Lecture 14

Physics of Bio-membrane

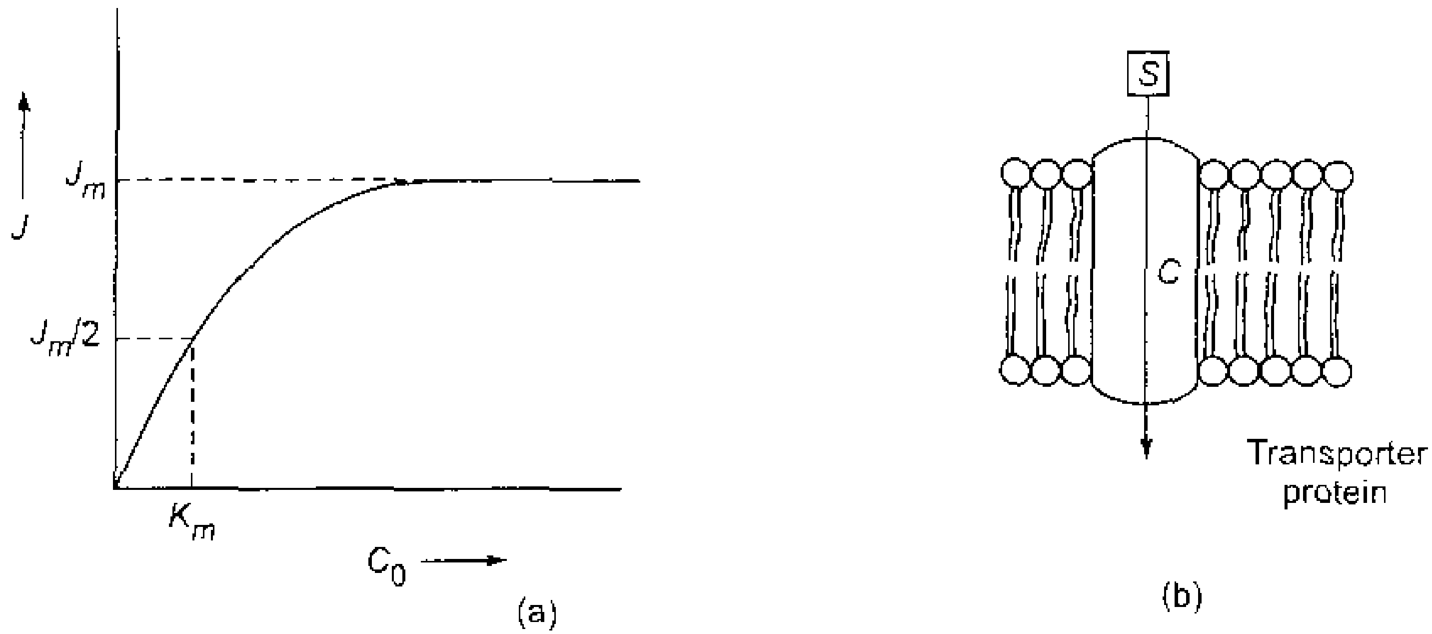
Part 2

Facilitated diffusion

- Fick's law shows that in case of simple diffusion the rate of diffusion (or flux) is proportional to concentration gradient

- However experimentally it is observed that
- 1. diffusion flux increases until a saturation value is reached. Example – diffusion of sugars, D-glucose
- 2. the presence of certain substances either promotes or inhibits diffusion of a particular molecule

- Therefore the transport is not simple, and does not occur only due to concentration gradient, this diffusion is facilitated by other substance and is called facilitated diffusion
- Such diffusion is facilitated by transporter molecule and depends on the concentration of transporter molecule



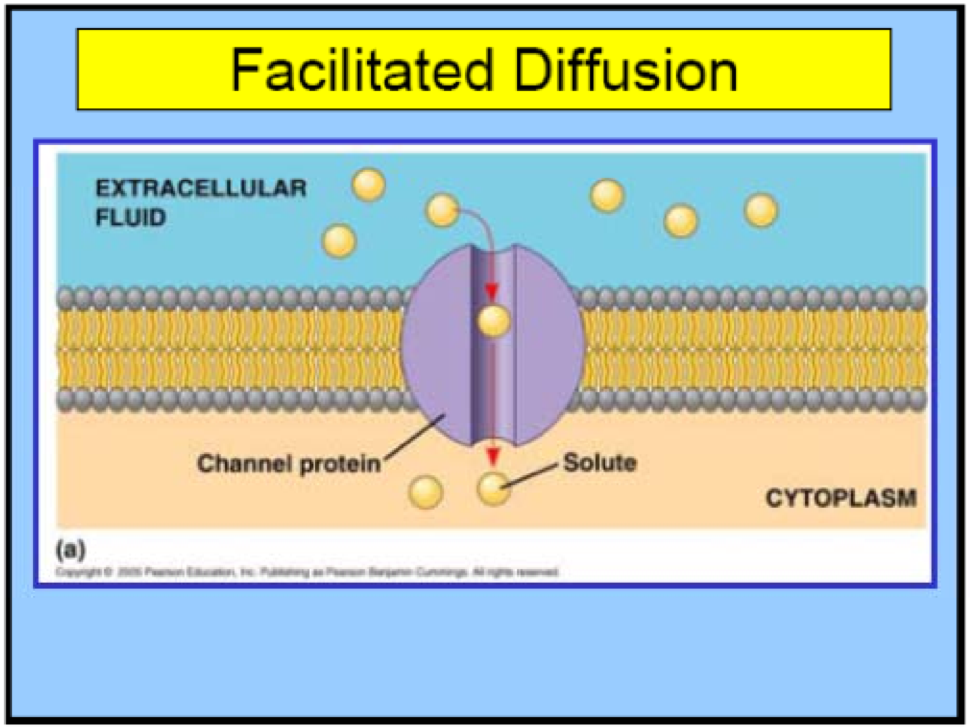
•a) The rate of facilitated diffusion J saturates at Jm;

