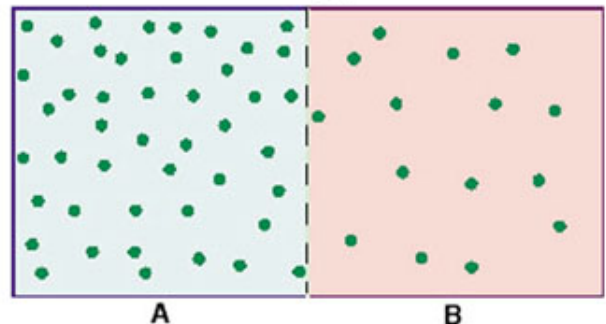
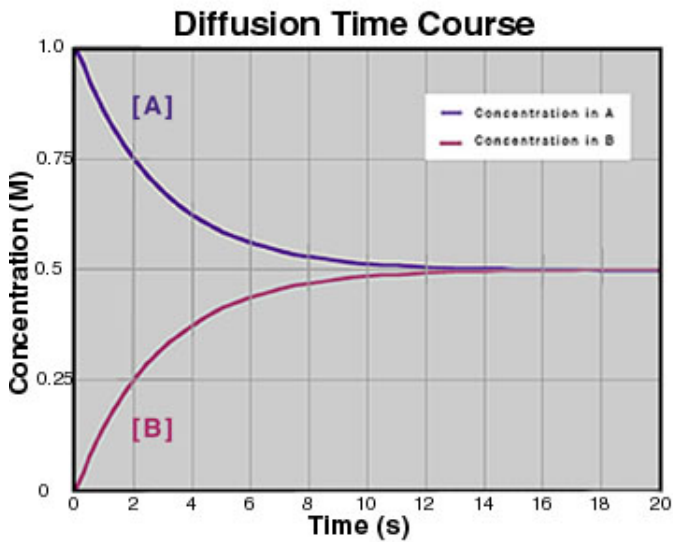
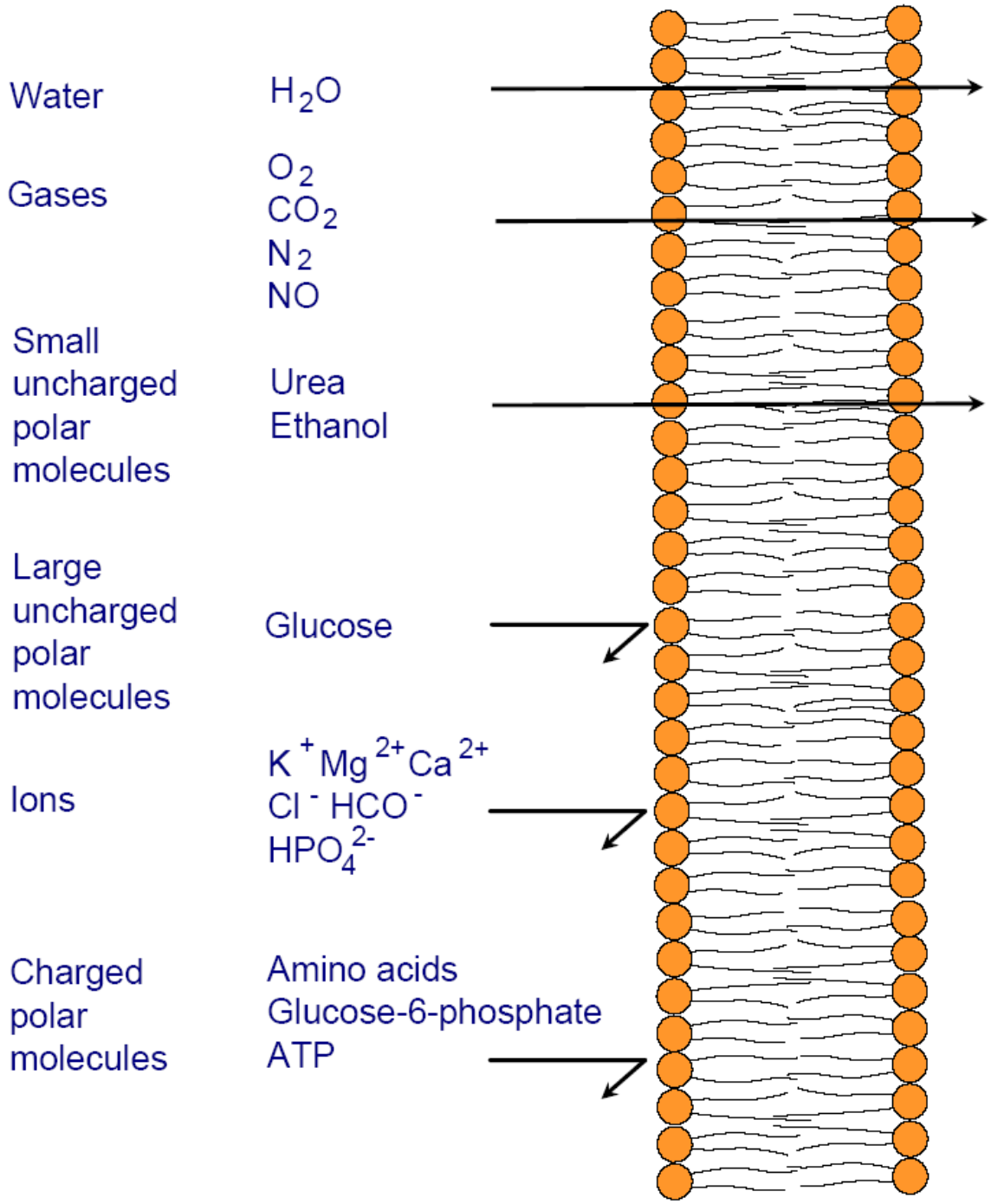
