Diffusion mediated transport: can we understand motion in small systems

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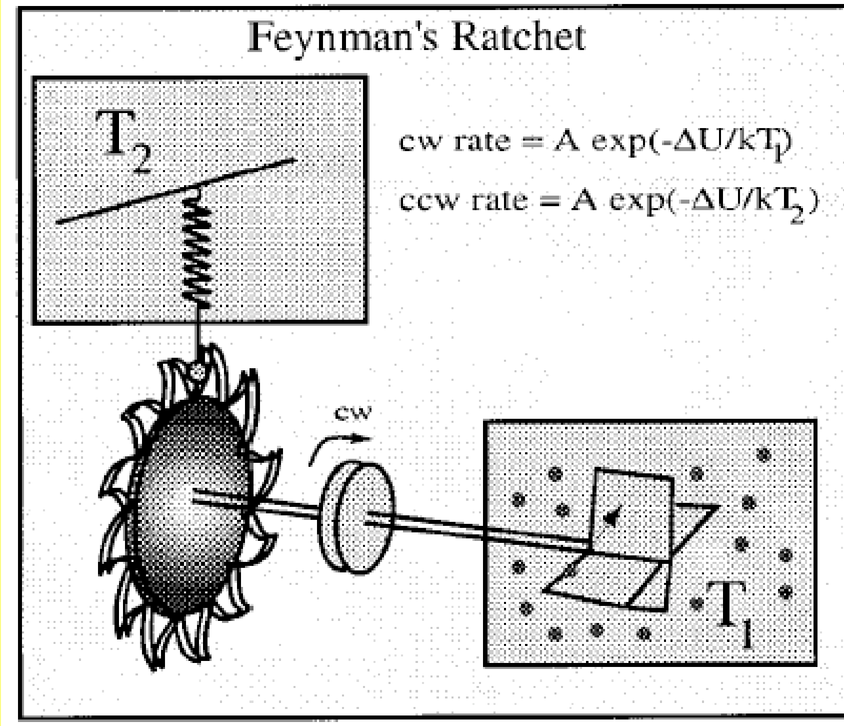
overview: diffusion mediated transport

Feynman 1966 (room at the bottom)
discussed possibility of a rachet and pawl device powered by fluctuations
concluded that it was impossible



in the meantime

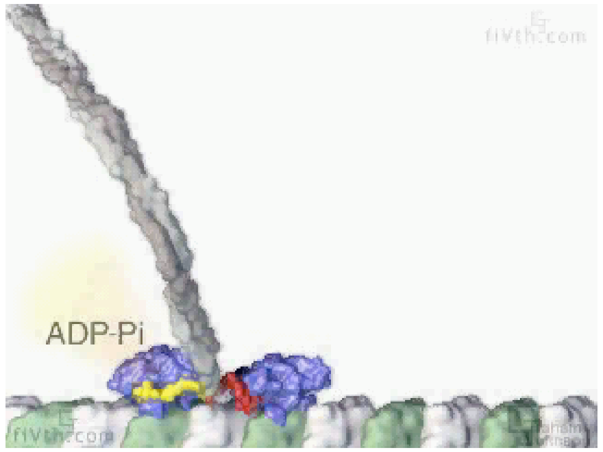
Huxley 1957 offered an extensive analysis for myosin as a motor responsible for muscle activity
myosin isolated from muscle ~ 1860

Vale et al. 1986 proposed kinesin molecular motors responsible for intracellular transport (and analogues in all eukarya!)
energetics: ATP → ADP + Pi hydrolysis reaction

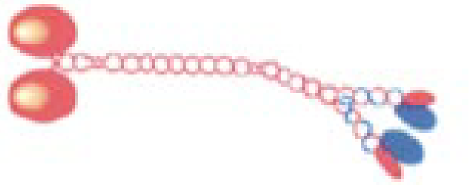
Also suggested as mechanism for
electron tunneling, lipid bilayers,
charged particles moving over interdigitated electrodes …
some surprises

some references
Doering, Ermentrout, Oster, Peskin
Astumian
Adjari, Prost, Jülicher, Parmeggiani
Palffy-Muhoray, Kosa, & E

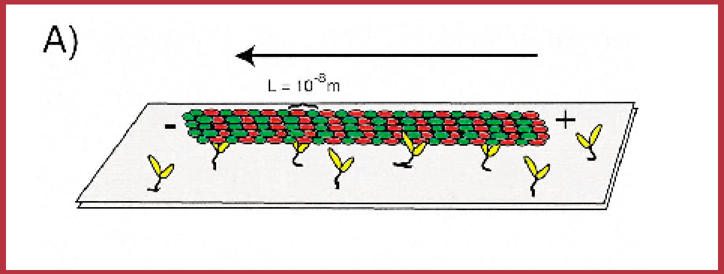
K & Kowalczyk
Heath, K, & Kowalczyk
Chipot, K, & Kowalczyk

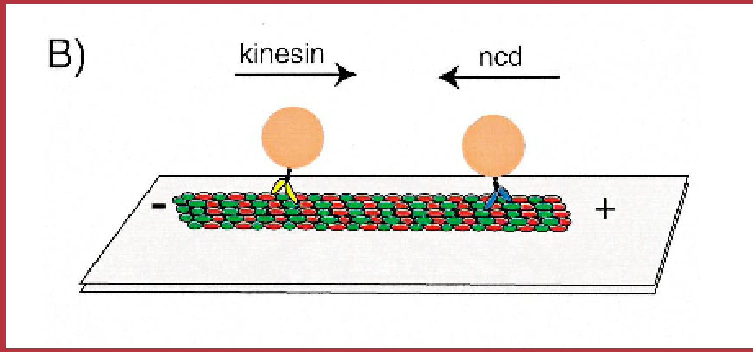


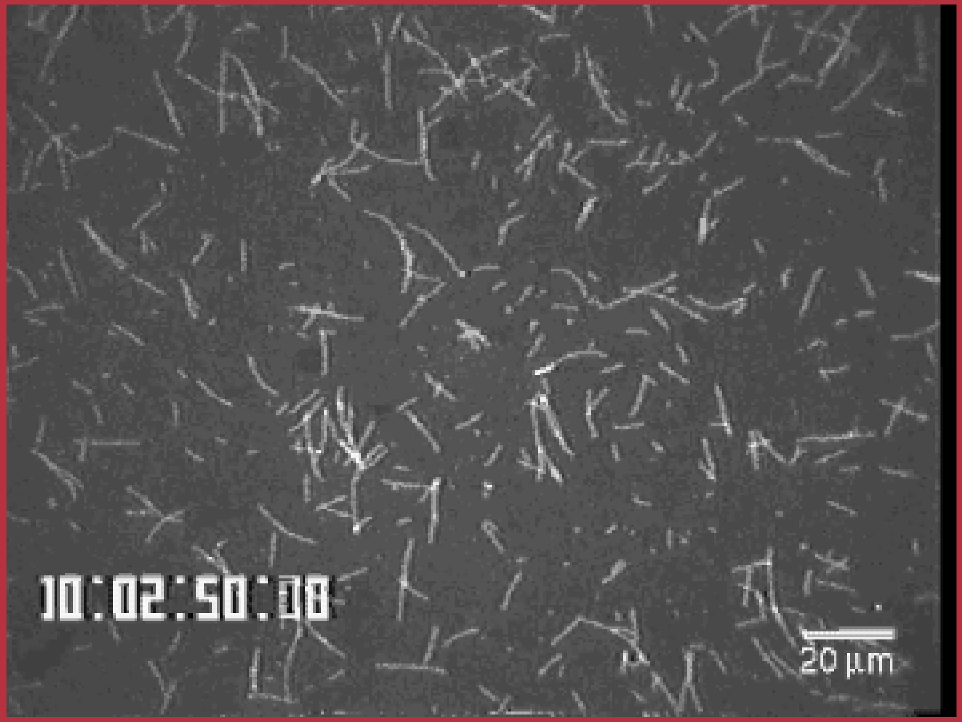
http://www.sciencemag.org
/feature/data/1049155s1.mov
Vale and Milligan



basic notion: equilibirum fluctuations do no work
nonequilibrium fluctuations can be 'oriented' to alter the state of the system,
for example, to exhibit transport







courtesy of Y. Hiratsuka

one of the groups attempting to engineer motors

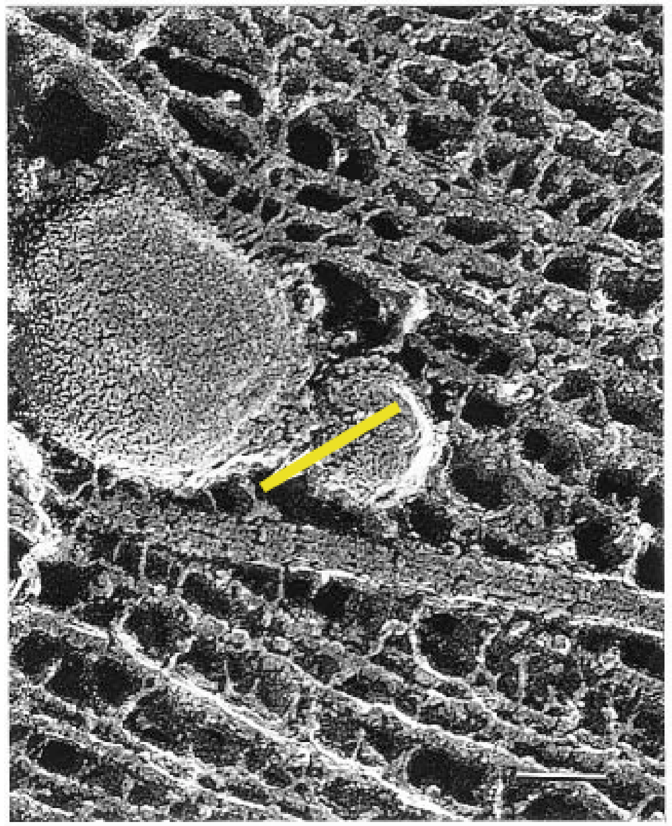
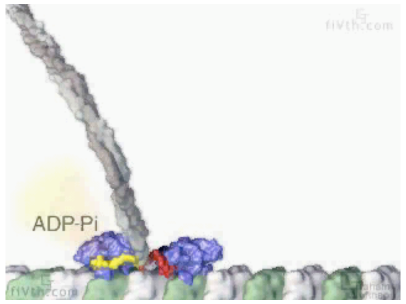


Fig. 1. Quick freeze–deep etch electron micrograph of mouse axon. A membranous organelle conveyed by fast transport is linked with a microtubule by a short cross-bridge (arrow), which could be a motor molecule. Scale bar, 50 nm.

Hirokawa, Science, 1998

energy transduction

- suggested mechanisms involve complicated chemistry and conformational changes scale where chemistry and mechanics coupled
- main interest: transduction mechanisms shape memory & magnetostriction began with J.L. Ericksen & R. James cf. Ball & James, Fonseca, Chipot & K



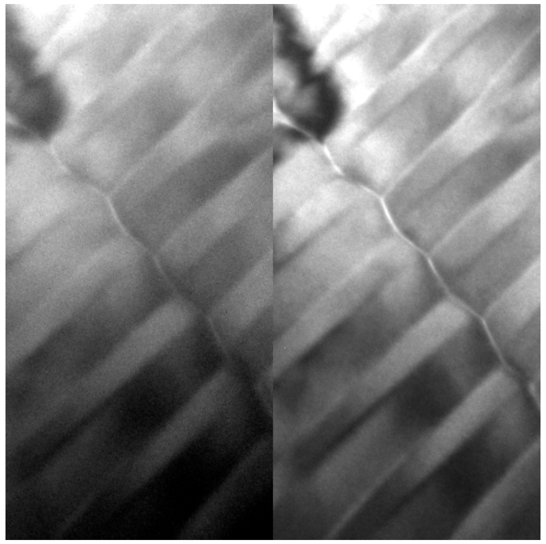
operation of a kinesin motor by ATP hydrolysis

$$\mathrm{ATP} \rightarrow \mathrm{ADP} + \mathrm{Pi}$$

shape memory NiTi
thermal/mechanical

ferromagnetic shape memory
$TbDyFe_2$
(giant magnetostrictive)
electromagnetic/mechanical

this configuration was predicted by our theory and first seen by Dooley & deGraef



Dooley & deGraef

significant differences

- design criteria for new active materials require minimum power consumption: transformation path as near equilibrium as possible

- biological systems like motors are very far from equilibrium

- minimum energy ... absolute
  metastable
  nonequilibrium .... how to assess?

