◉Sheet ○Slides

Number

5

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Vesicular Transport

We have talked about primary active transport and secondary active transport. Now we will talk about *vesicular transport which is a modality of active transport mechanism, it involves movement of particles in and out of the cell, and requires energy supplied by ATP.*

*** Structures involved in vesicular transport:**

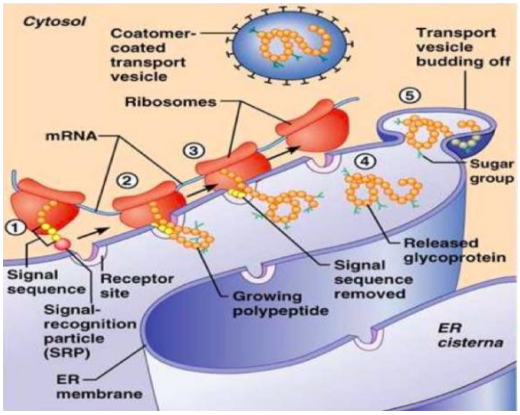
1- **Microtubules**, the cytoskeletal structures.
2- **Endoplasmic reticulum ER**: *a membranous structure lining another compartment inside the cell, and have different composition from the cytosol (like high amounts of proteins).* It synthesizes proteins and membrane structures.

In some cells, there is a higher concentration of calcium ions inside the ER, which is sometimes needed to control transport from ER to the cytosol. How to maintain this gradient? By active transport; calcium is transported through pumps across ER membrane from cytosol to the inside of ER.

ER synthesizes 2 types of proteins that are then transported towards the plasma membrane:

a) Secretory proteins → introduced inside this compartment then are engulfed by vesicles.
b) Functional proteins → remain inserted in the ER, HOW? they have an amino acid sequence that is more liposlouble so they get stuck into the membrane of ER.

- Both types of proteins are transported by vesicles to Golgi complex.



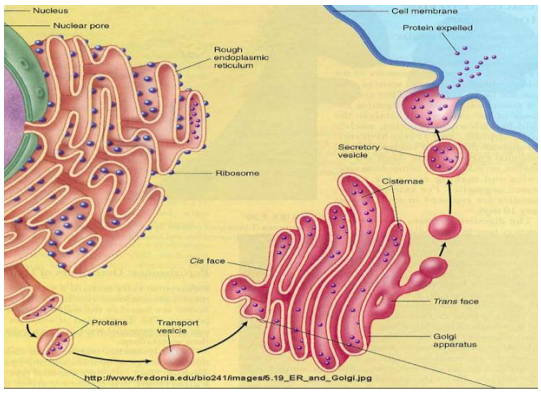
3- **Golgi complex**: sorts proteins synthesized in ER; rearrange the proteins into groups according to their final destination; Each protein has an address (an amino acid sequence), Golgi reads these addresses and packs each group of proteins together. Then they are sent to their destinations by new vesicles.

Vesicles:

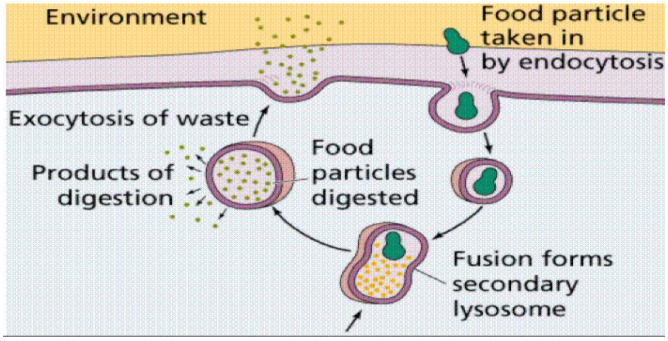
Endoplasmic reticulum generates vesicles that are transported towards Golgi complex in the following manner :
motor proteins attach vesicles to the microtubules and walk along microtubules by

the process of phosphorylation and dephosphorylation: *both induce motor protein to change shape, so it's switching continuously between 2 shapes as it walks along the microtubules.* Phosphorylation means that ATP molecules (energetic molecules) are consumed, so it is an active transport mechanism.

