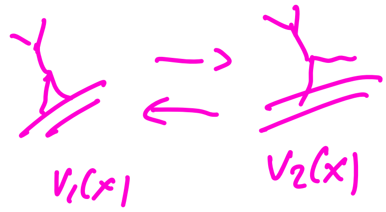
Last time:

* 2-state model for the stepping of molecular motor



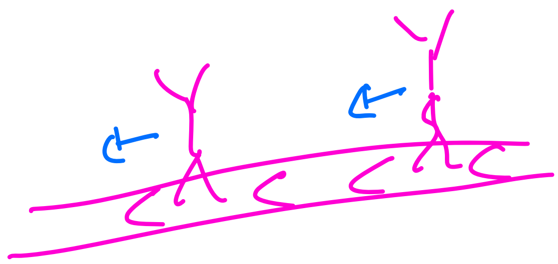
* coarse graining into Markov chain
  state $\varphi \Leftrightarrow$ position of the motor

* Transition rates $W(\varphi \to \varphi')$
* Master equation

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

Today:

* Collective motion of motors
  focus on difference between
  1 & 2 motors



* Detailed balance & TRS for Markov process

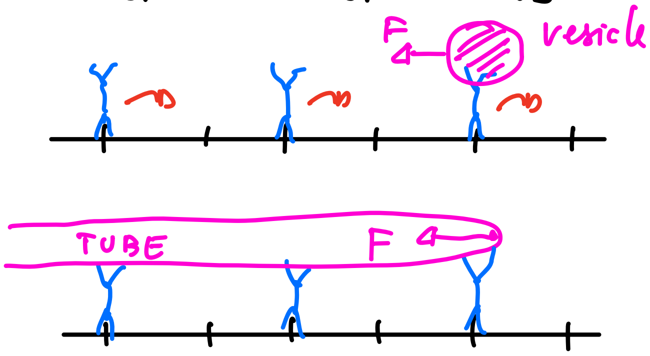
Application to molecular motors: the asymmetric simple exclusion process (ASEP)

TASEP introduced in [Mac Donald, Gibbs, Dipkin, Biopolymers 6, 1-25, 1968] to model ribosomes along DNA. Adapted in

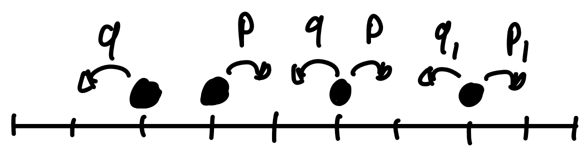
[O. Campas, et al Phys. Rev. Lett. 97, 038101 (2006)]

to model the collective motion of kinesins.

Two standard situations



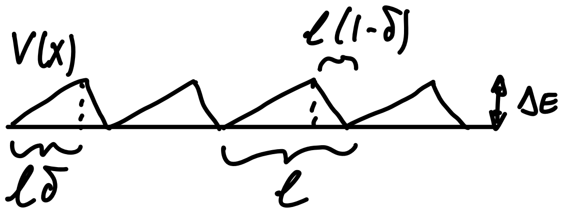
Model:



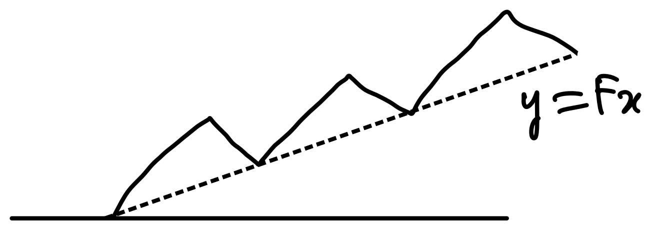
Particles hop at constant rates onto free sites.

Q: How to model the force applied to the first motor?

