Lecture 5: Markov State models and variational approach

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1.1 Variational principle

Let X_t be a reversible process in $\mathbb{R}^d$ and assume that X_t is ergodic with respect to a unique invariant density π. The associated semigroup is defined as

$$(T_t g)(x) = \mathbb{E}[g(X_t)|X_0 = x], \quad x \in \mathbb{R}^d . \tag{1.1}$$

Recall that we have

1. $T_{t+s}g = T_t \circ T_s g$, for $g \in L^2_\pi(\mathbb{R}^d)$ and $t, s \geq 0$,
2. $\langle T_t g_1, g_2 \rangle_\pi = \langle g_1, T_t g_2 \rangle_\pi$,

where the second claim follows from the reversibility of X_t, and $L^2_\pi(\mathbb{R}^d)$ is the Hilbert space induced by the weighted scalar product

$$\langle g_1, g_2 \rangle_\pi = \int_{\mathbb{R}^d} g_1 g_2 \pi dx , \quad g_1, g_2 : \mathbb{R}^d \to \mathbb{R} . \tag{1.2}$$

Let us fix $\tau > 0$ and denote the eigenvalues of T_τ by

$$1 = \nu_1 > \nu_2 \geq \nu_3 \geq \dots , \tag{1.3}$$

and the corresponding eigenfunctions are $\varphi_0 = \mathbf{1}, \varphi_1, \varphi_2, \dots$.

We know the following result from the previous lecture.

Theorem 1 (Variational principle).

$$\nu_2 = \max_{g \in L^2_\pi(\mathbb{R}^d), \langle g, \mathbf{1} \rangle_\pi = 0} \frac{\langle T_\tau g, g \rangle_\pi}{\langle g, g \rangle_\pi} . \tag{1.4}$$

The following lemma allows us to express the numerator in (1.4) more explicitly.

Lemma 1. For all $g_1, g_2 \in L^2_\pi(\mathbb{R}^d)$, we have

$$\langle T_\tau g_1, g_2 \rangle_\pi = \mathbb{E}_{X_0 \sim \pi}\left[g_1(X_\tau) g_2(X_0)\right] = \mathbb{E}_{X_0 \sim \pi}\left[g_1(X_0) g_2(X_\tau)\right] . \tag{1.5}$$

Proof. Using (1.1) and (1.2), we can derive

$$\begin{aligned} \langle T_\tau g_1, g_2 \rangle_\pi &= \int_{\mathbb{R}^d} (T_\tau g_1) g_2 \pi dx \\ &= \int_{\mathbb{R}^d} \mathbb{E}[g_1(X_\tau)|X_0 = x] g_2(x) \pi(x) dx \\ &= \int_{\mathbb{R}^d} \mathbb{E}[g_1(X_\tau) g_2(X_0)|X_0 = x] \pi(x) dx \\ &= \mathbb{E}_{X_0 \sim \pi}\left[g_1(X_\tau) g_2(X_0)\right] , \end{aligned} \tag{1.6}$$

which implies the first equality in (1.5). Similarly, we have

$$\langle g_1, T_\tau g_2\rangle_\pi = \mathbb{E}_{X_0\sim\pi}\big[g_1(X_0)g_2(X_\tau)\big]\,. \tag{1.7}$$

Since T_t is self-adjoint, i.e. $\langle T_\tau g_1, g_2\rangle_\pi = \langle g_1, T_t g_2\rangle_\pi$, we conclude that the right hands sides of (1.6) and (1.7) are equal, which implies the second equality in (1.5). □

Therefore, the identity (1.4) in Theorem 1 can be written explicitly as

$$\nu_2 = \max_{g\in L^2_\pi(\mathbb{R}^d),\, \langle g,\mathbf{1}\rangle_\pi=0} \frac{\mathbb{E}_{X_0\sim\pi}\big[g(X_0)g(X_\tau)\big]}{\mathbb{E}_\pi(g^2)}\,. \tag{1.8}$$

1.2 Markov state models

Let us consider a decomposition of the space $\mathbb{R}^d$ by disjoint subsets

$$\begin{aligned} & D_1, D_2, \dots, D_M \subset \mathbb{R}^d, \\ \text{such that} \quad & \bigcup_{i=1}^M D_i = \mathbb{R}^d, \text{ and } D_i\cap D_j = \emptyset, \quad 1\le i\ne j\le M\,. \end{aligned} \tag{1.9}$$

We solve the optimization problem in (1.8) using functions of the form

$$g(x) = \sum_{i=1}^M \omega_i \mathbb{1}_{D_i}(x)\,, \quad x\in\mathbb{R}^d\,, \quad \omega = (\omega_1,\dots,\omega_M)^\top \in \mathbb{R}^M\,, \tag{1.10}$$

where $\mathbb{1}_{D_i}(x)$ denotes the indicator function associated to the set D_i.

