Flux in an external Force

- Diffusing particles can be subjected to external forces

$$J = -D\left(\frac{\partial c}{\partial x}\right) + \underbrace{\left(\frac{f}{\xi}\right)c}_{}$$

flux of particles that results
from applied force f (e.g, gravity)

ξ is the friction coefficient

@equilibrium, $J=0$ and the contributios to the flux are equal

$$D\frac{\partial c}{\partial x} = \frac{cf}{\xi} \Longrightarrow \frac{\partial c}{\partial x} = \boxed{\frac{cf}{\xi D}}$$

Also,
@equilibrium, $c(x)$ will follow the Boltzman distribution

$$c(x) = C_o e^{\frac{-fx}{kT}} \qquad \left(\text{remember } f = \frac{\partial u}{\partial x}\right)$$

differentiate

$$\frac{\partial c}{\partial x} = \boxed{\frac{fc}{kT}}$$

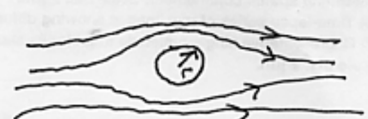
compare terms to get

$$\boxed{D = \frac{kT}{\cancel{f}\xi}} \quad \text{Einstein}$$

(friction slows down diffusion)

Add Stokes Law

$$\xi \cancel{\xi} = 6\pi\eta r$$



friction coefficient of a sphere in fluid of viscocity η

Stokes-Einstein:

$$\boxed{D = \frac{kT}{6\pi\eta r}}$$

Diffusion in a membrane

Saffman-Delbruck

membrane ~~thickn~~ viscocity
membrane thickness

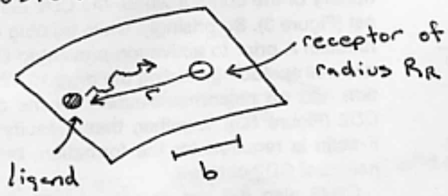
$$D = \frac{kT}{4\pi\eta_m h}\left(\ln\frac{\eta_m h}{\eta_w a} - 0.58\right)$$

protein radius
medium viscocity

- insensitive to medium viscocity and size
- sensitive to membrane thickness and viscocity

Diffusion-limited binding on a cell surface

- two molecules embedded in the cell membrane
- they diffuse in two dimensions
- diffusion coefficient is smaller than in solution



cylindrical coordinates @ steady-state

$$\nabla^2 C_L = 0$$

$$\cancel{\mathcal{D}_L}\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial C_L}{\partial r}\right) = 0$$

$$\frac{\partial C_L}{\partial r} = \frac{A}{r}$$

$$C_L(r) = A(\ln r + \ln B)$$

Boundary Conditions:

@ $r = R_R$ $\quad C_L = 0$ (ligand reacts w/ receptor)

@ $r = b$ $\quad C_L = C_0$ (arbitrary setting of the ½ way point as the bulk ~~diffusion~~ concentration)

$$0 = A\ln R_R B \implies B = \frac{1}{R_R}, \quad A = \frac{C_0}{\ln b/R_R}$$

$$C_0 = A\ln bB$$

$$\boxed{C_L(r) = C_0\frac{\ln(r/R_R)}{\ln(b/R_R)}}$$

collision frequency $= -J \cdot \text{Area}$

2D Area $= 2\pi R_R$

$$J = -\mathcal{D}_L\left.\frac{\partial C_L}{\partial r}\right|_{R_R} = -\frac{\mathcal{D}_L C_0}{R_R\ln(b/R_R)}$$

