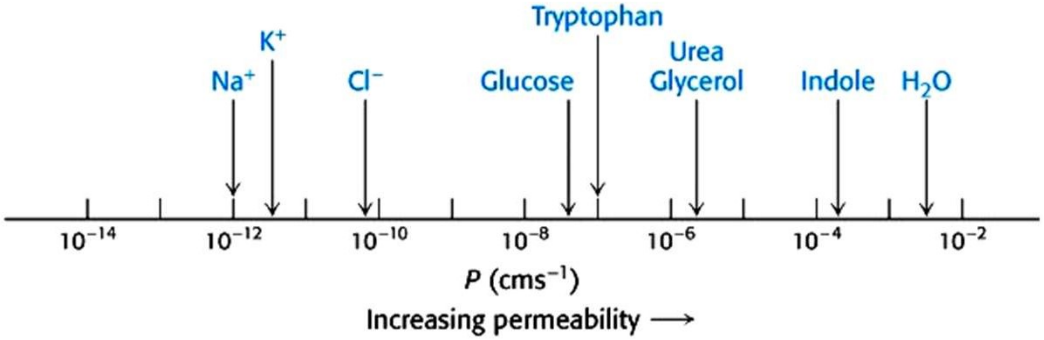
Transport Through Membranes

Voet & Voet, Chapter 20

- cells (and organelles in eukaryotes) are separated from their environment by membranes

Lipid bilayers are highly impermeable to ions and polar molecules

⇒ Specific transport proteins are needed for polar/ionic substances to enter the cell



Thermodynamics:

(J/mol)

Chemical potential $\mu_A = \mu_A^{o'} + RT\ln[\mathrm{A}]$

$$\mathrm{A(in)} \rightleftharpoons \mathrm{A(out)}$$

Membrane

Going from Out to In:

$$\Rightarrow \Delta\mu_A = \mu_A(\mathrm{in}) - \mu_A(\mathrm{out}) = RT\ln\frac{[\mathrm{A}]_{in}}{[\mathrm{A}]_{out}}$$

⇒ The net flow will always be from side of high [A] to side of low [A]

$$\boxed{[\mathrm{A}]_{in} < [\mathrm{A}]_{out} \Rightarrow \Delta\mu < 0 = \text{spontaneous}}$$

$$\boxed{[\mathrm{A}]_{in} > [\mathrm{A}]_{out} \Rightarrow \Delta\mu > 0 = \text{unfavorable}}$$

Ion Concentration Differences Generate Membrane Potentials

➢ ion transport systems maintain transmembrane concentration differences

$\Rightarrow$ Resulting charge differences generate an electric potential difference = membrane potential
$\Delta\Psi = \Psi(\text{in}) - \Psi(\text{out}) \approx 100$ mV

$\Rightarrow$ Only ionic substances will be affected

Electrochemical potential of A

$$\Delta\mu_A = \mu_A(\text{in}) - \mu_A(\text{out}) = RT \ln \frac{[\text{A}]_{in}}{[\text{A}]_{out}} + Z_A F \Delta\Psi$$

ionic charge of A

Faraday constant = 96,494 C/mol

Kinetics:

The driving force for the non-mediated flow of A through a medium is A's electrochemical potential gradient