•b) specific transporter protein C binds substance S and transports it across membrane

•Binding constant Km =concentration of protein C for which a diffusion is half max

•Facilitated diffusion is carried by two classes of transporters: channels and carriers

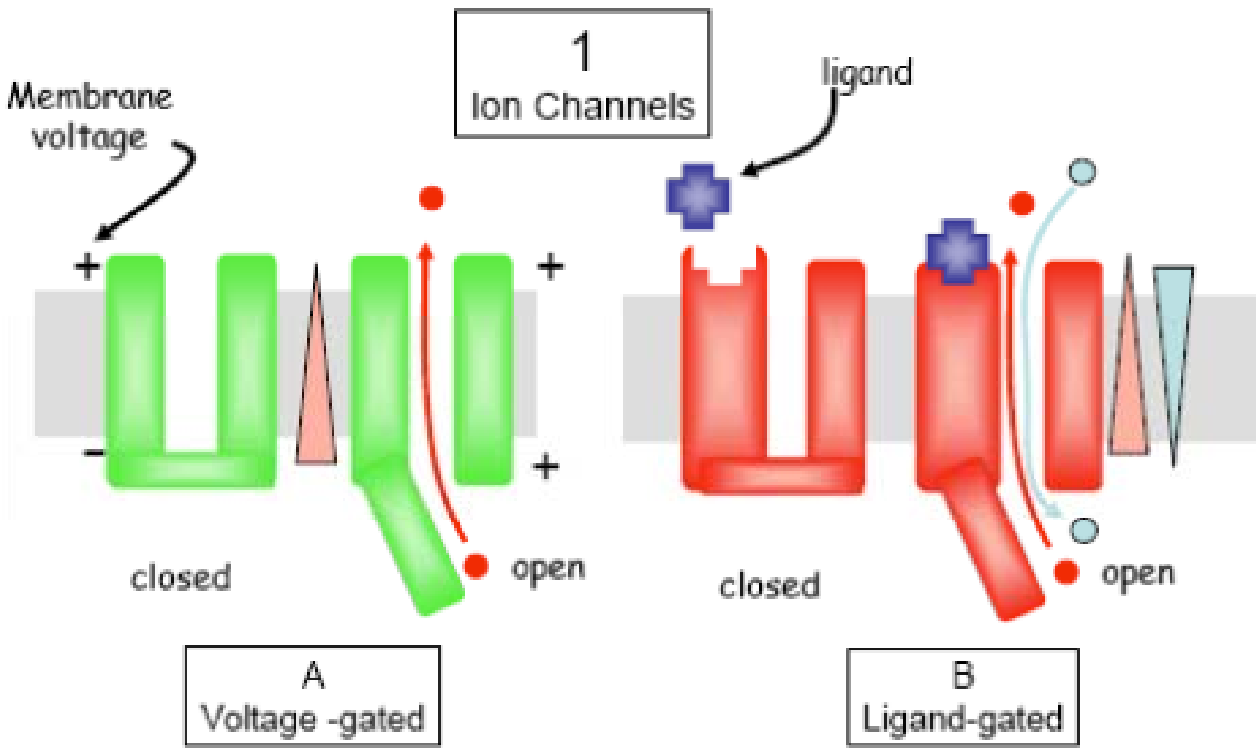
channels



Channels increase membrane permeability, and they are specific to certain ions or molecules, they have variable size of the pore and inner structure (charge, polarity),

example aquaporin – water transport, Na/K channels in neurons

Membrane Proteins Mediate Transport Across the Plasma Membrane



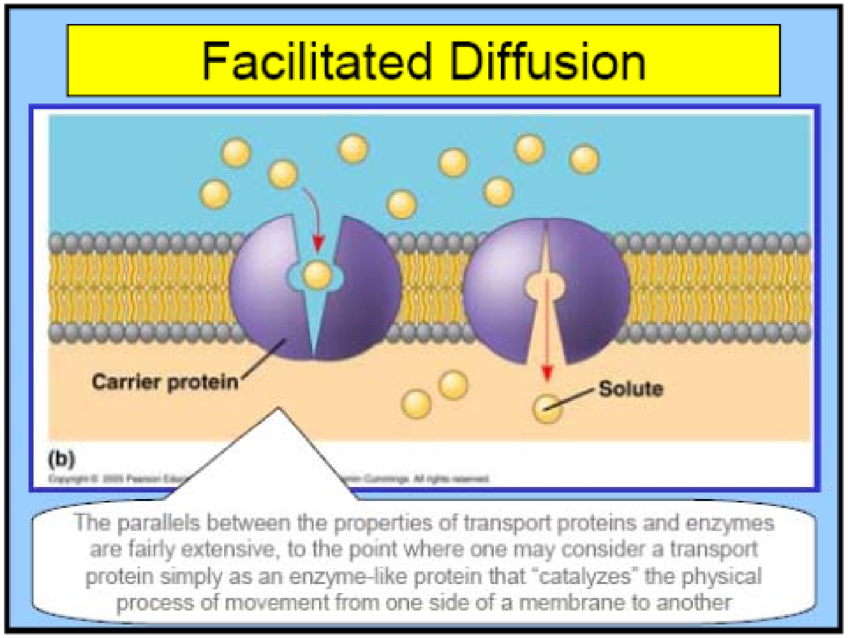
Because of selective transport the concentration of ions
is different inside and outside the cell

