Lecture 3

The Square Root Approximation of the Infinitesimal Generator

CONTENTS

A. Galerkin discretization of infinitesimal generator

Consider the backward Kolmogorov equation for an N_d-dimensional system

$$\frac{\partial f_t(x)}{\partial t} = \mathcal{Q} f_t(x)\,. \tag{1}$$

where $f_t(x) : \Gamma \subset \mathbb{R}^{N_d} \to \mathbb{R}$ and $f_t(x) \in L^\infty = \{f : \|f\|_\infty < \infty\}$ is an observable function, i.e. a function that represents a physical property or physical quantity that can be measured, and $\mathcal{Q}$ is a continuous operator called infinitesimal generator. We are interested in discretizing the infinitesimal generator $\mathcal{Q}$ into a transition rate matrix $\mathbf{Q}$.

For this purpose, we first discretize the space Γ with a Voronoi tessellation of k disjoint cells Γ_i such that $\Gamma = \cup_i^k \Gamma_i$, where each cell Γ_i id defined by the indicator function

$$\mathbf{1}_i(x) = \begin{cases} 1 & \text{if } \; x \in \Gamma_i \;, \\ 0 & \text{if } \; x \notin \Gamma_i \;. \end{cases} \tag{2}$$

The choice of the tessellation is arbitrary, it could be a tessellation made of either regular or irregular N_d-polytopes (polygons in 2D, polyhedra in 3D).

To discretize the continuous operator into a matrix of size $k \times k$, we could use the Galerkin projection

$$Q_{ij} = \frac{\langle \mathbf{1}_j,\, \mathcal{Q}\mathbf{1}_i \rangle_\pi}{\langle \mathbf{1}_i,\, \mathbf{1}_i \rangle_\pi}\,, \tag{3}$$

where Q_{ij} is the (ij)-entry of the matrix $\mathbf{Q}$ and we use the weighted scalar product

$$\langle f, g \rangle_\pi = \int_\Gamma f(x) g(x)\, \pi(x) dx\,. \tag{4}$$

Unfortunately, this route is not feasible, as $\mathbf{Q}$ is a differential operator and the indicator functions are step functions.

B. Galerkin discretization of the Koopman operator

Alternatively, we discretize the Koopman operator that acts on observable functions as

$$f_{t+\tau}(x) = \int_\Gamma p_\tau(x, y) f_t(y)\, dy \tag{5}$$

where $p_\tau(x, y) := p(y, t+\tau | x, t)$ is the conditional probability of finding the system in state x at time $t + \tau$, given it was in state y at time t.

Applying the Galerkin discretization, one obtains a transition probability matrix $\mathbf{T}_\tau$ with entries

$$\begin{aligned} K_{\tau,ij} &= \frac{\langle \mathbf{1}_j,\, \mathcal{K}_\tau \mathbf{1}_i \rangle_\pi}{\langle \mathbf{1}_i,\, \mathbf{1}_i \rangle_\pi} \\ &= \frac{\int_\Gamma \mathbf{1}_j(y) \int_\Gamma p_\tau(x, y) \mathbf{1}_i(x) \pi(x)\, dx\, dy}{\int_\Gamma \mathbf{1}_i(x) \mathbf{1}_i(x)\, \pi(x)\, dx} \\ &= \frac{\int_{\Gamma_j} \int_{\Gamma_i} p_\tau(x, y)\, \pi(x)\, dx\, dy}{\int_{\Gamma_i} \pi(x)\, dx} \\ &= \frac{1}{\pi_i} \int_{\Gamma_j} \int_{\Gamma_i} p_\tau(x, y)\, \pi(x)\, dx\, dy\,. \end{aligned} \tag{6}$$

The entries of eq. 6 are interpreted as probabilities

$$K_{\tau,ij} = \frac{\mathrm{Prob}\left[x_{t+\tau} \in \Gamma_j \text{ AND } x_t \in \Gamma_i\right]}{\mathrm{Prob}\left[x_t \in \Gamma_i\right]} \tag{7}$$

$$= \mathrm{Prob}\left[x_{t+\tau} \in \Gamma_j | x_t \in \Gamma_i\right]\,, \tag{8}$$

to jump from a state belonging to the cell Γ_i to the cell Γ_j within a lag time τ. The term π_i denotes the Boltzmann weight of the entire cell Γ_i.