$$J_A = -[\text{A}]u_A\left(\frac{d\mu_A}{dx}\right)$$

flux of A

mobility of A

For uncharged molecules $\Rightarrow$

Fick's first law

$$J_A = -D_A\left(\frac{d[\text{A}]}{dx}\right)$$

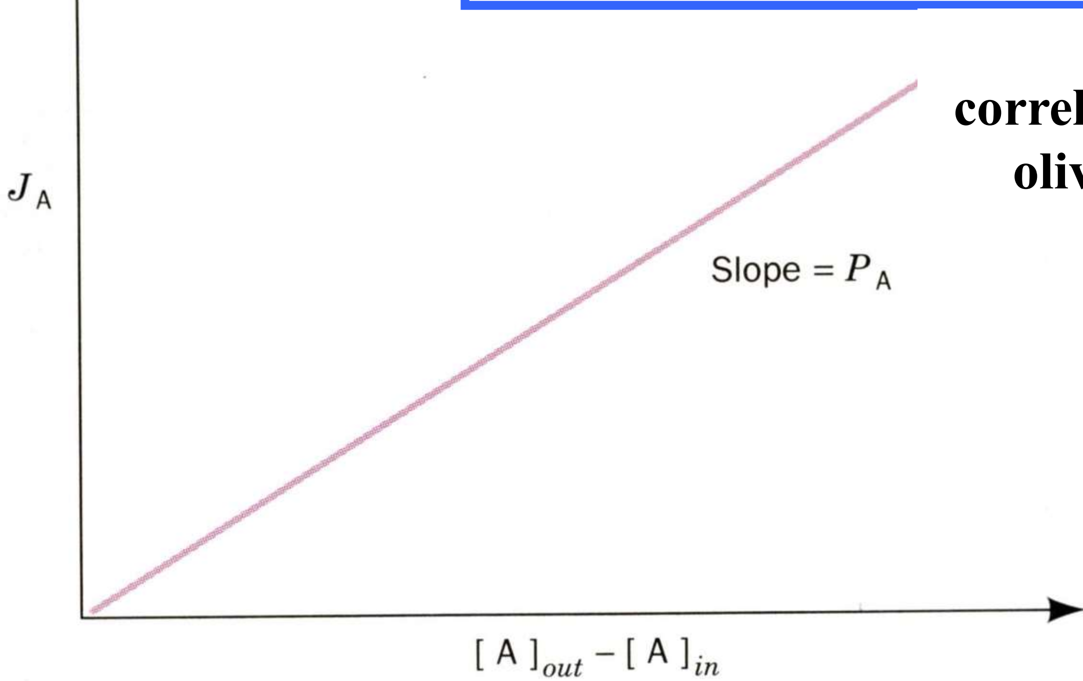
Diffusion coefficient = RTu_A

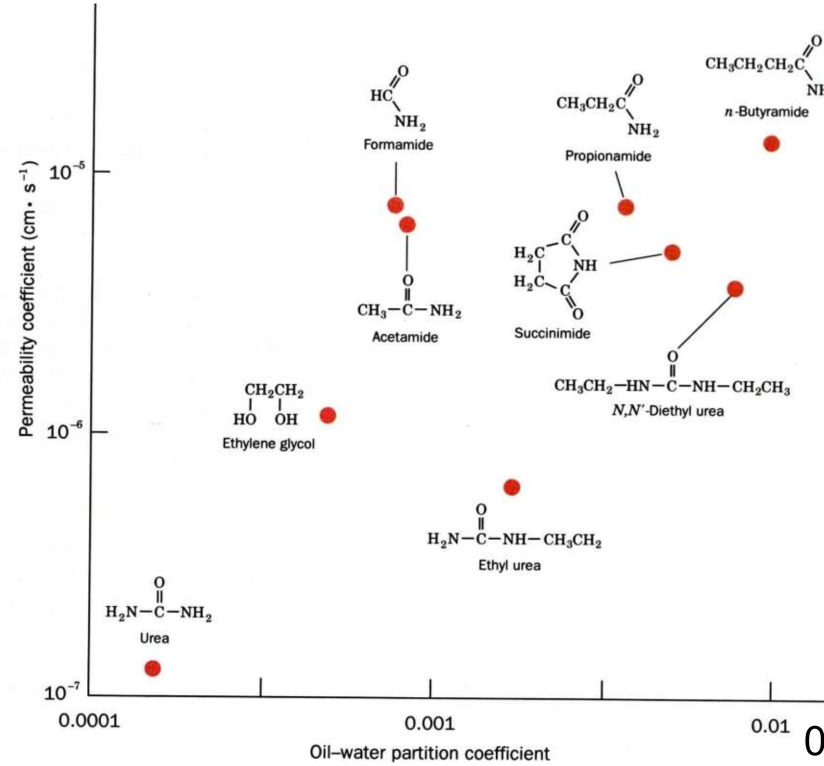
The Kinetics of Non-Mediated Transport of A Depends on A's Concentration Gradient and its Permeability Coefficient

