Rare Event in Stochastic Systems

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Outline for Section 1

Historical Background

Escape rate (Hoff and Arrhenius):

$$k = \nu \exp\left(-\frac{1}{k_B T} E\right) = \nu \exp\left(-\beta E\right) \tag{1}$$

where ν is the prefactor, k_B is the Boltzmann constant, T is the temperature and E is the energy barrier, $\beta = \frac{1}{k_B T}$[1].

[1] Hänggi et al. (1990).

Mean transition time:

$$\bar{t} \propto \frac{1}{k} \propto \exp\left(\frac{1}{k_B T} E\right), \tag{2}$$

which is exponentially large at small T (e.g. let $T \to 0^+$).

Rare event

The extremely low probability and long transition time of events is where the term *rare event* comes from.

Meaning

Rare event has little probability of occurrence, but it has large impact once it happens. For instance,

1. formation of cancer;
2. virus spreading;
3. system failure, e.g. breaking down of materials;
4. many others...

Therefore, one of the meanings of studying rare events is perhaps to understand the mechanics of dynamical systems so as to control risk.

Challenges

1. Complex dynamical system such as protein folding process[2];
2. High degree of freedom;
3. Expensive computational cost in direct simulation, even for small systems.

[2] Noé et al. (2009).

List of Methods

1. Transition State Theory (TST): classical method;
2. Large Deviation Principle (LDP): consider the vanishing noise case[3];
3. Transition Path Sampling (TPS);
4. Transition Path Theory (TPT): study statistics of ensemble reactive trajectories;
5. et al...

[3] Freidlin and Wentzell (2012).

Transition Problem

For an ergodic stochastic dynamical system $\{X_t\}_{t\in T}$ on state space S, we prescribe two disjoint subsets A and B of S:

- set A is the set where transition starts;
- set B is the set where transition ends.

In applications:

- (chemical kinetics): A is the reactant state, B is the product state;
- (biology): A is the health state, B is the body condition with cancer;
- (system control): A is the normal state, B is the failure state;
- et al...

Transition Problem

Definition (Reactive trajectory)

Reactive trajectory is a path starts from A directly to B without returning to A first.

For instance, state space $S = \{1, 2, 3, 4\}$, $A = \{1\}$, $B = \{4\}$, then

- $1 \to 2 \to 4$ is a reactive trajectory;
- $1 \to 2 \to 1 \to 2 \to 4$ is not.

Transition Problem

Here is a list of questions of interest:

1. What is the transition rate k^{AB}?
2. What is the most probable exit point in set A and what is the most probable entering point in set B?
3. How to get insight into transition mechanics?
4. Which is the path that dominates among all the transition paths, i.e. Most Probable Exit Path (MPEP)?

Outline for Section 2

Introduction of TPT

1. Firstly proposed by E and vanden Eijnden (2006);
2. Studying object: transition in ergodic stochastic dynamical system;
3. Assumption: ergodicity and strong Markov property in the system;
4. Advantage: no assumption on time-reversibility (sometimes called detailed balance); no assumption on the structure of set A and B.

Frontier Application

1. Lennard-Jones cluster LJ_{38}[4];
2. Conformation changes in trialanine[5];
3. Protein folding process[6];
4. many others...

[4] Cameron and Vanden-Eijnden (2014).
[5] Metzner et al. (2009).
[6] Noé et al. (2009).

General Definitions

Definition (Hitting time)

1. If $T = \mathbb{R}$, define hitting times as follow:

$$t^{AB,+}(t) := \inf\{s \geq t : X_s \in A \cup B\},$$
$$t^{AB,-}(t) := \sup\{s \leq t : X_s \in A \cup B\}.$$

2. If $T = \mathbb{Z}$, define hitting times as follow:

$$t^{AB,+}(n) := \inf\{m \geq n : X_m \in A \cup B\},$$
$$t^{AB,-}(n) := \sup\{m \leq n : X_m \in A \cup B\}.$$

Committor Functions

Definition (Forward committor functions $q^+(x)$)

The forward committor function $S \to [0,1]$, is defined as the probability of going to set B before reaching set A:

$$q^+(x) := \mathbb{P}_x[X_{t^{AB,+}(0)} \in B].$$

Definition (Backward committor function $q^-(x)$)

The backward committor function $S \to [0,1]$, is defined as the probability of coming from set A instead of set B:

$$q^-(x) := \mathbb{P}_x[X_{t^{AB,-}(0)} \in A].$$

Diffusion Process

We consider the following stochastic differential equation:

$$\dot{X}_t = b(X_t) + \sqrt{2D(X_t)}dW_t \tag{3}$$

where $X_t \in \mathbb{R}^d$, drift term $b : \mathbb{R}^d \to \mathbb{R}^d$, diffusion tensor $D : \mathbb{R}^d \to \mathbb{R}^d \times \mathbb{R}^d$, W_t is the Weiner process (Brownian motion).

Diffusion Process

The forward infinitesimal generator $\mathcal{L}$ takes the form of

$$\mathcal{L}f = b \cdot \nabla f + a : \nabla\nabla f, \tag{4}$$

and the generator for time-reversed process takes the form of

$$\begin{aligned}\mathcal{L}^- f = &-b \cdot \nabla f + \frac{2}{m}\mathrm{div}(am) \cdot \nabla f \\ &+ a : \nabla\nabla f.\end{aligned} \tag{5}$$

where $a := \sqrt{D}\sqrt{D}^T$ and m is the probability density at equilibrium.

Probability Density at Equilibrium and Probability Current

Fokker-Planck equation gives:

$$\frac{\partial}{\partial t}p(x,t) = -\nabla \cdot (b(x)p(x,t) - \text{div}(a(x)p(x,t))). \tag{6}$$

Definition (Probability current)

Probability current $J(x,t) := b(x)p(x,t) - \text{div}(a(x)p(x,t))$.

