Transport of Ions & Small molecules across membrane

(Day 5)

We note that lipid bilayer is highly impermeable to ions, because of charge and high degree of hydration of such molecules.

Relative permeability of membrane goes from

hydrophobic > small uncharged polar > large uncharged polar > ions

$$j_s = -P_s \Delta c$$

FLUX — Permeability constant — Concentration gradient

Hence we need membrane transport proteins.

- Transporters
- Channels

Some properties of membrane transport proteins :

1. specific - bacteria with single gene mutation unable to transport sugars
2. multipass - To allow hydrophilic molecules to pass easily

Transporters - undergo conformational changes to transfer bound solute (→ much faster)

Channels - interact with solute to be transported much more weakly.

→ allow solutes to move passively → down
- conc. gradient if uncharged
- electrochemical grad. if charged.

To pump against electrochemical gradients, active transport

Transporters and active membrane transport

- similar to an enzyme-substrate reaction
- each type of transporter has one or more specific binding sites for its solute substrate. It undergoes reversible conformation changes in order to transport the solute
- has characteristic V_{max} - with which it can flip b/w two conformational states.

Active transport
- Coupled transporters
- ATP-driven
- light-driven

First we talk about passive transport & ion channels.

- hydrophilic pores across membranes
- ion channels are selective and flip b/w open & closed states
- How are ion channels selective?

allow some ions to pass but not others ⇒ pore must be narrow enough in some places to force the permeating ions to initiate contact with walls of the channel

Selectivity filter - Permeation ions have to shed off their associated H_2O molecules to pass ⇒ limits rate of passage.
Flux ∝ conc., but saturates after some max. rate.

- Not continuously open:

Gated → opens to a specific stimulus (voltage, stress, ligand)

Bacterial K^+ channel

- exquisite ion selectivity with high conductance cannot be explained by pore size → because Na^+ is smaller
- high conductivity cannot be explained by K^+ binding sites, as that would slow down the passage.

- structure determined by X-ray crystallography

- Structure

1. Four identical transmembrane subunits.
2. cation-selective: negatively charged amino acids conc. at cytosolic entrance to repel anions
3. Each subunit

- 2 Transmembrane α-helices ⟹ tilted outward and form a cone.
- polypeptide chain that connects 2-alpha helices → forms selectivity filter (loop)

↳ 4 selectivity filters, form short narrow pore, lined by carbonyl Oxygen, to provide transient binding sites to dehydrated K^+.

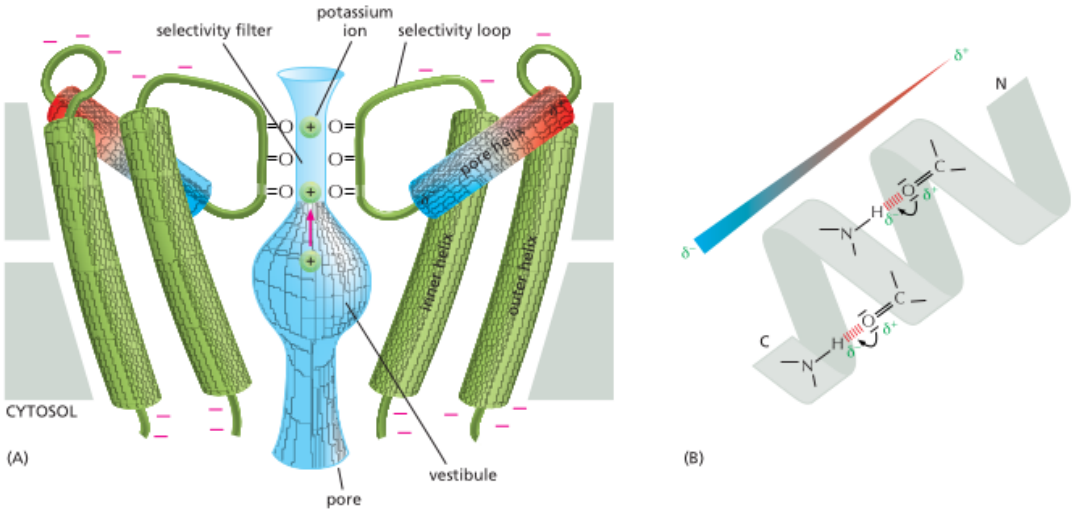

Figure 11–23 The structure of a bacterial K^+ channel. <ATTA> (A) Two transmembrane α helices from only two of the four identical subunits are shown. From the cytosolic side, the pore opens up into a vestibule in the middle of the membrane. The vestibule facilitates transport by allowing the K^+ ions to remain hydrated even though they are halfway across the membrane. The narrow selectivity filter links the vestibule to the outside of the cell. Carbonyl oxygens line the walls of the selectivity filter and form transient binding sites for dehydrated K^+ ions. The positions of the K^+ ions in the pore were determined by soaking crystals of the channel protein in a solution containing rubidium ions, which are more electron-dense but only slightly larger than K^+ ions; from the differences in the diffraction patterns obtained with K^+ ions and with rubidium ions in the channel, the positions of the ions could be calculated. Two K^+ ions occupy sites in the selectivity filter, while a third K^+ ion is located in the center of the vestibule, where it is stabilized by electrical interactions with the more negatively charged ends of the pore helices. The ends of the four pore helices (only two of which are shown) point precisely toward the center of the vestibule, thereby guiding K^+ ions into the selectivity filter. Negatively charged amino acids (indicated by *red* minus signs) are concentrated near the channel entrance and exit. (B) Because of the polarity of the hydrogen bonds (*red*) that link adjacent turns of an α helix, every α helix has an electric dipole along its axis, with a more negatively charged C-terminal end (δ^-) and a more positively charged N-terminal end (δ^+). (A, adapted from D.A. Doyle et al., *Science* 280:69–77, 1998. With permission from AAAS.)