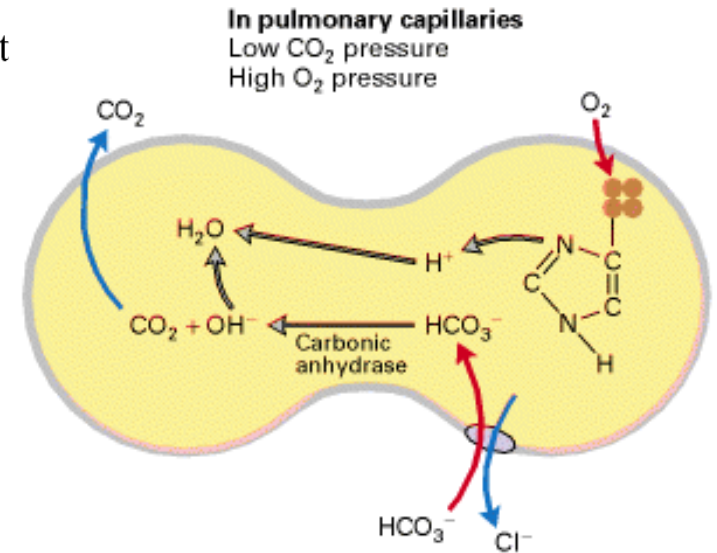
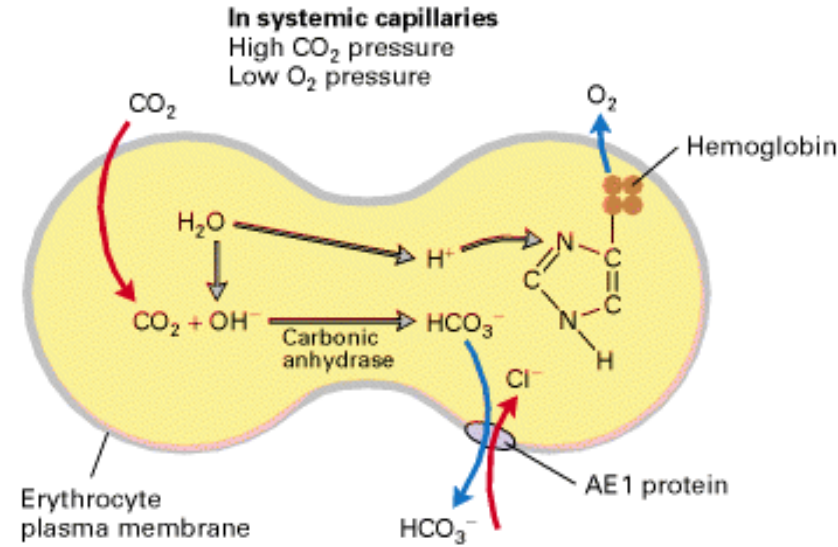
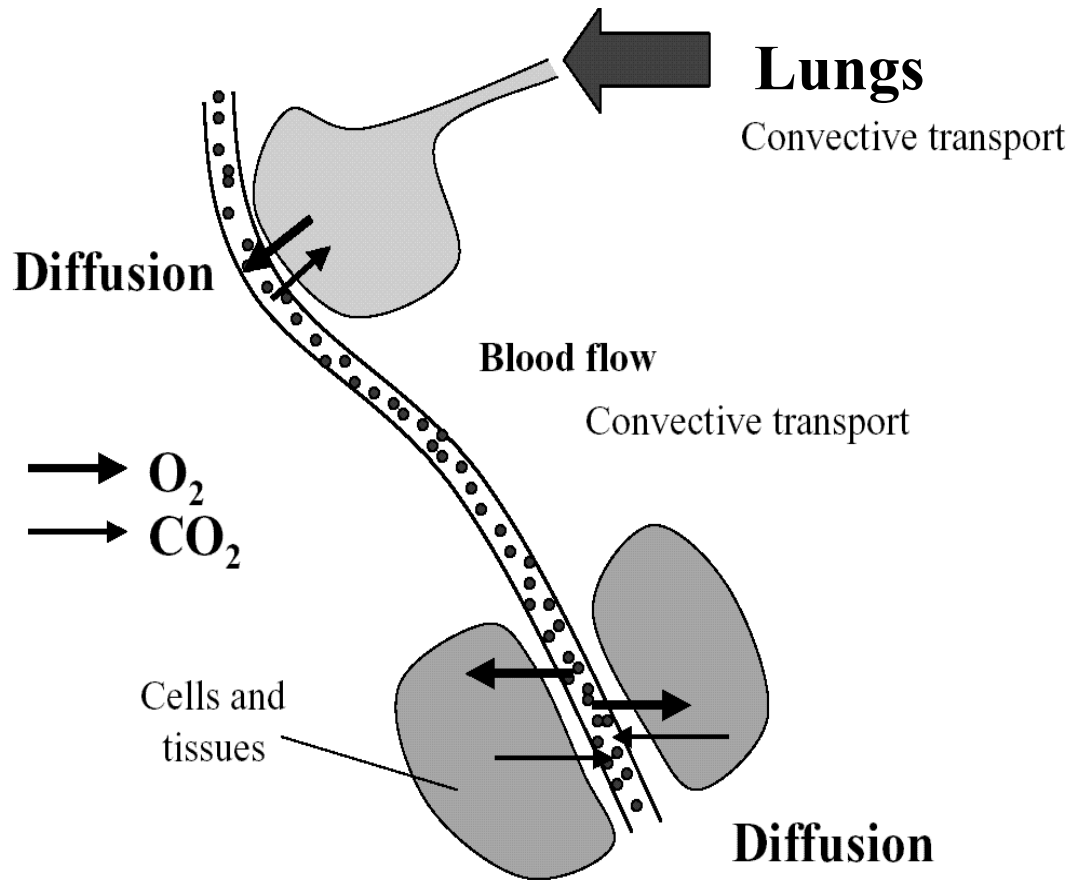