The probability density function at equilibrium $m(x)$ satisfies:

$$0 = -\nabla \cdot (b(x)m(x) - \text{div}(a(x)m(x))). \tag{7}$$

Reactive Trajectories

We want to extract all the reactive trajectories for a sample path $\omega \in \Omega$, stored in terms of their first exit time in A, denoted by t_n^A and first passage time to B, denoted by t_n^B.

Definition (Ensemble of Reactive Trajectory)

The set of reactive trajectories is described by $R := \cup_{n\in\mathbb{Z}}(t_n^A, t_n^B)$.

Define

$$\mathbf{1}_R(t) := \mathbf{1}_A(X_{t^{AB,-}(t)})\mathbf{1}_B(X_{t^{AB,+}(t)}),$$

which describes whether the system is in the process of transition.

Committor Functions

Committor functions satisfy the *backward Kolmogorov equation*:

$$\begin{cases} \mathcal{L}q^+(x) = 0 \\ q^+(x)\,|_{x\in A} = 0 \quad q^+(x)\,|_{x\in B} = 1 \end{cases} \tag{8}$$

and

$$\begin{cases} \mathcal{L}^- q^-(x) = 0 \\ q^-(x)\,|_{x\in A} = 1 \quad q^-(x)\,|_{x\in B} = 0 \end{cases} \tag{9}$$

The Distribution of Reactive Trajectories

The probability density $m^{AB}(x)$, which serves as the measure of distribution of reactive trajectories, satisfies:

$$m^{AB}(x) = q^{+}(x)q^{-}(x)m(x)/Z^{AB}, \tag{10}$$

where Z^{AB} is the factor for normalization.

Reactive Probability Flux

We want to find $J^{AB}(x)$ so that for any surface $E \subset S \setminus (A \cup B)$ (its enclosed space is E_a)

$$\int_E J^{AB}(x) \cdot \hat{n}(x)\, d\sigma(x) = \lim_{s\to 0} \frac{1}{s} \lim_{T\to\infty} \frac{1}{2T} \int_{-T}^{T} [\mathbf{1}_{E_a}(X(t))\mathbf{1}_{S\setminus E_a}(X(t+s)) - \mathbf{1}_{S\setminus E_a}(X(t))\mathbf{1}_{E_a}(X(t+s))]\mathbf{1}_R(t)\, dt. \tag{11}$$

Under ergodicity and strong Markov property, we can derive that

$$J^{AB} = q^- q^+ J + q^- ma\nabla q^+ - q^+ ma\nabla q^-. \tag{12}$$

Transition Rate and Mean Transition Time

For any surface $E \subset S \setminus (A \cup B)$,

$$k^{AB} = \int_E J^{AB}(x) \cdot \hat{n}(x)\, d\sigma(x), \tag{13}$$

which is the same for any E, due to the fact that $\nabla \cdot J^{AB}(x) = 0$ for $x \notin A \cup B$.

Mean transition time

$$\bar{t}^{AB} := \lim_{T\to\infty} \frac{1}{N_T} \int_{-T}^{T} \mathbf{1}_{S\setminus(A\cup B)}(X(t))\mathbf{1}_R(t)\, dt = \frac{Z^{AB}}{k^{AB}}, \tag{14}$$

where N_T means the number of reactive trajectories in time period $[-T, T]$.

Most Probable Exit and Entering Position

Most probable exit position in set A, denoted by x_1^*, is defined by

$$x_1^* := \arg\max_{x \in A} J^{AB}(x) \cdot \hat{n}(x).$$

Here $\hat{n}(x)$ is pointing outward of ∂A.

Most probable entering position in set B, denoted by x_2^*, is defined by

$$x_2^* := \arg\max_{x \in B} J^{AB}(x) \cdot \hat{n}(x).$$

Here $\hat{n}(x)$ is pointing inward of ∂B.

Markov Chain

We shall consider an ergodic Markov Chain.

- Without loss of generality, we might as well let $S = \mathbb{N}^+$.
- The time parameter $T = \mathbb{Z}$.
- The one-step transition matrix is denoted by P.
- Infinitesimal generator $\mathcal{L} := P - I$.
- The generator for reversed process is denoted by $\mathcal{L}^-$, which has the form of

$$\mathcal{L}^-_{ij} = \frac{\pi_j}{\pi_i}\mathcal{L}_{ji}. \tag{15}$$

Reactive Trajectories

Similarly, define the collection of reactive trajectories R by

$$R := \cup_{n\in\mathbb{Z}}[t_n^A, t_n^B],$$

where sample path X_n is in the process of A-B transition iff $t_n^A \leq n \leq t_n^B$.

Similarly, define $\mathbf{1}_R(n) := \mathbf{1}_A(X_{t^{AB,-}(n)})\mathbf{1}_B(X_{t^{AB,+}(n+1)})$.

Committor Functions

For forward committor function $q^+(x)$, $q_i^+ := q^+(i) = 1$ if $i \in B$; $q_i^+ = 0$ if $i \in A$. For $i \notin A \cup B$,

$$(\mathcal{L}q^+)_i = \sum_{j \in S} \mathcal{L}_{ij} q_j^+ = 0. \tag{16}$$

For backward committor function q^-, $q_i^- := q^-(i) = 1$ if $i \in A$; $q_i^- = 0$ if $i \in B$. For $i \notin (A \cup B)$,

$$(\mathcal{L}^- q^-)_i = \sum_{j \in S} \mathcal{L}_{ij}^- q_j^- = 0. \tag{17}$$

Probability Distribution of Reactive Trajectories

The probability distribution of reactive trajectories, defined on space $S \setminus (A \cup B)$, is denoted by $m^{AB}(\cdot)$. It takes the following form after derivation:

$$m^{AB}(i) = q_i^- \pi_i q_i^+ / Z^{AB}, \qquad \forall i \in S \setminus (A \cup B), \tag{18}$$

where $Z^{AB} := \sum_{i \in S} q_i^- \pi_i q_i^+ < 1$.

