Convergent discretisation schemes for transition path theory for diffusion processes

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Contents

Chapter 1

Introduction

In many areas one is interested in understanding the statistical behaviour of random dynamical systems. Often this amounts to understanding the transition events from a predefined set A which is called the *reactant* set to a predefined set B called the *product* set. In particular one is interested in statistics of those parts of trajectories of the process that exit set A and enter set B before returning to A, the so-called *reactive trajectories*. Figure 1.1 shows some examples of reactive trajectories.

By 'statistics of reactive trajectories' we mean calculating the net amount of reactive trajectories going through a given state, i.e. the so-called *probability current of reactive trajectories*, the frequency of transition between sets A and B, i.e. the so-called *reaction rate* and describing the mechanism of transition, i.e. the most probable *transition tubes* or *transition streamlines*. This problem of understanding statistics of reactive trajectories becomes more difficult in the scenario when the process is *metastable*, meaning that it spends long time intervals trapped in sets A and B and rarely transits between them.

For example, in chemistry one is often interested in transitions between stable conformations of molecules that occur as a result of collisions with atoms in the molecule's environment. These transition events are rare and happen at the timescale that is several orders of magnitude smaller than the timescale at which the random collisions with atoms happen. Therefore using simple Monte Carlo sampling of trajectories to obtain statistics requires significant computation time and is often impractical.

Transition path theory provides the means to describe the statistics of reactive trajectories using deterministic objects. These objects are the *committor function*, the *probability current of reactive trajectories* and the *streamlines of the probability current*. The committor function is one of the main objects of transition path theory. To every point or *state* in the state space of the random dynamical system, it assigns the probability of reaching the set B before reaching the set A, conditioned on starting from the given state. Using the committor function and an invariant probability density of the dynamical process one is then able to describe the statistics of reactive trajectories. In particular, one can obtain the probability density of observing a reactive trajectory at any state, i.e. the probability density of reactive trajectories. Furthermore, using the committor function and the invariant probability density one can obtain the probability current of reactive trajectories, the reaction rate and the streamlines.

Transition path theory for diffusion processes has been introduced in [14]. The committor function corresponding to a diffusion process is obtained by solving a boundary

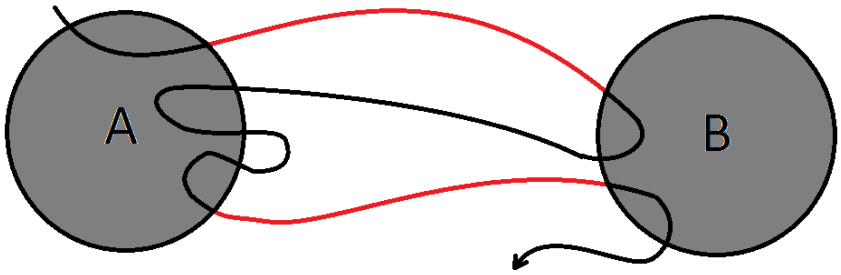


Figure 1.1: Reactive trajectories are depicted in red.

value problem for the backward Kolmogorov equation, which is a linear second order partial differential equation that involves an operator called the *infinitesimal generator* of the diffusion. Analytic solutions to such boundary value problems are in general not available.

Several techniques have been employed to discretise the continuous infinitesimal generator and numerically compute committor functions. These include a method based on finite differences [35] and on finite volumes [26] using uniform meshes. Finite element methods for non-uniform meshes of the continuous infinitesimal generator in 2 and 3 dimensions was suggested as being less prone to the curse of dimensionality compared to the standard finite differences approach [25]. Realisable discretisation schemes have been analysed in [3], for which the discretised infinitesimal operator yields the generator of a Markov jump process which can be simulated using Monte Carlo methods. Recently a discretisation scheme on a cloud of data points has been suggested for numerically calculating the committor function [24]. In addition, artificial neural networks have been employed in a discretisation scheme [22, 28].

In practice, the infinitesimal generator is often not available, whereas the diffusion process can be observed. Therefore one is interested in estimating the infinitesimal generator from observations. It was only after transition path theory was developed for Markov jump processes and Markov chains [32] that the framework of transition path theory became widely applicable. Continuous objects of transition path theory for diffusion processes are replaced with the discrete transition path theory objects corresponding to Markov jump processes on discrete (and often finite) state spaces. Therefore instead of analysing the transitions of a diffusion process between two subsets of the continuous state space, one approximates the diffusion process by a Markov jump process and analyses transitions between two disjoint subsets of nodes in the corresponding graph. In this way the problem of solving the partial differential equation is replaced by the problem of solving a system of linear equations. In connection to this approach, the following questions arise.

1. How should the state space be discretised?

2. How should the generator of the approximating Markov jump process or the transition probability matrix of the approximating Markov chain be estimated?

Discretisation approaches

The most popular discretisation schemes involve discretisation of both the state space and time, yielding a Markov chain called the Markov state model [5, 47, 48]. Standard Markov state models involve full partitions of the state space, and Galerkin approximation by characteristic functions of the partition sets. Voronoi tessellations have been used to partition the state space for Markov state models [29, 42]. In addition to discretisation of the state space, Markov state models involve a time discretisation which is achieved by choosing a lag time parameter. This parameter describes the time interval, or resolution, at which the process is observed.

When approximating the continuous process with the discrete Markov chain, we are also interested in the approximation errors that we make and whether such an approximation reproduces the long timescale behaviour of the original process. The long time behaviour of the Markov state models is analysed in [11], while a bound on the approximation error of the Markov state model has been provided in [44]. The error bound in [44] reveals a relationship between the accuracy of the approximation, the choice of the partition, and the lag time for which the transition probability matrix of Markov chain is computed. Specifically, increasing the number of sets in the partition decreases the approximation error of the Markov state model. However, it is not always practical to increase the number of sets in the partition. Therefore, adaptive discretisation techniques of the state space have been suggested in order to improve the approximation error of the model [42].

Spatial discretisation brings with it a problem of the effect of memory. Namely, a Markov chain is a memoryless process, meaning that the future of the process depends only on the present state, and is independent of the past. The process obtained by space and time discretisation is however not Markovian; see [43, Section 2.1] or [42].

The effect of memory can be counterbalanced by the choice of lag time parameter. The lag time needs to be adapted to the analysed process. However, there is no recipe that works for all cases. In general, increasing the lag time can improve the accuracy [42], while experimental results show that increasing the lag time and therefore reducing the time resolution of the model can increase the approximation error [47], and cause a systematic bias in calculating the transition path theory objects [51]. It is known that Markov state models in general can not reproduce the long time behaviour of the original process [39]. Some approaches therefore abandon altogether the assumption of Markovianity of the discretised process and include the history information [50, 51].

A hidden Markov model has been suggested for approximation of the non-Markovian process obtained by state space discretisation [39]. This approximation is shown to be accurate under certain assumptions on the eigenfunctions of the propagator, that is, the continuous analogue of the transition probability matrix of the dynamical system. However, these assumptions are often impossible to verify in practice because the eigenfunctions of the propagator are not known a priori. In [59], the assumptions on the eigenfunctions were weakened, and an approximation using a generalisation of hidden Markov models, the so-called 'observable operator models', was proposed.

An alternative approach is the use of milestoning [47, 48]. In the milestoning approach developed in [16], disjoint subsets or 'milestones' of the state space are preselected such that their union is a proper subset of the original state space. For example, one could choose the milestones to be hypersurfaces in state space. Afterwards the jump statistics between

the milestones are observed, usually by reinitialising the trajectories of the process from milestones. In principle, reinitialising is done according to the probability density of the position at which a long ergodic trajectory first hits the milestone. Milestoning renders a reduced representation of the original process while avoiding the need for decreasing the time resolution of the approximation. In addition, it avoids the problem of high computational cost due to partitions that consist of a large number of sets.

Unlike the Markov state model with full partitioning of state space, the milestoning approach is known to be robust to the effect of memory. Indeed, it has been shown in [55] that there exist milestones such that the transitions between them are statistically independent. Such milestones are isocommittor surfaces. Recently, isocommittor surfaces corresponding to the backward committor function have been proven to capture some kinetic features of the original system [30]. In particular, this choice of milestones enables exact calculation of the reaction rates of the process.

Edges of the sets in a Voronoi tessellation, i.e. of the Voronoi cells are suggested as milestones in the approach called Markovian milestoning [54]. The improvement in Markovian milestoning compared to the general milestoning procedure lies in the fact that the trajectories do not need to be reinitialised from milestones. Thus, one does not need to approximate the probability distribution for reinitialisation of trajectories. This is convenient as the probability distribution for reinitialisation of trajectories is not known in general [55].

Generator and transition probability matrix estimation

If the infinitesimal generator of the underlying process is unknown, the infinitesimal generator of the approximating Markov jump process has to be estimated from the observation data. Numerous approaches are developed for estimating the infinitesimal generator of a Markov jump process [33, 34].

Molecules in thermal equilibrium have reversible dynamics. Therefore it is desirable that the transition probability matrix obtained from observations satisfies the discrete detailed balance condition. A definition of reversibility and of detailed balance condition for diffusion processes is given in Section 2.5. For the detailed balance condition of a continuous time jump process on the discrete state space see [32]. Reversible maximum likelihood estimators of the transition probability matrix have been developed in [4, 38, 42, 53] while a Bayesian estimator is given in [52]. An approach using a Gibbs sampler is presented in [37].

Once the generator or the transition probability matrix has been approximated, the discrete committor function corresponding to the Markov jump process or Markov chain needs to be computed. Prinz et al. performed a numerical approximation and sensitivity analysis of the committor function [41]. Specifically, they quantified how sensitive the discrete committor function is to changes in the transition probability matrix and quantified its statistical uncertainty when the transition matrix is not exactly known. In [57] a graph transformation method has been suggested to calculate the discrete committor function. This method is based on the assumption that the dynamics can be modeled as a Markov chain and involves removing states from a Markov chain, one at a time followed by renormalising the transition probabilities.

Sampling of reactive trajectories

Sampling of the reactive trajectories by Monte Carlo method is often too time consuming due to the large range of timescales in the dynamics. Transition path theory therefore avoids sampling of reactive trajectories by solving partial differential equations. This is difficult in dimensions greater than three. Importance sampling technique on the path space using optimal control have been used to estimate committor values and avoid the sampling of reactive trajectories of the original process. The idea behind this approach is to change the measure which is sampled into a measure which is easier to sample. This is achieved by reweighting of the potential function such that the transitions occur more often. For a summary of the importance sampling techniques in molecular dynamics see [27].

Recently, theoretical approaches for generating reactive trajectories have been developed. Cameron et al. [7] propose a method that generates the reactive trajectories directly and a method that generates no-detour trajectories, i.e. trajectories that take productive steps towards the product state which can be understood as discrete versions of streamlines. In particular, they show how to obtain Markov jump processes from the original Markov jump process that generate the reactive or no-detour trajectories. The statistical analysis of these trajectories can be used to analyze the flows in networks. Their approach can be seen as an extension of transition path theory for Markov jump processes.

Similarly, transition path theory for diffusion processes has been extended by providing ways to generate reactive trajectories of the diffusion process [31]. The results in [31] use knowledge of the committor function to directly sample reactive trajectories without needing to sample long trajectories of the original process. Even though the true continuous committor function is not available in practice, these theoretical results may be useful in the design of numerical algorithms for sampling trajectories.

As in the approach of Cameron et al. [7] mentioned above, a Markov process that generates reactive trajectories is described in [56]. However, in [56] the *ergodicity* assumption of the analysed process is removed. The ergodicity assumption is one of the main assumptions of the transition path theory and it guarantees that the dynamical statistics of the process can be obtained by analysing only one inifinitely long trajectory of the process. Furthermore, in [56] it is shown how to generate nonreactive trajectories, i.e. trajectory segments that leave A and return to A before reaching B. They also study the ensemble of first passage paths, where a first passage path is a trajectory segment that starts outside B and ends at a point in B, thus containing both reactive and nonreactive parts. In the particular case when the jump processes is an ergodic Markov jump process, the analysis in [56] explains the relations between the study of the first passage paths and the study of the transition paths in transition path theory. Therefore, [56] can be seen as an extension of the discrete transition path theory framework of Metzner et al. [32] to non-ergodic systems. Algorithms for numerical computation of statistics of the first passage path ensemble are also provided.

Our approach

In this thesis, we extend the transition path theory to discrete-state space non-Markovian processes. More precisely, we develop the theory for analysing the statistics of reactive trajectories, for a process that is obtained from a continuous Markov process by discretising

the state space. We justify the introduced approach by proving convergence results and error bounds that show that the results of our approach approximate the results of transition path theory for diffusion processes. Our error bounds and convergence results hold in the case when the continuous Markov process is an ergodic diffusion process, whereas the definitions of the discrete transition path theory objects that we introduce are independent of the diffusion coefficients and can be applied to a wider spectrum of processes. To the best of our knowledge, our definitions, error bounds and convergence results are new.

The presented approach avoids solving the partial differential equation; this is also done in the transition path theory for Markov jump processes. However, by removing the assumption of Markovianity, our approach avoids estimating the generator matrix. This makes it more general than transition path theory for Markov jump processes.

In Chapter 2 of the thesis we provide an introduction to the theory of stochastic processes. In particular, we focus on diffusion processes, and provide the theory necessary for understanding the transition path theory for diffusion processes which is summarised in Chapter 3. In Chapter 4 we introduce our approach, define the discrete *committor function*, *isocommittor surfaces*, *probability current of reactive trajectories* and *streamlines*. Furthermore, we prove the error bounds that measure the discrepancy between the discrete objects we introduced and the corresponding continuous objects of transition path theory for diffusion processes. All of the provided error bounds scale linearly with the diameter of the largest cell in the partition. This provides the convergence in the limit of infinitely fine partition of the discrete objects we define to the continuous analogues in transition path theory for diffusion processes. Finally, in Chapter 5 we provide numerical results and use these to compare our approach to the approach of transition path theory for Markov chains, as well as to the finite differences approximation of objects from transition path theory for diffusion processes.

Notation

In this section we summarise some standard notation used throughout this thesis. The set of real numbers we denote by $\mathbb{R}$ and by $\overline{\mathbb{R}}$ we denote a two point compactification of real numbers, i.e. $\overline{\mathbb{R}} = \mathbb{R} \cup \{-\infty, \infty\}$. We use $\mathbb{R}_{\geq 0}$ to denote the set of nonnegative real numbers.

Let $(\Omega, \mathcal{A}, \mu)$ denote a measure space. $L^p(\Omega, \mathcal{A}, \mu; \mathbb{R})$, for $0 < p < \infty$ is a space of $\mathcal{A}$-measurable functions from Ω to $\mathbb{R}$ for which the p-th power of the absolute value is μ-integrable on Ω, i.e.

$$\|f\|_p := \left(\int_\Omega |f|^p \, \mathrm{d}\mu \right)^{\frac{1}{p}} < \infty.$$

We will shorten the notation and denote $L^p(\Omega, \mathcal{A}, \mu; \mathbb{R})$ by $L^p(\Omega, \mu)$ or $L^p(\mu)$ when there is no risk of confusion. $L^\infty(\Omega, \mathcal{A}, \mu; \mathbb{R})$ is a space of functions from Ω to $\mathbb{R}$ for which there exists $C \geq 0$ such that $|f(x)| \leq C$ for for μ-almost all $x \in \Omega$, and

$$\|f\|_\infty := \inf\{C \geq 0 \ : \ |f(x)| \leq C, \text{ for almost every } x \in \Omega\}.$$

The vector L^p norm we denote by $|\cdot|_p$, i.e. for $x \in \mathbb{R}^d$, where $d \in \mathbb{N}$, $|x|_p := \left(\sum_{i=1}^d |x_i|^p \right)^{\frac{1}{p}}$. We will use the standard notation for continuous functions, denoting by $f \in C^k(U; V)$ when $f : U \to V$ is k times continuously differentiable, i.e. when f has all the derivatives up to order k. If $U = U_1 \times U_2$ we denote $f \in C^{k,l}(U_1 \times U_2; V)$ if function f is C^k with respect to the first and C^l with respect to the second component. By $C_0(U; V)$ we denote the set of continuous functions $f : U \to V$ with compact support. Similarly $C_0^k(U; V)$ denotes the set of $f \in C^k(U; V)$ functions with compact support. Sometimes, when there is no risk of confusion, we will omit the codomain V from the notation.

Let X be a random variable. We denote the probability distribution of random variable X by $\mathbb{P} \circ X^{-1}$. By $\sigma(X)$ we denote the σ-algebra generated by X. The Borel σ-algebra on set S is denoted by $\mathcal{B}(S)$. In the special case of real numbers we denote $\mathcal{B} := \mathcal{B}(\mathbb{R})$ and $\mathcal{B}^d := \mathcal{B}(\mathbb{R}^d)$.

By $\delta(\cdot)$ we denote the Dirac delta measure at the origin, i.e. for every $f \in C_0^\infty(\mathbb{R}^d)$ and any $x \in \mathbb{R}^d$ we have

$$f(x) = \int_{\mathbb{R}^d} f(y) \delta(x - y).$$

The characteristic function of the set A we denote by $\mathbf{1}_A$, i.e.

$$\mathbf{1}_A(x) = \begin{cases} 1, & \text{if } \ x \in A \\ 0, & \text{if } \ x \notin A. \end{cases}$$

Chapter 2

Stochastic processes

In this chapter we present some prerequisites from probability theory, stochastic processes and diffusion processes which are necessary for understanding transition path theory, which will be presented in Chapter 3.

2.1 Probability theory background

Let $(\Omega_1, \mathcal{A}_1)$ and $(\Omega_2, \mathcal{A}_2)$ be measurable spaces. A random variable on $(\Omega_1, \mathcal{A}_1)$ that takes values in $(\Omega_2, \mathcal{A}_2)$ is a measurable function $X : \Omega_1 \to \Omega_2$, i.e. $X : \Omega_1 \to \Omega_2$ is a random variable if preimages of measurable sets in Ω_2 are measurable in Ω_1:

$$\forall\ A_2 \in \mathcal{A}_2, \quad X^{-1}(A_2) = \{\omega \in \Omega_1\ : X(\omega) \in A_2\} \in \mathcal{A}_1.$$

The triple $(\Omega_1, \mathcal{A}_1, \mathbb{P})$ where $\mathbb{P}$ is a probability measure, i.e. a measure for which $\mathbb{P}(\Omega_1) = 1$, is called a probability space.

The integral of the random variable X with respect to the probability measure $\mathbb{P}$ is called the expectation and it is denoted by

$$\mathbb{E}[X] = \int_{\Omega_1} X(\omega)\mathbb{P}(\mathrm{d}\omega).$$

Let $B \in \mathcal{A}_1$ such that $\mathbb{P}(B) > 0$. The conditional probability of an event $A \in \mathcal{A}_1$, conditioned on the event $B \in \mathcal{A}_1$ is defined as

$$\mathbb{P}(A|B) = \frac{\mathbb{P}(A \cap B)}{\mathbb{P}(B)}.$$

It can be shown that if $\mathbb{P}(B) > 0$, $\mathbb{P}(\ \cdot\ |B)$ is a probability measure on $(\Omega_1, \mathcal{A}_1)$ [23, Theorem 8.4].

In order to introduce conditional probabilities that allow conditioning on events of measure zero, we need to introduce a more general concept of conditional expectation. The conditional expectation of X given a σ-algebra $\mathcal{F} \subset \mathcal{A}_1$ denoted by $\mathbb{E}[X|\mathcal{F}]$, is a random variable Y such that Y is $\mathcal{F}$-measurable and for any $A \in \mathcal{F}$ we have $\mathbb{E}[\mathbf{1}_A X] = \mathbb{E}[\mathbf{1}_A Y]$ i.e.

$$\int_A X(\omega)\mathbb{P}(\mathrm{d}\omega) = \int_A Y(\omega)\mathbb{P}(\mathrm{d}\omega).$$

For $B \in \mathcal{A}_1$, the conditional probability of B given the σ-algebra $\mathcal{F}$ is given by $\mathbb{P}(B|\mathcal{F}) := \mathbb{E}[\mathbf{1}_B|\mathcal{F}]$.

Let X and Y be arbitrary random variables defined on the same probability space and $X \in L^1(\mathbb{P})$. Then we define

$$\mathbb{E}[X|Y] = \mathbb{E}[X|\sigma(Y)].$$

Let X, Y be random variables on a probability space $(\Omega_1, \mathcal{A}_1, \mathbb{P})$ such that $X, Y, XY \in L^1(\mathbb{P})$, and $\mathcal{F}' \subset \mathcal{F}$ be sub-σ-algebras of $\mathcal{A}_1$. Recall the following properties of the conditional expectation:

1. If Y is $\mathcal{F}$-measurable then
$$\mathbb{E}[XY|\mathcal{F}] = Y\mathbb{E}[X|\mathcal{F}]. \tag{2.1}$$

2.
$$\mathbb{E}[\mathbb{E}[X|\mathcal{F}]|\mathcal{F}'] = \mathbb{E}[\mathbb{E}[X|\mathcal{F}']|\mathcal{F}] = \mathbb{E}[X|\mathcal{F}']. \quad \text{(Tower law)} \tag{2.2}$$

3. If $\sigma(X)$ and $\mathcal{F}$ are independent then
$$\mathbb{E}[X|\mathcal{F}] = \mathbb{E}[X]. \tag{2.3}$$

Now let us turn to the question of defining the conditional probability, where the set we are conditioning on has a $\mathbb{P}$-measure zero. We define it using the factorisation lemma; see [23, Corollary 1.97].

Lemma 2.1.1 (factorisation lemma)**.** *Let $(\Omega_2, \mathcal{A}_2)$ be a measurable space and let Ω_1 be a nonempty set. Let $f : \Omega_1 \to \Omega_2$ be a map. A map $g : \Omega_1 \to \overline{\mathbb{R}}$ is $\sigma(f) - \mathcal{B}(\overline{\mathbb{R}})$ -measurable if and only if there is an $\mathcal{A}_2 - \mathcal{B}(\overline{\mathbb{R}})$-measurable map $\varphi : \Omega_2 \to \overline{\mathbb{R}}$ such that $g = \varphi \circ f$.*

Let X, Z be random variables such that X takes values in a measurable space $(E, \mathcal{E})$ and let Z be real valued and $\sigma(X) - \mathcal{B}(\overline{\mathbb{R}})$-measurable. For $f = X$ and $g = Z$, according to Lemma 2.1.1, there exists a $\mathcal{E} - \mathcal{B}(\overline{\mathbb{R}})$ measurable map φ such that $\varphi(X) = Z$.

Let now $X : (\Omega_1, \mathcal{A}_1) \to (E, \mathcal{E})$ and Y be such that $Y \in L^1(\mathbb{P})$ and $Z = \mathbb{E}[Y|X]$. By definition, Z is $\sigma(X) - \mathcal{B}(\overline{\mathbb{R}})$-measurable. For this special choice of random variables X and Z we know there exists a measurable function φ, such that $\varphi(X) = Z$, and therefore we define the conditional expectation of Y given $X = x$ by $\mathbb{E}[Y|X = x] := \varphi(x)$ and the conditional probability by $\mathbb{P}(A|X = x) := \mathbb{E}[\mathbf{1}_A|X = x]$ for $A \in \mathcal{A}$.

In general, the function $\mathbb{P}(\cdot|X = x)$ is not a probability measure, because there may exist x for which $\mathbb{P}(\cdot|X = x)$ is not defined. That implies that for any $A \in \mathcal{A}$ there might exist a null set $N_A \subset E$ such that for all $x \in N_A$, $\mathbb{P}(A|X = x)$ is not defined. Since in general, there are uncountably many $A \in \mathcal{A}$, we cannot claim that $\bigcup_{S \in \mathcal{A}} N_S$ is a null set. If, however, the σ-algebra $\mathcal{A}$ can be represented by countably many sets A, there exists a function called the *regular conditional distribution* that gives a probability measure for almost all $\omega \in \Omega$. This is derived in the remainder of this section. We first define a *transition kernel* [23, Definition 8.25].

Definition 2.1.2 (Transition kernel, Markov kernel)**.** Let $(\Omega_1, \mathcal{A}_1), (\Omega_2, \mathcal{A}_2)$, be measurable spaces. A map $\kappa : \Omega_1 \times \mathcal{A}_2 \to [0, \infty]$ is called a *$\sigma-$finite transition kernel* from Ω_1 to Ω_2 if:

(i) $\kappa(\cdot, A_2)$ is $\mathcal{A}_1$-measurable for any $A_2 \in \mathcal{A}_2$

(ii) $\kappa(\omega_1, \cdot)$ is a $\sigma-$finite measure on $(\Omega_2, \mathcal{A}_2)$ for any $\omega_1 \in \Omega_1$.

If in (ii) the measure is a probability measure for all $\omega_1 \in \Omega_1$, then κ is called a *stochastic kernel* or a *Markov kernel*.

Using transition kernels we define the regular conditional distribution [23, Definition 8.28].

Definition 2.1.3. Let $(\Omega_1, \mathcal{A}_1, \mathbb{P})$ be a probability space, $(E, \mathcal{E})$ be a measurable space, $Y : \Omega_1 \to E$ be a random variable, and $\mathcal{F}$ be a sub-σ-algebra of $\mathcal{A}_1$. A stochastic kernel $\kappa_{Y,\mathcal{F}}$ from $(\Omega_1, \mathcal{F})$ to $(E, \mathcal{E})$ is called a *regular conditional distribution* of Y given $\mathcal{F}$ if

$$\kappa_{Y,\mathcal{F}}(\omega, C) = \mathbb{P}\left(Y \in C | \mathcal{F}\right)(\omega)$$

for $\mathbb{P}-$almost all $\omega \in \Omega_1$ and for all $C \in \mathcal{E}$. If $\mathcal{F}$ is generated by a random variable X on $(\Omega_1, \mathcal{A}_1, \mathbb{P})$ that takes values in some measurable space $(E', \mathcal{E}')$, i.e. $\mathcal{F} = \sigma(X)$ then the stochastic kernel for all $\omega \in X^{-1}(\{x\})$ satisfies

$$\kappa_{Y,X}(x, C) = \mathbb{P}\left(Y \in C | X = x\right) = \kappa_{Y,\sigma(X)}(\omega, C) \tag{2.4}$$

is called a regular conditional distribution of Y given X. For $x \notin X(\Omega_1)$, $\kappa_{Y,X}(x, C)$ is the function from the factorisation lemma with an arbitrary value.

It can be shown [23, Theorem 8.37] that for a random variable Y on $(\Omega_1, \mathcal{A}_1, \mathbb{P})$ that takes values in a Borel space $(E, \mathcal{E})$ and for $\mathcal{F} \subset \mathcal{A}_1$, there exists a regular conditional distribution $\kappa_{Y,\mathcal{F}}$ of Y given $\mathcal{F}$. We list one more result [23, Theorem 8.38] that we use later in Section 4.

Theorem 2.1.4. *Let Y be a random variable on $(\Omega_1, \mathcal{A}_1, \mathbb{P})$ with values in a Borel space $(E, \mathcal{E})$. Let $\mathcal{F} \subset \mathcal{A}_1$ be a σ-algebra and let $\kappa_{Y,\mathcal{F}}$ be a regular conditional distribution of Y given $\mathcal{F}$. Further, let $f : E \to \mathbb{R}$ be measurable and $\mathbb{E}\left[|f(Y)|\right] < \infty$. Then*

$$\mathbb{E}\left[f(Y)|\mathcal{F}\right](\omega) = \int_E f(y)\kappa_{Y,\mathcal{F}}(\omega, \mathrm{d}y)$$

for $\mathbb{P}$-almost all ω.