Remember the ratchet



Apply F



Energy barrier δE: forward rate $p = p_0 e^{-\beta\Delta E} \Rightarrow p_1 = p_0 e^{-\beta[\Delta E + F\delta\ell]}$

$$= p e^{-\beta F\delta\ell}$$

backward rate $q = q_0 e^{-\beta\Delta E} \Rightarrow q_1 = q_0 e^{-\beta[\Delta E - F(1-\delta)\ell]}$

$$= q\, e^{+\beta F(1-\delta)\ell}$$

For clarity, introduce $\beta F\ell = f$

4.4.1) Isolated motor and stall force

On average, p_1 jumps to the right per unit time
q_1 ——— left ——— } mean speed $v_m = p_1 - q_1$

Let's prove it: $i(t)$ position of the motor at time t.

$$\langle i(t)\rangle = \sum_j j\, P(i(t)=j) \Rightarrow \partial_t \langle i(t)\rangle = \sum_j j\, \partial_t P(i(t)=j)$$

cumbersome notation $\Rightarrow P(j,t)$

Master equation $\partial_t P(\varphi) = \sum_{\varphi'\neq\varphi} W(\varphi'\to\varphi)P(\varphi') - W(\varphi\to\varphi')P(\varphi)$

* Here $\varphi \Leftrightarrow$ position j
* Identify all φ, φ' such that $W(\varphi\to\varphi')\neq 0$ or $W(\varphi'\to\varphi)\neq 0$ & $P(\varphi')\neq 0$

$\varphi \Leftrightarrow j \Rightarrow \varphi' \Leftrightarrow j\pm 1$

$$\begin{aligned}\partial_t P(j,t) &= W(j-1\to j)\,P(j-1) + W(j+1\to j)\,P(j+1) \\ &\quad - [W(j\to j-1) + W(j\to j+1)]\,P(j) \\ &= p_1 P(j-1) + q_1 P(j+1) - (p_1+q_1)P(j)\end{aligned}$$

$$\begin{aligned}\partial_t \langle j\rangle &= \sum_j p_1\, \underbrace{j\, P(j-1)}_{j=h+1} + q_1\, \underbrace{j\, P(j+1)}_{j=h-1} - (p_1+q_1)\underbrace{j\, P(j)}_{j=h} \\ &= \sum_h p_1 (h+1)P(h) + q_1(h-1)P(h) - (p_1+q_1)\,h\,P(h) \\ &= \sum_h (p_1-q_1)P(h) = (p_1-q_1)\sum_h P(h) = p_1 - q_1\end{aligned}$$

$$\Rightarrow \langle j(t)\rangle = \langle j(0)\rangle + (p_1-q_1)t \Rightarrow \boxed{v_m = p_1 - q_1}$$

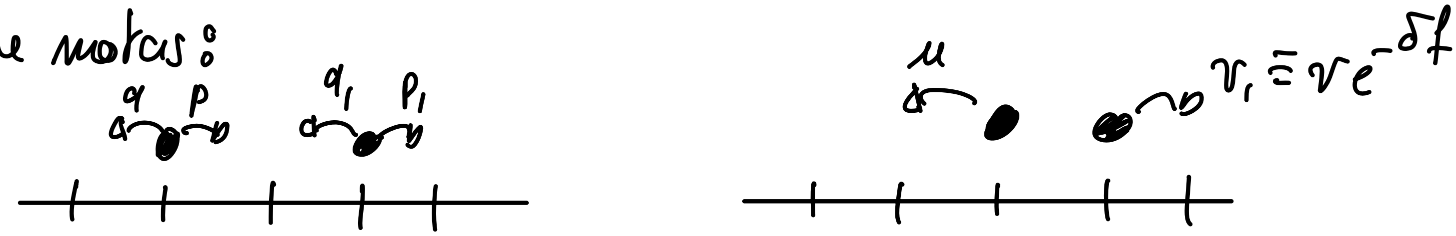
Stall force: Force f such that $v_{1m}(F) = 0$

$$\Longleftrightarrow p_1 = q_1 \Longleftrightarrow p e^{-\delta f} = q e^{(1-\delta)f}$$

