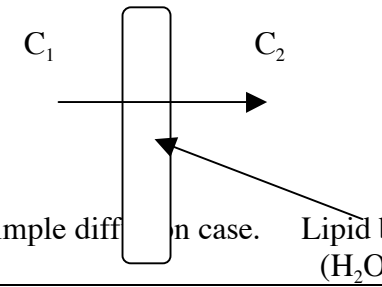
Chem 431A-L27-F'07 admin: Inclass Quiz 10 . Online quiz8 deadline is tonight (Chapt 10). Online quiz9 (Chapt 11) is Monday, Dec3 Today: membrane transport thermodynamics Wed: finish membranes; review guide posted Fri: talk + review	Last time: role of cholesterol, Started discussing transport thermodynamics

Today

For a solution: $G = RT\ln C$ so ΔG between 2 sides of memb: final – initial

$\Delta G = G_f - G_i = RT\ln C_f - RT\ln C_i = RT\ln(C_f/C_i)$



Simple diffusion case. Lipid bilayer membrane (H_2O diffuses easily!)

Process:

$C_1 \rightarrow C_2$ net charge transport

2 different aspects:

rate (kinetics) & spontaneity(thermodynamics)

$J = -P(C_2 - C_1)$ (1)$\Delta G = RT\ln(C_f/C_i)$

(2)$\Delta G = RT\ln(C_f/C_i) + ZF\Delta Y$

(3)$\Delta G = RT\ln(C_f/C_i) + \Delta G'$

permeability(deps on S solubility in memb.)

coupled chem rxns

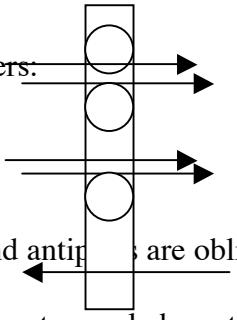
3 kinds of diffusion-driven transport

simple (nonmediated)	facilitated (mediated) (transporters,permeases)	
$\Delta G'=0$, "passive"	carrier	channel(pore)
slow	fast	very fast

factors to distinguish
speed, specificity
saturatable or not?
Competitive?
Can be inactivated?

Transporters are not really enzymes but function similarly (lower activation energy, can be inactivated or modified)

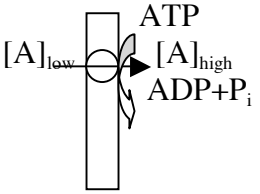
Kinds of transporters:



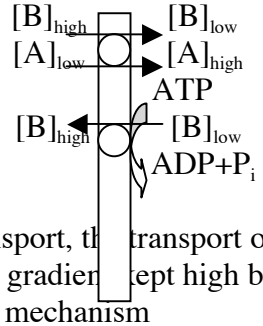
Symports and antiports are obligatory.

Active transport: coupled reactions usu. to ATP hydrolysis.

primary



secondary



In secondary active transport, the transport of A is by symport driven by B gradient kept high by another active transport mechanism

Thermodynamics of Transport Across Membranes

Like other processes, the Gibbs free energy change determines the direction in which a transport process occurs. The free energy change associated with movement of compound(s) across a biological membrane is a function of 1) the relative concentration of the material on both sides of the membrane, 2) the change in charge brought about by the movement of ionic compound(s) across the membrane, and 3) other energy releasing processes coupled to the transfer, such as hydrolysis of ATP. The Gibbs free energy for a transfer process of compound C from outside the membrane to inside the membrane is given by

$$\Delta G = RT\ln(C_{in}/C_{out}) + \Delta G',$$

where $\Delta G'$ depends on the particular transport process as follows:

$\Delta G' = 0$ for a diffusion-based process;

$\Delta G' = ZF\Delta\Psi$ for processes where net charge differences occur. F is the Faraday constant (96.5 kJ/mol/V), $\Delta\Psi$ is the membrane potential in volts, and Z is the charge of the ion; and

$\Delta G' = \Delta G$ process for processes coupled to the transport.

When ΔG for a transport is negative, movement of the compound(s) is favored in the direction for which it was calculated.

If the ΔG is positive, movement is favored in the reverse direction.

When $\Delta G = 0$, net movement is favored in neither direction. Note that at equilibrium for a diffusion-based process, $\Delta G = 0$, so $C_{in} = C_{out}$. Thus, a diffusion-based process results in equal conc'n's of the transported molecule inside and out.
These three scenarios (differences in concentration and charge, as well as the input of chemical energy) provide forces to transport molecules across membranes and are all used in biology.

The first diffusion-based process is called a **passive process**, because it employs no additional input of energy ($\Delta G' = 0$) and cannot move substances against a concentration gradient (from low to high concentration). All movement of molecules in diffusion-based processes is with the gradient (from high to low concentrations).

The processes that use energy from changes in potential or from energetically favorable chemical processes are called active transport processes. They can move substances against a concentration gradient using the additional contribution from $\Delta G'$ which is not available in diffusion-driven processes.

Students should be aware that both of these mechanisms can also be used to oppose transfer as well. Hence, electrical differences across a membrane may oppose a transfer instead of favor it and formation of ATP from ADP + Pi may be too energetically unfavorable of a barrier to allow a transfer to occur.

