First Passage Times in the Near-Continuum Limit of Birth-Death Processes

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Schlögl Model

$$2R + A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} 3R$$

$$R \underset{k_4}{\overset{k_3}{\rightleftharpoons}} B$$

- Introduced by Schlögl in 1972, as a catalysis model.
- Keep the concentrations N_A and N_B constant.
- Interested in the dynamics of $X(t) := N_R(t)$.
- The simplest description: deterministic, rate equation.



Deterministic Description

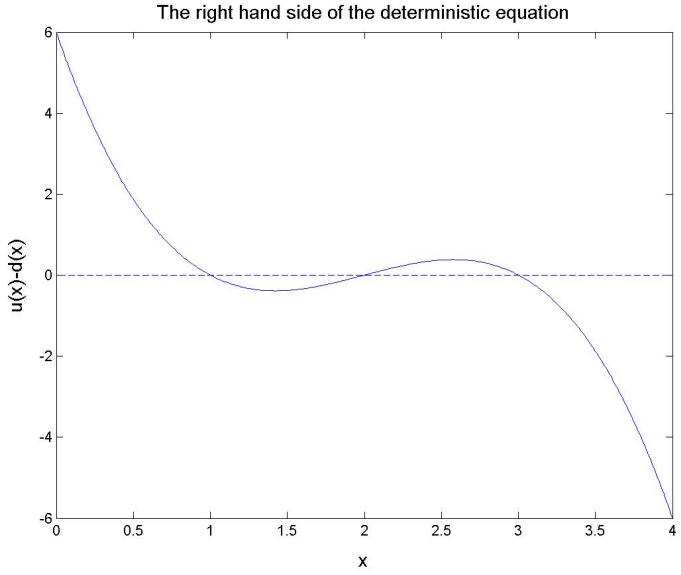
Proportion to the system size

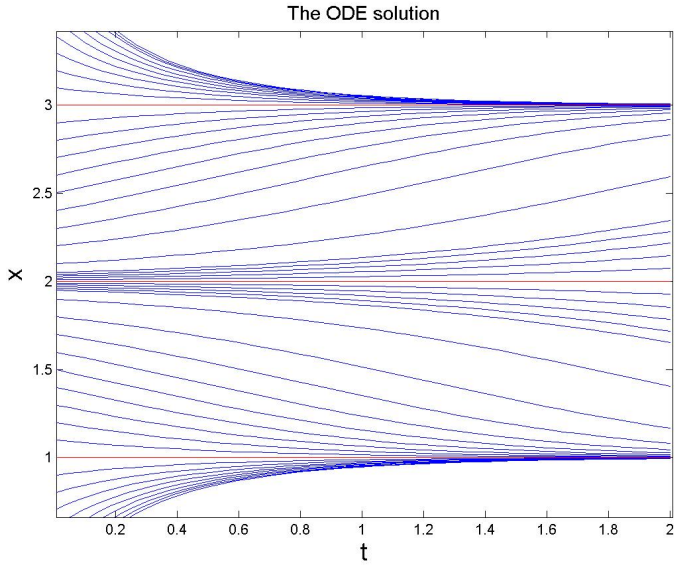
$$x(t) = \frac{X(t)}{N}$$

Governing ODE

$$\frac{dx}{dt} = k_1 x^2 + k_4 - k_2 x^3 - k_3 x = u(x) - d(x)$$

- Simple to analyze.
  Stable-Unstable-Stable.





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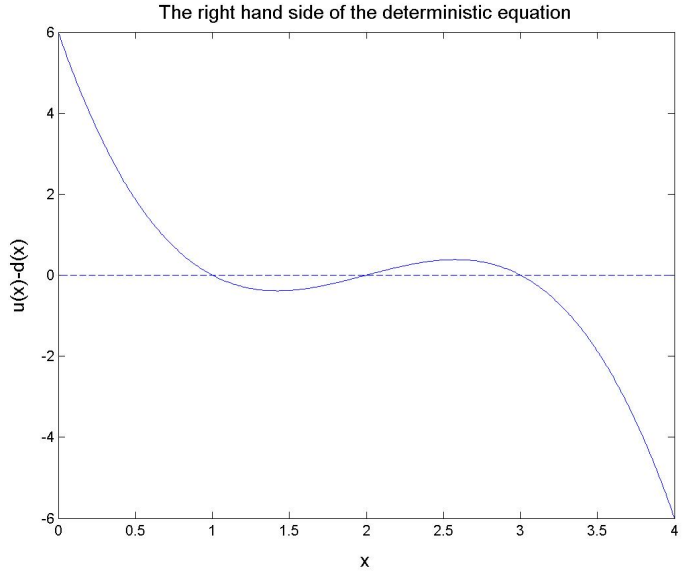
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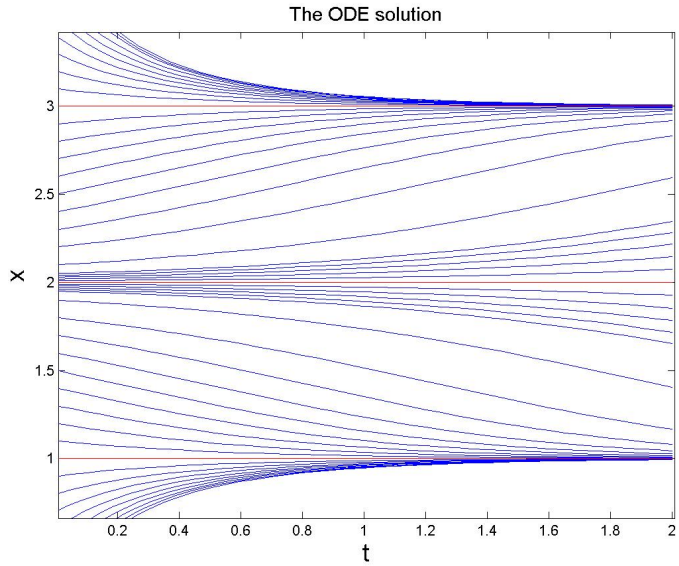
$$\frac{dx}{dt} = k_1 x^2 + k_4 - k_2 x^3 - k_3 x = u(x) - d(x)$$