2.2 Markov processes

Let $[t_0, T] \subset [0, \infty)$. A family of Ω_2-valued random variables $\{X_t\}_{t\in[t_0,T]}$ defined on a probability space $(\Omega_1, \mathcal{A}_1, \mathbb{P})$ is called a *stochastic process* or random process, and the set Ω_2 is called the *state space*. In the following, we will consider $\mathbb{R}^d$ valued stochastic processes, or more precisely we will have $(\Omega_2, \mathcal{A}_2) = (\mathbb{R}^d, \mathcal{B}^d)$ where $\mathcal{B}^d$ is the Borel σ-algebra on $\mathbb{R}^d$.

From the definition of a stochastic process it holds that for a fixed value $t \in [t_0, T]$, $X_t(\cdot)$ is an $\mathbb{R}^d$ valued random variable on $(\Omega_1, \mathcal{A}_1, \mathbb{P})$, while for a fixed $\omega \in \Omega_1$, $X.(\omega)$ is an $\mathbb{R}^d$ valued function defined on $[t_0, T]$. The function $X.(\omega) : [t_0, T] \to \mathbb{R}^d$, for a fixed $\omega \in \Omega_1$ is called a *sample path* (or sample trajectory or realisation) of the stochastic process.

A stochastic process defined on a probability space $(\Omega_1, \mathcal{A}_1, \mathbb{P})$ with index set $[t_0, T] \subset [0, \infty)$ satisfies the *Markov property* if for all $t_0 \leq s \leq t \leq T$ and all $B \in \mathcal{B}^d$ the following holds with probability 1:

$$\mathbb{P}(X_t \in B | \sigma([t_0, s])) = \mathbb{P}(X_t \in B | X_s)$$

where $\sigma([t_0, s]) = \sigma(X_t,\ t_0 \leq t \leq s)$ is the σ-algebra generated by the collection $\{X_t\}_{t_0 \leq t \leq s}$. The Markov property can be interpreted in the following way: When the present is known, information about the past of the Markov process does not bring any additional information about the probable development of the process in the future, i.e. given the present, the future of the Markov process is independent of its past.

Since $(\mathbb{R}^d, \mathcal{B}^d)$ is a Borel space, as mentioned in the previous section, Theorem 8.37 in [23] guarantees the existence of a regular conditional probability of X_t, given X_s. Therefore we define

$$P(s, x, t, B) := \mathbb{P}(X_t \in B | X_s = x).$$

The function $P(s, x, t, B)$ where $t_0 \leq s \leq t \leq T$, $x \in \mathbb{R}^d$, $B \in \mathcal{B}^d$ has the following properties:

1. For arbitrary $t_0 \leq s \leq t \leq T$ and $x \in \mathbb{R}^d$, $P(s, x, t, \cdot)$ is a probability measure on $\mathcal{B}^d$.
2. For arbitrary $t_0 \leq s \leq t \leq T$ and $B \in \mathcal{B}^d$, $P(s, \cdot, t, B) : \mathbb{R}^d \to [0, 1]$ is $\mathcal{B}^d$-measurable.
3. The Chapman-Kolmogorov equation holds, i.e. for any $x \in \mathbb{R}^d$,

$$P(s, x, t, B) = \int_{\mathbb{R}^d} P(u, y, t, B) P(s, x, u, dy),$$

   where $u \in (s, t)$ is arbitrary.

If in addition to conditions (1-3), for arbitrary $s \in [t_0, T]$ and $B \in \mathcal{B}^d$, it holds that

$$P(s, x, s, B) = \mathbf{1}_B(x), \tag{2.5}$$

then the function $P(t, x, s, B)$ is called the *transition probability* of Markov process.

A Markov process is called *time homogeneous* if the condition

$$P(s, x, t, B) = P(s + \tilde{h}, x, t + \tilde{h}, B)$$

holds for all $t_0 - \tilde{h} \leq s \leq t \leq T - \tilde{h}$ and all $\tilde{h} \in [0, T - t_0]$. Therefore, the transition probability for a time homogeneous Markov process depends only on the difference $h := t - s$ and can be written as

$$P(s, x, t, B) = P(h, x, B), \quad \text{for} \quad 0 \leq h \leq T - t_0.$$

We can then rewrite the Chapman-Kolmogorov equation for time homogeneous Markov process as

$$P(h_1 + h_2, x, B) = \int_{\mathbb{R}^d} P(h_2, y, B) P(h_1, x, \mathrm{d}y).$$

Every Markov process $\{X_t\}_{t \in [t_0, T]}$ can be transformed into a time homogeneous Markov process $\{Y_t\}_{t \in [t_0, T]} = \{(t, X_t)\}_{t \in [t_0, T]}$, by considering time as a state component [1, Remark

(2.2.9)]. The state space of $\{Y_t\}_{t\in[t_0,T]}$ is therefore $[t_0,T]\times\mathbb{R}^d$ and the transition probabilities of $\{Y_t\}_{t\in[t_0,T]}$, $P_Y(t,y,B)$ where $B=C\times D$, and $C\in\mathcal{B}([t_0,T])$, $D\in\mathcal{B}^d$ are given by

$$P_Y(t,y,C\times D)=P_Y(t,(s,x),C\times D)=P(s,x,s+t,D)\mathbf{1}_C(s+t).$$

At every time $t\in[t_0,T]$ the state of a Markov process is a random variable having some distribution. We assume that the distribution of X_{t_0} is absolutely continuous with respect to Lebesgue measure. The probability density ρ_{t_0} of X_{t_0} is a nonnegative function such that for all $B\in\mathcal{B}^d$

$$\mathbb{P}(X_{t_0}\in B)=\int_B\rho_{t_0}(x)\mathrm{d}x.$$

The function ρ_{t_0} is called the *initial probability density* of the process $\{X_t\}_{t\in[t_0,T]}$. Let $\{X_t\}_{t\in[t_0,T]}$ be a time homogeneous Markov process with initial density ρ_{t_0}. The probability of the Markov process $\{X_t\}_{t\in[t_0,T]}$ to visit some set $B\in\mathcal{B}^d$ at time t is then given by

$$\mathbb{P}(X_t\in B)=\int_{\mathbb{R}^d}P(t,x,B)\rho_{t_0}(x)\mathrm{d}x.$$

A probability measure μ on the state space $\mathbb{R}^d$ is called an *invariant probability measure* if the probability measure does not change under the stochastic dynamics of the Markov process, i.e. if for every $B\in\mathcal{B}^d$ it holds that

$$\int_{\mathbb{R}^d}P(t,x,B)\mu(\mathrm{d}x)=\mu(B). \tag{2.6}$$

Let an invariant probability measure be absolutely continuous with respect to Lebesgue measure. Then the Radon-Nikodym derivative $\rho(x)$ that satisfies

$$\rho(x)\mathrm{d}x=\mu(\mathrm{d}x)$$

is called the *invariant* or *equilibrium probability density*.

2.2.1 Infinitesimal operator

Let $\{X_t\}_{t\in[t_0,T]}$ denote a time homogeneous Markov process with transition probability $P(h,x,B)$. Let $B(\mathbb{R}^d):=B(\mathbb{R}^d;\mathbb{R})$ be the space of bounded, measurable, $\mathbb{R}$-valued functions on $\mathbb{R}^d$. Equip $B(\mathbb{R}^d)$ with the L^∞ norm. On $B(\mathbb{R}^d)$, we define the operator T_h as

$$T_hg(x)=\mathbb{E}_x[g(X_h)]=\int_{\mathbb{R}^d}g(y)P(h,x,\mathrm{d}y), \tag{2.7}$$

for $h\in[0,T-t_0]$, where $\mathbb{E}_x[g(X_h)]$ denotes the expectation of $g(X_h)$ conditioned on $X_{t_0}=x$. According to (2.5) it holds that $P(0,x,\cdot)=\mathbf{1}_\cdot(x)$. By substituting this into (2.7) we obtain $T_0g(x)=g(x)$. Therefore T_0 is the identity mapping.

For $g(x)=\mathbf{1}_B(x)$ we have

$$T_h\mathbf{1}_B(x)=P(h,x,B).$$

Therefore, transition operators T_h can be used to derive the transition probability. Moreover, there exists a single operator that can represent the dynamics of Markov process.

The *infinitesimal operator* or *generator* $\mathcal{A}$ of a time homogeneous Markov process $\{X_t\}_{t\in[t_0,T]}$ is defined by

$$\mathcal{A}g(x) = \lim_{h\to 0} \frac{T_h g(x) - g(x)}{h}, \quad g \in B(\mathbb{R}^d). \tag{2.8}$$

The value of $\mathcal{A}g(x)$ can be interpreted as the mean infinitesimal rate of change of $g(X_{t_0})$, given that $X_{t_0} = x$. We will denote the set of functions $g : \mathbb{R}^d \to \mathbb{R}$ for which this limit exists for all $x \in \mathbb{R}^d$ by $D_{\mathcal{A}}$.

As every Markov process $\{X_t\}_{t\in[t_0,T]}$ can be transformed into a time homogeneous Markov process $\{Y_t\}_{t\in[t_0,T]} = \{(t, X_t)\}_{t\in[t_0,T]}$ taking values in $[t_0, T] \times \mathbb{R}^d \subset \mathbb{R}^{d+1}$, we can define the transition operators $\{T_h\}_{h\in[t_0,T]}$ and the infinitesimal operator $\mathcal{A}$ of the process $\{Y_t\}_{t\in[t_0,T]}$ to be the same as those of $\{X_t\}_{t\in[t_0,T]}$. Namely, for $h \in [0, T - s]$, on the space of bounded measurable functions in $[t_0, T] \times \mathbb{R}^d$ we define

$$T_h g(s, x) = \mathbb{E}_{s,x}\left[g(s + h, X_{h+s})\right] = \int_{\mathbb{R}^d} g(s + h, y)P(s, x, s + h, \mathrm{d}y),$$

and

$$\mathcal{A}g(s, x) = \lim_{h\to 0} \frac{T_h g(s, x) - g(s, x)}{h}.$$

2.3 Diffusion processes

Diffusion processes are Markov processes that have continuous sample paths. In literature, there exist two approaches to studying them. The first approach involves posing constraints on transition probabilities, while the second studies the change of process $\{X_t\}_{t\in[t_0,T]}$ with respect to time, which leads to a stochastic differential equation.

We provide a definition of a diffusion process [1, Definition 2.5.1] based on the first approach.

Definition 2.3.1 (Diffusion process)**.** A Markov process $\{X_t\}_{t\in[t_0,T]}$ with almost certainly continuous sample functions is called a *diffusion process* if its transition probabilities $P(s, x, t, B)$, satisfy properties (2.9), (2.10), and (2.11) for every $s \in [t_0, T)$, $x \in \mathbb{R}^d$, and $\varepsilon > 0$:

$$\lim_{t\to s} \frac{1}{t - s} \int_{B(x,\varepsilon)^{\complement}} P(s, x, t, \mathrm{d}y) = 0, \tag{2.9}$$

there exists a function $b(s, x) : [t_0, T] \times \mathbb{R}^d \to \mathbb{R}^d$ such that

$$\lim_{t\to s} \frac{1}{t - s} \int_{B(x,\varepsilon)} (y - x)P(s, x, t, \mathrm{d}y) = b(s, x), \tag{2.10}$$

there exists a function $A(s, x) : [t_0, T] \times \mathbb{R}^d \to \mathbb{R}^{d\times d}$ such that

$$\lim_{t\to s} \frac{1}{t - s} \int_{B(x,\varepsilon)} (y - x)(y - x)^{\top} P(s, x, t, \mathrm{d}y) = A(s, x). \tag{2.11}$$

The functions b and A are referred to as the coefficients of the diffusion process. The function b is called the *drift vector* of the diffusion process and A is the *diffusion matrix*. The diffusion matrix is positive semidefinite and symmetric.

The condition (2.9) of Definition 2.3.1 implies that the probability of big changes in the value of X_t during the infinitesimally short time interval $[s,t]$ is vanishingly small. From condition (2.10) $b(s,x)$ can be interpreted as the mean velocity vector of $\{X_t\}_{t\in[t_0,T]}$ under the assumption that $X_s = x$ and from Condition (2.11) $A(s,x)$ can be interpreted as a measure of average fluctuations of $X_t - X_s$ around the mean, if $X_s = x$.

2.3.1 Stochastic differential

Differential equations of the form

$$\dot{X}_t = b(t,X_t) + \sigma(t,X_t)\xi_t, \quad t \in [t_0,T], \quad X_{t_0} = c$$

where ξ_t is m-dimensional white noise, X_t and b are $\mathbb{R}^d$-valued functions, σ is an $\mathbb{R}^{d\times m}$-valued function, and c is some random variable, often occur in the analysis of stochastic dynamic systems.

The above differential equation can also be written in integral form

$$X_t = c + \int_{t_0}^{t} b(s,X_s)\mathrm{d}s + \int_{t_0}^{t} \sigma(s,X_s)\mathrm{d}W_s, \quad t \in [t_0,T], \tag{2.12}$$

where W_t stands for the m-dimensional Wiener process. The first integral on the right-hand side of (2.12) is a Riemann integral, while the second one is an Itô stochastic integral. For the definition of Itô stochastic integral see [1, Section 4.4] or [23, Section 25].

We can therefore rewrite (2.12) as

$$\mathrm{d}X_t = b(t,X_t)\mathrm{d}t + \sigma(t,X_t)\mathrm{d}W_t, \quad t \in [t_0,T], \quad X_{t_0} = c \tag{2.13}$$

and say that the stochastic process $\{X_t\}_{t\in[t_0,T]}$ has the *stochastic differential* $b(t,X_t)\mathrm{d}t + \sigma(t,X_t)\mathrm{d}W_t$. Let now b and σ be defined and measurable on $[t_0,T]\times\mathbb{R}^d$. Equation (2.13) is called a *stochastic differential equation* and the random variable c is called the initial value of $\{X_t\}_{t\in[t_0,T]}$. Next we give a formulation [1, Theorem 5.3.8] of Itô's formula for computing how smooth functions act on stochastic differentials.

Theorem 2.3.2 (Itô's formula)**.** *Let the stochastic process $\{X_t\}_{t\in[t_0,T]}$ be defined by the stochastic differential equation*

$$\mathrm{d}X_t = b(t,X_t)\mathrm{d}t + \sigma(t,X_t)\mathrm{d}W_t,$$

and let $u \in C^{1,2}([t_0,T]\times\mathbb{R}^d;\mathbb{R}^k)$. Then the k-dimensional process $\{Y_t\}_{t\in[t_0,T]}$ where $Y_t = u(t,X_t)$ with initial value $Y_{t_0} = u(t_0,X_{t_0})$ also possesses a stochastic differential with respect to the same Wiener process W_t and

$$\mathrm{d}Y_t = \left(u_t(t,X_t) + u_x(t,X_t)b(t) + \frac{1}{2}\sum_{i,j=1}^{d} u_{x_ix_j}(t,X_t)(\sigma(t,X_t)\sigma(t,X_t)')_{ij} \right)\mathrm{d}t + u_x(t,X_t)\sigma(t,X_t)\mathrm{d}W_t$$

Itô's formula is a stochastic analogue of the chain rule.

2.3.2 Existence and uniqueness theorem

We give sufficient conditions for existence and uniqueness of a solution to the stochastic differential equation [1, Theorem 6.2.2].

Theorem 2.3.3 (Existence and uniqueness)**.** *Suppose that the stochastic differential equation* (2.13) *holds, with* c *being independent of* $W_t - W_{t_0}$*, for* $t \in [t_0, T]$ *and that* b *and* σ *are measurable functions on* $[t_0, T] \times \mathbb{R}^d$*. Suppose the following two properties hold:*

1. *There exists a constant* $K > 0$ *such that for all* $t \in [t_0, T]$*, and all* $x, y \in \mathbb{R}^d$

$$|b(t,x) - b(t,y)| + |\sigma(t,x) - \sigma(t,y)| \leq K|x - y|. \qquad \textit{(Lipschitz continuity)}$$

2. *For all* $t \in [t_0, T]$ *and all* $x \in \mathbb{R}^d$

$$|b(t,x)|^2 + |\sigma(t,x)|^2 \leq K^2(1 + |x|^2), \qquad \textit{(Linear growth)}$$

where $|\sigma|^2 = \sum \sigma_{ij}^2$*. Then the equation (2.13) has a unique solution* $\{X_t\}_{t\in[t_0,T]}$ *and this solution is almost surely continuous.*

The following theorem [1, Theorem 9.3.1] states the conditions under which the unique solution of (2.13) is a diffusion process.

Theorem 2.3.4. *Consider the stochastic differential equation* (2.13)*, and suppose that the conditions of Theorem 2.3.3 hold. If functions* b *and* σ *are continuous with respect to* t *then the solution* $\{X_t\}_{t\in[t_0,T]}$ *of equation (2.13) is a* d*-dimensional diffusion process on* $[t_0, T]$ *with drift vector* b *and diffusion matrix* $A(t,x) = \sigma(t,x)\sigma(t,x)^\top$*.*

2.3.3 Operators

In this section we establish a connection between the infinitesimal operator defined in Section 2.2.1 and a partial differential operator defined using diffusion coefficients. We will use this connection to show that under certain regularity conditions on the coefficients b and σ of the stochastic differential equation, the transition probability $P(s, x, t, B)$ can be uniquely determined from the drift vector b and the diffusion matrix $A = \sigma\sigma^\top$. We present the theory for time homogeneous diffusion processes. The following theorem [40, Theorem 7.3.3] expresses the infinitesimal generator as a partial differential operator.

Theorem 2.3.5. *Let* $\{X_t\}_{t\in[t_0,T]}$ *be a time homogeneous diffusion process given by*

$$\mathrm{d}X_t = b(X_t)\mathrm{d}t + \sigma(X_t)\mathrm{d}W_t, \quad X_{t_0} = c. \tag{2.14}$$

Let $\mathcal{A}$ *denote the generator of* $\{X_t\}_{t\in[t_0,T]}$ *defined in* (2.8) *and let* $D_{\mathcal{A}}$ *denote the set of all functions* $g : \mathbb{R}^d \to \mathbb{R}$ *for which* $\mathcal{A}g(x)$ *exists for all* $x \in \mathbb{R}^d$*. If* $g \in C_0^2(\mathbb{R}^d)$ *then* $g \in D_{\mathcal{A}}$ *and*

$$\mathcal{A}g(x) = \sum_{i=1}^{d} b_i(x)\frac{\partial g}{\partial x_i}(x) + \frac{1}{2}\sum_{i,j=1}^{d} a_{ij}(x)\frac{\partial^2 g}{\partial x_i \partial x_j}(x). \tag{2.15}$$

Thus, the generator of a diffusion process can be completely characterised by its diffusion coefficients.

Theorem 2.3.6. *[40, Theorem 7.4.1 and Theorem 8.1.1] Let $\{X_t\}_{t\in[t_0,T]}$ be a time homogeneous diffusion process given by*

$$\mathrm{d}X_t = b(X_t)\mathrm{d}t + \sigma(X_t)\mathrm{d}W_t \tag{2.16}$$

with generator $\mathcal{A}$ and let $g \in C_0^2(\mathbb{R}^d)$. Define

$$u(t,x) = \mathbb{E}_x\left[g(X_t)\right]$$

Then $u(t,x)$ is differentiable with respect to t, $u(t,\cdot) \in D_{\mathcal{A}}$ for each t and

$$\begin{array}{l} -\frac{\partial u(t,x)}{\partial t} + \mathcal{A}u(t,x) = 0, \qquad (t,x) \in [t_0,T]\times\mathbb{R}^d \\ u(t_0,x) = g(x), \quad x \in \mathbb{R}^d \end{array}. \tag{2.17}$$

The equation (2.17) is called *Kolmogorov's backward equation* where 'backward' corresponds to differentiation with respect to the backward time; for intuition on this matter see the nonhomogenous Kolmogorov's backward equation in [1, Theorem 2.6.3]. Kolmogorov's backward equation describes the evolution of the conditional expectations of functions of X_t. Compared to equation (2.8), Kolmogorov's backward equation is valid for any time t.

The evolution of the probability density of $\{X_t\}_{t\in[t_0,T]}$ is described by the *Fokker-Planck* equation or *Kolmogorov's forward* equation, given in the following theorem [1, Theorem 2.6.9]. Here 'forward' corresponds to differentiation of the transition density with respect to forward time t and state y. Let $\mathcal{A}^*$ be defined by

$$\mathcal{A}^*p = \frac{1}{2}\sum_{i,j=1}^{d}\frac{\partial^2(a_{ij}(y)p)}{\partial y_i \partial y_j} - \sum_{i=1}^{d}\frac{\partial\left(b_i(y)p\right)}{\partial y_i}. \tag{2.18}$$

Theorem 2.3.7. *Let $\{X_t\}_{t\in[t_0,T]}$ be a time homogeneous diffusion process for which the limit conditions* (2.9)*,* (2.10) *and* (2.11) *of Definition 2.3.1 hold uniformly in $s \in [t_0,T]$ and $x \in \mathbb{R}^d$ and let $p(t-s,x,y)$ be its transition density. If $p(\cdot,x,y) \in C^1((t_0,T);\mathbb{R})$ for every $x,y \in \mathbb{R}^d$, and $b_i(\cdot)p(t,x,\cdot) \in C^1(\mathbb{R}^d;\mathbb{R})$, $a_{ij}(\cdot)p(t,x,\cdot) \in C^2(\mathbb{R}^d;\mathbb{R})$, for $t,x \in [t_0,T]\times\mathbb{R}^d$, then for a fixed s and x, the transition density $p(t-s,x,y)$ is a fundamental solution of the following equation*

$$\frac{\partial p}{\partial t} = \mathcal{A}^*p. \tag{2.19}$$

Remark 2.3.8. *Since the invariant probability density $\rho(x)$ of a Markov process $\{X_t\}_{t\in[t_0,T]}$ is time independent,* (2.19) *reduces to*

$$\mathcal{A}^*\rho(x) = 0, \quad \forall x \in \mathbb{R}^d,$$

and it follows that the invariant probability density is the solution of the stationary forward Kolmogorov equation.

Remark 2.3.9. *The partial differential operator $\mathcal{A}^*$ is the L^2-adjoint of the operator $\mathcal{A}$, i.e. for every $u,v \in L^2(\mathbb{R}^d,\mathrm{d}x)$*

$$\int_{\mathbb{R}^d} v\mathcal{A}u\mathrm{d}x = \int_{\mathbb{R}^d} u\mathcal{A}^*v\mathrm{d}x.$$

For the boundary conditions under which the adjointness condition holds see for example [21, Section 2].

Next we give a guarantee [49, Theorem 2.2.9] for the uniqueness of the solution of the forward Kolmogorov equation (2.19) for time homogeneous diffusions.

Theorem 2.3.10. *Let $\mathcal{A}$ be given as in equation* (2.15) *with time independent coefficients, i.e. $a_{ij}(t,x) = a_{ij}(x)$ and $b_i(t,x) = b_i(x)$. Let $a_{ij}, b_i \in C^2(\mathbb{R}^d;\mathbb{R})$, let their first derivatives be bounded, and let their second derivatives have at most polynomial growth, that is there exist $C > 0$ and $r \in \mathbb{N} \cup \{0\}$ such that*

$$|f(x)| \leq C(1 + |x|^{2r}),$$

for $f = \frac{\partial^2 a_{ij}}{\partial x_k \partial x_l}$ or $f = \frac{\partial^2 b_i}{\partial x_k \partial x_l}$ and $k, l \in \{1, \dots d\}$. Then there exists a unique continuous transition probability $P(t,x,\mathrm{d}y)$ with transition density $p(t,x,y)$ satisfying

$$\int_{\mathbb{R}^d} \varphi(y)p(t,x,y)\mathrm{d}y = \varphi(x) + \int_0^t \int_{\mathbb{R}^d} \mathcal{A}\varphi(y)p(\tau,x,y)\mathrm{d}y\mathrm{d}\tau, \tag{2.20}$$

for any $\varphi \in C^2(\mathbb{R}^d;\mathbb{R})$ with bounded second order derivatives. Furthermore, for each measure ν with moments of all orders, there exists a measure $\mu(A,t)$ defined as

$$\mu(A,t) = \int_A \int_{\mathbb{R}^d} p(t,x,y)\nu(\mathrm{d}x)\mathrm{d}y, \quad A \in \mathcal{B}^d$$

such that μ is the unique solution of

$$\int_{\mathbb{R}^d} \varphi(y)\mu(\mathrm{d}y,t) - \int_{\mathbb{R}^d} \varphi(x)\nu(\mathrm{d}x) = \int_0^t \int_{\mathbb{R}^d} \mathcal{A}\varphi(y)\mu(\mathrm{d}y,\tau)\mathrm{d}\tau, \tag{2.21}$$

for any $\varphi \in C_0^2(\mathbb{R}^d;\mathbb{R})$.

Let us interpret the equation (2.20). The following computations are not rigorous, because the Dirac delta measure does not have a density. However, the computations are intended to communicate the main idea. Note first that $\varphi(x)$ can be written as

$$\varphi(x) = \int_{\mathbb{R}^d} \varphi(y)\delta(x-y) = \int_{\mathbb{R}^d} \varphi(y)p(0,x,y)\mathrm{d}y.$$

Using this in the first equality and the fact that $\mathcal{A}$ and $\mathcal{A}^*$ are adjoint in the second, we obtain

$$\begin{aligned}\int_{\mathbb{R}^d} \varphi(y)p(t,x,y)\mathrm{d}y &= \int_{\mathbb{R}^d} \varphi(y)p(0,x,y)\mathrm{d}y + \int_0^t \int_{\mathbb{R}^d} \mathcal{A}\varphi(y)p(\tau,x,y)\mathrm{d}y\mathrm{d}\tau \\ &= \int_{\mathbb{R}^d} \varphi(y)p(0,x,y)\mathrm{d}y + \int_{\mathbb{R}^d} \varphi(y) \int_0^t \mathcal{A}^* p(\tau,x,y)\mathrm{d}\tau\mathrm{d}y.\end{aligned}$$

Since the above equation holds for every $\varphi \in C^2(\mathbb{R}^d;\mathbb{R})$, it follows that

$$p(t,x,y) = p(0,x,y) + \int_0^t \mathcal{A}^* p(\tau,x,y)\mathrm{d}\tau.$$

Thus, by using the fundamental theorem of calculus we obtain

$$\frac{\partial p(\tau,x,y)}{\partial \tau} = \mathcal{A}^* p(\tau,x,y).$$

Therefore equation (2.20) of Theorem 2.3.10 tells us that the transition probability density $p(t,x,y)$ is the only solution to the forward Kolmogorov equation (2.19) for the initial condition $p(0,x,y)=\delta(x-y)$.

A more general result given in equation (2.21) tells us that for any initial distribution ν there exists a unique distribution μ that depends on ν and whose corresponding probability density $p_\mu(t,x,y)$, if it exists, solves the forward Kolmogorov equation (2.19).

2.4 Time reversed diffusion process

Let $\{X_t\}_{t\in[t_0,T]}$ be a diffusion process satisfying the stochastic differential equation

$$\mathrm{d}X_t = b(t,X_t)\mathrm{d}t + \sigma(t,X_t)\mathrm{d}W_t, \quad X_{t_0}=c.$$

In this section we introduce the time reversed process $\{X_t^r\}_{t\in[t_0,T]}$, give conditions that guarantee that $\{X_t^r\}_{t\in[t_0,T]}$ is also a diffusion process, and give explicit formulae for the diffusion coefficients of the time reversed process $\{X_t^r\}_{t\in[t_0,T]}$.

Let $\{X_t^r\}_{t\in[t_0,T]}$ denote the time reversal of the process $\{X_t\}_{t\in[t_0,T]}$, i.e. $X_t^r = X_{T-t}$. The Markov property treats past and future symmetrically, i.e. past and future are independent of each other given the present. Therefore, the time reversed process $\{X_t^r\}_{t\in[t_0,T]}$ is again a Markov process. The following result of [19, Theorem 2.1 and Theorem 3.1] gives conditions under which $\{X_t^r\}_{t\in[t_0,T]}$ is a diffusion process.

