Today: (I) Langevin equation for 2-state model

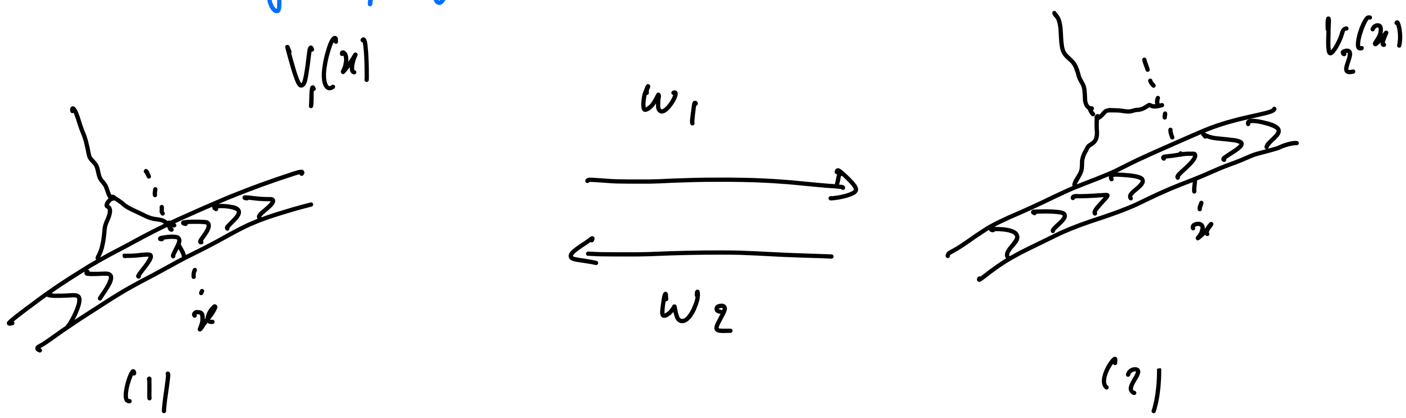
(II) Condition for steady current

(III) Collective behaviors of motors & lattice models

(I) Two-state model breaks detailed balance

State 1: strong coupling

State 2: weak coupling



$$\dot{x} = -V_1' + \sqrt{2T}\,\eta \qquad\qquad \dot{x} = -V_2' + \sqrt{2T}\,\eta$$

$P_i(x,t)$: Proba to be at x, in state i, at time t

$P(x,i,t+dt \mid y,j,t)$: Proba to transition from position y in state j at time t to position x in state i at time $t+dt$

Goal Compute $P_i(x,t+dt) - P(x,t)$ to order dt

Proba to switch from 1 to 2 in dt $= \omega_1 dt$ as $dt \to 0$

$\Rightarrow$ two switches $1 \to 2 \to 1$ occur with $p = \omega_1\omega_2 dt^2 \ll dt$

Conservation of probability.

$$\boxed{P(1,x,t+dt) = \int dy\, P_1(y,t)\, P(1,x,t+dt\,|\,1,y,t) + \int dy\, P_2(y,t)\, P(1,x,t+dt\,|\,2,y,t)}$$

$\Rightarrow$ we need to compute the conditional probabilities (a.k.a. "propagators")

① $P(1,x,t+dt\,|\,1,y,t) = P(\text{stay in state } 1) \times P(y \to x \text{ in } [t,t+dt]) + \mathcal{O}(dt^2)$

$\hookrightarrow 1 \xrightarrow{\omega_1 dt} 2 \xrightarrow{\omega_2 dt} 1$

* As $dt \to 0$ $P(1,x,t+dt\,|\,1,y,t) \to 0$ if $x-y = \mathcal{O}(1) \Rightarrow y$ needs to be close to x

only $y = x + dt^\alpha$; $\alpha > 0$ contribute.