- Simple to analyze.
  Stable-Unstable-Stable.

BUT

- Accurate only for large and well stirred systems.
- Does not detect intrinsic fluctuations.
- Switches between stable equilibriums are not allowed.
- Which of the two stable states is more stable?

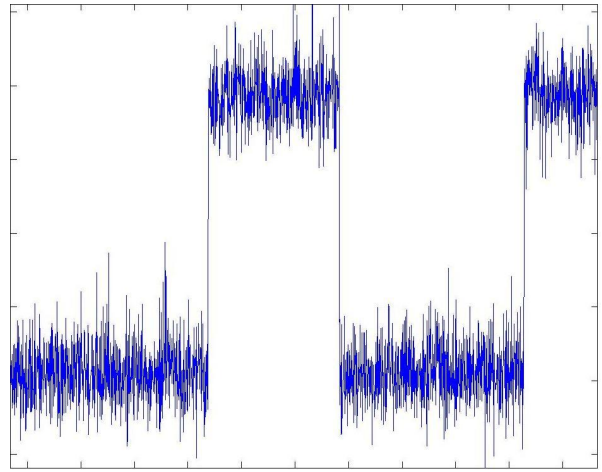




Discrete Model

$$2R + A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} 3R$$

$$R \underset{k_4}{\overset{k_3}{\rightleftharpoons}} B$$



$(N_R =)\ n \to n+1$ with rate $U_n = k_1 \dfrac{n(n-1)}{N} + k_4 N,$

$(N_R =)\ n \to n-1$ with rate $D_n = k_2 \dfrac{n(n-1)(n-2)}{N^2} + k_3 n.$

To determine which deterministically stable state is “more stable”, we need to compare the mean switching times between them, $\tau_{n_2 \to n_1}$ and $\tau_{n_1 \to n_2}$.

Backward Equation for Mean First Passage Time $n \to n_1$

$$-1 = U_n \tau_{n+1} - (U_n + D_n)\tau_n + D_n \tau_{n-1}$$

with boundary condition $\tau_{n_1} = 0$.

Exact Solution

$$\tau_n = (\tau_{n \to n_1}) = \sum_{m=n_1+1}^{n} \left[\frac{1}{D_m} + \prod_{i=1}^{m-1} \frac{D_i}{U_i} \sum_{j=m+1}^{\infty} \frac{1}{D_j} \prod_{k=1}^{j-1} \frac{U_k}{D_k} \right],$$

for $n > n_1$.

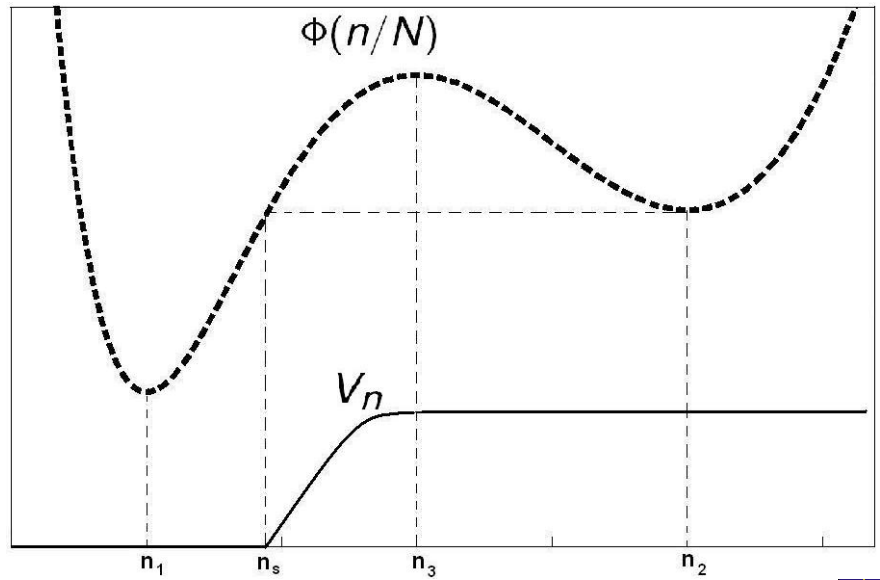
Large System Size Asymptotics

The leading order of the exponent $V_n = \lim_{N\to\infty} \frac{1}{N} \log \tau_{n\to n_1}$