Reactive Probability Current

Reactive probability current, denoted by J_{ij}^{AB}, is introduced to depict the contribution of jump between any two states i and j to the whole reactive trajectories: for $i \neq j$,

$$\begin{aligned} J_{ij}^{AB} = J^{AB}(i,j) &:= \lim_{T\to\infty} \frac{1}{2T+1} \sum_{n=-T}^{T} \mathbf{1}_{\{i\}}(X_n)\mathbf{1}_{\{j\}}(X_{n+1})\mathbf{1}_R(n) \\ &= q_i^- \pi_i P_{ij} q_j^+ = q_i^- \pi_i L_{ij} q_j^+. \end{aligned} \tag{19}$$

Set $J_{ii}^{AB} = 0, \ \forall i \in S$.

Transition Rate and Mean Transition Time

The transition rate k^{AB} is the frequency of occurrence of complete transition from set A to B,

$$\begin{aligned} k^{AB} &:= \lim_{T\to\infty} \frac{1}{2T+1} \sum_{n=-T}^{T} \mathbf{1}_A(X_n)\mathbf{1}_{S\setminus A}(X_{n+1})\mathbf{1}_R(n) \\ &= \sum_{i\in A, j\notin A} J_{ij}^{AB} = \sum_{i\in A, j\in S} J_{ij}^{AB}, \end{aligned} \tag{20}$$

Similarly, we might derive that the mean transition time $\bar{t}^{AB}$ is

$$\bar{t}^{AB} = 1 + \frac{Z^{AB}}{k^{AB}}. \tag{21}$$

Most Probable Exit and Entering Position

In Markov chain, the most probable exit position i^* in set A could be defined as the position, out of which the total reactive probability current achieves the maximum value among all:

$$i^* = \arg\max_{i\in A} \lim_{T\to\infty} \frac{1}{2T+1} \sum_{n=-T}^{T} \mathbf{1}_{\{i\}}(X_n)\mathbf{1}_R(n)$$
$$= \arg\max_{i\in A} \sum_{j\in S} J_{ij}^{AB}.$$

Similarly, the most probable entering position j^* into set B is

$$j^* = \arg\max_{j\in B} \sum_{i\in S} J_{ij}^{AB}.$$

Representative Dominant Transition Path

In the paper written by Metzner et al. (2009), representative dominant transition path is proposed as the path through which the reactive probability current achieves the maximum value among all.

From network flow J^{AB}, we could generate another network representing its net flow: the effective probability current J_{ij}^{+} is defined as

$$J_{ij}^{+} := \max(J_{ij}^{AB} - J_{ji}^{AB}, 0). \tag{22}$$

The capacity of a path $\varphi = (\varphi_0, \varphi_1, \cdots, \varphi_n)$ is limited by the weight of its bottleneck, which is defined as

$$(b_1, b_2) = \arg \min_{e=(i,j)\in\varphi} J_{ij}^{+}. \tag{23}$$

Definition (Representative dominant transition path (informal))

Representative dominant transition path is defined as the simple A-B transition path whose bottleneck has the highest weight.

Outline for Section 3

Double-well Potential

Let $b(x) = -\nabla V(x)$ and $D = \sigma^2 I$, where
$V(x) = V(x_1, x_2) = \frac{5}{2}(x_1^2 - 1)^2 + 5x_2^2$ and I is the identity matrix.

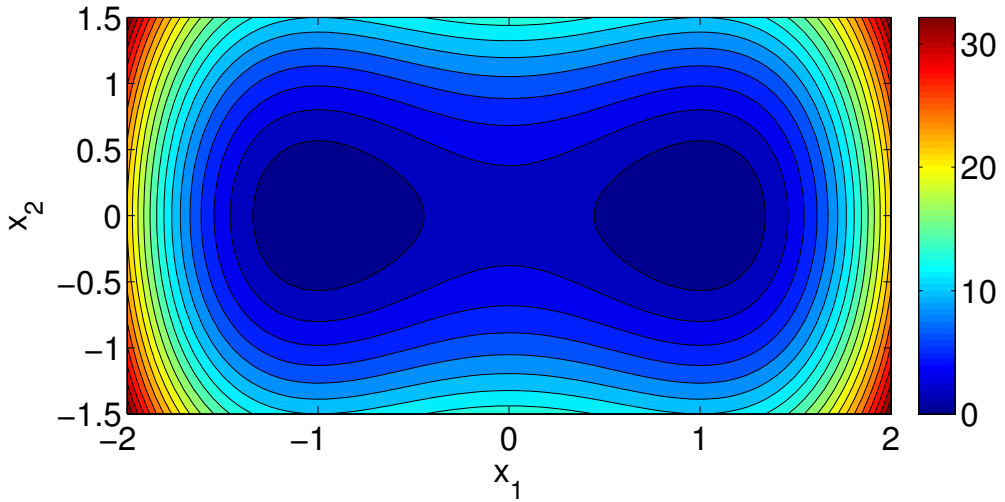


Figure: Potential $V(x_1, x_2)$.

There are two local minima $(\pm 1, 0)$ and a saddle point $(0, 0)$.

