Fluctuations in chemical reactions in a large volume

Khachik Sargsyan

GFD Summer Program, Woods Hole Oceanographic Institution

23 August, 2005

with Eric Vanden-Eijnden and Charlie Doering

Schlögl Model

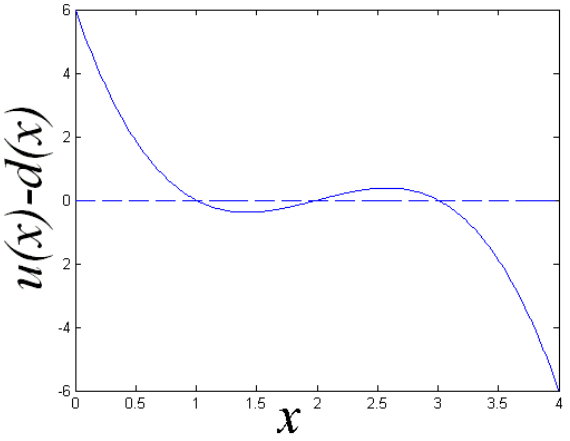
$$2X + A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} 3X$$

$$X \underset{k_4}{\overset{k_3}{\rightleftharpoons}} B.$$

- Introduced by Schlögl in 1972, as a catalysis model.
- Keep the concentrations [A] and [B] constant.
- Interested in the dynamics of [X].
- The simplest description: deterministic, governed by an ODE.

Deterministic description

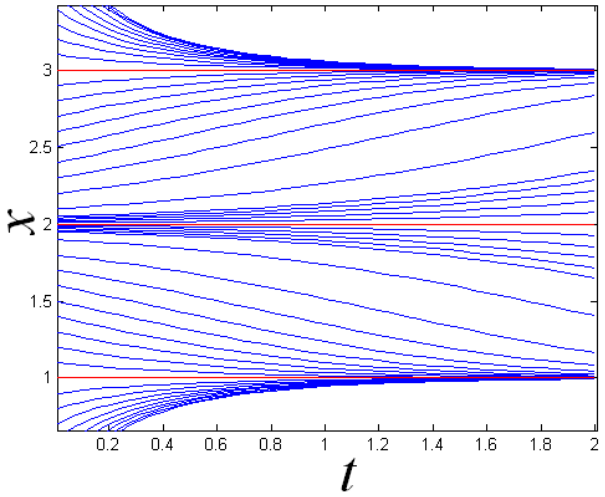
$$\frac{dx}{dt} = \tilde{k_1}x^2 + \tilde{k_4} - k_2x^3 - k_3x$$
$$= u(x) - d(x)$$



✓ Simple to analyze. Stable-Unstable-Stable.

But

- **Works 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 (KMC)

$$X \xrightarrow{U(X)} X+1 \qquad U(X) = \frac{k_1}{V} X(X-1) + k_4 V$$

$$X \xrightarrow{D(X)} X-1. \qquad D(X) = \frac{k_2}{V^2} X(X-1)(X-2) + k_3 X$$

- One-step Markov jump process.

- The *Master equation* for $P_n(t)=P\{X(t)=n\}$:

$$\frac{dP_n}{dt} = U(n-1)P_{n-1}(t) + D(n+1)P_{n+1}(t) - (U(n)+D(n))P_n(t)$$

Large volume regime

- Rescale the jump sizes and the rates.
- *Intensive variable* (concentration) $x=X/V=\varepsilon X$. $(\varepsilon=1/V)$.
- The Master Equation for $P_\varepsilon(x,t) = P\{X(t)=x/\varepsilon\}$

$$\partial_t P_\varepsilon(x,t)=\varepsilon^{-1}\,[u_\varepsilon(x-\varepsilon)\,P_\varepsilon(x-\varepsilon,t)-u_\varepsilon(x)\,P_\varepsilon(x,t)]+$$
$$+\varepsilon^{-1}[d_\varepsilon(x+\varepsilon)\,P_\varepsilon(x+\varepsilon,t)-d_\varepsilon(x)\,P_\varepsilon(x,t)]$$

where

$$u_\varepsilon(x)=u(x)+\varepsilon\,u_1(x)+O(\varepsilon^2) \quad \text{and} \quad d_\varepsilon(x)=d(x)+\varepsilon\,d_1(x)+O(\varepsilon^2)$$