# *Passive transport across the lipid bilayer*

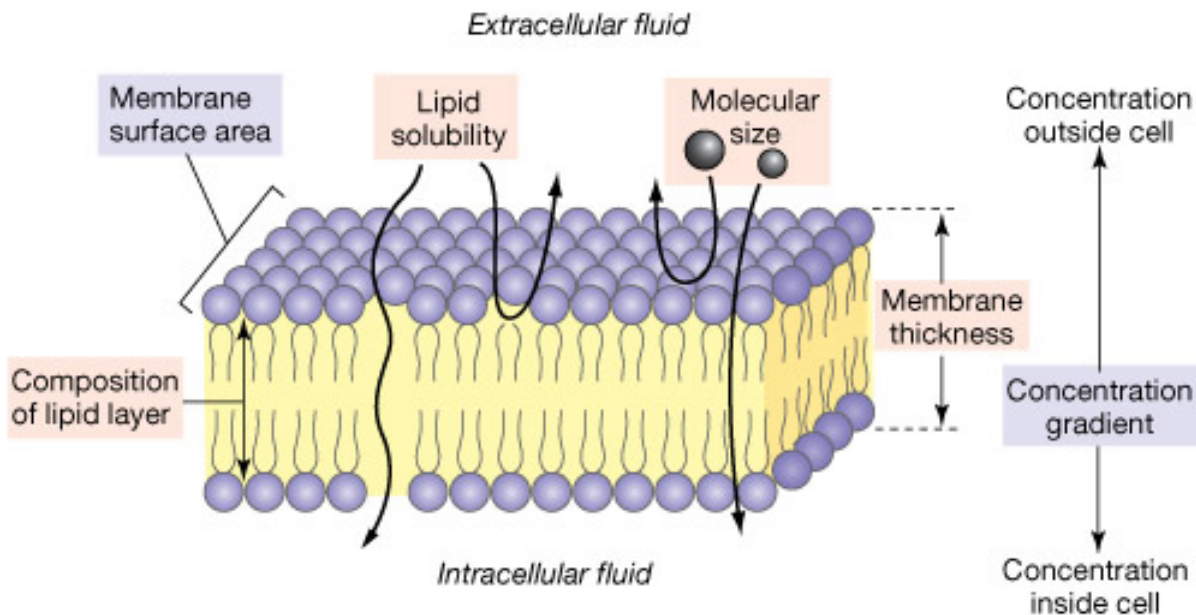


# Diffusion of gasses



# *Transmembrane diffusion: passive & down a concentration gradient*

*Rate factors: membrane, temperature, distance, & size*



## Factors affecting rate of diffusion through a cell membrane:

- Lipid solubility
- Molecular size
- Cell membrane thickness
- Concentration gradient
- Membrane surface area
- Composition of lipid layer

**Fick's Law of Diffusion** says:

$$\text{Rate of diffusion} \propto \frac{\text{available surface area} \cdot \text{concentration gradient}}{\text{membrane resistance} \cdot \text{thickness of membrane}}$$

## Membrane resistance

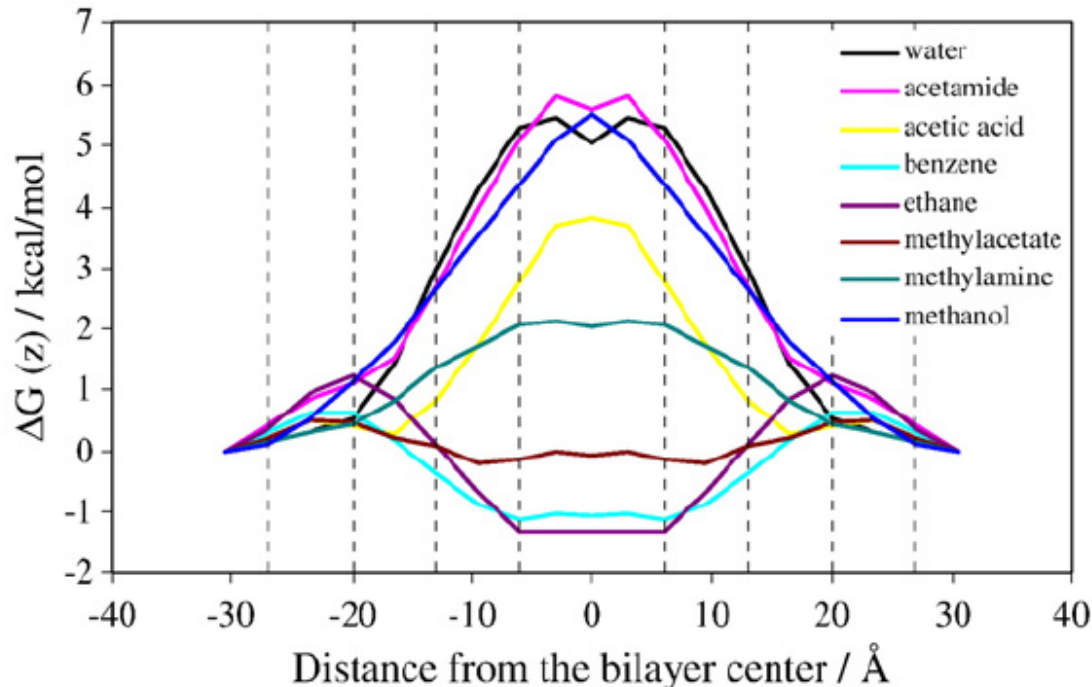
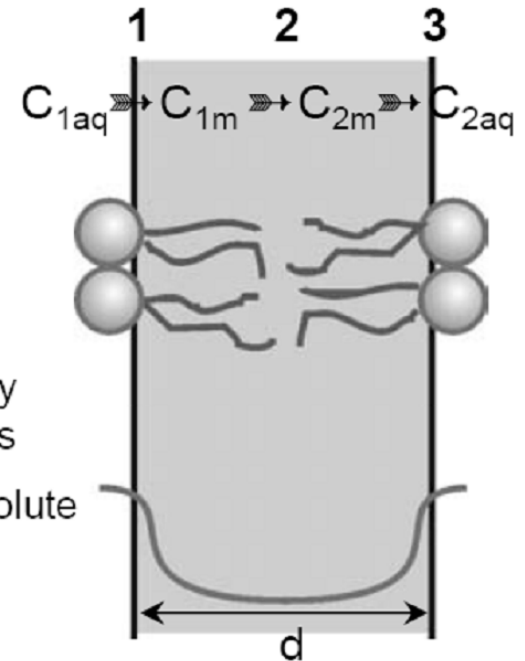
$$\text{Membrane resistance} \propto \frac{\text{lipid solubility}}{\text{molecular size}}$$

Changing the composition of the lipid layer can increase or decrease membrane resistance.

