Betterton

Molecular Motors

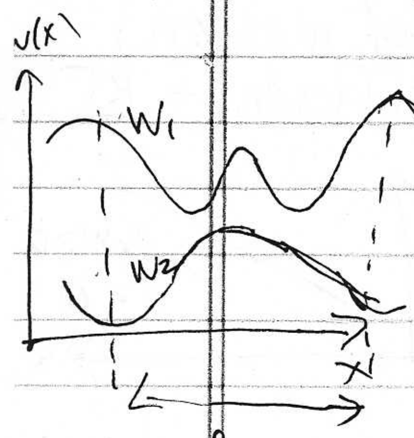
Boulder School 2007

Models of motor movement

1. Two-state model
   - Inspired by the observation that a motor protein has different conformations (shapes) in different nucleotide states. I.e., ATP-bound vs. ADP-bound

Idea: the particle (motor) randomly switches between 2 different states.

Assumptions:
- 1D motion - motion in x only
- 2 states - labeled 1 & 2
- Each state characterized by a <u>periodic potential</u> $W_j(x)$, with period ℓ



↳ Periodicity models the periodic track on which the motor moves

- Simplify: consider piecewise linear $W_j(x)$

- Random switching between the 2 states at rates $\omega_j(x)$, where ω_j is switching rate <u>from</u> state j

- Particle has diffusion coefficient D (for simplicity, same D in both states)

Formulation of the model: <u>Fokker-Planck equations</u>

$P_j(x)$ = probability ~~particle~~s density for particle in state j at position x

P_j changes due to
- diffusion
- force exerted by the potential
- switching between states

<u>Flux</u> J_j describes motion in a single potential

Diffusive flux:

$$\boxed{J_{j,\text{diff}} = -D\,\partial_x P_j}$$

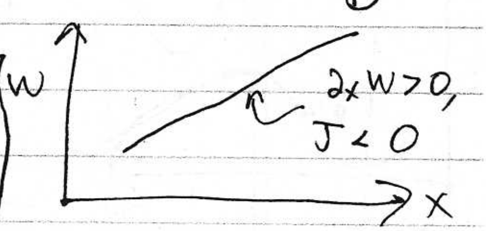
Net diffusive transport only if gradient $\neq 0$

Flux due to potential: (overdamped motion)

from $v = \frac{-F}{\gamma}$, where γ = drag coefficient $= \frac{kT}{D}$ and $J = vP$

use $F = -\partial_x W$,

$$\boxed{J_{j,W} = -D\,\partial_x\left(\frac{W_j}{kT}\right)P_j(x)}$$



Measure W in units of $kT \rightarrow$ drop factors of kT

$$\boxed{J = -D\left[P_j\,\partial_x W_j + \partial_x P_j\right]}$$

A flux of probability changes P_j

If have <u>no switching</u> between states, then

$$\partial_t P_j + \partial_x J_j = 0$$ ← conservation of probability

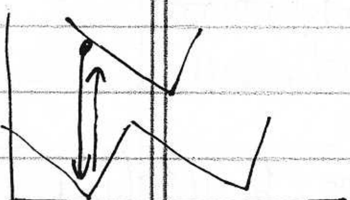
Note: with no applied force, this reduces to

$$\partial_t P_j = D\,\partial_{xx} P_j$$

The diffusion equation.

<u>Switching</u>: the rate of switching from state j at x is $\omega_j(x) P_j(x)$

Note: assume <u>x does not change</u> when switching



then have:

$$\boxed{\begin{aligned} \partial_t P_1 + \partial_x J_1 &= -\omega_1 P_1 + \omega_2 P_2 \quad (*)a \\ \partial_t P_2 + \partial_x J_2 &= \omega_1 P_1 - \omega_2 P_2 \quad (*)b \end{aligned}}$$

<u>Effective potential</u> at <u>steady state</u>

- Assume the system reaches steady state, so $\partial_t P_j = 0$
- Sum equations above $(*)$a & b

The $w_j P_j$ terms cancel. The result is

$$\partial_x J = 0$$

where $\boxed{J = J_1 + J_2 = -(\partial_x P + P\,\partial_x W)}$

$P = P_1 + P_2$ write $\lambda(x) = \frac{P_1(x)}{P(x)}$

then $\boxed{W(x') - W(0) = \int_0^{x'} dx^* \; \lambda \partial_x W_1 + (1-\lambda)\partial_x W_2}$

