Lecture 11: Transition path theory

2025–07–09

In the previous lecture, we have studied transition paths of Brownian dynamics from one local minimum point to another local minimum point in the zero-temperature (resp. zero-noise) limit. In this lecture, we introduce a framework, called transition path theory (TPT), for analyzing transition paths of diffusion processes at finite temperature [3, 1, 2].

1.1 TPT for Brownian dynamics

TPT applies to diffusion processes that are described by SDEs in a general form. For simplicity, we only present TPT for Brownian dynamics, which satisfies the SDE

$$dX_t = -\nabla V(X_t)\,dt + \sqrt{2\beta^{-1}}dB_t, \quad t \geq 0\,, \tag{1.1}$$

where $V : \mathbb{R}^d \to \mathbb{R}$ is a smooth potential function, B_t is a d-dimensional Brownian motion, and $\beta > 0$ is a constant whose inverse is proportional to the system's temperature. We assume that the process X_t is ergodic. From previous lectures, we know that its invariant density is

$$\pi(x) = \frac{1}{Z}\mathrm{e}^{-\beta V(x)}\,, \quad \text{where } Z = \int_{\mathbb{R}^d} \mathrm{e}^{-\beta V(x)}dx\,, \tag{1.2}$$

and its infinitesimal generator is

$$\mathcal{L}f = -\nabla V \cdot \nabla f + \frac{1}{\beta}\Delta f\,, \tag{1.3}$$

for a test function $f : \mathbb{R}^d \to \mathbb{R}$.

Assume that $A, B \subset \mathbb{R}^d$ are two disjoint closed subsets with smooth boundaries ∂A and ∂B, such that their union has non-empty complement, i.e.

$$A \cap B = \emptyset\,, \quad \text{and} \quad (A \cup B)^c = \mathbb{R}^d \setminus (A \cup B) \neq \emptyset\,. \tag{1.4}$$

We want to study the transition paths of X_t from the set A to the set B.

First of all, let us introduce the hitting times associated to sets A and B, respectively, as

$$\begin{aligned} \tau_{A,x} &= \inf\left\{t \geq 0 \,\middle|\, X_t \in A, \text{ starting from } X_0 = x\right\}, \\ \tau_{B,x} &= \inf\left\{t \geq 0 \,\middle|\, X_t \in B, \text{ starting from } X_0 = x\right\}. \end{aligned} \tag{1.5}$$

Since the process X_t is random, both $\tau_{A,x}$ and $\tau_{B,x}$ are random variables. Using the hitting times in (1.5), we can define the so-called (forward) *committor*, which plays a key role in TPT.

Definition 1 (Forward committor)**.** At any state $x \in \mathbb{R}^d$, the committor, denoted by $q(x)$, is the probability that X_t will hit B before it will hit A. Precisely, it is defined as

$$q(x) = P(\tau_{B,x} < \tau_{A,x})\,, \quad x \in \mathbb{R}^d\,. \tag{1.6}$$

It is well known that the committor solves a boundary value PDE problem, as is stated in the following result.

Proposition 1. The committor q solves

$$\begin{aligned} &\mathcal{L}q = 0, \quad \text{on } (A \cup B)^c \\ &q|_{\partial A} = 0, \quad q|_{\partial B} = 1\,, \end{aligned} \tag{1.7}$$

where $\mathcal{L}$ is the generator in (1.3).

Proof. We only present an informal proof.

First, notice that by definition it is obvious that the hitting times in (1.5) satisfy

$$\begin{aligned} \tau_{A,x} &= 0\,, \quad \forall x \in \partial A\,, \\ \tau_{B,x} &= 0\,, \quad \forall x \in \partial B\,, \end{aligned}$$

respectively. As a result, the boundary conditions in (1.7) directly follow from the definition of the committor in (1.6).

Next, we show that q satisfies the PDE $\mathcal{L}q = 0$ on $(A \cup B)^c$. For any $x \in (A \cup B)^c$, let $h > 0$ and define $t = h \wedge \tau_{A,x} \wedge \tau_{B,x}$, where $a \wedge b := \min\{a, b\}$. Assuming $X_0 = x$ and applying Ito's lemma, we obtain

$$q(X_t) = q(x) + \int_0^t \mathcal{L}q(X_s)ds + \sqrt{2\beta^{-1}} \int_0^t \nabla q(X_s) \cdot dB_s\,. \tag{1.8}$$