$$\Longleftrightarrow \boxed{f_s^{1m} = \ln \frac{p}{q}}$$

4.4.2) Two motors

For completeness, let us allow for short range interactions between the motors:



if $v_1 > p_1$ & $u > q \Rightarrow$ repulsive interactions

if $v_1 < p_1$ & $u < q \Rightarrow$ attractive interactions

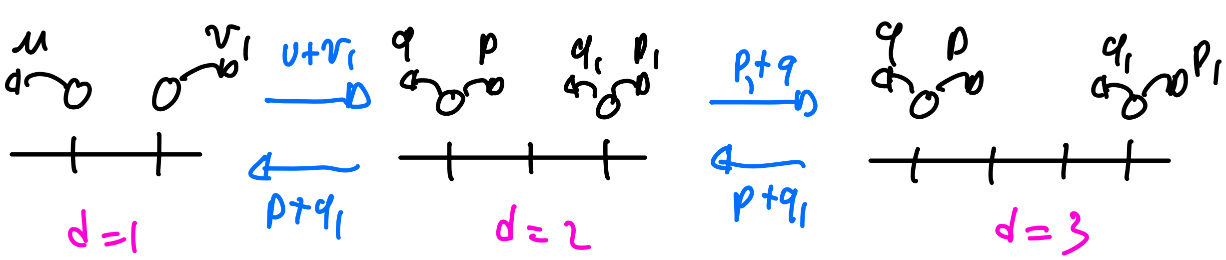
(otherwise, non reciprocal interactions)

Goal: characterize the motor cooperativity through v_{2m}, the speed in the presence of 2 motors

Intermediate step: characterize the distance between the motors

Average distance between two motors

Let's denote by $P_d(k)$ the probability that the distance between the motors equal k.



$$\partial_t P_d(1) = (p+q_1)\, P_d(2) - (u+v_1)\, P_d(1) \qquad (1)$$

$$\partial_t P_d(2) = (u+v_1)\, P_d(1) - (p+q_1)\, P_d(2) - (p_1+q)\, P_d(2) + (p+q_1)\, P_d(3) \qquad (2)$$

$$\vdots$$

$$\partial_t P_d(n) = (p_1+q)\, P_d(n-1) - (p+q_1)\, P_d(n) - (p_1+q)\, P_d(n) + (p+q_1)\, P_d(n+1) \qquad (n)$$

Steady state: $\partial_t P_d(i) = 0$; for any i.

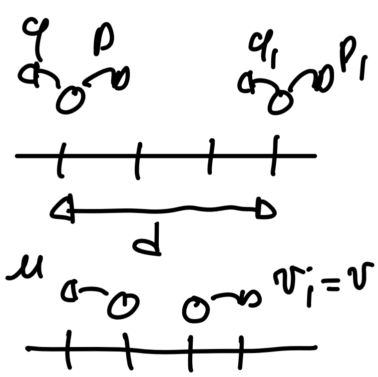
$(1) \Rightarrow P_d(2) = \frac{u+v_1}{p+q_1} P_d(1) \equiv r_1 P_d(1)$ where $r_1 = \frac{u+v_1}{p+q_1}$

$(1+2) \Rightarrow P_d(3) = \frac{p_1+q}{p+q_1} P_d(2) \equiv r P_d(1) = r\, r_1 P_d(1)$ where $r = \frac{p_1+q}{p+q_1}$

$(1+2+\dots+n) \Rightarrow P_d(n+1) = r P_d(n) = \dots = r^{n-1} r_1 P_d(1)$

Normalisation: $\sum_{k=1}^{\infty} P_d(k) = 1 \Leftrightarrow 1 = P_d(1)\left[1 + r_1 \sum_{k=0}^{\infty} r^k\right]$

Average distance between two motors



$v_1 = v e^{-\delta f}$

$p_1 = p\, e^{-\delta f} < p$

$q_1 = q\, e^{(1-\delta) f} > q$

$r = \frac{p_1+q}{p+q_1} < 1$

$\Rightarrow P_d(1) = \frac{1-r}{1-r+r_1}$ & $P_d(k \geq 2) = \frac{r_1(1-r)}{1-r+r_1} r^{k-2}$, $r_1 = \frac{u+v_1}{p+q_1}$

