At steady state, flux is constant $\qquad t_0 = \frac{1}{j(x_0)}$

$$t_0 = \frac{1}{j_0} = \frac{1}{D} \int_0^{x_0} e^{-U(x)/k_B T} \left\{ \int_x^{x_0} e^{U(y)/k_B T} \, dy \right\} dx$$

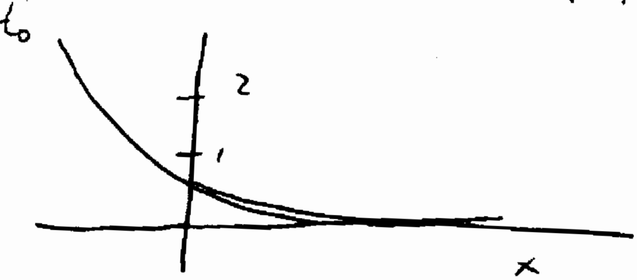
This integral needs to be solved for different choices of forces

① Free diffusion (No force) $\qquad U(x) = 0$

$$t_0 = \frac{1}{j_0} = \frac{1}{D} \frac{x_0^2}{2}$$

② Constant force $\qquad U(x) = -Fx$

$$t_0 = 2 \frac{x_0^2}{2D} \left(\frac{k_B T}{F x_0} \right)^2 \left\{ e^{-\frac{F(x_0)}{k_B T}} + \frac{F x_0}{k_B T} - 1 \right\}$$



'Downhill' movement $\qquad x_0 \to$ large

$$t_0 \to \frac{\gamma x_0}{F} \quad \frac{x_0}{V}$$

'Uphill' movement

$$t_0 \sim e^{F x_0 / k_B T}$$

like transfer over energy barrier

③ Harmonic potential $\qquad U(x) = \frac{1}{2} \kappa x^2$

$$t_0 = \frac{\gamma}{\kappa} \sqrt{\frac{\pi}{4}} \sqrt{\frac{k_B T}{U_0}} \, e^{U_0 / k_B T} \quad \text{for } U(x_0) \gg k_B T$$

Steady - state solutions to Fick equations

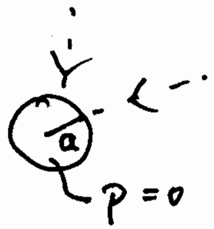
$$\frac{\partial p}{\partial t} = 0 = D \nabla^2 p$$

$$\nabla^2 p = 0 \qquad \text{Laplace equation}$$

For problems with radial symmetry

$$\frac{1}{r^2} \frac{d}{dr}\left(r^2 \frac{dp}{dr} \right) = 0$$

① Diffusion to spherical absorber



$r = a$

$p(r=a) = 0$

$p(r=\infty) = p_0$

Solution like in E & M (see Jackson, ch. 3)

$$p = A r^{\ell} + B r^{-\ell-1} \qquad p = u \cdot r \quad , \ell = 0$$

$$p = A - \frac{B}{r} \qquad \begin{array}{l} r \to \infty \Rightarrow A = p_0 \\ r \to a \Rightarrow B = -a p_0 \end{array}$$

$$p(r) = p_0 \left(1 - \frac{a}{r}\right)$$

Flux $\quad J = - D \frac{\partial p}{\partial r} = - D p_0 \frac{a}{r^2}$

current = flux × area

$$I = D p_0 \frac{a}{r^2} \cdot 4\pi a^2 = 4\pi D a p_0$$

$$I \propto a \qquad \left.\begin{array}{l} \text{Area} \propto a^2 \\ \text{conc. grad} \propto \frac{1}{a} \end{array}\right\} \propto a$$

(2) Diffusion to disk - like absorber

$p = 0$ at disk
$p = p_0$ $r \to \infty$

cylindrical coordinates

$$I = 4 D s p_0$$

again : proportional to s and not s^2

Electrical analogue

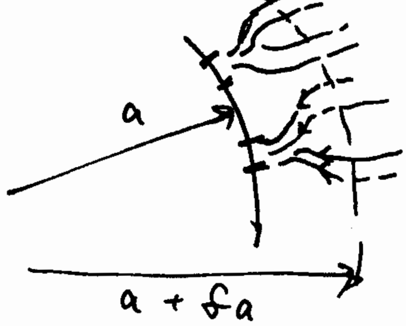
$$I = 4\pi D C p_0$$

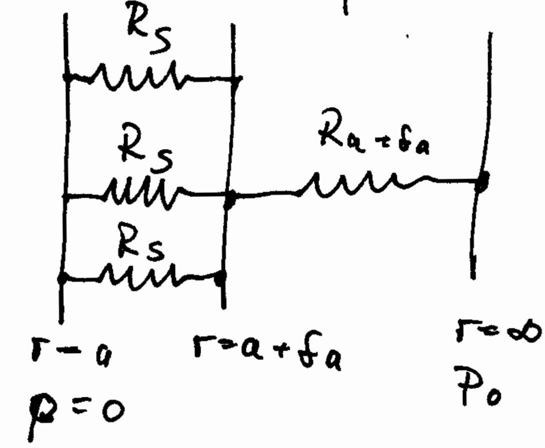
C: capacitance (cgs units) of an isolated conductor of that size and shape