Fick's first law simplifies for a membrane of thickness x to:

$$\boxed{J_A = \frac{D_A}{x}([\mathrm{A}]_{out} - [\mathrm{A}]_{in}) = P_A([\mathrm{A}]_{out} - [\mathrm{A}]_{in})}$$

permeability coefficient, correlates with A's partition coefficient between olive oil (≈ membrane interior) and water:





The Kinetics of Mediated Transport: E.g., Glucose Transport into Erythrocytes

The hints for a glucose transporter:

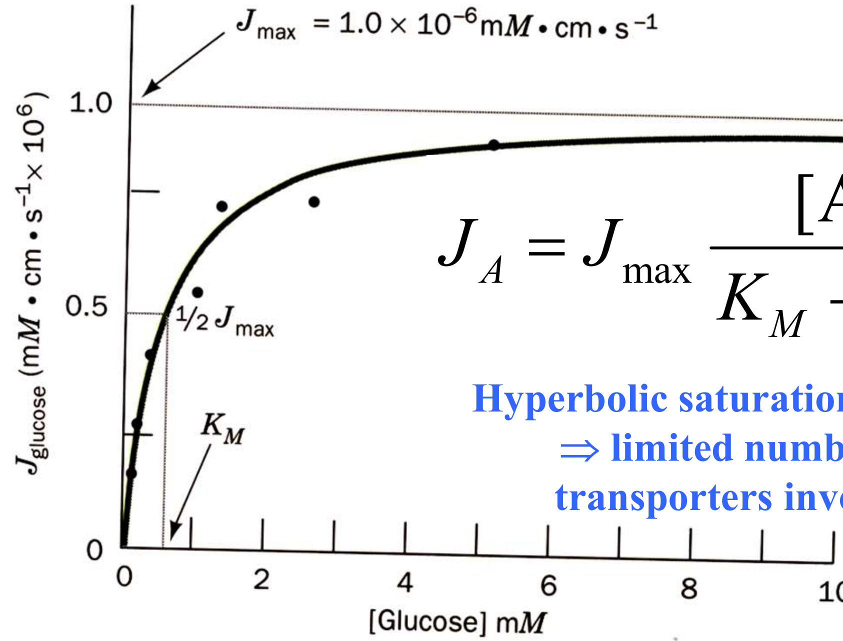
1.) Speed and Specificity

TABLE 18-1. Permeability Coefficients of Natural and Synthetic Membranes to D-Glucose and D-Mannitol at 25°C

Membrane Preparation	Permeability Coefficient ($cm \cdot s^{-1}$) D-Glucose	D-Mannitol
Synthetic lipid bilayer	2.4×10^{-10}	4.4×10^{-11}
Calculated nonmediated diffusion	4×10^{-9}	3×10^{-9}
Intact human erythrocyte	2.0×10^{-4}	5×10^{-9}

Source: Jung, C.Y., *in* Surgenor, D. (Ed.), *The Red Blood Cell,* Vol. 2, *p.* 709, Academic Press (1975).