- In our case:

$$u_\varepsilon(x) = k_1x(x-\varepsilon)+k_4 \qquad = (k_1x^2+k_4)-\varepsilon\,k_1x$$
$$d_\varepsilon(x) = k_2x(x-\varepsilon)(x-2\varepsilon)+k_3x = (k_2x^3+k_3x)-3\varepsilon\,k_2x^2+O(\varepsilon^2)$$

Small ε limits

- Expand the Master Equation:

$$\partial_t P(x,t)=\varepsilon^{-1}\,[u_\varepsilon(x-\varepsilon)\,P(x-\varepsilon,t)-u_\varepsilon(x)\,P(x,t)]+\varepsilon^{-1}[d_\varepsilon(x+\varepsilon)\,P(x+\varepsilon,t)-d_\varepsilon(x)\,P(x,t)]$$

$$= -\partial_x[(u(x)-d(x))P(x,t)]-\varepsilon\,\partial_x[(u_1(x)-d_1(x))P(x,t)]+\varepsilon\,\partial_{xx}[(u(x)+d(x))P(x,t)]/2+\ldots$$

- To $O(\varepsilon^0)$: $\partial_t P(x,t)= -\partial_x[(u(x)-d(x))P(x,t)]$.
  - ➢ Liouville equation, leads to the ODE for $x(t)$

$$\dot{x} = u(x) - d(x)$$

- To $O(\varepsilon^1)$:
  - ➢ Fokker-Planck equation, leads to the SDE for $x(t)$

$$dx = [u(x)-d(x)+\epsilon(u_1(x)-d_1(x))]dt+\sqrt{\epsilon(u(x)+d(x))}dW$$

❖ Only valid for up to moderate deviations, for fixed finite time intervals!

A bit of large deviations

- x_i i.i.d. with $E\, x_i = m$ and $E\, e^{\theta x_i} = M(\theta)$.
- Law of Large Numbers: $\dfrac{x_1 + \ldots + x_n}{n} \xrightarrow[n \to \infty]{} m$
- For $a > m$, $P(x_1 + \ldots + x_n \geq na) \to 0$ as $n \to \infty$.
- What is the rate of convergence?

$$P(x_1 + \ldots + x_n \geq na) = P(e^{\theta(x_1 + \ldots + x_n)} \geq e^{\theta n a}) \leq e^{-n\theta a}\, E\, e^{\theta(x_1 + \ldots x_n)} =$$
$$= e^{-n\theta a}\, M(\theta)^n = \exp[-n(\theta a - \log M(\theta))]. \qquad \text{All } \theta !$$

- The action (rate) function: $\phi(a) = \sup_\theta \{\theta a - \log M(\theta)\}$.
- Thm: The bound is sharp as $n \to \infty$

$$\log P(x_1 + \ldots + x_n \geq na) \sim -n\phi(a) \text{ as } n \to \infty$$

Back to the Master Equation

$$\partial_t P(x,t)=\varepsilon^{-1}\,[u_\varepsilon(x-\varepsilon)\,P(x-\varepsilon,t)-u_\varepsilon(x)\,P(x,t)]+\varepsilon^{-1}[d_\varepsilon(x+\varepsilon)\,P(x+\varepsilon,t)-d_\varepsilon(x)\,P(x,t)]$$

Rare event (large deviation) ansatz: $P(x,t) = e^{-\phi(x,t)/\varepsilon}$.