$$V_n \sim \begin{cases} 0 & \text{for} \quad n \in [n_1, n_s] \\ \Phi(n/N) - \Phi(n_2/N) & \text{for} \quad n \in [n_s, n_3] \\ \Phi(n_3/N) - \Phi(n_2/N) & \text{for} \quad n \in [n_3, \infty) \end{cases}$$

$$\Phi(n/N) = -\int_0^{n/N} \log \frac{u(x)}{d(x)}\, dx,$$

$$\Phi(n_s/N) = \Phi(n_2/N).$$

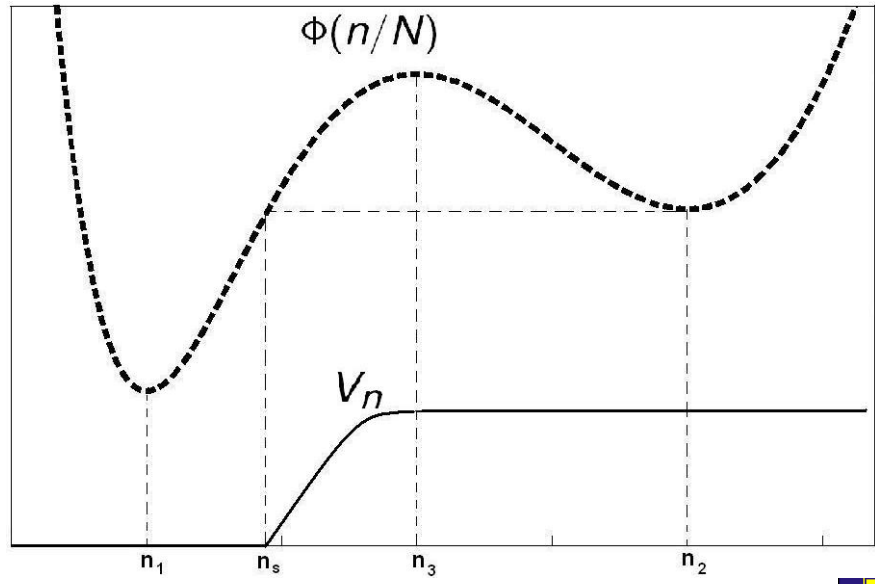


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V_n is not a constant!



Discrete Exponential (Large Deviation or Rare Event) Ansatz

$$\tau_n = \sigma_n e^{NV_n}$$

into

$$-1 = U_n \tau_{n+1} - (U_n + D_n)\tau_n + D_n \tau_{n-1}$$

to get (in the leading order)

$$V_n - V_{n-1} = 0$$

or

$$V_n - V_{n-1} = \frac{1}{N} \ln \frac{D_n}{U_n}.$$

But which one to choose?

Discrete Exponential (Large Deviation or Rare Event) Ansatz

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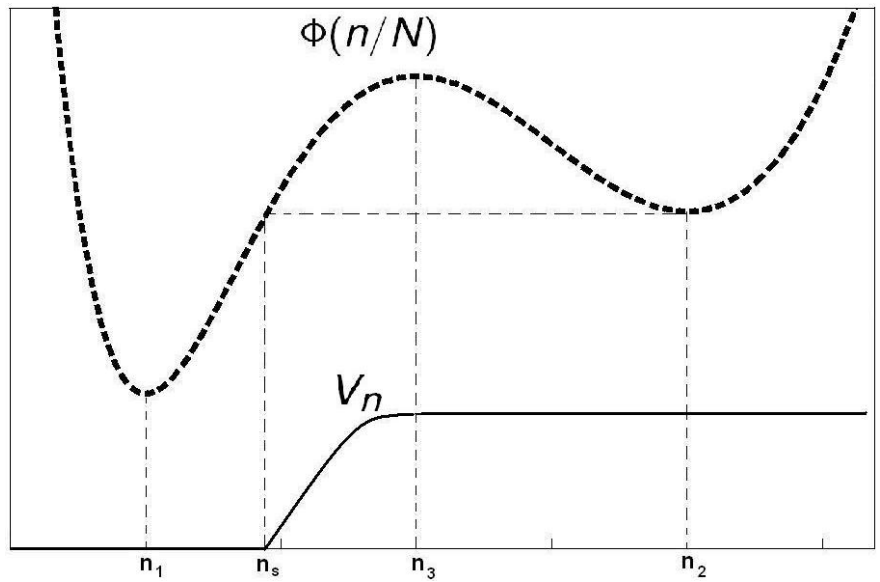
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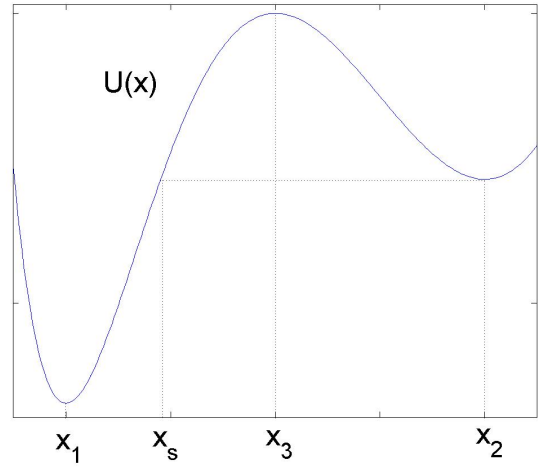
$$V_n - V_{n-1} = \frac{1}{N} \ln \frac{D_n}{U_n}.$$