Comment: $P_d(k) \underset{k\to\infty}{\sim} C e^{-k \ln r} \Rightarrow \langle k \rangle$ finite, scales as $\frac{1}{\ln r}$ as $r \to 1$

In this case, $\langle h \rangle$ finite $\Rightarrow$ the two motors go at the same average speed

Mean speed of the first motor

$$v_{2M} = \langle v \rangle = v_{isolated} \times p(isolated) + v_1 P_d(1)$$

$$= (p_1 - q_1)\left[1 - P_d(1)\right] + v_1 P_d(1)$$

$$= (p_1 - q_1)\frac{\Omega_1}{1-\Omega+\Omega_1} + v_1 \frac{1-\Omega}{1-\Omega+\Omega_1} = \frac{(p_1-q_1)(u+v_1) + v_1(p+q_1-p_1-q)}{p+q_1-p_1-q+u+v_1}$$

$$= \frac{u(p_1-q_1) + v_1(p-q)}{p+q_1-p_1-q+u+v_1}$$

Stall force f such that $v^{2M}(f) = 0$

$$u\, e^{-\delta f}(p - q e^{f}) + v e^{-\delta f}(p-q) = 0 \iff u q e^{f} = up + vp - vq$$

$$f_S^{2M} = \ln\left[\frac{p}{q} + \frac{v}{u}\underbrace{\left(\frac{p}{q} - 1\right)}_{>0}\right] > \ln\frac{p}{q} = f_S^{1M}$$

Whatever the interactions between the motors, the stall force to stop the 1st motor is always larger when there is a 2nd motor behind it. This is because the presence of the second motor prevents backward fluctuations of the 1st motor.

Speed of the first motor

The second motor increases the stall force, does it increase the speed?

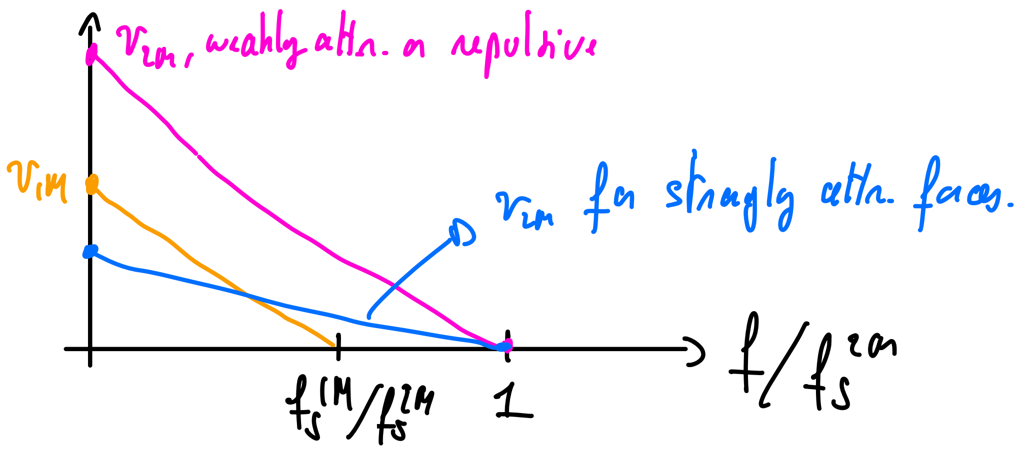
$$v_{2M} - v_{1M} = \frac{u(p_1-q_1) + v_1(p-q)}{p+q_1-p_1-q+u+v_1} - \frac{(p_1-q_1)(p+q_1-p_1-q+u+v_1)}{\underbrace{p-p_1}_{>0} + \underbrace{q_1-q}_{>0} + \underbrace{u+v_1}_{>0}} \Rightarrow \text{denominator is} > 0$$

$$\text{Sign}(v_{2M}-v_{1M}) = \text{Sign}\left[v_1(p-q) - (p_1-q_1)(p+q_1-p_1-q) - v_1(p_1-q_1)\right]$$
$$= \text{Sign}\left[(v_1-(p_1-q_1))(\underbrace{p-p_1}_{\geq 0} + \underbrace{q_1-q}_{\geq 0})\right]$$
$$= \text{Sign}\left[v - p + qe^{f}\right]$$