Taking expectation on both sides, we have

$$\mathbb{E}\big(q(X_t) \,\big|\, X_0 = x\big) = q(x) + \int_0^t \mathbb{E}\Big(\mathcal{L}q(X_s)\Big|X_0 = x\Big)ds\,, \tag{1.9}$$

where the last term in (1.8) vanishes because its mean is zero. To proceed, notice that the committor defined in (1.6) can be written as

$$q(x) = \mathbb{E}\big(\mathbb{1}_{\{\tau_{B,x} < \tau_{A,x}\}}\big)\,.$$

Therefore, for the left hand side of (1.9), we can derive

$$\begin{aligned} \mathbb{E}(q(X_t) \,|\, X_0 = x) =& \mathbb{E}\Big(\mathbb{E}(\mathbb{1}_{\{\tau_{B,X_t} < \tau_{A,X_t}\}})\Big|X_0 = x\Big) \\ =& \mathbb{E}\big(\mathbb{1}_{\{\tau_{B,x} < \tau_{A,x}\}}\big) \\ =& q(x)\,. \end{aligned}$$

Substituting the above identity into (1.9), we obtain

$$\int_0^{h\wedge\tau_{A,x}\wedge\tau_{B,x}} \mathbb{E}\big(\mathcal{L}q(X_s)\big|X_0 = x\big)\,ds = 0\,.$$

Since the identity above is true for any $h > 0$, we conclude that the equation $\mathcal{L}q(x) = 0$ must hold. □

The next result states that, for Brownian dynamics (1.1), the committor also

solves an optimization problem.

Proposition 2. For any C^1-smooth function $f : (A \cup B)^c \to \mathbb{R}$, which satisfies the boundary conditions

$$f|_{\partial A} = 0, \quad f|_{\partial B} = 1\,, \tag{1.10}$$

we have

$$\begin{aligned} &\frac{1}{\beta}\int_{(A\cup B)^c} |\nabla f(x)|^2 \pi(x) dx \\ =&\frac{1}{\beta}\int_{(A\cup B)^c} |\nabla q(x)|^2 \pi(x) dx + \frac{1}{\beta}\int_{(A\cup B)^c} |\nabla (f-q)(x)|^2 \pi(x) dx\,, \end{aligned} \tag{1.11}$$

where π is the invariant density in (1.2). Therefore, the committor q solves the minimization problem

$$\min_f \Big(\frac{1}{\beta}\int_{(A\cup B)^c} |\nabla f(x)|^2 \pi(x) dx\Big) \tag{1.12}$$

among all C^1-smooth function $f : (A \cup B)^c \to \mathbb{R}$ with the boundary conditions in (1.10).

Proof. Let us define $g = f - q$ and compute

$$\begin{aligned} &\frac{1}{\beta}\int_{(A\cup B)^c} |\nabla f(x)|^2 \pi(x) dx \\ =&\frac{1}{\beta}\int_{(A\cup B)^c} |\nabla (q+g)(x)|^2 \pi(x) dx \\ =&\frac{1}{\beta}\int_{(A\cup B)^c} |\nabla q(x)|^2 \pi(x) dx + \frac{1}{\beta}\int_{(A\cup B)^c} |\nabla g(x)|^2 \pi(x) dx \\ &+ \frac{2}{\beta}\int_{(A\cup B)^c} \nabla g(x)\cdot \nabla q(x) \pi(x) dx\,. \end{aligned}$$

Therefore, it is sufficient to prove that the third term on the right hand side of the last equality above vanishes. To this end, notice that, since both f and q satisfy the same boundary conditions on ∂A and ∂B, their difference $g = f - q$ is zero on $\partial A \cup \partial B$. Applying the divergence theorem

on $(A\cup B)^c$ and using the invariant density in (1.2), we can derive

$$\begin{aligned}
&\int_{(A\cup B)^c} \nabla g(x)\cdot\nabla q(x)\pi(x)dx\\
=&\frac{1}{Z}\int_{(A\cup B)^c} \nabla g(x)\cdot\nabla q(x)\mathrm{e}^{-\beta V(x)}\,dx\\
=&\frac{1}{Z}\int_{\partial A\cup\partial B} g(x)\,\mathbf{n}(x)\cdot\nabla q(x)\mathrm{e}^{-\beta V(x)}\,dx-\frac{1}{Z}\int_{(A\cup B)^c} g(x)\,\mathrm{div}\Big(\nabla q(x)\mathrm{e}^{-\beta V(x)}\Big)\,dx\\
=&\frac{1}{Z}\int_{\partial A\cup\partial B} g(x)\,\mathbf{n}(x)\cdot\nabla q(x)\mathrm{e}^{-\beta V(x)}\,dx-\frac{\beta}{Z}\int_{(A\cup B)^c} g(x)\mathcal{L}q(x)\,\mathrm{e}^{-\beta V(x)}dx\\
=&0\,,
\end{aligned}$$

where $\mathbf{n}(x)$ is the normal direction of $(A\cup B)^c$, the third equality follows from the identity $\mathrm{div}\Big(\nabla q(x)\mathrm{e}^{-\beta V(x)}\Big)=\beta\mathrm{e}^{-\beta V(x)}\mathcal{L}q(x)$, which can be verified directly using (1.3), and the last equality follows from the fact that g is zero on $\partial A\cup\partial B$ and $\mathcal{L}q=0$ on $(A\cup B)^c$. This shows the identity (1.11). The second claim that q solves the minimization problem (1.12) is a direct consequence of (1.11). □