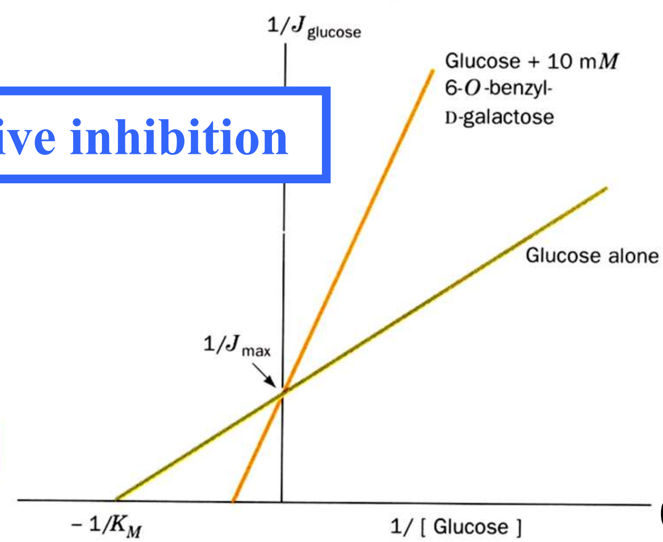
2.) Saturation kinetics like an enzyme



$$J_A = J_{max} \frac{[A]}{K_M + [A]}$$

Hyperbolic saturation function
⇒ limited number of transporters involved

3.) Specific competitive inhibition

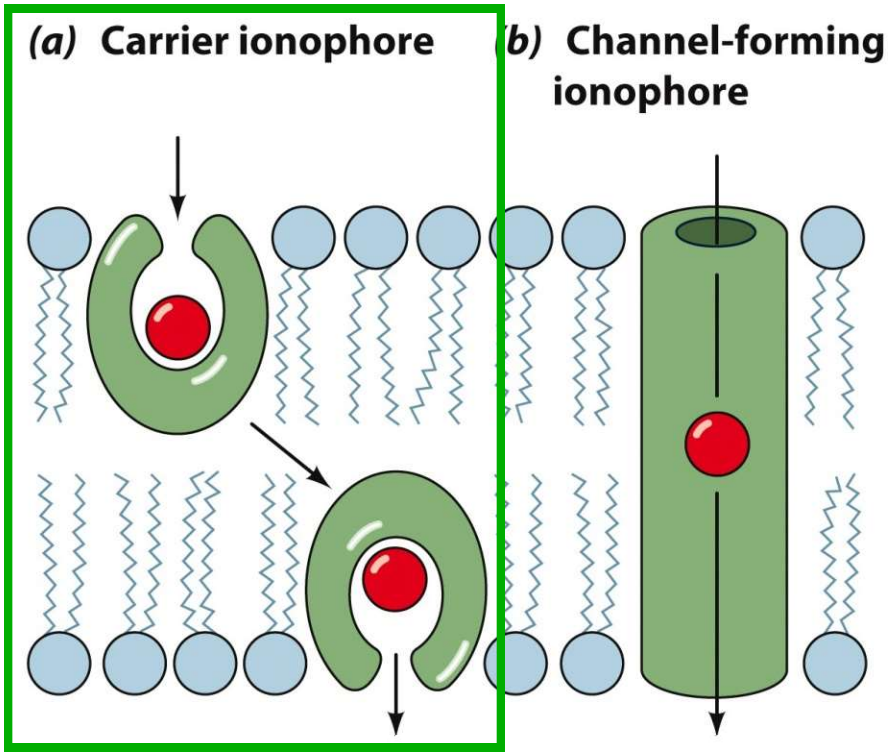


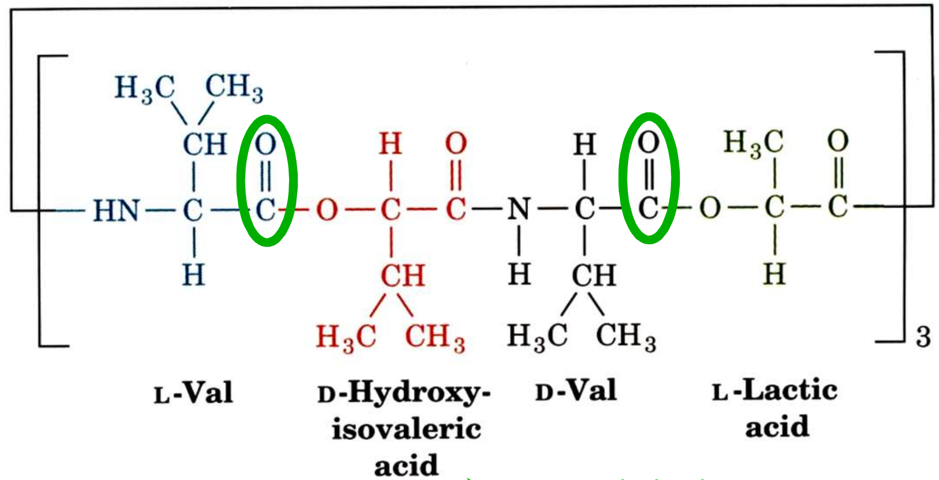
4.) Specific chemical inactivation

$HgCl_2$ reduces permeability for glucose to that of mannitol
⇒ transporter contains an -SH