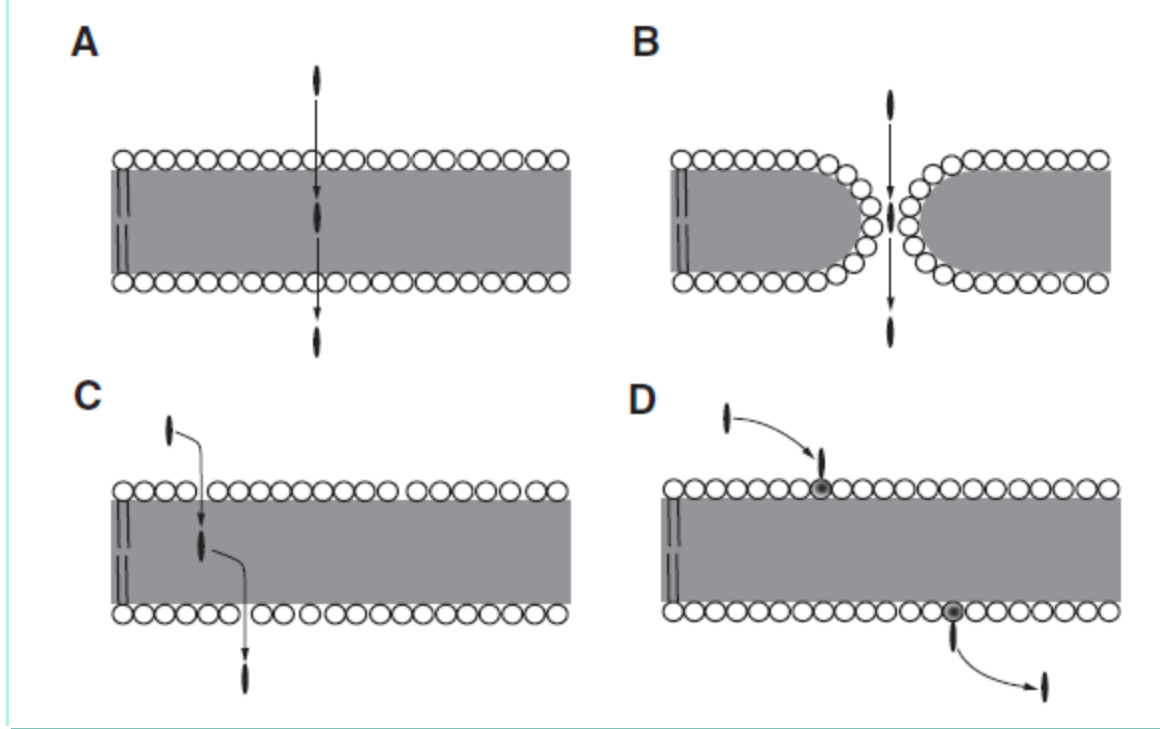
# Membrane permeability to nonelectrolytes

Steps (any can be rate limiting)

- 1) enter the membrane (potential barrier)
- 2) diffusion through the bilayer core
- 3) exit the membrane (potential barrier)



Free energy profiles  
for selected solutes  
in a DPPC bilayer at  
323 °K.



Membrane passive transport mechanisms.

(A) Solubility-diffusion model.

(B) Transient pore model.

(C) Head-group gated model.

(D) Lipid flipping-carrier model.

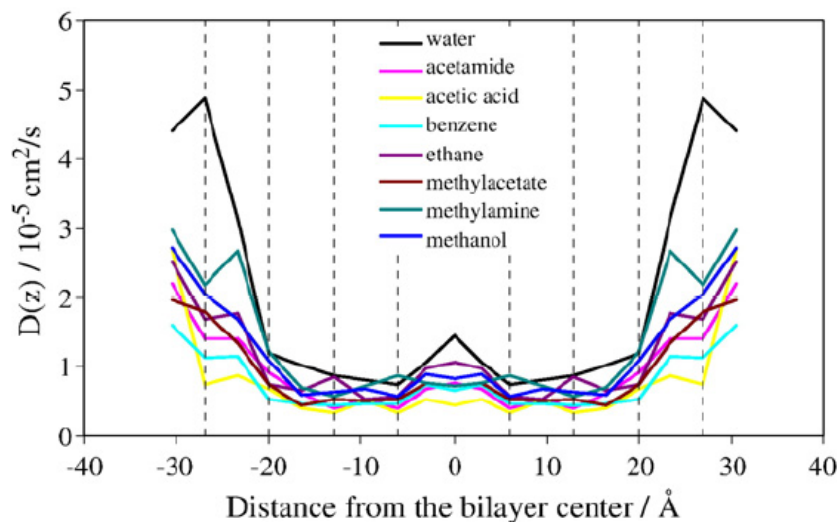
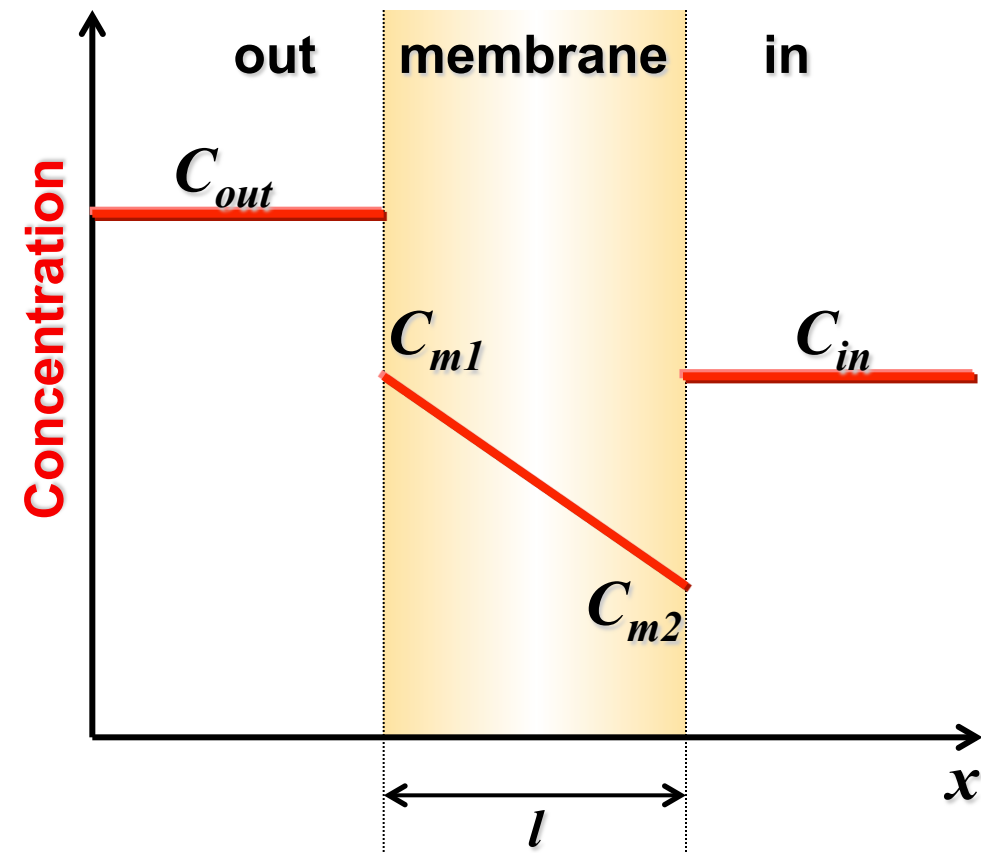
Circles represent lipid head groups and the gray area indicates the hydrophobic region occupied by lipid acyl chains. The black oval is the solute molecule.