Theorem 2.4.1. *Let $b(t,X_t)$ and $\sigma(t,X_t)$ be such that the conditions of Theorem 2.3.3 hold. Let the law of X_{t_0} have a density ρ_{t_0} such that for some $\lambda<0$*

$$\int_{\mathbb{R}^d} \rho_{t_0}^2(x)(1+|x|^2)^\lambda \mathrm{d}x < \infty.$$

If either of the following two conditions hold

i) there exists $\alpha>0$ such that $A(t,x)>\alpha I$,

ii) $\frac{\partial^2 a_{ij}}{\partial x_i \partial x_j} \in L^\infty((t_0,T)\times\mathbb{R}^d)$, for all $i,j\in\{1,\dots,d\}$,

then $\{X_t^r\}_{t\in[t_0,T]}$ is a diffusion process which satisfies the stochastic differential equation

$$\mathrm{d}X_t^r = b^r(t,X_t^r)\mathrm{d}t + \sigma^r(t,X_t^r)\mathrm{d}W_t, \quad X_{t_0}^r = X_T$$

where

$$b_i^r(t,x) = -b_i(T-t,x) + \frac{1}{\rho(T-t,x)}\sum_{j=1}^d \frac{\partial\left(a_{ij}(T-t,x)\rho(T-t,x)\right)}{\partial x_j} \tag{2.22}$$

with $\rho(t,x)$ denoting the density of X_t, and $a_{ij}^r(t,x) = a_{ij}(T-t,x)$.

The infinitesimal generator of the time reversed process is then given by

$$\mathcal{A}^r = \sum_{i=1}^d b_i^r(t,x)\frac{\partial}{\partial x_i} + \frac{1}{2}\sum_{i,j=1}^d a_{ij}(T-t,x)\frac{\partial^2}{\partial x_i \partial x_j}. \tag{2.23}$$

One might notice that in Theorem 2.4.1 the assumptions differ from the assumptions given in [19]. In particular, we omit the assumption of Borel-measurability of functions $b(t, X_t)$ and $\sigma(t, X_t)$ because it is implied by the Lipschitz continuity. Namely, every Lipschitz continuous function is continuous, hence Borel-measurable. Furthermore, the linear growth condition in [19]

$$|b(t,x)| + |\sigma(t,x)| \leq K(1+|x|), \tag{2.24}$$

is equivalent to the linear growth condition in Theorem 2.3.3. We show this using the inequality $ab \leq \frac{1}{2}(a^2+b^2)$. By multiplying this inequality by 2 and adding a^2+b^2 to both sides we obtain

$$(a+b)^2 \leq 2(a^2+b^2). \tag{2.25}$$

Let (2.24) hold. Therefore

$$|b(t,x)|^2 + |\sigma(t,x)|^2 + 2\,|b(t,x)|\,|\sigma(t,x)| \leq K^2(1+|x|)^2 \leq 2K^2(1+|x|^2).$$

where the first inequality was obtained by squaring (2.24) and the second using (2.25). Since $2\,|b(t,x)|\,|\sigma(t,x)| \geq 0$ the linear growth condition from Theorem 2.3.3 holds with constant $\sqrt{2}K$.
Let now the linear growth condition from Theorem 2.3.3 hold, i.e. let

$$|b(t,x)|^2 + |\sigma(t,x)|^2 \leq K^2(1+|x|^2).$$

By multiplying the previous inequality by 2 we obtain

$$\begin{aligned}(|b(t,x)| + |\sigma(t,x)|)^2 &\leq 2(|b(t,x)|^2 + |\sigma(t,x)|^2) \leq 2K^2(1+|x|^2)\\ &\leq 2K^2(1+|x|^2) + 4K^2\,|x| = 2K^2(1+|x|)^2,\end{aligned}$$

where we used (2.25) in the first and the fact that $4K^2\,|x| \geq 0$ in the last inequality. After taking the square root we see that the condition (2.24) holds with constant equal to $\sqrt{2}K$.

2.5 Reversibility

In this section, we focus only on time homogeneous diffusion processes. A diffusion process is *time reversible* or *reversible* if the original and time reversed process are probabilistically the same.

Let $\{X_t\}_{t\in[t_0,T]}$ be a time homogeneous Markov process given by

$$\mathrm{d}X_t = b(X_t)\mathrm{d}t + \sigma(X_t)\mathrm{d}W_t, \quad X_{t_0} = c,$$

taking values in $\overline{S} = S \cup \partial S$, where $S \subset \mathbb{R}^d$, and let $p(t,x,y)$ be its transition probability density. Note that due to the assumption of time homogeneity, the diffusion coefficients are independent of t. Let $\{X_t^r\}_{t\in[t_0,T]}$ be the time reversal of the process $\{X_t\}_{t\in[t_0,T]}$ and let $p^r(t,x,y) := p(t,y,x)$ be its transition probability density. With this notation in mind, a diffusion process is time reversible if $p(t,x,y) = p(t,y,x)$.

In the remainder of this section we will give a necessary and sufficient condition for a diffusion process to be reversible. We introduce symmetric diffusions for this reason.

A diffusion process is *v-symmetric* if for some function $v(x) > 0$ on $\overline{S}$, the transition probability density $p(t, x, y)$ satisfies the following condition:

$$\frac{p(t,x,y)}{v(y)} = \frac{p(t,y,x)}{v(x)}. \tag{2.26}$$

A function $p(t, x, y)$ is a *minimal fundamental solution* of the time homogeneous backward Kolmogorov equation (2.17) if for any other fundamental solution $u(t, x, y)$ of the backward Kolmogorov equation it holds that $p(t, x, y) \leq u(t, x, y)$, for all $t \in [t_0, T]$, $x, y \in \mathbb{R}^d$.

In the following theorem we give a necessary and sufficient condition [21, Theorem 4.1] for the minimal fundamental solution of the backward Kolmogorov equation to be v-symmetric.

Theorem 2.5.1. *Let $v \in C^2(\bar{S}; \mathbb{R}_{>0})$ and let $p(t, x, y)$ be the minimal fundamental solution of the backward Kolmogorov equation (2.17). $p(t, x, y)$ is v-symmetric if and only if*

$$\sum_{j=1}^{d} a_{ij}(x) \frac{\partial v}{\partial_{x_j}} = \left(2b_i - \sum_{j=1}^{d} \frac{\partial a_{ij}(x)}{\partial x_j} \right) v. \tag{2.27}$$

The equation (2.27) is called the *detailed-balance* equation. However, in the community of chemical physics and Markov state models the equation

$$p(t, x, y)\rho(x) = p(t, y, x)\rho(y).$$

is known as the detailed-balance equation.

The following result due to Kolmogorov [21, Theorem 4.2] gives a necessary and sufficient condition for the existence of a function $v(x)$ for which the solution of the backward Kolmogorov equation is v-symmetric.

Theorem 2.5.2. *The minimal fundamental solution of the backward Kolmogorov equation* (2.17) *is v-symmetric for some function v if and only if there exists a scalar function $\varphi(x) \in C^2(S; \mathbb{R})$ such that the following holds*

$$2b_i - \sum_{j=1}^{d} \frac{\partial a_{ij}(x)}{\partial x_j} = \sum_{j=1}^{d} a_{ij}(x) \frac{\partial \varphi(x)}{\partial x_j}$$

We now state the necessary and sufficient condition for the reversibility of a diffusion process [21, Theorem 6.1].

Theorem 2.5.3. *Let $p(t, x, y)$ be the minimal fundamental solution of the backward Kolmogorov equation (2.17). The time-homogeneous diffusion process $\{X_t\}_{t \in [t_0, T]}$ with transition density $p(t, x, y)$ is time reversible if and only if $\{X_t\}_{t \in [t_0, T]}$ has an equilibrium density $v(x)$ with respect to which $p(t, x, y)$ is v-symmetric.*

The function $p(t, x, y)$ can be interpreted as the transition probability density of a diffusion on the domain $\overline{S}$. On a compact domain $\overline{S}$ the minimality condition is not needed. For more details on existence of the minimal fundamental solution see [21, Section 2]. From the definition of a reversible diffusion process it follows that the equilibrium densities of a diffusion process and its time reversal coincide.

Lemma 2.5.4. *Let $\{X_t\}_{t\in[t_0,T]}$ be a reversible time homogeneous process with equilibrium density $\rho(x)$. Then $\rho(x)$ is also an equilibrium density of the time reversed process $\{X_t^r\}_{t\in[t_0,T]}$.*

Proof. The claim follows from the fact that for a reversible process $p^r(t,x,y) = p(t,x,y)$. Namely, it holds that

$$\int_{\mathbb{R}^d}\int_B p^r(t,x,y)\mathrm{d}y\ \mu(\mathrm{d}x) = \int_{\mathbb{R}^d}\int_B p(t,x,y)\mathrm{d}y\ \mu(\mathrm{d}x) = \mu(B),$$

where $\mu(\mathrm{d}x) = \rho(x)\mathrm{d}x$ and we used the definition of the invariant probability measure (2.6) in the second equality. Therefore by (2.6) ρ is an equilibrium density of the time reversed process $\{X_t^r\}_{t\in[t_0,T]}$. □

Theorem 2.5.5. *Let $\{X_t\}_{t\in[t_0,T]}$ be a diffusion process with time independent coefficients and generator $\mathcal{A}$. Let $\mathcal{A}^r$ be the generator of the time reversed process $\{X_t^r\}_{t\in[t_0,T]}$. If $\{X_t\}_{t\in[t_0,T]}$ is reversible, then the generators of these two processes are the same, i.e.*

$$\mathcal{A} = \mathcal{A}^r.$$

Proof. From the formula (2.23) for the generator of the time reversed process, $\mathcal{A}^r$ is given by

$$\mathcal{A}^r = \sum_{i=1}^d b_i^r(x)\frac{\partial}{\partial x_i} + \frac{1}{2}\sum_{i,j=1}^d a_{ij}(x)\frac{\partial^2}{\partial x_i\partial x_j}.$$

Substituting the expression (2.22) for b_i^r and the equilibrium density $\rho(x)$ instead of $p(T-t,x)$, which we may do due to Lemma 2.5.4, we have

$$\begin{aligned}\mathcal{A}^r =& \sum_{i=1}^d\left(-b_i(x) + \frac{1}{\rho(x)}\sum_{j=1}^d\frac{\partial\left(a_{ij}(x)\rho(x)\right)}{\partial x_j}\right)\frac{\partial}{\partial x_i}\\ &+\frac{1}{2}\sum_{i,j=1}^d a_{ij}(x)\frac{\partial^2}{\partial x_i\partial x_j}.\end{aligned} \tag{2.28}$$

From Theorem 2.5.3 it follows that the transition probability density of $\{X_t\}_{t\in[t_0,T]}$ is symmetric with respect to $\rho(x)$ and by Theorem 2.5.1 the symmetry condition is equivalent to the detailed balance condition, i.e.

$$\sum_{j=1}^d a_{ij}(x)\frac{\partial\rho(x)}{\partial x_j} = \left(2b_i(x) - \sum_{j=1}^d\frac{\partial a_{ij}(x)}{\partial x_j}\right)\rho(x)$$

holds, or equivalently

$$2b_i(x)\rho(x) = \sum_{j=1}^d a_{ij}(x)\frac{\partial\rho(x)}{\partial x_j} + \sum_{j=1}^d\frac{\partial a_{ij}(x)}{\partial x_j}\rho(x) = \sum_{j=1}^d\frac{\partial(a_{ij}(x)\rho(x))}{\partial x_j}. \tag{2.29}$$

By substituting (2.29) into (2.28) we obtain

$$\begin{aligned}\mathcal{A}^r &= \sum_{i=1}^{d} \left(-b_i(x) + 2b_i(x)\right) \frac{\partial}{\partial x_i} + \frac{1}{2} \sum_{i,j=1}^{d} a_{ij}(x) \frac{\partial^2}{\partial x_i \partial x_j} \\ &= \sum_{i=1}^{d} b_i(x) \frac{\partial}{\partial x_i} + \frac{1}{2} \sum_{i,j=1}^{d} a_{ij}(x) \frac{\partial^2}{\partial x_i \partial x_j} = \mathcal{A}.\end{aligned}$$

□

2.6 Smoluchowski dynamics

Smoluchowski dynamics is described by the following stochastic differential equation

$$\mathrm{d}X_t = -\Gamma^{-1} \nabla V(X_t) \mathrm{d}t + \sqrt{2\beta^{-1}} \Gamma^{-\frac{1}{2}} \mathrm{d}W_t, \tag{2.30}$$

where $X_t \in \mathbb{R}^d$ represents the position of a particle at time t, $\Gamma = \mathrm{diag}(\gamma_1, ..., \gamma_d)$ is a diagonal matrix with friction coefficients $\gamma_i > 0$, and the function $V : \mathbb{R}^d \to \mathbb{R}$ is a potential. The parameter β represents the inverse temperature and it is related to the actual temperature $\mathcal{T}$ of the system by

$$\beta = \frac{1}{k_B \mathcal{T}},$$

where k_B denotes the Boltzmann constant.

By setting $b = -\Gamma^{-1} \nabla V$ and $\sigma = \sqrt{2\beta^{-1}} \Gamma^{-1/2}$ in equation (2.15), we obtain the infinitesimal operator of Smoluchowski dynamics,

$$\mathcal{A} = -\Gamma^{-1} \nabla V(x) \cdot \nabla + \frac{1}{\beta} \sum_{i=1}^{d} \gamma_i^{-1} \frac{\partial^2}{\partial x_i^2}.$$

Similarly, by equation (2.18) the adjoint operator $\mathcal{A}^*$ is given by

$$\mathcal{A}^* p = \beta^{-1} \sum_{i=1}^{d} \gamma_i^{-1} \frac{\partial^2 p}{\partial x_i^2} + \sum_{i=1}^{d} \gamma_i^{-1} \frac{\partial V(x)}{\partial x_i} \frac{\partial p}{\partial x_i} + \sum_{i=1}^{d} \gamma_i^{-1} \frac{\partial^2 V(x)}{\partial x_i^2} p. \tag{2.31}$$

The invariant probability density of the process defined by (2.30) is given by

$$\rho(x) = Z^{-1} e^{-\beta V(x)}$$

where

$$Z = \int_{\mathbb{R}^d} e^{-\beta V(x)} \mathrm{d}x.$$

Indeed, we check that the invariant density ρ satisfies the forward Kolmogorov equation (2.19), with $\mathcal{A}^*$ given in equation (2.31).

$$\begin{aligned}\mathcal{A}^* \rho(x) &= \beta^{-1} \sum_{i=1}^{d} \gamma_i^{-1} \frac{\partial^2 (Z^{-1} e^{-\beta V})}{\partial x_i^2} + \sum_{i=1}^{d} \frac{\partial V}{\partial x_i} \frac{\partial (Z^{-1} e^{-\beta V})}{\partial x_i} + Z^{-1} e^{-\beta V} \sum_{i=1}^{d} \gamma_i^{-1} \frac{\partial^2 V}{\partial x_i^2} \\ &= Z^{-1} e^{-\beta V} \sum_{i=1}^{d} \gamma_i^{-1} \left(\beta \left(\frac{\partial V}{\partial x_i} \right)^2 - \frac{\partial^2 V}{\partial x_i^2} + \frac{\partial^2 V}{\partial x_i^2} - \beta \sum_{i=1}^{d} \left(\frac{\partial V}{\partial x_i} \right)^2 \right) = 0\end{aligned}$$

Since

$$2b_i - \sum_{j=1}^{d} \frac{\partial a_{ij}}{\partial x_j} = -2\gamma_i^{-1} \frac{\partial V}{\partial x_j},$$

and

$$\sum_{j=1}^{d} a_{ij} \frac{\partial \varphi(x)}{\partial x_j} = 2\beta^{-1}\gamma_i^{-1} \frac{\partial \varphi(x)}{\partial x_i},$$

where we used that a_{ij} is constant in the first equality and that is zero for $i \neq j$, there exists a scalar function $\varphi(x) \in C^2(S;\mathbb{R})$ such that

$$2b_i - \sum_{j=1}^{d} \frac{\partial a_{ij}}{\partial x_j} = \sum_{j=1}^{d} a_{ij} \frac{\partial \varphi(x)}{\partial x_j}.$$

The function φ is a scalar multiple of $V \in C^2(S;\mathbb{R})$, i.e. $\varphi = -\beta V(x)$. Then by Theorem 2.5.2, the minimal fundamental solution of the backward Kolmogorov equation corresponding to the Smoluchowski dynamics is v-symmetric for some function v. The function v is related to φ in the following way: $v(x) := e^{\varphi(x)}$, i.e. by Theorem 2.5.1 the minimal fundamental solution of the backward Kolmogorov equation corresponding to the Smoluchowski dynamics is symmetric with respect to the function $v = e^{-\beta V(x)}$. Since ρ is a scalar multiple of v by (2.26) the minimal fundamental solution of the backward Kolmogorov equation corresponding to the Smoluchowski dynamics is ρ-symmetric as well. By Theorem 2.5.3 it follows that the Smoluchowski process $\{X_t\}_{t\in[t_0,T]}$ given in (2.30) is *time reversible*.

2.7 Dirichlet problem

Let L be a linear second order partial differential operator on the space of $C^2(\mathbb{R}^d;\mathbb{R})$ defined by

$$L = \frac{1}{2} \sum_{i,j=1}^{d} a_{ij}(x) \frac{\partial^2}{\partial x_i \partial x_j} + \sum_{i=1}^{d} b_i(x) \frac{\partial}{\partial x_i} + c(x),$$

with real coefficients $a_{ij}(x)$, $b_i(x)$, and $c(x)$. If the matrix $A(x) = \sigma(x)\sigma(x)^\top$ is positive definite on a bounded domain D, i.e.

$$\xi' A(x) \xi > 0, \quad \forall \xi \in \mathbb{R}^n, \ \xi \neq 0, \quad \forall x \in D, \tag{2.32}$$

then the partial differential operator L satisfying condition (2.32) is called *elliptic*. If instead of condition (2.32) there exists a constant $k > 0$ such that

$$\xi' A(x) \xi \geq k|\xi|^2, \quad \forall \xi \in \mathbb{R}^n, \ \xi \neq 0, \quad \forall x \in D,$$

then the operator L is called *uniformly elliptic*.
For a given $g \in C(D)$ and function $\phi \in C(\partial D)$, consider the problem of finding a solution $u \in C^2(D;\mathbb{R})$ of the boundary problem:

$$\begin{aligned} Lu(x) &= g(x) \quad x \in D \\ u(x) &= \phi(x) \quad x \in \partial D. \end{aligned} \tag{2.33}$$

The problem defined in equation (2.33) is called a *Dirichlet problem.* The following theorem gives a sufficient condition for existence and uniqueness [17, Section 6.5] of a solution of the Dirichlet problem.

Theorem 2.7.1 (Existence and uniqueness)**.** *Let L be a uniformly elliptic partial differential operator on D with uniformly Lipschitz continuous coefficients b_i and a_{ij} on $\overline{D}$ and coefficient $c \leq 0$ which is uniformly Hölder continuous on $\overline{D}$. Let $\partial D \in C^2$. For any g uniformly Hölder continuous on $\overline{D}$ and any ϕ continuous on ∂D, the Dirichlet problem* (2.33) *has a unique solution.*

The unique solution whose existence is guaranteed in the previous theorem has the form given in the following theorem [17, Theorem 6.5.1]. The representation of the unique solution follows from Itô's formula given in Theorem 2.3.2.

Theorem 2.7.2. *Let the conditions of Theorem 2.7.1 hold. The unique solution of the Dirichlet problem (2.33) is given by*

$$u(x) = \mathbb{E}_x\left[\phi(X_\tau)\exp\left[\int_0^\tau c(X_s)\mathrm{d}s\right]\right] - \mathbb{E}_x\left[\int_0^\tau g(X_t)\exp\left[\int_0^t c(X_s)\mathrm{d}s\right]\mathrm{d}t\right],$$

where τ is the exit time from D, i.e,

$$\tau = \inf\{t > t_0 \mid X_t \in D^{\complement}\}.$$

Chapter 3

Transition path theory for diffusion processes

In this section we summarise the main ideas of the transition path theory. Transition path theory is a statistical theory developed for the analysis of rare transition events of a diffusion process, between two pre-specified subsets of the state space of the diffusion. More precisely, it provide us with tools to describe the mechanism of transitions, i.e. the paths of transitions, their probability density and reaction rates.

In this section we consider an ergodic diffusion process $\{X_t\}_{t>0}$ taking values in $S \subset \mathbb{R}^d$, given by the following stochastic differential equation

$$\mathrm{d}X_t = b\left(X_t\right)\mathrm{d}t + \sigma(X_t)\mathrm{d}W_t \tag{3.1}$$

where $X_t \in S$, $b(X_t) \in \mathbb{R}^d$ is the drift vector, $\sigma(X_t) \in \mathbb{R}^{d\times d}$ and W_t is a d-dimensional Brownian motion. Note that the process given in equation (3.1) is time homogeneous.

A diffusion process is called ergodic if it has a unique invariant measure and its stationary statistics can be realised by an infinitely long trajectory, i.e. b and σ are such that there exists a unique invariant probability measure $\mu(\mathrm{d}x) = \rho(x)\mathrm{d}x$, where ρ denotes the equilibrium probability density function and

$$\lim_{T\to\infty} \frac{1}{T}\int_0^T f(X_s)\mathrm{d}s = \int_{\mathbb{R}^d} f(y)\rho(y)\mathrm{d}y,$$

for all $f \in L^1(\mu)$.

Let $A, B \subset S$ be two μ-measurable, disjoint sets with smooth boundaries. By ergodicity it follows that the process $\{X_t\}_{t>0}$ makes the transition from set A to set B, as well as the transition from B to A, infinitely often. We are interested in understanding how these transitions occur. While having knowledge of μ suffices for obtaining the proportion of time that the process spends in a predefined open set $C \subset S \setminus (A \cup B)$, as $\frac{\mu(C)}{\mu(S\setminus(A\cup B))}$, this does not give us the proportion of time that the process spends in the set C while making transitions from A to B, because this quantity does not differentiate between transitions from A to B or from B to A. To be able to understand the statistics of transitions between sets A and B, we need to introduce new notions, such as the notion of reactive trajectories, committor functions and probability density of reactive trajectories.

3.1 Reactive trajectories and their probability density

Let us define the set of *reactive times* R as the set of times that the process spends while transitioning from A to B, i.e. $R = \bigcup_{i\in\mathbb{N}} \left(t_i^-,\ t_i^+\right)$, where t_i^- and t_i^+ for all $i \in \mathbb{N}$ are such that $X_{t_i^-} \in \partial A$, $X_{t_i^+} \in \partial B$ and $X_t \in S \setminus (A \cup B)$, for all $t \in (t_i^-,\ t_i^+)$.

A portion of a trajectory during which the process makes a transition between the sets A and B is called an *AB-reactive trajectory*, that is, an AB-reactive trajectory is a trajectory segment corresponding to a reactive time $(t_i^-,\ t_i^+)$, for some $i \in \mathbb{N}$. Unless otherwise stated, in the following text we are interested in transitions from A to B. Thus we simplify the notation and refer to AB-reactive trajectories as *reactive trajectories*. The ensemble of reactive trajectories is the set of all reactive trajectories. By ergodicity and the definition of the reactive times R, the ensemble of reactive trajectories is $\{X_t\}_{t\in R}$.

We wish to obtain the probability distribution of reactive trajectories μ_R which is the invariant probability distribution with respect to which reactive trajectories are ergodic, i.e. for any μ-measurable set $C \subset S \setminus (A \cup B)$ it holds

$$\lim_{T\to\infty} \frac{\int_{R\cap[0,T]} \mathbf{1}_C(X_t)\mathrm{d}t}{\int_{R\cap[0,T]} \mathrm{d}t} = \mu_R(C).$$

Important objects for expressing the probability distribution of reactive trajectories μ_R are the forward and backward committor functions.

3.2 Committor functions

The *forward committor function* $q : S \setminus (A \cup B) \to [0,1]$ is defined at any point $x \in S \setminus (A \cup B)$ as the probability of reaching first B rather than A when starting from point x. Similarly, the *backward committor function* $q_b : S \setminus (A \cup B) \to [0,1]$ is defined at any point $x \in S \setminus (A \cup B)$ as the probability that a trajectory arriving at x last came from A, rather than B.

Note that we can extend the definitions of q and q_b onto the whole space S, while preserving the interpretation of values of committor functions as probabilities. We define $q(x) = 0$ for all $x \in A$ and $q(x) = 1$ for all $x \in B$. Similarly, we have $q_b(x) = 1$ for $x \in A$ and $q_b(x) = 0$ for $x \in B$.

Remark 3.2.1. *The backward committor function can be interpreted as the forward committor function of the time reversed diffusion process $\{X_t^r\}_{t>0}$, when the roles of the sets A and B are reversed, i.e. when we observe transitions from B to A of the process $\{X_t^r\}_{t>0}$.*

Let $\tau_{A\cup B}$ denote the *first hitting time* of the process $\{X_t\}_{t>0}$ with respect to the set $A \cup B$, i.e.

$$\tau_{A\cup B}(\{X_t\}_{t\geq 0}) = \inf\{t \geq 0 : X_t \in A \cup B\}. \tag{3.2}$$

Then the forward committor function can be expressed as

$$q(x) = \mathbb{P}(X_{\tau_{A\cup B}} \in B | X_0 = x) = \mathbb{E}_x\left[\mathbf{1}_B(X_{\tau_{A\cup B}})\right]. \tag{3.3}$$

As defined in Section 2.3.3 the generator of the diffusion process given in (3.1) is the second order partial differential operator given by

$$\mathcal{A} = \frac{1}{2}\sum_{i,j=1}^{d} a_{ij}\frac{\partial^2}{\partial x_i \partial x_j} + \sum_{i=1}^{d} b_i \frac{\partial}{\partial x_i} \tag{3.4}$$

where a_{ij} are the elements of the diffusion matrix A of the process (3.1) defined by $A(X_t) = \sigma(X_t)\sigma(X_t)^T \in \mathbb{R}^{d\times d}$. The forward committor function satisfies the backward Kolmogorov equation (2.17) associated with process (3.1)

$$\begin{aligned} &\mathcal{A}q = 0, \quad x \in S \setminus (A \cup B) \\ &q|_{\partial A} = 0, \quad q|_{\partial B} = 1. \end{aligned} \tag{3.5}$$

From Theorem 2.7.2 for the case that the operator L is given by $\mathcal{A}$ (and thus $c(x) = 0$), it follows that if there exists a solution to problem (3.5), it is equal to $\mathbb{E}_x\left[\mathbf{1}_B(X_{\tau_{A\cup B}})\right]$. According to the expression of the forward committor given in equation (3.3), we see that $q(x)$ is the solution of (3.5).

Similarly, the backward committor function satisfies the backward Kolmogorov equation associated with the time reversed process

$$\begin{aligned} &\mathcal{A}^r q_b = 0, \quad x \in S \setminus (A \cup B) \\ &q_b|_{\partial A} = 1, \quad q_b|_{\partial B} = 0, \end{aligned} \quad .$$

where $\mathcal{A}^r$ is the generator of the time reversed process $\{X_t^r\}_{t>0}$, defined in Section 2.4.

If the process (3.1) is reversible, from Theorem 2.5.5 it follows that $\mathcal{A} = \mathcal{A}^r$ and therefore

$$q_b(x) = 1 - q(x). \tag{3.6}$$

In the following theorem [14, Proposition 2] we give the expression of the probability density of reactive trajectories using the forward and backward committor functions.