Derivation of W: from terms

$$\partial_x(P_1 \partial_x W_1 + P_2 \partial_x W_2)$$

use $P_1 = \lambda P$ and $P_2 = (1-\lambda)P$

$$= \partial_x\Big[P(x)\underbrace{\big(\lambda(x)\partial_x W_1 + (1-\lambda(x))\partial_x W_2\big)}_{\partial_x W}\Big]$$

From these expressions, we can see 2 useful results:

1. If W_1 and W_2 are <u>symmetric</u>, there can be no motion.

- Note: $\lambda(x)$ has the same symmetry as the potentials $\Rightarrow$ if $W_{1,2}(x)$ ~~is~~ are symmetric, so is $\lambda(x)$.
- If $W_j(x)$ is symmetric, $\partial_x W_j$ is antisymmetric

Then $\lambda(x)\,\partial_x W_1$ and $(1-\lambda(x))\,\partial_x W_2$ are both antisymmetric functions

$\Rightarrow$ The integral — the effective potential — is zero, on average

$\Rightarrow$ Flat effective potential

$\Rightarrow$ No net motion.

$$\boxed{\text{2. If switching occurs at equilibrium, there can be no net motion.}}$$

If the switching is at equilibrium, at steady state the system must have probabilities that obey the Boltzmann distribution.

$$P_2(x) = P_1(x)\, e^{-(W_2(x) - W_1(x))}$$

$$P = P_1 + P_2 = P_1\left(1 + e^{W_1 - W_2}\right)$$

$$\lambda(x) = \frac{1}{1+e^{W_1-W_2}} \qquad 1-\lambda(x) = \frac{e^{W_1-W_2}}{1+e^{W_1-W_2}}$$

The integrand in the eff. potential is:

$$\lambda\,\partial_x W_1 + (1-\lambda)\,\partial_x W_2$$

$$= \frac{\partial_x W_1 + e^{W_1-W_2}\,\partial_x W_2}{1+e^{W_1-W_2}}$$

$$= \frac{e^{-W_1}\,\partial_x W_1 + e^{-W_2}\,\partial_x W_2}{e^{-W_1} + e^{-W_2}}$$

$$= \partial_x \ln\left(e^{-W_1} + e^{-W_2}\right)$$

Therefore the effective potential is

$$W(x) = e^{-W_1(x)} + e^{-W_2(x)} + \text{const.}$$

↳ This function is periodic, so on long length scales $\underline{W(x) \text{ is flat}}$

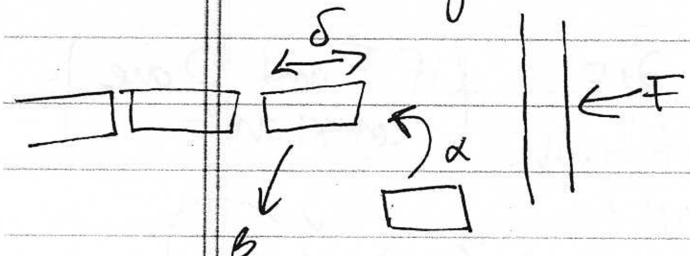
$\Rightarrow$ No net motion.

This model can not in general be solved analytically. Analytic solutions have been derived in some special cases, such as assuming piecewise linear potentials and slow switching.

In more general cases, the equations are integrated numerically.

2. Polymerization Ratchet

Model of a polymer growing near a wall
↳ e.g. an actin filament near a cell membrane



- Fluctuating wall
- Monomer size δ
  On rate α
  Off rate β

Wall has force F applied
diffusion coefficient D

Calculation: Place origin at tip of filament
$p(x)$ = probability the wall (particle) is at position x
(Really $p(x)dx$ is prob. particle is between x and $x+dx$)