Ionophores Help Our Understanding

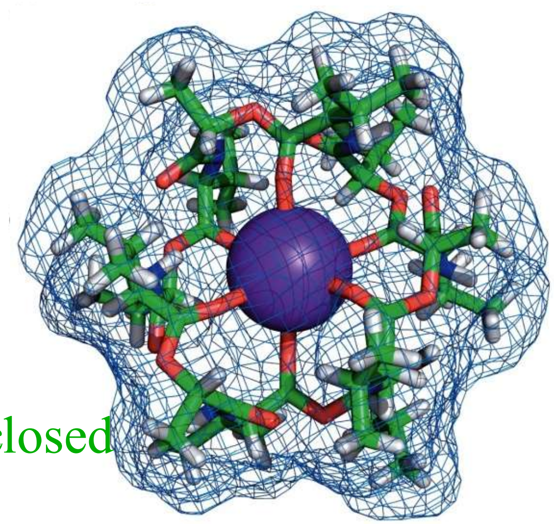
Ionophore = Substance that increases permeability of membranes to particular ions





<u>Valinomycin</u>

- an antibiotic, transports 10^4 K^+/s across membrane
- forms zigzag backbone where valine C=O's coordinate K^+
- hydrophobic methyls and isopropyls project outward



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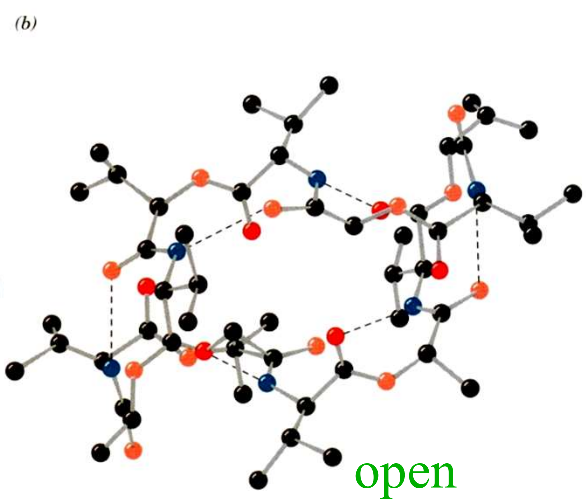


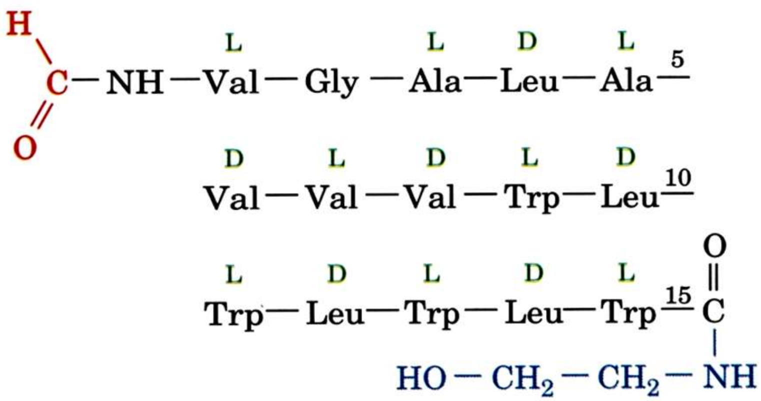
open

Valinomycin octahedrally chelates K^+ (r = 1.33 Å) and Rb^+ (r = 1.49 Å); Na^+ (r = 0.95 Å) or Li^+ (r = 0.60 Å) are too small

⇒ 10,000-fold specificity for K^+ over Na^+ (record!)

