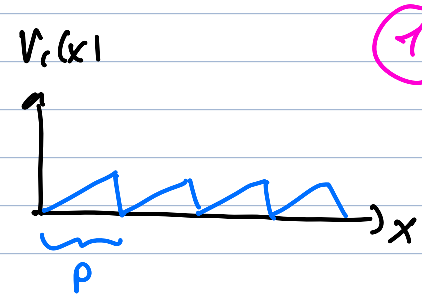
4.3) A simple example



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

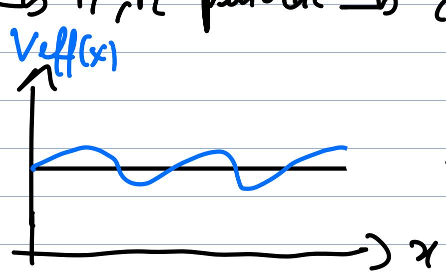
$\Rightarrow$ Brownian dynamics in an effective potential

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

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

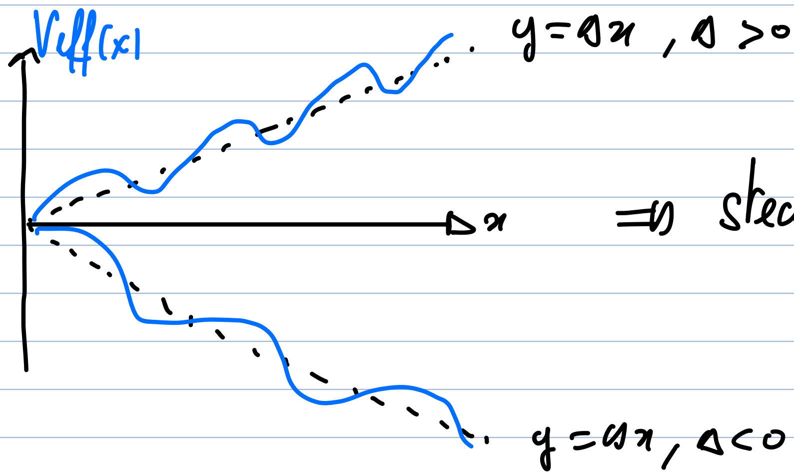
V_1, V_2 periodic $\Rightarrow P_1, P_2$ periodic $\Rightarrow \lambda(x)$ periodic

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

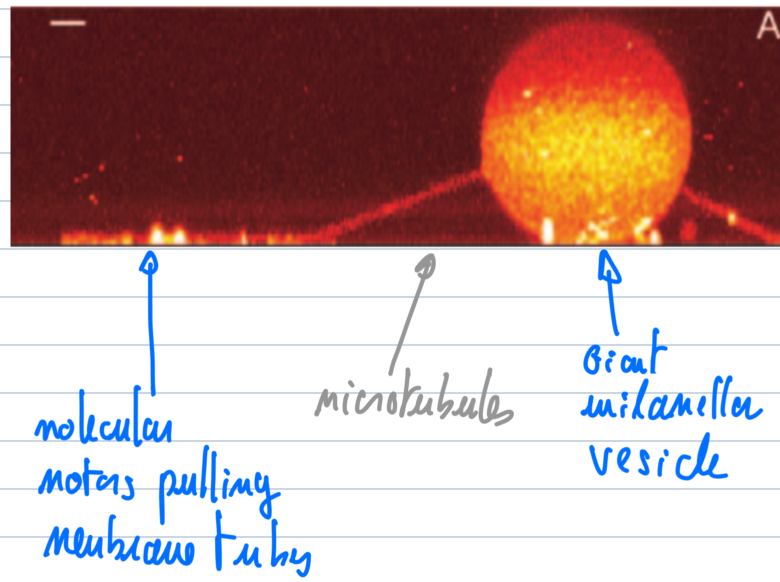
Comment: $\partial_t P_i = -H_{FP}^i P_i$ satisfies detailed balance with $P_s^i = \frac{1}{Z} e^{-\beta V_i}$

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

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.