2 cases:

$$\frac{\partial p}{\partial t} = \frac{\partial}{\partial x}\left(\frac{D}{kT} F p + D\frac{\partial p}{\partial x}\right) + \alpha\, p(x+\delta, t) - \beta\, p(x,t))$$

for $x < \delta$

$$\partial_t p = \partial_x\left(\frac{D}{kT} F p + D\partial_x p\right) + \alpha\left[p(x+\delta,t) - p(x,t))\right] + \beta\left[p(x-\delta,t) - p(x,t))\right]$$

for $x > \delta$

First 2 terms: Diffusion with drift

Drift: $v = -\frac{F}{\gamma}$ ← drag coeff. $= \frac{KT}{D}$

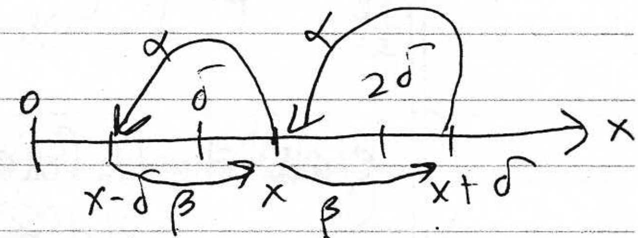
Flux $J = -p v$

$= -\frac{D}{KT} F p$

Then $\partial_t p = -\partial_x J = \frac{DF}{KT} \partial_x p$ (if F and D are constant)

Diffusion: $J = -D \partial_x p$

$\partial_t p = D \partial_{xx} p$



Rate terms: $\alpha p(x+\delta, t)$ addition: decreases particle position by δ

$\alpha p(x)$

- 2nd term not allowed if $x < \delta$ because $x \geq 0$ always

$\beta p(x, t)$ removal: increases particle position by δ

$\beta p(x-\delta, t)$

- 2nd term not allowed if $x < \delta$

Solution: Require $-\frac{\partial p}{\partial x}\Big|_0 + \frac{F}{KT} p\Big|_0 = 0$ no flux

- p continuous: $p(x=\delta-\varepsilon) = p(x=\delta+\varepsilon)$

Goal: solve for steady state $p(x,t)$

Ratchet velocity is

$$v = \delta \left[\frac{\alpha \int_\delta^\infty p(x)dx - \beta \int_0^\infty p(x)dx}{\underbrace{\int_0^\infty p(x)dx}_{=1 \text{ if } p(x) \text{ normalized}}} \right]$$

keep this term so we can neglect normalization

(Homework: solve for $p(x)$ at steady state, and determine v
↳ Assume $\beta \ll \alpha$)

Result: If polymerization and depolymerization are slow compared to ~~a~~ the time for the particle to diffuse by ~~[illegible]~~ δ

$$\frac{1}{\alpha} \gg \frac{\delta^2}{D} \qquad \frac{1}{\beta} \gg \frac{\delta^2}{D}$$

Then $p(x) \simeq p_0 e^{-\frac{Fx}{kT}}$ solution to the diffusion eqn with $F = \text{const}$.

$$\int_\delta^\infty p(x)dx = \frac{p_0}{F/kT} e^{-\frac{F\delta}{kT}}$$

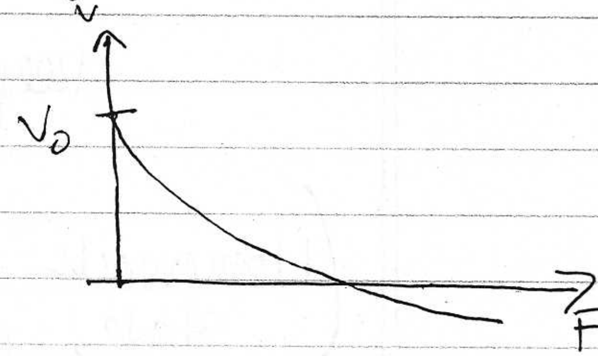
$$\int_0^\infty p(x)dx = \frac{p_0}{F/kT}$$

So

$$\boxed{v = \delta\left[\alpha e^{-\frac{F\delta}{kT}} - \beta\right]}$$

Effective monomer on rate is $\alpha e^{-\frac{F\delta}{kT}}$

Probability of finding a gap of size δ is $\exp\left(-\frac{F\delta}{kT}\right)$



Zero load: $F = 0$

$$\boxed{v = \delta(\alpha - \beta)}$$

Stall force: $v=0$ when

$$\alpha e^{-F\delta/kT} = \beta$$

$$\boxed{F_{stall} = -\frac{kT}{\delta} \ln\left(\frac{\beta}{\alpha}\right)}$$

(Note: if $\beta < \alpha$ — which is necessary for polymerization — then $F_{stall} > 0$)