$\Rightarrow$ proba to stay in (1) $= 1 - \omega_1(x)dt + \mathcal{O}(dt^{1+\alpha})$

since $\omega_1(y') = \omega_1(x) + \underbrace{(x-y')}_{\mathcal{O}(dt^\alpha)}\omega_1'(x)$

* $P(y \to x \text{ in } [t,t+dt]) = P_1(x,t+dt\,|\,y,t) \simeq P_1(x,t\,|\,y,t) + dt\, \partial_{\tilde t} P_1(x,\tilde t\,|\,y,t)\big|_{\tilde t = t}$

but $P_1(x,t\,|\,y,t) = \delta(x-y)$

and $\partial_{\tilde t} P_1(x,\tilde t\,|\,y,t)\big|_{\tilde t = t} = -H_{FP}^1 P_1$; where $H_{FP}^1 = -\dfrac{\partial}{\partial x}\left[k_B T \dfrac{\partial}{\partial x} + U_1'(x) \right]$

[also works with $H_{FP}^{1\dagger}(y)$]

$\Rightarrow P(y \to x \text{ in } [t,t+dt]) = (1 - dt\, H_{FP}^1)\,\delta(x-y)$

* Together: $P(1,x,t+dt\,|\,1,y,t) = (1 - \omega_1(x)dt)(1 - dt\, H_{FP}^1)\,\delta(x-y)$

$\simeq (1 - \omega_1(x)dt - dt\, H_{FP}^1)\,\delta(x-y)$

$$\Rightarrow \boxed{\int dy\, P(1,x,t+dt\,|\,1,y,t)\, P_1(y,t) = (1 - \omega_1(x)dt - dt\, H_{FP}^1)\, P_1(x,t)}$$

(2) $P(1,x,t+dt|2,y,t) = (\text{proba } 2 \to 1) \times (\text{proba } y \to x)$

$$= \left[\omega_2(x)dt + o(dt)\right]\left[1 - dt\, H_{FP}\right]\delta(x-y)$$

$$\simeq \omega_2(x)\, dt\, \delta(x-y)$$

$$\Rightarrow \boxed{\int dy\, P(1,x,t+dt|2,y,t)\, P_2(y,t) \simeq \omega_2(x)\, dt\, P_2(x,t)}$$

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All in all:

$$P_1(x,t+dt) = P_1(x,t) - dt\left(H^1_{FP} + \omega_1(x)\right)P_1 + \omega_2\, dt\, P_2$$

$$\Rightarrow \begin{cases} \underbrace{\partial_t P_1(x,t) =}_{\substack{\text{rate of change of the}\\ \text{probability to be in}\\ \text{state } i \text{ at } x,t}} & \underbrace{-H^1_{FP}\, P_1(x,t)}_{\substack{\text{Motion within}\\ \text{the state.}\\ \Rightarrow -\partial_x J_i}} & \underbrace{-\omega_1(x) P_1}_{\substack{\text{loss or gain}\\ \text{due to hops}\\ \text{from 1 to 2}}} & \underbrace{+\omega_2(x) P_2}_{\substack{\text{loss or gain}\\ \text{due to hops}\\ \text{from 2 to 1.}}} \\ \partial_t P_2(x,t) = & -H^2_{FP}\, P_2(x,t) & +\omega_1(x) P_1 & -\omega_2(x_2) P_2 \end{cases}$$

Switching rates:

Let us forget space and focus on $\underset{V_1(x)}{\text{State } 1} \underset{W_2(x)}{\overset{W_1(x)}{\rightleftarrows}} \underset{V_2(x)}{\text{State } 2}$

Dynamics $\partial_t P_1 = -\omega_1 P_1 + \omega_2 P_2$ & $\partial_t P_2 = +\omega_1 P_1 - \omega_2 P_2$

Steady state $\omega_1 P_1 = \omega_2 P_2$

(1) **Thermally activated switch:**

$$\left.\begin{aligned} \omega_1^{th}(x) &= \omega(x)\, e^{\beta V_1(x)} \\ \omega_2^{th}(x) &= \omega(x)\, e^{\beta V_2(x)} \end{aligned}\right\} P_i = \frac{1}{Z_1} e^{-\beta V_i(x)} \quad \text{such that } P_i \omega_i = \omega(x)$$

② **Chemically activated switch:** $(1), ATP \underset{\omega_1}{\overset{\omega_2}{\rightleftharpoons}} (2), ADP + P$

$$\omega_1^{ch}(x) = \gamma(x)\, \omega_1^{th}(x)\, e^{\beta \Delta\mu_{ATP}}$$

$$\omega_2^{ch}(x) = \gamma(x)\, \omega_2^{th}(x)\, e^{\beta[\Delta\mu_{ADP} + \Delta\mu_P]} \quad ; \quad \Delta\mu_i = \mu_i - \mu_i^{eq} \quad ; \quad \mu_i = \mu_i^{std} + \ln [i]$$

Excess of ATP favors $1 \to 2$ while excess of ADP favors $2 \to 1$

If $\Delta\mu_{ATP} \neq \Delta\mu_{ADP} + \Delta\mu_P$, then $\frac{\omega_1^{ch}}{\omega_2^{ch}} \neq \frac{\omega_1^{th}}{\omega_2^{th}}$ which leads to a competition between the steady states

$\to$ the system will be out of equilibrium.