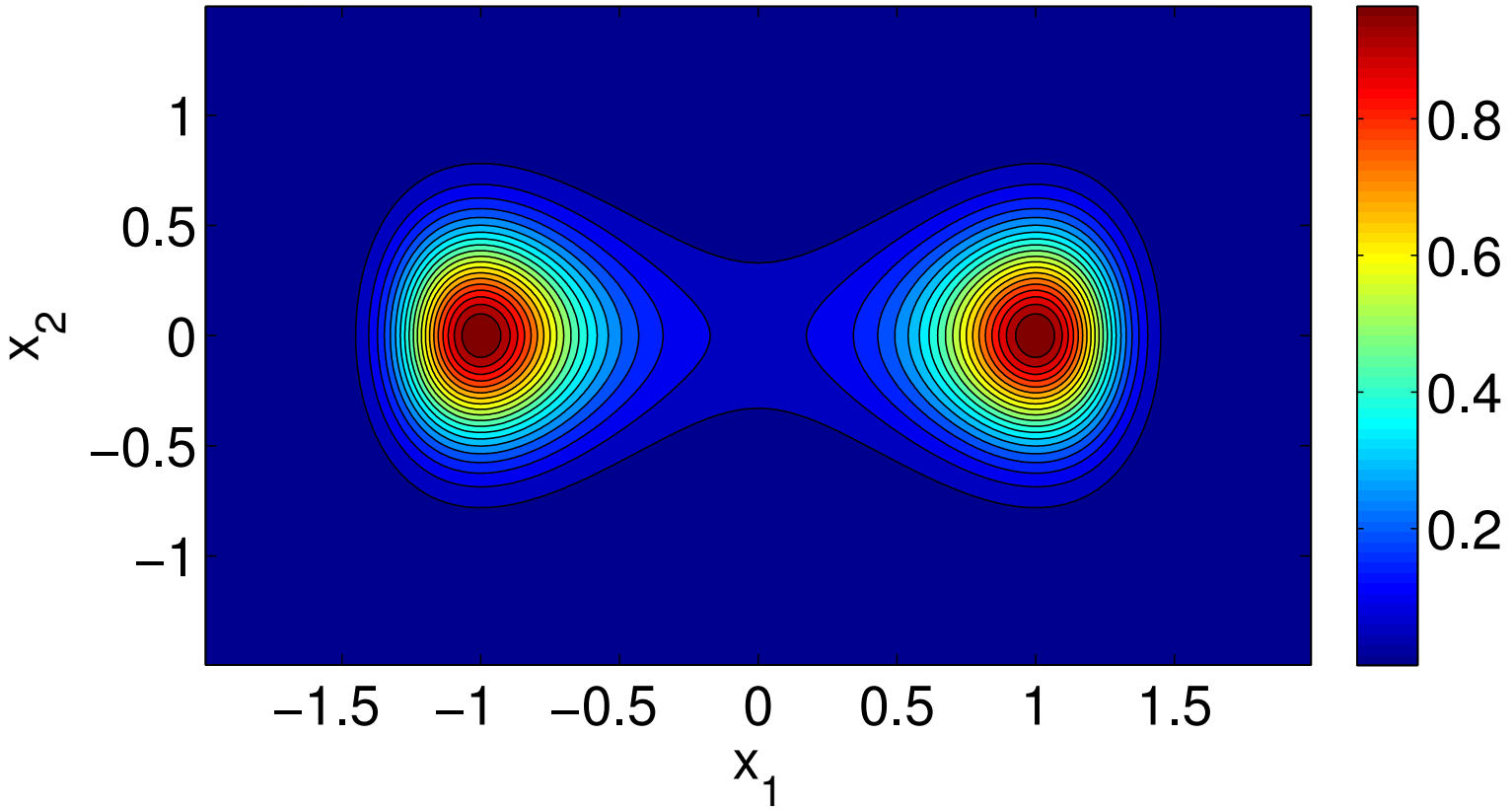
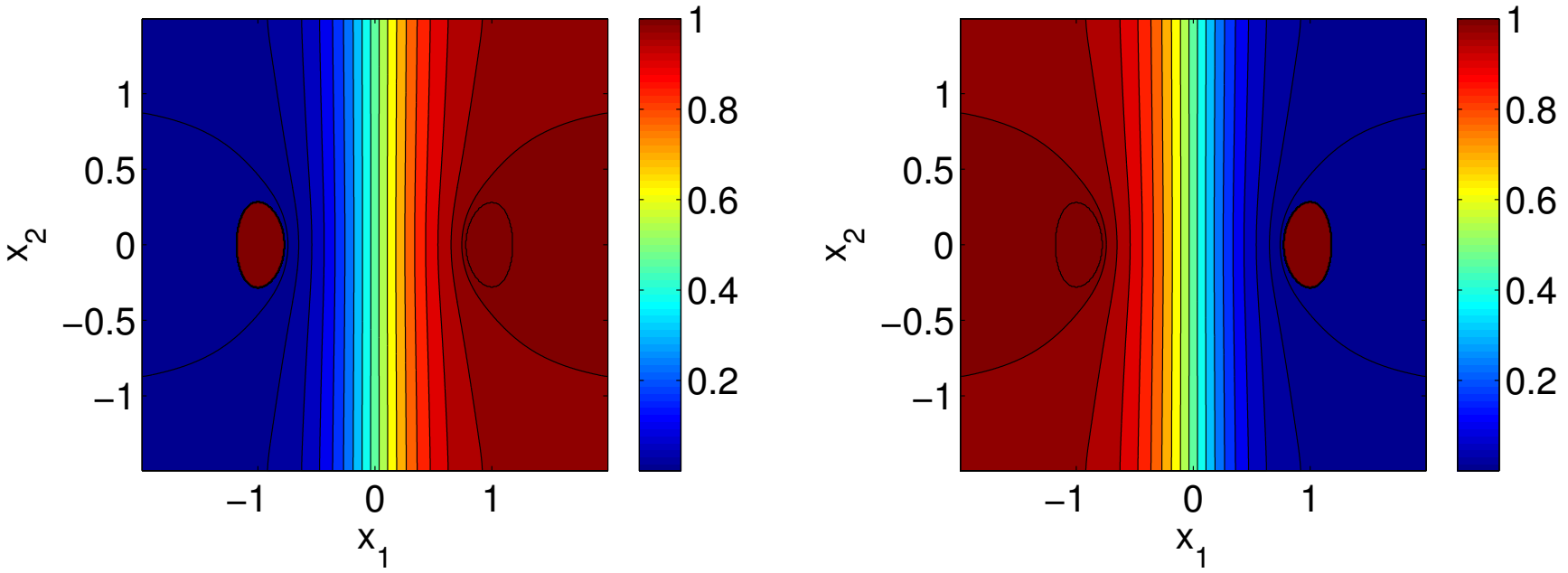


Figure: Probability density $m(x)$ at equilibrium.