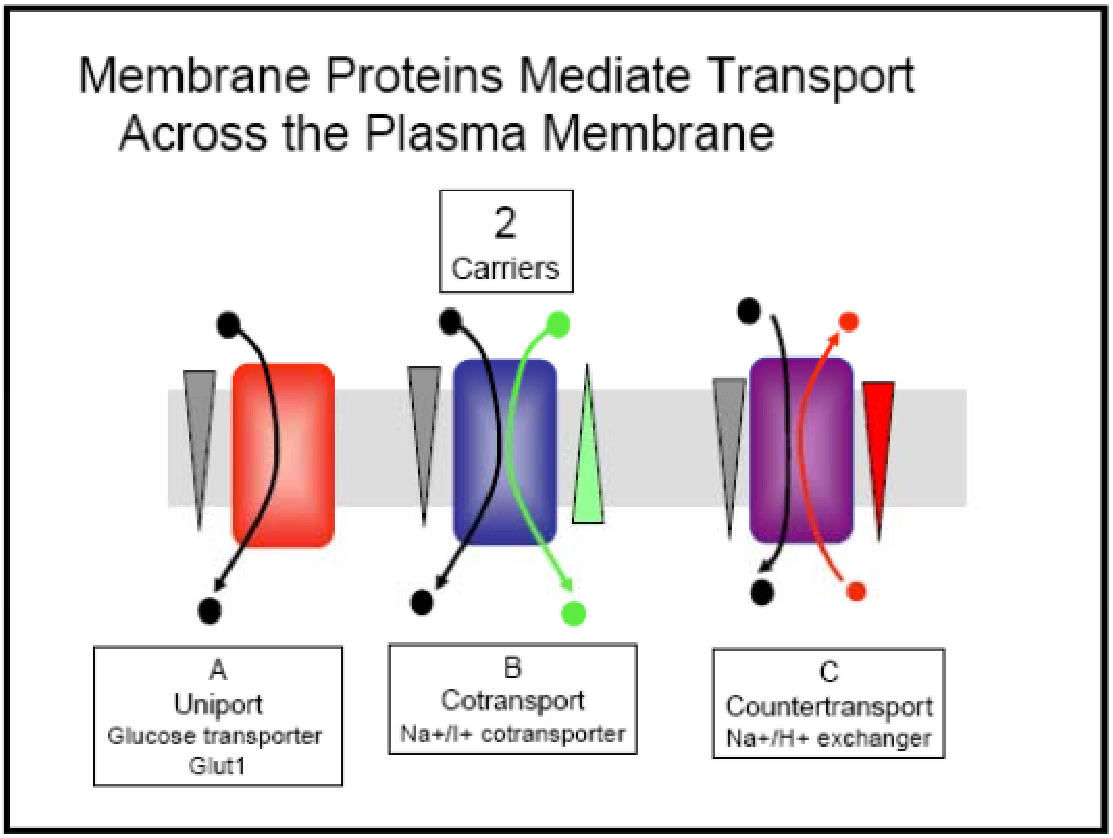
Ionic concentration in mammalian cells (in mM at pH 7.4)

Ion	Intracellular	Extracellular
Na^+	5–15	145
K^+	140	5
Mg^{2+}	30	1–2
Ca^{2+}	1–2	2.5–5
H^+ (pH 7.4)	4×10^{-5}	4×10^{-5}
Cl^-	4	110

carriers

- Molecules, which promote ion transport across membrane (carriers or ionofores)
- Example valinomycin
- They are hydrophobic outside and have hydrophilic cavity in the center, so that ion moves in
- Specific carrier for each ion, the structure of cavity is such that it accommodates the ion
- Valynomicin has 15 A cavity K+ fits, but Na+ does not bind properly there



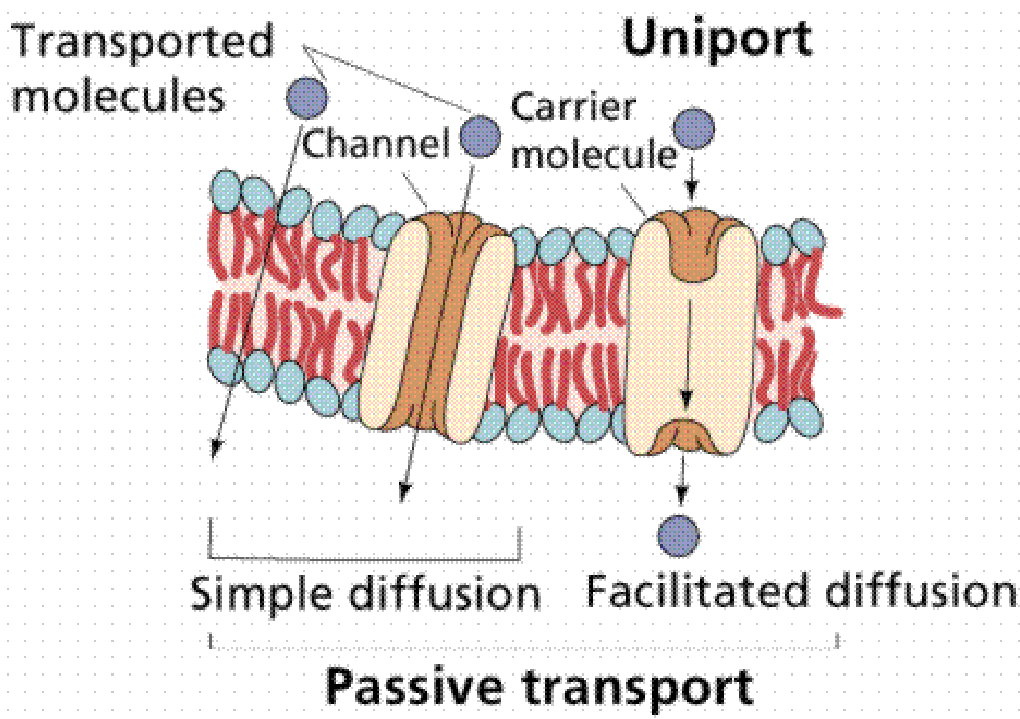


Types of transport molecules

Uniport transports one solute at a time.
Symport (co-transport) transports the solute and a co-transported solute at the same time in the same direction.
Antiport (counter-transport) transports the solute in (or out) and the co-transported solute the opposite direction. One goes in the other goes out or vice-versa.