* if $f > f_s^{2M}$, $v_{2M} = v_{1M} = 0$
* if $f_s^{2M} > f > f_s^{1M}$, $v_{2M} > 0 = v_{1M}$
* if $f_s^{1M} > f$, then $v_{2M} > v_{1M} \Leftrightarrow v > p - qe^{f} \underset{f=0}{\simeq} p-q$

If attractive forces are strong, $v < p-q$ & $v_{2M} < v_{1M}$

If ——————— are weak, or interactions are repulsive $v_{2M} > v_{1M}$



N body: [O. Campàs, et al Phys. Rev. Lett. 97, 038101 (2006)]

5 Detailed balance for Markov Processes

Langevin equations : continuous time & continuous space

Markov processes : continuous time & discrete space

(Markov chain : discrete time & discrete space)

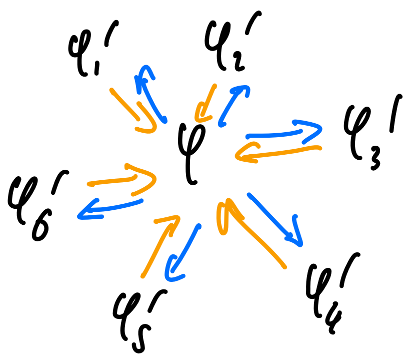
These can be seen as different level of coarse-graining, as above, or as dealing with observables of different nature (continuous position x vs discrete number of particles n_i).

The notion of time reversal symmetry & detailed balance extend to the discrete case.

5.1) Detailed balance at the rate level

$$\partial_t P(\varphi) = \sum_{\varphi' \neq \varphi} W(\varphi' \to \varphi) P(\varphi') - \sum_{\varphi' \neq \varphi} W(\varphi \to \varphi') P(\varphi)$$

Steady state: $\partial_t P(\varphi) = 0 \Rightarrow \forall \varphi,\ \underbrace{\sum_{\varphi' \neq \varphi} W(\varphi' \to \varphi) P(\varphi')}_{\text{probability flux into } \varphi} = \underbrace{\sum_{\varphi' \neq \varphi} W(\varphi \to \varphi') P(\varphi)}_{\text{probability flux out of } \varphi}$



This is called global balance, the sum of ingoing fluxes is balanced by the sum of outgoing fluxes, leaving $P(\varphi)$ constant.

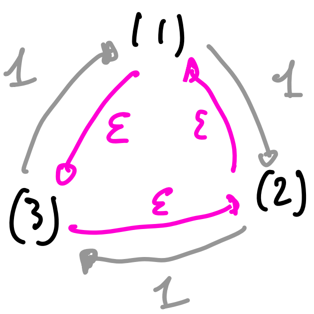
Detailed Balance (DB) is a stronger constraint: $W(\varphi' \to \varphi) P(\varphi') = W(\varphi \to \varphi') P(\varphi)$

It enforces the balance between each pair of state and guarantees that the dynamics is time reversible in the steady state since

$$P(\varphi,t';\varphi',t) = P(\varphi,t'|\varphi',t)\,P(\varphi',t) \underset{t'=t+dt}{\approx} W(\varphi'\to\varphi)\,dt\,P(\varphi',t)$$
$$= W(\varphi\to\varphi')\,dt\,P(\varphi,t)$$