(a) Forward committor function q^+. (b) Backward committor function q^-.

Figure: Committor functions.

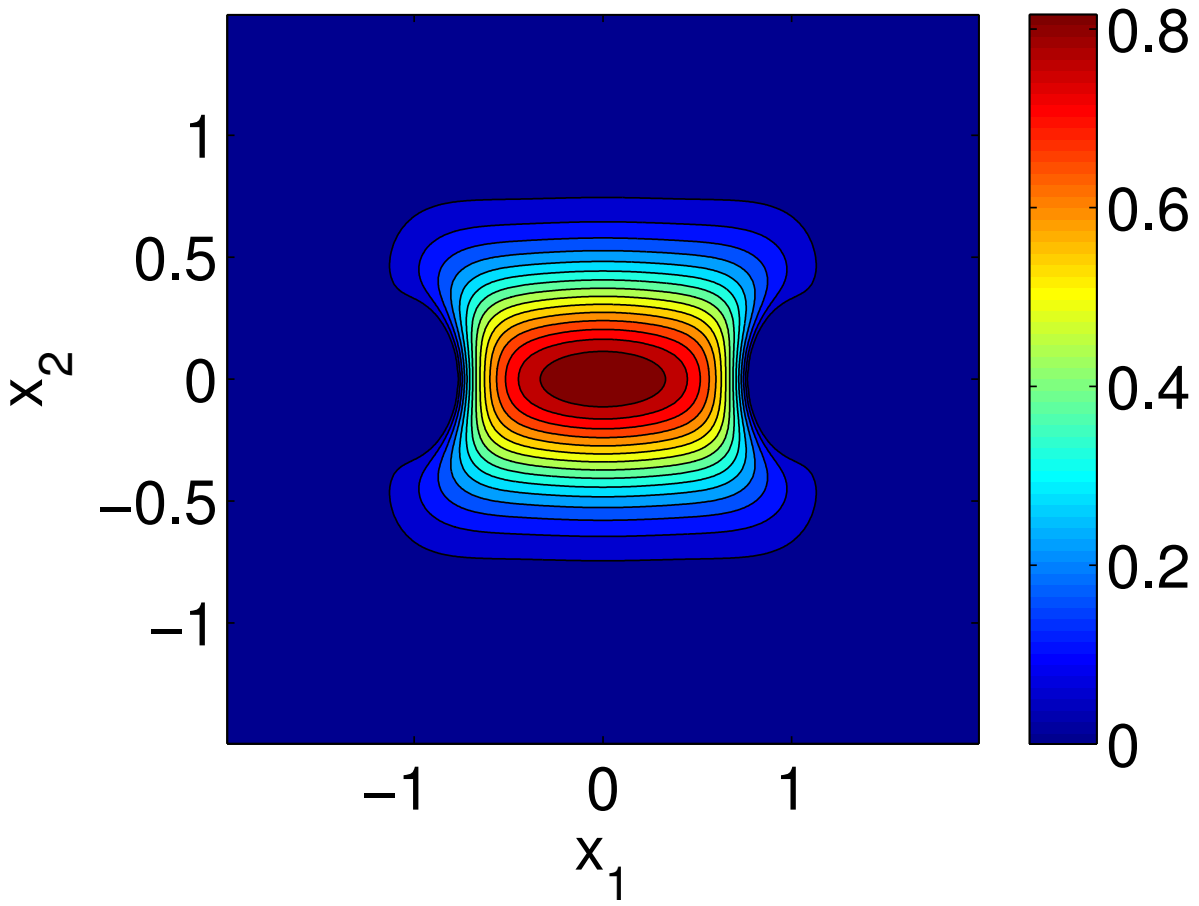


Figure: Probability density of reactive trajectories $m^{AB}(x)$.