Theorem 3.2.2. *If the probability distribution of reactive trajectories μ_R admits a density $\rho_R : S \to \mathbb{R}_{\geq 0}$ with respect to Lebesgue measure, then ρ_R satisfies*

$$\rho_R(x) = Z_R^{-1} q(x) q_b(x) \rho(x)$$

where

$$Z_R = \int_{S\setminus(A\cup B)} q(x) q_b(x) \rho(x) \mathrm{d}x.$$

We refer to the function ρ_R in Theorem 3.2.2 as the probability density of reactive trajectories. High values of ρ_R indicate the regions where reactive trajectories spend long times. Such regions are called *bottlenecks*. While ρ_R offers useful information on the regions in which the reactive trajectories spend long times, it is also useful for determining the regions that are likely to be visited by reactive trajectories, regardless of the time spent in the region. This information can be described by the *hitting point distribution* of reactive trajectories, which is defined as the distribution of points where the reactive trajectories hit a surface while crossing it.

3.3 Hitting point distribution

Let $\mathcal{S}$ be a codimension 1 piecewise continuously differentiable surface in $S \setminus (A \cup B)$ and let $\sigma_{\mathcal{S}}(\mathrm{d}x)$ denote the surface measure on $\mathcal{S}$ with respect to Lebesgue measure. Define a probability distribution ν_S supported on $\mathcal{S}$ that is induced by the invariant probability measure μ on S according to

$$\nu_{\mathcal{S}}(\mathrm{d}x) = C_{\mathcal{S}}^{-1}\rho(x)\sigma_{\mathcal{S}}(\mathrm{d}x),$$

where

$$C_{\mathcal{S}} = \int_{\mathcal{S}} \rho(x)\sigma_{\mathcal{S}}(\mathrm{d}x).$$

The probability distribution ν_S gives the probability that the diffusion hits a subset of the surface $\mathcal{S}$ when passing through $\mathcal{S}$.

For any μ-measurable set $C \subset S \setminus (A \cup B)$ and an ε-slab around $\mathcal{S}$, i.e. $\mathcal{S}_\varepsilon := \{x \mid \exists y \in \mathcal{S},\ \|x - y\| \leq \varepsilon\}$, we define the *hitting point distribution* of the surface $\mathcal{S}$ as

$$\nu_{\mathcal{S},R}(C \cap \mathcal{S}) = \lim_{\varepsilon \to 0} \lim_{T \to \infty} \frac{\int_{R \cap [0,T]} \mathbf{1}_{C \cap \mathcal{S}_\varepsilon}(X_t)\mathrm{d}t}{\int_{R \cap [0,T]} \mathbf{1}_{\mathcal{S}_\varepsilon}(X_t)\mathrm{d}t}. \tag{3.7}$$

The following theorem [14, Proposition 3] gives us an expression for the probability distribution of the hitting points of the reactive trajectories on $\mathcal{S}$ in terms of the forward and backward committors and the equilibrium probability density ρ.

Theorem 3.3.1. *Let $\mathcal{S} \subset S \setminus (A \cup B)$ be a C^1 surface, and let $\nu_{\mathcal{S},R}$ be the corresponding hitting point distribution. Then the following holds:*

$$\nu_{\mathcal{S},R}(\mathrm{d}x) = C_{\mathcal{S},R}^{-1} q(x) q_b(x) \rho(x) \sigma_{\mathcal{S}}(\mathrm{d}x),$$

with

$$C_{\mathcal{S},R} = \int_{\mathcal{S}} q(x) q_b(x) \rho(x) \sigma_{\mathcal{S}}(\mathrm{d}x).$$

Let $\mathcal{M} \subset S$ be a set whose boundary is of codimension 1, such that $A \subset \mathrm{int}(\mathcal{M})$ and $B \subset \mathrm{int}(\mathcal{M}^C)$. The boundary $\mathcal{S} = \partial\mathcal{M}$ is then called a *dividing surface*.

For a given reactive trajectory $\{X_t\}_{t \in (t_i^-, t_i^+)}$ and a C^1 dividing surface $\mathcal{S}$, we define the *last hitting point* on $\mathcal{S}$ as the point on the surface $\mathcal{S}$ that is last visited by the reactive trajectory, i.e. the last hitting point is some $x \in \mathcal{S}$ such that

$$X_{t_i^*} = x, \quad \text{for some} \quad t_i^* \in (t_i^-, t_i^+) \quad \text{and} \quad X_t \in \mathrm{int}(\mathcal{M}^C) \quad \forall t \in (t_i^*, t_i^+).$$

The *last hitting point distribution* $\nu_{\mathcal{S},R}^l$ of reactive trajectories on $\mathcal{S}$ is defined such that for any μ-measurable set $C \subset S \setminus (A \cup B)$

$$\nu_{\mathcal{S},R}^l(C \cap \mathcal{S}) = \lim_{N \to \infty} \frac{1}{N-1} \sum_{i=1}^{N} \mathbf{1}_{C \cap \mathcal{S}}(X_{t_i^*}). \tag{3.8}$$

We now choose the surface $\mathcal{S}$ to be a level set of the committor function. Level sets of the committor function are called *isocommittor surfaces* and we denote them by

$$q_a = \{x :\ q(x) = a\}. \tag{3.9}$$

By definition, $\{q_a\}_{a\in(0,1)}$ form a partition of the state space S, that is

$$q_a \cap q_{a'} = \emptyset \text{ for } a \neq a', \text{ and } \bigcup_{a\in(0,1)} q_a = S.$$

The isocommittor surface defined in equation (3.9) is continuously differentiable because it is the level set of the committor function $q(x)$, which is itself twice continuously differentiable on the interior of $S \setminus (A \cup B)$, as it satisfies the Dirichlet problem (3.5). Furthermore, the isocommittor surface q_a is for every $a \in (0,1)$ a dividing surface, under the assumption that q has no critical points on $S \setminus (A \cup B)$. In particular, for every $a \in (0,1)$ it holds that $A \subset \bigcup_{\alpha\in[0,a)} q_\alpha$ and $B \subset \left(\bigcup_{\alpha\in[0,a)} q_\alpha\right)^{\complement}$ and q_a is a codimension 1 surface in $S \setminus (A \cup B)$. It is known that when one chooses a dividing surface $\mathcal{S}$ to be an isocommittor surface q_a for some $a \in (0,1)$, the hitting point distribution and the last hitting point distribution on $\mathcal{S}$ coincide. We state this in the following theorem [14, Proposition 4].

Theorem 3.3.2. *For every $a \in (0,1)$*

$$\nu_{q_a,R} \equiv \nu^l_{q_a,R},$$

where $\nu_{q_a,R}$ denotes the hitting point distribution defined in equation (3.7) *and $\nu^l_{q_a,R}$ denotes the last hitting point distribution given in equation* (3.8)*.*

This implies that reactive trajectories get conserved, in the sense that the probability of reactive trajectories hitting the surface q_a and the probability of reactive trajectories leaving the surface q_a are the same for any subset of q_a.

3.4 Probability current of reactive trajectories

On its own, the probability density of reactive trajectories does not describe the mechanism of reaction. In order to characterise the reaction pathway the probability current of reactive trajectories is defined.
The *probability current* of reactive trajectories $J_R(x)$ is a vector field $J_R : S \setminus (A \cup B) \to \mathbb{R}^d$ such that for every region C whose boundary is piecewise continuously differentiable and $\partial C \subset S \setminus (A \cup B)$, it holds that

$$\begin{aligned}\lim_{s\to 0^+} \frac{1}{s} \lim_{T\to\infty} \frac{1}{T} \int_{\mathcal{R}\cap[0,T]} \mathbf{1}_C(X_t)\, \mathbf{1}_{C^{\complement}}(X_{t+s}) - \mathbf{1}_{C^{\complement}}(X_t)\, \mathbf{1}_C(X_{t+s})\, \mathrm{d}t \\ = \int_{\partial C} J_R(x) \cdot n_C(x) \sigma_C(\mathrm{d}x),\end{aligned} \tag{3.10}$$

where $n_C(x)$ is the outward pointing unit normal on ∂C and $\sigma_C(\mathrm{d}x)$ is the surface measure on C, i.e. the surface measure induced by Lebesgue measure. The probability current can be interpreted as the probability of AB-reactive trajectories crossing the surface ∂C in one direction minus the probability of reactive trajectories crossing this surface in the opposite direction, i.e. the net probability flux of reactive trajectories crossing the surface ∂C in an infinitesimal time period.

The following theorem [32, Equation (3.15)] gives the expression for the probability current using committors, diffusion coefficients, and the equilibrium density.

Theorem 3.4.1. *The probability current of reactive trajectories can be expressed as*

$$J_{R,i}(x) = q(x)q_b(x)J_i(x) + q_b(x)\rho(x)\frac{1}{2}\sum_{j=1}^{d} a_{ij}(x)\frac{\partial q(x)}{\partial x_j} - q(x)\rho(x)\frac{1}{2}\sum_{j=1}^{d} a_{ij}(x)\frac{\partial q_b(x)}{\partial x_j},$$

where

$$J_i(x) = b_i(x)\rho(x) - \frac{1}{2}\sum_{j=1}^{d}\frac{\partial}{\partial x_j}(a_{ij}(x)\rho(x)).$$

The probability current is divergence free. This was stated without proof in [32]. We provide a proof in Appendix A. As a consequence, by Gauss' theorem, the probability current over the surface ∂C of any set C contained in $S \setminus (A \cup B)$ is zero i.e.

$$\int_{\partial C} J_R(x) \cdot n_C(x)\sigma_C(\mathrm{d}x) = \int_C \operatorname{div} J_R(x)\mathrm{d}x = 0.$$

Thus the definition of $J_R(x)$ given in (3.10) is independent of the choice of the set C.

Note that (3.10) is the definition from [32]. The definition of the probability current given in equation (50) of [14] is

$$\lim_{s\to 0^+}\frac{1}{s}\lim_{T\to\infty}\frac{1}{T}\int_0^T \mathbf{1}_C(X_t)\,\mathbf{1}(\tau_B^-(t) < \tau_A^-(t)) \times \mathbf{1}_{C^{\complement}}(X_{t+s})\,\mathbf{1}(\tau_B^+(t+s) < \tau_C^+(t+s)) = \int_{\partial C} J_R(x) \cdot n_C(x)\sigma_C(\mathrm{d}x), \tag{3.11}$$

where for an arbitrary set $D \subset S$

$$\tau_D^+(t) = \inf\{t' \geq t : X_{t'} \in \overline{D}\}, \text{ and } \tau_D^-(t) = \sup\{t' \leq t : X_{t'} \in \overline{D}\}.$$

The difference between (3.10) and (3.11) is twofold. First, (3.11) does not represent a net probability, but the probability of crossing the surface ∂C in one direction only, in particular, when going from A to B. The probability current J_R defined in (3.11) is divergence free as well; see Remark A.0.3. Therefore, the definition of $J_R(x)$ at any point x is independent of the surface ∂C. Thus in [14] the surface ∂C is assumed to be a dividing surface, that is $A \subset C$ and $B \subset C^{\complement}$. The second difference between the two corresponding definitions is the condition on trajectories being reactive at time t. In (3.10) this condition is given in the domain of integration and can be expressed as the probability of trajectory coming last from A and going to B next, rather than returning to A. In contrast, in (3.11) the condition is expressed as the probability of coming last from A and going to set B next, rather than returning to the set C.

3.5 Reaction rate

The *reaction rate* k_R is defined as the integral of the probability current over any dividing surface $\mathcal{S} = \partial C$ that is a boundary of the region $C \subset S$,

$$k_R = \int_{\mathcal{S}} n_C(x) \cdot J_R(x)\sigma_{\mathcal{S}}(\mathrm{d}x), \tag{3.12}$$

where $n_C(x)$ denotes the unit normal on ∂C pointing towards B. Since the probability current is divergence free, the probability flux over any dividing surface equals the total probability flux of reactive trajectories. Therefore the reaction rate is independent of the set C and represents the average number of crossings from set A to set B per unit of time, i.e. the frequency of reactive trajectories

$$k_R = \lim_{T\to\infty} \frac{N_T^R}{T}, \tag{3.13}$$

where N_T^R represents the number of reactive trajectories that occur until time T.

The reaction rate of transitions from set B to set A is also k_R, because every AB-reactive trajectory corresponds to a BA-reactive trajectory. Namely, every time the process trasitions from set A to set B, it has to to return from set B to set A in order to make another transition from A to B. Therefore, in any time interval, the number of AB-reactive trajectories and the number of BA-reactive trajectories can differ by one at most.

Theorem 3.5.1. *[32, Equation 3.19] The reaction rate can be expressed as:*

$$k_R = \int_{S\setminus(A\cup B)} \rho(x) \frac{1}{2} \sum_{i,j=1}^{d} a_{ij}(x) \frac{\partial q(x)}{\partial x_i} \frac{\partial q(x)}{\partial x_j} \mathrm{d}x.$$

The result above does not imply that the average time necessary for the process to go from A to B is the same as the average time the process takes to go from B to A. Let us denote the total time in $[0, T]$ during which the last visited set by the trajectory is set A by T_A, and the analogous time for B by T_B. Then we have $T_A + T_B = T$. We compute the average time the process takes to go from set A to set B, t_{AB} and the average time the process takes to go from set B to set A, t_{BA} as

$$t_{AB} = \lim_{T\to\infty} \frac{T_A}{N_T^R}, \quad \text{and} \quad t_{BA} = \lim_{T\to\infty} \frac{T_B}{N_T^R}.$$

These two average transition times differ and rates t_{AB}^{-1} and t_{BA}^{-1} differ from the reaction rate k_R.

If we define

$$\rho_A = \lim_{T\to\infty} \frac{T_A}{T}, \quad \rho_B = \lim_{T\to\infty} \frac{T_B}{T}, \tag{3.14}$$

then since $T_A + T_B = T$ we have $\rho_B = 1 - \rho_A$ and

$$\rho_A = \int_S \rho(x) q_b(x) \mathrm{d}x, \quad \rho_B = 1 - \int_S \rho(x) q_b(x) \mathrm{d}x = \int_S \rho(x)(1 - q_b(x)) \mathrm{d}x.$$

Using (3.13) and (3.14) the following expressions [15, Equation 34] for the average times t_{AB} and t_{BA} hold:

$$t_{AB} = \frac{\rho_A}{k_R} \quad \textit{and} \quad t_{BA} = \frac{\rho_B}{k_R}.$$

Therefore, the time necessary to go from A to B is the same as the time necessary to go from B to A only if $\rho_A = 1/2$.

3.6 Streamlines and transition tubes

Let the equation

$$\frac{\mathrm{d}s(\tau)}{\mathrm{d}\tau} = J_R(s(\tau)), \quad s(0) = x \in \partial A \tag{3.15}$$

admit a unique solution for every $x \in \partial A$. The solution $s(\tau)$ of (3.15) is called the *transition streamline* corresponding to $x \in \partial A$. For each initial condition the corresponding streamline connects the sets A and B and represents the averaged behaviour of reactive trajectories. A bundle of streamlines with initial conditions belonging to some set $A' \subset \partial A$ is called the *transition tube* corresponding to A'.

3.7 Transition path theory for Smoluchowski diffusion

In this section we show the transition path theory objects on an example - the Smoluchowski diffusion process introduced in Section 2.6. Recall that the stochastic differential equation of Smoluchowski diffusion is given by

$$\mathrm{d}X_t = -\Gamma^{-1}\nabla V(X_t)\mathrm{d}t + \sqrt{2\beta^{-1}}\Gamma^{-\frac{1}{2}}\mathrm{d}W_t,$$

where $\Gamma \in \mathbb{R}^d$ is a diagonal matrix with friction coefficients γ_i, $\beta = 1/k_B\mathcal{T}$ is the inverse temperature parameter, k_B is the Boltzmann constant and $V : \mathbb{R}^d \to \mathbb{R}$ is a potential function. The corresponding infinitesimal operator is given by

$$\mathcal{A} = -\Gamma^{-1}\nabla V(x)\cdot\nabla + \frac{1}{\beta}\sum_{i=1}^{d}\gamma_i^{-1}\frac{\partial^2}{\partial x_i^2}.$$

Therefore, according to equation (3.5) the corresponding forward committor q is a solution of the system

$$\begin{aligned} -\Gamma^{-1}\nabla V(x)\cdot\nabla q(x) + \frac{1}{\beta}\sum_{i=1}^{d}\gamma_i^{-1}\frac{\partial^2 q(x)}{\partial x_i^2} &= 0, && x \in S\setminus(A\cup B)\\ q(x) &= 0, && x \in \partial A\\ q(x) &= 1, && x \in \partial B. \end{aligned}$$

Since the Smoluchowski dynamics is reversible as shown in the end of Section 2.6, the backward committor q_b is given by $q_b(x) = 1 - q(x)$ (3.6). Since the invariant probability density of the Smoluchowski diffusion process is the Boltzmann density given by

$$\rho(x) = Z^{-1}e^{-\beta V(x)}, \qquad Z = \int_{\mathbb{R}^d} e^{-\beta V(x)}\mathrm{d}x,$$

by Theorem 3.2.2 the probability density of reactive trajectories is given by

$$\rho_R(x) = Z_R^{-1}q(x)(1-q(x))e^{-\beta V(x)},$$

where

$$Z_R = \int_{S\setminus(A\cup B)} q(x)(1-q(x))e^{-\beta V(x)}.$$

The probability current of reactive trajectories corresponding to the Smoluchowski dynamics [35] is given by

$$J_R(x) = Z^{-1}\beta^{-1}e^{-\beta V(x)}\Gamma^{-1}\nabla q(x) \tag{3.16}$$

Thus by (3.12) the corresponding reaction rate over a dividing surface $\mathcal{S} = \partial C$ for some region $C \subset S$ is given by

$$k_R = Z^{-1}\beta^{-1}\int_{\mathcal{S}} e^{-\beta V(x)} n_C(x) \cdot \Gamma^{-1}\nabla q(x)\sigma_C(\mathrm{d}x),$$

or alternatively, by Theorem 3.5.1

$$k_R = Z^{-1}\beta^{-1}\int_{S\setminus(A\cup B)} e^{-\beta V(x)}\nabla q(x)^\top\Gamma^{-1}\nabla q(x)\mathrm{d}x.$$

Chapter 4

Convergent discretisation schemes

In this chapter, we define transition path theory objects for projections of diffusion processes onto discrete state spaces, where the discrete state spaces are generated by partitions of state space. We show that in the limit of small partition width - i.e. in an appropriate 'continuum limit' - the objects we define converge to the corresponding objects of transition path theory for diffusion processes. More precisely, we define the discrete analogues of the committor function, isocommittor surfaces, probability current, and streamlines defined in Chapter 3. We prove the convergence of the committor function, probability current and streamlines with respect to an appropriate metric, to the respective continuous objects of diffusion processes. These results are based on the results of [9].

4.1 Setup

Let $X = \{X_t\}_{t\geq 0}$ be an ergodic diffusion process taking values in a bounded subset $S \subset \mathbb{R}^d$ with reflecting boundary conditions. Suppose that the invariant measure μ of X is absolutely continuous with respect to Lebesgue measure, so that there exists a density $p : S \to \mathbb{R}$ such that for all $t \geq 0$,

$$\mu(A) = \mu_t(A) := \mathbb{P}(X_t \in A) = \int_A p(x)\mathrm{d}x, \quad \forall A \in \mathcal{B}(S).$$

We consider a partition of the state space S, i.e. a collection $\{S_1, \ldots, S_n\}$ of nonempty subsets of S such that $\cup_{j=1}^n S_j = S$, and $S_i \cap S_j$ have Lebesgue measure zero for $i \neq j$. In particular, we consider a Voronoi tessellation of S associated to a finite set of *generators* $\{g_1, \ldots, g_n\} \subset S$ for some $n \in \mathbb{N}$. A Voronoi tessellation is a collection $\{S_1, \ldots, S_n\}$ of nonempty subsets of S, where each Voronoi cell S_i is defined by

$$S_i := \{x \in S \ : \ |x - g_i|_2 \leq |x - g_j|_2 , \quad \forall j \neq i\}.$$

That is, S_i is the closed set consisting of all points in state space that are closer to the generator g_i than to any other generator. Since every Voronoi cell S_i is a closed neighbourhood of its generator g_i, it has strictly positive Lebesgue measure. Observe that

$$S = \bigcup_{i=1}^n S_i, \quad S_i \cap S_j = \partial S_i \cap \partial S_j, \ i \neq j,$$

so that Voronoi cells intersect at most at their boundaries, which are sets of strictly positive codimension and hence have Lebesgue measure zero; note that this intersection may be empty. This motivates the following definition.

Definition 4.1.1. Two distinct Voronoi cells S_i and S_j are *adjacent* if they share a common facet, i.e. if

$$\dim(S_i \cap S_j) = d - 1.$$

Given a Voronoi tessellation $\{S_i\}_{i\in I}$, with $I = \{1, \dots n\}$ the dual object is the Delaunay graph $G = (I, E)$ with vertex set I and edge set E consisting of all pairs (i, j) such that S_i and S_j are adjacent.

Recall that, given a nonempty set $A \subset \mathbb{R}^d$, the Euclidean *diameter* of A is defined by

$$\operatorname{diam}(A) = \sup\{|x - y|_2 \ : \ x, y \in A\}.$$

This leads us to the next definition.

Definition 4.1.2. The *width* ρ of a Voronoi tessellation $\{S_i\}_{i\in I}$ is the largest Euclidean diameter of the Voronoi cells, i.e.

$$\rho(\{S_i\}_{i\in I}) := \max_{i\in I} \operatorname{diam}(S_i).$$

When there is no risk of confusion, we will omit the argument $\{S_i\}_{i\in I}$ of the width and simply write ρ. The smaller (respectively larger) the width, the finer (resp. coarser) the tessellation. We are interested in obtaining error bounds in the limit of small width, i.e. as ρ decreases to 0. As ρ decreases to zero, the number n of cells in the Voronoi tessellation must increase to infinity. The converse is not true: it is possible for the number of cells to increase to infinity, while the width ρ stays bounded away from zero. For example, let a sequence of partitions $\{\{S_i^{(k)}\}_{i\in I(k)}\}_{k\in\mathbb{N}}$ be generated by the strictly increasing nested sequence of collections of generators $\{\{g_i^{(k)}\}_{i\in I(k)}\}_{k\in\mathbb{N}}$, that is, $\{\{g_i^{(k)}\}_{i\in I(k)}\}_{k\in\mathbb{N}}$ is such that $\left|\{g_i^{(k)}\}_{i\in I(k)}\right| < \left|\{g_i^{(l)}\}_{i\in I(l)}\right|$ and $\{g_i^{(k)}\}_{i\in I(k)} \subset \{g_i^{(l)}\}_{i\in I(l)}$ when $k < l$. That implies that the sequence of partitions $\{\{S_i^{(k)}\}_{i\in I(k)}\}_{k\in\mathbb{N}}$ is refined as $k \to \infty$ by adding new generator points to the existing generators. If there exists a subset of the state space in which no new generator point is added, that is if there exists a set $C \subset S$ and some $n \in \mathbb{N}$ such that

$$\left(\{g_i^{(k+1)}\}_{i\in I(k+1)} \setminus \{g_i^{(k)}\}_{i\in I(k)}\right) \cap C = \emptyset$$

for all $k > n$, then the diameter of the cells inside C does not decrease. Therefore, in this case, the width of partitions does not decrease to zero, even though the number of cells increases to infinity as $k \to \infty$. With this example in mind, we will impose a constraint on the Voronoi tessellations that we use to discretise state space, namely that as the width decreases to zero, the Voronoi cells shrink in a uniformly controlled way to their associated generators. This uniform controlled shrinkage describes the continuum limit in which the objects we define in this chapter converge to the objects of the transition path theory for diffusion processes.

Given a Voronoi tessellation $\{S_i\}_{i\in I}$ with finite index set I and its associated Delaunay graph $G = (I, E)$, we construct a jump process $Y = \{Y_t\}_{t\geq 0}$ on the index set I, by setting

$Y_t = i$ whenever $X_t \in S_i$. For the case that $X_t \in S_i \cap S_j$ for a pair (S_i, S_j) of adjacent Voronoi cells, then we set $Y_t = k \in \{i, j\}$, where k is the index set of the cell such that the diffusion process X was 'most recently' in the interior of S_k prior to time t. To be precise, if there exists some $\varepsilon > 0$ such that $X_s \in S_k$ for all $s \in (t - \varepsilon, t)$, then we set $Y_t = k$. The jump process Y is non-Markovian, i.e. it is not memoryless which shows in the increased probability of recrossing back after the process Y crosses a boundary of a cell; see [43, non-MarkovianSection 2.1] or [42].

We write $A, B \subset S$ to denote the reactant and product sets of states for the diffusion process of interest. We will assume that A and B are simply connected, open and that their closures are disjoint.

In the following section we define the first object of our transition path theory on discrete state spaces, namely the committor of the process $\{Y_t\}_{t\geq 0}$ with state space $\{S_i\}_{i\in I}$. Furthermore, we prove the convergence of our discrete committor to the continuous (forward) committor function defined in (3.3), in the limit of small partition width.

4.2 Committors

Recall the forward committor function $q : S \to [0, 1]$ defined in (3.3). For $i \in I$ where $I := \{1, \ldots, n\}$, define

$$\hat{q}_i = \frac{1}{\mu(S_i)} \langle q, \mathbf{1}_{S_i} \rangle_\mu, \tag{4.1}$$

where $\mathbf{1}_{S_i} : S \to \{0, 1\}$ is the indicator function of S_i and $\langle \cdot, \cdot \rangle_\mu$ is the inner product with respect to the invariant measure μ of the process X_t, i.e.

$$\langle v, w \rangle_\mu = \int_S v(x) w(x) \mu(\mathrm{d}x).$$

Using the collection $\{\hat{q}_i\}_{i\in I}$, we can construct a function that is piecewise constant on the interiors of the Voronoi cells, the *projected forward committor function* $\hat{q} : S \to [0, 1]$:

$$\hat{q}(x) := \sum_{i\in I} \hat{q}_i \mathbf{1}_{\mathrm{int}(S_i)}(x). \tag{4.2}$$

Note that we are abusing notation, by using $\hat{q}$ to denote the function constructed from the numbers $\hat{q}_i$, $i \in I$. Later, we will write $\hat{q}|_{S_i}$ to denote the restriction of the function $\hat{q}$ to the set S_i.

To complete the definition of $\hat{q}$, we need to specify its values on the intersections of the closed Voronoi cells. However, since the union of the intersections has Lebesgue measure zero and since we will measure the error of $\hat{q}$ with respect to q using an L^p norm, the values that we prescribe will not be important. One straightforward assignment is as follows: If $x \notin \mathrm{int}(S_i)$ for all $i \in I$, then there must be a nonempty set $C \subset I$ such that $x \in \partial S_c$ for all $c \in C$; for such x, define $\hat{q}(x)$ according to

$$\hat{q}(x) = \max_{c\in C(x)} \hat{q}_c.$$

Other assignments are possible, e.g. the minimum or the mean of $\hat{q}_c$ over $c \in C$.

Now we define the *discrete forward committor function* $\tilde{q} : I \to [0, 1]$, which is the forward committor function that corresponds to the time continuous process $\{Y_t\}_{t\geq 0}$ on the discrete state space. We will make the following assumption.

Assumption 4.2.1. *The sets A and B are open convex sets such that $\overline{A} \cap \overline{B} = \emptyset$ and there exist disjoint subsets $J, K \subset I$ such that $\overline{A} = \cup_{j\in J} S_j$ and $\overline{B} = \cup_{k\in K} S_k$.*

Thus, J and K are the metastable sets for the jump process Y that correspond to the metastable sets A and B for the diffusion process X. The assumption is justified in the limit of small width, since one can approximate any convex body by collections of arbitrarily small Voronoi cells [46].