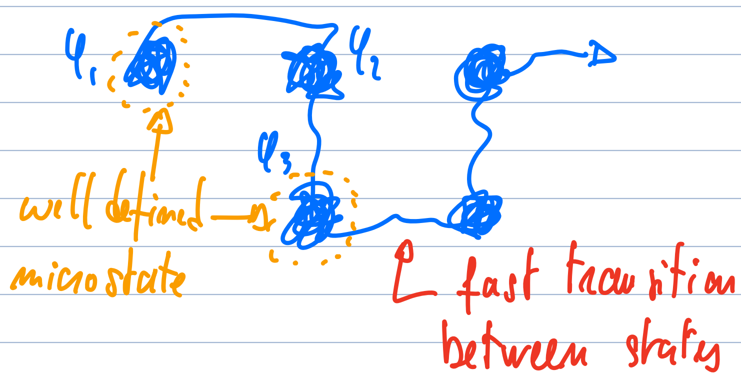


[Roux et al., PNAS 99, 5394 (2002)]

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:

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

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

Comments: . Beautiful idea

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

$$W(\varphi_h \to \varphi_i)\,dt \simeq \int_{\varphi_i} dx_i \; P(x_i, t+dt, x_h, t) \quad \text{for any } x_h \in C_h .$$

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

"Proof"

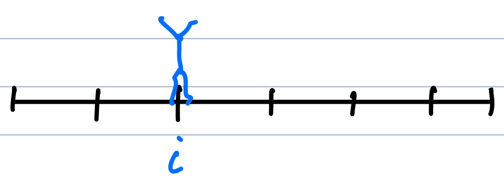
$$P(\varphi_i, t+dt ; \varphi_h, t) = W(\varphi_h \to \varphi_i)\,dt\; P(\varphi_h) ; \quad P(\varphi_h) = \int_{x_h \in \varphi_h} dx_h \; P(x_h)$$

$$\Rightarrow W(\varphi_h \to \varphi_i)\,dt = \int_{\varphi_i} dx_i \int_{\varphi_h} dx_h \; \frac{P(x_i, t+dt \mid x_h, t)\, P(x_h, t)}{P(\varphi_h)}$$

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

$$\Rightarrow W(\varphi_h \to \varphi_i)\,dt = \int_{\varphi_i} dx_i \; P(x_i, t+dt \mid x_h^0, t) \; \underbrace{\frac{\int dx_h \; P(x_h, t)}{P(\varphi_h)}}_{=1} \qquad \text{qed.}$$

Model:



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

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

Evolution of $P(\varphi,t)$

$$P(\varphi, t+dt) = P(\varphi,t) \times \text{Proba}\left(\text{stay in } \varphi \text{ in } [t,t+dt]\right)$$

$$+ \sum_{\varphi' \neq \varphi} P(\varphi',t) \times \text{Proba}\left(\text{go from } \varphi' \text{ to } \varphi \text{ in } [t,t+dt]\right)$$

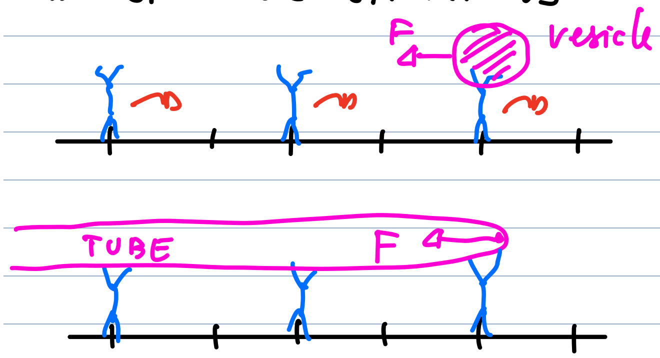
$$= P(\varphi,t) \times \underbrace{\Big(1 - \sum_{\varphi' \neq \varphi} W(\varphi \to \varphi')dt\Big)}_{1-\text{proba to leave}} + \sum_{\varphi' \neq \varphi} W(\varphi' \to \varphi)dt + \underbrace{O(dt^2)}_{\text{proba}(n>1 \text{ configuration changes})}$$

Master equation:

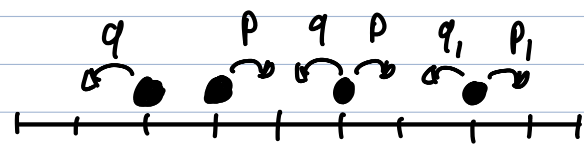
$$\partial_t P(\varphi) = \underbrace{\sum_{\varphi' \neq \varphi} W(\varphi' \to \varphi) P(\varphi',t)}_{\text{gain term due to incoming transition}} - \underbrace{\sum_{\varphi' \neq \varphi} W(\varphi \to \varphi') P(\varphi,t)}_{\text{loss due to outgoing transitions.}}$$