③ **In practice, both processes:** $\omega_i(x) = \omega_i^{th}(x) + \omega_i^{ch}(x)$

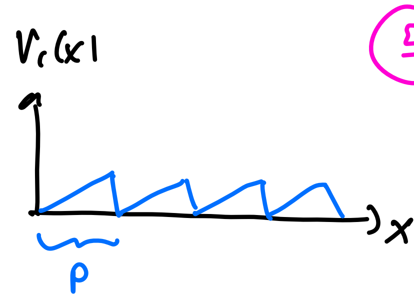
④ **Diffusion:**

In the presence of diffusion in each state, the Brownian dynamics is also trying to lead to $\frac{1}{Z} e^{-\beta V_i(x)}$, which is compatible with $\omega_i^{th}(x)$ but not with $\omega_i^{ch}(x)$ if $\Delta\mu \equiv \Delta\mu_{ATP} - \Delta\mu_{ADP} + \Delta\mu_P > 0$

Comment: As time goes on, $[ATP] \to [ATP]^{eq}$ & the environment relaxes to equilibrium $\Rightarrow$ need to maintain $\Delta\mu > 0$. This is why we eat & breathe.

Conclusion: $\Delta\mu \neq 0$ drives the system out of equilibrium $\Rightarrow$ is this sufficient to induce a current?

4.3) A simple example



[Jülicher, Ajdari, Prost; RMP 69, 1269, (1997)]

$V_2 = 0$, ω_1 & ω_2 constant, $V_1(x)$ periodic with period p

Dynamics: $$\partial_t P_1(x,t) = \frac{\partial}{\partial x}\left[T\frac{\partial}{\partial x} + V_1'(x)\right]P_1 - \omega_1 P_1 + \omega_2 P_2$$

$$\partial_t P_2(x,t) = T\frac{\partial^2}{\partial x^2}P_2 + \omega_1 P_1 - \omega_2 P_2$$

$$P_{tot}(x) = P_1(x) + P_2(x) \Rightarrow \partial_t P_{tot}(x) = T\frac{\partial^2}{\partial x^2}P_{tot} + \frac{\partial}{\partial x}\left[V_1'(x)P_1(x)\right]$$

$$= T\frac{\partial^2}{\partial x^2}P_{tot} + \frac{\partial}{\partial x}\left[V_{eff}'(x)P_{tot}(x)\right]$$

where $V_{eff}'(x) = \lambda(x)V_1'(x)$ & $\lambda(x) = \frac{P_1(x)}{P_{eff}(x)}$

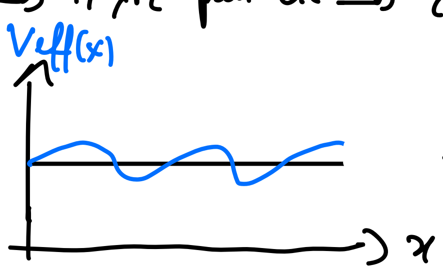
$\Rightarrow$ Brownian dynamics in an effective potential