  "all stable systems are alike; each metastable system loses stability in its own way" Tolstoy

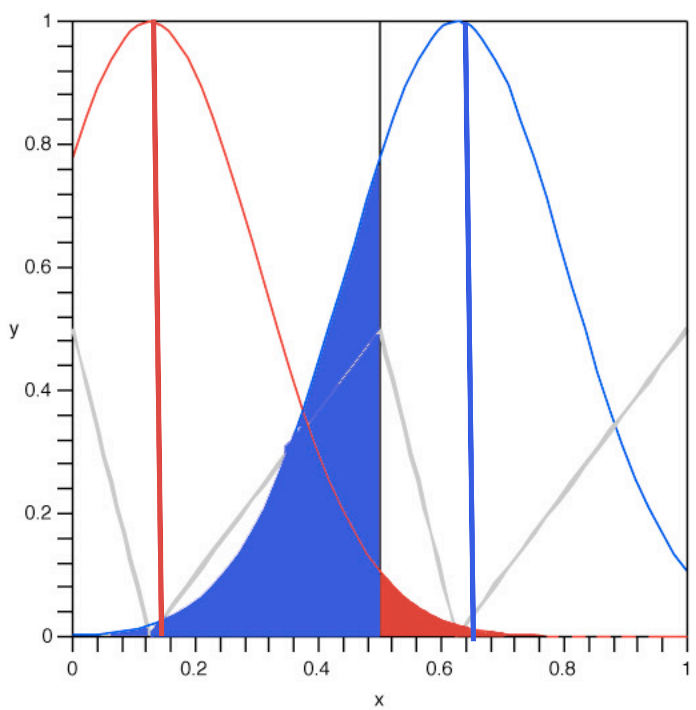
CuAlNi shape memory mosaic of lamellar twins is close to equilibrium. (Chu & James)

today's outline

- motion at small scales and Monge-Kantorovich problem
- flashing rachet
- dissipation and Wasserstein
- multiple state motors
- game time

- # Flashing rachet
  Astumian

diffusion interchanged with transport in anisotropic potential



Dirac masses of same height located asymmetrically in period basin

- diffusion spreads mass
- transport collects mass to special sites
- each process taken separately does not move density
- asymmetric drift is a key for transport
- not the whole story

$$\frac{\partial \rho}{\partial t} = \sigma \frac{\partial^2 \rho}{\partial x^2} + \frac{\partial}{\partial x}(\psi' \rho) \quad in\ \Omega, 0 < t \leq T_{tr},$$

$$\sigma \frac{\partial}{\partial x}\rho + \psi' \rho = 0 \quad on\ \partial\Omega, 0 < t \leq T_{tr}$$

$$\frac{\partial \rho}{\partial t} = \sigma \frac{\partial^2 \rho}{\partial x^2} \quad in\ \Omega, T_{tr} < t \leq T = T_{diff} + T_{tr},$$

$$\sigma \frac{\partial}{\partial x}\rho = 0 \quad on\ \partial\Omega, T_{tr} < t \leq T$$

Flashing rachet

$$\frac{\partial \rho}{\partial t} = \sigma \frac{\partial^2 \rho}{\partial x^2} + f(t) \frac{\partial}{\partial x} (\psi' \rho) \quad in \quad \Omega, t > 0,$$

$$\sigma \frac{\partial}{\partial x} \rho + f(t) \psi' \rho = 0 \quad on \ \partial\Omega, t > 0$$

$$f(t) = \begin{matrix} 1 & 0 \le t \le T_{tr} \\ 0 & T_{tr} \le t \le T_{diff} + T_{tr} = T \end{matrix}$$

study (unique) periodic solution

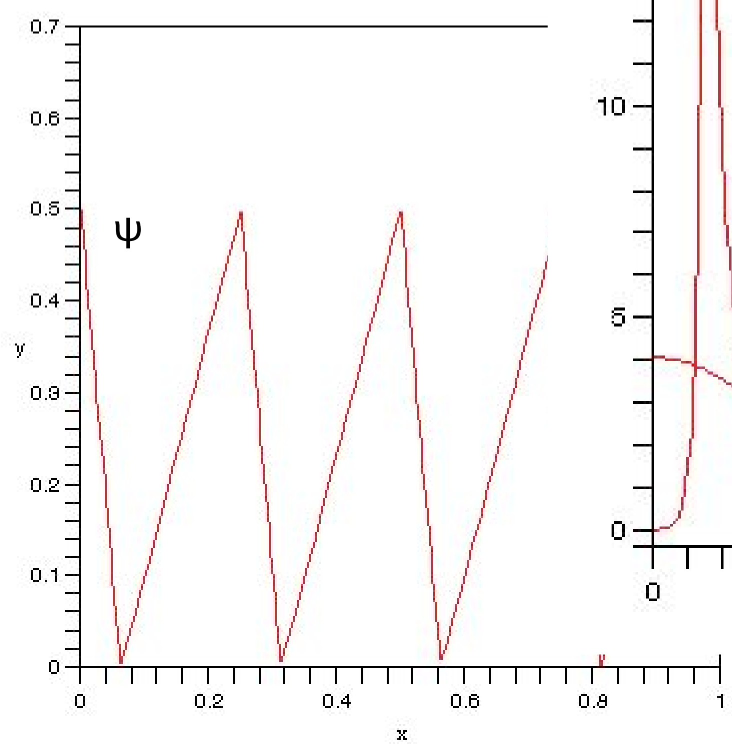
use the transport/diffusion to construct a Markov chain paradigm

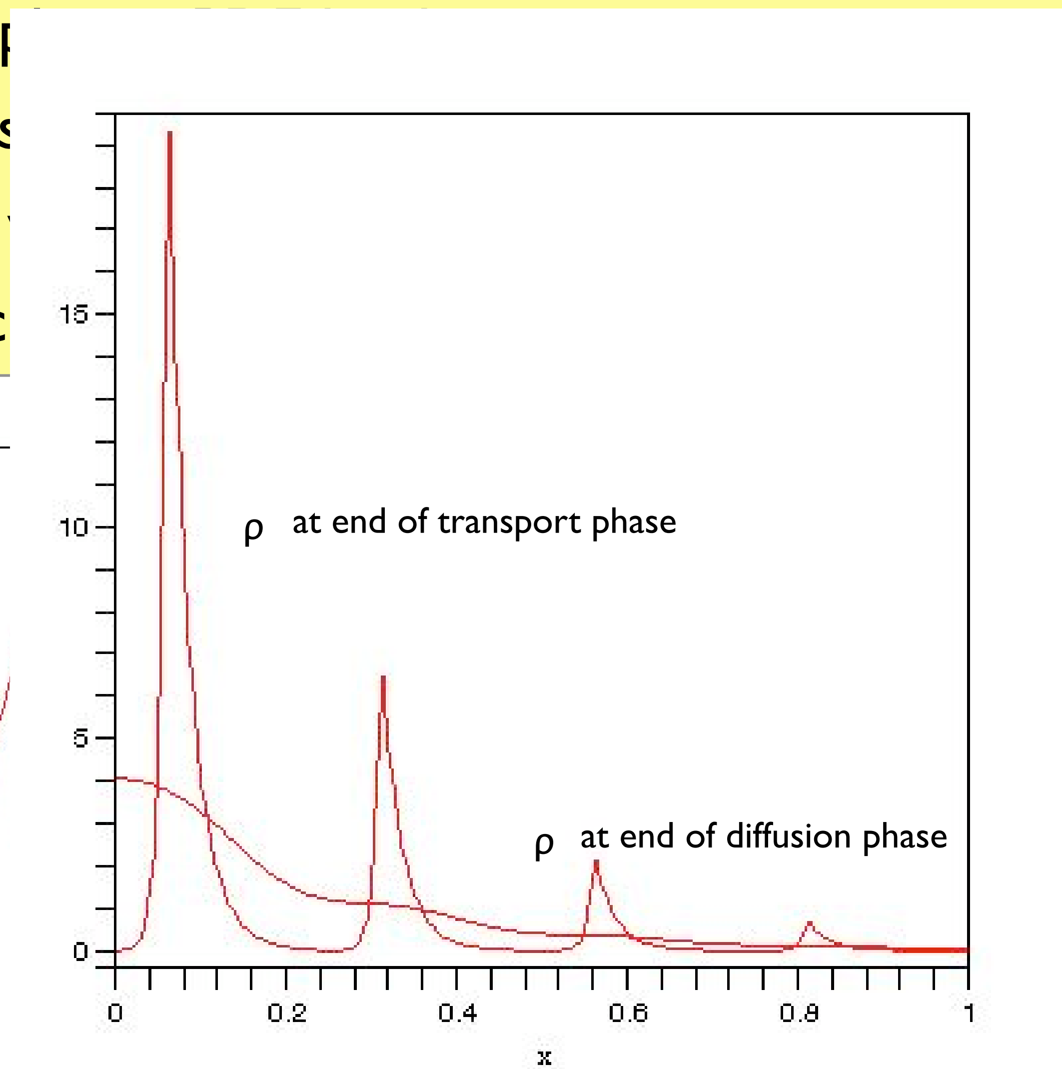
rep

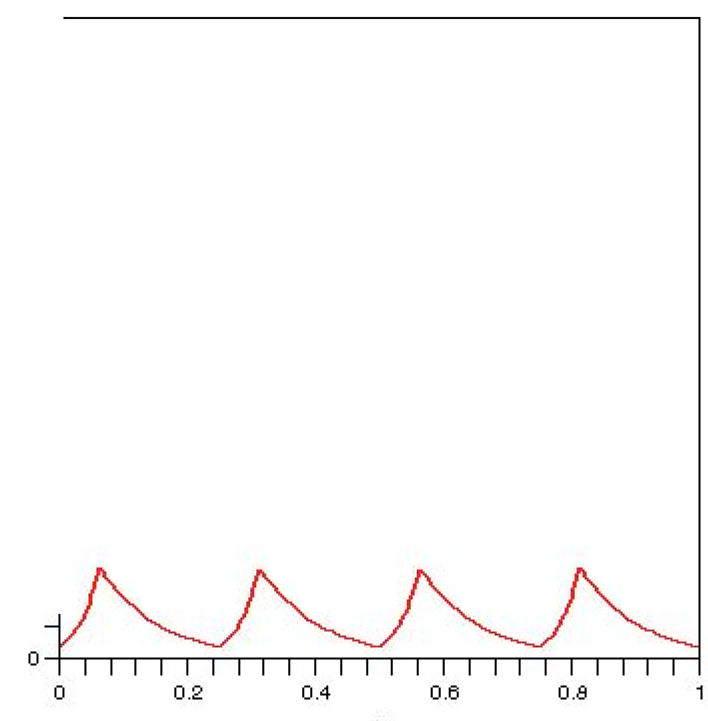
periodic s tor of the Markov chain

in

Markov c







there is a unique periodic solution $\rho^\sharp$ for each T_{tr}, T_{diff}

it is stable: if ρ is any solution of the Flashing Rachet problem then

$$\int_\Omega |\rho - \rho^\sharp| dx \leq C\ e^{-ct} \quad \text{or} \quad d(\rho, \rho^\sharp) \leq C\ e^{-ct}$$