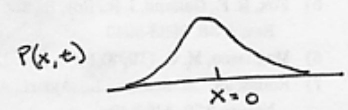
$$\text{collision frequency} = (2\pi R_R)\left(\frac{\mathcal{D}_L C_0}{R_R\ln b/R_R}\right)$$

$$= \underbrace{\left(\frac{2\pi\mathcal{D}_L}{\ln b/R_R}\right)}_{k^+}C_0$$

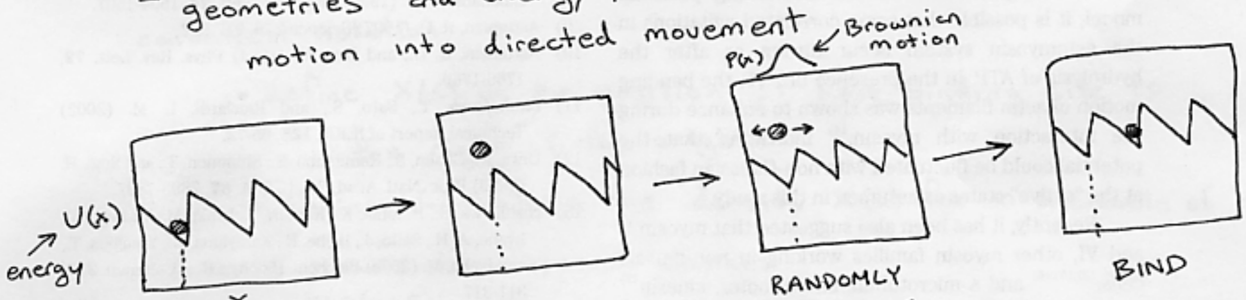
k^+: diffusion-limited association rate

Brownian Ratchets

- convert Brownian motion into directed movement
- Brownian motion is uniform



- geometries and energy potentials can covert the random motion into directed movement



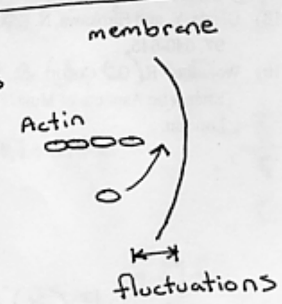
Diffusion Eqn: $\frac{\partial P(x,t)}{\partial t} = -\frac{\partial}{\partial x}\left[\frac{U(x)}{\xi}P(x,t)\right] + D\frac{\partial^2 P(x,t)}{\partial x^2}$

~~Diffusion Equation~~

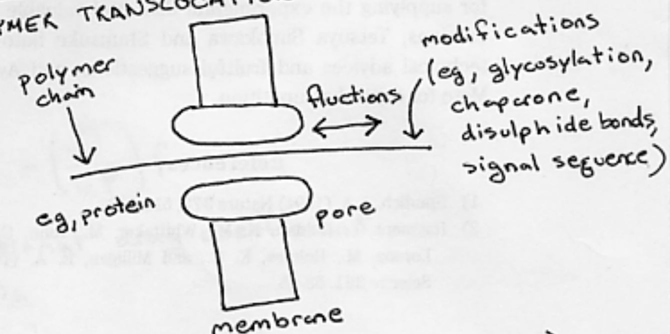
• Does not violate 2° law of thermo: chemical bond energy drives the flow

Many examples of Brownian Ratchets in Biology

• MEMBRANE PROTRUSIONS



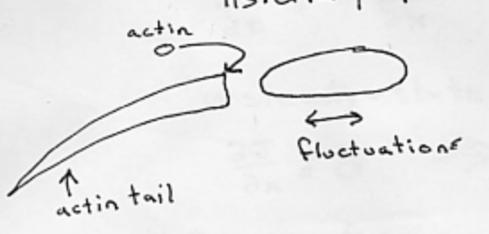
• POLYMER TRANSLOCATION



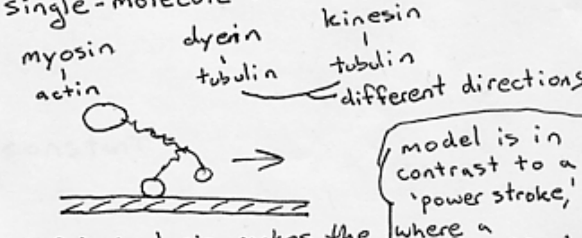
(Ooi + Weiss, Cell, 1992)