Think simpler

$T(x)$ is MFPT from x to x_1.

$$-1 = -U'(x)T'(x) + \epsilon T''(x)$$



Exact solution

$$T(x) = \frac{1}{\epsilon} \int_0^x \int_y^\infty e^{-\frac{U(z)-U(y)}{\epsilon}} dzdy$$

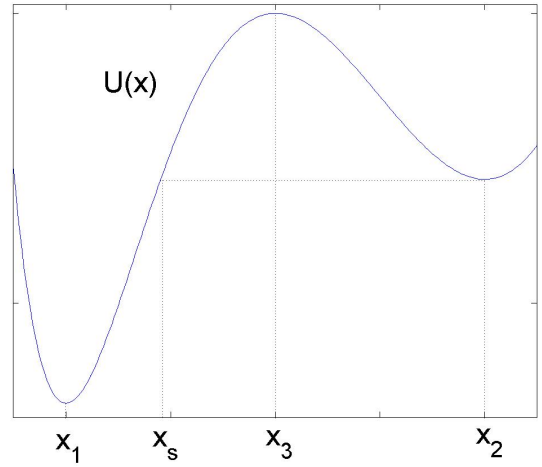
Asymptotics

$$\epsilon \log T(x) \sim \begin{cases} 0 & \text{for} \quad x \in [x_1, x_s] \\ U(x) - U(x_2) & \text{for} \quad x \in [x_s, x_3] \\ U(x_3) - U(x_2) & \text{for} \quad x \in [x_3, \infty) \end{cases}$$

Think simpler

$T(x)$ is MFPT from x to x_1.

$$-1 = -U'(x)T'(x) + \epsilon T''(x)$$



Exponential ansatz $T(x) = z(x)e^{\Phi(x)/\epsilon}$ leads to (in the leading order)

$$0 = -U'(x)\Phi'(x) + \Phi'(x)^2$$

$$\Phi'(x) = 0 \qquad \text{or} \qquad \Phi'(x) = U'(x)$$

One-step Markov Jump Process $X(t)$

$$\begin{aligned} U_n \qquad & n \to n+1, \\ D_n \qquad & n \to n-1. \end{aligned}$$

Master Equation

$$\frac{dP_n(t)}{dt} = U_{n-1}P_{n-1}(t) + D_{n+1}P_{n+1}(t) - (U_n + D_n)P_n(t)$$

for the probabilities $P_n(t) = \mathbb{P}\{X(t) = n\}$.

- Rescale the jump sizes and the rates,
- Rates $u(x) := \epsilon U_n$ and $d(x) := \epsilon D_n$,
- *Intensive variable* $x = n/N = \epsilon n$.

Rescaled Master Equation

$$\frac{\partial P_\epsilon(x,t)}{\partial t} = \epsilon^{-1}\{u(x-\epsilon)P_\epsilon(x-\epsilon,t) - u(x)P_\epsilon(x,t)\}+$$
$$+\epsilon^{-1}\{d(x+\epsilon)P_\epsilon(x+\epsilon,t) - d(x)P_\epsilon(x,t)\},$$

for the probabilities $P_\epsilon(x,t) = \mathbb{P}\{X(t) = x/\epsilon\}$.

Expansion up to the order $\mathcal{O}(\epsilon^0)$

- Liouville Equation: $\frac{\partial P(x,t)}{\partial t} = -\frac{\partial}{\partial x}\left[(u(x) - d(x))P(x,t)\right]$,
- Leads to the ODE: $\dot{x} = u(x) - d(x)$.

- Rescale the jump sizes and the rates,
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Rescaled Master Equation

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for the probabilities $P_\epsilon(x,t) = \mathbb{P}\{X(t) = x/\epsilon\}$.

Expansion up to the order $\mathcal{O}(\epsilon^1)$

- Fokker-Planck Equation: $\frac{\partial P(x,t)}{\partial t} = -\frac{\partial}{\partial x}\left[(u(x) - d(x))P(x,t)\right] + \frac{\epsilon}{2}\frac{\partial^2}{\partial x^2}\left[(u(x) + d(x))P(x,t)\right]$,
- Leads to the SDE: $dx = (u(x) - d(x))\,dt + \sqrt{\epsilon(u(x) + d(x))}\,dW$.