Csizar-Kullback Talagrand

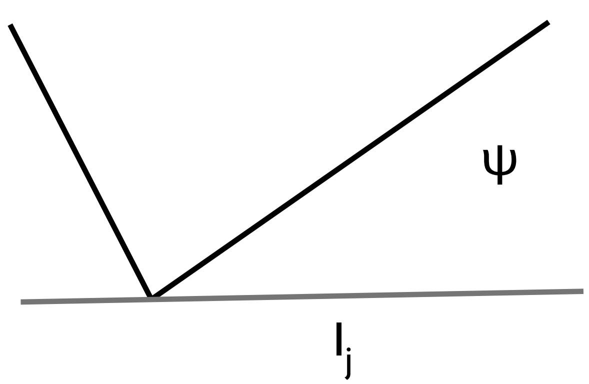
because

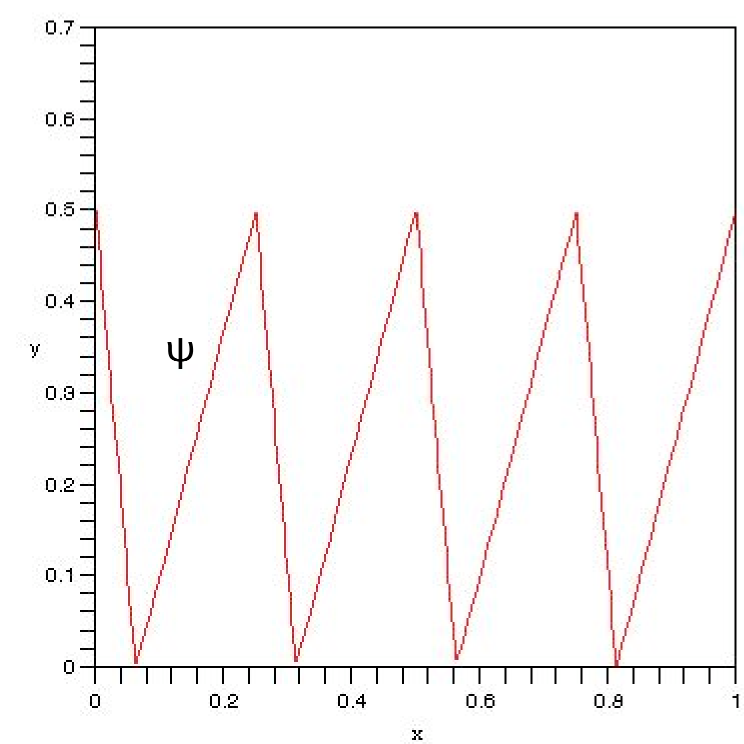
for ρ_1, ρ_2 solutions of (the same) Fokker-Planck Equation

$$\int_\Omega \rho_1\ log \frac{\rho_1}{\rho_2} dx \leq C\ e^{-ct}$$

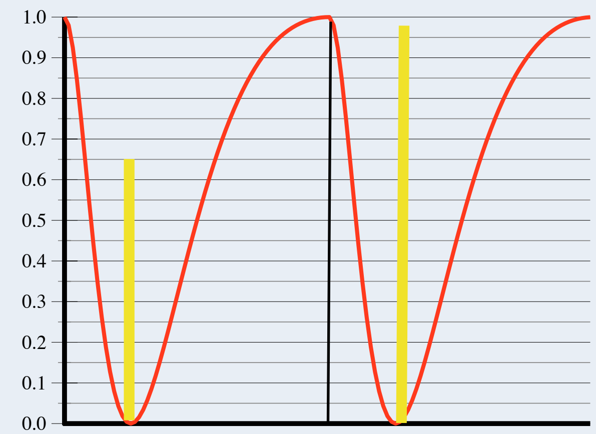
from log-Sobolev inequality

suppose ψ periodic with period intervals I_j, j = 1…n





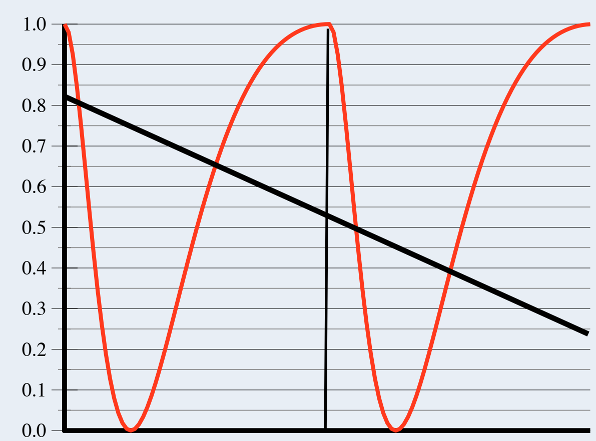
Markov Chain Paradigm for the Flashing Rachet



begin with density at Dirac masses

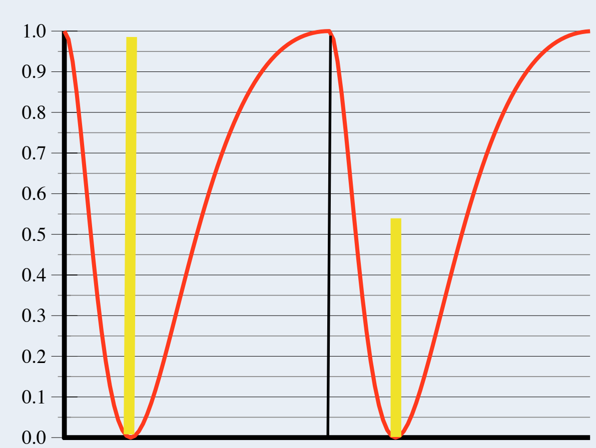
$$\mu^* = \mu_1^* \delta_{a_1} + \mu_2^* \delta_{a_2}$$

Compare Markov chain
on Dirac masses
(measures)
with density:
use Wasserstein metric



density diffuses for t = T_{diff}

$$w_t = \sigma w_{xx} \ in \ \Omega, \ t > 0$$
$$w_x = 0 \ on \ \partial\Omega, \ t > 0$$
$$w|_{t=0} = \mu^* \ in \ \Omega$$



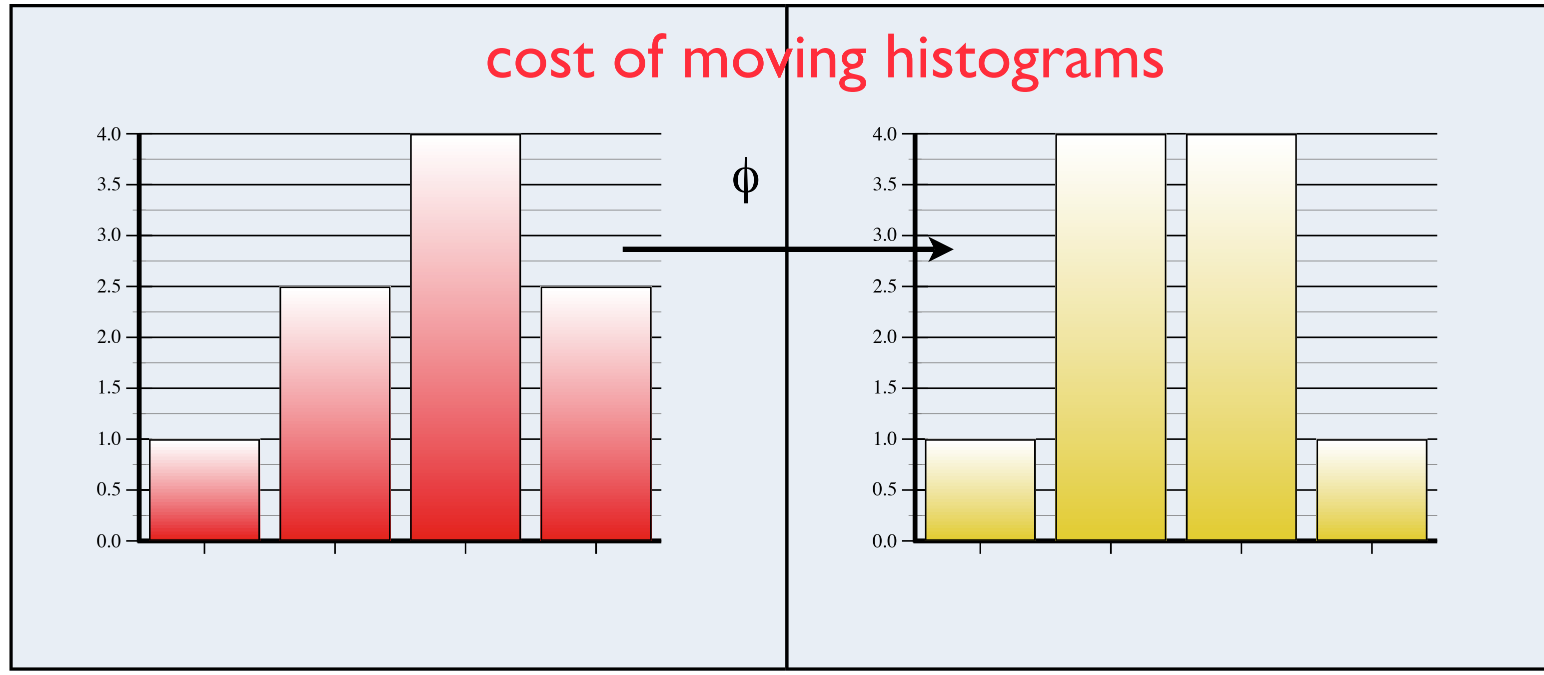
accumulate density at Dirac masses

$$\mu = \mu_1 \delta_{a_1} + \mu_2 \delta_{a_2}$$

this is a Markov chain:

$$\mu = \mu^* P$$

Monge-Kantorovich Problem
Wasserstein Metric



f, f^* probability densities on Ω

$$
\begin{aligned}
d(f, f^*)^2 &= \min \int_{\Omega \times \Omega} |x-y|^2 dp(x,y) \\
&= \int_{\Omega} |x - \phi(x)|^2 \, f^*(x) dx
\end{aligned}
$$

transfer function

$$\int_{\Omega} \zeta(y) f(y) dy = \int_{\Omega} \zeta(\phi(x)) f^*(x) dx$$

p joint distribution with marginals f, f^*
ϕ Monge Kantorovich transfer function

Wasserstein metric induces weak* topology on measures
ϕ is solution of Monge-Ampère Eq.