Passive Transport

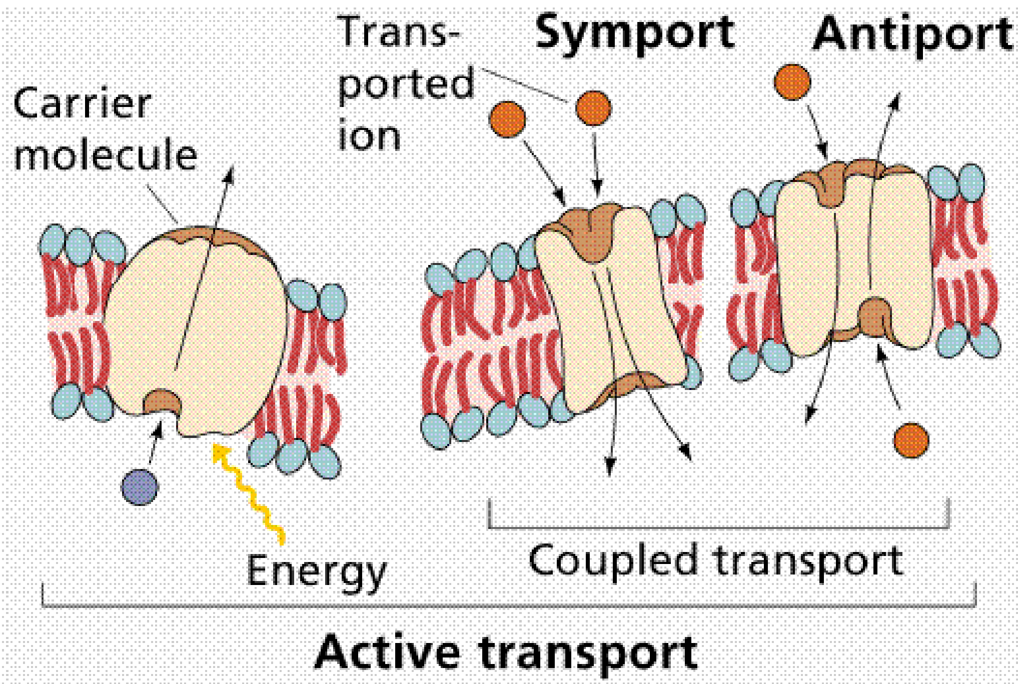
- Passive transport requires no energy from the cell. Examples include the simple diffusion of oxygen and carbon dioxide, osmosis of water, and facilitated diffusion.



The transport proteins integrated into the cell membrane are highly selective about the chemicals they allow to cross. Transport can be simple diffusion or carrier-assisted facilitated transport. Both simple diffusion and facilitated diffusion are driven by concentration gradient and/or potential gradient.

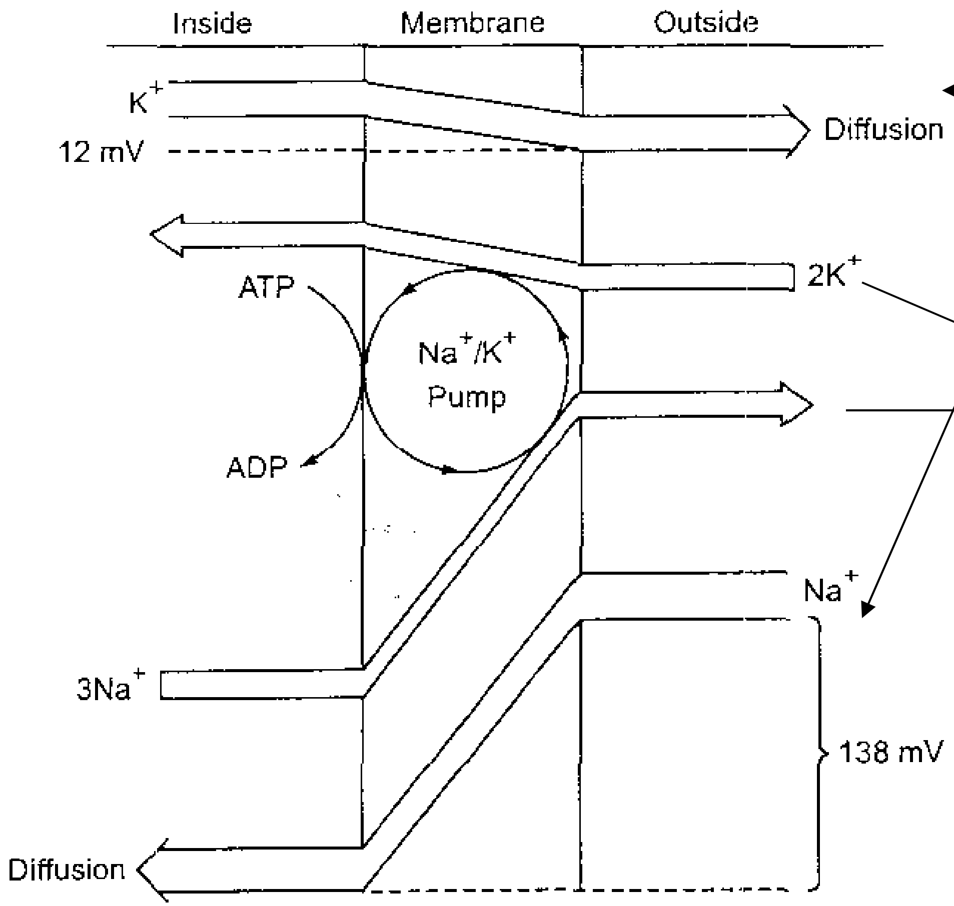
Active transport

- Active transport requires cell to spend energy, usually in the form of ATP. Examples include transport of large molecules (non-lipid soluble) and the sodium-potassium pump.