Rare event (large deviation) ansatz $P(x,t) = e^{-\Phi(x,t,\epsilon)/\epsilon}$ (same ϵ!).

Rescaled Master Equation

$$\frac{\partial P(x,t)}{\partial t} = \epsilon^{-1}\{u(x-\epsilon)P(x-\epsilon,t) - u(x)P(x,t)\} + \epsilon^{-1}\{d(x+\epsilon)P(x+\epsilon,t) - d(x)P(x,t)\}$$

$$-\epsilon^{-1} e^{-\Phi(x,t)/\epsilon} \frac{\partial \Phi(x,t)}{\partial t} = \epsilon^{-1} u(x) \left[e^{-\Phi(x-\epsilon,t)/\epsilon} - e^{-\Phi(x,t)/\epsilon} \right] +$$

$$+\epsilon^{-1} d(x) \left[e^{-\Phi(x+\epsilon,t)/\epsilon} - e^{-\Phi(x,t)/\epsilon} \right]$$

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Hamilton-Jacobi Equation

$$\Phi_t + u(x)(e^{\Phi_x} - 1) + d(x)(e^{-\Phi_x} - 1) = 0$$

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Fokker-Planck Approximation

$$\frac{\partial P(x,t)}{\partial t} = -\frac{\partial}{\partial x}\left[(u(x) - d(x))P(x,t)\right] + \frac{\epsilon}{2}\frac{\partial^2}{\partial x^2}\left[(u(x) + d(x))P(x,t)\right]$$

The *wrong* Hamilton-Jacobi Equation

$$\Phi_t + (u(x) - d(x))\Phi_x + \frac{u(x) + d(x)}{2}(\Phi_x)^2 = 0$$

[Not so] Rare event (moderate deviation) ansatz $P(x,t) = e^{-\Phi(x,t)/\delta}$ with $\delta = \epsilon^{\alpha}$ for $0 < \alpha < 1$.

Now both Master and Fokker-Planck Equations lead to the same

Hamilton-Jacobi Equation

$$\Phi_t + (u(x) - d(x))\Phi_x + \frac{\epsilon}{\delta}\frac{u(x)+d(x)}{2}(\Phi_x)^2 + o\left(\frac{\epsilon}{\delta}\right) = 0$$

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Take-Home Message

Fokker-Planck approximation is valid only for up to moderate deviations $e^{-\Phi(x,t)/\delta}$, NOT for large deviations $e^{-\Phi(x,t)/\epsilon}$!

Back to solving Hamilton-Jacobi

$$\Phi_t + u(x)(e^{\Phi_x} - 1) + d(x)(e^{-\Phi_x} - 1) = \Phi_t + H(x, \Phi_x) = 0$$

- Read off the Hamiltonian

$$H(x, p) = u(x)(e^p - 1) + d(x)(e^{-p} - 1),$$

- Set up the Hamiltonian System

$$\begin{cases} \frac{dx}{dt} = u(x)e^p - d(x)e^{-p} \\ \frac{dp}{dt} = -u'(x)(e^p - 1) - d'(x)(e^{-p} - 1), \end{cases}$$

- Along the Hamiltonian paths,

$$\frac{d\Phi}{dt} = \Phi_t + \Phi_x \frac{dx}{dt} = -H(x, p) + p\frac{dx}{dt} = L\left(x, \frac{dx}{dt}\right)$$

as claimed in Freidlin-Wentzell theory.

Freidlin-Wentzell LD Theory

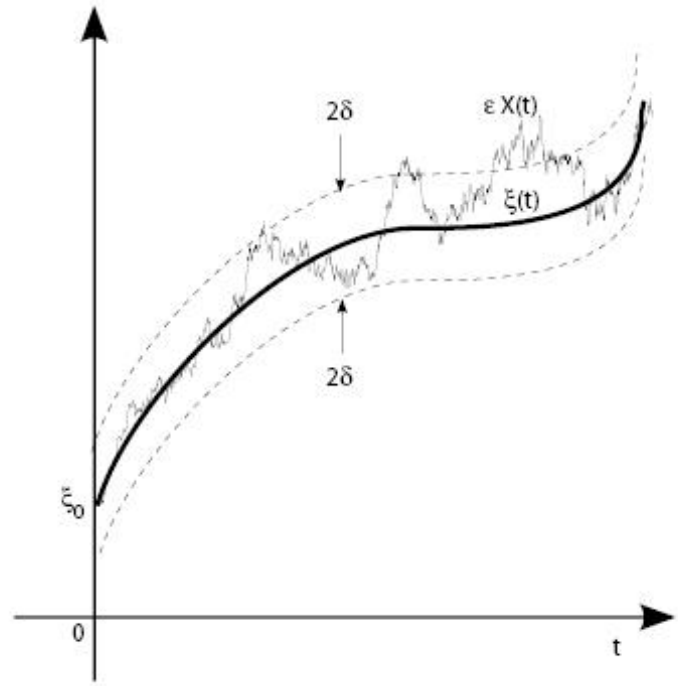
$$\lim_{\epsilon \to 0} \epsilon \log \mathbb{P}\{\epsilon X(t) \in S\} = - \inf_{\substack{\xi(\cdot) \in S \\ \xi(0)=\xi_0}} I_0^T[\xi]$$