Extensive current literature
recent books and notes
Villani, Rachev ; Ambrosio, Evans

Remarks

many paths f(x,t), 0 ≤ t ≤ τ, from f*(x) to f(x) Eulerian
or ϕ(x,t), 0 ≤ t ≤ τ, (transfer functions) Langrangian

$$\int_\Omega \zeta(y) f(y,t) dy = \int_\Omega \zeta(\phi(x,t)) f^*(x) dx$$

$$v(y,t) = \phi_t(x,t)$$

$$\Longrightarrow \quad \frac{1}{2\tau} d(f, f^*)^2 \leqq \frac{1}{2} \int_0^\tau \int_\Omega v^2 f dx dt$$

$$\frac{1}{2\tau} d(f, f^*)^2 = \frac{1}{2} \int_0^\tau \int_\Omega v^2 f dx dt$$

$f_t + (vf)_x = 0$ continuity equation

$v_t + v v_x = 0$ optimality condition (Burgers)

Brenier & Benamou

$g(x,t,a)$ Green's function with pole at a for Neuman Problem:

$$\begin{aligned} g_t &= \sigma g_{xx} \; in \; \Omega, \; t>0 \\ g_x &= 0 \; on \; \partial\Omega, \; t>0 \\ g &= \delta_a \; in \; \Omega, \; t=0 \end{aligned}$$

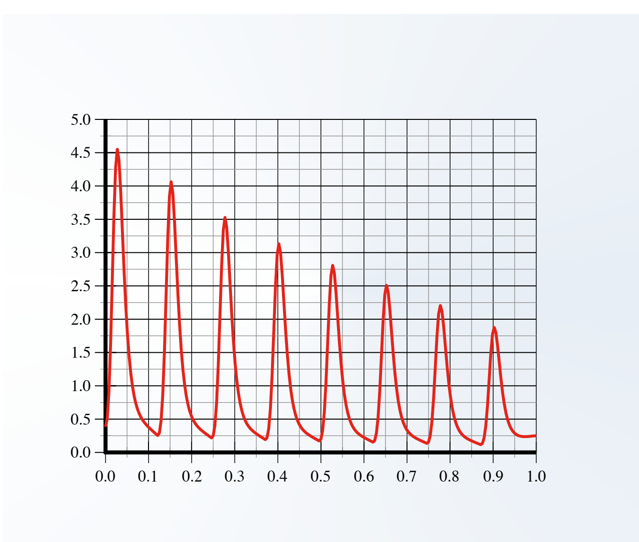
$$w(x,t) = \sum \mu_i^* g(x,t,a_i)$$

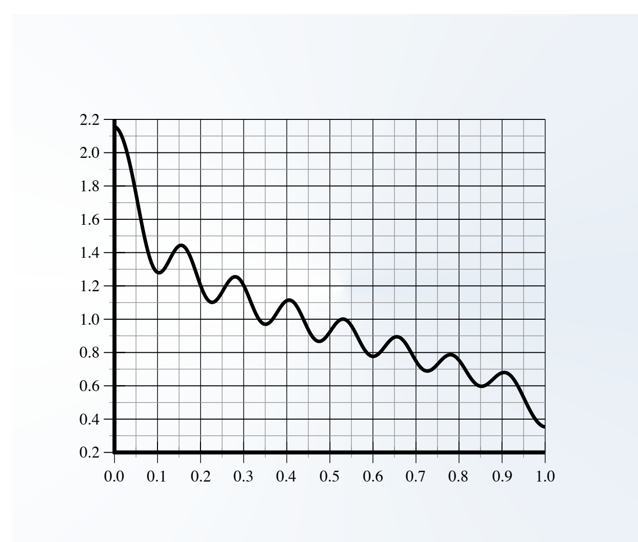
$$\mu_i^* = \int_{I_i} \rho_i^\sharp(x,0)dx$$

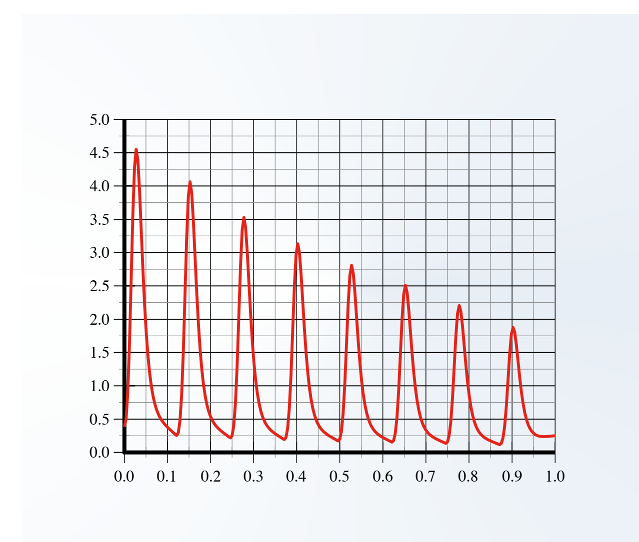
$$\mu_j = \int_{I_j} \sum \mu_i^* g(x, T_{diff}, a_i)dx \qquad P_{ij} = \int_{I_j} g(x, T_{diff}, a_i)dx$$

$\mu = \mu^* P$ $\Rightarrow$ Markov chain is ergodic has unique stationary state $\mu^\sharp$ $\qquad \rho = \rho^\sharp$

follow a period







$\rho(x, T_{tr})$

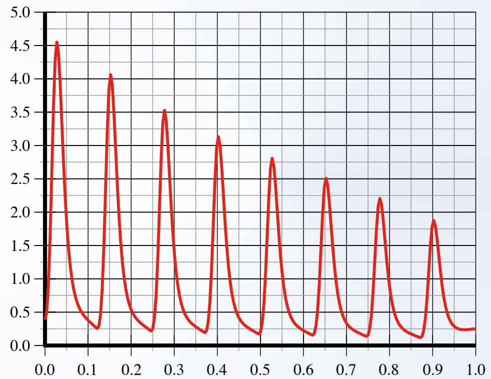
μ^*

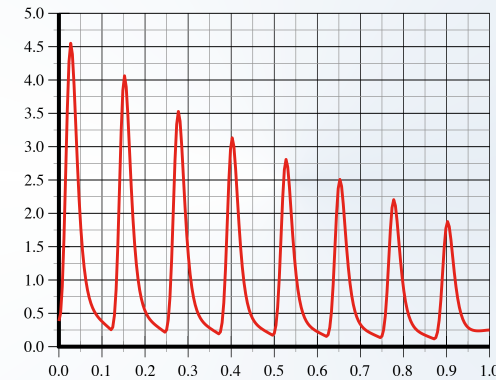
$\rho(x, T_{diff} + T_{tr}) = \rho(x, T)$

$w(x, T_{diff})$

$\rho(x, T)$

$\mu = \mu^* P$





$$\rho(x, T_{tr})$$
$$\mu^*$$

$$\rho(x, T_{diff} + T_{tr}) = \rho(x, T)$$
$$w(x, T_{diff})$$

$$\rho(x, T)$$
$$\mu = \mu^* P$$

$$d(\rho|_{T_{tr}}, \mu^*) \leq \epsilon$$

$$d(\rho|_T, w|_{T_{diff}}) \leq \epsilon$$

$$d(\rho|_T, \mu) \leq \epsilon$$

transport phase
most difficult estimate

log-Sobolev + Talagrand or analogous:
d of two solutions of diffusion equation decreases exponentially

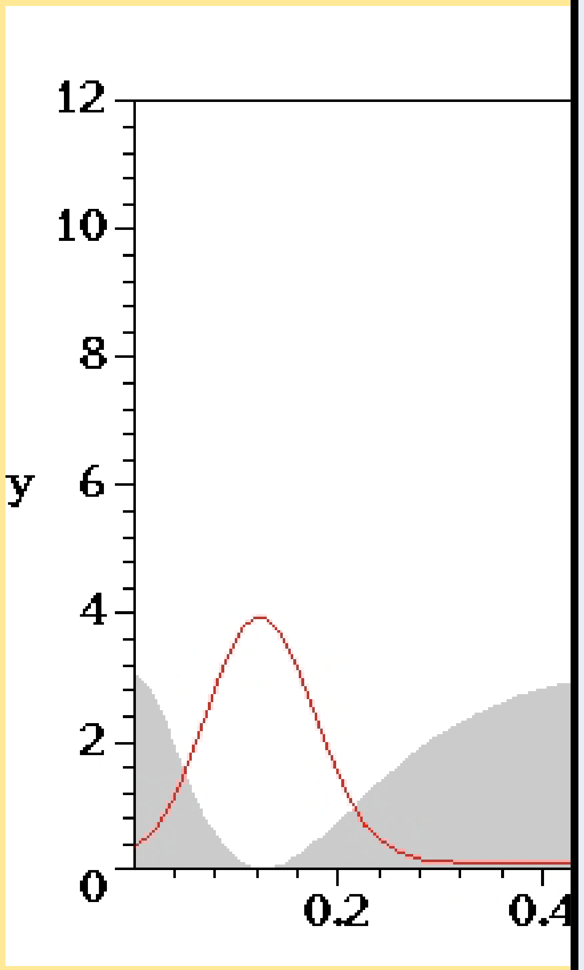
estimate
know how to work with Wasserstein metric

$$d(\mu^*, \mu^* P)^2 \leq 2\epsilon$$

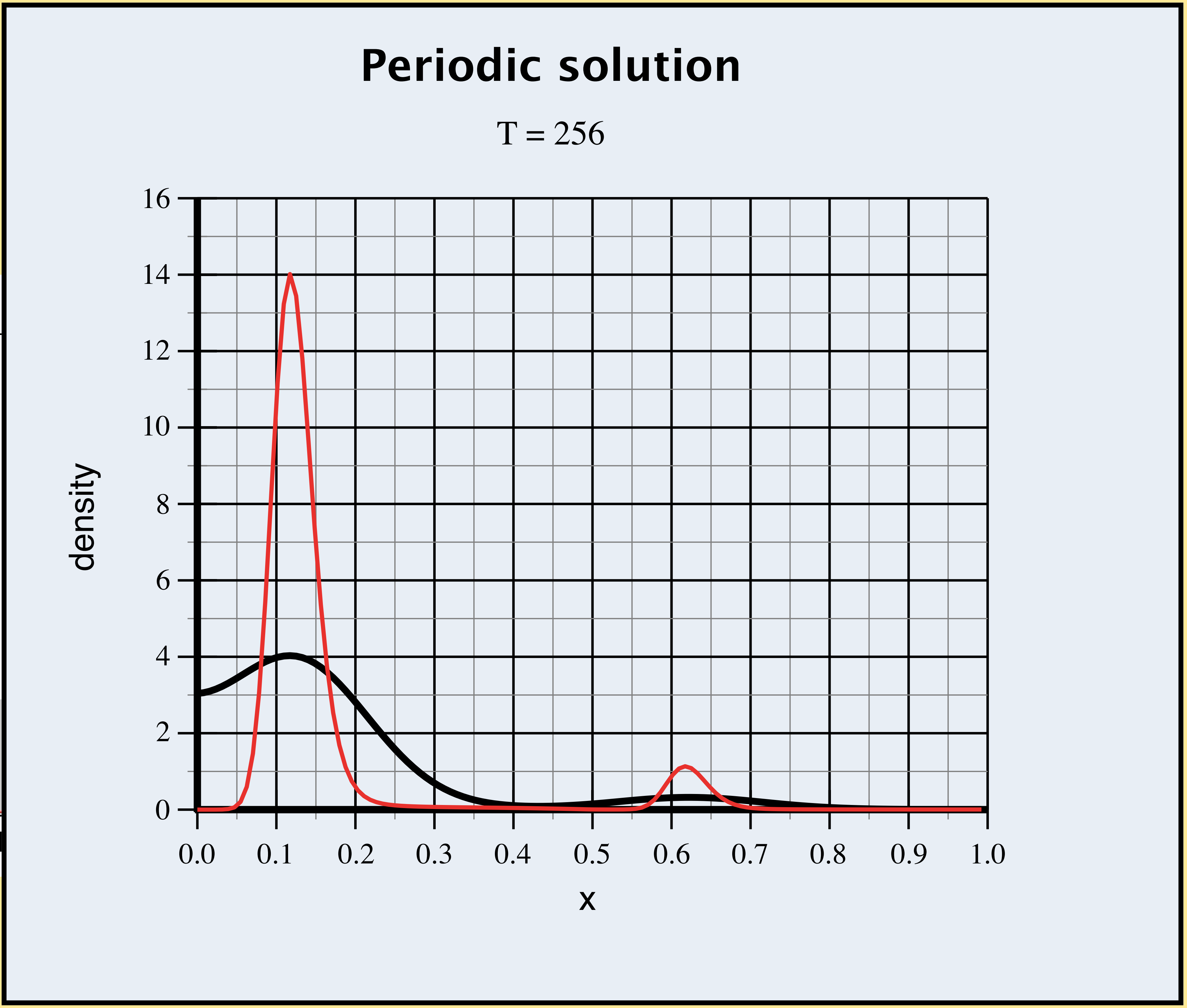
iterates of a Markov chain close
can only happen if they are close to the stationary state and then ρ is too.