Then DB $\Rightarrow P(\varphi,t+dt;\varphi',t) = P(\varphi',t+dt;\varphi,t)$

example: Invariance by rotation $\Rightarrow$ steady state $P(i)=\frac{1}{3}$



Let's check that it satisfies global balance

flux out of (i) : $(1+\varepsilon)\times\frac{1}{3}$
flux into (i) : $(1+\varepsilon)\times\frac{1}{3}$
$\Big\}$ global balance

However $P(i)\,W(i\to i+1) = \frac{1}{3}\times 1 = \frac{1}{3}$ while $P(i+1)\,W(i+1\to i) = \varepsilon/3$

$\Rightarrow$ No detail balance if $\varepsilon\neq 1$.

This fits our intuition: if $\varepsilon<1$, the CW rotation is more likely than the time reversed, CCW, rotation.

Comment: DB is a joint property of the rates and the steady state distribution.

5.2) At the trajectory level

Escape rate: $r(\varphi) = \sum_{\varphi'\neq\varphi} W(\varphi\to\varphi')$ is the total rate at which the system hops out of configuration φ.

Escape time: τ is the first time at which the system escapes φ, given that it is in φ at time 0. Q: $P(\tau)=?$

$\tau = N dt$ & work in the limit $N\to\infty$, $dt\to 0$, $N dt=\tau$ constant

$$\text{Proba}(\varphi\to\varphi' \text{ during } dt) = W(\varphi\to\varphi')\,dt + O(dt^2)$$

$$\text{Proba}(\text{out of } \varphi \text{ during } dt) = \sum_{\varphi'\neq\varphi} W(\varphi\to\varphi')\,dt + O(dt^2) \simeq r(\varphi)\,dt$$

$$\text{Proba}(\text{stay in } \varphi \text{ during } dt) = 1 - r(\varphi)\,dt$$

$$\text{Proba}\,(1^{st}\text{ escape in }[\tau,\tau+dt]) = \underbrace{[1-r(q)\,dt]^N}_{\text{does not escape in the } N \text{ first time intervals}} \cdot \underbrace{r(q)\,dt}_{\text{then it escapes}}$$

$$\simeq e^{-N r(q)\,dt}\, r(q)\,dt = r(q)\, e^{-\tau r(q)}\, dt$$

$\Rightarrow$ the probability density to exit at τ is $\boxed{P(\tau) = r(q)\, e^{-\tau r(q)}}$

<u>Comment:</u> (i) $P(\tau > t) = \int_t^\infty d\tau\, P(\tau) = e^{-t r(q)}$ $\Rightarrow$ the probability to remain in q decreases exponentially in time.

(ii) $W(q\to q')\,dt$ is the probability that the system jumps out of q AND into q'.

<u>Q:</u> Given that the system hops out of q, what is the proba that it goes into a specific q'?

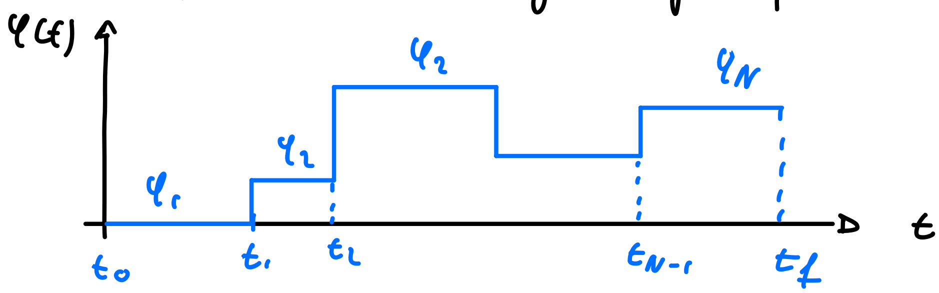
$$P(q\to q' \,\&\, \text{jump in the next } dt) = W(q\to q')\,dt = P(q\to q' \mid \text{jump}) \times \underbrace{P(\text{jump})}_{r(q)\,dt}$$

$$\Rightarrow P(q\to q' \mid \text{jump}) = \frac{W(q\to q')}{\sum_{q''\neq q} W(q\to q'')}$$

This is the basis of the tower-sampling algorithm

Probability of a full trajectory

A trajectory is defined as a sequence of configurations q_i and jump times t_i, at which the system goes from q_i to q_{i+1}.