Given J and K, define the first hitting time of the jump process Y of $J \cup K$ by

$$\tau_{J\cup K}(Y) := \inf\{t \geq 0 \ : \ Y_t \in J \cup K\}.$$

Lemma 4.2.2. *The first hitting time $\tau_{J\cup K}(Y)$ of the jump process Y and the first hitting time $\tau_{A\cup B}(X)$ of the diffusion X defined in* (3.2) *coincide, i.e.*

$$\tau_{J\cup K}(Y) = \tau_{A\cup B}(X). \tag{4.3}$$

Proof. Let us observe a trajectory $\{X_t\}_{t\geq 0}$ of the process X initiated from a point in $S \setminus (\overline{A} \cup \overline{B})$ and let τ denote the first time the trajectory reaches the set $A \cup B$, i.e.

$$\tau := \inf\{t \geq 0 : X_t \in A \cup B\}.$$

Then there exist ε such that the trajectory $X_t \in S\setminus(A\cup B)$ for $t \in (\tau-\varepsilon, \tau)$, $X_\tau \in \partial A \cup \partial B$ and $X_t \in A \cup B$ for $(\tau, \tau+\varepsilon)$. Let ε be small such that $X_t \in \text{int}(S_i) \subset S \setminus (A \cup B)$ for some $i \in I$, for all $(\tau-\varepsilon, \tau)$. Given our definition of Y, then $Y_t = i$, for $t \in (\tau-\varepsilon, \tau)$ and $Y_\tau = i$. If $X_t \in A$ for $t \in (\tau, \tau+\varepsilon)$ then $Y_t \in J$ for $t \in (\tau, \tau+\varepsilon)$, due to Assumption 4.2.1. Otherwise, if $X_t \in B$ for $t \in (\tau, \tau+\varepsilon)$ then $Y_t \in K$ for $t \in (\tau, \tau+\varepsilon)$. Since A and B are disjoint, we have that $\tau = \inf\{t \geq 0 : Y_t \in J \cup K\}$, i.e. $\tau_{J\cup K}(Y) = \tau_{A\cup B}(X)$. □

We now define the discrete forward committor, the first object of our discrete transition path theory.

Definition 4.2.3. The *discrete forward committor* at any $i \in I$ is the probability that starting from the state i, the process Y reaches K before J:

$$\tilde{q}_i := \frac{\mathbb{P}\left(Y_{\tau_{J\cup K}} \in K, \ Y_0 = i\right)}{\mathbb{P}\left(Y_0 = i\right)}. \tag{4.4}$$

We will prove that $\hat{q}_i = \tilde{q}_i$ for all i, using the notion of a regular conditional distribution defined in Definition 2.1.3. The existence of the regular conditional distribution of Y defined on the probability space $(\Omega, \mathcal{A}, \mathbb{P})$ given some sub-σ algebra $\mathcal{F} \subset \mathcal{A}$ is given in [23, Theorem 8.37].

Lemma 4.2.4. *The committor function q given in* (3.3) *is a regular conditional probability.*

Proof. Recall the definition of the regular conditional probability (2.4). By setting the random varaibles Y and X and the set C in (2.4) to be $X_{\tau_{A\cup B}(X)}$ and X_0 and the set B respectively, we obtain

$$\kappa_{X_{\tau_{A\cup B}(X)}, X_0}(x, B) = \mathbb{P}\left(X_{\tau_{A\cup B}(X)} \in B | X_0 = x\right),$$

which is the definition of the forward committor function (3.3). □

The following lemma is a corollary of Theorem 2.1.4 and we will use it in our proof of the convergence of the discrete forward committor function $\tilde{q}$ defined in (4.4) to the continuous committor function q defined in (3.3).

Lemma 4.2.5. *Let X and Y be random variables on $(\Omega_1, \mathcal{A}_1, \mathbb{P})$, taking values in the measurable spaces $(E', \mathcal{E}')$ and $(E, \mathcal{E})$ respectively. Then for any $C \in \mathcal{E}$ and $D \in \mathcal{E}'$,*

$$\mathbb{P}\left(Y \in C, X \in D\right) = \int_D \kappa_{Y,X}(x, C)\mathbb{P} \circ X^{-1}(\mathrm{d}x).$$

Proof. By definition of expectation

$$\mathbb{E}\left[\mathbf{1}_D(X)\mathbb{E}[\mathbf{1}_C(Y)|\sigma(X)]\right] = \int_\Omega \mathbf{1}_D\left(X(\omega)\right)\mathbb{E}[\mathbf{1}_C(Y)|\sigma(X)](\omega)\mathbb{P}(\mathrm{d}\omega). \tag{4.5}$$

Using Theorem 2.1.4 in the first equality, (2.4) in the second, and the fact that a stochastic kernel is a probability measure for fixed $\omega \in \Omega$ in the third equality we obtain:

$$\begin{aligned}\mathbb{E}\left[\mathbf{1}_C(Y)|\sigma(X)\right](\omega) &= \int_E \mathbf{1}_C(y)\kappa_{Y,\sigma(X)}(\omega, \mathrm{d}y) = \int_E \mathbf{1}_C(y)\kappa_{Y,X}(X(\omega), \mathrm{d}y) \\ &= \kappa_{Y,X}(X(\omega), C).\end{aligned} \tag{4.6}$$

Using (4.6) in the first equation and the change of variables formula in the second we have:

$$\begin{aligned}\int_\Omega \mathbf{1}_D\left(X(\omega)\right)\mathbb{E}[\mathbf{1}_C(Y)|\sigma(X)](\omega)\mathbb{P}(\mathrm{d}\omega) &= \int_\Omega \mathbf{1}_D\left(X(\omega)\right)\kappa_{X,Y}\left(X(\omega), C\right)\mathbb{P}(\mathrm{d}\omega) \\ &= \int_E \mathbf{1}_D(x)\kappa_{X,Y}(x, C)\mathbb{P} \circ X^{-1}(\mathrm{d}x).\end{aligned} \tag{4.7}$$

Let $\mathcal{G} := \{\emptyset, \Omega\}$ be the trivial σ-algebra on Ω. By using the property of conditional expectation (2.1) in the first, (2.3) in the second and the tower law (2.2) in the third equality we obtain:

$$\begin{aligned}\mathbb{E}\left[\mathbf{1}_D(X)\mathbb{E}[\mathbf{1}_C(Y)|\sigma(X)]\right] &= \mathbb{E}\left[\mathbb{E}[\mathbf{1}_D(X)\mathbf{1}_C(Y)|\sigma(X)]\right] \\ &= \mathbb{E}\left[\mathbb{E}[\mathbf{1}_D(X)\mathbf{1}_C(Y)|\sigma(X)]|\mathcal{G}\right] \\ &= \mathbb{E}[\mathbf{1}_D(X)\mathbf{1}_C(Y)] = \mathbb{P}(Y \in C, X \in D).\end{aligned} \tag{4.8}$$

Finally, combining (4.5), (4.7) and (4.8) proves the claim

$$\mathbb{P}(Y \in C, X \in D) = \int_E \mathbf{1}_D(x)\kappa_{X,Y}(x, C)\mathbb{P} \circ X^{-1}(\mathrm{d}x).$$

□

We now use the previous lemma to prove that the projected forward committor $\hat{q}$ and the discrete forward committor $\tilde{q}$ are equal.

Proposition 4.2.6. *Suppose that Assumption 4.2.1 holds. Let the projected forward committor $\hat{q}_i$ and discrete forward committor $\tilde{q}_i$ be defined as in* (4.1) *and* (4.4)*, respectively. Assume that X_0 is distributed according to the equilibrium distribution μ. Then $\hat{q}_i = \tilde{q}_i$, for all $i \in I$.*

Proof. Let $i \in I$ be arbitrary. Recall from (4.1) that

$$\hat{q}_i = \frac{1}{\mu(S_i)} \langle q, \mathbf{1}_{S_i} \rangle_\mu = \frac{1}{\mu(S_i)} \int_S q(x) \mathbf{1}_{S_i}(x) \mu(\mathrm{d}x).$$

The definition (4.4), equation (4.3), the construction of Y, and the hypothesis that X_0 is distributed according to the equilibrium measure μ imply that

$$\begin{aligned} \tilde{q}_i &= \frac{\mathbb{P}\left(Y_{\tau_{J \cup K}(Y)} \in K,\ Y_0 = i\right)}{\mathbb{P}\left(Y_0 = i\right)} = \frac{\mathbb{P}\left(X_{\tau_{A \cup B}(X)} \in B,\ X_0 \in S_i\right)}{\mathbb{P}(X_0 \in S_i)} \\ &= \frac{\mathbb{P}\left(X_{\tau_{A \cup B}(X)} \in B,\ X_0 \in S_i\right)}{\mu(S_i)}. \end{aligned}$$

Thus, to prove the proposition, it suffices to show that

$$\int_S q(x) \mathbf{1}_{S_i}(x) \mu(\mathrm{d}x) = \mathbb{P}\left(X_{\tau_{A \cup B}(X)} \in B,\ X_0 \in S_i\right).$$

By Lemma 4.2.4, the left-hand side can be rewritten in terms of a regular conditional probability,

$$\begin{aligned} \int_S q(x) \mathbf{1}_{S_i}(x) \mu(\mathrm{d}x) &= \int_S \mathbf{1}_{S_i}(x) \kappa_{X_{\tau_{A \cup B}(X)}, X_0}(x, B) \mu(\mathrm{d}x) \\ &= \int_{S_i} \kappa_{X_{\tau_{A \cup B}(X)}, X_0}(x, B) \mu(\mathrm{d}x). \end{aligned}$$

Using that $\mu = \mathbb{P} \circ X_0^{-1}$ and Lemma 4.2.5, we obtain

$$\begin{aligned} \int_{S_i} \kappa_{X_{\tau_{A \cup B}(X)}, X_0}(x, B) \mu(\mathrm{d}x) &= \int_{S_i} \kappa_{X_{\tau_{A \cup B}(X)}, X_0}(x, B) \mathbb{P} \circ X_0^{-1}(\mathrm{d}x) \\ &= \mathbb{P}(X_{\tau_{A \cup B}(X)} \in B, X_0 \in S_i), \end{aligned}$$

yielding the desired conclusion. □

The following lemma guarantees that in every cell there exists a point at which the value of the continuous committor function equals that of the projected committor function. We shall use the lemma later to prove the convergence of the discrete forward committor function $\tilde{q}$ to the continuous forward committor function q.

Lemma 4.2.7. *Let $\{S_i\}_{i \in I}$ be a Voronoi tessellation of S, and let $\hat{q}_i$ be defined as in* (4.1)*. For every $i \in I$, there exists some $x_i \in S_i$ such that $q(x_i) = \hat{q}_i$.*

Proof. If q is constant on S_i, then because $\hat{q}_i$ is the μ-weighted average of the values of q in the interior of S_i, q must equal $\hat{q}_i$ on S_i, and so there exist uncountably many x_i which satisfy the desired property. Therefore, suppose that q is not constant on S_i, and partition S_i into the disjoint subsets $S_i^- := \{x \in S_i \ : \ q(x) < \hat{q}|_{S_i}\}$, $S_i^+ := \{x \in S_i \ : \ q(x) > \hat{q}|_{S_i}\}$ and $S_i^0 := \{x \in S_i \ : \ q(x) = \hat{q}|_{S_i}\}$. Since q is continuous and not constant on S_i, there must exist some $a \in S_i^-$ and $b \in S_i^+$. It follows from the intermediate value theorem that there exists a $t \in (0, 1)$ such that $x_i(t) := (1-t)a + tb$ satisfies $q(x_i(t)) = \hat{q}_i$. Since $a, b \in S_i$ and since any Voronoi cell S_i is convex, it follows that $x_i(t)$ belongs to S_i. □

Remark 4.2.8. *Note that Lemma 4.2.7 still holds if set S_i is only pathwise connected. Namely, if S_i is pathwise connected, that means that for every $x, y \in S_i$, there exists a continuous function $f : [0,1] \to S_i$ such that $f(0) = x$ and $f(1) = y$. Therefore, for the points a and b from the proof of Lemma 4.2.7 there exists a point $c \in (0,1)$ such that $q(f(c)) = \hat{q}_i$ since q is continuous and thus maps intervals to intervals.*

Next, we show that our choice of the projected committor function (4.1) is valid, by proving an error bound for the error incurred when approximating the true forward committor q with the projected forward committor $\hat{q}$ defined in (4.2).

Theorem 4.2.9 (Error bound for projected committor)**.** *Suppose that the forward committor $q : S \to [0,1]$ has bounded derivatives of first order, i.e. $\nabla q \in L^\infty$, and let $p \in [1, \infty)$. If there exists a constant K independent of x and x_i such that for close enough $x, x_i \in S$*

$$|q(x) - q(x_i) - \langle \nabla q(x_i), x - x_i \rangle| \leq K |x - x_i|_2 , \tag{4.9}$$

then there exists some $C > 0$ that depends only on q, such that for any Voronoi tessellation $\{S_i\}_{i \in I}$ of S with width ρ, the corresponding projected committor function $\hat{q}$ satisfies

$$\|q - \hat{q}\|_{L^p(\mu)} \leq C\rho.$$

In particular, as the width of the Voronoi tessellation decreases to zero, the $L^p(\mu)$ error of $\hat{q}$ decreases linearly with ρ.

Proof. It suffices to prove the first statement, since the second statement follows from the first. Fix an arbitrary $p \in [1, \infty)$, and fix an arbitrary $i \in I$. By Lemma 4.2.7, there exists an $x_i \in S_i$ such that $q(x_i) = \hat{q}_i = \hat{q}|_{S_i}$.

Computing the $L^p(\mu)$-error of the restrictions of q and $\hat{q}$ to S_i, using that $\hat{q}|_{S_i} = q(x_i)$ by definition of x_i, we obtain

$$\begin{aligned}
\| (q - \hat{q}) |_{S_i} \|^p_{L^p(\mu)} &= \int_{S_i} |q(x) - \hat{q}(x)|^p \, \mu(\mathrm{d}x) = \int_{S_i} |q(x) - q(x_i)|^p \, \mu(\mathrm{d}x) \\
&= \int_{S_i} |q(x) - q(x_i) - \langle \nabla q(x_i), x - x_i \rangle + \langle \nabla q(x_i), x - x_i \rangle|^p \, \mu(\mathrm{d}x) \\
&\leq 2^{p-1} \left(\int_{S_i} |q(x) - q(x_i) - \langle \nabla q(x_i), x - x_i \rangle|^p \, \mu(\mathrm{d}x) + \int_{S_i} |\langle \nabla q(x_i), x - x_i \rangle|^p \, \mu(\mathrm{d}x) \right) \\
&\leq 2^{p-1} \left(\int_{S_i} (K |x - x_i|_2)^p \, \mu(\mathrm{d}x) + \int_{S_i} (\|\nabla q\|_\infty |x - x_i|_2)^p \, \mu(\mathrm{d}x) \right) \\
&\leq 2^{p-1} \left(K^p \rho^p \mu(S_i) + \|\nabla q\|^p_\infty \rho^p \mu(S_i) \right)
\end{aligned}$$

where we used the inequality $(a+b)^p \leq 2^{p-1}(a^p + b^p)$ in the first inequality, (4.9) and the Cauchy-Schwarz inequality in the second and the fact that $x, x_i \in S_i$ implies that $|x - x_i| \leq \rho$ in the third. Therefore, we have that

$$\begin{aligned}
\|q - \hat{q}\|^p_{L^p(\mu)} &= \sum_{i \in I} \|(q - \hat{q})|_{S_i}\|^p_{L^p(\mu)} \\
&\leq 2^{p-1} \left(K^p \rho^p \left(\sum_{i \in I} \mu(S_i) \right) + \|\nabla q\|^p_\infty \rho^p \left(\sum_{i \in I} \mu(S_i) \right) \right). \\
&\leq (2(\|\nabla q\|_\infty + K)\rho)^p
\end{aligned}$$

where we used that $\sum_{i\in I}\mu(S_i) = 1$, $2^{p-1} < 2^p$ and $a^p + b^p \leq (a+b)^p$, for $a, b \geq 0$ and $p \geq 1$ in the second inequality. This proves the claim for $C = 2\left(\|\nabla q\|_\infty + K\right)$. □

Inequality (4.9) is inspired by the Taylor expansion of q about x_i:

$$q(x) = q(x_i) + \langle \nabla q(x_i), x - x_i\rangle + \mathcal{R}\left(|x - x_i|_2\right), \quad x, x_i \in S.$$

In particular, by (4.9) we assume that the remainder of the first order Taylor expansion of q about x_i, $\mathcal{R}(|x - x_i|_2)$ is bounded by $K\,|x - x_i|_2$ with K that does not depend on the point of expansion x_i.

In an analogous way to how in (4.2) we defined the function $\hat{q} : S \to [0,1]$ using the finite collection $\{\hat{q}_i\}_{i\in I}$ of values, using the collection $\{\tilde{q}_i\}_{i\in I}$ we can define a function $\tilde{q} : S \to [0,1]$ that is constant on the interior of each S_i with value $\tilde{q}_i$. The values of $\tilde{q}$ on the boundaries of Voronoi cells are not important for the error analysis, so we will not specify them here. This yields the following corollary.

Corollary 4.2.10 (Error bound for discrete committor)**.** *Suppose that Assumption 4.2.1 and the assumptions of Theorem 4.2.9 hold. Then for the same scalar C as in Theorem 4.2.9, it holds that for any Voronoi tessellation $\{S_i\}_{i\in I}$ of S with width ρ, the function $\tilde{q}$ satisfies*

$$\|q - \tilde{q}\|_{L^p(\mu)} \leq C\rho,$$

and the $L^p(\mu)$ error of $\tilde{q}$ decreases linearly with the width ρ.

Proof. The result follows from Theorem 4.2.9 and Proposition 4.2.6. □

Corollary 4.2.10 implies that for a sequence of partitions with widths decreasing to zero, the error between the discrete committor function $\tilde{q}$ and the continuous committor function q corresponding to the diffusion process decreases to zero linearly with the width. In the following section we define the discrete isocommittor surfaces using the discrete committor function defined in this section.

4.3 Isocommittor surfaces

Let us recall the definition of the isocommittor surface corresponding to a diffusion process. For a given value a in the unit interval $[0,1]$, the corresponding isocommittor surface q_a is the a-level set of the forward committor q, i.e.

$$q_a := \{x \in S \ : \ q(x) = a\}.$$

We assume q_a to be a surface of codimension 1 for $a \in (0,1)$. Note that by definition of q given in (3.3) $q_0 = A$, and $q_1 = B$. Therefore the dimension of q_a changes at the endpoints of the unit interval, because for $a \in \{0,1\}$ q_a is not a surface, but a full dimensional set. Thus there is a disagreement between mathematical and linguistic description of sets q_a for $a \in \{0,1\}$.

We describe a procedure for obtaining reasonable discrete isocommittor surfaces. We make the following assumption.

Assumption 4.3.1. *The true forward committor q defined in* (3.5) *is globally Lipschitz continuous with constant $K > 0$, i.e.*

$$|q(x) - q(y)| \leq K |x - y|_2 , \quad \forall x, y \in S.$$

Remark 4.3.2. *Globally Lipschitz continuously differentiable functions have bounded derivatives, therefore, the assumption that $\nabla q \in L^\infty$ used in Theorem 4.2.9 is implied by Assumption 4.3.1. Furthermore, the global Lipschitz continuity of q is implied by $\nabla q \in L^\infty$ under the assumption that S is open and convex. Namely, by the mean value theorem, for every $x, y \in C$, there exists a $\beta(x, y) \in (0, 1)$ such that*

$$q(y) - q(x) = \nabla q((1 - \beta)x + \beta y) \cdot (y - x).$$

Using the Cauchy-Schwarz inequality it follows then that

$$|q(y) - q(x)| \leq |\nabla q((1 - \beta)x + \beta y)| \, |y - x| \leq \|\nabla q\|_\infty |y - x| .$$

Here we could bound the ∇q at the given point since $q \in C^2$, as it satisfies (3.5)*. This implies that q is Lipschitz continuous on S. Therefore, on the interior of the convex state space S the global Lipschitz continuity of continuously differentiable committor function q is equivalent to $\nabla q \in L^\infty$.*

Fix a Voronoi tessellation $\{S_i\}_{i \in I}$ with width ρ. Recall the definitions (4.4) and (4.1) of $\tilde{q}_i$ and $\hat{q}_i$ respectively, and that $\tilde{q}_i = \hat{q}_i$ by Proposition 4.2.6. We shall use the following lemma.

Lemma 4.3.3. *Suppose that Assumption 4.3.1 holds with the constant K. Let $\{S_i\}_{i \in I}$ be a Voronoi tessellation with width ρ. Then for any $i \in I$, it holds that*

$$\tilde{q}_i - K\rho \leq q(y) \leq \tilde{q}_i + K\rho, \quad \forall y \in S_i.$$

Proof. Fix an arbitrary $i \in I$. Given Assumption 4.2.1, it holds that

$$|q(x) - q(y)| \leq K |x - y| \leq K\rho, \quad \forall x, y \in S_i.$$

Now recall that, by Lemma 4.2.7, there exists at least one $x_i \in S_i$ such that $q(x_i) = \hat{q}_i$. Hence by Proposition 4.2.6, $q(x_i) = \tilde{q}_i$. Therefore, we have

$$|\tilde{q}_i - q(y)| = |q(x_i) - q(y)| \leq K |x_i - y| \leq K\rho,$$

which proves the claim. □

Definition 4.3.4. Suppose that Assumption 4.3.1 holds with the constant $K > 0$ and suppose we have a Voronoi tessellation $\{S_i\}_{i \in I}$ of width ρ, together with the associated set $\{\tilde{q}_i\}_{i \in I}$ of discrete committor values. For a given $a \in (0, 1)$ the corresponding *discrete isocommittor surface* $\tilde{q}_a(\rho)$ is defined by the index set I_a and corresponding subset of state space,

$$I_a := \{i \in I \ : |\tilde{q}_i - a| \leq K\rho\}, \quad \tilde{q}_a(\rho) := \cup_{i \in I_a} S_i. \tag{4.10}$$

Note that the discrete isocommittor surface $\tilde{q}_a$, unlike q_a, is not a surface as it has full dimension d. Definition 4.3.4 is motivated by Corollary 4.2.10, which suggests that as the width decreases, the deviation of $\tilde{q}_i(x)$ from $q(x)$ at any point $x \in S_i$ is small. Therefore, for $a \in (0,1)$ there should exist a set of indices I such that the deviation of $\tilde{q}_i$ from a is not too large for all $i \in I$.

The following lemma suggests that our definition is reasonable because the discrete isocommittor "surface" contains the true isocommittor surface.

Lemma 4.3.5. *Fix an arbitrary $a \in (0,1)$ and let q_a denote the corresponding continuous isocommittor surface. Then $q_a \subset \tilde{q}_a(\rho)$.*

Proof. Let S_i be a partition set such that $S_i \cap q_a \neq \emptyset$, and suppose that $i \notin I_a$. According to Definition 4.3.4, if $i \notin I_a$, then either $\tilde{q}_i < a - K\rho$ or $\tilde{q}_i > a + K\rho$. If $\tilde{q}_i < a - K\rho$, then the right inequality of Lemma 4.3.3 yields that $q(y) \leq \tilde{q}_i + K\rho < a$, for all $y \in S_i$. This implies that $q_a \cap S_i = \emptyset$, which contradicts the assumption that $S_i \cap q_a$ is nonempty. Similarly, if $\tilde{q}_i > a + K\rho$, then the left inequality of Lemma 4.3.3 yields that $a < \tilde{q}_i - K\rho \leq q(y)$ for all $y \in S_i$, which again produces a contradiction with the assumption that $S_i \cap q_a$ is nonempty. Thus, if $S_i \cap q_a$ is nonempty, then i must belong to I_a. By definition of the discrete isocommittor $\tilde{q}_a(\rho)$, it follows that $S_i \subset \tilde{q}_a(\rho)$.

Since S_i was taken to be an arbitrary partition set that had nonempty intersection with q_a, it follows that every such partition set is contained in $\tilde{q}_a(\rho)$. Since q_a is contained in the union of sets S_i such that $S_i \cap q_a$ is nonempty, and since every such S_i is contained in $\tilde{q}_a(\rho)$, it follows that q_a is contained in $\tilde{q}_a(\rho)$. □

In the following proposition we define an envelope $D_a(\rho)$ of the continuous isocommittor surface q_a as a full dimensional set which depends on the partition width ρ and contains the discrete isocommittor surface $\tilde{q}_a$.

Proposition 4.3.6. *Suppose that Assumption 4.3.1 holds. Let $a \in (0,1)$ be arbitrary, and let $\{S_i\}_{i \in I}$ be an arbitrary Voronoi tessellation of S with width ρ. Let $\tilde{q}_a(\rho)$ be the associated discrete isocommittor surface given in Definition 4.3.4. There exists a set $D_a(\rho)$, that depends solely on q, a and ρ such that $D_a(\rho) \supset \tilde{q}_a(\rho)$.*

Proof. Let $a \in (0,1)$ be arbitrary. Fix an arbitrary Voronoi tessellation $\{S_i\}_{i \in I}$ with width ρ, let I_a be as in (4.10), and fix an arbitrary $i \in I_a$. Then by definition of I_a given in (4.10) it holds that

$$a - K\rho \leq \tilde{q}_i \leq a + K\rho.$$

Combining these inequalities with the result of Lemma 4.3.3 yields

$$a - 2K\rho \leq q(y) \leq a + 2K\rho, \quad \forall y \in S_i.$$

Therefore, it holds that

$$|q(y) - a| \leq 2K\rho, \quad \forall y \in S_i, \ \forall i \in I_a. \tag{4.11}$$

For any $\rho' > 0$ not necessarily equal to ρ, define the set

$$D_a(\rho') := \{x \in S \ : \ |q(x) - a| \leq 2K\rho'\}. \tag{4.12}$$

From the definition of q_a and $D_a(\rho')$, it follows that $q_a \subset D_a(\rho')$, for any $\rho' > 0$. From (4.11), it follows that $S_i \subset D_a(\rho)$ for all $i \in I_a$. Thus

$$\tilde{q}_a(\rho) = \bigcup_{i \in I_a} S_i \subset D_a(\rho).$$

Therefore $\tilde{q}_a(\rho) \subset D_a(\rho)$ which proves the claim.

□

Suppose that Assumption 4.3.1 holds. Let a sequence $\{\rho_k\}_{k\in\mathbb{N}} \subset (0, +\infty)$ be decreasing to zero and for each ρ_k, let $\{S_i^{(k)}\}_{k\in I(k)}$ be an arbitrary Voronoi tessellation of S with width ρ_k. Fix $a \in (0, 1)$ and let $\{\tilde{q}_a(\rho_k)\}_{k\in\mathbb{N}}$ be the associated sequence of discrete isocommittor surfaces and $\{D_a(\rho_k)\}_{k\in\mathbb{N}}$ the sequence of envelopes defined in (4.12). By Lemma 4.3.5 and Proposition 4.3.6 we then have

$$q_a \subset \tilde{q}_a(\rho_k) \subset D_a(\rho_k), \tag{4.13}$$

for every $a \in (0, 1)$ and every ρ_k. Note that when $\{\rho_k\}_{k\in\mathbb{N}}$ decreases to zero, the sequence of envelopes $\{D_a(\rho_k)\}_{k\in\mathbb{N}}$ decreases to q_a. Thus the sequence of discrete isocommittor surfaces $\{\tilde{q}_a(\rho_k)\}_{k\in\mathbb{N}}$ decreases to q_a when $\{\rho_k\}_{k\in\mathbb{N}}$ decreases to zero. Therefore, Definition 4.3.4 of the discrete isocommittor surfaces is reasonable.

In the preceding section and this section we defined the discrete committor function and the discrete isocommittor surfaces on the Voronoi tessellation, respectively. We proved the convergence of the discrete committor function to the committor function of transition path theory for diffusion processes. For the isocommittor surfaces, we did not prove the convergence result in the Hausdorff metric, but we provided the set inequality (4.13) which implies that the discrete isocommittor surfaces decrease to the continuous isocommittor surfaces of transition path theory for diffusion processes when the partition width decreases. Note however, that we have not used any properties of the Voronoi tessellation except that the Voronoi cells are pathwise connected sets; see Remark 4.2.8. The following step is to define the discrete probability current and prove its convergence to the probability current of the transition path theory for diffusion processes. In order to achieve this we will use more of the properties of the Voronoi tessellation. In particular, we will use that the partition sets in the Voronoi tessellation are polytopes. Therefore, in the following section we digress and summarise some properties of polytopes that we will use in the proof of the convergence of the discrete probability current that we give in Section 4.5. The results presented in the following section are based on the results of [10].

