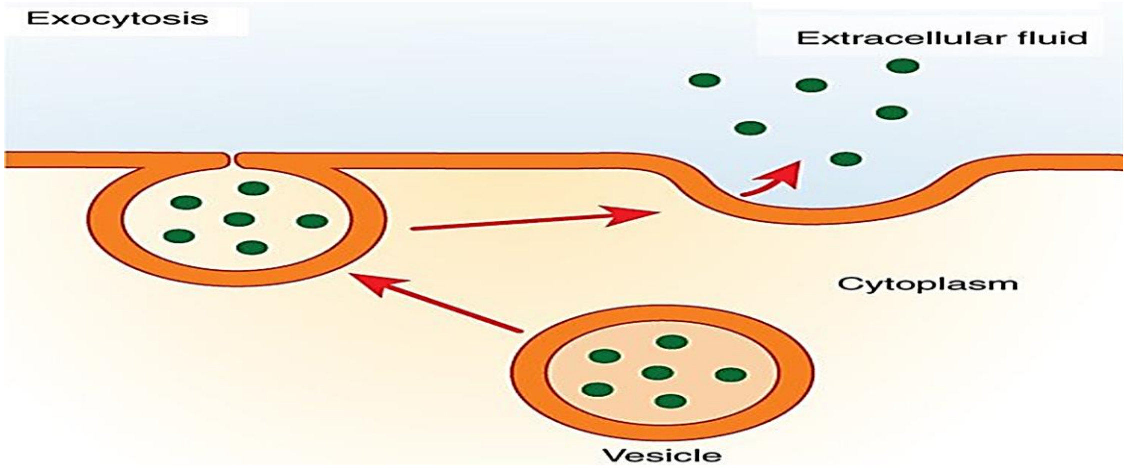


# 2. EXOCYTOSIS

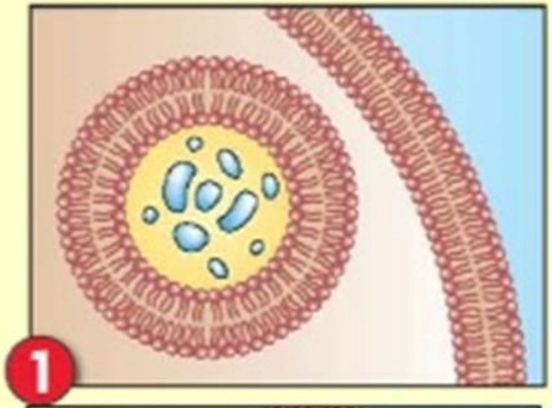
- This is the reverse of endocytosis.
- It is also called cell vomiting.
- It is also an **active process** (requiring energy) by means of which secretory granules (or vesicles) are **extruded out of the cell**.
- The membrane of the granule or vesicle fuses with the cell membrane, then the area of fusion breaks down and its contents are expelled outside the cell while the cell membrane remains intact.
- **Examples:**

1- Pancreatic cells secrete insulin into the blood by exocytosis.

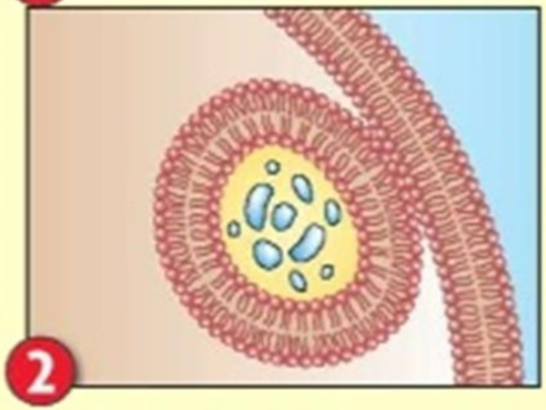
2- Neurons use exocytosis to release neurotransmitters that signal other neurons or muscle cells.



# Process of Exocytosis




The cell forms a vesicle around material that needs to be expelled from the cell.




The vesicle is transported to the cell membrane.


The vesicle membrane fuses with the cell membrane and releases the contents from the cell.


THANK
YOU