$$\boxed{V_{eff}(x) = V_{eff}(0) + \int_0^x du\, \lambda(u) V_1'(u)}$$

let $\Delta = \int_0^p dx\, \lambda(x) V_1'(x)$

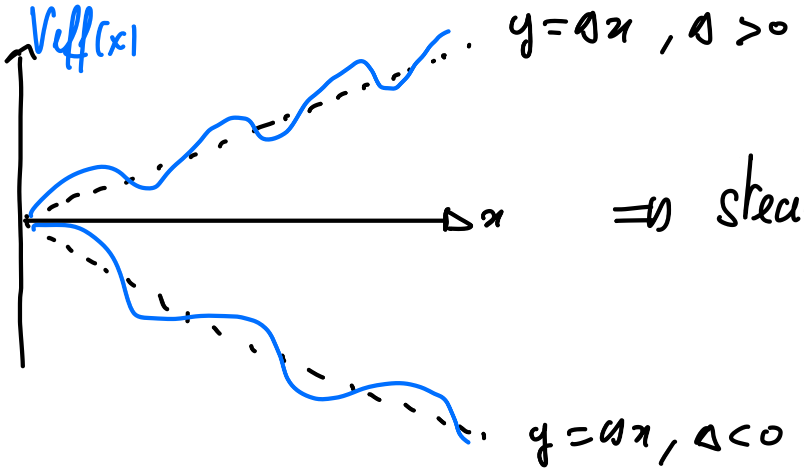
V_1, V_2 periodic $\Rightarrow P_1, P_2$ periodic $\Rightarrow \lambda(x)$ periodic

If $\Delta = 0$ then



$\Rightarrow$ no current.

If $\Delta \neq 0$, then



$\Rightarrow$ steady current.

What is the condition for $\Delta = 0$?

(i) if $V_1(x) = V_1(-x) \Rightarrow P_1$ & P_2 even $\Rightarrow \lambda(x) = \lambda(-x)$, $V_1'(x)$ odd $\Big\}$ $\lambda V_1'$ odd & $\Delta = 0$

(ii) otherwise, Δ is generically non-zero & the dynamics leads to a non zero current

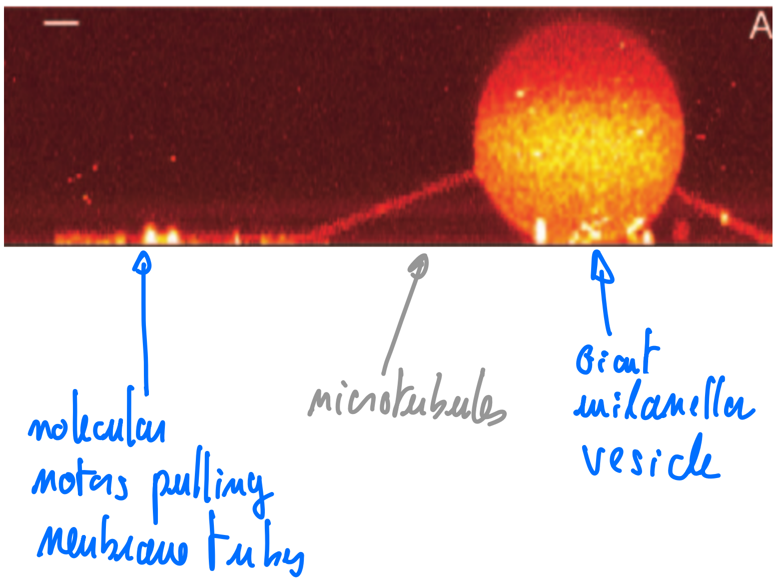
Comment: $\partial_t P_i = -H^i_{FP} P_i$ satisfies detailed balance with $P^i_s = \frac{1}{Z} e^{-\beta V_i}$

$\partial_t P_i = -\omega_i P_i + \omega_j P_j$ ———— $\frac{P_i}{P_j} = \frac{\omega_j}{\omega_i}$

It is the competition between the two processes that prevents the relaxation towards a time-reversal symmetric steady state

4.4) Collective behaviors of molecular motors

Idea: Model the collective behavior of molecular motors, e.g. when they pull on membrane tubes.

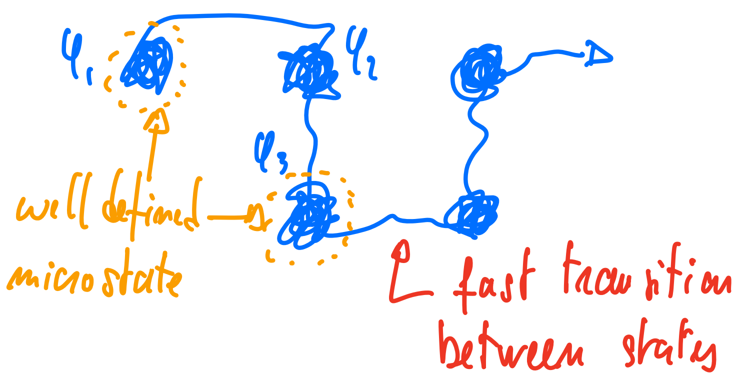


[Roux et al., PNAS 99, 5394 (2002)]

Problem: The model above is useful to understand why motors walk processively but it is far too detailed to study the large scale properties of $N \gg 1$ interacting motors.