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

Two standard situations



Model:

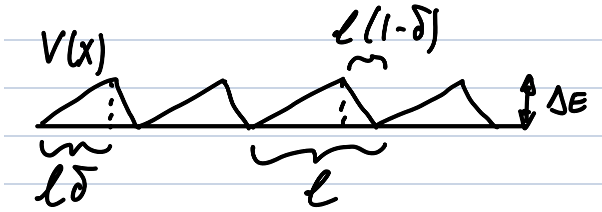


[Mac Donald, Gibbs, Dipkin, Biopolymers 6, 1-25, 1968] to model ribosomes along DNA.

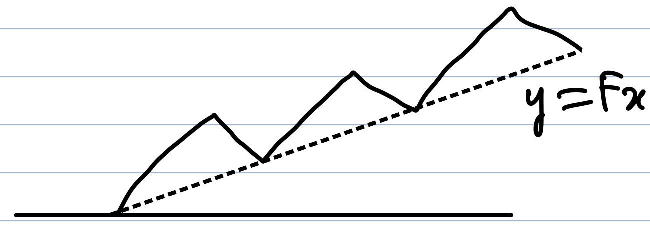
Particles hop at constant rates onto free sites.

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

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

Choose units such that $\beta F \ell = 1$

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 $W(\varphi' \to \varphi) \neq 0$ & $P(\varphi') \neq 0$

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

$$\partial_t P(j,t) = W(j-1 \to j)\, P(j-1) + W(j+1 \to j)\, P(j+1)$$
$$- [W(j \to j-1) + W(j \to j+1)]\, P(j)$$
$$= p_1 P(j-1) + q_1 P(j+1) - (p_1 + q_1) P(j)$$

$$\partial_t \langle j \rangle = \sum_j p_1\, j\, P(j-1) + q_1\, j\, P(j+1) - (p_1+q_1)\, j\, P(j)$$

$$\qquad\quad j=h+1 \qquad\qquad j=h-1 \qquad\qquad\qquad j=h$$

$$= \sum_h p_1 (h+1) P(h) + q_1 (h-1) P(h) - (p_1+q_1)\, h\, P(h)$$

$$= \sum_h (p_1-q_1) P(h) = (p_1-q_1) \sum_h P(h) = p_1 - q_1$$

$$\Rightarrow \langle j(t) \rangle = \langle j(0) \rangle + (p_1-q_1)\, t \Rightarrow \boxed{v_{1M} = p_1 - q_1}$$

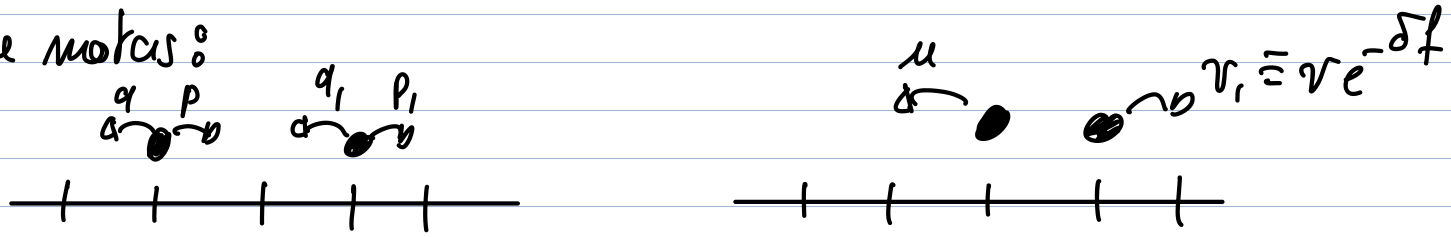
Stall force: Force f such that $v_{1M}(F) = 0$