Define $\hat\pi = (\hat\pi_1,\dots,\hat\pi_M)^\top \in \mathbb{R}^M$, where

$$\hat\pi_i = \mathbb{E}_{x\sim\pi}\big[\mathbb{1}_{D_i}(x)\big] = \int_{\mathbb{R}^d} \mathbb{1}_{D_i}(x)\pi(x)dx\,. \tag{1.11}$$

Since the sets $D_1, D_2, \dots, D_M$ form a disjoint decomposition of $\mathbb{R}^d$ (see (1.9)), we have

$$\sum_{i=1}^M \hat\pi_i = \sum_{i=1}^M \int_{\mathbb{R}^d} \mathbb{1}_{D_i}(x)\pi(x)dx = \int_{\mathbb{R}^d}\pi(x)dx = 1\,. \tag{1.12}$$

Computing the expectations in (1.8) using (1.10), we have the following result.

Lemma 2. For functions g in (1.10), we have the following expressions.

1. $\langle g, \mathbf{1}\rangle_\pi = \mathbb{E}_\pi g = \sum_{i=1}^M \omega_i\hat\pi_i$.
2. $\mathbb{E}_\pi g^2 = \sum_{i=1}^M \omega_i^2\hat\pi_i$.
3. $\mathbb{E}_{X_0\sim\pi}\big[g(X_\tau)g(X_0)\big] = \sum_{i,j=1}^M \omega_i\omega_j \mathbb{E}_{X_0\sim\pi}\big[\mathbb{1}_{D_i}(X_0)\mathbb{1}_{D_j}(X_\tau)\big]$.

Proof. The first and the third claims follow directly using the expression of g in (1.10). For the second, using the fact that D_i form a disjoint decomposition of $\mathbb{R}^d$ (see (1.9)), we have

$$\begin{aligned}\mathbb{E}_\pi g^2 =& \int_{\mathbb{R}^d} g^2(x)\pi(x)dx \\ =& \sum_{i,j=1}^M \omega_i\omega_j \int_{\mathbb{R}^d} \mathbb{1}_{D_i}(x)\mathbb{1}_{D_j}(x)\pi(x)dx \\ =& \sum_{i=1}^M \omega_i^2 \int_{\mathbb{R}^d} \mathbb{1}_{D_i}(x)\pi(x)dx \\ =& \sum_{i=1}^M \omega_i^2 \hat{\pi}_i \,.\end{aligned}$$

□

Let us define the matrix $\hat{P} \in \mathbb{R}^{M\times M}$ whose entries are

$$\hat{P}_{ij} = \frac{\mathbb{E}_{X_0\sim\pi}\big[\mathbb{1}_{D_i}(X_0)\mathbb{1}_{D_j}(X_\tau)\big]}{\mathbb{E}_{x\sim\pi}\big[\mathbb{1}_{D_i}(x)\big]}\,, \quad 1 \le i,j \le M\,. \tag{1.13}$$

We have the following result.

Lemma 3. The matrix $\hat{P}$ satisfies the following two properties.

1. $\sum_{j=1}^M \hat{P}_{ij} = 1$, for $1 \le i \le M$.
2. $\hat{\pi}_i\hat{P}_{ij} = \hat{\pi}_j\hat{P}_{ji}$, for all $1 \le i,j \le M$.

Proof. Concerning the first claim, using (1.13) and the fact that the sets D_j form a disjoint decomposition of $\mathbb{R}^d$ (see (1.9)), we have

$$\begin{aligned}\sum_{j=1}^M \hat{P}_{ij} =& \sum_{j=1}^M \frac{\mathbb{E}_{X_0\sim\pi}\big[\mathbb{1}_{D_i}(X_0)\mathbb{1}_{D_j}(X_\tau)\big]}{\mathbb{E}_{x\sim\pi}\big[\mathbb{1}_{D_i}(x)\big]} \\ =& \frac{\mathbb{E}_{X_0\sim\pi}\big[\mathbb{1}_{D_i}(X_0)\big]}{\mathbb{E}_{x\sim\pi}\big[\mathbb{1}_{D_i}(x)\big]} \\ =& 1\,.\end{aligned}$$