C. The Square Root Approximation of the infinitesimal generator

In order to derive the entries of the matrix $\mathbf{Q}$, we use the definition of infinitesimal generator as

$$\begin{aligned}\mathcal{Q}f(x) &= \lim_{\tau\to 0^+} \frac{\mathcal{K}_\tau - \mathcal{I}}{\tau} f(x) \\ &= \left.\frac{\partial \mathcal{K}_\tau}{\partial \tau}\right|_{\tau=0} f(x)\,,\end{aligned} \tag{9}$$

where $\mathcal{I}$ is the identity operator. Correspondingly, from eq. 9, we define the entries of the matrix $\mathbf{Q}$, describing the rate between two adjacent cells Γ_i and Γ_j as

$$Q_{ij,\,\text{adjacent}} = \left.\frac{\partial K_{\tau,\,ij}}{\partial \tau}\right|_{\tau=0} \tag{10}$$

Inserting the definition of $K_{\tau,\,ij}$ (eq. 6) into eq. 10 yields

$$Q_{ij,\,\text{adjacent}} = \frac{1}{\pi_i}\int_{\Gamma_j}\int_{\Gamma_i} \left.\frac{\partial p_\tau(x,y)}{\partial \tau}\right|_{\tau=0} \pi(x)\,dx\,dy\,. \tag{11}$$

The conditional probability $p_\tau(x,y)$ is solution of the Fokker-Planck equation, which, written in terms of the flux, reads

$$\frac{\partial p_\tau(x,y)}{\partial \tau} = -\nabla_y \cdot \mathbf{J}_\tau(x,y)\,, \tag{12}$$

where $\nabla_y \cdot \mathbf{J}_\tau(x,y)$ expresses the divergence of the flux vector.

Then, we rewrite eq. 11 as

$$Q_{ij,\,\text{adjacent}} = \frac{1}{\pi_i}\int_{\Gamma_j}\int_{\Gamma_i} -\nabla_y \cdot \mathbf{J}_{\tau=0}(x,y)|_{x=y}\,\pi(x)\,dx\,dy\,. \tag{13}$$

Here we can apply the divergence theorem, also known as Gauss's theorem:

$$\int_\Gamma \nabla_x \cdot f(x)\,dx = \int_{\partial\Gamma} f(x)\cdot \mathbf{n} dS(x)\,, \tag{14}$$

where $\int_\Gamma dx$ denotes a volume integral, $\int_{\partial\Gamma} dS(x)$ denotes a surface integral and $\mathbf{n}$ is a outward unit normal vector. Then, applying the Gauss's theorem, eq. 13 yields

$$\begin{aligned}Q_{ij,\,\text{adjacent}} &= \frac{1}{\pi_i}\int_{\Gamma_j}\int_{\partial\Gamma_i} \mathbf{J}_{\tau=0}(x,y)|_{x=y}\,\pi(x)\,\mathbf{n}_i dS(x)\,dy \\ &= \frac{1}{\pi_i}\int_{\partial\Gamma_i\partial\Gamma_j} \mathbf{J}_{\tau=0}(z)\,\pi(z)\,\mathbf{n}_i dS(z)\,,\end{aligned} \tag{15}$$

where the variable z denotes the only points on the intersecting surface $\partial\Gamma_i\partial\Gamma_j$, i.e. the only points that satisfy $x = y$. The quantity $\mathbf{J}_{\tau=0}(z)$ denotes the flux of the states through the infinitesimal intersecting surface. We now make the following assumptions:

1. The flux between two adjacent cells Γ_i and Γ_j is a constant, and it does not depend on the potential energy function $V(x)$:

$$\mathbf{J}_{\tau=0}(z) = \mathbf{J}_{ij}\,. \tag{16}$$

2. The Voronoi cells are so small that within a cell Γ_i, the potential energy function $V(x)$ and the Boltzmann weight $\pi(x)$ are constant. Then, we can write

$$\pi_i = \int_{\Gamma_i} \pi(x)\,dx \approx \pi(x_i)\mathcal{V}_i\,, \tag{17}$$

where $\mathcal{V}_i$ is the volume of the cell Γ_i and

$$\pi(x_i) = \exp\left(-\beta V(x_i)\right)\,, \tag{18}$$

with x_i center of the cell Γ_i.