- The same ε !!

$$-\varepsilon^{-1}e^{-\phi(x)/\varepsilon}\,\phi_t = \varepsilon^{-1}(u(x)+O(\varepsilon))(e^{-\phi(x-\varepsilon)/\varepsilon}-e^{-\phi(x)/\varepsilon})+\varepsilon^{-1}(d(x)+O(\varepsilon))(e^{-\phi(x+\varepsilon)/\varepsilon}-e^{-\phi(x)/\varepsilon}).$$

leads to $$\phi_t+u(x)(e^{\phi_x}-1)+d(x)(e^{-\phi_x}-1)=0.$$

While the Fokker-Planck equation (SDE)

$$P_t=-[(u_\varepsilon(x)-d_\varepsilon(x))\,P]_x+\varepsilon\,[(u_\varepsilon(x)+d_\varepsilon(x))\,P]_{xx}/2$$ with $P(x,t) = e^{-\phi(x,t)/\varepsilon}$ ansatz

implies $$\phi_t+[u(x)-d(x)]\phi_x+[u(x)+d(x)]^2\,(\phi_x)^2/2=0.$$

Why ε ?

Why $e^{-\phi(x,t)/\varepsilon}$?

Use $P(x,t) = e^{-\phi(x,t)/\delta}$ for $1 \gg \delta \gg \varepsilon$.

Think of $\delta = \varepsilon^{\alpha}$ for $0 < \alpha < 1$. Moderate deviations.

Then both the Master Equation and the Fokker-Planck Equation lead to:

$$\phi_t + (u(x) - d(x))\phi_x + \frac{\epsilon}{\delta}\frac{u(x)+d(x)}{2}\phi_x^2 + o(\tfrac{\epsilon}{\delta}) = 0.$$

✓ FPE valid only for up to moderate deviations $e^{-\phi(x,t)/\delta}$,
NOT for large deviations $e^{-\phi(x,t)/\varepsilon}$!

Solving for $\phi(x,t)$

- Back to the ansatz $P(x,t)=e^{-\phi(x,t)/\varepsilon}$.
- Plug into the Master Equation to obtain

$$\phi_t + u(x)(e^{\phi_x}-1)+d(x)(e^{-\phi_x}-1)=0.$$

- Hamilton-Jacobi form $\phi_t+H(x,\phi_x)=0$.
- Read off the Hamiltonian $H(x,p)=u(x)(e^{p}-1)+d(x)(e^{-p}-1)$,