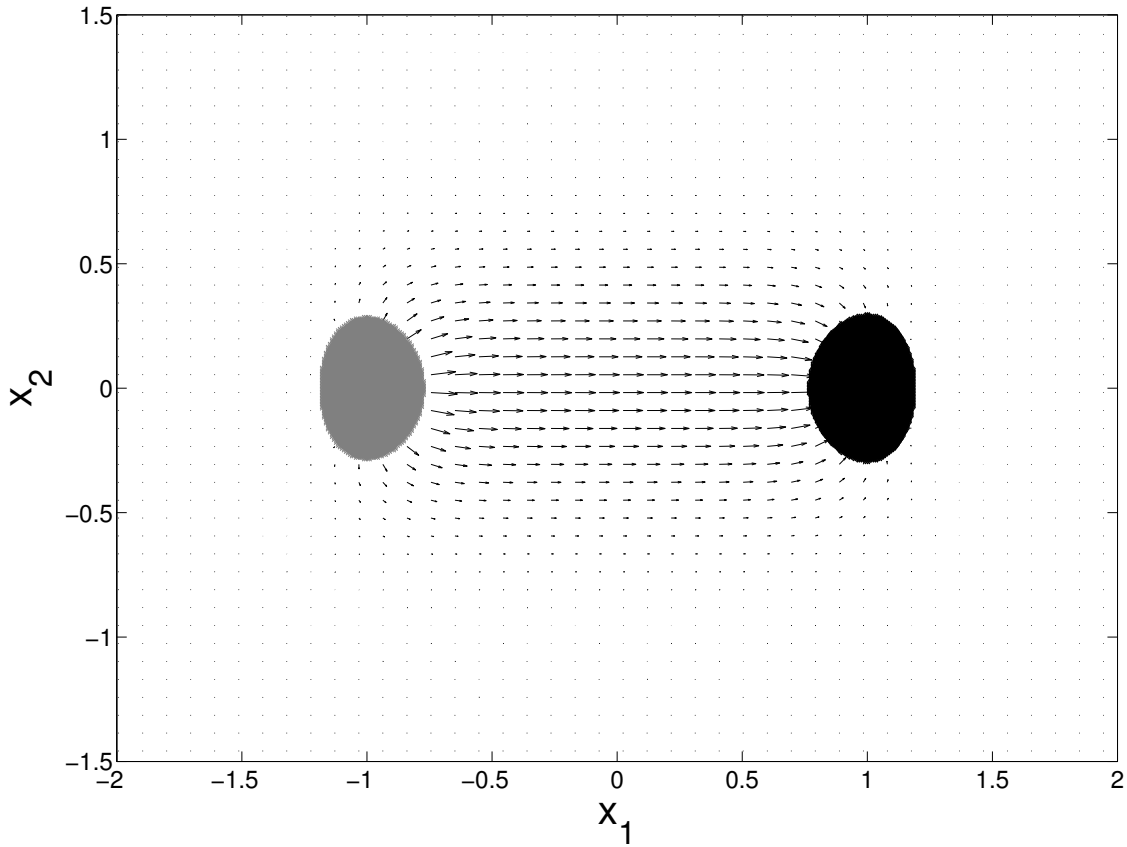


Figure: The vector field J^{AB}. Set A is colored in gray; set B is colored in black.

Triple-well Potential

Change $b(x)$ to be $-\nabla V(x)$ where

$$\begin{aligned} V(x_1, x_2) = & 3\exp\left(-x_1^2 - (x_2 - 1/3)^2\right) - 3\exp\left(-x_1^2 - (x_2 - 5/3)^2\right) \\ & - 5\exp\left(-(x_1 - 1)^2 - x_2^2\right) - 5\exp\left(-(x_1 + 1)^2 - x_2^2\right) \\ & + 0.2x_1^4 + 0.2(x_2 - 1/3)^4. \end{aligned}$$

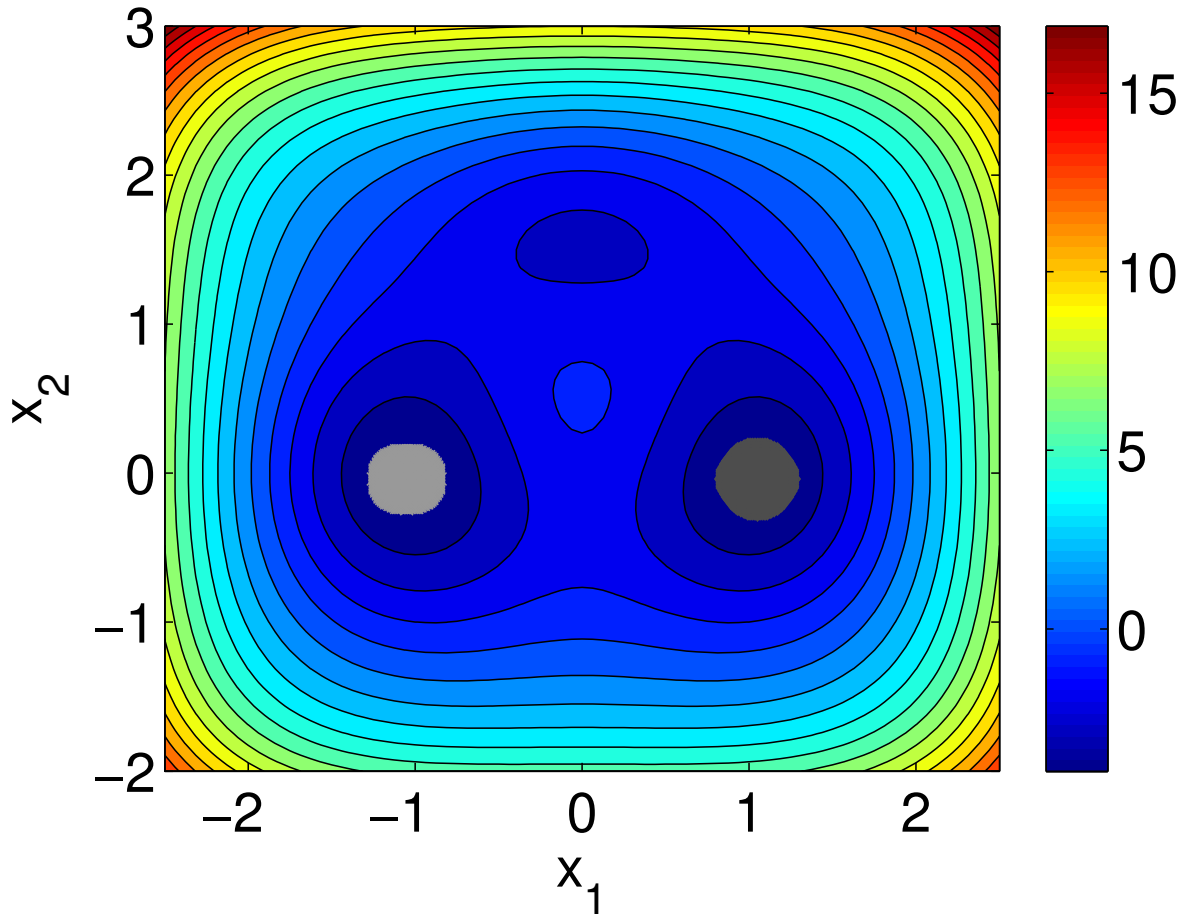
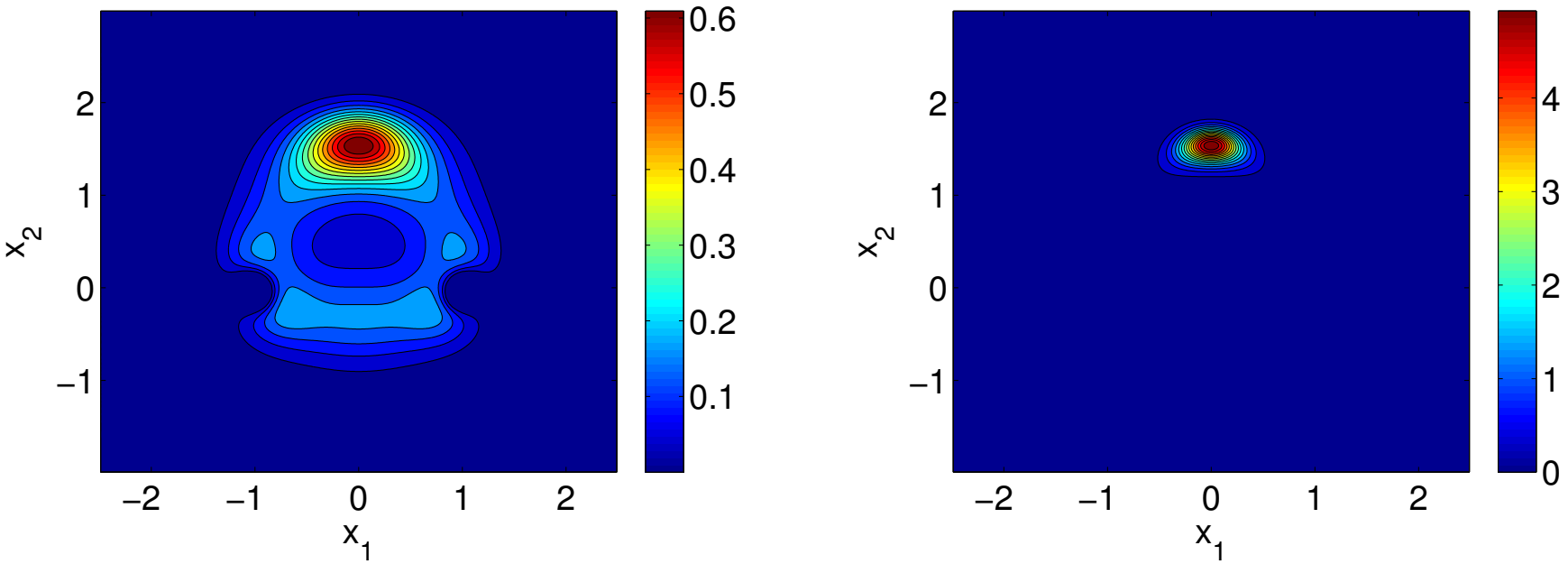