The probability to go from φ to φ' in $[t, t+dt]$ is $W(\varphi\to\varphi')dt$

→ independent from $\varphi(s \le t)$ → Markovian dynamics.

⇒ $P[\text{trajectory } \varphi(t)] = \prod_k P[\text{transition from } \varphi_k \text{ to } \varphi_{k+1}]$

Let us denote by $P(\varphi)$ the steady state proba to be in φ and compare the probability of $\varphi(t)$ & $\varphi^R(t) = \varphi(t^R = t_f - t)$.

$$P(\{\varphi(t)\}) = \underbrace{P(\varphi_1)}_{\text{start at } \varphi_1} \times \underbrace{r(\varphi_1)\, e^{-r(\varphi_1)(t_1-t_0)}}_{\text{jump out at } t_1} \cdot \underbrace{\frac{W(\varphi_1\to\varphi_2)}{r(\varphi_1)}}_{\text{go to } \varphi_2} \times \underbrace{r(\varphi_2)\, e^{-r(\varphi_2)(t_2-t_1)} \cdot \frac{W(\varphi_2\to\varphi_3)}{r(\varphi_2)}}_{\text{same for } \varphi_2\to\varphi_3}$$

$$\times \cdots \times \underbrace{r(\varphi_{N-1})\, e^{-r(\varphi_{N-1})(t_{N-1}-t_{N-2})} \cdot \frac{W(\varphi_{N-1}\to\varphi_N)}{r(\varphi_{N-1})}}_{\text{same for } \varphi_{N-1}\to\varphi_N} \cdot \underbrace{e^{-r(\varphi_N)(t_f - t_{N-1})}}_{\text{stay in } \varphi_N \text{ in } [t_{N-1}, t_f]}$$

The factors $r(\varphi_i)$ cancel out.

$$P(\{\varphi(t)\}) = P(\varphi_1) \times \prod_{i=1}^{N-1} W(\varphi_i \to \varphi_{i+1}) \times \prod_{i=1}^{N} e^{-r(\varphi_i)(t_i - t_{i-1})} \quad \text{with } t_N \equiv t_f$$

Detailed balance $P(\varphi_i)\, W(\varphi_i\to\varphi_{i+1}) = W(\varphi_{i+1}\to\varphi_i)\, P(\varphi_{i+1})$

$$\underbrace{P(\varphi_1)\, W(\varphi_1\to\varphi_2)}_{W(\varphi_2\to\varphi_1)\,\underbrace{P(\varphi_2)\, W(\varphi_2\to\varphi_3)}_{W(\varphi_3\to 2)\, P(\varphi_3)}}\; W(\varphi_2\to\varphi_3) \dots W(\varphi_{N-1}\to\varphi_N)$$

$$\cdots\quad W(\varphi_N\to\varphi_{N-1})\, P(\varphi_N)$$

$$\Rightarrow \underbrace{P(\varphi_1)}_{\text{proba to start in } \varphi_1} \underbrace{\prod_i W(\varphi_i\to\varphi_{i+1})}_{\text{proba of forward transitions}} = \underbrace{\prod_i W(\varphi_{i+1}\to\varphi_i)}_{\text{Proba of backward transitions}} \underbrace{P(\varphi_N)}_{\text{proba to start in } \varphi_N}$$

$$\Rightarrow P(\{\varphi(t)\}) = P(\varphi_N) \times \prod_{i=1}^{N-1} W(\varphi_{i+1}\to\varphi_i) \times \prod_{i=1}^{N} e^{-\lambda(\varphi_i)(t_i-t_{i-1})} \qquad (*)$$

