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Chapter 10

Membrane Transport

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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 μ = the electrochemical potential

Recall from Chapter 3

$\mu = \mu^o + RT\ln C + ZF\Psi$

where C is the concentration (actually the activity), Z is the charge, F is the Faraday constant (96.5 kJ/volt-mol) and Ψ 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 μ^o is the same on both sides of the membrane, this term cancels out.

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Thermodynamics of Transport, con't.

Therefore the free energy of transport is given by

$$\Delta G = \underbrace{nRT\ln\frac{C_2}{C_1}}_{\text{chemical work}} + \underbrace{nZF\Delta\Psi}_{\text{electrical work}}$$

See Figures 10.1 and 10.2

Remember if ΔG is negative, the process is spontaneous, and ΔG represents the maximum work we can get from the process. If ΔG is positive, the process is not spontaneous, and ΔG 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 +).

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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

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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

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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

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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 HCO_3^- and Cl^-
  - (See model, Figure 10.7)

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Active Transport, ATP Driven

Energy of ATP hydrolysis used to do work of transport

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

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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^{2+} ATPase

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

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H^+ ATPases

- Gastric H^+, K^+ ATPase
  - K^+, Cl^- **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

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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**)

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Light Driven **Transport**

- 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

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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

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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.

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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

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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

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Ionophores

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