$$d(\rho, \mu^\sharp)^2 \leq 4\epsilon$$

investigate properties of $\mu^\sharp, \quad P$



y
0
2
4
6
8
10
12
0.2
0.4

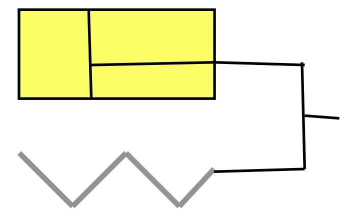


Periodic solution
T = 256
density
x
0
2
4
6
8
10
12
14
16
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0

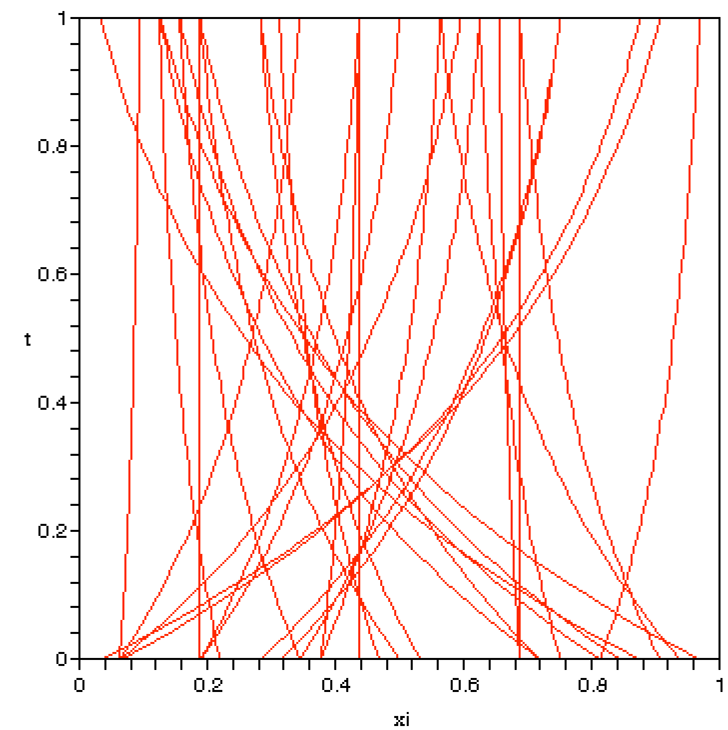
Dissipation and Wasserstein

ensemble of small bodies (large proteins)
motion in a highly viscous environment

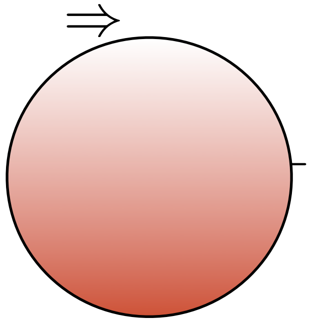
spring-mass-dashpot



$$m\frac{d^2\xi}{dt} + \gamma\frac{d\xi}{dt} + \psi'(\xi) = 0$$
$$\xi(0) = x$$
$$\xi'(0) = 0$$



$\Rightarrow$



$$-\gamma\int_0^\tau (\frac{d\xi}{dt})^2 dt + \psi(\xi(\tau)) - \psi(x) = 0$$

kinetic energy

dissipation

Re $_{\text{large yacht}}$ = 10^6

Re $_{\text{auto}}$ = 10^7

Re $_{\text{kinesin}}$ = 0.05

$$Re = \frac{\rho L v}{\eta}$$

distribute over Ω = (0,1) with density f*

$$\gamma\int_0^\tau\int_\Omega(\frac{d\xi}{dt})^2 f^* dx dt + \int_\Omega \big(\psi(\xi(\tau,x))f^* + \sigma\ f^*\log f^*\big)dx$$

$$\xi(t,x) = \phi(x,t)\ \ f(y,t)$$

$$\frac{d\xi}{dt} = \phi_t(x,t) = v(y,t)$$

we know what this is:
minimum value is Wasserstein metric

$$\gamma\int_0^\tau\int_\Omega v^2 f dy dt + \int_\Omega \big(\psi f + \sigma\ f\log f\big)dy$$

ensemble starts at f^*
assumes new configuration f

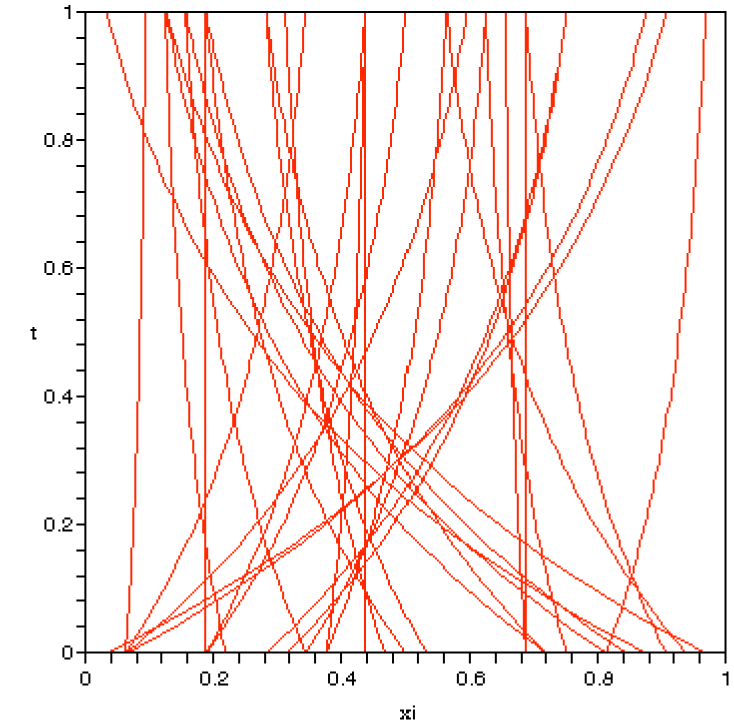
$$\frac{1}{2\tau}d(f,f^*)^2 + \int_\Omega \big(\psi f + \sigma\ f\log f\big)dx = \min$$

Can now evolve through many relaxation times τ

given f_{k-1} determine f_k from the variational principle with $f^* = f_{k-1}, f = f_k$

$$f^{(\tau)}(x,t) = f_k(x), (k-1)\tau < t \le k\tau$$

$lim_{\tau \to 0} f^{(\tau)}(x,t) = ?$



$$f^{(\tau)} \to f \quad where$$

$$\frac{\partial f}{\partial t} = \sigma \frac{\partial^2 f}{\partial x^2} + \frac{\partial}{\partial x}(\psi' f) \quad in\ \Omega, \quad t > 0,$$

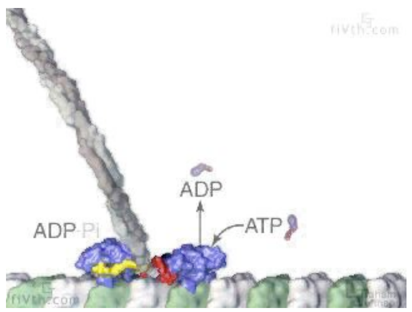
$$\sigma \frac{\partial}{\partial x} f + \psi' f = 0 \quad on\ \partial\Omega, \quad t > 0$$

Fokker-Planck

Otto, Jordan,K,Otto
many authors
Agueh, Petrelli, Tudorascu

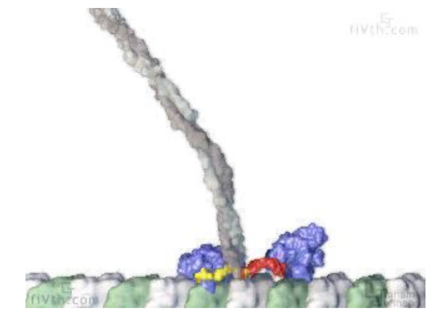
multiple state motors: a look at conventional kinesin

cartoon of conformational change and response to potential



leading head binds
undergoes conformational change

trailing head swings
forward



new leading head binds

sort heads:

type 1 bind at even labled sites ρ_1 density $-\nu_1 \quad \nu_2$ rates

type 2 bind at odd labled sites ρ_2 density $\nu_1 \quad -\nu_2$ rates

$$P = \mathbf{1} + \tau \begin{pmatrix} -\nu_1 & \nu_2 \\ \nu_1 & -\nu_2 \end{pmatrix}$$

$$\rho^* \rightarrow \rho^* P \qquad \rho^* P \rightarrow \rho \qquad \nu_1 > 0, \nu_2 > 0$$

note that P is a probability matrix

apply ideas of dissipation to obtain a variational principle

$$\sum_{i=1}^{2} \frac{1}{2\tau} d(\rho_i, (\rho^* \ P)_i)^2 + \sum_{i=1}^{2} \int_\Omega (\psi_i \ \rho_i + \sigma \ \rho_i \ log \ \rho_i) dx = min$$

$$\int_\Omega \rho_i \ dx = \int_\Omega (\rho^* \ P)_i \ dx$$

variational principle

variational principle/dissipation principle

- separates free energy, dissipation, and conformational change
- determines an implicit scheme
- always has a solution: functional is superlinear

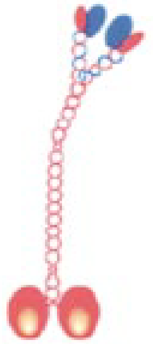
Oster, Mogilner
Elston

more detailed modeling from very different viewpoint

Analysis: embark on known path for existence (Jordan, K, Otto & Otto & others)

is the dissipation principle powerful enough to solve our problem?
are Monge-Kantorovich transport methods sufficiently well developed?

- existence & uniqueness
- existence & uniqueness of stationary solution
- trend to equilibrium
- character of stationary solution



system of evolution equations obtained from implicit scheme:

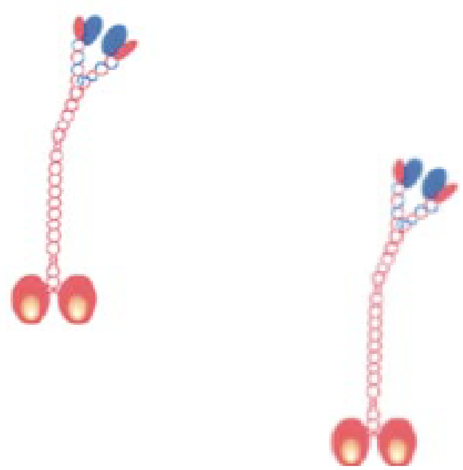
recover familiar equations
Adjari and Prost
Oster, Ermentrout, Peskin

note: can use conventional
J.-L. Lions method as well to
investigate system

$$\frac{\partial \rho_1}{\partial t} = \frac{\partial}{\partial x}\big(\sigma \frac{\partial \rho_1}{\partial x} + \psi_1' \rho_1\big) - \nu_1 \rho_1 + \nu_2 \rho_2$$
$$\frac{\partial \rho_2}{\partial t} = \frac{\partial}{\partial x}\big(\sigma \frac{\partial \rho_2}{\partial x} + \psi_2' \rho_2\big) + \nu_1 \rho_1 - \nu_2 \rho_2$$
$$\sigma \frac{\partial \rho_1}{\partial x} + \psi_1' \rho_1 = 0$$
$$\sigma \frac{\partial \rho_2}{\partial x} + \psi_2' \rho_2 = 0$$
$$\rho_i(x,0) = \rho_i^0 \ \geq \ 0, \qquad in\ \Omega, \quad i \ = \ 1,2$$
$$\int_\Omega \big(\rho_1 + \rho_2\big)\ dx = 1$$

Role of asymmetry

asymmetry of the potentials is thought to play an important role in motor processivity, similar to the flashing rachet