3. The potential over the boundary $\partial\Gamma_i\partial\Gamma_j$ is approximated as

$$V(z) := \frac{V(x_i) + V(x_j)}{2}\,. \tag{19}$$

The Boltzmann distribution over the boundary $\partial\Gamma_i\partial\Gamma_j$ is approximated as

$$\begin{aligned}\pi(z) &:= \exp\left(-\beta\frac{V(x_i) + V(x_j)}{2}\right)\\ &= \sqrt{\exp\left(-\beta V(x_i)\right)\exp\left(-\beta V(x_j)\right)}\\ &= \sqrt{\pi(x_i)\pi(x_j)}\,.\end{aligned} \tag{20}$$

Inserting eqs. 16, 17 and 20 into eq. 15 yields

$$\begin{aligned}Q_{ij,\,\text{adjacent}} &= \frac{1}{\pi(x_i)\mathcal{V}_i}\mathbf{J}_{ij}\int_{\partial\Gamma_i\partial\Gamma_j}\sqrt{\pi(x_i)\pi(x_j)}\mathbf{n}_i dS(z)\\ &= \mathbf{J}_{ij}\frac{\sqrt{\pi(x_i)\pi(x_j)}}{\pi(x_i)\mathcal{V}_i}\int_{\partial\Gamma_i\partial\Gamma_j}\mathbf{n}_i dS(z)\\ &= \mathbf{J}_{ij}\frac{\mathcal{S}_{ij}}{\mathcal{V}_i}\sqrt{\frac{\pi(x_j)}{\pi(x_i)}}\,.\end{aligned} \tag{21}$$

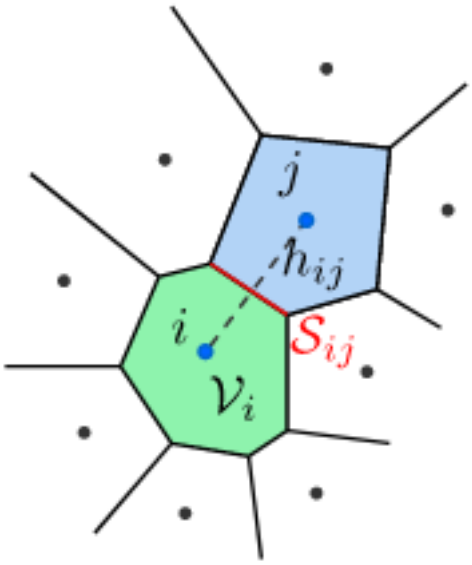

FIG. 1. Adjacent Voronoi cells.

1. *Derivation of the flux term*

In what follows, we derive an analytical expression for the flux term $\mathbf{J}_{ij}$. First, we recall the integral definition of the gradient. Consider a vector field $f(x) : \Gamma \subset \mathbb{R}^{N_d} \to \mathbb{R}$, then the gradient of f is defined as the surface integral

$$\nabla f(x) = \lim_{\mathcal{V}\to 0} \frac{1}{\mathcal{V}} \int_{\mathcal{S}} f(x) \cdot \mathbf{n} \, \mathrm{d}S(x) \,, \tag{22}$$

where $\mathcal{V}$ is a small volume containing x and $\mathcal{S}$ is the area of the surface of the volume.

We now use the assumption that the flux does not depend on the potential, and we derive $\mathbf{J}_{ij}$ from the Fokker-Planck equation with position-dependent diffusion $D(x)$ without the drift term, also known as diffusion equation or Fick's second law:

$$\frac{\partial \rho_t(x)}{\partial t} = D(x) \Delta \rho_t(x) \,, \tag{23}$$

Inserting eq. 22 into eq. 23 yields

$$\frac{\partial \rho_t(x)}{\partial t} = D(x) \lim_{\mathcal{V}\to 0} \frac{1}{\mathcal{V}} \int_{\mathcal{S}} \nabla \rho_t(x) \cdot \mathbf{n} \, \mathrm{d}S(x) \,, \tag{24}$$