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

- Along the Hamiltonian paths

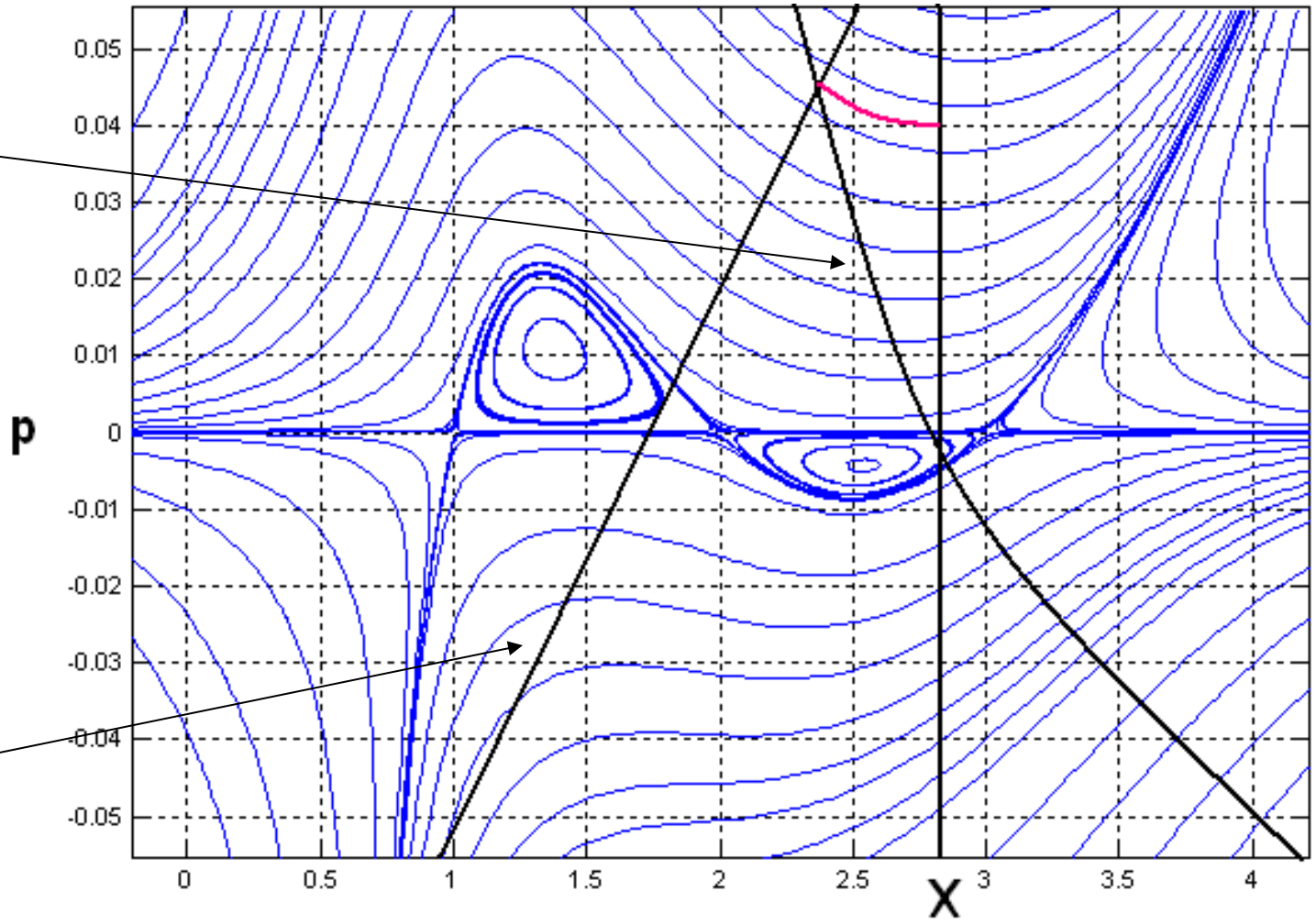
$$\frac{d\phi}{dt} = \phi_t+\phi_x\frac{dx}{dt} = -H(x,p)+p\frac{dx}{dt} = L\left(x, \frac{dx}{dt}(x,p)\right) =$$
$$= u(x)(pe^{p} - e^{p} + 1) - d(x)(pe^{-p} + e^{-p} - 1).$$

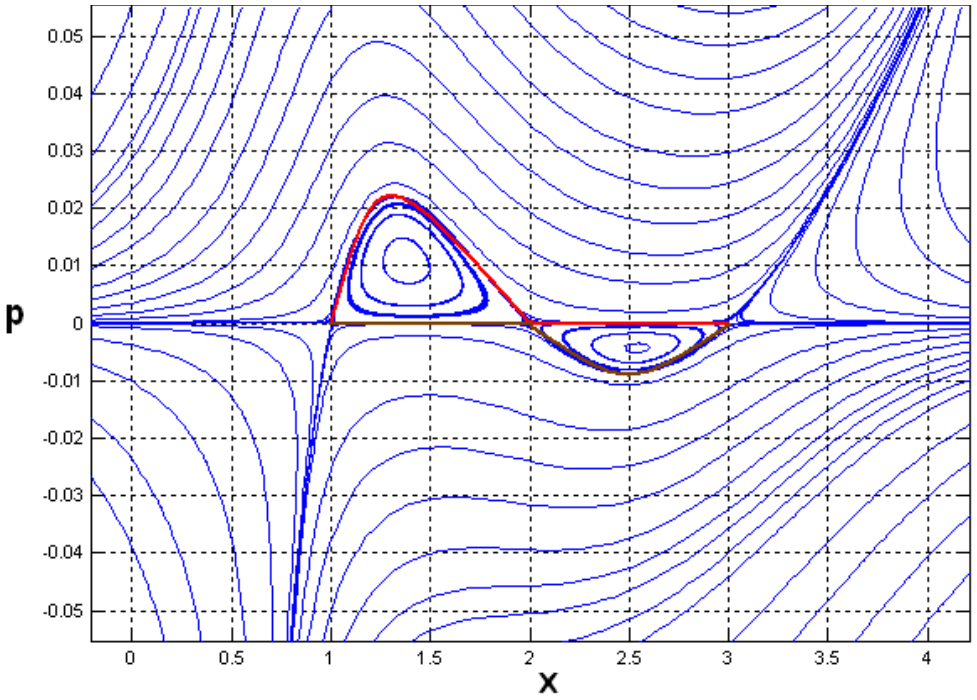
- By Hamilton's principle:

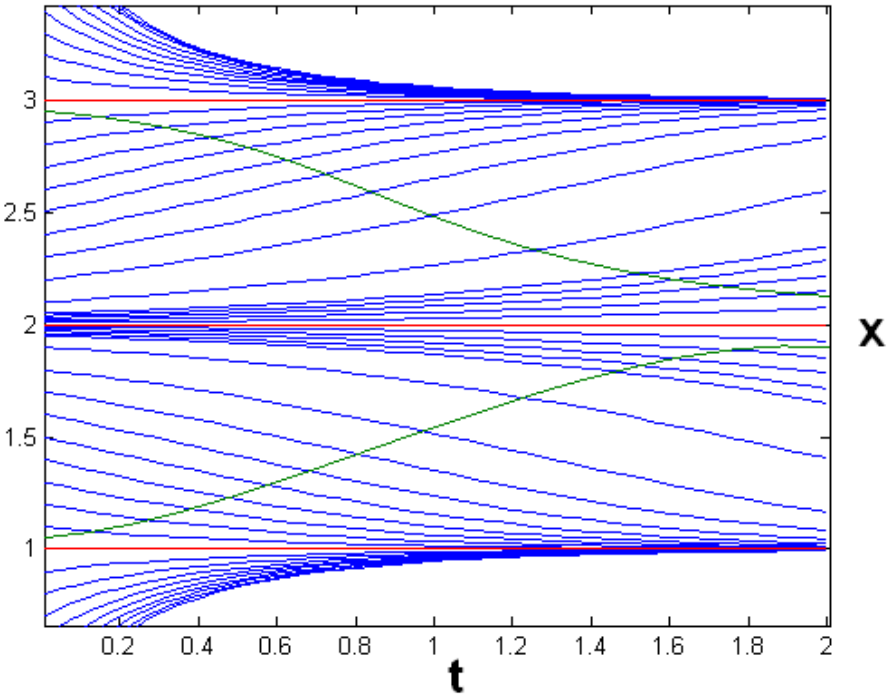
$$\phi(x,t) = \min\{\int_0^t L(x, \frac{dx}{ds})ds : x(0) = x_0,\ x(t) = x\}$$