• BACTERIA MOTILITY

listeria propulsion



• single-molecule motors



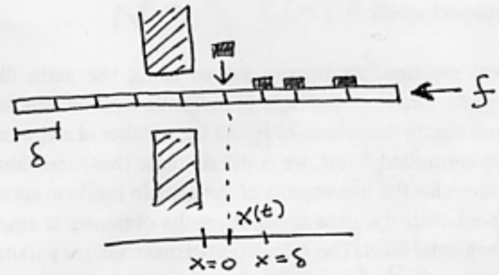
model is in contrast to a 'power stroke,' where a conformational change drives the motion

ATP hydrolysis makes the Brownian motion unidirectional

cycles through the states:

1. binding of ATP weakens attachment to fiber
2. motor fluctuates until it reaches next site
3. ATP hydrolysis relaxes the head enough to bind tightly

Derivation for a Translocation Ratchet

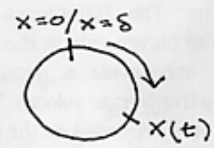


perfect ratchet: each time the rod shifts to the right, it is ratcheted

convenient notation:

- define $x(t)$ as the position of first binding site to the right of the origin
- define $c(x,t)$ as the density $x(t)$ for an ensemble of rods

converts x-axis to a circular domain



2 (odd) boundary conditions

$$J(0,t) = J(\delta,t)$$

$$c(\delta,t) = 0$$

drift velocity: $\dfrac{-f}{\xi} = -\left(\dfrac{D}{kT}\right)f$

frictional drag coefficient

$$J(x) = \frac{-Df}{kT}c - D\frac{\partial c}{\partial x}$$

$$\frac{\partial c}{\partial t} = -\frac{\partial J}{\partial x}$$

@ steady-state

$$\frac{\partial J}{\partial x} = 0 \implies J = \text{constant}$$

$$\frac{\partial c}{\partial x} + \left(\frac{f}{kT}\right)c + (J) = 0$$

constants

$\Downarrow$ solve w/ boundary conditions

$$c(x) = \frac{kTJ}{Df}\left[e^{\frac{f(\delta - x)}{kT}} - 1\right]$$

Calculate the number of rods in the ensemble

$$N = \int_0^\delta c(x)\,dx$$

$$= \frac{kTJ}{\mathcal{D}f}\int_0^\delta \left[e^{\frac{f\delta}{kT}} e^{\frac{-x}{kT}} - 1\right] dx$$

$$= \frac{J\delta^2}{\mathcal{D}}\left(\frac{kT}{f\delta}\right)\left[e^{\frac{f\delta}{kT}} - 1 - \frac{f\delta}{kT}\right]$$

Now, calculate the velocity of the rod

$$V = \frac{\delta J}{N}$$ ← flux is the average rate from left to right

Define ω = dimensionless work (force × distance)

$$\omega = \frac{f\delta}{kT}$$ ← scaled by thermal energy

$$\boxed{V = \left(\frac{2\mathcal{D}}{\delta}\right)\underbrace{\left[\frac{\omega^2/2}{(e^\omega - 1) - \omega}\right]}}$$

as $\omega \to 0$, this term $\to 1$

(if you don't believe me, try it in Excel)

so, as $f \to 0$, $V \to \frac{2\mathcal{D}}{\delta}$

maximum velocity for perfect ratchet

say, $\delta = 100$ nm (length of average unfolded protein)

$\mathcal{D} \sim 1 \frac{\mu m^2}{s}$ (average longitudinal diffusion coefficient)

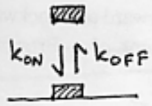
$$V \sim \frac{2(1)}{(0.1)} = 20 \frac{\mu m}{s}$$

spacing of ~~actin~~ dynein binding sites: ~~10 nm~~ 8 nm

$\mathcal{D} = 0.05 \frac{\mu m^2}{s}$ $\quad V_{max} = \frac{2(0.05)}{0.008} = 12.5 \frac{\mu m^2}{s}$

(actual is $0.8 \frac{\mu m}{s}$)

velocity Equation for imperfect translocation ratchet



$$V = \frac{2\mathcal{D}}{\delta}\left[\frac{\frac{1}{2}\omega^2}{\frac{(e^\omega - 1)}{1 - K(e^\omega - 1)} - \omega}\right]$$

$$K = \frac{k_{OFF}}{k_{ON}}$$