On a Voronoi tessellation of the space, the discrete Laplacian on a small Voronoi cell Γ_j is

$$\Delta \rho_t(x)|_{x=x_j} = \frac{1}{\mathcal{V}_j} \sum_{i\sim j} \nabla \rho_t(x)|_{x=x_j} \cdot \mathbf{n}_{ji} \mathcal{S}_{ji} \,, \tag{25}$$

where the notation he Voronoi cells Γ_i, with $i \sim j$, are the cells adjacent to Γ_j. The term $\nabla\rho_t(x)|_{x=x_j} \cdot \mathbf{n}_{ji}$ is the gradient in the direction $j \to i$ (directional derivative), which can be approximated by the finite difference

$$\nabla\rho_t(x)|_{x=x_j} \cdot \mathbf{n}_{ji} \approx \frac{\rho_t(x_i) - \rho_t(x_j)}{h_{ji}}\,, \tag{26}$$

where $h_{ji} = x_j - x_i$ is the distance between the centers of the cells Γ_j and Γ_i. Inserting this finite difference into eq. 25 yields

$$\Delta\rho_t(x)|_{x=x_j} = \frac{1}{\mathcal{V}_j}\sum_{i\sim j}\frac{\rho_t(x_i) - \rho_t(x_j)}{h_{ji}}\mathcal{S}_{ji}\,. \tag{27}$$

Assuming that the density $\rho_t(x)$ is approximately constant within cell Γ_i (assumption 2), we have $\rho_{t,\,i} \approx \int_{\Gamma_i}\rho_t(x_i)\,\mathrm{d}x = \rho_t(x_i)\mathcal{V}_i$. Substituting $\rho_t(x_i) = {}^{\rho_{t,\,i}}\!/_{\mathcal{V}_i}$ in eq. 27 and inserting into eq. 24 yields

$$\frac{\partial}{\partial t}\frac{\rho_{t,\,j}}{\mathcal{V}_j} = D_{ij}\frac{1}{\mathcal{V}_j}\sum_{i\sim j}\frac{\frac{\rho_{t,\,i}}{\mathcal{V}_i} - \frac{\rho_{t,\,j}}{\mathcal{V}_j}}{h_{ij}}\mathcal{S}_{ij} \tag{28}$$

$$\frac{\partial}{\partial t}\rho_{t,\,j} = D_{ij}\sum_{i\sim j}\frac{\frac{\rho_{t,\,i}}{\mathcal{V}_i} - \frac{\rho_{t,\,j}}{\mathcal{V}_j}}{h_{ij}}\mathcal{S}_{ij} \tag{29}$$

$$= \sum_{i\sim j} D_{ij}\frac{1}{h_{ij}}\frac{\mathcal{S}_{ij}}{\mathcal{V}_i}\rho_{t,\,i} - D_{ij}\frac{1}{h_{ij}}\frac{\mathcal{S}_{ij}}{\mathcal{V}_j}\rho_{t,\,j} \tag{30}$$

$$= \sum_{i\sim j} Q_{ij,\,\text{adjacent}}\rho_{t,\,i} - Q_{ji,\,\text{adjacent}}\rho_{t,\,j}\,. \tag{31}$$

Eq. 31 is a master equation. Comparing eq. 31 with eq. 21, we obtain the equality

$$Q_{ij,\,\text{adjacent}} = \mathbf{J}_{ij}\,\frac{\mathcal{S}_{ij}}{\mathcal{V}_i} \tag{32}$$

$$= D_{ij}\frac{\mathcal{S}_{ij}}{h_{ij}\mathcal{V}_i} \tag{33}$$

where we used that $\sqrt{\frac{\pi(x_j)}{\pi(x_i)}} = 1$ because we assumed a constant potential. Finally the flux is defined as

$$\mathbf{J}_{ij} = \frac{D_{ij}}{h_{ij}}\,. \tag{34}$$

The term D_{ij} represents the diffusion along the intersecting surface between the two cells Γ_i and Γ_j. As for the potential energy $V(x)$, it can be approximated as

$$D_{ij} = \frac{D(x_i) + D(x_j)}{2}\,. \tag{35}$$

2. SqRA for regular grids

If the state-space Γ is discretized using a regular N-dimensional grid, then the SqRA formula simplifies as

$$Q_{ij,\,\text{adjacent}} = D_{ij}\frac{\mathcal{S}_{ij}}{h_{ij}\,\mathcal{V}_i}\sqrt{\frac{\pi(x_j)}{\pi(x_i)}} \tag{36}$$

$$= D_{ij}\frac{1}{h_{ij}^2}\sqrt{\frac{\pi(x_j)}{\pi(x_i)}}\,. \tag{37}$$

3. Transition rate matrix

The formula defined in eq. 21 with the flux term in eq. 34 defines the transition rate between adjacent subsets of the state space. The complete transition rate matrix $\mathbf{Q}$ is written as

$$Q_{ij} = \begin{cases} D_{ij}\dfrac{\mathcal{S}_{ij}}{h_{ij}\,\mathcal{V}_i}\sqrt{\dfrac{\pi(x_j)}{\pi(x_i)}} & \text{if } i \sim j \\ -\displaystyle\sum_{\substack{j=1 \\ j\neq i}}^{k} Q_{ij} & \text{if } i = j \\ 0 & \text{else} \end{cases}\,. \tag{38}$$