or

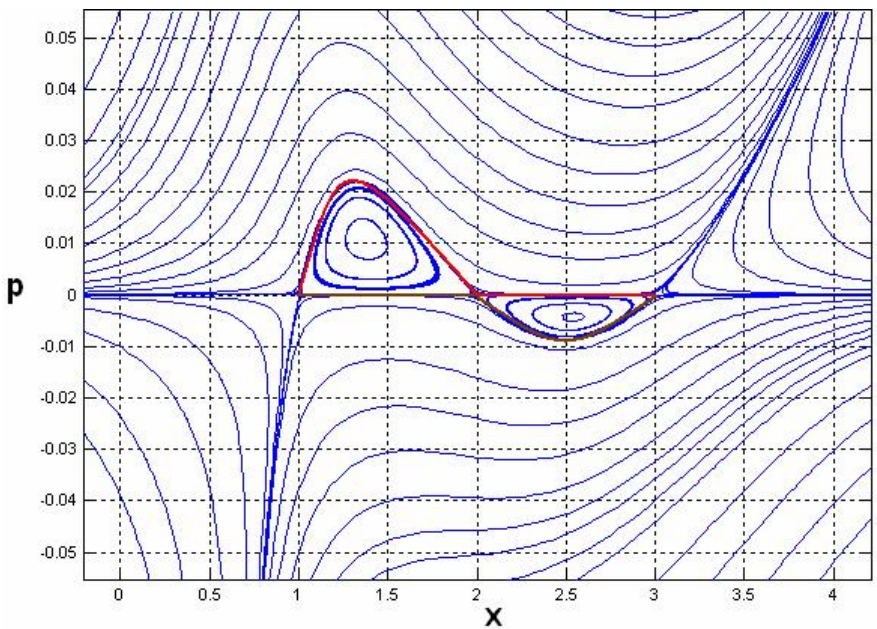
$$\lim_{\delta \to 0} \lim_{\epsilon \to 0} \epsilon \log \mathbb{P}\{ \sup_{0 \le t \le T} |\epsilon X(t) - \xi(t)| < \delta\} = -I_0^T[\xi]$$