(3) Cell absorption

N disk like absorbers (radius s) on surface of a sphere with radius a

N resistors in parallel

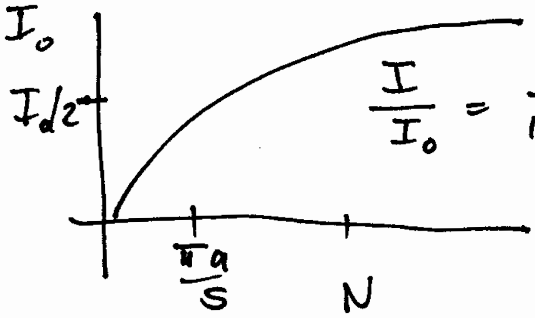




lines of flux radial for $r > a + \delta a$, i.e constant p but converge on disks

$$R = R_{a+\delta} + R_s/N$$

$=$ [illegible] $a+\delta a$



$$\frac{I}{I_0} = \frac{1}{1+\pi a/Ns}$$

limits

N small $I \sim 4 D N s p_0$

N large $I \sim 4\pi D a p_0$

Diffusion coefficients for proteins

$D_t = \frac{kT}{\gamma_t}$ [$\mu m^2/s$] translational (lateral) diff. coeff.

$D_r = \frac{kT}{\gamma_r}$ [$1/s$] rotational diff. coeff.

More general:

$$\begin{pmatrix} u^\infty - u \\ \Omega^\infty - \Omega \end{pmatrix} = \frac{1}{\eta} \begin{pmatrix} a & b^t \\ b & c \end{pmatrix} \begin{pmatrix} F \\ T \end{pmatrix}$$

F → Force
T → Torque

u : transl. velocity field of fluid

Ω : rotational velocity field of fluid

"Put" protein in fluid
Solve Stokes equations to get $u, u^\infty, \Omega, \Omega^\infty$
Easy for simple shapes → Einstein solution for sphere
Numerical for real proteins

$$D^t = \frac{1}{3}\frac{kT}{\eta}\,\mathrm{tr}(a)$$

$$D_r = \frac{1}{3}\frac{kT}{\eta}\,\mathrm{tr}(c)$$

Experimental : fluorescence photolysis measurements
sees lateral movement
use D_r [D_ℓ] relationship to get D_r

Order of magnitude estimates

	water	lipid membrane	
D_t / D_ℓ	$100\ \mu m^2/s$	$1\ \mu m^2/s$	(less for high prot conc.
D_r	$1 \times 10^7/s$	$1 \times 10^5/s$	or low L/P lipid-to-protein ratios)

More general Stat Mech

$$m_i \frac{d^2}{dt^2} r_i = -\frac{\partial}{\partial r_i} U(r_1 \dots r_N) \quad \text{Newton's Eq.}$$

Stochastic DE

$$\partial_t \, x(t) = \underbrace{A\,(x(t),t)}_{\text{drift}} + \underbrace{B(x(t),t) \cdot \eta(t)}_{\text{noise}}$$

Choice of A and B and η determines SDE
This is very general
For each set of Newton's Eq. there is a corresponding SDE
We are not really interested in $x(t)$, but in $P(x,t \mid x_0,t_0)$ → Fokker-Planck Eq.

Langevin Eq.

$$m\ddot{r} = -\gamma \dot{r} + F(r) + \sigma\,\xi(t)$$

→ corresponding F-P Eq.
limit of strong friction $|\gamma \dot{r}| \gg |m\ddot{r}|$
(white noise)
Eq. distribution: Boltzmann $p_0(r) = N e^{-U/kT}$
potential $U(r)$

F-P Eq. is called Smoluchowski Eq.

$\Rightarrow \sigma^2 = 2k_B T \gamma$

In order for system to attain thermal equilibrium, there needs to be a temperature-dep. relationship between amplitude of fluctuating and dissipative forces

· Fluctuation - Dissipation theorem