# Fick's law for passive transport of neutral particles through the membrane:

Fick's 1<sup>st</sup> law

$$J_x = -D \frac{\partial C}{\partial x}$$

$$J_x = \frac{1}{s} \frac{\partial m}{\partial t} = -D \frac{C_{m1} - C_{m2}}{l}$$



Diffusion coefficient profiles for selected solutes in a DPPC bilayer at 323 °K.

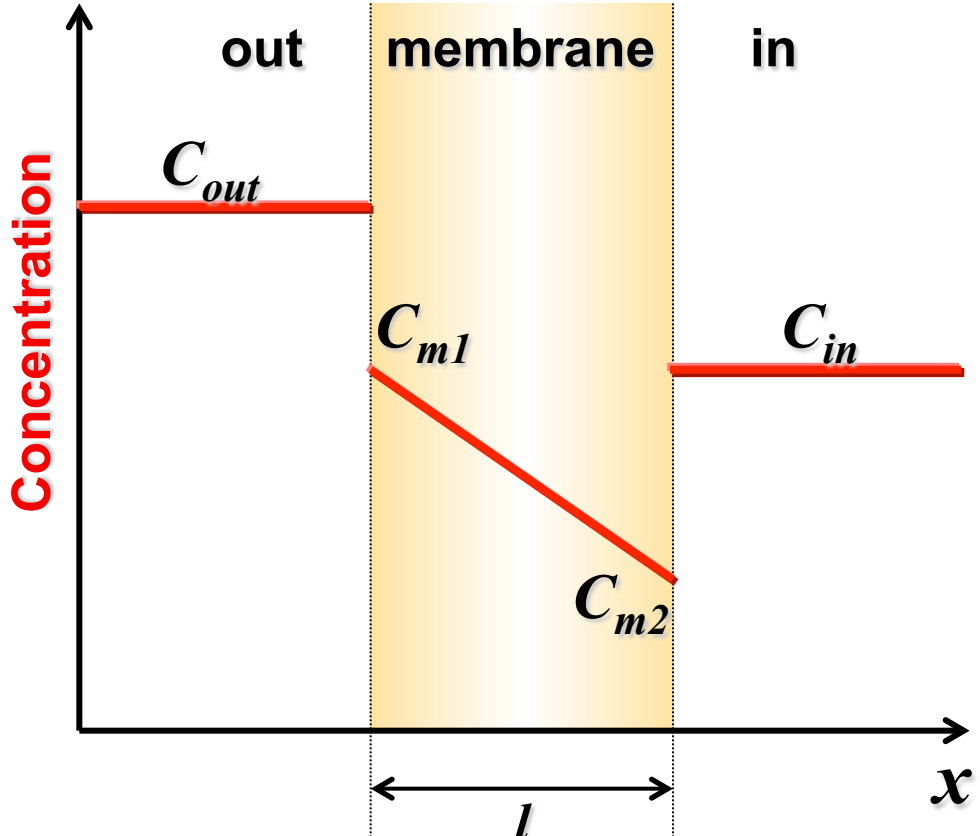
# The membrane:water partition coefficient ( $K_p$ )

The chemical potential in the water phase ( $\mu_w$ ) = the chemical potential in the membrane ( $\mu_m$ ):

$$\mu_w = \mu_w^o + RT \ln C_w = \mu_m = \mu_m^o + RT \ln C_m$$

The concentration at the surface of the membrane ( $C_m$ )

