

## Biochemistry 462a – Membrane Transport

### Reading - Chapter 12

### Practice problems - Chapter 12: 8; Lipids extra problems

## Cellular Transport

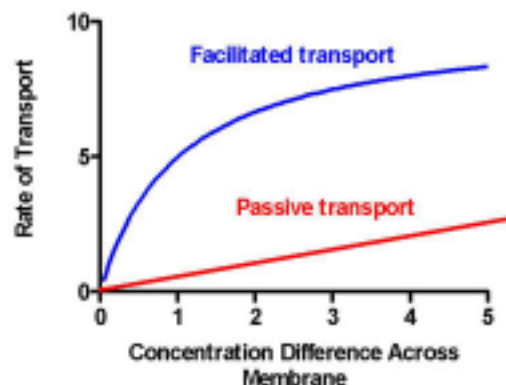
### Ion Transport

- The free energy of transporting material across a membrane depends on the concentration gradient across the membrane:  $\Delta G = RT\ln[C_2/C_1]$ .
- This equation dictates that material will move from the compartment of higher concentration to that of lower concentration and that  $\Delta G = 0$ , when  $C_1 = C_2$ .
- There are three circumstances under which such equalization can be circumvented:
  - **The transported substances may be bound by a macromolecule inside the cell**, which lowers the free concentration of the substance within the cell, e.g.,  $O_2$  binding by hemoglobin.
    - It is the free concentration that is used in the above equation.
  - The presence of a **membrane potential** influences the distribution of ions.
    - For an ion of charge  $Z$ ,  $\Delta G = RT\ln[C_2/C_1] + ZF\Delta\Psi$ , where  $F$  is the Faraday constant and  $\Delta\Psi$  is the membrane potential.
    - **If  $\Delta\Psi$  is negative, going from outside to inside, then the transport of cations into the cell is favored over anions. The opposite would be true if  $\Delta\Psi$  were positive.**
  - If some thermodynamically favorable process is coupled to transport, then  $\Delta G = RT\ln[C_2/C_1] + \Delta G'$ .
    - This is the general case of **active transport** in which the cell expends energy to drive uptake of a needed compound or secretion of a waste product.

### Cells take up materials by either

**Passive transport or diffusion**, which depends on the concentration gradient across the membrane.

**Facilitated diffusion/transport**, which is mediated by proteins in the membrane which either create **pores** through which the material can move or serve as **carriers** to move the material from one side of the membrane to the.



- Some antibiotics serve as **ionophores**, which form pores in the membrane through which ions, which are essential for the cell, diffuse out of the cell.
- **Active transport** allows cells to transport materials against a concentration gradient.
  - Ion pumps couple ATP hydrolysis to ion transport.
  - The  $\text{Na}^+\text{-K}^+$  pump maintains a high concentration of  $\text{K}^+$  and a low concentration of  $\text{Na}^+$  within the cell.
  - It pumps  $\text{Na}^+$  out of the cell against a concentration gradient and takes  $\text{K}^+$  into the cell against a concentration gradient.
  - The pump is driven by ATP hydrolysis.
- **Cotransport** utilizes a favorable gradient for one compound to drive the uptake of a second compound.
  - Sodium-glucose cotransport is one example, but many others are known, especially in the mitochondrial membrane.

### **Anatomy of proton pumping**

The energy needed to produce ATP comes from the oxidation of food. Ultimately the energy comes from the reduction of oxygen to water. This reaction is carried out in the electron transport chain, which is a series of linked oxidation-reduction enzymes found in the inner mitochondrial membrane. During passage of electrons along this chain, protons are pumped across the inner mitochondrial membrane generating a proton gradient that is the driving force for the synthesis of ATP. One of the components of the electron transfer chain, is cytochrome c oxidase. The structure of cytochrome c oxidase has been determined and a proposal has been made for the channel through the proton moves across the membrane. This chime script shows how this might work.

### **The Potassium Channel**

Recently the structure of the potassium ion channel has been solved. This page gives some of the details.

## Gaseous anesthetics

Halothane,  $\text{CHBrClCF}_3$ , is a gaseous anesthetic.

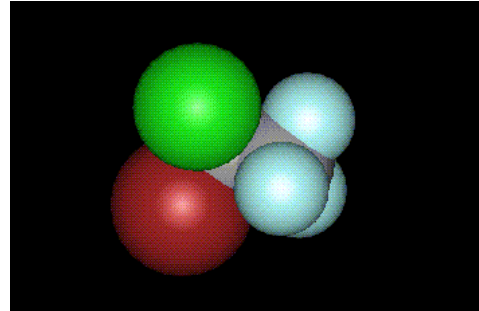
These types of anesthetics are secreted from the body unchanged.

The potency of these anesthetics is directly proportional to their solubility in lipid solvents.

It seems likely that these compounds act by dissolving in the hydrocarbon portion of the lipid bilayer.

The addition of these molecules to the hydrocarbon core would alter the properties of the bilayer, e.g., fluidity (like adding more cholesterol).

The altered membrane properties probably affect ion transport and nerve conduction.



## Inhibiting the $\text{Na}^+\text{-K}^+\text{-ATPase}$ makes the heart work stronger

Digitalis, which is prepared from the purple foxglove (*Digitalis purpurea*), is a cardiac glycoside. The active ingredient is digitoxin, shown below. Digitoxin (see below) contains three sugar residues (purple), which account for the glycoside in the name. The other part is the aglycon (blue), which resembles a sterol. The aglycon dissolves the membrane and the glycoside helps to improve water solubility.

- Digitoxin inhibits the  $\text{Na}^+\text{-K}^+\text{-ATPase}$  transport system, leading to a loss of  $\text{K}^+$  from the heart cells and an increase of  $\text{Na}^+$  in heart cells.
- The increased  $\text{Na}^+$  activates a  $\text{Na}^+\text{-Ca}^{+2}$  pump that exchanges intracellular  $\text{Na}^+$  for extracellular  $\text{Ca}^{+2}$ .
- The increase in intracellular  $\text{Ca}^{+2}$  enhances myocardial contraction.
- This causes more force to be generated without increased oxygen consumption.
- Digitoxin also slows the heart rate, which allows more filling of the heart and improves cardiac output.