*** Types of vesicular transport:**



1- **Exocytosis** new secretory vesicles are formed by Golgi complex carrying proteins designated to the plasma membrane. First, these vesicles dock at the membrane. Then they fuse with it releasing their contents to the ECF.



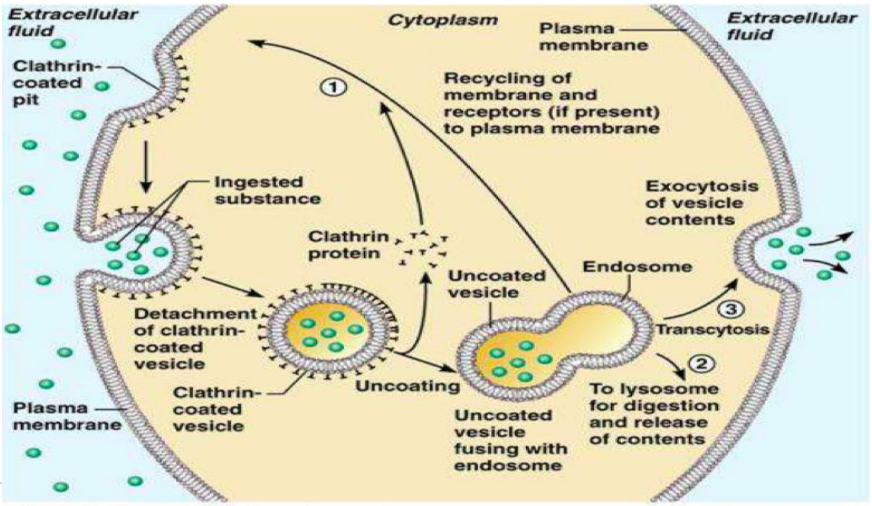
2- **Endocytosis** the movement of particles **e.g.(**neurotransmitters, hormones, digestive enzymes**)** into the cell by vesicles; reverse of exocytosis. Lysosomes have highly enzymatic content which digest food particles.

Wastes are released by exocytosis.

10:00

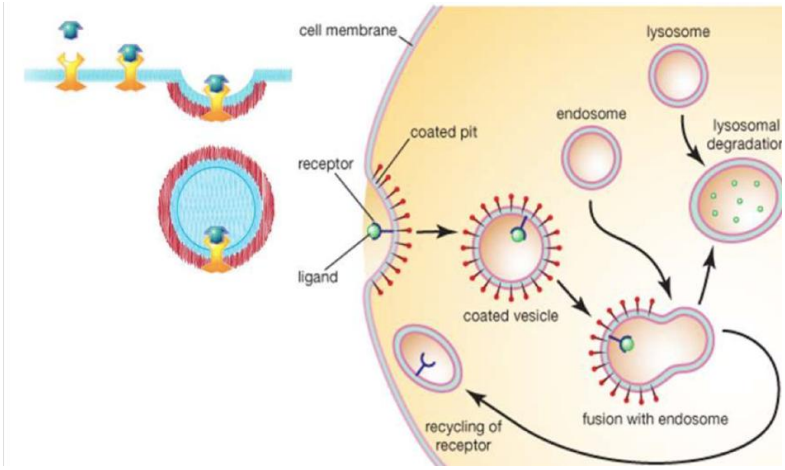
3- **Phagocytosis** solid particles **e.g. (**bacteria, viruses, dead cells**)** engulfed by pseudopods to form pseudosomes, these particles are then destroyed. Phagocytosis can be considered in some cases as receptor mediated endocytosis; immune cells cannot engulf antigens unless they are bound to an antibody, the antibody has a part that binds with the cell, the binding of this part activates phagocytosis allowing the immune cell to ingulf the antibody and the antigen.

4- **Transcytosis** vesicles formed by endocytosis at one pole of the cell are transported to the other pole of the cell where they are involved in exocytosis.