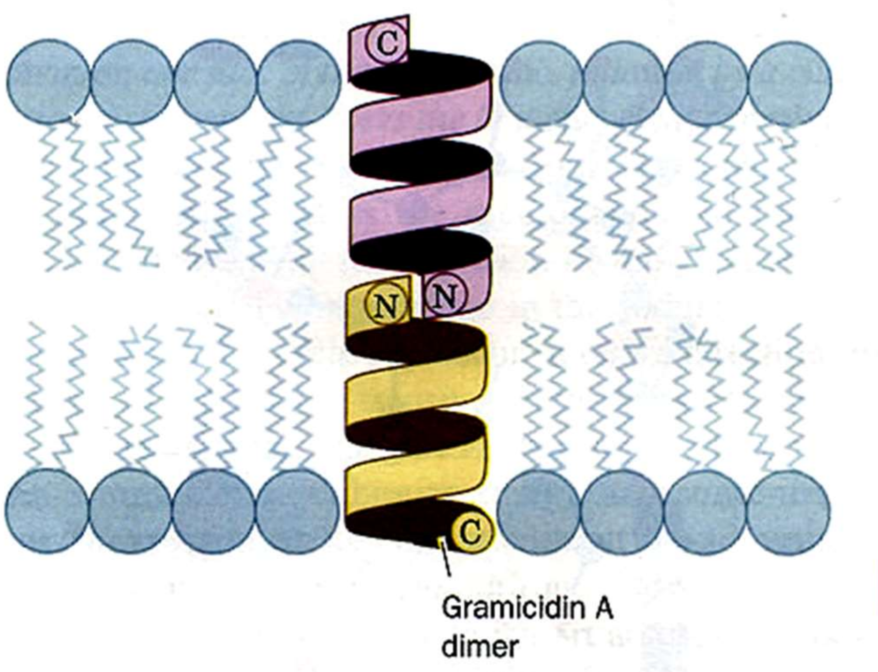
Gramicidin A: Channel-Forming Ionophore

- ➢ an antibiotic from *Bacillus brevis*, transports 10^7 K^+/s across membrane
- ➢ 15 alternating D- and L-amino acids, blocked termini
- ➢ permits passage of H^+, alkali cations; but blocked by Ca^{2+}



Gramicidin A

➢ head-to-head dimers:



➢ "β helix":

♣ rolled up parallel β sheet;

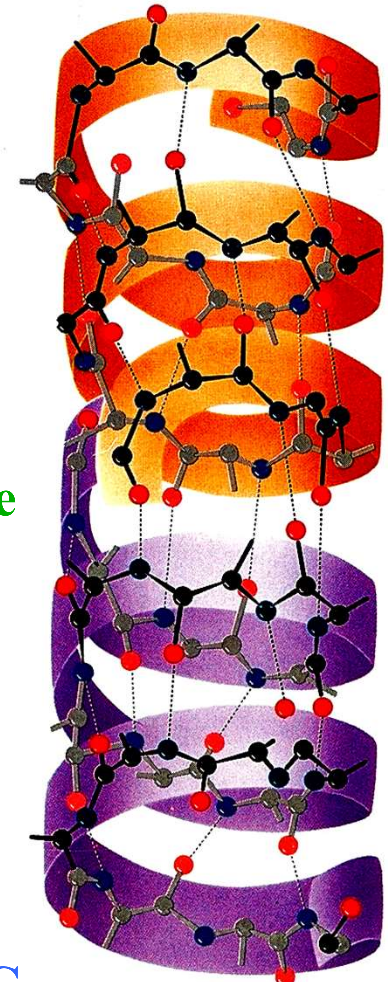
♣ right handed;

♣ 6-7 residues/turn;

♣ alternating D-, L-amino acids necessary to generate hydrophobic exterior;

♣ polar backbone groups line central channel;

♣ Trp side chains oriented with their polar N-H groups directed towards bilayer surface ⇒ orientation perpendicular to membrane!



➢ Download structure 1MAG from http://www.rcsb.org/ View w/ PyMOL Viewer