Active transport occurs in the absence of concentration gradient or electric potential gradient or pressure,
Active transport can move ions and molecules even against these gradients!
But energy is required

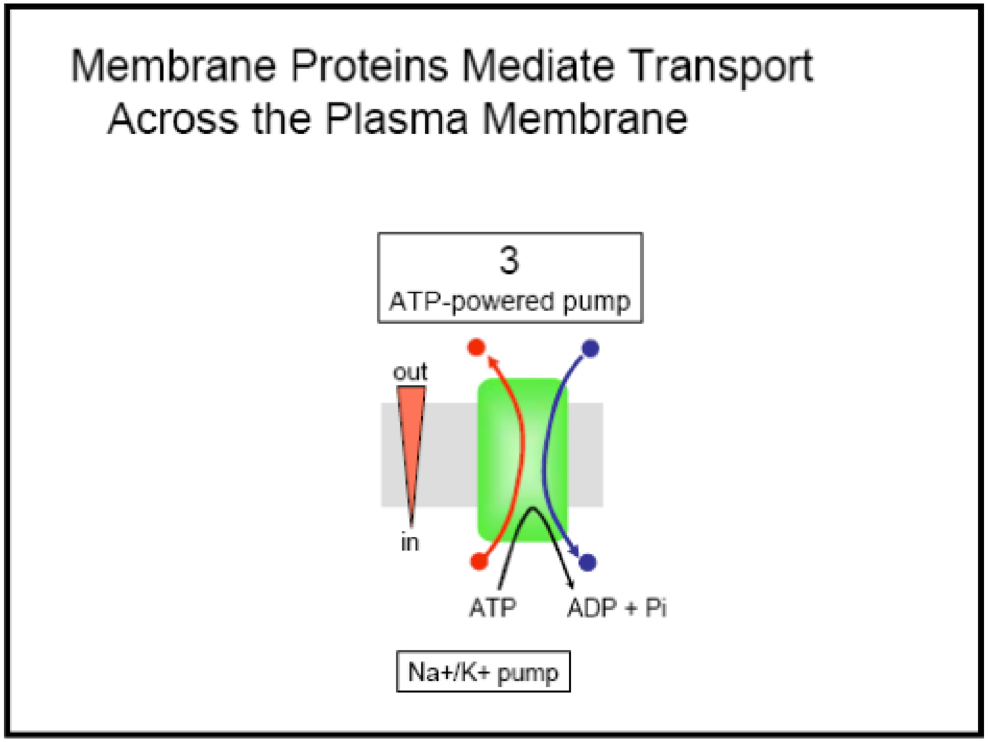
active transport, Na-K pump



Passive transport through channels due to concentration and electrical potential gradient

Active transport . The Na – K pump actively drives Na+ out and K+ in

active transport



Active transport requires energy, which is supplied by ATP,

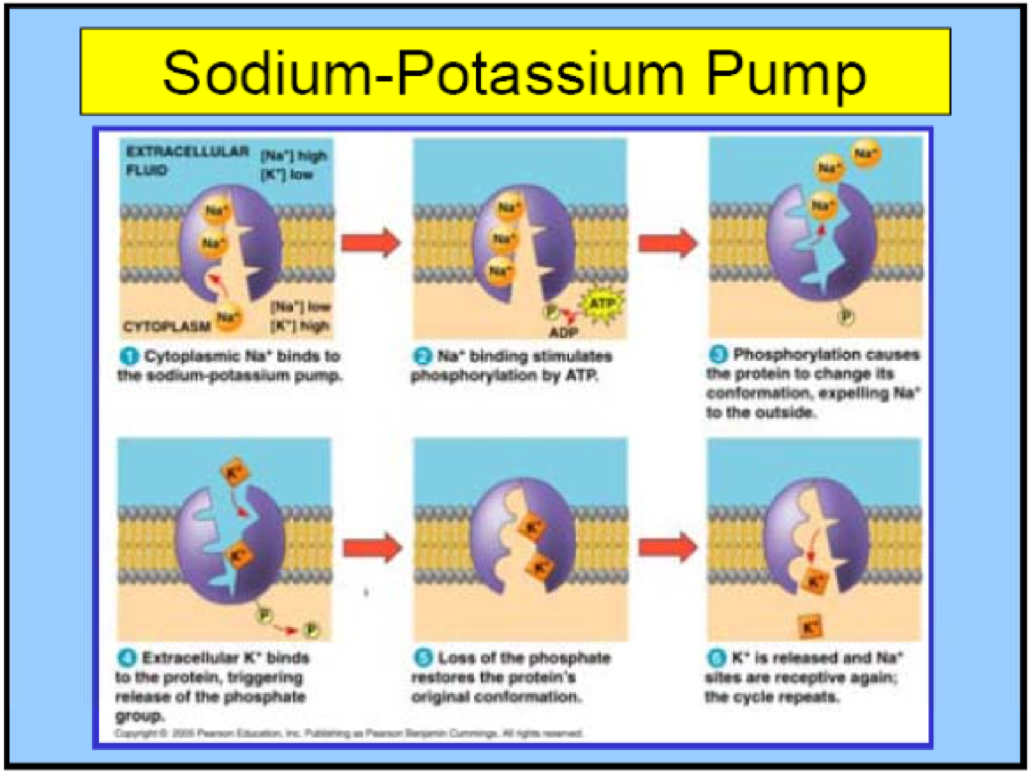
Hydrolysis of ATP provides energy, 1 ATP – 1 cycle