$$C_m = C_w \exp\left(\frac{\mu_w^o - \mu_m^o}{RT}\right)$$

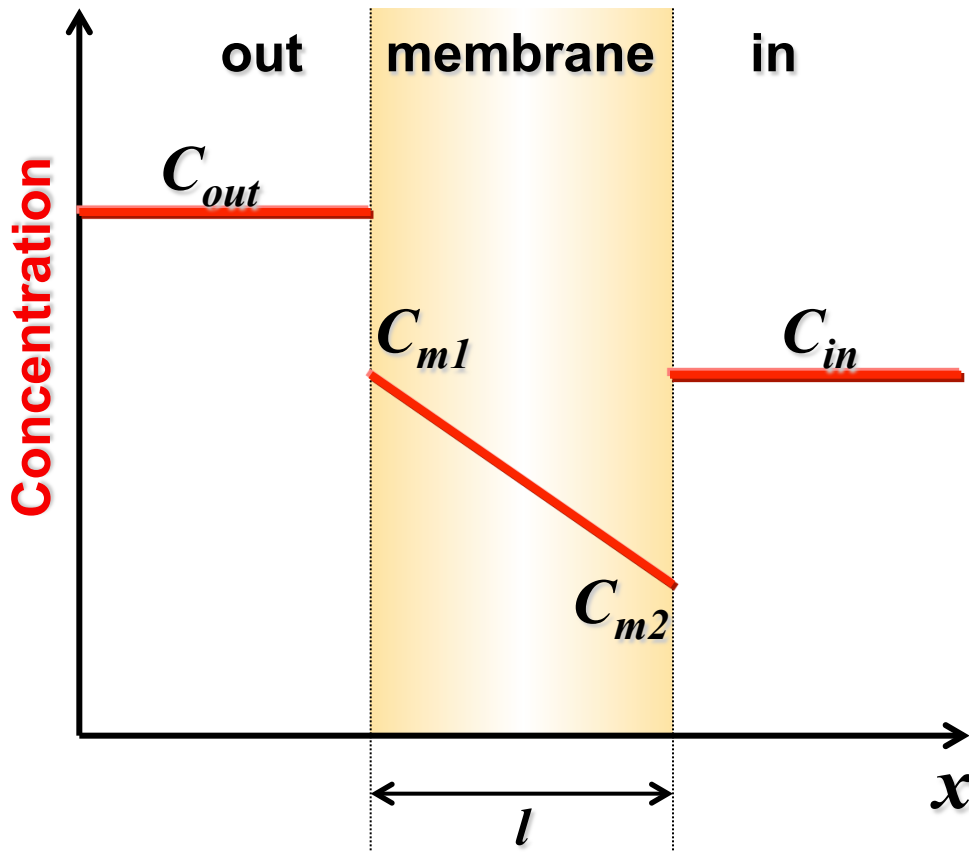


$$K = \frac{C_m}{C_w} = \exp\left(\frac{\mu_w^o - \mu_m^o}{RT}\right)$$

$C_m$  – concentration just inside the hydrophobic core of the bilayer,  
 $C_w$  – concentration in the aqueous solution.

$$K = \frac{C_{m1}}{C_{out}} = \frac{C_{m2}}{C_{in}}$$

# *Fick's law for passive transport of neutral particles through the membrane:*



*Flux, and therefore the rate of transfer across the membrane are proportional to the partitioning coefficient.*

*Partitioning coefficient is a quantitative measure of the how lipophilic is the compound.*

*Higher partitioning coefficient indicates better solubility and faster transport across the membrane*



$$J_x = -D \frac{\partial C}{\partial x}$$

$$J = -\frac{D}{d} \exp\left(\frac{\mu_w^o - \mu_m^o}{RT}\right) (C_i - C_o)$$

$$P = \left(\frac{D}{d}\right) \exp\left(\frac{\mu_w^o - \mu_m^o}{RT}\right)$$

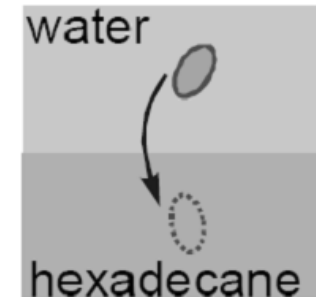
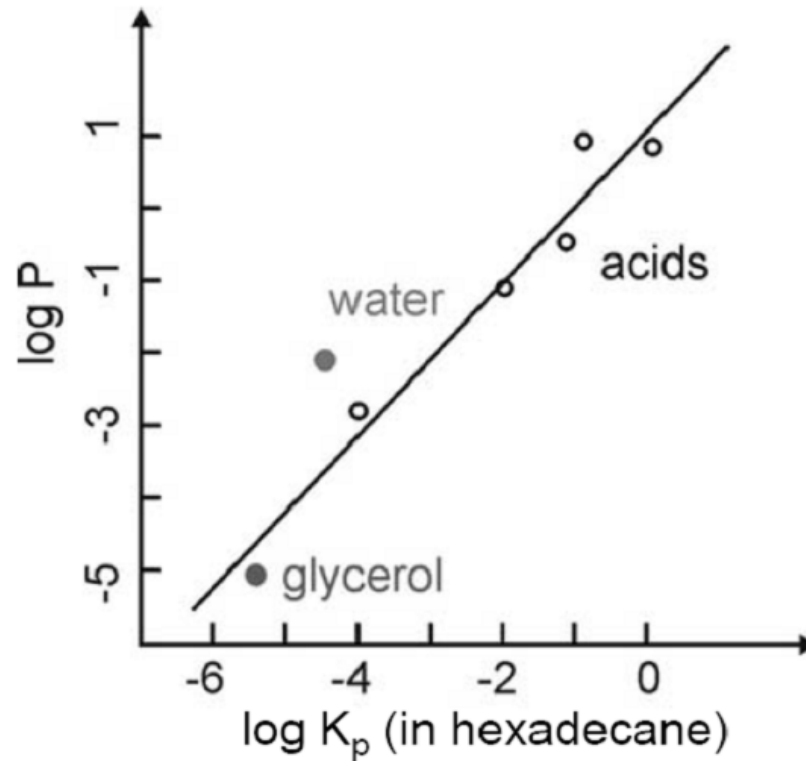
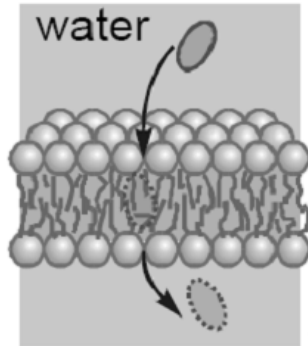
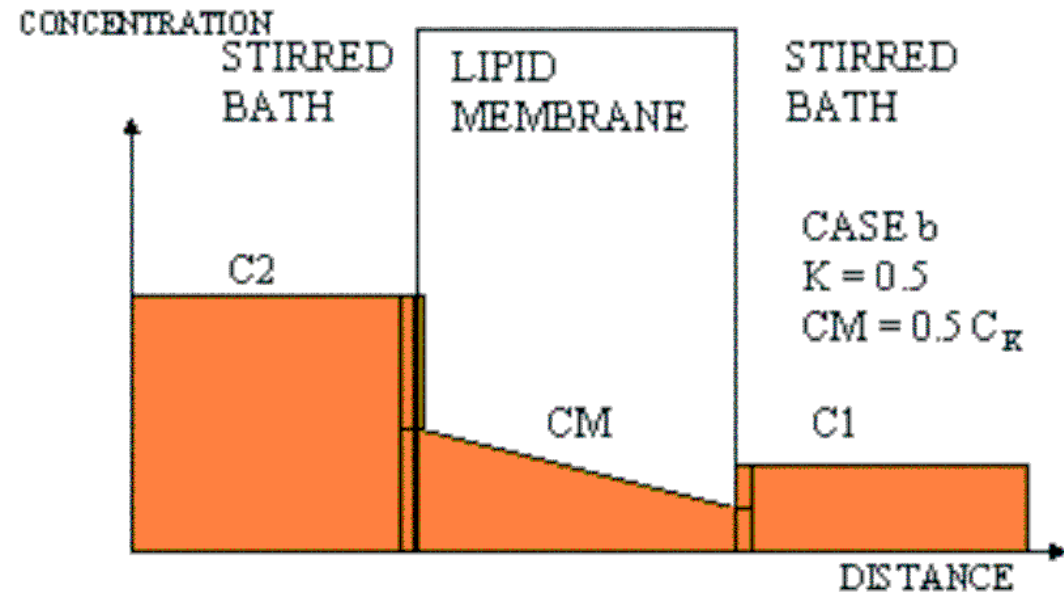
*The permeability coefficient*