Next, we introduce several quantities in TPT. Consider an infinitely long trajectory $(X_t)_{t\in[0,+\infty)}$ of the process (1.1). We define

$$\tau_A^{(1)}=\inf\big\{t>0\,\big|\,X_t\in A\big\}\,, \tag{1.13}$$

and, for $k\geq 1$,

$$\begin{aligned}
\tau_B^{(k)}=&\inf\big\{t\,\big|\,t>\tau_A^{(k)}\,,X_t\in B\big\}\,,\\
\tau_A^{(k+1)}=&\inf\big\{t\,\big|\,t>\tau_B^{(k)}\,,X_t\in A\big\}\,.
\end{aligned} \tag{1.14}$$

In words, $\tau_B^{(k)}$ is the first time when the process hits B after it hit A at $t=\tau_A^{(k)}$, and $\tau_A^{(k+1)}$ is the first time when the process hits A after it hit B at $t=\tau_B^{(k)}$. We also define

$$\sigma_A^{(k)}=\sup\big\{t\,|\,\tau_A^{(k)}<t<\tau_B^{(k)},\,X_t\in A\big\}\,,\quad k\geq 1\,, \tag{1.15}$$

which is the last time between $[\tau_A^{(k)},\tau_B^{(k)}]$ when the process is in A. These times satisfy

$$0\leq\tau_A^{(1)}\leq\sigma_A^{(1)}<\tau_B^{(1)}<\tau_A^{(2)}\leq\sigma_A^{(2)}<\tau_B^{(2)}<\cdots<\tau_A^{(k)}\leq\sigma_A^{(k)}<\tau_B^{(k)}\leq\cdots\,. \tag{1.16}$$

A trajectory segment is called a *reactive segment* if it came from A and then goes to B without returning to A. Using (1.14) and (1.15), we can see that the reactive segments correspond to time intervals

$$[\sigma_A^{(1)},\tau_B^{(1)}],\ [\sigma_A^{(2)},\tau_B^{(2)}],\ \ldots,\ [\sigma_A^{(k)},\tau_B^{(k)}],\ \ldots\,. \tag{1.17}$$

Alternatively, a time interval $[t_1,t_2]$ corresponds to a reactive segment, if and only if

$$X_{t_1}\in A,\quad X_{t_2}\in B,\quad \text{and } X_t\in(A\cup B)^c,\ \forall\ t_1<t<t_2\,.$$

For any $T > 0$, let M_T be the total number of reactive segments that occur within time $[0, T]$. In other words, M_T is the maximal integer k such that $\tau_B^{(k)} \le T$.

Let us introduce the mean reaction time of the process.

Definition 2 (Mean reaction time). The mean reaction time is defined as the average length of reactive segments, namely,

$$t_{AB}^R = \lim_{T\to+\infty} \frac{\sum_{k=1}^{M_T}(\tau_B^{(k)} - \sigma_A^{(k)})}{M_T}\,. \tag{1.18}$$

Similar to the forward committor in Definition 1, we also need to introduce the backward committor.

Definition 3 (Backward committor). At any state $x \in \mathbb{R}^d$, the backward committor, denoted by $q^-(x)$, is the probability that the process X_t came from A rather than B. Precisely, it is defined as

$$q^-(x) = P\big(t \in [\tau_A^{(k)}, \tau_B^{(k)}), \text{for some } k \ge 1 \;\big|\; X_t = x\big)\,. \tag{1.19}$$

For any $x \in (A \cup B)^c$, we define the *reactive density* at x, denote by $\pi^R(x)$, as the density of being at x conditioned on that it belongs to a reactive segment. Using the forward and backward committors in Definition 1 and Definition 3, respectively, we can express the reactive density as

$$\pi^R(x) = Z_{AB}^{-1}\pi(x)q^-(x)q(x)\,, \tag{1.20}$$

where (by ergodicity) the normalizing constant Z_{AB} is the percentage of time that the process spends on reactive segments, namely,

$$Z_{AB} = \int_{(A\cup B)^c} \pi(x)q^-(x)q(x)dx = \lim_{T\to+\infty} \frac{\sum_{k=1}^{M_T}(\tau_B^{(k)} - \sigma_A^{(k)})}{T}\,. \tag{1.21}$$

Note that the backward committor for the process X_t from A to B is actually the forward committor for the time-reversal of X_t from B to A. For a reversible process X_t, e.g. the Brownian dynamics (1.1) considered in this lecture, the statistics of X_t is the same as the statistics of the time-reversal of X_t. In this case, the backward committor is related to the forward committor by the following simple relation

$$q^-(x) = 1 - q(x), \quad x \in \mathbb{R}^d\,,$$

and therefore the reactive density in (1.20) becomes

$$\pi^R(x) = Z_{AB}^{-1}\pi(x)(1-q(x))q(x)\,.$$

The last quantity we introduce is the transition rate from A to B.