Membrane asymmetry is necessary for active transport

Ion channel has a binding site and is coupled with ATP

Fluid mosaic , membrane http://www.youtube.com/watch?v=Qqsf_UJcfBc&feature=related

active transport of Na+ and K+



Transport of Na and K ions is coupled –

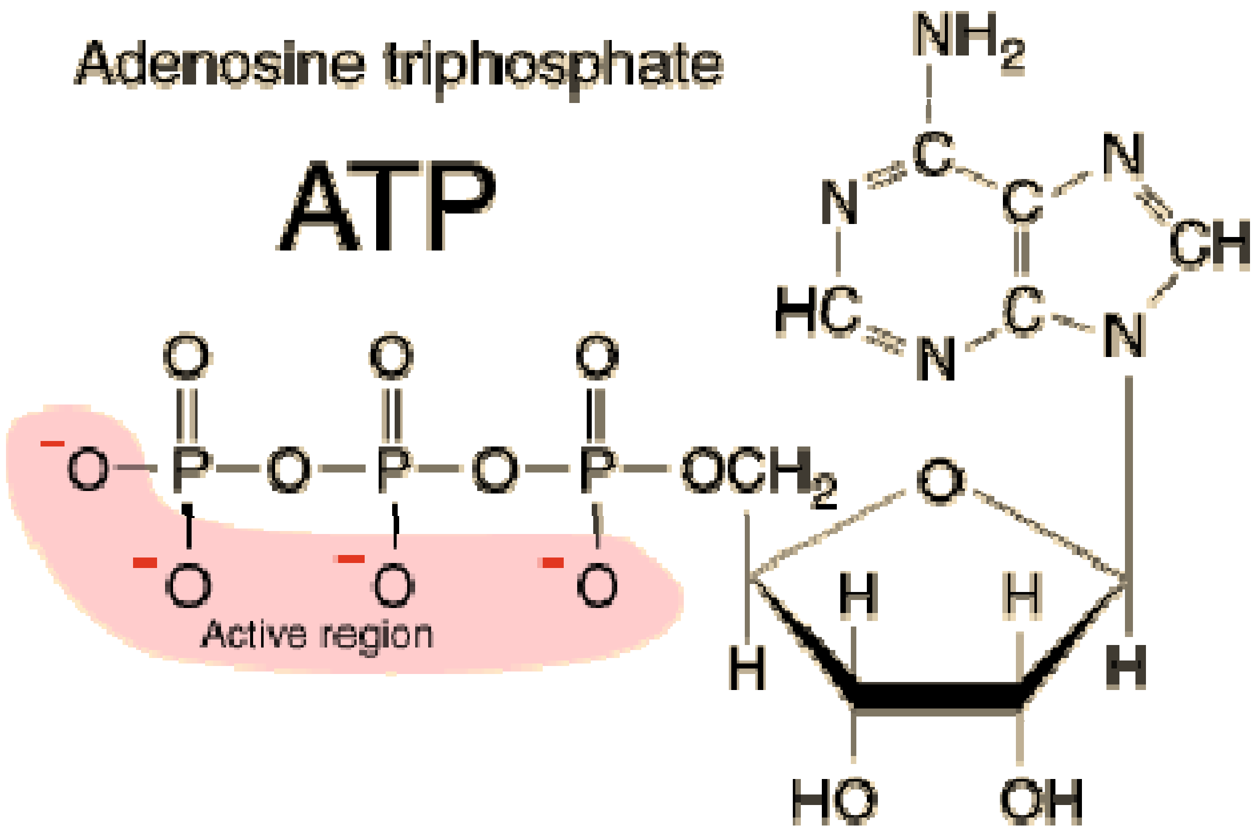
Na+ is transported – activate transport of K+ and visa versa

Ion channel – has binding site to Na+ on one side and K+ on the other side

protein C binds 3Na+ - reacts with ATP – changes conformation to C', transport Na+ to the outer side.

In C' conformation it has higher binding affinity to K+ , it looses 3Na+ on the other side and binds 2K+

http://www.youtube.com/watch?v=YA4Eng4CyZg&feature=related



ATP converts to ADP - the energy is released

7.3 kilocalories per mole = 30.6 kJ/mol.

This is about the same as the energy in a single peanut.

The structure of ATP has an ordered carbon compound as a backbone, but the part that is really critical is the phosphorous part - the triphosphate. Three phosphorous groups are connected by oxygens to each other, and there are also side oxygens connected to the phosphorous atoms. Negatively charged oxygens repel each other. There is a lot of potential energy here. If you remove just one of these phosphate groups from the end (ATP – to ADP – adenosine diphosphate), so that there are just two phosphate groups, the molecule is much happier and energy is released.

protein C binds 3Na+ - reacts with ATP – phosphorylates and changes conformation to C’, transport Na+ to the outer side.