Permeability coefficients are a combined property of the solute *and* the membrane system.

$$P = \frac{DK_P}{d}$$

*P in membranes is strongly correlated with K for nonpolar solvent*

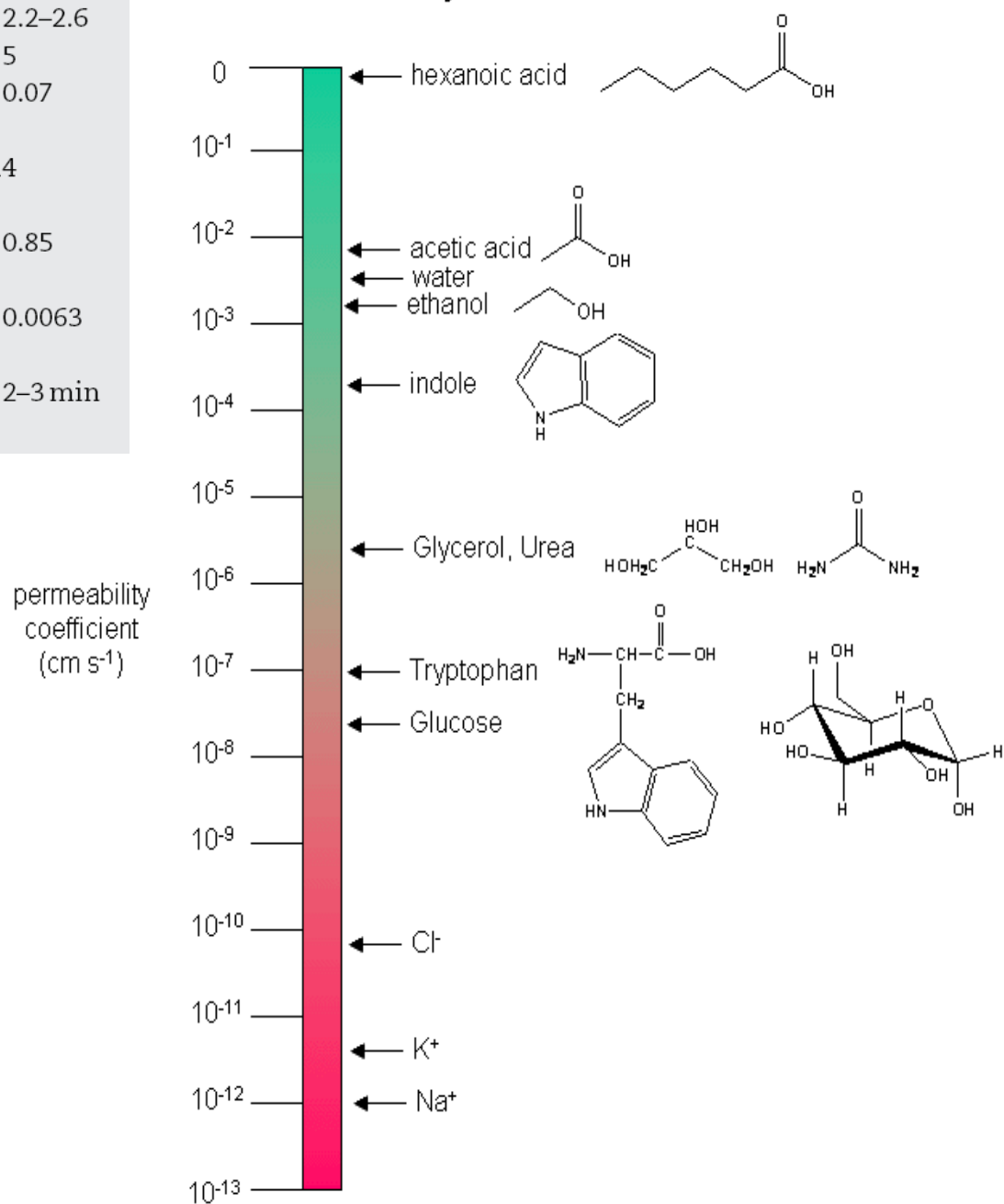
$$J = -\frac{D}{d} K (C_i - C_o)$$



Properties	Water	Urea	Thiourea
Molecular weight	18	60	76
Molecular radius (Å) <sup>a,b,c</sup>	1.5–1.9	2.4–2.7	2.2–2.6
Number of H bonds <sup>d,c</sup>	4	5	5
Permeability coefficient ( $\times 10^{-5}$ cm/s) <sup>d</sup>	915	23.9	0.07
Ea for permeability (kcal/mol) <sup>e,c</sup>	6	11	14
Reflection coefficient ( $\sigma$ ) <sup>f,g,c</sup>	0.002	0.55–0.79	0.85
Partition coefficient ( $k_{\text{ether}}$ ) <sup>d</sup>	0.003	0.00047	0.0063
Half time for exchange <sup>h,i,j,b</sup>	4.2 ms	0.03–0.3 s	2–3 min