5- **Pinocytosis** movement of ECF **e.g.(**solutes in ECF**)** into the cell by infolding of plasma membrane to form a pinocytic vesicle. Used by bacteria to engulf water.

6- **Receptor mediated endocytosis (stimulated process)** the binding of a ligand to the receptor activates endocytosis in which clathrin-coated pits infold to form a vesicle containing ligand. This vesicle fuses with endosome before its contents are degraded by lysosomes. The receptor is then recycled.

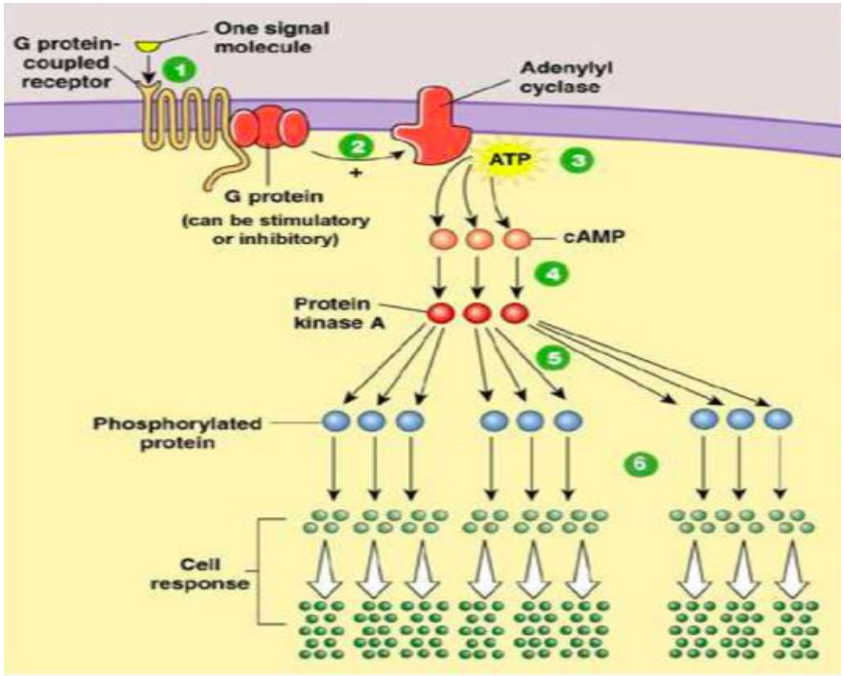


Control of Transport

Is the process of transport across plasma membrane controlled?
It is highly controlled

What is the link between enzymes and transport?

You have seen the aspects of the control, as in the activation of the enzyme adenylate cyclase increases concentration of cyclic AMP. This increase can change the activity of channels **e.g.(** K channels, Ca channels, Na channels **).**