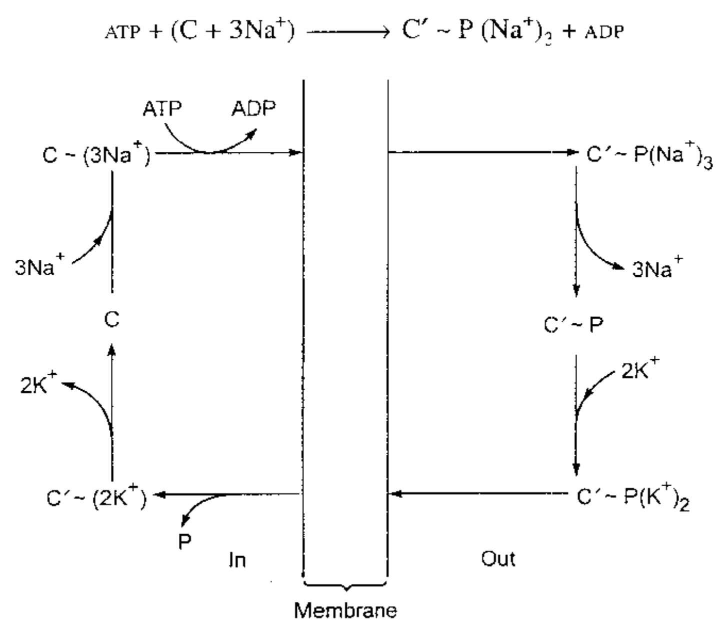
Essential role of protein C is to couple ion transport and ATP hydrolysis

$$C'\sim P(Na^{+})_3 + 2K^{+} \rightarrow C'\sim P(K^{+})_2 + 3Na^{+}$$

In C’ conformation it has higher binding affinity to K+ , it looses 3Na+ on the other side and binds 2K+

because of this the bond with phosphate group is weaker and protein C’ dephosphorylates back and changes conformation to initial conformation C, and the circle repeats

$$C'\sim P(K^{+})_2 \rightarrow C + P + 2K^{+}$$



Why Na+ and K+ is important?

- It is believed now that circulation of Na+/K+ ions mediates and regulates the transport of all other molecules and ions across the membrane
- Na+/K+ ion pump creates an ions gradient across membrane, creates the potential gradient
- sodium-potassium pump is important in nerve cells. Na+ is maintained at low concentrations inside the cell and K+ is at higher concentrations. The reverse is the case on the outside of the cell. When a nerve message is propagated, the ions pass across the membrane, thus sending the message. After the message has passed, the ions must be actively transported back to their "starting positions" across the membrane.
- sodium-potassium pump is important in plasma membrane energetics, by coupling to the ATP hydrolysis it captures the energy in the form of electro-chemical potential across the membrane - membrane is energized in this state, and uses the energy to transport other molecules and ions

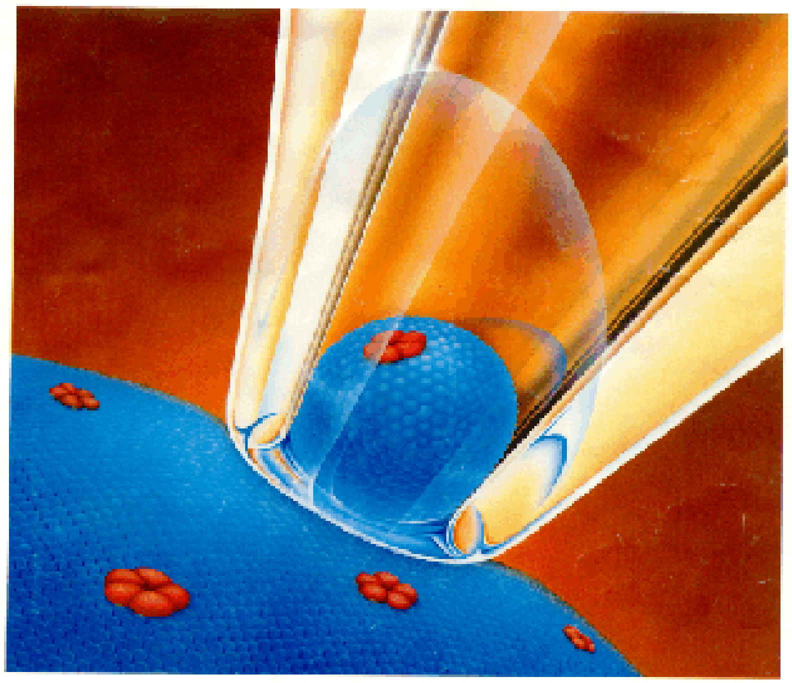
Action potential

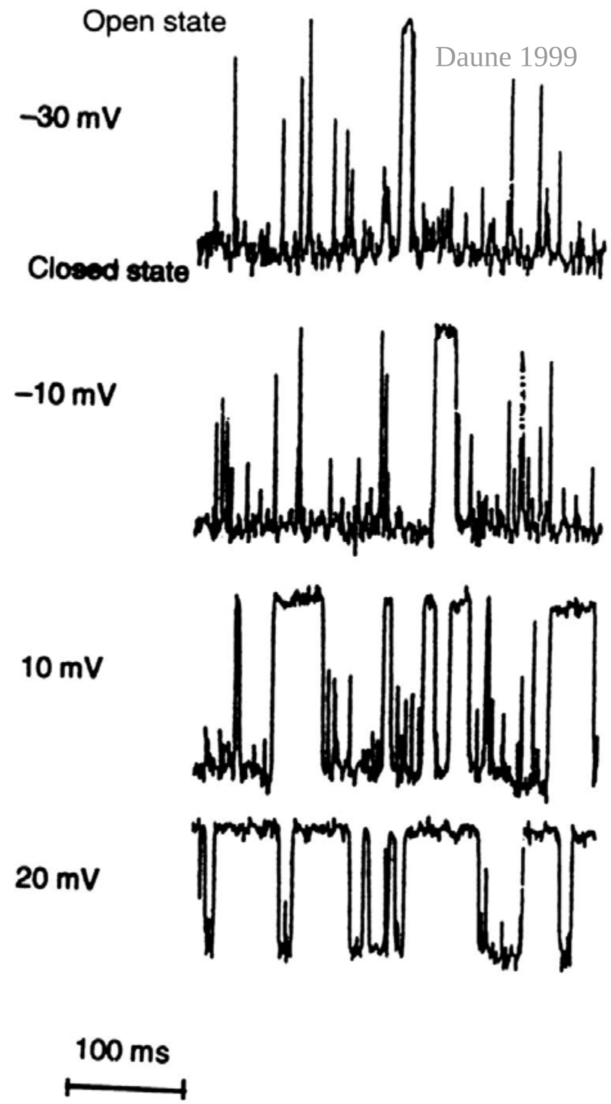
http://www.youtube.com/watch?v=U0NpTdge3aw&feature=related