Definition 4 (Transition rate). The transition rate from A to B is defined as

$$k_{AB} = \lim_{T\to+\infty} \frac{M_T}{T}\,, \tag{1.22}$$

where M_T is the total number of reactive segments within time $[0, T]$.

As a simple property, we have the following lemma.

Lemma 1. $k_{AB} = k_{BA}$.

Proof. Notice that, along an infinitely long trajectory of X_t, there is exactly one reactive segment from B to A between two consecutive reactive segments from A to B. The conclusion follows immediately from this observation and Definition 4. □

The following lemma reveals the connection between the transition rate and the mean reaction time in Definition 2.

Lemma 2.

$$k_{AB} = \frac{Z_{AB}}{t^R_{AB}}\,. \tag{1.23}$$

Proof. Using (1.18), (1.21), and (1.22), we can derive

$$\begin{aligned} k_{AB} =& \lim_{T\to+\infty} \frac{M_T}{T} \\ =& \lim_{T\to+\infty} \frac{M_T}{\sum_{k=1}^{M_T}(\tau_B^{(k)} - \sigma_A^{(k)})} \times \lim_{T\to+\infty} \frac{\sum_{k=1}^{M_T}(\tau_B^{(k)} - \sigma_A^{(k)})}{T} \\ =& \frac{Z_{AB}}{t^R_{AB}}\,. \end{aligned}$$

□

The results above are true for both reversible and non-reversible processes. In the reversible case considered in this lecture, we also have the following result, which connects the transition rate and the committor. For brevity, we omit its proof and refer to [3] for derivations.

Proposition 3. For the Brownian dynamics in (1.1), we have

$$k_{AB} = \frac{1}{\beta} \int_{(A\cup B)^c} |\nabla q(x)|^2 \pi(x) dx\,. \tag{1.24}$$

Combining Propositions 2–3, we can conclude that the transition rate k_{AB} for Brownian dynamics is identical to the minimum of the optimization problem in (1.12).

Remark. Proposition 2 provides a way to numerically compute the com-

mittor q by solving the optimization problem (1.12) under the boundary condition in (1.10). Specifically, assuming states $X_1, X_2, \ldots, X_N$ are sampled from a long trajectory of (1.1), we can represent the committor q by neural networks and train it with the loss function

$$\begin{aligned}\text{Loss}(q) =& \frac{1}{\beta N}\sum_{n=1}^{N} |\nabla q(X_n)|^2 \mathbb{1}_{(A\cup B)^c}(X_n) \\ &+ \frac{\lambda_1}{N}\sum_{n=1}^{N}\Big(|q(X_n)|^2 \mathbb{1}_A(X_n)\Big) + \frac{\lambda_2}{N}\sum_{n=1}^{N}\Big(|q(X_n)-1|^2 \mathbb{1}_B(X_n)\Big).\end{aligned}$$

where the first term is a Monte Carlo estimator of the integral in (1.24), the two terms in the second line are penalty terms to impose the boundary condition in (1.10), and $\lambda_1, \lambda_2 > 0$ are tunable parameters.

Proposition 3 implies that solving the minimization problem (1.12) for the committor also gives an estimation of the transition rate.

1.2 TPT for Markov chains

TPT can be generalized to Markov chains. Here, we only introduce the committor for Markov chains. A comprehensive discussion of TPT for Markov chains is presented in [2].

Consider a Markov chain with finite number of states $\mathcal{D} = \{1, 2, \ldots, m\}$, whose dynamics is described by a probability transition matrix $P \in \mathbb{R}^{m\times m}$, where P_{ij} is the probability of jumping to the state j when the Markov chain is currently at the state i, for $i, j \in \mathcal{D}$.

Assume that $A, B \subset \mathcal{D}$ are two disjoint subsets. The committor from set A to set B is an m-dimensional vector, which can be defined in a similar way as in Definition 1. The following result is a counterpart of Proposition 1 in the discrete setting.

Proposition 4. The committor q solves

$$\begin{cases} \sum_{j=1}^{m} P_{ij} q_j = q_i, & i \in (A\cup B)^c, \\ q_i = 0, & i \in A, \\ q_i = 1, & i \in B. \end{cases} \tag{1.25}$$

We refer to [2] for the proof of Proposition 4, as well as for the other quantities in the discrete setting, such as reactive segments, mean reaction time, and transition rates.

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