

Lecture Notes for October 21, 2005

ACTIVE TRANSPORT

Active transport is defined as mass transport from a region of lower to a region of a higher electrochemical potential. It is transport that requires chemical or photochemical energy. Active transport across biological membranes occurs via “enzymes” that are divided into four groups:

- 1) Ion-translocating ATP-ases
- 2) H^+ -transporting electron transfer chains
- 3) Group-translocating enzymes
- 4) Photochemically-driven transporters e.g. bacteriorhodopsin.

1. Ion translocating ATP-ases

Two types of ATP-ases are distinguished: (i) P-type and (ii) the so-called F/V/A type. The P-type includes Na^+/K^+ ATPase, which is crucial for maintaining the concentration gradient across the cell membrane, the Ca^{2+} ATPases found in sarcoplasmic and endoplasmic reticulum, the H^+/K^+ ATPase involved in acid extrusion, and an H^+ ATPase found in the plasma membranes and in plant cells. The source of energy for these pumps is ATP that the ATPases hydrolyze. ATPases use cytosolic ATP. Typically they transport one type of an ion or a molecule; the Na^+/K^+ and H^+/K^+ ATPases are exceptions that they cause exchange of two ions: potassium is brought into the cell and sodium (proton) is taken out of the cell.

The process of pumping performed by the Na^+/K^+ ATPase consists of the following steps:

- Binding of three sodium ions inside the cell to the ATPase
- Hydrolysis of ATP by ATPase
- ATPases undergoes a conformation change
- Sodium ions dissociate from the enzyme outside of the cell
- Potassium ions bind to ATPase and are released inside the cell

The F/V/A-type ATPases include the F ATP-ases used for synthesis of ATP in mitochondria.

ATP-ases couple a chemical reaction to vectorial movement of an ion. The following criteria must be fulfilled to enable pumping:

- The energetics must be such that the chemical reaction releases more free energy that is required for ion translocation;
- The chemical reaction and ion translocation must be coupled processes;
- The enzyme must change its affinity for the ions during the translocation cycle.

For ions transport, the change in the electrochemical potential of the transported ion is:

$$\Delta\mu_j = \mu_{j,final} - \mu_{j,initial} = RT \ln C_{j,final} + z_j F \psi_{final} - RT \ln C_{j,initial} - z_j F \psi_{initial} \quad (1)$$

$$\Delta\mu_j = RT \ln \frac{C_{j,final}}{C_{j,initial}} + z_j F (\psi_{final} - \psi_{initial}) \quad (2)$$

The total free energy change required for transport is the sum of the electrochemical potential $\Delta\mu_j$ for each of the transported ions multiplied by the stoichiometry n_j for that ion:

$$\Delta G_{ions} = \sum_j n_j \Delta\mu_j \quad (3)$$

If one defines n_j as positive for ions transported from outside to inside and negative for ions transported from inside to outside:

For the chemical reaction, the free energy change is:

$$\Delta G_{ATP} = \Delta G_{ATP}^o + RT \ln \frac{[ADP][P_i]}{[ATP]} \quad (4)$$

Where $\Delta G_{ATP}^o = -30.3 \text{ kJ/mol}$

The transport can occur if:

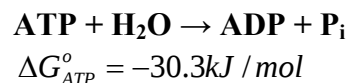
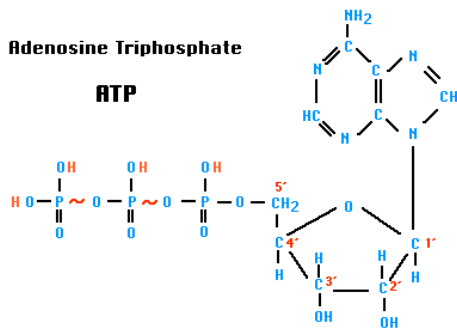
$$\Delta G_{ATP} + \Delta G_{ions} \leq 0 \quad (5)$$

Equation (5) emphasizes that the ATPases catalyze coupled reactions.

Example 1

Calculate the minimum free energy required to operate the Na^+/K^+ pump. Assume that the sodium concentration outside the cell is 20 times higher than inside the cell. The resting potential of the membrane is -0.07 mV.

$$\Delta\mu = (8.314) (310) \ln(20) + (96500) (0.07) = 7721 + 6755 = 14.5 \text{ kJ/mol}$$



It is feasible to pump 2 sodium ions per ATP hydrolyzed.

INDIRECT Active Transport

Indirect active transport uses the downhill flow of an ion to pump some other molecule or ion against its gradient. The driving ion is usually sodium (Na^+) with its gradient established by the Na^+/K^+ ATPase.

Symport Pumps

In this type of indirect active transport, the driving ion (Na^+) and the pumped molecule pass through the membrane pump in the **same** direction.

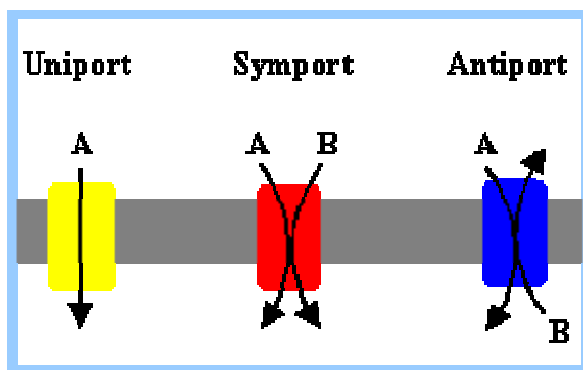
For example:

- **The $\text{Na}^+/\text{glucose}$ transporter.** This transmembrane protein allows sodium ions and glucose to enter the cell together. The sodium ions flow **down** their concentration gradient while the glucose molecules are pumped **up** theirs. Later the sodium is pumped back out of the cell by the Na^+/K^+ pump.

Antiport Pumps

In antiport pumps, the driving ion (usually sodium) diffuses through the pump in one direction providing the energy for the active transport of some other molecule or ion in the opposite direction.

For example: Ca^{2+} ions are pumped out of cells by a sodium-driven antiport pump.



Schematic visualization of symport and antiport pumps.

<http://www.rpi.edu/dept/bcbp/molbioc hem/MBWeb/mb1/part2/carriers.htm>

Example 2

The Na⁺/glucose Cotransporter

The active transport of glucose is mediated by the **Na⁺/glucose cotransporter**.

- sodium DOWN its gradient of about
 - 140 **mM** outside to
 - 10 **mM** inside
- while glucose is going UP its gradient (0.005 **mM** -> 5 **mM**).

According to eq. (4)

$$\Delta\mu = (8.314) (310) \ln (10/140) + (+1) 96\,500 (-0.07) = -6.8 \text{ kJ/mol} - 6.7 \text{ kJ/mol} = \mathbf{-13.5 \text{ kJ/mol}}$$

However for moving glucose up the concentration gradient one needs energy of at least: $(8.314) (310) \ln (5/0.005) = 17.8 \text{ kJ/mol}$

For moving glucose one needs therefore at least 2 sodium ions!