Quantitative Physiology: Cells and Tissues **Lecture 4: September 13, 2006**
(Volume 1: 3.6-3.6.1.2; 3.7-3.7.2)

Review of Lecture 3

Fick's first law: $\phi(x,t) = -D \dfrac{\partial c(x,t)}{\partial x}$

Continuity equation: $-\dfrac{\partial \phi(x,t)}{\partial x} = \dfrac{\partial c(x,t)}{\partial t}$

Diffusion equation: $\dfrac{\partial c(x,t)}{\partial t} = D \dfrac{\partial^2 c(x,t)}{\partial x^2}$

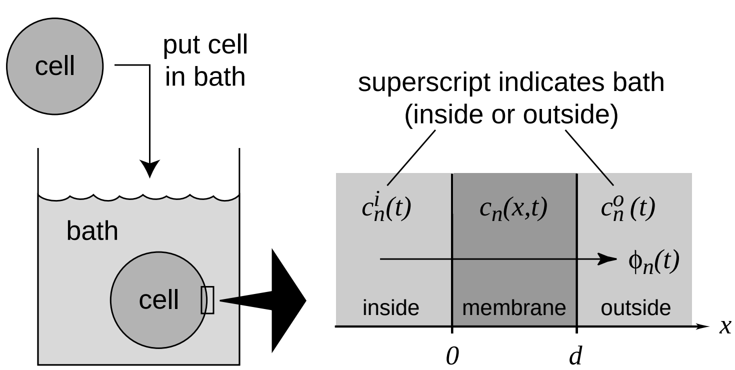
Solutions to diffusion equation:

- Equilibrium: $\phi=0$ & $\partial/\partial t$ (everything)=0
- Steady-state: $\partial/\partial t$ (everything)=0
- Impulse response: gaussian function of space; $\sigma=\sqrt{2Dt}$

Importance of Scale

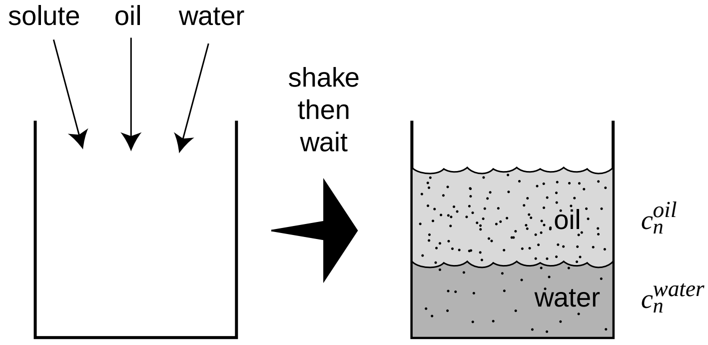
$t_{1/2} = \dfrac{x_{1/2}^2}{D}$ $\quad D = 10^{-5}\,\dfrac{\text{cm}^2}{\text{s}}$	$x_{1/2}$	$t_{1/2}$
membrane sized	10 nm	$\frac{1}{10}$ µsec
cell sized	10 µm	$\frac{1}{10}$ sec
dime sized	10 mm	10^5 sec ≈ 1 day