The driving force for passive transport is simply the process of diffusion. Though this may be masked a bit by movement of molecules through pores or via carrier molecules, the end result of passive transport is always an equal concentration of the transported molecule on both sides of the membrane.
KINETICS of Transport. Some considerations:
Consider $C_1 = 10$ || $C_2 = 1$ (we know $J_{1->2}$=+)

One defines the net rate of transport, J ($J_{1->2}$) in terms of membrane thickness (d), the diffusion coefficient (D), the partition coefficient (K), and the concentration difference ($C_2 - C_1$) of the compound across the membrane. This is simplified to
$J = -P(C_2 - C_1)$, where P is the permeability coefficient (explain the – sign)

The slow process of diffusion is insufficient to transport many needed molecules across cellular membranes, so cells have evolved a variety of mechanisms for speeding up diffusion. This process, called **facilitated transport,** includes (1) pore-facilitated transport and (2) carrier-facilitated transport. (due to membrane proteins called: *transporters or permeases*. It is important to note, however, that though pores or carriers speed the diffusion process, the driving force for each process is still diffusion, with all of its built-in limitations.	Active transport, on the other hand, *couples* transport of compounds across the membrane to energetically favorable processes, such as hydrolysis of ATP. Because of the additional energy provided by the coupled process, active transport systems can "pump" molecules against a concentration gradient. Thus, with active transport provided by the sodium-potassium pump, cells can maintain a higher concentration of potassium ions inside of the cell than outside and a higher concentration of sodium ions outside than inside.

Example: sodium-glucose cotransport system - energy for the transport is provided by the high sodium ion concentration outside the cell compared to inside. This might seem to be a passive transport process, because diffusion of sodium ions into the cell carries glucose with it. It is not, however, because the sodium ions are pumped back out as they enter the cell, so the sodium ion concentration never comes to equilibrium inside and outside the cell. The sodium-glucose cotransport system is thus an active transport system that derives its energy	from another active transport system-the sodium ion gradient maintained by the sodium-potassium pump .**Diffusion** - Diffusion happens, and there is very little cells can do about it. Tables list permeability coefficients for selected ions and molecules through membranes. Because the driving force for diffusion is a concentration gradient, active transport pumps, such as the sodium-potassium pump, create gradients of these two ions that are continually (though slowly) degraded by diffusion.

4 ways to distinguish simple (nonmediated) vs facilitated (mediated) diffusion: (1) speed and specificity (e.g. glucose vs mannitol) (2) saturation (graph:hyperbola vs straight line)	(3) competition (hyperbola shifts to right with a competing similar solute (4) inactivation: (protein modifying reagents)

Facilitated transport (or facilitated diffusion) - Includes pore-facilitated transport and carrier-facilitated transport systems. One notable feature of facilitated transport systems is that even though the driving force is also the process of diffusion and the	end result is the same as diffusion. Facilitated transport systems speed up diffusion by a factor of up to 10,000,000-fold. Note: pore-facilitated much faster than carrier facilitated transport. Na^+ and K^+ have no facilitated transport and thus diffuse very slowly.

Pore-facilitated transport examples – $Cl\text{-}HCO_3$ exchanger of the erythrocyte is an example of a pore-facilitated transport system. It contains a highly specific channel to transport bicarbonate ions out of cells as it transports chloride ions in. It is an *anion-exchanger*(AE protein). Note net charge difference in the	and sodium ions to pass through it. Still another pore-facilitated system is that of the glucose transport protein of erythrocytes which strongly favors transport of D-glucose over other sugars. Carrier-facilitated transport - Valinomycin, an *antibiotic*, is an example of a carrier-facilitated

transport is zero, exchange is *electroneutral* and so there is no electrical polarization of the membrane.
-a cotransport system (obligat, 2 ions same dirxn)
(compare: antiport vs symport vs uniport)
Another kind of pore is gramicidin A, which is a simple 15-residue polypeptide that allows potassium

transport system. It contains a hydrophobic exterior for interacting with the hydrophobic portion of the membrane's lipid bilayer and an interior designed specifically to accommodate a potassium ion. It transports by the mechanism. How does it kill germs

increase transport simply as the concentration of transported molecule increases.

An ionophore is a system that transports ions. If the result of the transfer is a change in charge, the process is called electrogenic; if there is no charge difference, it is called electroneutral.

Active Transport Mechanisms

Active transport mechanisms use energy sources to "pump" ions against concentration gradients. It is estimated that cells expend about 25% of their ATP just on active transport. Three common active transport mechanisms are described below.

Ion pumps - Directly couple ATP hydrolysis to transport. A well-studied example is the sodium-potassium pump of the plasma membrane (Figure 10.26). Note that in one turn of the multistep cycle, two potassiums are pumped in, three sodiums are pumped out, and one ATP is cleaved. The pump can be blocked by ouabain which, in the heart, stimulates contraction because sodium concentration increases and stimulates the sodium-calcium pump to remove sodium and import calcium. Increasing calcium leads to stronger muscular contraction.

Cotransport Systems - The sodium-glucose cotransport system relies on the concentration gradient built up by the sodium-potassium pump to drive the import of glucose into cells. In this case, sodium outside the cell binds to the receptor and, upon binding of a glucose molecule, the sodium concentration gradient drives the sodium inward and glucose is carried with it

Transport by Modification - This system relies upon covalently modifying a molecule during (or shortly after) passive or facilitated transport so that it can no longer pass back through the membrane. For example, the phosphotransferase system of E. coli uses ATP to phosphorylate sugars as they are transported into the cell. The phosphorylated sugars cannot pass back out.

Important terminology for active transport mechanisms:
Antiport - moves one or more molecules in as it moves one or more molecules out
Symport - moves all molecules in same direction
Electrogenic - causes change in charge as a result of transport
Electroneutral - causes no change in charge as a result of transport