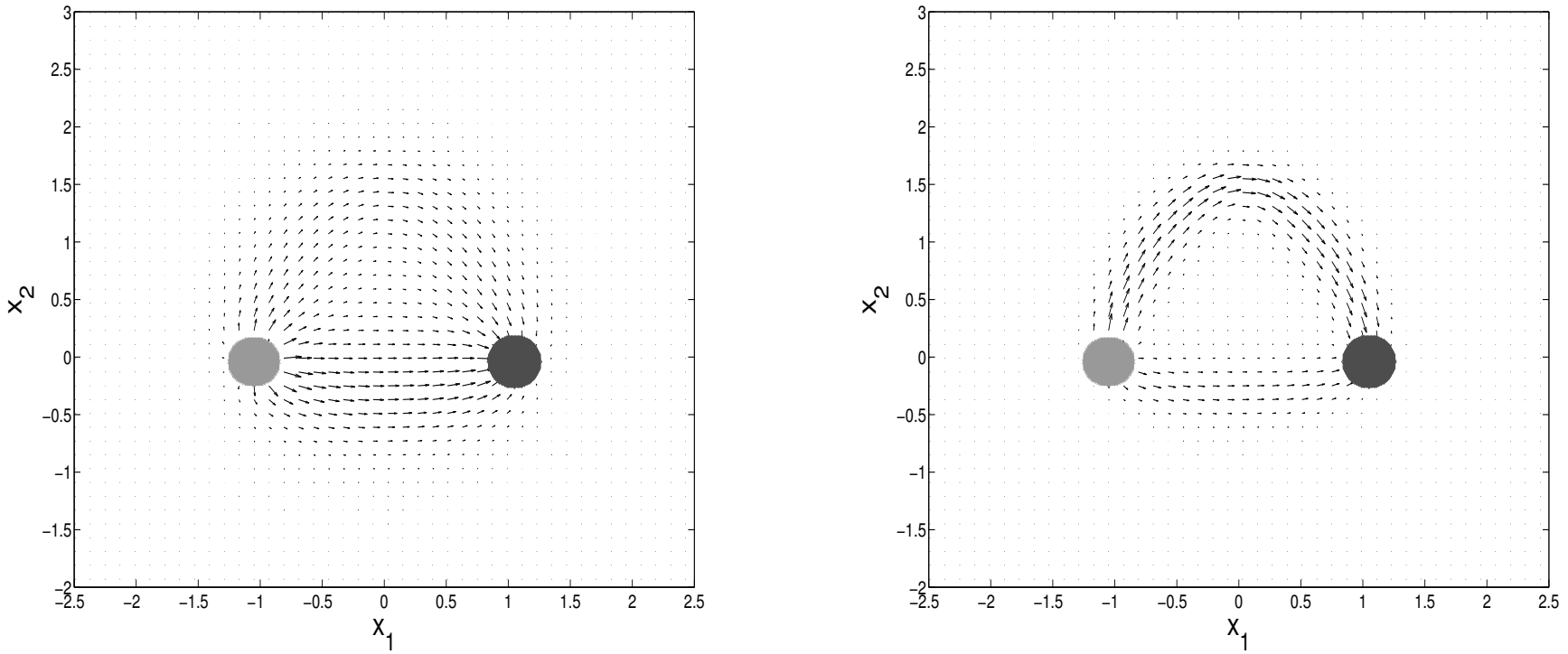
Figure: Potential $V(x_1, x_2)$. Set A is colored in light gray, set B in dark gray.