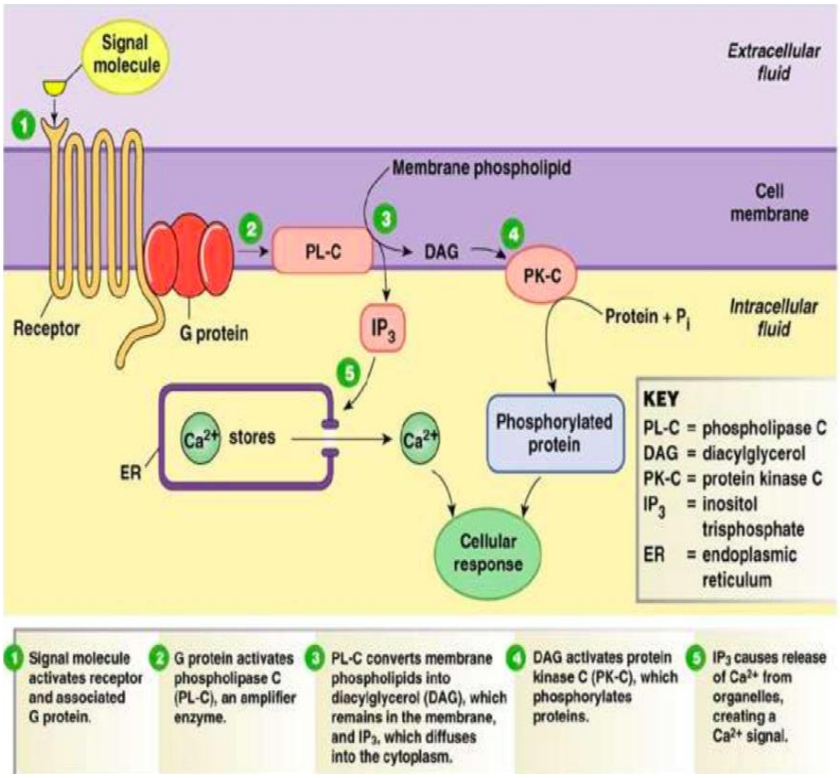


Direct activation of channels (to get more transport)

chemical gated channels: *channels activated by the binding of ligand to receptors.*

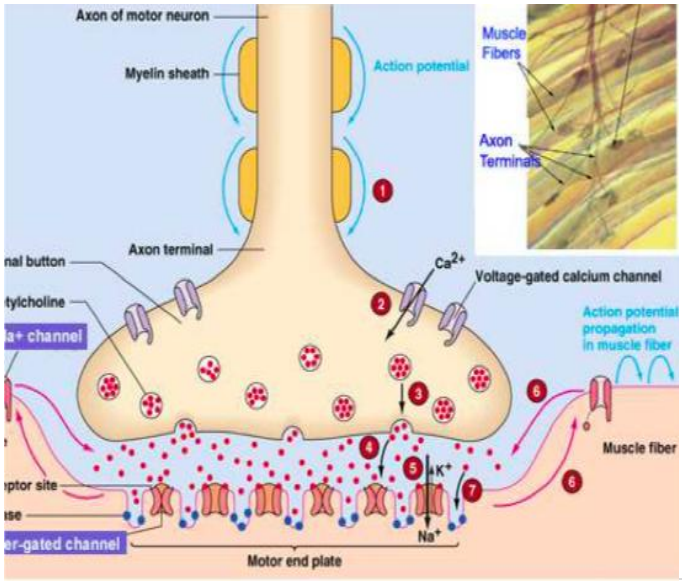
Phospholipase biphosphate splits PL-C into inositol triphosphate IP_3 and diacylglycerol DAG, splitting it between the phosphate group and the glycerol.

→On the endoplasmic reticulum of some cells, there are receptors for the IP_3. the binding of IP_3 can cause activation of Ca channels (*a chemical gated channel*). Since the concentration of calcium ions inside ER is higher, calcium ions will diffuse towards the cytosol. So, we can increase the transport of Ca ions thus changing the activity of the cell by increasing the calcium concentration inside the cytosol.



To get less transport → inactivation of channels

Control of Exocytosis



Also, vesicular transport is highly controlled.

Nerves have terminals at the end of axons which are the storage of neurotransmitters. A nerve terminal contains plenty of vesicles that carry the neurotransmitters, **where are these vesicles formed?** in the cell body which is 20-30 cm far. Then they

are transported to the terminals by vesicular transport.

Release of neurotransmitters once we have a change in the electrical activity, Ca channels are activated and calcium ions are transported down the chemical gradient. Assuming that the vesicles and the axon terminal membrane are both negative, repulsion will occur. BUT as the Ca++ concentration increases inside the terminal, the polarity of the vesicles will change allowing them to dock on the membrane.

After docking to the membrane, vesicles release the neurotransmitters by exocytosis. To sum up, increasing Ca++ concentration inside the terminal activated exocytosis of neurotransmitters.