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

$$\Leftrightarrow \boxed{f_s^{1M} = \ln \frac{p}{q}}$$

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

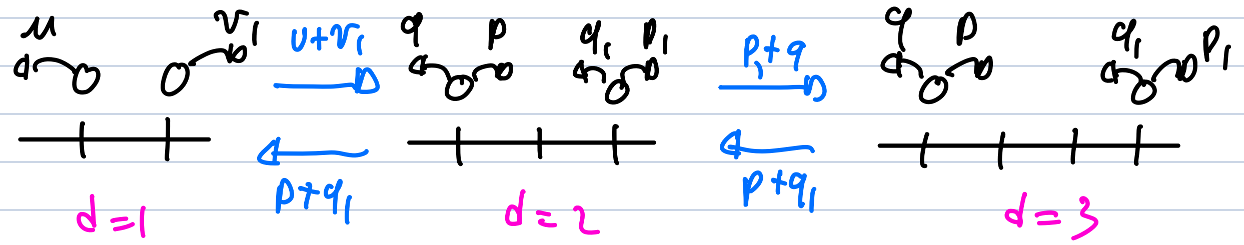
(otherwise, non reciprocal interactions)

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.

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

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

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

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

(i) if $r > 1$, the steady state is not normalizable

$\Leftrightarrow p_1 + q > p + q_1$, the motors move away from eachother on average

(ii) if $r < 1$, $\displaystyle 1 + r_1 \sum_k r^k = 1 + \frac{r_1}{1-r} = \frac{1+r_1-r}{1-r}$

$$\Rightarrow P_d(1) = \frac{1-r}{1-r+r_1} \quad \& \quad P_d(k \geq 2) = \frac{r_1(1-r)}{1-r+r_1} r^{k-2}$$

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

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

Mean speed of the first motor

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

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

$$= (p_1-q_1)\frac{r_1}{1-n+r_1} + v_1 \frac{1-n}{1-n+r_1} = \frac{(p_1-q_1)(u+v_1) + v_1(p+q_1-p_1-q)}{p+q_1-p_1-q+u+v_1}$$

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

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

$$u e^{-\delta f}(p-qe^{f}) + v e^{-\delta f}(p-q) = 0$$

$$\Leftrightarrow \quad u q e^{f} = up + vp - vq$$

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

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?

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

$$\mathrm{Sign}(v_{2M}-v_{1M}) = \mathrm{Sign}\left[v_1(p-q) - (p_1-q_1)(p+q_1-p_1-q) - v_1(p_1-q_1)\right]$$

$$= \mathrm{Sign}\left[(v_1-(p_1-q_1))(\underbrace{p-p_1}_{\geq 0}+\underbrace{q_1-q}_{\geq 0})\right]$$

$$= \mathrm{Sign}\left[v-p+qe^{f}\right]$$

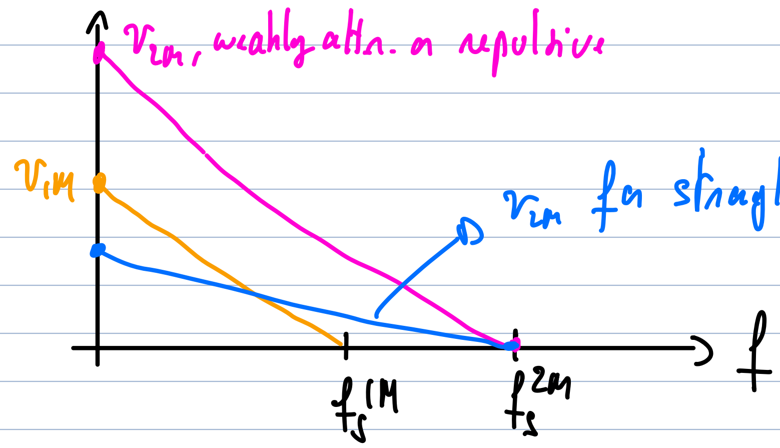
* if $f > f_s^{2M}$, $v_{2M} = v_{1M} = 0$
* if $f_s^{2M} > f > f_s^{1M}$, $v_{2M} > 0 = v_{1M}$
* if $f_s^{1M} > f$, then $v_{2M} > v_{1M} \Leftrightarrow v > p - qe^{f} \underset{f=0}{\simeq} p-q$

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

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

$\Rightarrow$ Quite rich physics

sketch



N body: [O. Campas, Y. Kafri, K. B. Zeldovich, J. Casademunt, J.-F. Joanny, Phys. Rev. Lett. 97, 038101 (2006)]