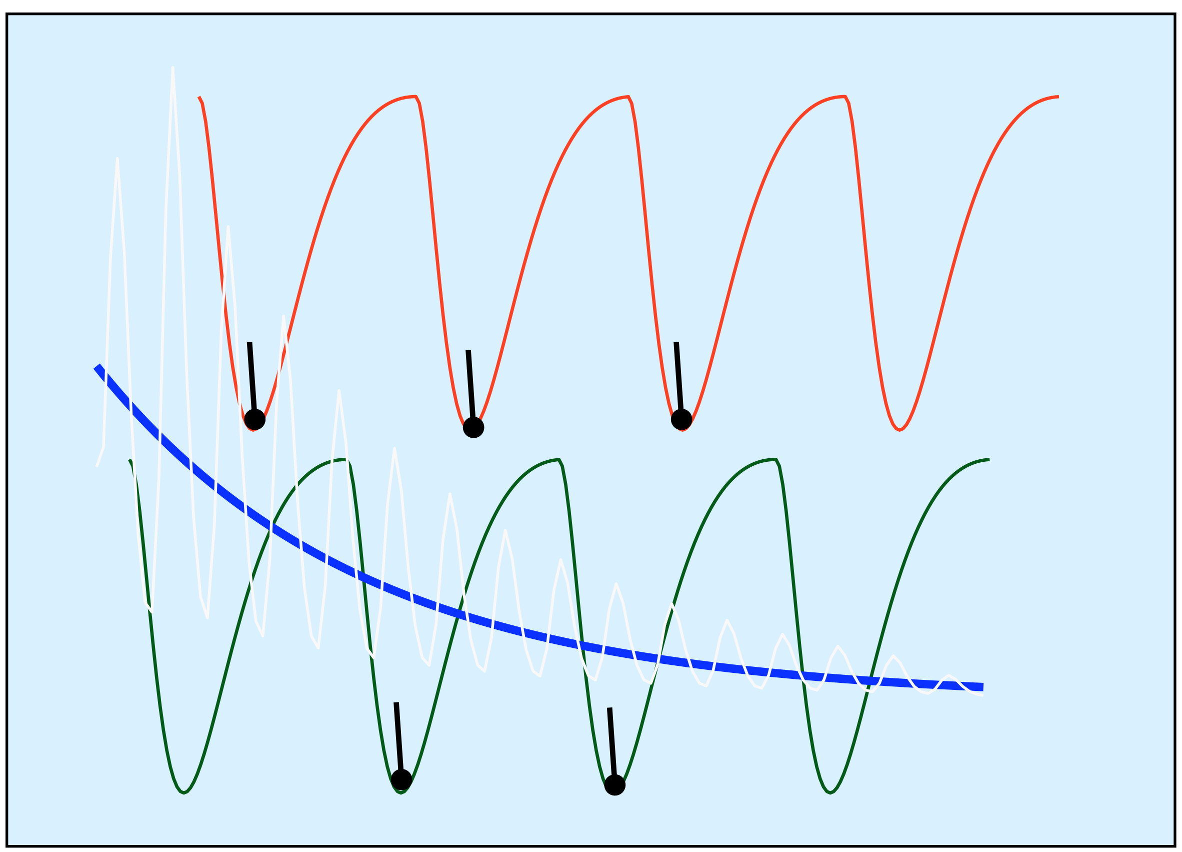
motors distributed about red well bottom; some change conformation from asymmetry, most move left to a green well bottom with probability p

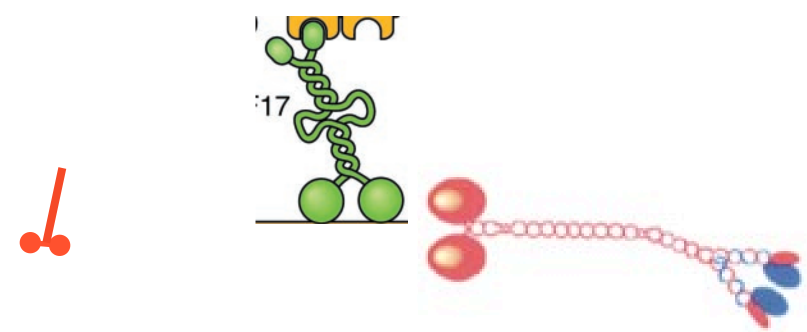
some change conformation; most move left with probability p

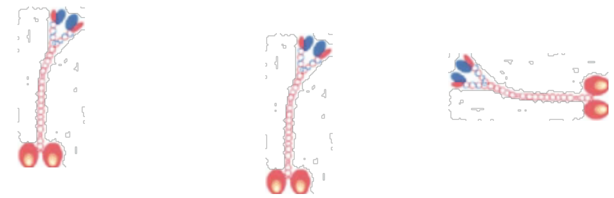
corresponds to trials with a biased coin

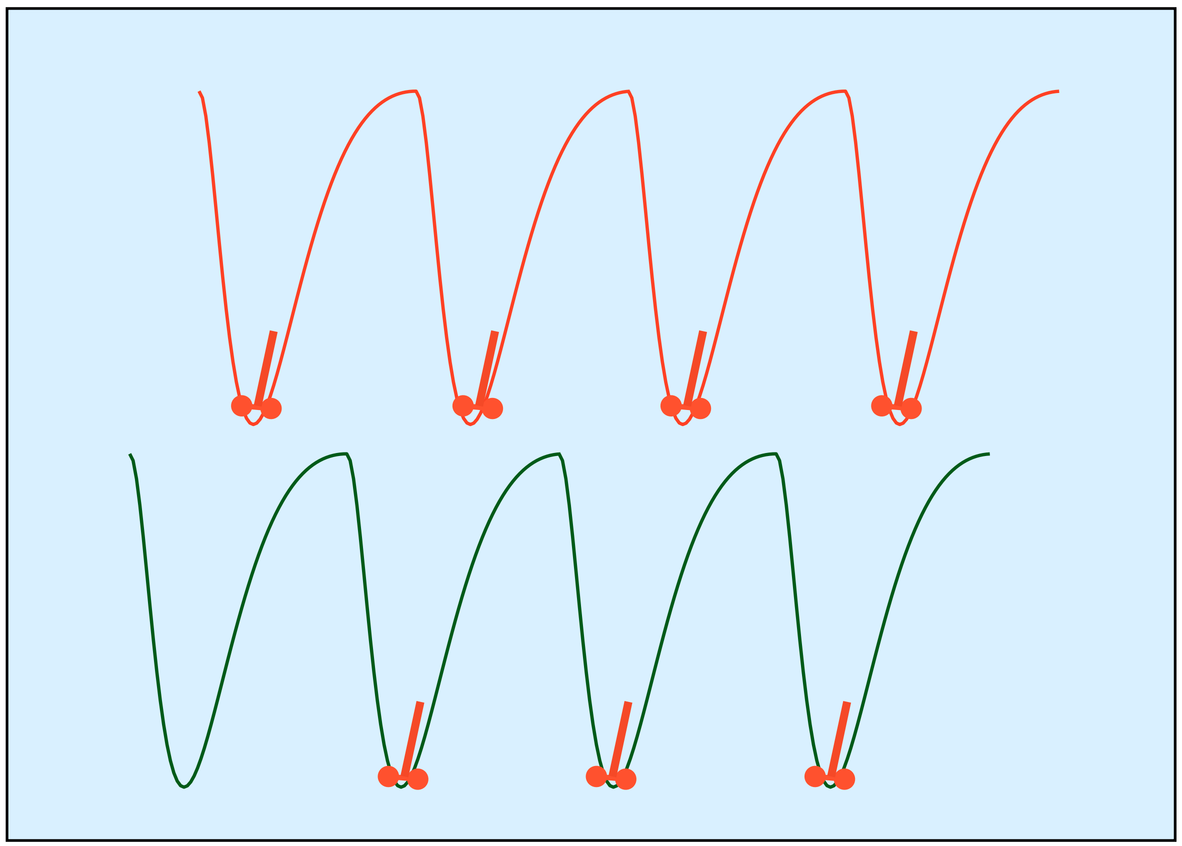
stationary distribution is exponentially decaying

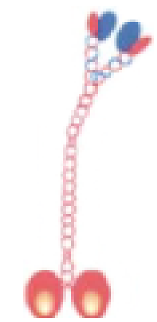
correct but does not translate to a proof



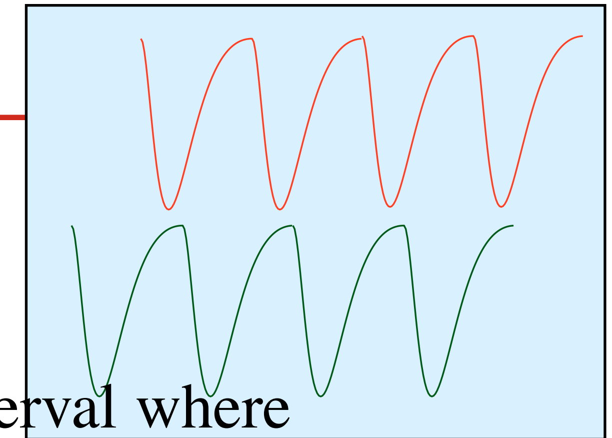








Character of stationary solution

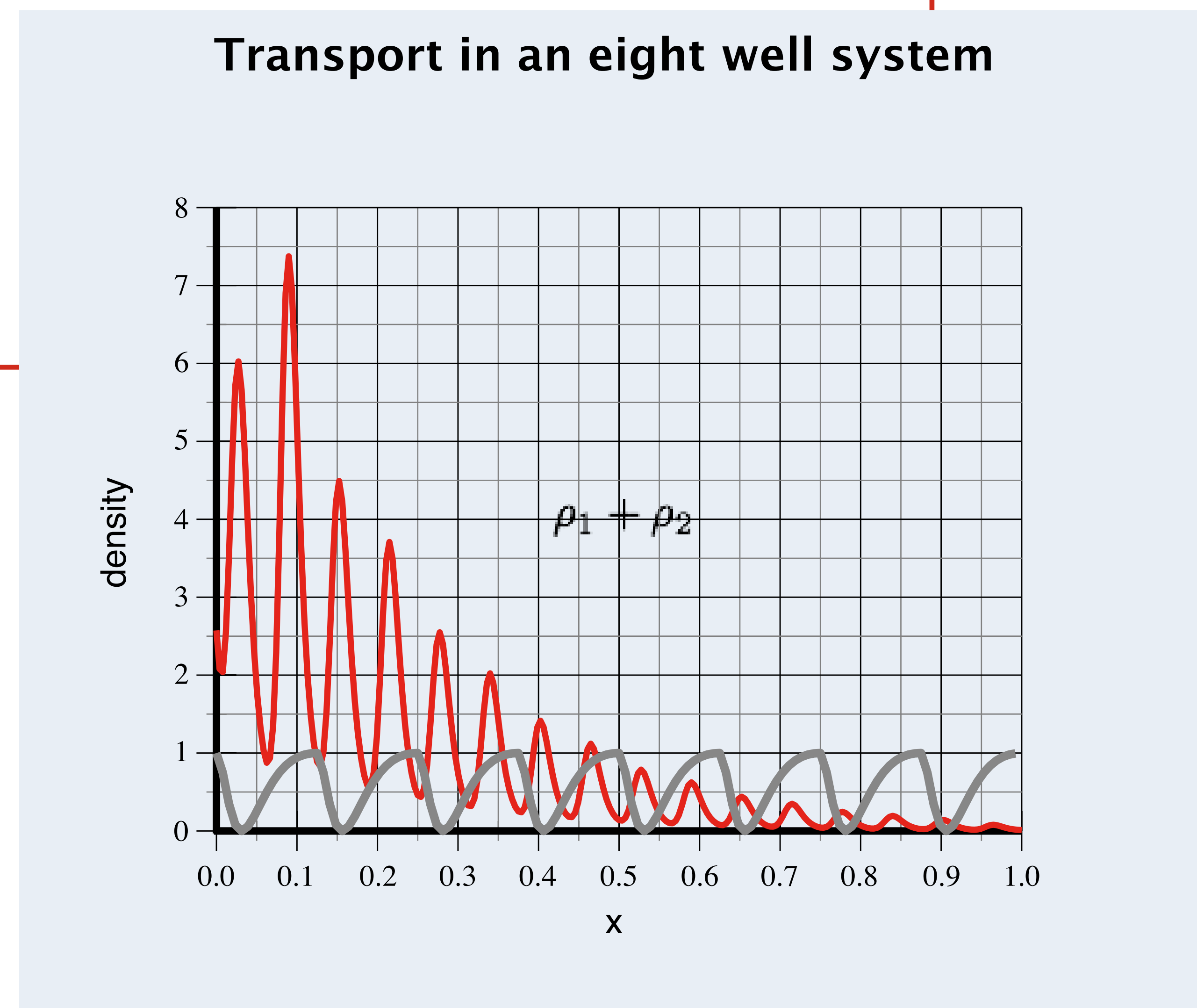


Assume that

1. ψ_i, ν_i periodic of period $1/N$ on Ω
2. $\psi_1' > 0$ on each interval where $\psi_2' \leqq 0$ and $\psi_2' > 0$ on each interval where $\psi_1' \leqq 0$
3. $\nu_i > 0$