Solution: coarse grain the microstates corresponding to the residency of a motor (head) on a tubulin monomer into 1 macrostate & average over all possible trajectories from 1 state to the next to compute the corresponding transition rate.

Langevin dynamics in $\mathbb{R}^N$



Transition rate:

$$\int_{\varphi_i} dx_i \, \frac{1}{V_k} \int_{\varphi_k} dx_k \, P(x_i, t+dt \,|\, x_k, t) \equiv \underbrace{W(\varphi_k \to \varphi_i)}_{\text{transition rate from configuration } i \text{ to } j.} dt$$

$$V_k = \int_{\varphi_k} dx_k$$

Comments: . Beautiful idea

- requires scale separation to identify states correctly. This amounts to requiring Dynkin's condition that $P(x_i, t+dt \mid x_k)$ is $\sim$ constant for x_k in φ_k so that

$$W(\varphi_k \to \varphi_i)\, dt \simeq \int_{\varphi_i} dx_i \; P(x_i, t+dt, x_k, t) \text{ for any } x_k \in C_k .$$

- in practice, computing $W(\varphi_k \to \varphi_i)$ from the dynamics is horribly difficult, except in the simplest of cases (e.g. Arrhenius in 1d)

"Proof"

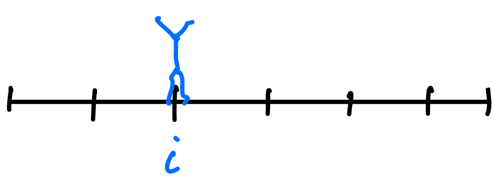
$$P(\varphi_i, t+dt; \varphi_k, t) \equiv W(\varphi_k \to \varphi_i)\, dt\; P(\varphi_k); \quad P(\varphi_k) = \int_{x_k \in \varphi_k} dx_k \; P(x_k)$$

$$\Rightarrow W(\varphi_k \to \varphi_i)\, dt = \int_{\varphi_i} dx_i \int_{\varphi_k} dx_k \; \frac{P(x_i, t+dt \mid x_k, t)\, P(x_k, t)}{P(\varphi_k)}$$

Dynkin, $P(x_i, t+dt \mid x_k, t) \simeq P(x_i, t+dt \mid x_k^0, t)$; $x_k^0 \in \varphi_k$

$$\Rightarrow W(\varphi_k \to \varphi_i)\, dt = \int_{\varphi_i} dx_i \; P(x_i, t+dt \mid x_k^0, t) \underbrace{\frac{\int dx_k \; P(x_k, t)}{P(\varphi_k)}}_{=1} \quad \text{qed.}$$

Model:



$\varphi_i \Leftrightarrow$ motor attached to monomer i.

Set of configurations $\{\varphi\}$ and transition rates between them.

Evolution of $P(\varphi,t)$

$$P(\varphi, t+dt) = P(\varphi,t) \times \text{Proba}(\text{stay in } \varphi \text{ in } [t,t+dt])$$
$$+ \sum_{\varphi' \neq \varphi} P(\varphi',t) \times \text{Proba}(\text{go from } \varphi' \text{ to } \varphi \text{ in } [t,t+dt])$$
$$= P(\varphi,t) \times \underbrace{\Big(1 - \sum_{\varphi' \neq \varphi} W(\varphi \to \varphi')dt\Big)}_{1-\text{proba to leave}} + \sum_{\varphi' \neq \varphi} W(\varphi' \to \varphi) dt \underbrace{+ O(dt^2)}_{\text{proba}(n>1 \text{ configuration changes})}$$

Master equation:

$$\partial_t P(\varphi) = \underbrace{\sum_{\varphi' \neq \varphi} W(\varphi' \to \varphi) P(\varphi',t)}_{\text{gain term due to incoming transition}} - \underbrace{\sum_{\varphi' \neq \varphi} W(\varphi \to \varphi') P(\varphi,t)}_{\text{loss due to outgoing transitions.}}$$