Reversed traj

(i) transitions $\quad \varphi_1^R = \varphi_N \,,\ \varphi_2^R = \varphi_{N-1} \ \dots,\ \varphi_N^R = \varphi_1$

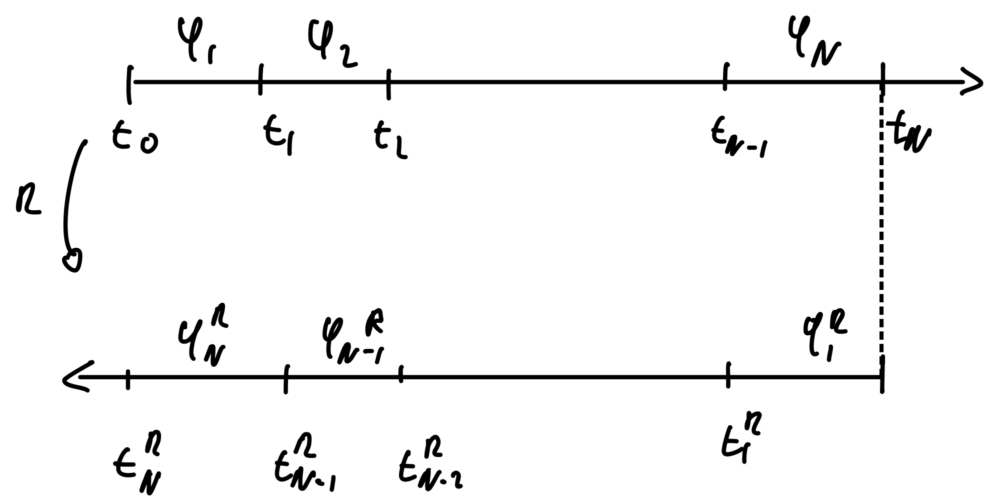
$$\Rightarrow \prod_{i=1}^{N-1} W(\varphi_{i+1}\to\varphi_i) = \prod_{i=1}^{N-1} W(\varphi_i^R \to \varphi_{i+1}^R)$$

(ii) waiting times

The waiting times are symmetric so we expect $\prod_i e^{-\lambda(\varphi_i)(t_i-t_{i-1})}$ to transform symmetrically into $\prod_i e^{-\lambda(\varphi_i^R)(t_i^R-t_{i-1}^R)}$

① $\lambda(\varphi_i) = \lambda(\varphi^R_{N-i+1})$

② $|t_i - t_{i-1}| = |t^R_{N-i} - t^R_{N-i+1}|$



$$e^{-\lambda(\varphi_i)(t_i-t_{i-1})}$$
$$\parallel$$
$$e^{-\lambda(\varphi_i)|t_i-t_{i-1}|}$$
$$\parallel$$
$$e^{-\lambda(\varphi^R_{N+1-i})|t^R_{N-i}-t^R_{N-i+1}|}$$
$$\parallel$$
$$e^{-\lambda(\varphi^R_{N+1-i})(t^R_{N+1-i}-t^R_{N-i})}$$

$$\Rightarrow \prod_i e^{-\lambda(\varphi_i)(t_i-t_{i-1})} = \prod_i e^{-\lambda(\varphi_i^R)(t_i^R-t_{i-1}^R)}$$

Thus (*) reads:

$$P(\{\varphi(t)\}) = P(\varphi_1^R)\cdot \prod_{i=1}^{N-1} W(\varphi_i^R\to\varphi_{i+1}^R) \times \prod_{i=1}^{N} e^{-\lambda(\varphi_i^R)(t_i^R-t_{i-1}^R)} = P(\{\varphi^R(t)\})$$

DB at the rates level thus imposes reversibility at the trajectory level!

Comments: If we sum over all possible trajectories between φ_1 & φ_N, we find

$$P_{ss}(\varphi_1, t_0)\, P(\varphi_N, t_f \mid \varphi_1, t_0) = P_{ss}(\varphi_N, t_f)\, P(\varphi_1, t_f \mid \varphi_N, 0)$$