4.4 Properties of polytopes

We begin with the definition of a d-dimensional polytope P in $\mathbb{R}^d$. Let $N \in \mathbb{N}$. For $i \in \{1, \ldots, N\}$, let $a_i \in \mathbb{R}^d$ satisfy $|a_i|_2 = 1$, $a_i \neq a_j$ for $i \neq j$, and let $b_i \in \mathbb{R}$. The set $\{x \in \mathbb{R}^d \ : \ a_i^\top x = b_i\}$ defines a hyperplane with normal vector a_i and b_i is the offset of the hyperplane from the origin; see [6, Section 2.2.1]. The set $H_i := \{x \in \mathbb{R}^d \ : \ a_i^\top x \leq b_i\}$ defines a half-space. We define a polytope to be the intersection of half-spaces, i.e. $P = \cap_{i=1}^N H_i$.

Note that P can be written as a system of linear inequalities

$$P = \{x \in \mathbb{R}^d : Ax \preceq b\}, \tag{4.14}$$

where $A \in \mathbb{R}^{N\times d}$ has row vectors $a_i^\top$ and vector $b \in \mathbb{N}$ has components b_i and $\preceq$ denotes the componentwise inequality between vectors. The terminology is not standard and in some uses a polytope may be an unbounded or a nonconvex set. The polytopes we discuss in this thesis are bounded and convex.

Note that a polytope $P \subset \mathbb{R}^d$ defined in (4.14) need not have the full dimension d. This means that the intersection of two halfspaces is at most $d-1$-dimensional, i.e. there exist $i, j \in \{1, \dots, N\}$, $i \neq j$ such that $\dim(H_i \cap H_j) \leq d-1$. A facet of the polytope is the intersection of one of the supporting hyperplanes $\{x \ : \ a_i^\top x = b_i\}$ with the polytope itself:

$$\{x \in \mathbb{R}^d : a_i^\top x = b_i\} \cap P.$$

An outer unit normal associated to a facet of a polytope P is a unit vector that is orthogonal to the facet and points out of P.

In the following proposition we prove that for $d > 1$ any d-dimensional polytope in $\mathbb{R}^d$ has at least $d+1$ facets.

Proposition 4.4.1. *Let $P \in \mathbb{R}^d$ be a polytope given by $P = \{x \in \mathbb{R}^d : Ax \preceq b\}$ where $d > 1$. Then the matrix $A \in \mathbb{R}^{N\times d}$ is such that $N \geq d+1$.*

Proof. We prove the claim by induction.
Base case: Let $d = 2$. A full-dimensional polytope in $\mathbb{R}^2$ with the smallest number of facets is a triangle, which has $3 = d+1$ facets.
Suppose that the claim holds for a $(d-1)$-dimensional polytope.
Induction step: Let $d \geq 3$, and assume that there exists a d-dimensional polytope with only d facets. These d facets are $(d-1)$-dimensional polytopes. Furthermore, each facet intersects at most $d-1$ other facets, since there are d facets in total by assumption. This yields that there exist $(d-1)$-dimensional polytopes with at most $d-1$ facets, which contradicts the base case. Thus any d-dimensional polytope must have at least $d+1$ facets. □

Corollary 4.4.2. *Let P be a d-dimensional polytope in $\mathbb{R}^d$ given by* (4.14)*. Then A has at least d linearly independent rows, i.e. P has at least d linearly independent outer unit normals.*

Proof. By Proposition 4.4.1, P has at least $d+1$ facets, and therefore at least $d+1$ outer normals. We will prove by contradiction that there exist d linearly independent outer normals.

Suppose P has no more than $d-1$ linearly independent outer normals. Then the normals to the facets of P span at most a $(d-1)$-dimensional space, which implies that there exists a hyperplane H in $\mathbb{R}^d$ containing all the outer normals of P. Let v be normal to H, and let n be an arbitrary outer normal associated to some facet F of P. Then v and n are orthogonal, which implies that v is parallel to F, and thus F is unbounded along the direction of v. This implies that P is unbounded, which produces the desired contradiction. □

Let

$$A = U\Sigma V^\top$$

denote the singular value decomposition of A, where $U \in \mathbb{R}^{N\times N}$ and $V \in \mathbb{R}^{d\times d}$ are orthogonal matrices with columns $\{u_1, \ldots, u_N\}$ and $\{v_1, \ldots, v_d\}$ forming orthonormal bases of $\mathbb{R}^N$ and $\mathbb{R}^d$ respectively, and $\Sigma \in \mathbb{R}^{N\times d}$ is a diagonal matrix with the singular values $\sigma_1, \ldots, \sigma_d$ of matrix A on the diagonal. In the following we assume that $\sigma_1 \geq \sigma_2 \geq \cdots \geq \sigma_d$. Then $\sigma_{\min} := \sigma_d > 0$, since $\operatorname{rank}(A) = d$ by Corollary 4.4.2. The matrix A can be written as a sum of rank one matrices in the following way:

$$A = \sum_{i=1}^{d} \sigma_i u_i v_i^\top. \tag{4.15}$$

In the remainder of this section we establish the connection between the geometry of a polytope and the smallest singular value of the corresponding matrix A of unit normals. We first define the Chebyshev centre and the inner radius of a polytope.

The centre of the largest ball inscribed in the polytope is known as the *Chebyshev centre* of the polytope [6, Section 4.3.1] and it is the point that lies furthest away from any point on the boundary of the polytope. Let us denote the Chebyshev centre of the polytope P by x_c.

Let the *inner radius* of a polytope $P \subset \mathbb{R}^d$ be defined as the radius of the largest ball inscribed in P. We denote the inner radius of P by $\operatorname{inrad}(P)$. According to the definition of the Chebyshev centre, the problem of finding $\operatorname{inrad}(P)$ is equivalent to the problem of finding the largest ball inscribed in P that is centred at x_c. More precisely, the problem of finding $\operatorname{inrad}(P)$ is equivalent to maximising the radius r of the ball $B(x_c, r)$ such that $B(x_c, r) \subset P$, i.e.

$$\operatorname{inrad}(P) := \sup\{r > 0 : B(x_c, r) \subset P\}.$$

This implies that every point $x \in B(x_c, r)$ satisfies all the inequality constraints of (4.14), i.e.

$$a_i^\top x \leq b_i, \text{ for all } i \in \{1, \ldots, N\} \quad \text{for all } x \in B(x_c, r). \tag{4.16}$$

Since $B(x_c, r)$ can be written as $B(x_c, r) = \{x_c + u \ : \ |u|_2 \leq r\}$, (4.16) can be rewritten as the linear program

$$\begin{aligned} &\text{maximise} && r \\ &\text{subject to} && |u|_2 \leq r \\ &&& a_i^\top (x_c + u) \leq b_i, \quad i \in \{1, \ldots, N\}. \end{aligned} \tag{4.17}$$

The solution of the linear program (4.17) corresponding to the Chebyshev centre x_c is $\operatorname{inrad}(P)$. Since $\sup\{a_i^\top u \ : |u|_2 \leq r\} = r\,|a_i|_2$, we arrive at the following formulation of the linear program (4.17):

$$\begin{aligned} &\text{maximise} && r \\ &\text{subject to} && a_i^\top x_c + r\,|a_i|_2 \leq b_i, \quad i \in \{1, \ldots, N\}. \end{aligned} \tag{4.18}$$

Now, since the rows of the matrix A have unit norms, we can compactly rewrite (4.18) as

$$\begin{aligned} &\text{maximise} && r \\ &\text{subject to} && Ax_c + re \preceq b, \end{aligned} \tag{4.19}$$

where $e = [1, \ldots, 1]^\top \in \mathbb{R}^N$.

Using the inner radius of a set, we define the degeneracy ratio of a set. We will use this to characterise the geometry of polytopes. We define the *degeneracy ratio* of a d-dimensional set P by

$$\delta(P) := \frac{\text{inrad}(P)}{\text{diam}(P)},$$

to quantify how close a d-dimensional set P is to being $(d-1)$-dimensional. Note that $\delta(P) \leq 1/2$, since $\frac{\text{diam}(P)}{2} \geq \text{inrad}(P)$ for any set P, with equality attained for d-dimensional Euclidean balls.

Recall that a homothetic transformation is a similarity mapping that preserves the proportion of distances of any point of a set P to a preselected fixed point. Therefore the image of a set P under homotheties is a scaled version of P. Since the scaling factor appears in both the numerator and the denominator of the degeneracy ratio, we conclude that the degeneracy ratio $\delta(P)$ is invariant under homotheties.

We motivate the degeneracy ratio as follows: Suppose that P_1 and P_2 are d-dimensional sets with $\delta(P_1) < \delta(P_2)$, and let P_1' be a homothetic image of P_1 such that $\text{diam}(P_1') = \text{diam}(P_2)$ and $\delta(P_1') = \delta(P_1)$; then

$$\frac{\text{inrad}(P_1')}{\text{diam}(P_1')} = \frac{\text{inrad}(P_1)}{\text{diam}(P_1)} < \frac{\text{inrad}(P_2)}{\text{diam}(P_2)}. \tag{4.20}$$

Since $\text{diam}(P_1') = \text{diam}(P_2)$, it holds that P_1' and P_2 are of equal 'size' in the sense that the minimal circumscribed balls of P_1' and P_2 have the same radius. On the other hand, from (4.20) it follows that $\text{inrad}(P_1') < \text{inrad}(P_2)$ which means that P_1' is 'thinner' than P_2, because the radius of the maximal inscribed ball of P_1' is smaller than that of the maximal inscribed ball of P_2. Loosely speaking, the set P_2 is closer to being d-dimensional than the set P_1'. The set P_1' will be at most $d-1$-dimensional when $\text{inrad}(P_1')$ equals zero.

We will relate the degeneracy ratio of a polytope P to the smallest singular value corresponding to the polytope P, i.e. the smallest singular value of matrix A. In particular let $\{P_k\}_{k\in\mathbb{N}}$ be a sequence of d-dimensional polytopes and $\{A_k\}_{k\in\mathbb{N}}$ be the sequence of the matrices of unit normals corresponding to $\{P_k\}_{k\in\mathbb{N}}$. We prove that when the sequence of polytopes is such that the corresponding smallest singular value decreases to zero, the degeneracy ratio of the polytopes decreases to zero, i.e. if $\sigma_{\min}(A_k) \to 0^+$ then $\delta(P_k) \to 0^+$.

In the following lemma we prove that the inner radius of a polytope is invariant under translations.

Lemma 4.4.3. *Let P be a polytope given by* (4.14)*. If P' is a polytope obtained from P by translation, i.e.*

$$P' = \{x \in \mathbb{R}^d \ : \ x - s \in P\},$$

for some $s \in \mathbb{R}^d$, then $\text{inrad}(P') = \text{inrad}(P)$.

Proof. Let x_c denote the Chebyshev centre of P and r denote the inner radius of P, i.e. $r = \text{inrad}(P)$. Thus x_c and r satisfy (4.19).

Let P' be given as in the statement of the lemma. Then

$$P' = \{x \in \mathbb{R}^d \ : \ A(x-s) \preceq b\} = \{x \in \mathbb{R}^d \ : \ Ax \preceq b'\},$$

where $b' = b + As$. By adding As to both sides of the constraint in (4.19) we obtain the following linear program that optimises for $\text{inrad}(P')$

$$\begin{array}{ll} \text{maximise} & r \\ \text{subject to} & Ax'_c + re \preceq b', \end{array} \tag{4.21}$$

where $x'_c = x_c + s$. Since the constraint sets in (4.21) and (4.19) are related by translation, the solutions of the linear programs in (4.19) and (4.21) are the same, and thus $\text{inrad}(P') = \text{inrad}(P)$. □

Note that any polytope P can be translated such that $0 \in \text{int}(P)$. The following lemma provides the information on the sign of the offsets b_i of the facets of the polytope P when $0 \in \text{int}(P)$.

Lemma 4.4.4. *If P is a d-dimensional polytope given by* (4.14) *such that $0 \in \text{int}(P)$, then $b_i > 0$ for all $i \in \{1, \ldots, N\}$.*

Proof. If $0 \in P$ then $x = 0$ satisfies the inequality constraint in (4.14), which implies that $b_i \geq 0$ for all $i \in \{1, \ldots, N\}$. Suppose that there exists some $i \in \{1, \ldots, N\}$ such that $b_i = 0$. Then for $x = 0$, $a_i^\top x = 0 = b_i$, and hence the origin lies on a supporting hyperplane of the polytope P, and thus the origin belongs to the boundary of P. Taking the contrapositive, if the origin lies in the interior of P, then for all $i \in \{1, \ldots, N\}$, $b_i > 0$. □

Lemma 4.4.4 will be useful in proving the relation between the minimal singular value of A and the degeneracy ratio of P which we give in the following theorem. Recall the singular value decomposition (4.15) of the matrix A; $\sigma_d(A)$ denotes the smallest singular value of A.

Theorem 4.4.5. *Let $P = \{x \in \mathbb{R}^d \,:\, Ax \preceq b\}$ be a d-dimensional polytope with $0 \in \text{int}(P)$, and let σ_d be the smallest strictly positive singular value of the matrix A. Then*

$$\delta(P) < \sigma_d(A).$$

Proof. By singular value decomposition, v_d denotes the right singular vector of A corresponding to $\sigma_d(A)$. The intersection of $\text{span}(v_d)$ and the polytope P is a line segment. Let $f, g \in \partial P$ denote the end points of this line segment, i.e. points where $\text{span}(v_d)$ intersects ∂P. Then $f = \lambda_1 v_d$ and $g = \lambda_2 v_d$ for some $\lambda_1, \lambda_2 \in \mathbb{R}$. Since $0 \in \text{int}(P)$ and $0 \in \text{span}(v_d)$, it holds that the line segment connecting f and g contains the origin $0 \in \mathbb{R}^d$ and therefore

$$\text{sign}(\lambda_1) = -\,\text{sign}(\lambda_2). \tag{4.22}$$

Since $f, g \in \partial P$ there exist $i, j \in \{1, \ldots, N\}$ such that f and g satisfy $Ax \preceq b$ with equality for components i and j, that is $(Af)_i = b_i$ and $(Ag)_j = b_j$ or equivalently

$$\exists\ i, j \text{ such that } a_i^\top f = b_i \text{ and } a_j^\top g = b_j. \tag{4.23}$$

If $i = j$, then the two distinct points f and g lie on the hyperplane $\{x \in \mathbb{R}^d \,:\, a_i^\top x = b_i\}$. More precisely, they lie on the facet $\{x \in \mathbb{R}^d \,:\, a_i^\top x = b_i\} \cap P$. Since the line segment connecting f and g contains the origin $0 \in \mathbb{R}^d$, the origin belongs to the facet $\{x \in \mathbb{R}^d \,:\, a_i^\top x = b_i\} \cap P$. This contradicts the assumption that $0 \in \text{int}(P)$. Therefore $i \neq j$.

The points f and g are mapped by the linear mapping A to the points

$$f' := Af = A\lambda_1 v_d = \sum_{i=1}^{d} \sigma_i u_i v_i^\top \lambda_1 v_d = \sigma_d \lambda_1 u_d \tag{4.24}$$

and

$$g' := Ag = A\lambda_2 v_d = \sum_{i=1}^{d} \sigma_i u_i v_i^\top \lambda_2 v_d = \sigma_d \lambda_2 u_d \tag{4.25}$$

respectively, where we used (4.15) in the second equations of both (4.24) and (4.25), and the fact that $\{v_1, \ldots, v_d\}$ form an orthonormal system in the third equations of both (4.24) and (4.25).

The length of the line segment connecting the points f and g in $\mathbb{R}^d$ is

$$|f - g|_2 = |\lambda_1 v_d - \lambda_2 v_d|_2 = |\lambda_1 - \lambda_2| \, |v_d|_2 = |\lambda_1 - \lambda_2| \,, \tag{4.26}$$

where we used that $|v_d|_2 = 1$ in the last equality. Analogously using $|u_d|_2 = 1$ we obtain the length of the line segment connecting f' and g' in $\mathbb{R}^N$:

$$|f' - g'|_2 = |\sigma_d \lambda_1 u_d - \sigma_d \lambda_2 u_d|_2 = \sigma_d \, |\lambda_1 - \lambda_2| \, |u_d|_2 = \sigma_d \, |\lambda_1 - \lambda_2| \,. \tag{4.27}$$

Due to the linearity of the mapping A, the line segment connecting f and g is mapped to the line segment connecting f' and g'. According to (4.23), $f'_i = b_i$ and $g'_j = b_j$. Furthermore,

$$g'_i = (\sigma_d \lambda_2 u_d)_i = (\sigma_d \lambda_1 u_d)_i \frac{\lambda_2}{\lambda_1} = f'_i \frac{\lambda_2}{\lambda_1} = b_i \frac{\lambda_2}{\lambda_1},$$

where we used (4.25) in the first equality and (4.24) in the third. Let $b' \in \mathbb{R}^N$ be such that $b'_k := g'_k$ for all $k \in \{1, \ldots N\} \setminus \{i\}$ and $b'_i = b_i$. Consider the triangle with vertices f', g' and b'. This triangle is right-angled with right angle at the vertex b', because the line segment between f' and b' is contained in the hyperplane $\{x \in \mathbb{R}^N \ : \ x_i = b_i\}$ and the line segment between g' and b' is contained in the hyperplane $\{x \in \mathbb{R}^N \ : \ x_j = b_j\}$ and these two hyperplanes are orthogonal to each other because $i \neq j$. Since g' and b' differ in the i-th coordinate only, the length of the side connecting g' and b' is

$$\left| b_i - b_i \frac{\lambda_2}{\lambda_1} \right| = b_i \left| 1 + \left| \frac{\lambda_2}{\lambda_1} \right| \right| = b_i \left(1 + \left| \frac{\lambda_2}{\lambda_1} \right| \right),$$

where we used Lemma 4.4.4 and (4.22) in the first equality and the fact that $1 + \left|\frac{\lambda_1}{\lambda_2}\right|$ is positive in the second. Furthermore, since the triangle formed by b', f' and g' is right angled with right angle at the vertex b', it follows that the hypotenuse is given by the line segment joining f' and g', and that the length of the hypotenuse is greater than the length of the line segment connecting g' and b'. Therefore

$$\sigma_d \, |\lambda_1 - \lambda_2| \geq b_i \left(1 + \left| \frac{\lambda_2}{\lambda_1} \right| \right) > b_i, \tag{4.28}$$

where we used (4.27). The last inequality uses the fact that the absolute value is non-negative and that λ_1 and λ_2 are nonzero.

The radius of the largest inscribed ball in P solves the linear program (4.19). By Lemma 4.4.3, we know that the inner radius of a polytope is invariant under translations. Therefore, we may assume without loss of generality that $x_c = 0$. Substituting $x_c = 0$ into the linear program (4.19) yields that the radius $\mathrm{inrad}(P)$ of the largest inscribed ball in P satisfies $\mathrm{inrad}(P)e \preceq b$, where $e = [1, \dots, 1]^\top \in \mathbb{R}^N$. In particular, it follows that

$$\mathrm{inrad}(P) \leq b_i \quad \text{for every} \quad i \in \{1, \dots, N\}. \tag{4.29}$$

Therefore it follows that for some $i \in \{1, \dots, N\}$

$$\sigma_d \ \mathrm{diam}(P) \geq \sigma_d \, |f - g|_2 = \sigma_d \, |\lambda_1 - \lambda_2| > b_i \geq \mathrm{inrad}(P),$$

where we used that f and g are in ∂P in the first inequality, equation (4.26) in the equality, and (4.28) and (4.29) in the second and third inequalities respectively. Finally,

$$\sigma_d > \frac{\mathrm{inrad}(P)}{\mathrm{diam}(P)} = \delta(P).$$

□

Theorem 4.4.5 gives a geometric interpretation of the shape of a polytope whose smallest singular value is close to zero. In particular, if the smallest singular value of the polytope P is close to zero, the radius of the largest inscribed ball in P, $\mathrm{inrad}(P)$ is small compared to its diameter, which means that P is 'thin' in the direction of the right singular vector corresponding to the smallest singular value of matrix A in (4.14). This result is interesting in its own right and to the best of our knowledge it is the only result relating the smallest singular value corresponding to a polytope to the shape of the polytope. Theorem 4.4.5 will be the crucial ingredient in the proof of convergence of the discrete probability current which we define in the following section.

4.5 Probability current

In this section we define a *discrete probability current of reactive trajectories* $\tilde{J}_R$ which is obtained by observing the diffusion process in the state space discretised by a Voronoi partition. As with Sections 4.2 and 4.3 we assume that we can observe the continuous process $\{Y_t\}_{t \geq 0}$. This means that at any moment $t \geq 0$ we know in which Voronoi cell S_i the diffusion process $\{X_t\}_{t \geq 0}$ is located. However, we cannot detect the exact location of the diffusion process within the cell.

Recall that the probability current $J_R : S \setminus (A \cup B) \to \mathbb{R}^d$ (3.10) represents the probability of the flow of reactive trajectories. We repeat the definition from (3.10) below for convenience. This definition was taken from [32, Equation (3.14)]. On any surface ∂S_i, which is the boundary of $S_i \subset S \setminus (A \cup B)$ it is defined implicitly via

$$\lim_{s \to 0^+} \frac{1}{s} \lim_{T \to \infty} \frac{1}{T} \int_{\mathcal{R} \cap [0,T]} \mathbf{1}_{S_i}(X_t) \, \mathbf{1}_{S_i\complement}(X_{t+s}) - \mathbf{1}_{S_i\complement}(X_t) \, \mathbf{1}_{S_i}(X_{t+s}) \, \mathrm{d}t$$
$$= \int_{\partial S_i} J_R(y) \cdot n_{S_i}(y) \sigma_{S_i}(\mathrm{d}y)$$

Notice that for a Voronoi cell S_i we have

$$\int_{\partial S_i} J_R(y) \cdot n_{S_i}(y) \sigma_{S_i}(\mathrm{d}y) = \sum_{k \in \mathcal{N}_i} \int_{\partial S_i \cap \partial S_k} J_R(y) \cdot n_{ik}(y) \sigma_{S_i \cap S_k}(\mathrm{d}y),$$

where $\mathcal{N}_i$ denotes the set of indices of cells adjacent to S_i, i.e.

$$\mathcal{N}_i := \{j \in I \ : \ \dim(\partial S_i \cap \partial S_j) = d - 1\},$$

and $n_{ik} \in \mathbb{R}^d$ is the unit vector that points out of S_i and is orthogonal to the hyperplane that contains the facet $\partial S_i \cap \partial S_k$. Thus, for any $k \in \mathcal{N}_i$ we have

$$\begin{aligned} \alpha_{ik} &:= \lim_{s \to 0^+} \frac{1}{s} \lim_{T \to \infty} \frac{1}{T} \int_{\mathcal{R} \cap [0,T]} \mathbf{1}_{S_i}(X_t) \, \mathbf{1}_{S_k}(X_{t+s}) - \mathbf{1}_{S_k}(X_t) \, \mathbf{1}_{S_i}(X_{t+s}) \, \mathrm{d}t \\ &= \int_{\partial S_i \cap \partial S_k} J_R(y) \cdot n_{ik} \sigma_{S_i \cap S_k}(\mathrm{d}y) \end{aligned} \tag{4.30}$$

Following the same strategy as for the discrete committor function, we define the discrete probability current $\tilde{J}_R : S \setminus (A \cup B) \to \mathbb{R}$ to be a piecewise constant function, equal to some vector $\tilde{J}_{R,i} \in \mathbb{R}^d$ on the interiors of each Voronoi cell $\mathrm{int}(S_i)$. Choosing a piecewise constant function motivates the relation

$$\int_{\partial S_i \cap \partial S_k} J_R(y) \cdot n_{ik} \sigma_{S_i \cap S_k}(\mathrm{d}y) = \tilde{J}_{R,i} \cdot n_{ik} \sigma(\partial S_i \cap \partial S_k), \quad \forall k \in \mathcal{N}_i.$$

Since we can observe the process $\{Y_t\}_{t \geq 0}$, we can approximate the quantity α_{ik} by using sample data from reactive trajectories. Combining (4.30) with the preceding equation, it follows that for every $k \in \mathcal{N}_i$ we want to have

$$\alpha_{ik} = n_{ik} \cdot \tilde{J}_{R,i} \sigma(\partial S_i \cap \partial S_k).$$

We can rewrite the above as a matrix-vector equation

$$N_i \tilde{J}_{R,i} = \hat{\alpha}_i \in \mathbb{R}^{\#\mathcal{N}_i}, \tag{4.31}$$

where $\hat{\alpha}_i$ is a vector of length $\#\mathcal{N}_i$ with k-th entry given by $(\hat{\alpha}_i)_k = \alpha_{i,k}/\sigma(\partial S_i \cap \partial S_k)$, and N_i is a $(\#\mathcal{N}_i) \times d$ matrix with real entries such that the k-th row is n_{ik}^T. A necessary condition for the existence of a solution $\tilde{J}_{R,i}$ to the equation (4.31) is that $\hat{\alpha}_i$ must belong to the column space of N_i. However, we do not expect the latter condition to hold in general, since Proposition 4.4.1 indicates that $\#\mathcal{N}_i \geq d+1$, so the column space of N_i will be a subspace of strictly positive codimension. However, according to Corollary 4.4.2, the rank of matrix N_i is d. As a consequence, we can substitute the problem given in equation (4.31) with the normal equation

$$N_i^\top N_i \tilde{J}_{R,i} = N_i^\top \hat{\alpha}_i \in \mathbb{R}^d. \tag{4.32}$$

Since $N_i \in \mathbb{R}^{\#\mathcal{N}_i \times d}$ has rank d, the square matrix $N_i^\top N_i \in \mathbb{R}^{d \times d}$ has full rank and thus it is invertible. Therefore, we can define the discrete probability current $\tilde{J}_R$ on the interior of every Voronoi cell using equation (4.32). Note however, that solving (4.32), as well as

storing the matrix $N_i^\top N_i$ will be computationally expensive for large d, since in the case of meshless discretisations $N_i^\top N_i$ is not sparse.

We now extend the definition of the discrete probability current to the boundaries of Voronoi cells. Let 2^I denote the power set of any countable set I. Define the maps

$$\begin{aligned} h_1 &: \left(\bigcup_{i\in I} \operatorname{int}(S_i)\right)^{\complement} \to 2^I, \quad x \mapsto \{i \in I : x \in \partial S_i\} \\ h_2 &: 2^I \to I, \qquad\qquad\qquad J \mapsto j^* := \operatorname{argmax}\left\{\left|\tilde{J}_{R,j}\right|_2 : j \in J\right\} \\ h &: \left(\bigcup_{i\in I} \operatorname{int}(S_i)\right)^{\complement} \to I, \quad x \mapsto h_2 \circ h_1(x). \end{aligned}$$

The map h_1 assigns to every point x on a boundary of some Voronoi cell S_i, the set of indices of all Voronoi cells that share a facet containing x with the cell S_i. This set of indices includes i as well. To this set of indices of Voronoi cells, the map h_2 assigns the index of the cell in the given set for which the discrete probability current in its interior has the maximal norm. Finally, we are able to give a definition of the discrete probability current on $S \setminus (A \cup B)$.