The second lines guarantees that the sum of the rows is zero. This property is analogous to the sum of the rows of the transition probability matrix $\mathbf{T}(\tau)$ that must be equal 1. The third line is because we do not expect transitions between non-adjacent Voronoi cells in an infinitesimal time.

4. Derivation of the master equation from the transition rate matrix

Consider the Fokker-Planck equation

$$\frac{\partial \rho_t(x)}{\partial t} = \mathcal{Q}^*\rho_t(x)\,, \tag{39}$$

where $\mathcal{Q}^*$ is the adjoint of the infinitesimal generator $\mathcal{Q}$.

Consider now the k-dimensional column vector $\vec{\rho}_t$, whose entries $\rho_{t\,1}, \rho_{t\,2}, ..., \rho_{t\,k}$ take the values of the continuous function $\rho_t(x)$ at the centers $x_1, x_2, ...x_k$ of the Voronoi cells. The

Fokker-Planck equation, in its operator form, is discretized by means of the rate matrix defined $\mathbf{Q}$ as

$$\frac{\partial \vec{\rho}^{\top}}{\partial t} = \vec{\rho}_t^{\top} \mathbf{Q} \,. \tag{40}$$

Note that $\vec{\rho}_t^{\top}$ is the transpose row vector, then the product in eq.40 is a left multiplication product:

$$\frac{\partial \vec{\rho}^{\top}}{\partial t} = \sum_{i=1}^{k} \rho_{t,\,i} Q_{ij} \,. \tag{41}$$

To rewrite eq. 41 as a master equation, we split the sum as

$$\frac{\partial \vec{\rho}^{\top}}{\partial t} = \sum_{\substack{i=1 \\ i \neq j}}^{k} \rho_{t,\,i} Q_{ij} + \rho_{t,\,j} Q_{jj} \,. \tag{42}$$

Inserting the second option in eq. 38 yields

$$\begin{aligned} \frac{\partial \vec{\rho}^{\top}}{\partial t} &= \sum_{\substack{i=1 \\ j \neq i}}^{k} \rho_{t,\,i} Q_{ij} - \rho_{t,\,j} \sum_{\substack{i=1 \\ i \neq j}}^{k} Q_{ji} \\ &= \sum_{\substack{i=1 \\ i \neq j}}^{k} \rho_{t,\,i} Q_{ij} - \rho_{t,\,j} Q_{ji} \,. \end{aligned} \tag{43}$$

D. SqRA for the overdamped Langevin dynamics

Consider the stochastic differential equation for the overdamped Langevin dynamics for a one-dimensional particle:

$$dx_t = -\frac{\nabla V(x_t)}{m\gamma} dt + \sqrt{2D}\, \eta_t \tag{44}$$

where

- m is the mass of a particle;
- γ is a friction coefficient representing the interaction between the particle and the surroundings;
- k_B is the Boltzmann constant, T is the temperature;
- D is the diffusion constant, and is written as

$$D = \frac{k_B T}{m\gamma} \,; \tag{45}$$

- η_t is a Gaussian white noise that satisfies

$$\begin{cases} \langle \eta_t \rangle = 0 \,, \\ \langle \eta_t,\, \eta_{t'} \rangle = \delta(t - t') \,. \end{cases} \tag{46}$$

Then, the associated SqRA rate matrix is written as

$$Q_{ij} = \begin{cases} D \dfrac{\mathcal{S}_{ij}}{h_{ij}\, \mathcal{V}_i} \sqrt{\dfrac{\pi(x_j)}{\pi(x_i)}} & \text{if } i \sim j \\ -\displaystyle\sum_{\substack{j=1 \\ j \neq i}}^{k} Q_{ij} & \text{if } i = j \\ 0 & \text{else} \end{cases} . \tag{47}$$