Concerning the second claim, using (1.13) and the second equality in Lemma 1, we have

$$\hat{\pi}_i\hat{P}^{(M)}_{ij} = \mathbb{E}_{X_0\sim\pi}\big[\mathbb{1}_{D_i}(X_0)\mathbb{1}_{D_j}(X_\tau)\big] = \mathbb{E}_{X_0\sim\pi}\big[\mathbb{1}_{D_i}(X_\tau)\mathbb{1}_{D_j}(X_0)\big] = \hat{\pi}_j\hat{P}_{ji}\,.$$

□

The first claim of Lemma 3 implies that $\hat{P}$ is a probability matrix, which defines a Markov chain on the finite space $\mathcal{D} = \{1, 2, \dots, M\}$. The second claim implies that the Markov chain satisfies detailed balance condition with the stationary distribution $\hat{\pi}$, defined in (1.11).

Let us define inner product in $\mathbb{R}^M$ weighted by $\hat{\pi}$ as

$$\langle \omega, \omega' \rangle_{\hat{\pi}} = \sum_{i=1}^{M} \omega_i \omega'_i \hat{\pi}_i, \quad \omega, \omega' \in \mathbb{R}^M . \tag{1.14}$$

Then, for a function g in (1.10) with coefficients $\omega \in \mathbb{R}^M$, the claims in Lemma 2 can be written as

$$\begin{aligned} \langle g, \mathbf{1} \rangle_{\pi} &= \sum_{i=1}^{M} \omega_i \hat{\pi}_i = \langle \omega, \mathbf{1}_M \rangle_{\hat{\pi}} \\ \mathbb{E}_{\pi} g^2 &= \sum_{i=1}^{M} \omega_i^2 \hat{\pi}_i = \langle \omega, \omega \rangle_{\hat{\pi}} \\ \mathbb{E}_{X_0 \sim \pi} \big[g(X_\tau) g(X_0) \big] &= \sum_{i,j=1}^{M} \omega_i \omega_j \mathbb{E}_{X_0 \sim \pi} \big[\mathbb{1}_{D_i}(X_0) \mathbb{1}_{D_j}(X_\tau) \big] = \langle \hat{P} \omega, \omega \rangle_{\hat{\pi}} . \end{aligned}$$

where $\mathbf{1}_M$ denotes the vector in $\mathbb{R}^M$ with all components 1. Therefore, by solving (1.8) with functions of the form (1.10), we end up with the optimization problem

$$\max_{\omega \in \mathbb{R}^M, \langle \omega, \mathbf{1}_M \rangle_{\hat{\pi}} = 0} \frac{\langle \hat{P} \omega, \omega \rangle_{\hat{\pi}}}{\langle \omega, \omega \rangle_{\hat{\pi}}} . \tag{1.15}$$

associated to the Markov chain defined by $\hat{P}$.

Recall that, as a probability matrix, the largest eigenvalue of $\hat{P}$ is $\hat{\nu} = 1$ with the corresponding right eivenvector $\mathbf{1}_M$. Denote by $\hat{\nu}_2$ the second largest eigenvalue of $\hat{P}$. The following result states the connection among the solution to (1.15), the eigenvalue $\hat{\nu}_2$ associated to the Markov chain, and the eigenvalue ν_2 of the operator T_τ associated to X_t.

Proposition 1. We have

$$\nu_2 \geq \max_{\omega \in \mathbb{R}^M, \langle \omega, \mathbf{1}_M \rangle_{\hat{\pi}} = 0} \frac{\langle \hat{P} \omega, \omega \rangle_{\hat{\pi}}}{\langle \omega, \omega \rangle_{\hat{\pi}}} = \hat{\nu}_2 . \tag{1.16}$$

Proof. The first equality follows from the fact that the maximization problem in (1.15) is equivalent to (1.8) for functions of the form (1.10) (i.e. we are solving (1.8) in a subspace). The second equality follows from the variational principle for the second largest eigenvalue of $\hat{P}$. □