Definition 4.5.1. The *discrete probability current* $\tilde{J}_R : S \setminus (A \cup B) \to \mathbb{R}^d$ associated to a Voronoi tessellation $\{S_i\}_{i\in I}$ is given by the function:

$$\tilde{J}_R(x) := \begin{cases} \tilde{J}_{R,i} & x \in \operatorname{int}(S_i) \\ \tilde{J}_{R,h(x)} & \text{otherwise.} \end{cases}$$

The function $\tilde{J}_R$ is piecewise constant on the interiors of the Voronoi cells, and for any x not in the interior of a Voronoi cell, the probability current is the L^2-norm maximising current chosen from among the cells whose boundary contains x. For the purposes of establishing a convergence of $\tilde{J}_R$ to J_R in the $L^2(S \setminus (A \cup B), \mu; \mathbb{R}^d)$ topology the definition of $\tilde{J}_R$ on the complement of the interiors is not important, as this set has Lebesgue measure zero. However, for the purposes of defining discrete streamlines, which we consider in Section 4.6, this case is important.

Remark 4.5.2. *Note that Definition 4.5.1 does not require the knowledge of the stochastic differential equation corresponding to the diffusion process X. Therefore, the definition can potentially be applied to a wider spectrum of continuous processes with different boundary conditions. However, the convergence results we prove below hold only in the case when X is an ergodic diffusion process.*

Let us denote $M_i := N_i^\top N_i$ and $\beta_i := N_i^\top \hat{\alpha}_i$. Equation (4.32) then becomes

$$M_i \tilde{J}_{R,i} = \beta_i.$$

Note that the singular values of the matrix M_i are equal to the squared singular values of the matrix N_i. Indeed, let $N_i = U\Sigma V^\top$ be a singular value decomposition of matrix N_i, then $M_i = N_i^\top N_i = \left(U\Sigma V^\top\right)^\top U\Sigma V^\top = V\Sigma^\top\Sigma V^\top$ is the singular value decomposition of matrix M_i.

Since the matrix N_i is determined by the polytope S_i, we may consider the smallest and largest singular values $\sigma_{\min}(N_i)$ and $\sigma_{\max}(N_i)$ of N_i, i.e.

$$\sigma_{\min}(S_i) := \sigma_{\min}(N_i) = \sqrt{\sigma_{\min}(M_i)}, \quad \sigma_{\max}(S_i) := \sigma_{\max}(N_i) = \sqrt{\sigma_{\max}(M_i)}. \tag{4.34}$$

We use this property in the proof of the following theorem to show that when J_R belongs to a certain class of functions, then the error between $\tilde{J}_R$ and J_R is bounded on every cell in $S \setminus (A \cup B)$, and approaches zero in the limit of small partition width.

Theorem 4.5.3 (Error bound for discrete probability current)**.** *Let J_R be a globally Lipschitz function on $S \setminus (A \cup B)$ with Lipschitz constant L, and let $\{S_i\}_{i \in I}$ be a Voronoi tessellation of S with width ρ. Then for every $i \in I \setminus (J \cup K)$, there exists some $C_i > 0$ that does not depend on ρ, such that*

$$\left| \tilde{J}_{R,i} - J_R(x) \right|_2 \leq \rho C_i, \quad \forall x \in S_i.$$

In particular, for any well defined discrete probability current $\tilde{J}_R : S \setminus (A \cup B) \to \mathbb{R}^d$ that is equal to $\tilde{J}_{R,i}$ on $\operatorname{int}(S_i)$ for every $i \in I \setminus (J \cup K)$, we have

$$\left\| \tilde{J}_R - J_R \right\|_{L^2(S \setminus (A \cup B), \mu; \mathbb{R}^d)} \leq \rho \max_{i \in I} C_i. \tag{4.35}$$

Proof. The second statement follows from the first. Namely, the first statement proves the convergence of $\tilde{J}_R$ to J_R on the interior of each cell S_i for $i \in I \setminus (J \cup K)$. Since the complement of interiors of cells has Lebesgue measure zero, it does not affect the convergence of $\tilde{J}_R$ to J_R in the $L^2(S \setminus (A \cup B), \mu; \mathbb{R}^d)$ topology. Thus it suffices to prove the first statement.

Fix an arbitrary $x \in S_i$ with $i \in I \setminus (J \cup K)$. According to Corollary 4.4.2, the matrix N_i has full rank. Therefore M_i is invertible and we can write

$$\begin{aligned}
\left| \tilde{J}_{R,i} - J_R(x) \right|_2 &= \left| M_i^{-1} M_i \left(\tilde{J}_{R,i} - J_R(x) \right) \right|_2 \\
&\leq \sigma_{\max}\left({M_i}^{-1} \right) \left| M_i \left(\tilde{J}_{R,i} - J_R(x) \right) \right|_2 \\
&= \frac{1}{\sigma_{\min}(M_i)} \left| M_i \left(\tilde{J}_{R,i} - J_R(x) \right) \right|_2 \\
&= \frac{1}{\sigma^2_{\min}(S_i)} \left| M_i \left(\tilde{J}_{AB,i} - J_{AB}(x) \right) \right|_2 .
\end{aligned} \tag{4.36}$$

where we used the following inequality from linear algebra

$$\sigma_{\min}(G) \left| x - y \right|_2 \leq \left| G(x - y) \right|_2 \leq \sigma_{\max}(G) \left| x - y \right|_2 ,$$

where G is a d-dimensional matrix, to obtain the inequality, for $G = M_i$, and (4.34) to obtain the last equality.

For $H \in \mathbb{R}^{d_1 \times d_2}$ and $v \in \mathbb{R}^d_2$ it follows from the Cauchy-Schwarz inequality that

$$|Hv|_2^2 = \sum_{i=1}^{d_1} \left(\sum_{j=1}^{d_2} h_{ij} v_j \right)^2 = \sum_{i=1}^{d_1} \left(\left| \sum_{j=1}^{d_2} h_{ij} v_j \right| \right)^2 = \sum_{i=1}^{d_1} \left| h_i^\top v \right|^2 \leq \sum_{i=1}^{d_1} |h_i|_2^2 \, |v|_2^2 ,$$

where $h_i^\top$ is the i-th row of H. Therefore

$$\begin{aligned}\left|M_i\left(\tilde{J}_{R,i}-J_R(x)\right)\right|_2^2 &= \left|N_i^\top N_i\left(\tilde{J}_{R,i}-J_R(x)\right)\right|_2^2 \\ &\leq \sum_{j=1}^{d}|{n_{ij}}^*|_2^2\left|N_i\left(\tilde{J}_{R,i}-J_R(x)\right)\right|_2^2, \end{aligned} \tag{4.37}$$

where $({n_{ij}}^*)^\top$ is the j-th row of matrix ${N_i}^\top$, i.e. ${n_{ij}}^*$ is the j-th column of N_i. Since the rows of the matrix N_i are unit normals for all $j \in \{1,\dots,\#\mathcal{N}_i\}$, we know that the absolute value of each entry of vector n_{ij} is at most one. Thus the absolute value of each entry of matrix N_i is bounded from above by one. Therefore

$$|{n_{ij}}^*|_2^2 \leq \#\mathcal{N}_i. \tag{4.38}$$

It follows from (4.31) that

$$\left|N_i(\tilde{J}_{R,i}-J_R(x))\right|_2^2 = \sum_{j=1}^{d}\left|n_{ij}\cdot\left(\tilde{J}_{R,i}-J_R(x)\right)\right|^2 = \sum_{j=1}^{d}\left|\alpha_{i,j}-n_{ij}\cdot J_R(x)\right|^2. \tag{4.39}$$

By (4.30)

$$\begin{aligned}|\alpha_{i,j}-n_{ij}\cdot J_R(x)| &= \left|\frac{1}{\sigma(\partial S_i\cap\partial S_j)}\int_{\partial S_i\cap\partial S_j} n_{ij}\cdot(J_R(y)-J_R(x))\,\sigma_{\partial S_i\cap\partial S_j}(\mathrm{d}y)\right| \\ &\leq \frac{1}{\sigma(\partial S_i\cap\partial S_j)}\int_{\partial S_i\cap\partial S_j}|n_{ij}|_2\,|J_R(y)-J_R(x)|_2\,\sigma_{\partial S_i\cap\partial S_j}(\mathrm{d}y) \\ &\leq \frac{1}{\sigma(\partial S_i\cap\partial S_j)}\int_{\partial S_i\cap\partial S_j} L\,|y-x|_2\,\sigma_{\partial S_i\cap\partial S_j}(\mathrm{d}y) \\ &\leq \frac{L\rho}{\sigma(\partial S_i\cap\partial S_j)}\sigma(\partial S_i\cap\partial S_j) = L\rho, \end{aligned} \tag{4.40}$$

where we used the Cauchy-Schwarz inequality to obtain the first inequality, the fact that n_{ij} is a unit vector for all $i \in I$ and $j \in \{1,\dots,\#\mathcal{N}_i\}$ and the Lipschitz continuity of J_R to obtain the second inequality, and the fact that $|x-y|_2 \leq \rho$ for any $x, y \in \partial S_i \subset S_i$ in the last inequality. Combining the inequalities (4.36), (4.37), (4.38), (4.39) and (4.40) yields

$$\begin{aligned}\left|\tilde{J}_{R,i}-J_R(x)\right|_2 &\leq \frac{1}{\sigma_{\min}^2(S_i)}\left|M_i\left(\tilde{J}_{AB,i}-J_{AB}(x)\right)\right|_2 \\ &\leq \frac{1}{\sigma_{\min}^2(S_i)}\sqrt{\sum_{j=1}^{d}|{n_{ij}}^*|_2^2\left|N_i\left(\tilde{J}_{R,i}-J_R(x)\right)\right|_2^2} \\ &\leq \frac{1}{\sigma_{\min}^2(S_i)}\sqrt{\#\mathcal{N}_i\sum_{j=1}^{d}\left|\alpha_{i,j}-n_{ij}\cdot J_R(x)\right|^2} \\ &\leq \frac{1}{\sigma_{\min}^2(S_i)}\sqrt{\#\mathcal{N}_i d\,(L\rho)^2} \\ &= L\rho\frac{\sqrt{\#\mathcal{N}_i d}}{\sigma_{\min}^2(S_i)} \end{aligned}$$

so that the desired error bound holds with $C_i := \sqrt{\#\mathcal{N}_i d}L\sigma_{\min}^{-2}(S_i)$. □

Define the *smallest singular value of a Voronoi tessellation* $\{S_i\}_{i\in I}$ via

$$\sigma_{\min}(\{S_i\}_{i\in I}) := \min_{i\in I} \sigma_{\min}(S_i),$$

and let

$$\#\mathcal{N}_{\max}(\{S_i\}_{i\in I}) := \max_{i\in I}(\#\mathcal{N}_i).$$

The error bound (4.35) of Theorem 4.5.3 can then be written as

$$\left\|\tilde{J}_R - J_R\right\|_{L^2(S\setminus(A\cup B),\mu;\mathbb{R}^d)} \leq \sqrt{\#\mathcal{N}_{\max}(\{S_i\}_{i\in I})d}L\left(\sigma_{\min}(\{S_i\}_{i\in I})\right)^{-2}\rho. \tag{4.41}$$

To obtain a convergence theorem from the bound above, we must ensure that the sequence $\left\{\#\mathcal{N}_{\max}(\{S_i^{(k)}\}_{i\in I(k)})\right\}_{k\in\mathbb{N}}$ associated to the sequence of Voronoi tessellations with decreasing widths remains bounded and that the sequence $\left\{\sigma_{\min}(\{S_i^{(k)}\}_{i\in I(k)})\right\}_{k\in\mathbb{N}}$ remains bounded away from zero. For the first sequence to be bounded we introduce an additional assumption which uniformly bounds the number of facets of every Voronoi cell.

Assumption 4.5.4. *The sequence of Voronoi tessellations* $\{\{S_i^{(k)}\}_{i\in I(k)}\}_{k\in\mathbb{N}}$ *is such that there exists a constant* $K_1 > 0$ *such that* $\#\mathcal{N}_{\max}(\{S_i^{(k)}\}_{i\in I(k)}) \leq K_1$*, i.e. the maximal number of neighbours of a cell in the partition* $\{S_i^{(k)}\}_{i\in I(k)}$ *is bounded from above by* K_1*, for every* $k \in \mathbb{N}$*.*

To achieve that the sequence $\left\{\sigma_{\min}(\{S_i^{(k)}\}_{i\in I(k)})\right\}_{k\in\mathbb{N}}$ remains bounded away from zero we use the degeneracy ratio defined in Section 4.4. Theorem 4.4.5 gives a necessary condition for the smallest singular value of a polytope to be close to zero, namely that the degeneracy ratio of the polytope must be close to zero. Therefore, by contraposition, keeping the degeneracy ratio of all polytopes in a partition bounded away from zero ensures that the smallest singular value for any polytope in the partition stays bounded away from zero. This motivates the following assumption.

Assumption 4.5.5. *For the sequence of Voronoi tessellations* $\{\{S_i^{(k)}\}_{i\in I(k)}\}_{k\in\mathbb{N}}$ *there exists a constant* $K_2 > 0$ *such that* $\delta(S_i^{(k)}) \geq K_2$ *for all* $i \in I(k)$ *and all* $k \in \mathbb{N}$*.*

Finally, we prove the convergence of the discrete probability current $\tilde{J}_R$ to the continuous probability current J_R.

Proposition 4.5.6. *Let* J_R *be a globally Lipschitz function on* $S \setminus (A \cup B)$ *with Lipschitz constant* L*. Let* $\{\rho_k\}_{k\in\mathbb{N}}$ *be an arbitrary sequence in* $(0,\infty)$ *decreasing to zero and for each* k*, let* $\{S_i^{(k)}\}_{i\in I(k)}$ *be a Voronoi tessellation with width* ρ_k*. Let the sequence of partitions* $\{\{S_i^{(k)}\}_{i\in I(k)}\}_{k\in\mathbb{N}}$ *satisfy Assumptions 4.5.4 and 4.5.5 with constants* $K_1 > 0$ *and* $K_2 > 0$ *respectively. If* $\tilde{J}_R^{(k)}$ *denotes the discrete probability current corresponding to partition* $\{S_i^{(k)}\}_{i\in I(k)}$ *then, for every* $x \in S \setminus (A \cup B)$ *there exists a constant* $C > 0$ *independent of* k *such that*

$$\left|\tilde{J}_R^{(k)}(x) - J_R(x)\right|_2 \leq C\rho_k. \tag{4.42}$$

Furthermore

$$\|\tilde{J}_R^{(k)} - J_R\|_{L^2(S\setminus(A\cup B),\mu;\mathbb{R}^d)} \leq C\rho_k.$$

Proof. Since Assumption 4.5.5 is satisfied with constant K_2 for all $k \in \mathbb{N}$ it follows that the smallest degeneracy ratio over all cells and all partitions stays bounded away from zero. Equivalently, there exists $K_2 > 0$ such that

$$\delta(S_i) \geq K_2, \quad \text{for all} \quad i \in I(k) \quad \text{and all} \quad k \in \mathbb{N}.$$

By Theorem 4.4.5 then

$$\sigma_{\min}(S_i) \geq K_2, \quad \text{for all} \quad i \in I(k) \quad \text{and for all} \quad k \in \mathbb{N},$$

which implies

$$\sigma_{\min}(\{S_i\}_{i \in I(k)}) \geq K_2 \quad \text{for all} \quad k \in \mathbb{N}.$$

Using the error bound from the proof of Theorem 4.5.3, the discrepancy at any point $x \in S \setminus (A \cup B)$ becomes

$$\left| \tilde{J}_R^{(k)}(x) - J_R(x) \right|_2 \leq C \rho_k,$$

for

$$C = \frac{\sqrt{dK_1}L}{\sigma_{\min}^2(\{S_i^{(k)}\}_{i \in I(k)})} \leq \frac{\sqrt{dK_1}L}{K_2^2},$$

where we used Assumption 4.5.4 to bound the maximal number of neighbours of a cell in $\{S_i^{(k)}\}_{i \in I(k)}$ for any $k \in \mathbb{N}$ by K_1 and Assumption 4.5.5 to bound the degeneracy ratio of all the cells in the partition from away from zero and thus bound the smallest singular value of all cells away from zero by Theorem 4.4.5.

Furthermore, using (4.42) in the first inequality, the constant C given above in the second, and the fact that $\mu(S \setminus (A \cup B)) \leq \mu(S) = 1$ in the last equality it follows that

$$\begin{aligned}
\|\tilde{J}_R^{(k)} - J_R\|_{L^2(S \setminus (A \cup B), \mu; \mathbb{R}^d)} &= \left(\int_{S \setminus (A \cup B)} \left| \tilde{J}_R^{(k)}(x) - J_R(x) \right|_2^2 \mu(\mathrm{d}x) \right)^{\frac{1}{2}} \\
&\leq \frac{\sqrt{dK_1}L}{\sigma_{\min}^2(\{S_i^{(k)}\}_{i \in I(k)})} \rho_k \left(\int_{S \setminus (A \cup B)} \mu(\mathrm{d}x) \right)^{\frac{1}{2}} \\
&\leq \frac{\sqrt{dK_1}L \sqrt{\mu(S \setminus (A \cup B))}}{K_2^2} \rho_k \leq \frac{\sqrt{dK_1}L}{K_2^2} \rho_k.
\end{aligned}$$

□

The most relevant result of this section is given in Theorem 4.5.3. This theorem is an important ingredient for proving the convergence of the discrete streamlines, which we shall define in the next section, to their continuous counterparts from the transition path theory for diffusion processes.

4.6 Streamlines

We introduce the *discrete streamlines* using the discrete probability current defined in the previous section. In order to be able to compare the discrete and the continuous streamline and prove the convergence of the former to the latter in the limit of small width, we fix

a starting point to be the same for both the continuous and discrete streamlines and let them evolve for the same time interval.

As given in Section 3.6, a streamline of diffusion process transition path theory between the reactant set A and the product set B for a given initial condition $s_0 \in \partial A$ is the solution $\{s(t)\}_{t\in[0,T(s_0)]}$ of the initial value problem

$$s(0) = s_0, \quad \frac{\mathrm{d}s}{\mathrm{d}t}(t') = J_R(s(t')), \quad t' \in [0, T(s_0)] \tag{4.43a}$$

$$T(s_0) := \inf\{t' > 0 \ : \ s(t') \in B\}. \tag{4.43b}$$

We make the following assumption.

Assumption 4.6.1. *For all $s_0 \in \partial A$, $T(s_0)$ is finite and strictly positive.*

We define the discrete streamline $\tilde{s}$ on the partitioned state space such that it starts from the same initial point $\tilde{s}_0 := s_0 \in \partial A$ and such that it evolves for the same amount of time $T(s_0)$ as the continuous streamline. For the definition we use the discrete probability current $\tilde{J}_R : S \setminus (A \cup B) \to \mathbb{R}^d$ defined in Section 4.5. Since $\tilde{J}_R$ is piecewise constant on the interiors of the cells of a Voronoi tessellation, we would like to use (4.43) to construct for every initial condition $\tilde{s}_0$ a streamline that is *piecewise linear* on the interiors of the Voronoi cells. Since the discrete probability current converges to the true probability current in the L^2-topology, we expect that for any given initial condition $s_0 \in \partial A$, the discrete streamline starting at s_0 converges to the true streamline starting at s_0.

A problem with the approach described above is that the discrete probability current $\tilde{J}_R$ is not continuous. Hence, the standard existence and uniqueness theorems for solutions of ordinary differential equations do not apply. Nevertheless, we can define a continuous, piecewise linear trajectory that solves the analogue of (4.43a) with J_R replaced by $\tilde{J}_R$: since the differential equation (4.43a) can be written in integral form as

$$s(t') = s_0 + \int_0^{t'} J_R(s(r))\mathrm{d}r, \quad 0 \le t' \le T(s_0), \tag{4.44}$$

we define the discrete streamline in the following way.

Definition 4.6.2. The *discrete streamline* $\tilde{s}$ with an initial point $\tilde{s}_0 \in \partial A$ is given by

$$\tilde{s}(t') = \tilde{s}_0 + \int_0^{t'} \tilde{J}_R(\tilde{s}(r))\mathrm{d}r, \quad 0 \le t' \le T(\tilde{s}_0). \tag{4.45}$$

Note that if $\tilde{s}_0 = s_0$, then the upper time limit in (4.45) equals $T(s_0)$.

In the remainder of this section we give an error bound for the discrete streamlines in a fixed partition and show that for a sequence of partitions of decreasing width this error bound decreases linearly with the width of partition. In order to prove this we will need the integral form of Grönwall's inequality [2].

Theorem 4.6.3 (Grönwall-Bellman inequality)**.** *Let $y(t)$, $f(t)$ and $g(t)$ be non-negative functions on $[0, T]$. If $f(t)$ is nondecreasing and*

$$y(t) \le f(t) + \int_0^t g(s)y(s)\mathrm{d}s \quad \textit{for all} \quad t \in [0, T],$$

then

$$y(t) \le f(t) \exp\left(\int_0^t g(s)\mathrm{d}s\right) \quad \textit{for all} \quad t \in [0, T].$$

Theorem 4.6.4 (Error bound for discrete streamlines)**.** *Let $J_R : S \setminus (A \cup B) \to \mathbb{R}^d$ be a globally Lipschitz vector field with Lipschitz constant L, and let $\{S_i\}_{i\in I}$ be a Voronoi tessellation of S with width $\rho > 0$ and let $K_1 > 0$ be such that $\#\mathcal{N}_{\max}(\{S_i\}_{i\in I}) \le K_1$. Let there exist $K_2 > 0$ for which $\delta(S_i) \ge K_2$ for all $i \in I$. Fix $s_0 = \tilde{s}_0 \in \partial A$, and let s and $\tilde{s}$ be the true and discrete streamlines defined according to* (4.44) *and* (4.45) *respectively. If Assumption 4.6.1 holds, then*

$$\|s - \tilde{s}\|_{L^2([0,T(s_0)],\mathrm{d}t)} \le C\rho$$

where C does not depend on ρ.

Proof. Fix an arbitrary $t \in [0, T(s_0)]$. Since $s_0 = \tilde{s}_0$ from (4.44) and (4.45) it follows that

$$|s(t) - \tilde{s}(t)|_2 \le \int_0^t \left| J_R(s(r)) - \tilde{J}_R(\tilde{s}(r)) \right|_2 \mathrm{d}r.$$

By the triangle inequality and Lipschitz continuity of J_R, we have

$$\begin{aligned}\left| J_R(s(r)) - \tilde{J}_R(\tilde{s}(r)) \right|_2 &\le |J_R(s(r)) - J_R(\tilde{s}(r))|_2 + \left| J_R(\tilde{s}(r)) - \tilde{J}_R(\tilde{s}(r)) \right|_2 \\ &\le L\,|s(r) - \tilde{s}(r)|_2 + \left| J_R(\tilde{s}(r)) - \tilde{J}_R(\tilde{s}(r)) \right|_2.\end{aligned}$$

Recall that Proposition 4.5.6 yields

$$\left| \tilde{J}_R(x) - J_R(x) \right|_2 \le \frac{\sqrt{dK_1}L}{K_2^2}\rho.$$

Therefore,

$$\left| J_R(\tilde{s}(r)) - \tilde{J}_R(\tilde{s}(r)) \right|_2 \le \rho L\sqrt{dK_1}K_2^{-2}, \quad \forall r \in [0, T(s_0)].$$

Combining the preceding estimates yields

$$\begin{aligned}|s(t) - \tilde{s}(t)|_2 &\le \int_0^t \left(\rho L\sqrt{dK_1}K_2^{-2} + L\,|s(r) - \tilde{s}(r)|_2 \right) \mathrm{d}r \\ &\le \rho L\sqrt{dK_1}K_2^{-2}t + L\int_0^t |s(r) - \tilde{s}(r)|_2\,\mathrm{d}r\end{aligned}$$

By the Grönwall-Bellman inequality given in Theorem 4.6.3, for

$$y(t) := |s(t) - \tilde{s}(t)|_2, \quad f(t) := \rho L\sqrt{dK_1}K_2^{-2}t \quad \text{and} \quad g(t) := L$$

it follows that for all $t \in [0, T(s_0)]$

$$|s(t) - \tilde{s}(t)|_2 \le \rho L\sqrt{dK_1}K_2^{-2}t\exp\left(\int_0^t L\mathrm{d}s\right) = \rho L\sqrt{dK_1}K_2^{-2}t\exp(Lt),$$

and therefore

$$|s(t) - \tilde{s}(t)|_2 \le \rho L\sqrt{dK_1}K_2^{-2}\exp(LT(s_0))\,T(s_0), \quad \forall t \in [0, T(s_0)].$$

Since the right-hand side of the inequality above does not depend on t, the desired conclusion follows from:

$$\begin{aligned}\|\tilde{s} - s\|_{L^2([0,T(s_0)],\mathrm{d}t)} &= \left(\int_0^{T(s_0)} |\tilde{s}(t) - s(t)|_2^2 \,\mathrm{d}t\right)^{\frac{1}{2}} \\ &\leq \frac{\sqrt{dK_1} L \exp\left(LT(s_0)\right) T(s_0)}{K_2^2} \rho \left(\int_0^{T(s_0)} \mathrm{d}t\right)^{\frac{1}{2}} \\ &= \frac{\sqrt{dK_1} L \exp\left(LT(s_0)\right) T(s_0)^{\frac{3}{2}}}{K_2^2} \rho.\end{aligned}$$

□

The final step is to prove convergence of the discrete streamlines, given a sequence of Voronoi tessellations with decreasing widths.

Corollary 4.6.5 (Convergence of discrete streamlines)**.** *Let $\{\rho_k\}_{k\in\mathbb{N}}$ be an arbitrary sequence in $(0,\infty)$ decreasing to zero. For each k, let $\{S_i^{(k)}\}_{i\in I(k)}$ be a Voronoi tessellation of width ρ_k, such that Assumptions 4.5.4 and 4.5.5 hold with constants K_1 and K_2 respectively, where both K_1 and K_2 are independent of k. Fix $s_0 = \tilde{s}_0 \in \partial A$, let s be the streamline generated by s_0, and let $\tilde{s}^{(k)}$ be the discrete streamline generated by $\tilde{s}_0$ and the discrete probability current associated to $\{S_i^{(k)}\}_{i\in I(k)}$. Under Assumption 4.6.1 there exists some $C > 0$ that does not depend on k, such that*

$$\left\|s - \tilde{s}^{(k)}\right\|_{L^2([0,T(s_0)],\mathrm{d}t)} \leq C\rho_k.$$

Proof. By Theorem 4.6.4, we have

$$\left\|s - \tilde{s}^{(k)}\right\|_{L^2([0,T(s_0)],\mathrm{d}t)} \leq L\exp(LT(s_0))T(s_0)^{\frac{3}{2}}\sqrt{dK_1}K_2^{-2}\rho_k,$$

which proves the claim for $C = L\exp(LT(s_0))T(s_0)^{\frac{3}{2}}\sqrt{dK_1}K_2^{-2}$. □

Since the constant C in Corollary 4.6.5 is finite, we have proven the convergence of the discrete streamlines to the continuous streamlines of the diffusion process in the limit of partition width decreasing to zero.

Chapter 5

Numerical example

In this section we present an example on which we compare our approach and the approach for transition path theory (TPT) for Markov chains [36]. To the best of our knowledge, there are no theoretical results that prove the convergence of the objects of transition path theory for Markov jump processes or Markov chains to the objects of transition path theory for diffusions, and we do not aim to investigate this convergence in the experiments shown in this section. That being said, we will not perform the state space discretisation refinement. Instead, we will fix one discretisation of the state space and investigate if the transition path theory objects for Markov chains differ from those of our approach for the same discretisation. In addition, we present the results of the TPT for diffusion processes obtained using the finite differences approximation and use them as the ground truth for comparison with other two approaches.