Methods to measure conductance of single ion channels

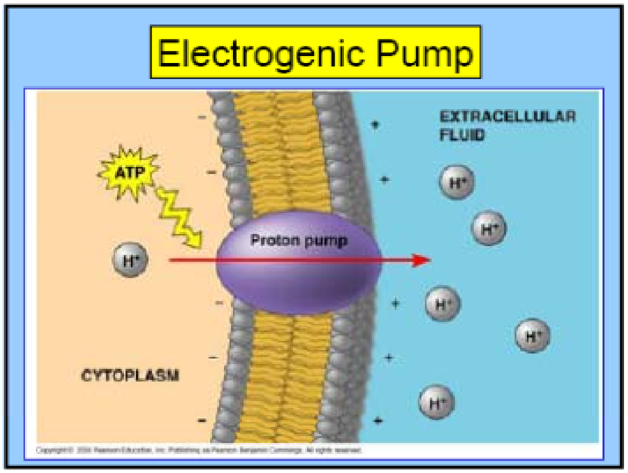
Patch-clamp: Glass pipette with tiny opening is used to measure membrane current

www-users.york.ac.uk/ ~fjm3/techpc.htm





Chemi–Osmotic theory of active transport



- Mitchel hypothesis:
- There are only two kinds of pumps in a living cell :
- 1. Na+/K+ pump in a cytoplasmic membrane
- 2. proton pump in internal membranes

  http://www.youtube.com/watch?v=Yr97niwxGHw

- The fundamental process of cell energetics is to maintain the circulation of proton or Na+ current across biological membranes. These membranes are regarded as alive (or energized) only if these pumps are functional

- In general, according to chemi-osmotic theory, there are two reversible transport systems associated with a pump. The first system pumps the ions across membrane at the cost of some energy source. The second transport system returns the ions back under the potential gradient and couples the energy release to useful work (transport other molecules, synthesizing ATP, contracting the muscles, propagating nerve impulses). An efficient coupling of both channels requires that membrane should be insulating and close to have no leakage of current .

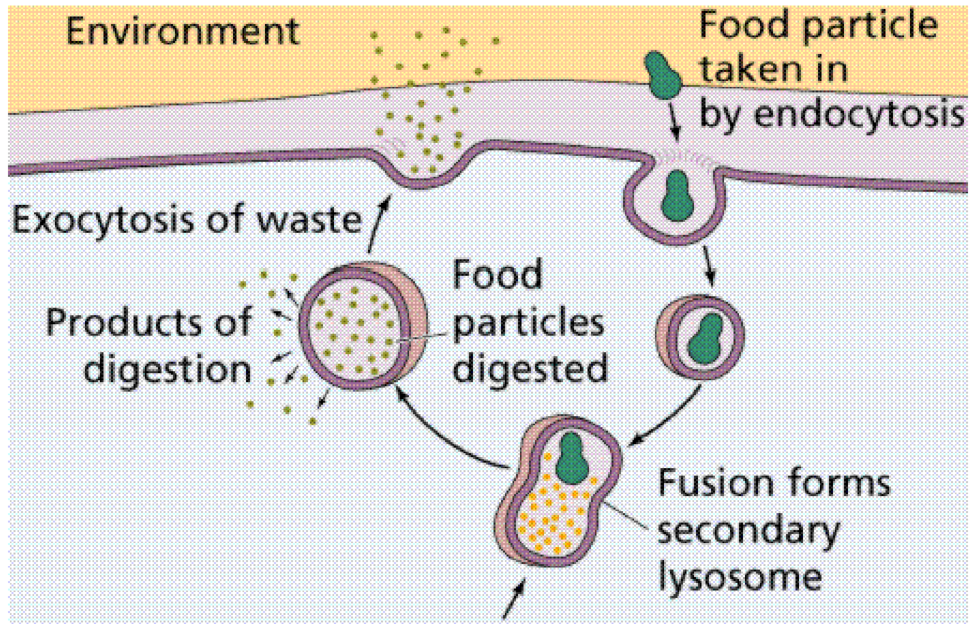
- The sodium pump creates an electric potential ~50-100mV across cell membrane
- The proton pump in mitochondria creates a potential 200mV, coming from two sources: electrical potential due to membrane asymmetry, and chemical potential due to difference in pH (concentration of H^+ ions)

- Chemi-osmotic theory states that energized state of H pump membrane contains a force which moves proton across the membrane. In respiration and photosynthesis it is electron transport which initiates translocation of protons in opposite direction. The energy is used to synthesize ATP

- Chemi-osmotic theory is related to electron coupling in oxidative phosphorylation in mitochondrial membrane. It states:
- two transport systems (primary and secondary) exist,
- Primary system trans-locates ions and initiate chemical reaction,
- Primary system equals to active transport described earlier
- Secondary system catalyses transport but not coupled with chemical reaction, equals to carrier or facilitated transport

Other types of transport

- **Vesicle-mediated transport**
- **V**esicles and vacuoles that fuse with the cell membrane may be utilized to release or transport chemicals out of the cell or to allow them to enter a cell.
- Exocytosis is transport out of the cell.
- Endocytosis is the case when a molecule causes the cell membrane to bulge inward, forming a vesicle.
- Phagocytosis is the type of endocytosis where an entire cell is engulfed.



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