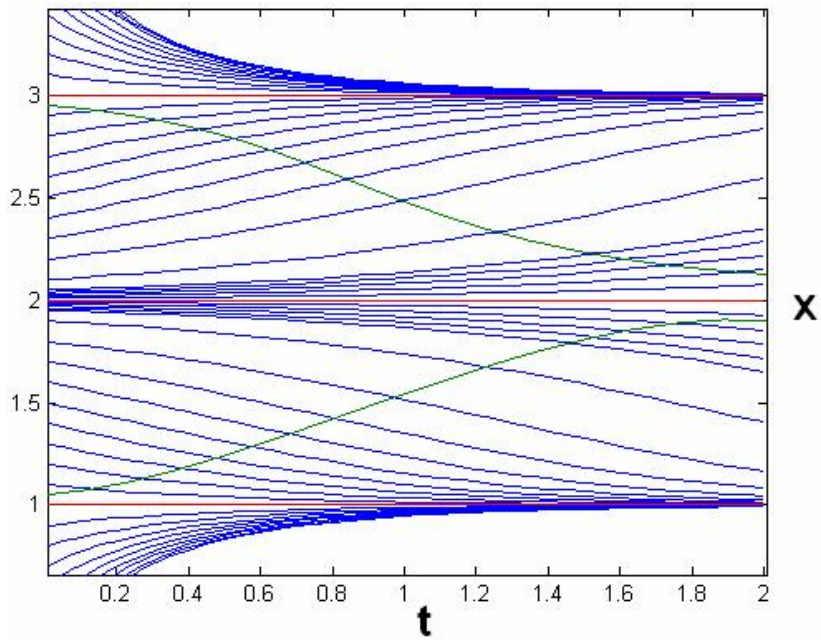
Action Functional

$$I_0^T[\xi] = \int_0^T L(\xi(s), \xi'(s)) ds$$

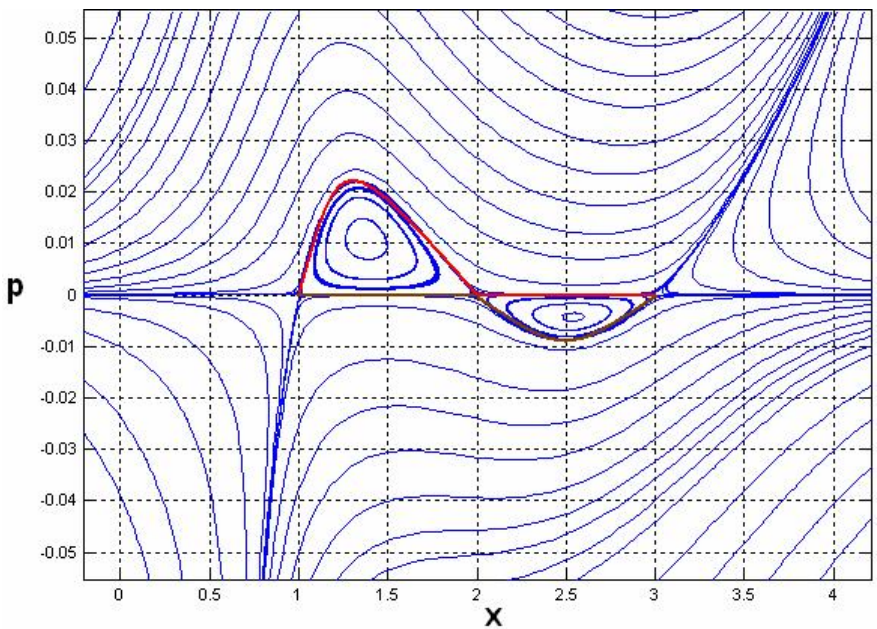


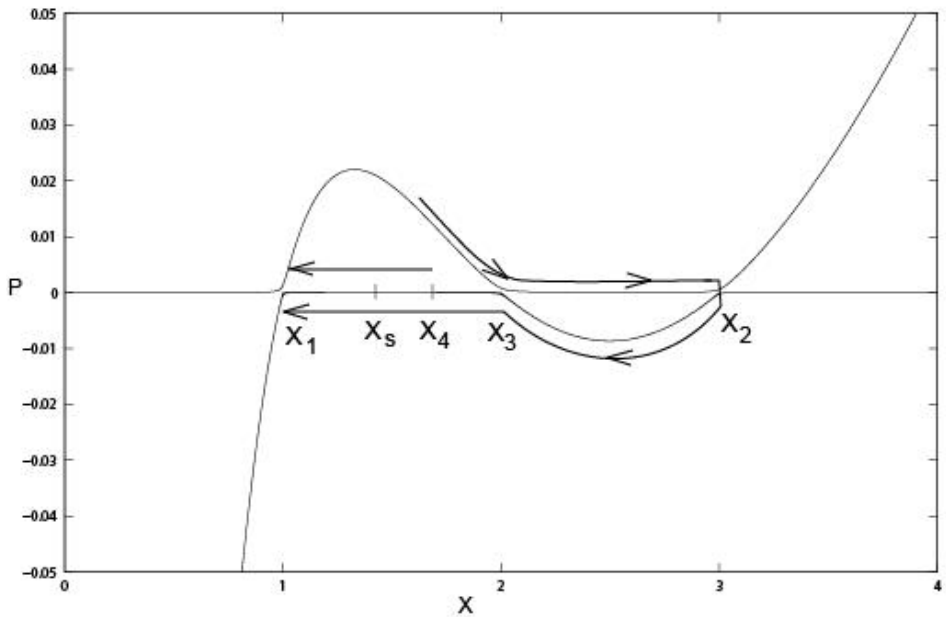
- Backward Equation $-1 = \mathcal{L}T$ for mean switching times leads to Homogeneous H-J Equation $H(x, \Phi_x) = 0$ for the exponent function.
- For One-Step MJP: $H(x,p) = u(x)(e^p - 1) + d(x)(e^{-p} - 1) = 0$. $p = 0$ (deterministic path) or $p = \log(d(x)/u(x))$.
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Messages

- Fokker-Planck (diffusion) approximation may give the opposite answer to the relative stability question,
- MFPT exponent is not necessarily piecewise-constant over the range of state variables,
- MFPT may not be dominated by the most likely path.

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Susceptible-Infected-Susceptible

- n = number of infected people,
- N = total number of people (kept constant),
- $1 < \Lambda$ = infection rate.

$$n \to n+1 \qquad \text{with rate} \quad \lambda_n = \Lambda n \left(1 - \frac{n}{N}\right),$$
$$n \to n-1 \qquad \text{with rate} \quad \mu_n = n.$$

Mean Extinction Time τ_n is the Mean First Passage Time from the state n to the state 0.

Backward Equation

$$-1 = \lambda_n \tau_{n+1} - (\lambda_n + \mu_n)\tau_n + \mu_n \tau_{n-1}$$

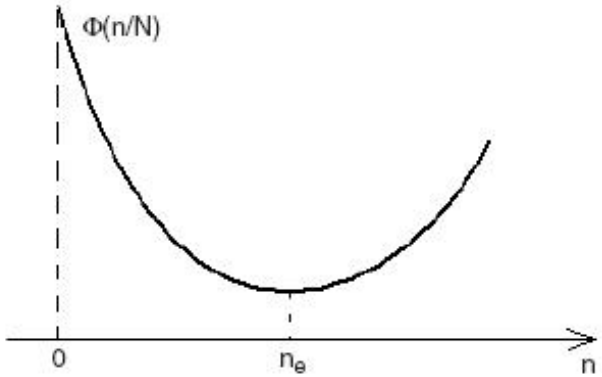
with boundary condition $\tau_0 = 0$.