***Physicochemical  
and RBC  
distributional  
properties for  
water, urea and  
thiourea***

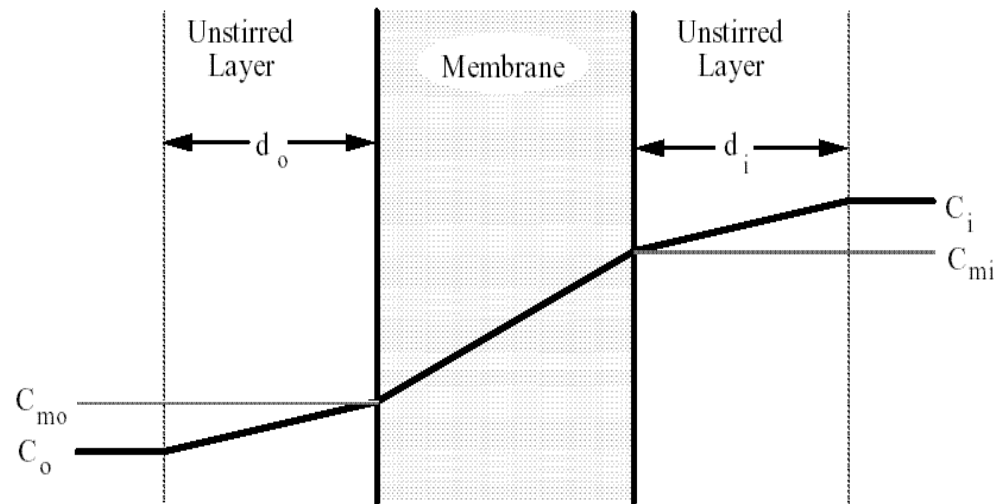
**Membrane Permeability Coefficients**



# Unstirred Layers

*Molecule diffusion across the aqueous layers adjacent to either surface of the membrane.*

*1  $\mu\text{m}$  to 500  $\mu\text{m}$  thickness.*



- ✚ It is most prominent for relatively nonpolar compounds – the diffusion across the membrane itself will be relatively fast.
- ✚ For water soluble compounds – diffusion across the unstirred layers will have relatively less effect.

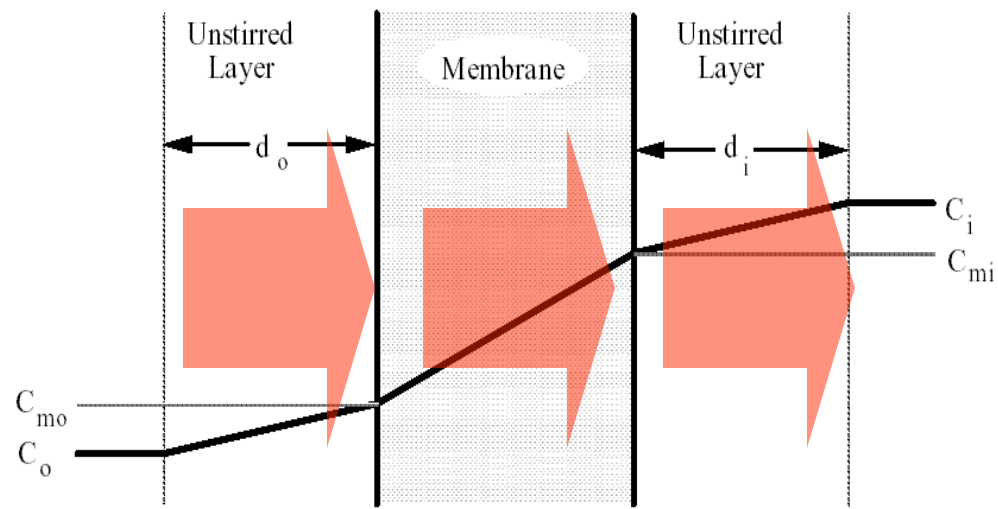
✚ P – a membrane permeability coefficient

✚ D – an aqueous diffusion constant.

✚  $d_i$  and  $d_o$  – the thicknesses of unstirred layers.

✚  $C_i$  and  $C_o$  – the bulk concentrations of the compound,

✚  $C_{mi}$  and  $C_{mo}$  – the concentrations at the surface of the membrane.



■ The flow through the membrane is

$$J_m = P(C_{mi} - C_{mo})$$

■ The flow through the unstirred layers

$$J_o = \frac{D}{d_o} (C_{mo} - C_o)$$

$$J_i = \frac{D}{d_i} (C_i - C_{mi})$$

At steady-state

$$J_m = J_i = J_o = J$$

Therefore

$$\frac{J}{P} = C_{mi} - C_{mo}$$

$$\frac{Jd_i}{D} = C_i - C_{mi}$$

$$\frac{Jd_o}{D} = C_{mo} - C_o$$

After summing:

$$J \left( \frac{1}{P} + \frac{d_i}{D} + \frac{d_o}{D} \right) = C_i - C_o$$

The effect of unstirred layers is to decrease the permeability so the apparent permeability coefficient ( $P_{app}$ ) is smaller than P:

$$\frac{1}{P_{app}} = \frac{1}{P} + \frac{d_i}{D} + \frac{d_o}{D}$$