Chapter 10

Membrane Transport

Thermodynamics of Transport

- Free Energy change is given by difference in electrochemical potential and the quantity transported
  \[ \Delta G = n(\mu_2 - \mu_1) \]
  where \( \mu \) = the electrochemical potential
  Recall from Chapter 3
  \[ \mu = \mu^\circ + RT \ln C + ZF \Psi \]
  where \( C \) is the concentration (actually the activity), \( Z \) is the charge,
  \( F \) is the Faraday constant (96.5 kJ/volt-mol) and \( \Psi \) is the electrical potential of the solution

We did not discuss the electrical component in Chapter 3. Recall that what we are calling \( C \) here is really the activity, i.e. the concentration relative to the standard state. Review your standard state conventions.

Because \( \mu^\circ \) is the same on both sides of the membrane, this term cancels out.

Remember if \( \Delta G \) is negative, the process is spontaneous, and \( \Delta G \) represents the maximum work we can get from the process. If \( \Delta G \) is positive, the process is not spontaneous, and \( \Delta G \) is the minimum work required to realize it. The first term is negative when a substance is moving from a high concentration to a lower concentration \( (C_2 < C_1) \). The second term is negative when a positive ion \( (Z \) is +) moves to a lower potential \( (\Delta \Psi \) is -) or a negative ion \( (Z \) is -) moves to a higher potential \( (\Delta \Psi \) is +).

Therefore the free energy of transport is given by

\[ \Delta G = nRT \ln \frac{C_2}{C_1} + nZF \Delta \Psi \]

chemical work  electrical work

See Figures 10.1 and 10.2
Topic Outline

- Passive Diffusion
- Facilitated Diffusion
- Active Transport
  - Driven by ATP hydrolysis (ATPase’s)
  - Driven by light
  - Driven by ion gradients
- Group Translocation
- Membrane Pores
- Ionophore Antibiotics

Passive Diffusion

- Usually no special protein involved
- Usually substances can dissolve in hydrocarbon layer of membrane
- Transported species moves down electrochemical gradient
- Rate is proportional to concentration of diffusing species

Facilitated Diffusion

- Transported species moves down electrochemical gradient
- Usually faster than passive processes
- Membrane protein or other “carrier” involved
- Important distinguishing features:
  - Rate of transport is saturable (See Fig. 10.3)
  - Specificity toward transported species
  - Can have specific inhibitors
Examples of Facilitated Diffusion

- Glucose transporter in erythrocytes
  - Example of **uniport**
  - Specific inhibitor, Figure 10.6
  - (See model, Figure 10.5)
- Anion transporter of erythrocytes
  - Example of **antiport**
  - Exchange of $\text{HCO}_3^-$ and $\text{Cl}^-$
  - (See model, Figure 10.7)

Active Transport, ATP Driven

*Energy of ATP hydrolysis used to do work of transport*

- $\text{Na}^+$, $\text{K}^+$ ATPase
- $\text{Ca}^{2+}$ ATPase
- $\text{H}^+$ ATPases
  - Gastric $\text{H}^+$, $\text{K}^+$ exchange
  - Cellular vacuoles
  - Osteoclast
  - Mitochondrial and chloroplast ATPase (later chapters)
- MDR ATPase

Na$^+$, K$^+$ ATPase

- Pumps Na$^+$ out of cells, K$^+$ in (2K$^+$/3Na$^+$)
- Ion gradients important in nerve transmission, and in “cotransport” of other species
- Two subunits, see Fig 10.9 for membrane model
- Phosphorylation/dephosphorylation and two protein conformations involved
  - See Fig. 10.11 for suggested mechanism
- Specific inhibitor—cardiac glycosides (Fig 10.2)

Inhibitors of the Na$^+$, K$^+$ ATPase can cause high blood pressure!
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**Ca\textsuperscript{2+} ATPase**

- Ca\textsuperscript{2+} is a cellular “second messenger” in virtually all cells
- Normally Ca\textsuperscript{2+} is kept low by pumping it into cellular vesicles called the **sarcoplasmic reticulum**.
- Pumping is by an ATP driven Ca\textsuperscript{2+} ATPase
- Some protein homology to Na\textsuperscript{+}, K\textsuperscript{+} ATPase
  - (See Fig 10.13)
  - Membrane model (Fig 10.14); mechanism (Fig 10.15)

**H\textsuperscript{+} ATPases**

- Gastric H\textsuperscript{+}, K\textsuperscript{+} ATPase
  - K\textsuperscript{+}, Cl\textsuperscript{-} symport makes it an HCl pump
  - See Figure 10.16
- Vacuoles and Osteoclast
  - See Figure 10.17
- Mitochondrial and Chloroplast ATPases
  - Will discuss later. Role of these pumps is to use proton gradient to drive synthesis of ATP rather than ATP hydrolysis to drive pumping of protons

**Multidrug Resistance**

- Many transporters found that transport peptides or other molecules out of the cell
- Examples
  - Transport of a-factor peptide in yeast
  - Transport of drugs out of mammalian cells by an inducible protein called **P-glycoprotein**
  - (protein is responsible for acquisition of drug resistance, and is referred to as **MDR ATPase**
Light Driven 

- Bacteriorhodopsin
  - a major membrane protein of *Halobacterium halobium*, forming purple patches in membrane
  - Retinal bound as Schiff base to lysine residue
  - Light absorption promotes trans to cis isomerization of the retinal
  - Conformational changes during isomerizations results in pumping protons out of cells
    - See Figure 10.22

Light Driven Transport, con’t.

- Halorhodopsin
  - Also in *Halobacterium halobium*
  - Also retinal bound Schiff base to lysine residue
  - Cl⁻ pumped instead of H⁺
  - Folding of halorhodopsin in membrane
    - See Figure 10.23
  - Helical Wheel model comparing halorhodopsin and bacteriorhodopsin
    - See Figure 10.24

Ion Gradient Driven Active Transport

*Also called Secondary Active Transport*

- Best known systems coupled to Na⁺ or H⁺ gradients. Favorable ion gradient can drive unfavorable gradient of transported species
- **Symport**
  - Substance transported in same direction of ion.
- **Antiport**
  - Substance transported in opposite direction of ion.
- Many amino acid and sugar transport systems

This is called secondary active transport because the ion gradients were developed by the “primary” active transport, often an ATPase.
Group Translocation

- Special classification to describe active sugar transport in bacteria
- Sugar is phosphorylated during transport
- Energy for phosphorylation from phosphoenolpyruvate (a glycolysis intermediate)
- Several proteins involved that are transiently phosphorylated at histidine residues
  - See Figure 10.27

Specialized Membrane Pores

- Porins
  - Pore forming proteins
  - Relatively non-specific
  - Outer membranes of bacteria and mitochondria
  - Range of structures. Some are toxins
- Gap Junctions
  - Forms connections between cells
    - See Fig 10.37
  - Don’t worry about details

Ionophores

- Small molecule toxins—antibiotics
- Mobile carrier
  - Valinomycin as example
    - See Figure 10.40
- Channel forming
  - Gramicidin as example
    - See Figure 10.41