Trace backward the line $x=X$ by time T

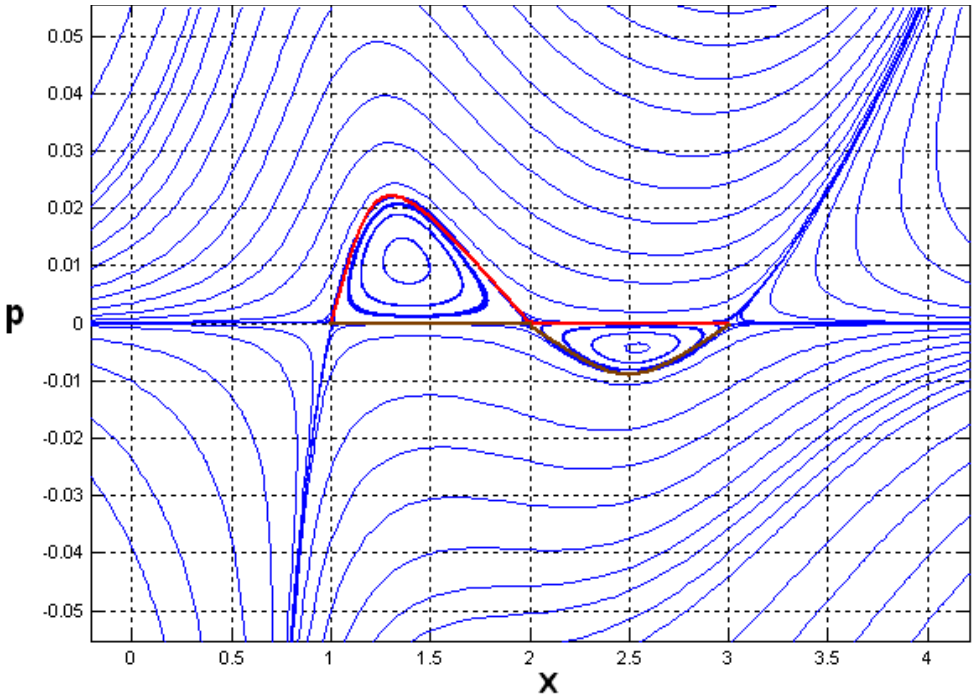
$p=\phi_0'(x)$

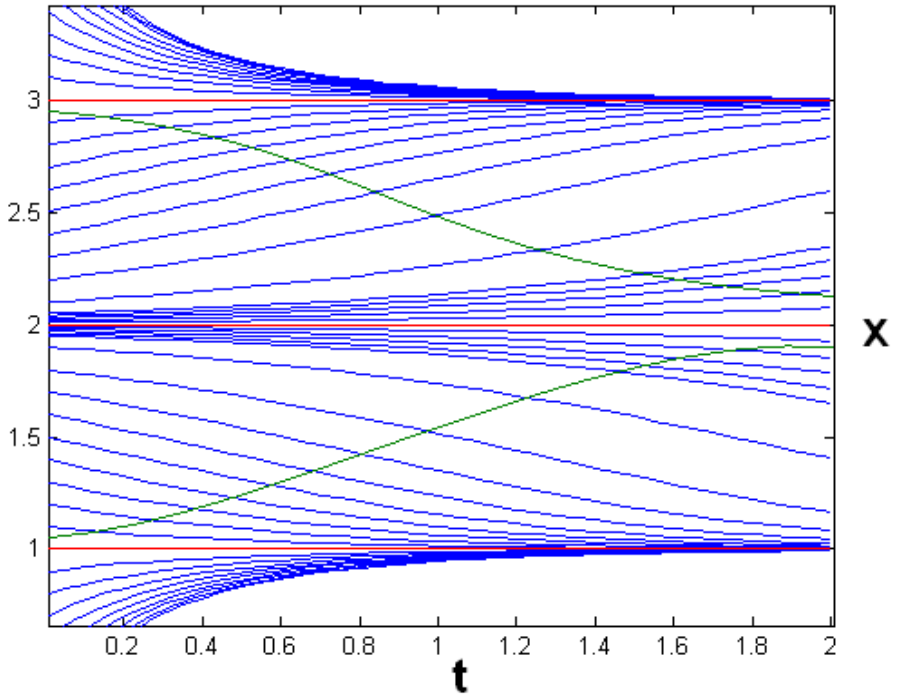






- Rare events correspond to the heteroclinic connections.
  - They satisfy $H(x,p)=u(x)(e^{p}-1)+d(x)(e^{-p}-1)=0$.
    - Hence $p=0$ or $p=\log(d(x)/u(x))$.
    - The action functions along these paths are $\phi(x,t)=\int(p\,x^{0}-H)dt=\int p\,dx$
- The deterministic paths are the ones with $p=0$.
  - $\frac{dx}{dt}=\frac{\partial H}{\partial p}=u(x)-d(x).$





- Back to the question: which one is "more stable" ?
  - Compare the mean first passage times T_{13} and T_{31}.

o Use the correct expansion of backward equations, the analysis is the same.

o There are paths of <u>finite action</u> both from 1 to 3 and vice versa.