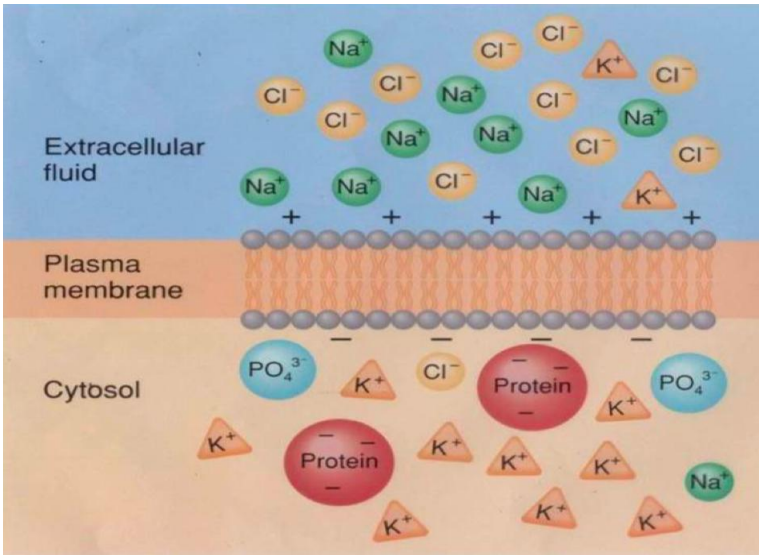
20:00

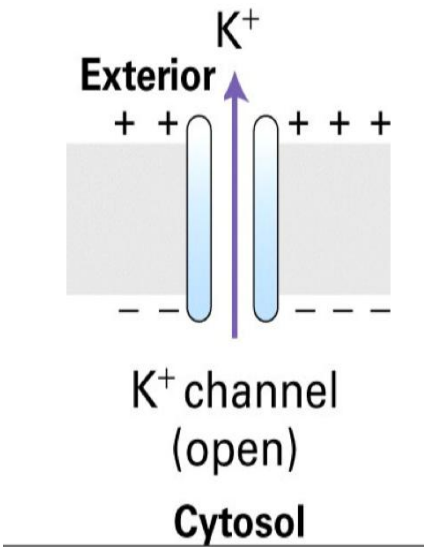
Transport of Ions across Plasma Membrane

Until now, we have discussed the transport of molecules in general regardless of their polarity. We will focus now on the transport of charged particles, the outcomes of it, and how we can change the activity of channels across excitable cells' membranes.

Examples of excitable cells → cardiac muscle cells, skeletal muscle cells, smooth muscle cells, neural cells.

The plasma membrane separates two compartments, each with different composition.





By concentration gradient, there is a high tendency for sodium to move from outside to inside, and a high tendency for potassium to move from inside to outside.
Assuming that the membrane is only permeable for potassium; will the movement of

potassium ions stop when the concentrations on both sides are equal? No.
during the movement of ions another event takes place; developing of **potential** across the membrane. When the **electrochemical equilibrium** is reached the created potential will prevent any net movement (even if the conc. of ions is still high in the ECF and low in the ICF).

Net diffusion:: *potassium is still moving from outside to inside and from inside to outside, but the difference between these movements is zero.*

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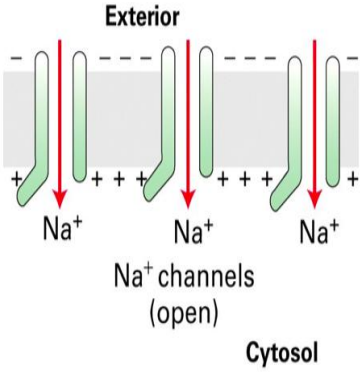


Assuming permeability for Na+ only, the inside of the cell becomes positive in respect to the outside due to the movement of sodium ions from the outside towards cytosol.

The case is the same when assuming permeability for Cl- only.

The Equilibrium Potential for an Ion

→ *the equilibrium resulting from the movement of this specific ion across the membrane*

→ **How to measure it?**
by placing an electrode across the membrane and another electrode outside the membrane

→ **How to calculate it**?