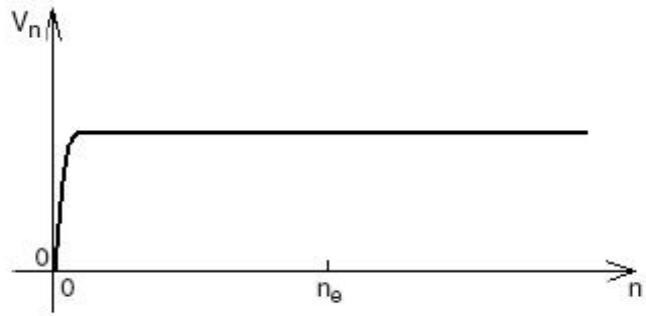
The Exact Solution

$$\tau_n = \sum_{m=1}^{n} \left[\frac{1}{\mu_m} + \prod_{i=1}^{m-1} \frac{\mu_i}{\lambda_i} \sum_{j=m+1}^{\infty} \frac{1}{\mu_j} \prod_{k=1}^{j-1} \frac{\lambda_k}{\mu_k} \right]$$

$$\Phi(x) = -\int_0^x \log \frac{\bar{\lambda}(\xi)}{\bar{\mu}(\xi)} d\xi$$

$$V_n = \lim_{N \to \infty} \frac{1}{N} \log \tau_n$$



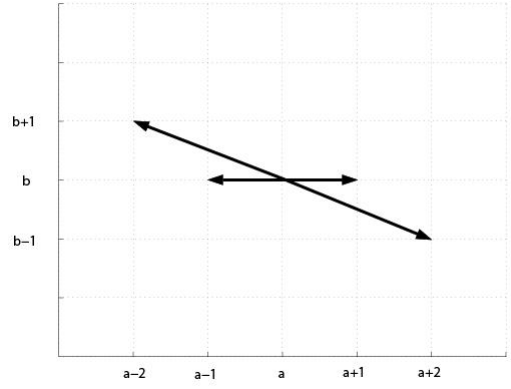


Fast Dimerization

$$A \underset{\gamma}{\overset{\delta}{\rightleftharpoons}} \emptyset$$

$$A + A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B$$

$k_1, k_2 \gg \delta, \gamma$

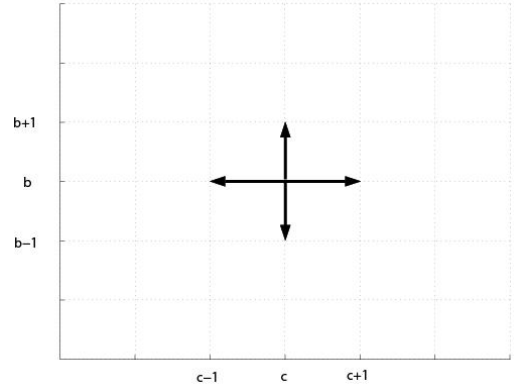


$C = A + 2B$

$$C \underset{\gamma}{\overset{\delta}{\rightleftharpoons}} \emptyset$$

$$\emptyset \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B$$

$$C \underset{\gamma_{eff}}{\overset{\delta_{eff}}{\rightleftharpoons}} \emptyset$$



Invariant measure of the fast process for a given c

$$P_{a,\,b|\,c} = P_0 \frac{k_1^b k_2^{a/2}}{a!b!}\delta_{a+2b,c} = P_0 \frac{k_1^b k_2^{\frac{c-2b}{2}}}{(c-2b)!b!} \approx \frac{1}{d\sqrt{2\pi}} e^{-\frac{(b-b_0)^2}{2d^2}},$$

with

$$b_0(c) = \left(\frac{c}{2} + \frac{k_2}{8k_1}\right) - \frac{k_2}{8k_1}\sqrt{1 + 8c\frac{k_1}{k_2}},$$
$$d(c)^2 = \frac{b_0}{1+4\sqrt{b_0 k_1/k_2}}.$$

The effective rates

$$\delta_{eff}(c) = \sum_{b=0}^{c/2} \delta(c-2b)\frac{P_0}{(c-2b)!b!} k_1^b k_2^{\frac{c-2b}{2}} \approx \delta(c - 2b_0(c)),$$
$$\gamma_{eff}(c) = \sum_{b=0}^{c/2} \gamma\frac{P_0}{(c-2b)!b!} k_1^b k_2^{\frac{c-2b}{2}} = \gamma.$$

For large b_0,

$$d \sim b_0^{1/4}$$

Acknowledgements

- Charlie Doering
- Len Sander
- Peter Smereka
- Joe Conlon
- Bob Ziff
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- Peter Miller
- Danny Forger
- Aaron King
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- Geophysical Fluid Dynamics Program, Woods Hole Oceanographic Institution

Friends and Family

Thank You!