- Jumps not allowed by the deterministic description.
- Allowed by FPE, <u>but</u> with wrong mean first passage times.

o The rates k_i may be tuned to achieve $T_{13}=T_{31}$.

Conclusions

- Stochastic Differential Equation or Fokker-Planck Equation are not always good enough approximations of a Markov jump process!
  - ➢ if we are interested in rare events.
    - ✓ Expand the exponent of a function, not the function itself!
- The action for a large deviation event allows classical mechanics interpretation.
  - ➢ in fact, it satisfies Hamilton-Jacobi equation.
- Naturally, one stable state is more stable than the other.
  - ➢ mean times of jumps from one to the other can be calculated by the correct expansion of the backward equations.

Future work:

- Multiple dimensions
- Multiple time scales

Acknowledgements

- Eric Vanden-Eijnden
- Charlie Doering
- All the GFD Fellows and Staff



LD Theorem for Markov jump processes

$$\lim_{\varepsilon \to 0} \varepsilon \log P\{x(t) \in F[0,T] \mid X(0)=x\} =$$

$$= -\inf\{I_{0T}(r) : r \in F[0,T],\ r(0)=x\}$$

where $I_{0T}(r)=\int_0^T l(r(s), r^0(s))\, ds,$

$l(x,x^0)=\sup_\theta \{\theta x^0 - h(x,\theta)\},$

$h(x,\theta)=\log M(x,\theta)=u(x)(e^{\theta}-1)+d(x)(e^{-\theta}-1).$

$F[0,T]$ is any set of right continuous functions.

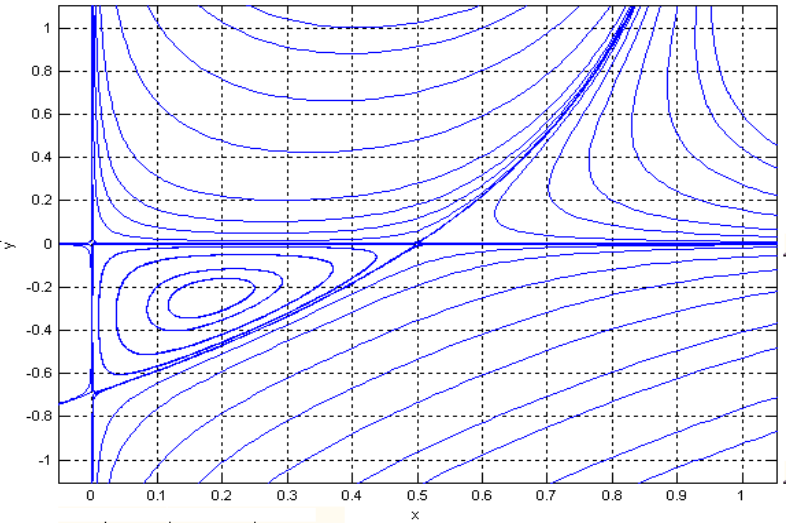
Another simple model

- Susceptible-Infected-Susceptible

  $I \to I+1$ with rate $\Lambda\, I\, S$

  $I \to I\text{-}1$ with rate I

- The deterministic version: $\frac{dx}{dt} = \Lambda x(1-x) - x$
- Absorbing state, x=0.
- Stable equilibrium, if $\Lambda > 1$.
- Infinite action for paths from the absorbing state.





• In our case
(in fact, for all one-step Markov jump processes):

$$L\left(x, \frac{dx}{dt}\right) = \frac{dx}{dt} \log \frac{\frac{dx}{dt} + \sqrt{\left(\frac{dx}{dt}\right)^2 + 4u(x)d(x)}}{2u(x)} +$$

$$+ u(x) + d(x) - \sqrt{\left(\frac{dx}{dt}\right)^2 + 4u(x)d(x)}.$$