Then

$$\rho_1(x) + \rho_2(x) \leqq K e^{-\frac{cN}{\sigma}(x - \frac{1}{N})}, \; x \geqq \frac{1}{N}$$



proof based on studying system of ODE's

$$\rho_1 \quad \rho_2 \quad \phi = \sigma\rho_1' + \psi_1\rho_1'$$

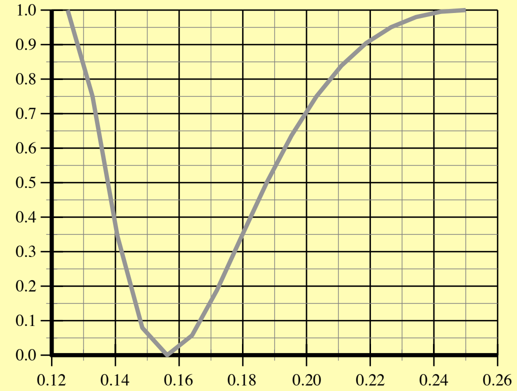
$$\begin{aligned} \sigma\rho_1' &= \phi - \psi_1'\rho_1 \\ \sigma\rho_2' &= -\phi - \psi_2'\rho_2 \\ \phi' &= \nu_1\rho_1 - \nu_2\rho_2 \\ \phi(0) &= \phi(1) = 0 \end{aligned}$$

$$\frac{d}{dx}\hat{\rho} = A\hat{\rho} \qquad A = \frac{1}{\sigma}\begin{pmatrix} -\psi_1' & 0 & 1 \\ 0 & -\psi_2' & -1 \\ \sigma\nu_1 & -\sigma\nu_2 & 0 \end{pmatrix}$$

Mechanisms of diffusion mediated transport

basic notion: nonequilibrium fluctuations can be 'oriented' to alter the state of the system, for example, to exhibit transport; actual biological function extraordinarily complex

equations illustrate rich and diverse mechanisms to achieve this



Flashing rachet (Astumian et al.)

diffusion and transport in alternate potential is periodic and asymmetric in its period basin

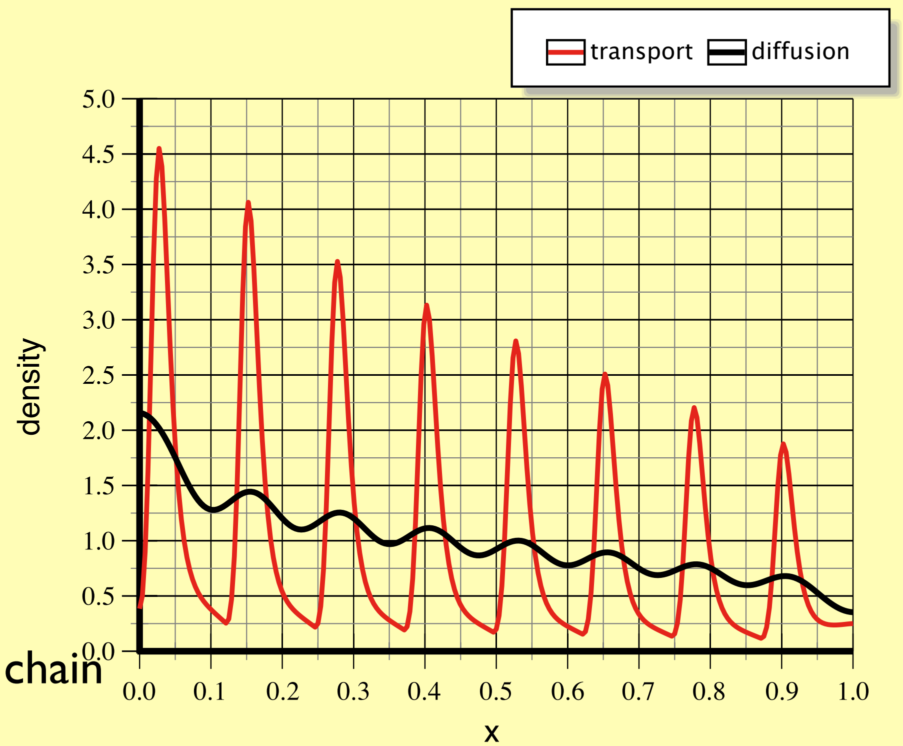
$$\frac{\partial \rho}{\partial t} = \frac{\partial}{\partial x}(\sigma \frac{\partial \rho}{\partial x} + \psi' \rho)$$

alternates with

$$\frac{\partial \rho}{\partial t} = \sigma \frac{\partial^2 \rho}{\partial x^2}$$

there is a periodic solution
can estimate transport with Markov chain
(K & Kowalczyk)

Flashing Rachet: eight well system

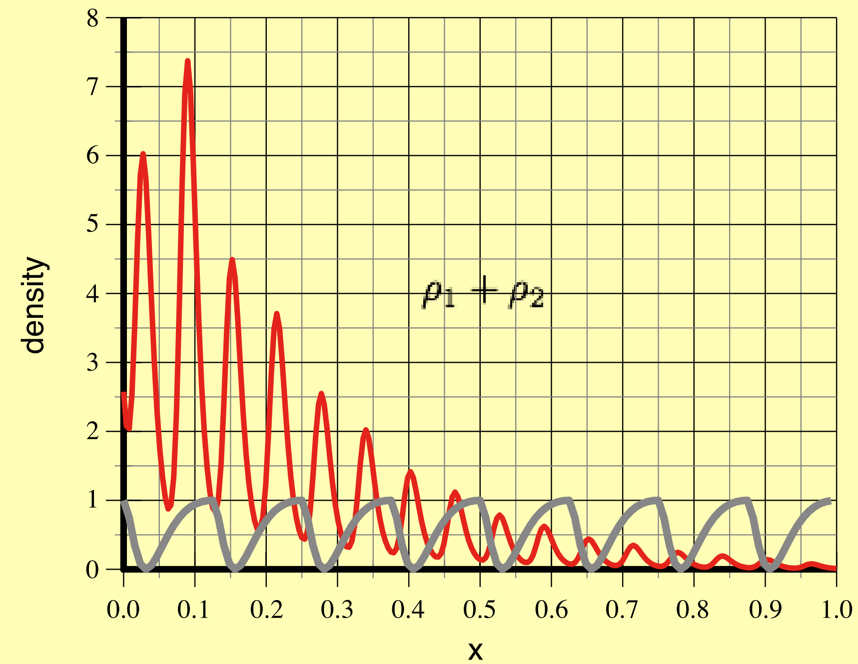


Transport in an eight well system

Multiple state molecular motor (Adjari & Prost; Oster, Ermentrout, Peskin, Doering and others)

diffusion and transport in several potentials with state changes among the wells like hand over hand motion (conventional kinesin).

$$\frac{\partial \rho}{\partial t} = \frac{\partial}{\partial x}(\sigma \frac{\partial \rho}{\partial x} + \rho \psi') + \rho \nu \qquad \rho = (\rho_1, \rho_2)$$



potentials are asymmetric as before
stationary state decays exponentially: like trials with a biased coin
(Chipot, Hastings, K, Kowalczyk)

Parrondo Paradox

winning through losing

pair of coin toss games

win or lose $$ each trial

Harmer & Abbot
Nature 1999

a-game
toss a fair coin

$p_a = 0.5$

$E_a = 0$

b-game
coin played depends on present capital

3 divides present capital otherwise

$p_b = \epsilon$

$p_b' = 0.75 - \epsilon$

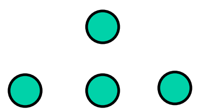
$E_b = 0$

but playing according to the schedule *a, b, a, b, a, b,* ...is winning!

essence of the game is an illusion: naive idea of fairness

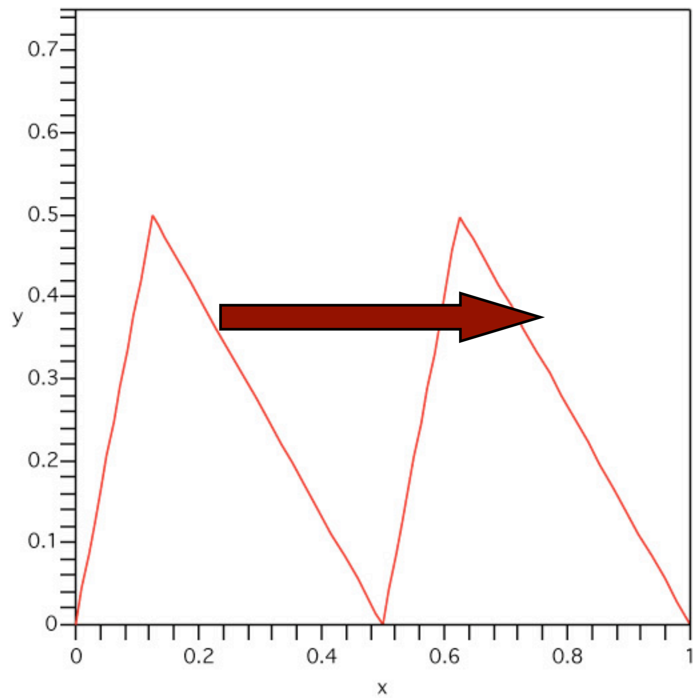
magic lies in maintaining that illusion as long as possible.

look at finite difference scheme
b-game looks like random walk with piecewise constant drift



$$\rho_k^{i+1} - \rho_k^i = \frac{1}{2}(\rho_{k+1}^i - 2\rho_k^i + \rho_{k-1}^i) - \frac{1}{2}(\lambda_{k+1}\rho_{k+1}^i - \lambda_{k-1}\rho_{k-1}^i)$$

$$\text{where } \lambda_k = 2p_b - 1 \ or \ 2p_b' - 1 \text{ depending on k mod 3}$$



alternating a-game/b-game looks like flashing rachet

potential plot enhances the illusion

what we call a
spare parts story

frequency of coin play actually governed by a Markov chain P_b (3 x 3)

fair coin game governed by Markov chain P_a

Parrondo game corresponds to periodic transition matrix, P_a, P_b, P_a, etc.

limit cycle near stationary state of product P_bP_a

for special game here, corresponds to b-game with tails replaced by heads

original b-game losing means concatenated game winning something more fascinating is true