Nernest equation $\mathrm{E} = \frac{RT}{ZF}\ ln\ \frac{[C]_{out}}{[C]_{in}}$

R :gas contant [C] :ion concentration

T :absolute temperature F :faraday's constant

Z :valence (for Ca++ : 2) (for K+ : 1)

concentration is not measured in moles but instead, in **equivalents**: *takes valence into consideration, and it refer to the mole concentration of the ion that can replace one mole of H+.*
(1mol Ca++ replaces 2 mol H+)
(1mol K+ replaces 1 mol H+)

Electro-chemical Equilibrium Energy $E_{eq\,(ion)}$

$\Delta G_{conc} + \Delta G_{volt} = 0$

ΔE due to concentration differences + ΔE caused by the electrical properties of ions (one energy is working against the other)

$$zFV - RT \ln \frac{C_o}{C_i} = 0$$

$$V = \frac{RT}{zF} \ln \frac{C_o}{C_i} = 2.3 \frac{RT}{zF} \log_{10} \frac{C_o}{C_i}$$

$$E_{eq,K+} = 61.54mV \log \frac{[K^+]_o}{[K^+]_i}$$

The permeability for only a single ion is an assumption. In fact, the plasma membrane is usually permeable for both ions **e.g. (**permeable for Na+ and K**)**. BUT the permeability for one ion is much higher than the other. The potential created by the movement of the ion that the membrane is more permeable to will be closer to the equilibrium potential of that ion.

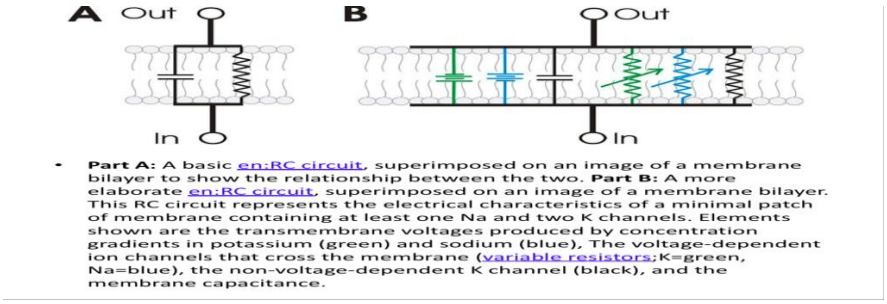
e.g. Na+/K+: the membrane is more permeable to K+ so the potential will be closer to the equilibrium potential of potassium { close to -95 BUT NOT equal to -95 }

Ion	Extracellular (mM)	Intracellular (mM)	Nernst Potential (mV)
Na^+	145	15	60
Cl^-	100	5	−80
K^+	4.5	160	−95
Ca^{2+}	1.8	10^{-4}	130

The membrane acts as an electric circuit

1- it has high resistance for the electrical activity

2- it separate the charges (functioning like capacitors)



- **Part A:** A basic en:RC circuit, superimposed on an image of a membrane bilayer to show the relationship between the two. **Part B:** A more elaborate en:RC circuit, superimposed on an image of a membrane bilayer. This RC circuit represents the electrical characteristics of a minimal patch of membrane containing at least one Na and two K channels. Elements shown are the transmembrane voltages produced by concentration gradients in potassium (green) and sodium (blue), The voltage-dependent ion channels that cross the membrane (variable resistors; K=green, Na=blue), the non-voltage-dependent K channel (black), and the membrane capacitance.

A: a basic en:RC circuit, superimposed on an image of a membrane bilayer to show the relationship between the two. B: a more elaborate en:RC circuit, superimposed on an image of a membrane bilayer. This RC circuit represents the electrical characteristics of a minimal patch of membrane containing at least one Na and two K channels. Elements shown are the transmembrane voltages produced by concentration gradients in K (green) and Na (blue), the voltage-dependent ion channels that cross the membrane (variable resistors; K= green, Na= blue), the non-voltage-dependent K channel (black), and the membrane capacitance.

46:00

THE END