(a) $\sigma = 1/\sqrt{1.67}$.

(b) $\sigma = 1/\sqrt{6.67}$.

Figure: Probability density of reactive trajectories $m^{AB}(x)$ under different noise σ.



(a) $\sigma = 1/\sqrt{1.67}$.

(b) $\sigma = 1/\sqrt{6.67}$.

Figure: Probability flux $J^{AB}(x)$ under different noise σ.

Markov Chains

Consider a randomly generated Markov Chain $\{X_n\}_{n\in\mathbb{Z}}$ with state space $S = \{1, 2, 3, 4\}$ as an example. Let $A = \{1\}$ and $B = \{4\}$.

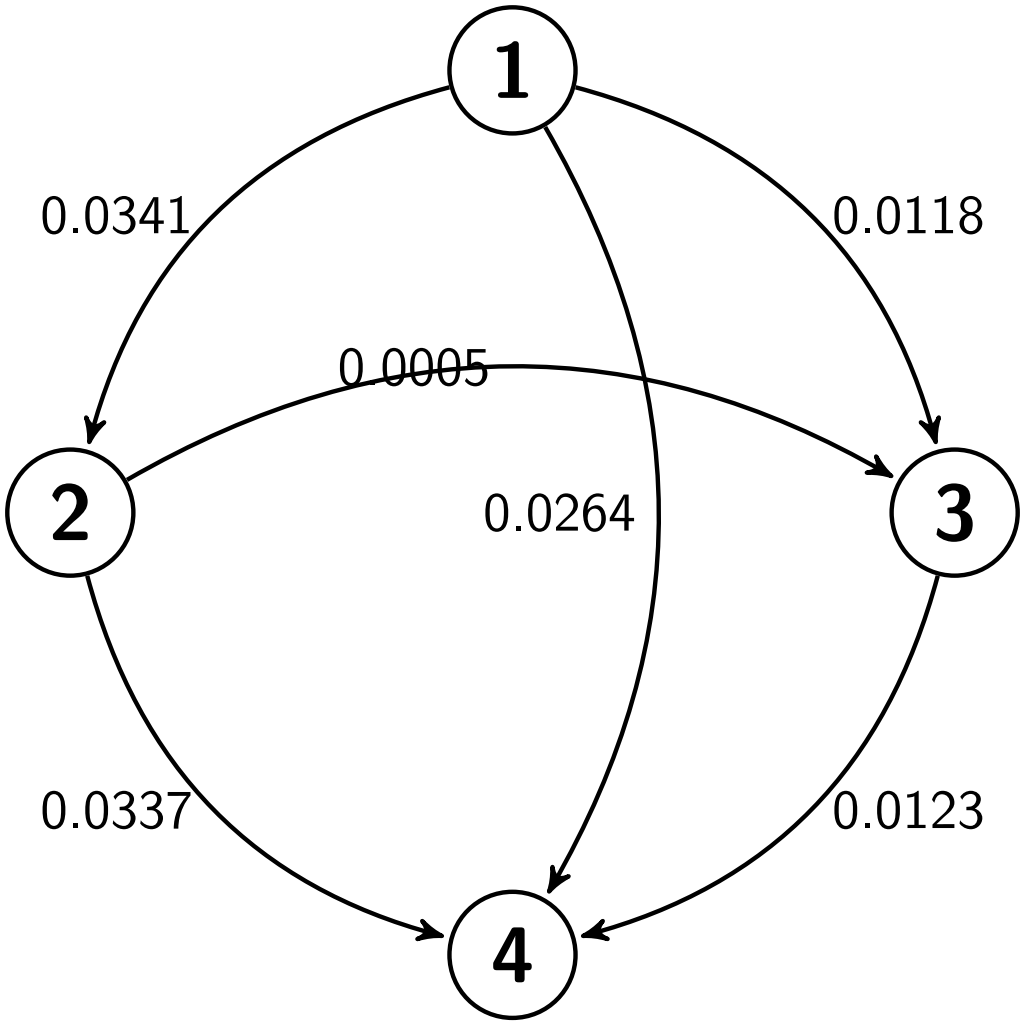
$$P = \begin{bmatrix} 0.4539 & 0.2906 & 0.1907 & 0.0648 \\ 0.3537 & 0.4600 & 0.0362 & 0.1501 \\ 0.5584 & 0.0211 & 0.3236 & 0.0968 \\ 0.1737 & 0.5098 & 0.1597 & 0.1568 \end{bmatrix}$$

Probability current J^{AB} is

$$J^{AB} = \begin{bmatrix} 0 & 0.0341 & 0.0118 & 0.0264 \\ 0 & 0 & 0.0012 & 0.0337 \\ 0 & 0.0008 & 0 & 0.0123 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

while effective probability current J^{+} is

$$J^{+} = \begin{bmatrix} 0 & 0.0341 & 0.0118 & 0.0264 \\ 0 & 0 & 0.0005 & 0.0337 \\ 0 & 0 & 0 & 0.0123 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$



Representative dominant transition path $\varphi^* = (1, 2, 4)$.

Outline for Section 4

Summary

- Transition path theory provides us with a new perspective to consider the ensemble behavior of reactive trajectories, different from classical methods such as TST, LDP, large fluctuation.
- The advantage of TPT is that many statistics can be computed and the assumption in TPT is weak.
- Weakness of TPT: cannot handle high-dimensional problem directly, due to its cost in solving committor functions.

Outlook and Further Work

- How to reduce the computational cost in solving committor function?
- How to perform local analysis on the operator $\mathcal{L}$ so that the computational cost might be reduced?
- How representative is the representative dominant transition path in e.g. real physical and biological system?

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