In practice, we need to evaluate $\hat{\pi}$ and $\hat{P}$. To this end, notice that ergodic theorem implies, with probability one,

$$\begin{aligned} \hat{\pi}_i &= \int_{\mathbb{R}^d} \mathbb{1}_{D_i}(x) \pi(x) dx = \lim_{T \to \infty} \frac{1}{T} \int_0^T \mathbb{1}_{D_i}(X_t) dt \\ \hat{P}_{ij} &= \frac{\mathbb{E}_{X_0 \sim \pi} \big[\mathbb{1}_{D_i}(X_0) \mathbb{1}_{D_j}(X_\tau) \big]}{\mathbb{E}_{x \sim \pi} \big[\mathbb{1}_{D_i}(x) \big]} = \frac{\lim\limits_{T \to \infty} \frac{1}{T} \int_0^T \mathbb{1}_{D_i}(X_t) \mathbb{1}_{D_j}(X_{t+\tau}) dt}{\lim\limits_{T \to \infty} \frac{1}{T} \int_0^T \mathbb{1}_{D_i}(X_t) dt} , \end{aligned} \tag{1.17}$$

which can be approximated using long trajectory of the process X_t.

1.3 Generalization

When the dimension is high, constructing a decomposition of the state space, as we did in the previous section, may become infeasible. Also, we may want to solve (1.8) with functions that are more sophisticated than the piece-wise functions, e.g. with functions represented by artificial neural networks. For these reasons, in the following we develop an alternative algorithmic approach for solving (1.8).

We can impose the constraint in (1.8) by adding a penalty term, which results in uncontrained problem:

$$\min_{g\in\Phi}\Big[-\frac{\langle T_\tau g, g\rangle_\pi}{\langle g, g\rangle_\pi}+\alpha\big(\mathbb{E}_\pi g\big)^2\Big] \tag{1.18}$$

where Φ is a parametrized space of functions, and $\alpha > 0$ is a relative large constant. Notice that we have transformed the maximization problem (1.8) to a minimization problem by including a minus sign in front of the objective.

By ergodic theorem, we have the approximations

$$\begin{aligned}
\langle T_\tau g, g\rangle_\pi &= \mathbb{E}_{X_0\sim\pi}\big[g_1(X_\tau)g_2(X_0)\big] \approx \frac{1}{N}\sum_{n=0}^{N-1} g(X_n)g(X_{n+n'})\,,\\
\langle g, g\rangle_\pi &= \int_{\mathbb{R}^d} g^2(x)\pi(x)dx \approx \frac{1}{N}\sum_{n=0}^{N-1} g^2(X_n)\,,\\
\langle g, \mathbf{1}\rangle_\pi &= \int_{\mathbb{R}^d} g(x)\pi(x)dx \approx \frac{1}{N}\sum_{n=0}^{N-1} g(X_n)\,,
\end{aligned} \tag{1.19}$$

where $(X_n)_{0\le n<N}$ are states along the trajectory of X_t sampled at the time $t_n = nh$, h is the step-size, and we assume that $\tau = n'h$ for some integer n'.

Substituting the above approximations into (1.18), we obtain the objective function:

$$\mathrm{Loss}(g) = \min_{g\in\Phi}\Big[-\frac{\frac{1}{N}\sum_{n=0}^{N-1} g(X_n)g(X_{n+n'})}{\frac{1}{N}\sum_{n=0}^{N-1} g^2(X_n)}+\alpha\Big(\frac{1}{N}\sum_{n=0}^{N-1} g(X_n)\Big)^2\Big]. \tag{1.20}$$

The above approach can also be applied to solve the smallest nonzero eigenvalue of generators. Consider the Brownian dynamics X_t in $\mathbb{R}^d$

$$dX_t = -\nabla V(X_t)\,dt + \sqrt{2\beta^{-1}}dB_t\,,\quad t>0 \tag{1.21}$$

whose the generator is

$$\mathcal{L}g = -\nabla V\cdot\nabla g + \frac{1}{\beta}\Delta g\,. \tag{1.22}$$

Recall that the smallest nonzero eigenvalue of $\mathcal{L}$ satisfies the variational principle

$$\lambda_2 = \min_{g\in L^2_\pi(\mathbb{R}^d),\langle g,\mathbf{1}\rangle_\pi=0}\frac{\frac{1}{\beta}\mathbb{E}_\pi|\nabla g|^2}{\langle g, g\rangle_\pi}\,. \tag{1.23}$$

The corresponding loss objective is

$$\mathrm{Loss}(g) = \min_{g\in\Phi}\Big[\frac{\frac{1}{N}\sum_{n=0}^{N-1} |\nabla g(X_n)|^2}{\frac{1}{N}\sum_{n=0}^{N-1} g^2(X_n)}+\alpha\Big(\frac{1}{N}\sum_{n=0}^{N-1} g(X_n)\Big)^2\Big]. \tag{1.24}$$