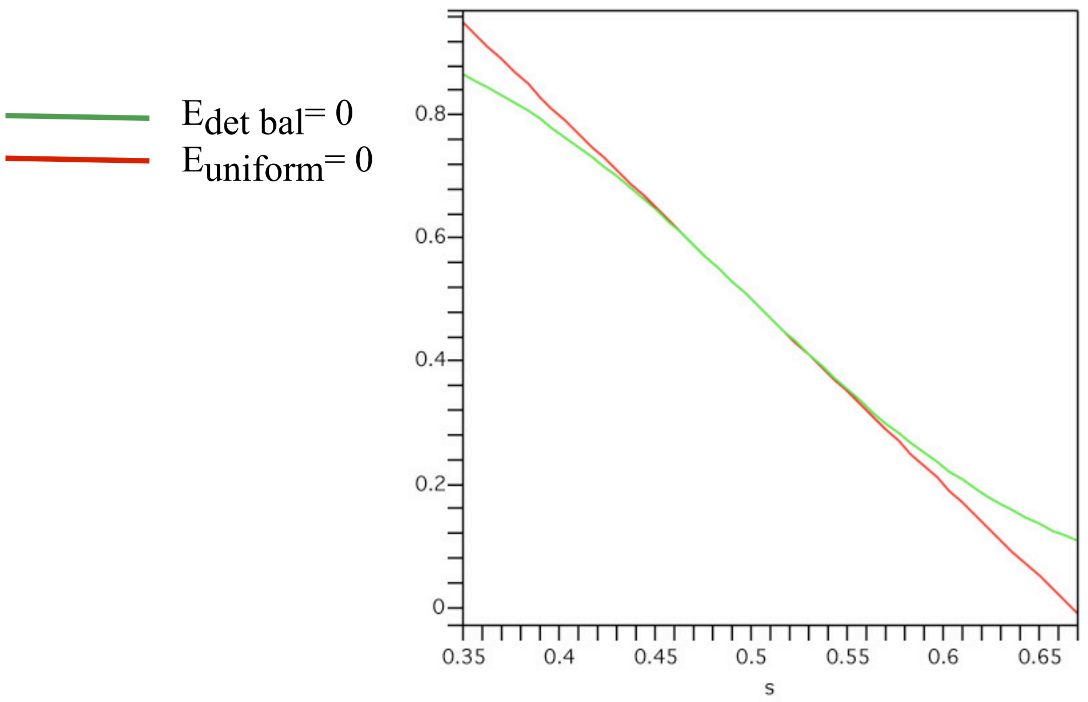
about game played with capital mod **4**

$P_b P_a = P_a^2$

means: starting from uniform distribution returns to uniform distribution after one a-game/b-game cycle for any b-game

winning or losing depends on

E_b(uniform distribution)



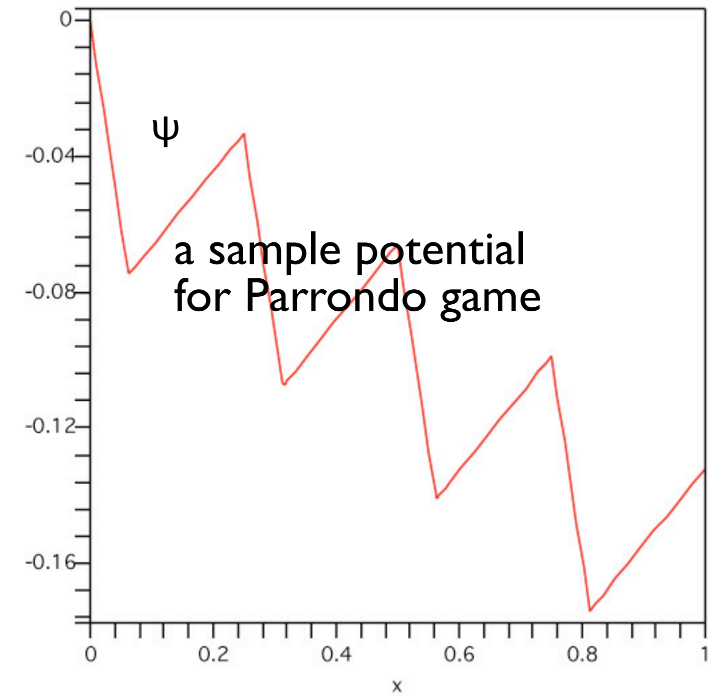
this is a new rachet mechanism like a screw with stripped threads:
turning it always resets to the initial position

Parrondo game works on potential difference

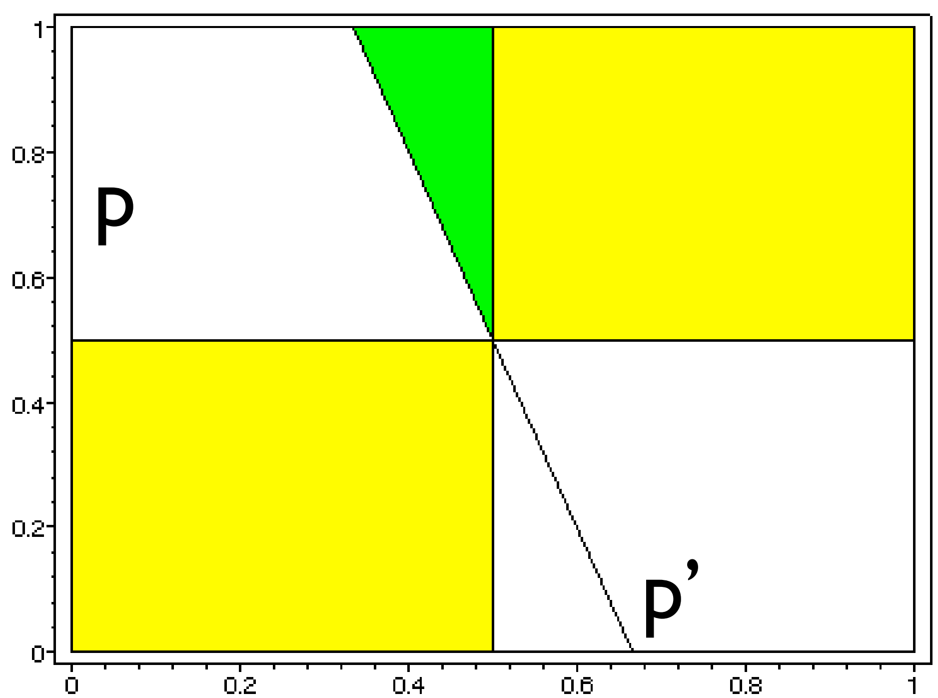
Brownian rachet (what we have been studying) works on geometry of potential

can find parameters so Parrondo wins and rachet moves to left

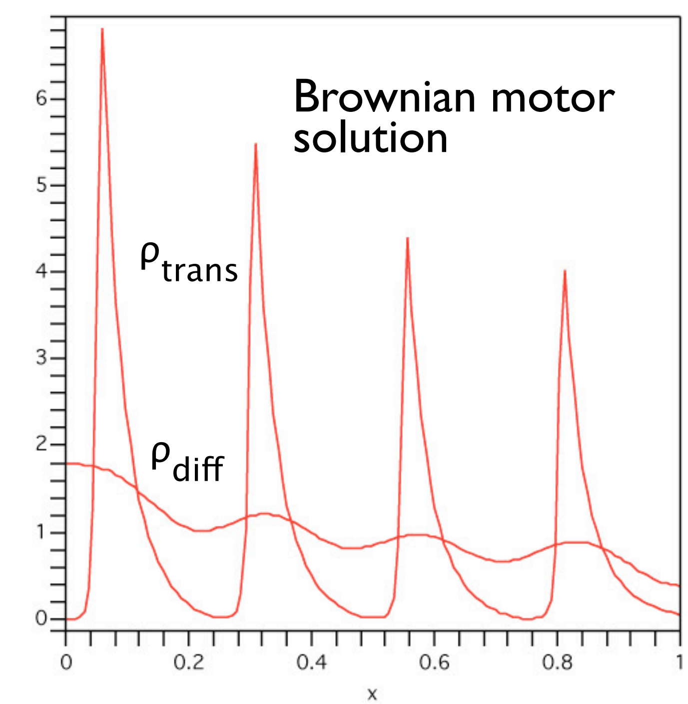
also related to stochastic time?

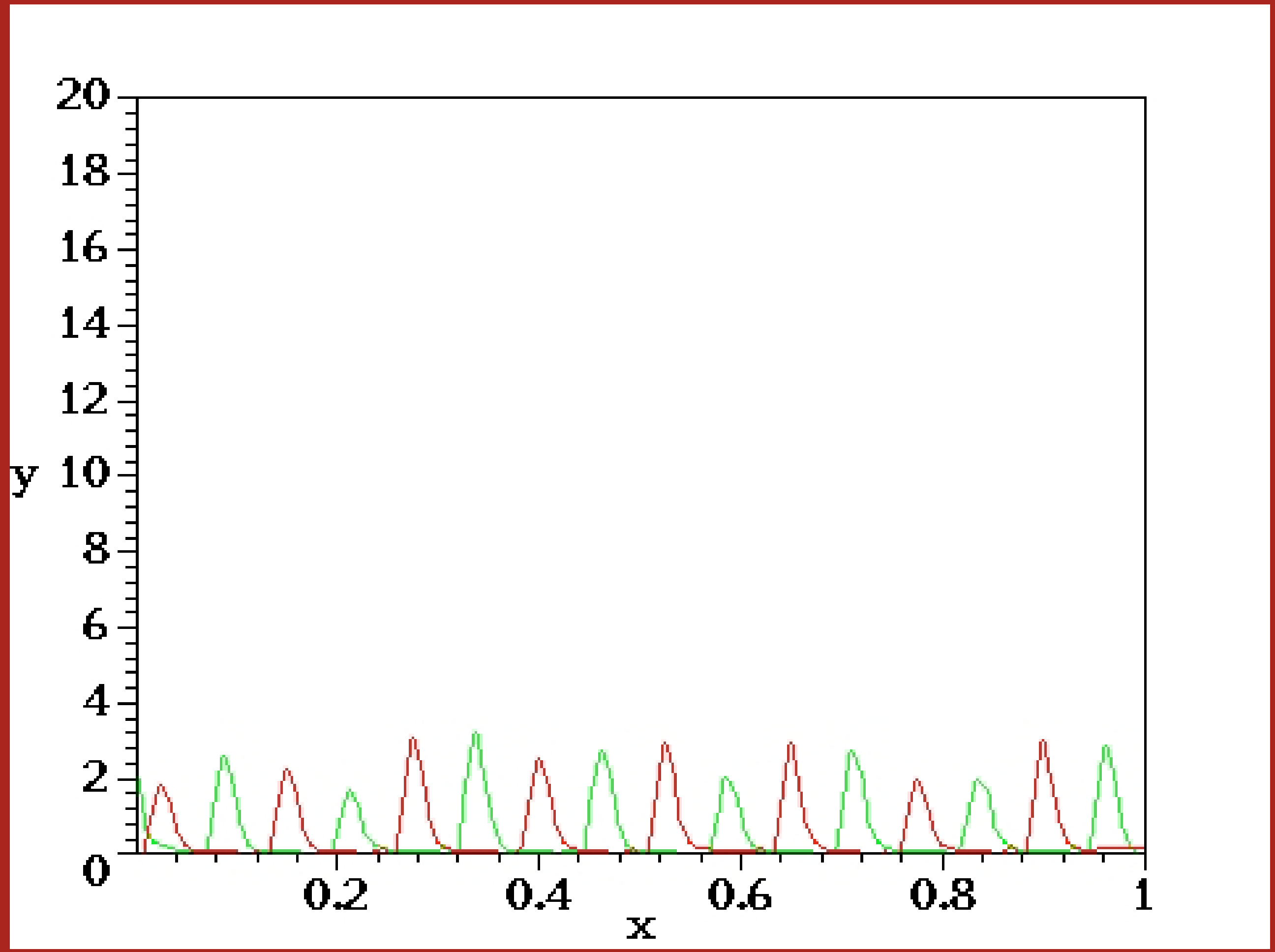


in green triangle Parrondo is winning
and rachet moves left



Alex Bogomolny
http://www.cut-the-knot.org/ctk/Parrondo.shtml





20
18
16
14
12
y
10
8
6
4
2
0
0.2
0.4
0.6
0.8
1
x