Membrane Diffusion: Two-Compartment Geometry



reference direction for flux is outward

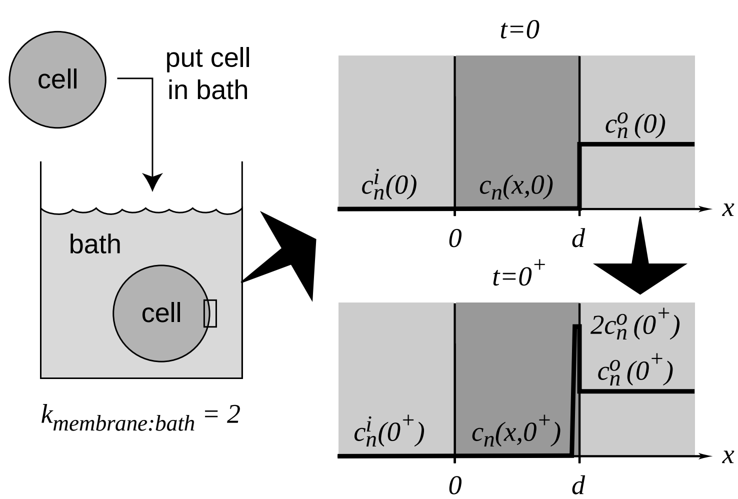
Step 1: Dissolve



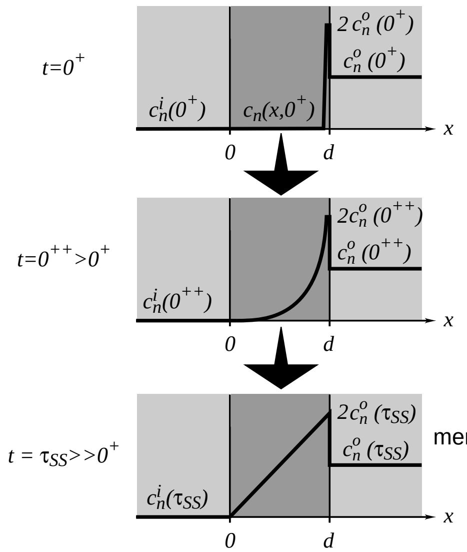
Equilibrium characterized by relative solubilities
of solute n in oil and water

partition coefficient $k_{oil:water} = \dfrac{c_n^{oil}}{c_n^{water}}$

Assume Dissolving is fast relative to diffusing



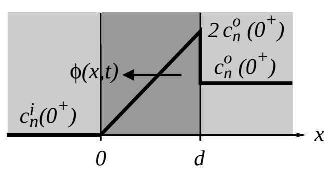
Step 2: Solute diffuses though membrane



steady state
membrane time constant

$$\tau_{SS} = \frac{d^2}{\pi^2 D}$$

Step 3: Solute enters the cell



$$c_n(x,t) = c_n(0,t) + \frac{x}{d}(c_n(d,t) - c_n(0,t))$$
$$= k_n c_n^i(t) + \frac{k_n x}{d}(c_n^o(t) - c_n^i(t))$$

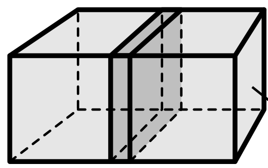
$$k_n = k_{membrane:bath} = k_{membrane:cytoplasm}$$

Fick's law: $\phi_n(t) = -D_n \frac{\partial c_n(x,t)}{\partial x}$
$$= -D_n \frac{c_n(d,t) - c_n(0,t)}{d}$$
$$= \frac{D_n k_n}{d}(c_n^i(t) - c_n^o(t))$$

$$\boxed{\phi_n(t) = P_n (c_n^i(t) - c_n^o(t)) \;;\; P_n = \frac{D_n k_n}{d}}$$

Fick's law for membranes
P_n = permeability of membrane to solute n

Step 4: Concentration in cell changes: two-compartment diffusion



Assume

- $\mathcal{V}_i$ and $\mathcal{V}_o$ constant
- well-stirred baths: $c_n^i(t)$, $c_n^o(t)$
- solute is conserved and membrane is thin: $c_n^i(t)\mathcal{V}_i + c_n^o(t)\mathcal{V}_o = N_n$
- membrane always in steady state: $\phi_n(t) = P_n(c_n^i(t) - c_n^o(t))$

By continuity,

$$A\phi_n(t) = -\frac{d}{dt}(c_n^i(t)\mathcal{V}_i) = \frac{d}{dt}(c_n^o(t)\mathcal{V}_o)$$

$$\frac{d}{dt}c_n^i(t) = -\frac{AP_n}{\mathcal{V}_i}(c_n^i(t) - c_n^o(t)) = -\frac{AP_n}{\mathcal{V}_i}\left(c_n^i(t) - \frac{1}{\mathcal{V}_o}N_n + c_n^i(t)\frac{\mathcal{V}_i}{\mathcal{V}_o}\right)$$

$$\frac{d}{dt}c_n^i(t) + AP_n(\frac{1}{\mathcal{V}_i} + \frac{1}{\mathcal{V}_o})c_n^i(t) = \frac{AP_nN_n}{\mathcal{V}_i\mathcal{V}_o}$$

First-order linear differential equation with constant coefficients, therefore

$$c_n^i(t) = c_n^i(\infty) + [c_n^i(0) - c_n^i(\infty)]e^{-t/\tau_{EQ}}$$

$$c_n^i(\infty) = \frac{N_n}{\mathcal{V}_i + \mathcal{V}_o} \qquad \tau_{EQ} = \frac{1}{AP_n(\frac{1}{\mathcal{V}_i} + \frac{1}{\mathcal{V}_o})}$$