The example we chose is a 2-dimensional Smoluchowski diffusion process with the triple well potential. We introduced the Smoluchowski diffusion in Section 2.6, but for convenience we repeat here the corresponding stochastic differential equation:

$$\mathrm{d}X_t = -\Gamma^{-1}\nabla V(X_t)\mathrm{d}t + \sqrt{2\beta^{-1}}\Gamma^{-\frac{1}{2}}\mathrm{d}W_t,$$

where $V : \mathbb{R}^d \to \mathbb{R}$ denotes the potential function, β is an inverse temperature parameter, i.e. $\beta = \frac{1}{k_B \mathcal{T}}$ with Boltzmann constant denoted by k_B and $\Gamma \in \mathbb{R}^{d\times d}$ is a diagonal matrix with friction coefficients on the diagonal.

In our example $d = 2$, we choose $\beta = 1.67$, $\Gamma = \mathbb{I}$ and the potential function is given by

$$\begin{aligned} V(x,y) = {} & 3e^{-x^2-\left(y-\frac{1}{3}\right)^2} - 3e^{-x^2-\left(y-\frac{5}{3}\right)^2} \\ & - 5e^{-(x-1)^2-y^2} - 5e^{-(x+1)^2-y^2} \\ & + \frac{1}{5}x^4 + \frac{1}{5}(y-\frac{1}{3})^4, \end{aligned} \tag{5.1}$$

on the state space $S = \{(x,y) \in \mathbb{R}^2 \ : \ -2 \le x \le 2,\ -1.5 \le y \le 2.5\}$. Figure 5.1 shows the graph of the potential function $V(x,y)$ which is also called the energy landscape. We employed reflective boundary conditions.

For the reactant and product state A' and B' we choose basins on the energy landscape containing minima of the potential function $(\pm 1, 0)$. In particular we choose $A' = \{(x,y) \in S \ : \ V(x,y) \le -3,\ x \le 0\}$ and $B' = \{(x,y) \in S \ : \ V(x,y) \le -3,\ x \ge 0\}$.

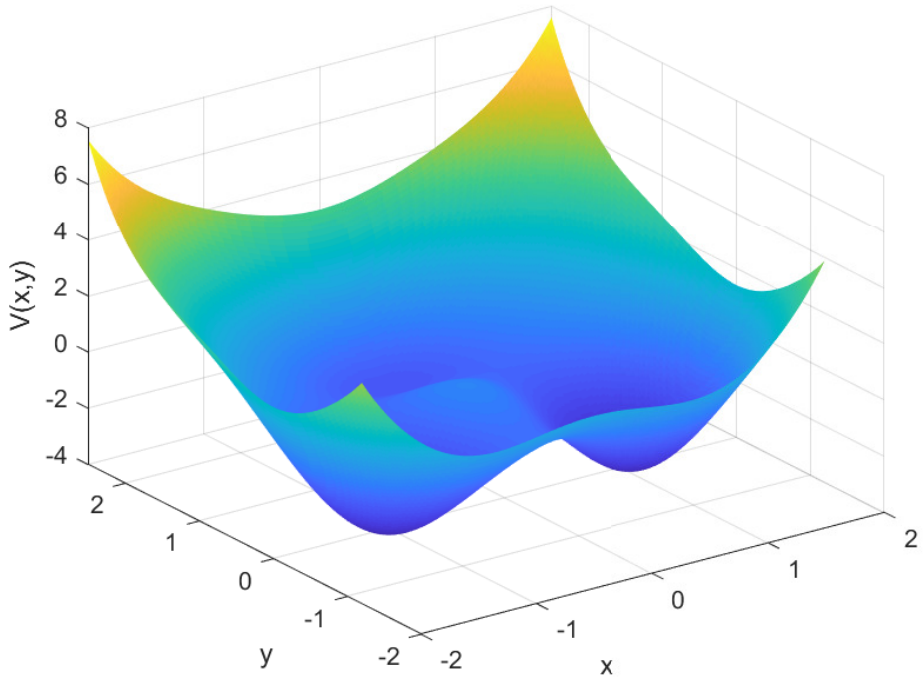


Figure 5.1: Potential function $V(x, y)$ given in (5.1) on S

We discretise the state space S by a uniform 20×20 mesh. The uniform mesh is a special case of a Voronoi tessellation, where each partition set is a square. For the chosen state space S, the partition sets $\{S_1, \ldots, S_{400}\}$ are squares with side length 0.2. We made the choice to use a uniform discretisation in order to be able to compare the results of our approach and the results of the transition path theory for Markov chains with the numerical solution obtained using the finite difference approach. The discrete reactant set A we obtain as a set of those partition sets for which at least one vertex of the partition set belongs to the set A'. Similarly, we define the discrete product set B to be the set of partition sets with at least one vertex belonging to B'. See Figure 5.2 for an illustration.

In order to obtain the committor and the probability current of our approach or the transition probabilty matrix of the Markov chain TPT we need to simulate the diffusion process on the continuous state space and project it to the discretised state space. We simulate the diffusion process using the Euler-Maruyama method with the time step $\Delta t = 0.001$.

5.1 Committor function

Our approach

In order to compute the discrete committor function $\tilde{q}$ of our approach, from each partition set S_i, $i \in \{1, \ldots, 400\}$ we sampled 10^4 trajectories. The initial condition of each trajectory

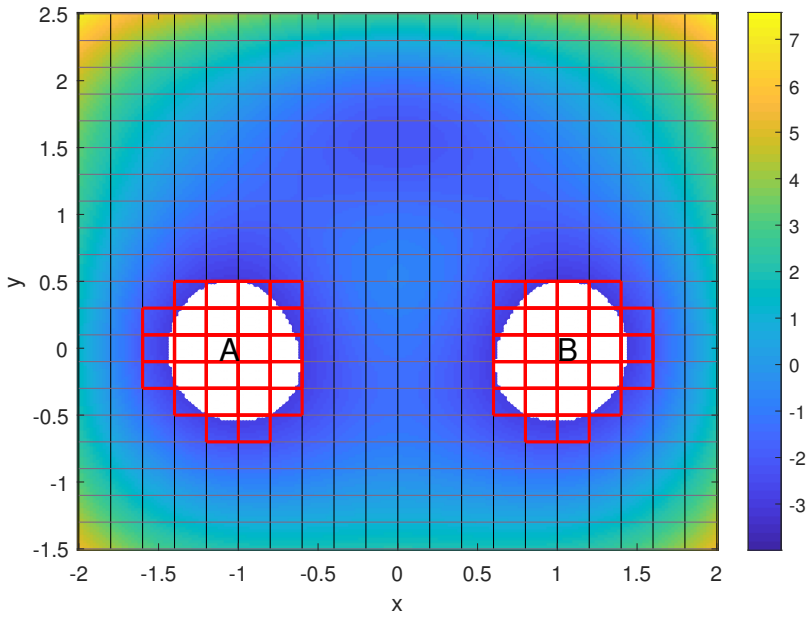


Figure 5.2: Colors correspond to the values of the potential function $V(x, y)$ as denoted in colourbar on the right. Continuous sets A' and B' are denoted in white. The 20×20 discretisation of the state space is shown. Partition sets that belong to the discrete sets A and B are outlined in red.

was drawn from the uniform distribution on S_i. We terminated each trajectory when it reached $A \cup B$, i.e. one of the sets A or B. Then we computed the discrete committor value on each of the partition sets as the relative frequency of trajectories that reach B.

Transition path theory for Markov chains

In order to obtain the transition probability matrix of the Markov chain, starting from each partition set S_i, $i \in \{1, \ldots, 400\}$ we simulated 2×10^5 short trajectories. The initial condition of each trajectory was drawn from the uniform distribution on S_i. Every short trajectory was ℓ time steps long, where the time step is $\Delta t = 0.001$. We compared the performance for the whole range of parameters $\ell \in [1, 200]$, meaning that we sampled the whole range of transition probability matrices, depending on the parameter ℓ by observing the state that the process reached after $\ell \Delta t$ time steps – the so called lag time. If a trajectory starting in S_i ended in a point in S_j for some $j \in \{1, \ldots, 400\}$, we considered this as a transition from S_i to S_j, regardless of the partition sets visited at intermediate time steps. By doing this for every partition set S_i we counted the transitions that occur between S_i and each of the remaining partition sets S_j, $j \neq i$. In this way we obtained the count matrix for the lag time $\tau = \ell \Delta t$[1]. We normalised the count matrix row-wise in order to obtain the row-stochastic matrix. The procedure that we used to obtain the transition probability matrix is summarised in Algorithm 1 with $\#cells := 400$, $\#iterations := 2 \times 10^5$

[1]The choice of lag time was suggested to be the one for which the implied timescales converge [42]. However, implied timescales do not converge in this example so we chose the whole range of lag time parameters τ. Selecting a large lag time parameter was advised in [42, 44].

and $\ell \in [1, 200]$.

input : zero matrix $C \in \mathbb{R}^{\#cells \times \#cells}$, parameter ℓ
output: transition probability matrix $\hat{P}$

for $i = 1 : \#cells$ **do**
  for $j = 1 : \#iterations$ **do**
    select a point $p \in S_i$ from the uniform distribution on S_i;
    simulate a trajectory T of length ℓ steps such that $T_0 = p$;
    find $j \in \{1, \ldots, 400\}$ such that $T_\ell \in S_j$;
    $C_{i,j} \longleftarrow C_{i,j} + 1$;
  end
end
$\hat{P} \longleftarrow$ row-wise normalised C

Algorithm 1: Estimates the transition probability matrix $\hat{P}$ of the Markov chain on the discretised state space for a given parameter ℓ denoting the length of sampled trajectories.

These matrices with parameter $\ell \in [1, 200]$ were used to obtain the range of committor functions $q^{MC}(\ell)$ of Markov chains using the PyEMMA package [45]. We compare the committor function of TPT for Markov chains with the discrete committor function obtained using our approach later in this section.

Numerical approximation using the finite differences method

Since we observe the two-dimensional Smoluchowski diffusion for which we know the stochastic differential equation, we can numerically estimate the committor function using the centred finite differences method. For this method we have used a finer discretisation of the state space with mesh width 0.05, however in order to compare these results with the committor function of our approach and with the committor function of TPT for Markov chains, we use only the values of the finite differences committor function on the coarser grid with mesh width 0.2, as we did in the other two cases. We denote this approximation by q^{FD} and we use it as ground truth against which we compare the committor function of our approach and that of TPT for Markov chains.

Results

In Figure 5.3 we compare the committor function of our approach $\tilde{q}$ and the committor functions of TPT for Markov chains $q^{MC}(\ell)$, for a range of parameters $\ell \in [1, 200]$, in L^2-norm to the ground truth q^{FD}. Since the committor function of our approach does not depend on the lag time parameter, the shown error is constant with respect to ℓ. As suggested in [42,44] the error of the committor function of TPT for Markov chains decreases as we increase the lag time parameter. The minimal error occurs at about $\ell = 95$, and any further increase in parameter ℓ yields the slight increase in the error. While sampling more than 10^4 trajectories starting from each partition set could decrease the error of the discrete committor function of our approach $\tilde{q}$, it is also costly. Therefore we observe that

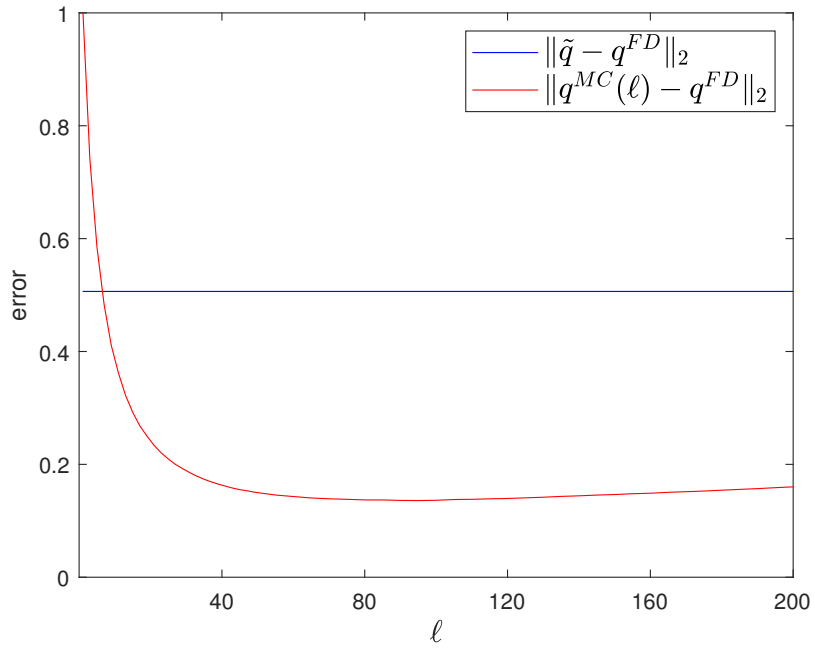


Figure 5.3: The error between the ground truth q^{FD} and the committor function of TPT for Markov chains ($q^{MC}(\ell)$) with lag time $\ell\Delta t$ shown in red and between the ground truth q^{FD} and the discrete committor function of our approach $\tilde{q}$ shown in blue.

for the right choice of the lag time parameter the committor function of TPT for Markov chains can approximate the ground truth better than our approach on this fixed partition.

5.2 Probability current

Our approach

In order to compute the discrete probability current of our approach we need to estimate the net flow of reactive trajectories. We estimate the net flow of reactive trajectories from 10^5 reactive trajectories that we sampled by generating one long trajectory with 5.1×10^9 steps starting from the point $(-1, 0)$ in S.

Recall that the net flow of reactive trajectories $\alpha_{j,k}$ for any two adjacent partition sets S_j, S_k is given in (4.30) by

$$\alpha_{jk} := \lim_{s\to 0^+} \frac{1}{s} \lim_{T\to\infty} \frac{1}{T} \int_{\mathcal{R}\cap[0,T]} \mathbf{1}_{S_j}(X_t)\, \mathbf{1}_{S_k}(X_{t+s}) - \mathbf{1}_{S_k}(X_t)\, \mathbf{1}_{S_j}(X_{t+s})\, \mathrm{d}t.$$

For any two adjacent partition sets S_j, S_k where $j, k \in \{1, \ldots, 400\}$ we compute the net flow of reactive trajectories $\alpha_{j,k}$ by

$$\alpha_{j,k} = \frac{1}{\#steps} \sum_{i=1}^{10^5} \left(\sum_{t=1}^{length(T^i)-1} \mathbf{1}_{S_j}(X_t)\mathbf{1}_{S_k}(X_{t+1}) - \mathbf{1}_{S_k}(X_t)\mathbf{1}_{S_j}(X_{t+1}) \right),$$

where $\#steps = 5.1 \times 10^9$, the first sum goes through all reactive trajectories and the second counts the net transitions between adjacent partition sets S_j and S_k that occur within the i-th reactive trajectory T^i.

Using the $\alpha_{j,k}$ that we obtain in this way, we obtain the discrete probability current $\tilde{J}_{R_i}$ for each of the partition sets S_i, $i \in \{1, \ldots, 400\}$ using normal equations (4.32). We repeat the normal equations here

$$N_i^\top N_i \tilde{J}_{R,i} = N_i^\top \hat{\alpha}_i \in \mathbb{R}^d, \tag{5.2}$$

where $N_i \in \mathbb{R}^{\#\mathcal{N}_i \times d}$ is a matrix for which the j-th row is an outer unit normal to the j-th facet of S_i, $\#\mathcal{N}_i$ is the number of adjacent partition sets to the partition set S_i, and $\hat{\alpha}_i$ is a vector in $\mathbb{R}^{\#\mathcal{N}_i}$ such that

$$(\hat{\alpha}_i)_k = \alpha_{i,k}/\sigma(\partial S_i \cap \partial S_k). \tag{5.3}$$

For every two adjacent partition sets S_i and S_k the surface measure $\sigma(\partial S_i \cap \partial S_k) = 0.2$, since in our discretisation each partition set is a square with side length 0.2.

The number $\#\mathcal{N}_i$ of partition sets adjacent to the partition set S_i depends on the position of the set in the state space. The partition set S_i whose boundaries lie in the interior of the state space S have four immediate neighbours. The matrix N_i of the unit normals is

$$N_i = \begin{bmatrix} -1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & -1 \end{bmatrix},$$

where the rows of matrix N_i viewed from top to bottom correspond to the left, right, top and bottom neighbours of the the partition set S_i. The partition sets whose one side is contained in the boundary of S have three immediate neighbours, and the unit normal corresponding to the side aligned with the boundary of S is omitted such that the corresponding matrix N_i has only three rows. The partition sets lying in the corners of S whose 2 sides align with the boundary of S have only two immediate neighbours and the corresponding matrix N_i has two rows. Note that regardless of the number of rows of the matrix N_i corresponding to the partition set S_i, (5.2) is a system of 2 linear equations with a solution $\tilde{J}_{R,i}$. The procedure for obtaining the discrete probability current that we just described is summarised in Algorithm 2.

input : partition, net flow estimate $\alpha_{j,k}$ for every two adjacent partition sets S_j, S_k
output: discrete probability current

for *every partition set* S_i **do**
  for *all neighbours* S_k *of* S_i **do**
    obtain outer unit normal to S_i on joint facet $S_k \cap S_i$;
    calculate $(\hat{\alpha}_i)_k$ using (5.3);
  end
  solve system of equations (5.2);
end

Algorithm 2: Obtains the discrete probability current from the estimates of the net flow between every two adjacent partition sets.

Transition path theory for Markov chains

As mentioned in Section 5.1, we obtained a whole range of transition probability matrices of the Markov chain, depending on the lag time parameter. We used these transition probability matrices to obtain the range of probability currents of Markov chains using the PyEMMA package. The probability current of Markov chains is a scalar valued function that to each pair of adjacent partition sets (S_j, S_k) assigns the net flow of reactive trajectories $f^+_{j,k}$ between those partition sets [36]. Using the normal equations (5.2) with $\alpha_{i,k}$ replaced by the net flow $f^+_{i,k}$ estimated using the TPT for Markov chains, we obtain the piecewise constant vector field J^{MC}_R, i.e. J^{MC}_R is obtained using Algorithm 2 with $\alpha_{i,k} := f^+_{i,k}$. We repeated this procedure for different values of parameter ℓ, obtaining the range of discrete probability currents $J^{MC}_R(\ell)$, for $\ell \in [1, 200]$. These vector fields we then compared to the discrete probability current $\tilde{J}_R$ that we obtained using our approach and the finite differences approximation of the probability current of the underlying diffusion process. We describe the procedure used to obtain the finite differences approximation below.

Numerical approximation using the finite differences method

As mentioned in Section 5.1, we can numerically estimate the committor function using the centred finite differences method, since in our example the stochastic differential equation is known and the problem is 2-dimensional. Using the same method we approximate the gradient of the committor function and compute the probability current using (3.16). The estimate of the probabilty current using finite differences on the grid of width 0.2 we denote by J^{FD}_R. For brevity we sometimes refer to the finite differences approximation of probability current J^{FD}_R as the ground truth.

Results

We compare the probability current of our approach $\tilde{J}_R$ with the discrete probability current of the transition path theory for Markov chains $J^{MC}_R(\ell)$ while we use the probability current obtained using the finite differences method J^{FD}_R as the ground truth. In Figures 5.4 and 5.5, we compare $J^{MC}_R(95)$ and $\tilde{J}_R$ to the ground truth J^{FD}_R respectively using the Matlab built-in function 'quiver'. In Figure 5.4 presented is the probability current of Markov chains computed using the lag time $\tau = 95\Delta t$ that corresponds to the minimal error of the committor function of TPT for Markov chains, which was shown in Figure 5.3. The lengths of vectors in Figures 5.4 and 5.5 are scaled such that they do not overlap, and therefore these two figures are intended to merely show that the directions of the probability current of transition path theory for Markov chains $J^{MC}_R(95)$ and the probability current of our approach $\tilde{J}_R$ do not differ drastically from the directions of the ground truth J^{FD}_R.

Notice the discrepancies that occur on the boundary of the set B between the probability current of TPT for Markov chains $J^{MC}_R(95)$ and the finite differences approximation of the probability current of TPT for diffusion processes J^{FD}_R. In particular, $J^{MC}_R(95)$ is zero on some cells close to the set B which one can recognise as a missing red arrow over the existing black arrow in Figure 5.4. This occurs because the implementation of TPT for Markov chains includes the cells into sets A and B depending on their committor values,

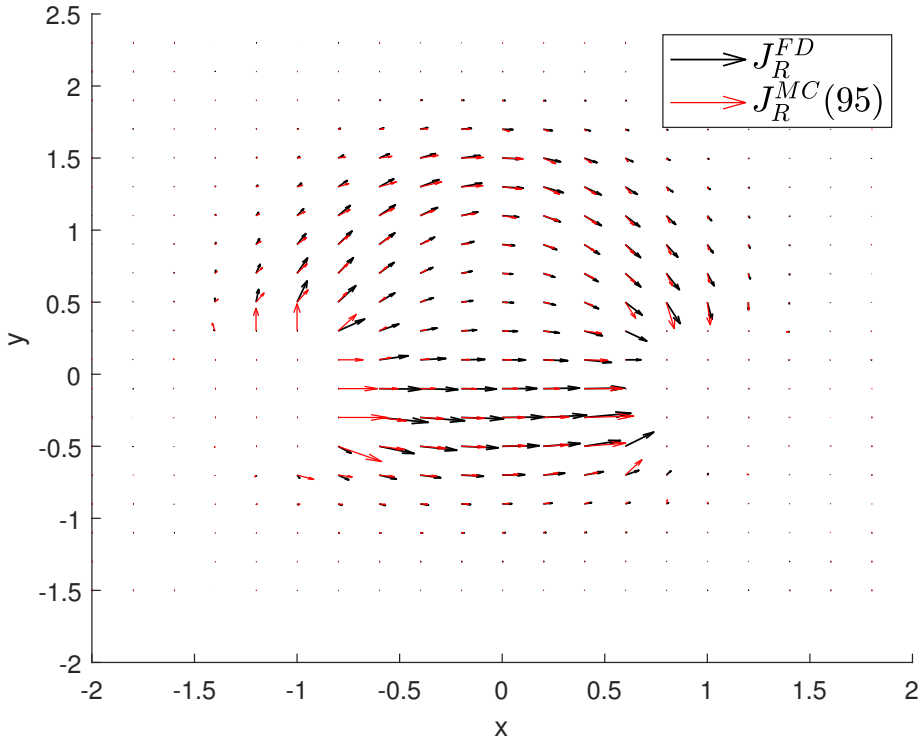


Figure 5.4: Velocity plot of the probability current for Markov chains ($J_R^{MC}(95)$) with lag time $\tau = 95\Delta t$ compared with the ground truth (J_R^{FD}).

i.e. if they are close to 0 or 1 respectively. We will therefore ignore the discrepancies in probability current that occur in these regions, as they result from the used implementation of TPT for Markov chains, and not the approach itself.

In order to closer investigate the discrepancies between $\tilde{J}_R$, $J_R^{MC}(\ell)$ and J_R^{FD}, we investigate separately the following two criteria: the angle alignment between the vectors of $\tilde{J}_R$, $J_R^{MC}(\ell)$ and J_R^{FD} and the discrepancies in the lengths of the vectors of the probability current between $\tilde{J}_R$, $J_R^{MC}(\ell)$ and J_R^{FD}. We first investigate the angle alignment between the directions of the vectors of the probability current regardless of their intensities. In Figure 5.6 we compare the angle alignment between the vectors of probability current obtained using the TPT for Markov chains and that of our approach with the ground truth on every partition set. The angle discrepancies in degrees are colour-coded; dark red corresponds to large angle discrepancies of 50° or more[2] and dark blue corresponds to almost perfect alignment, i.e. angle discrepancies of only a few degrees. We observe that the biggest discrepancies in angles for both of the approaches occur close to the boundary of the state space. This is to be expected in our approach, and can be explained by the statistical error. Namely, very few reactive trajectories populate these regions and therefore the obtained statistics is insufficient to describe the probability current of reactive trajectories. It is interesting to observe that the directions of $\tilde{J}_R$ on the partition sets

[2]In order to achieve better visibility of the discrepancies in the central part of the state space, we have thresholded the angles greater than 50°. The discrepancies greater than 50° are presented as the discrepancy of 50° degrees and depicted in dark red.

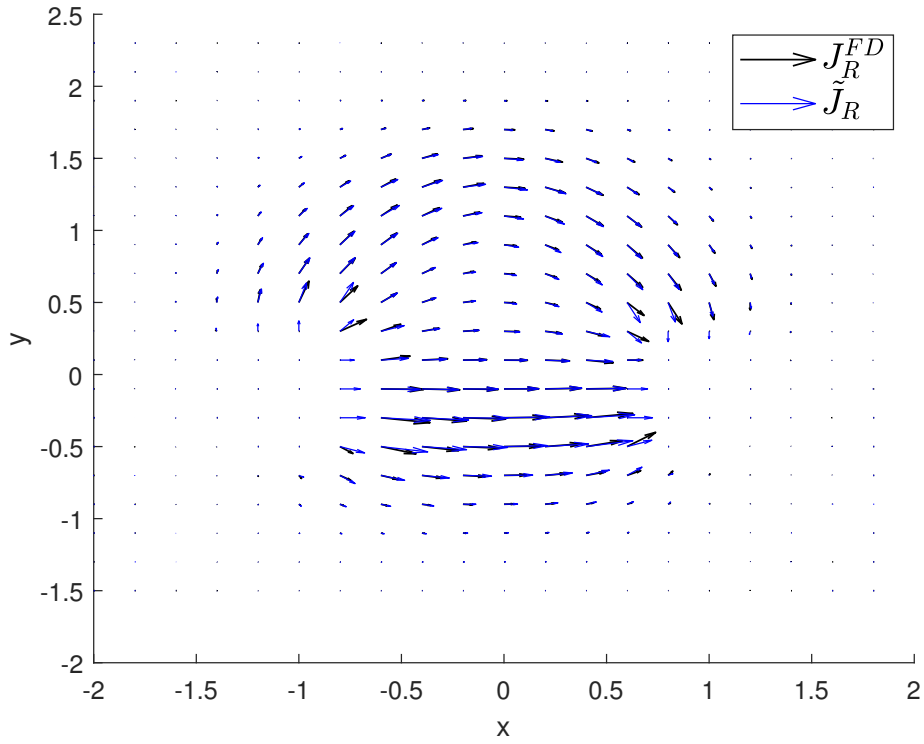


Figure 5.5: Velocity plot of the discrete probability current obtained using our approach ($\tilde{J}_R$) compared with the ground truth (J_R^{FD}).

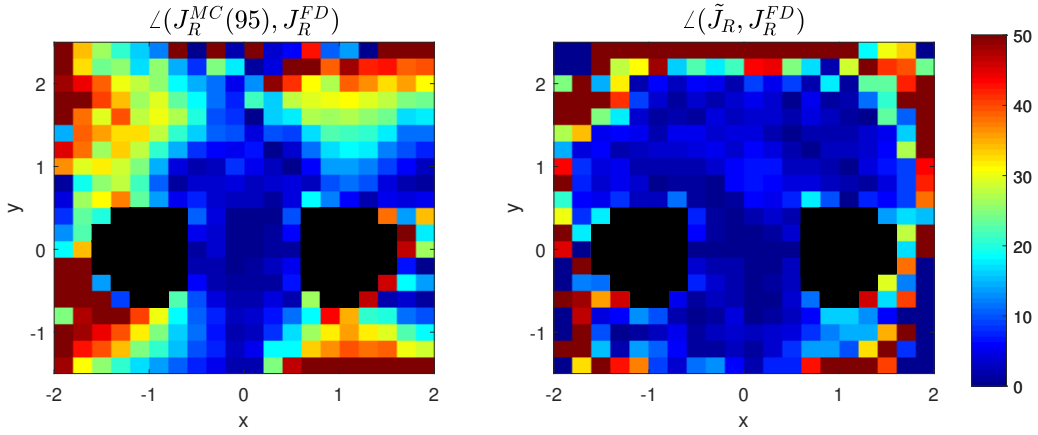


Figure 5.6: Angle discrepancies of the estimated probability current vectors. As shown in the colourbar, the dark red colour denotes the biggest difference amounting to angle discrepancies of 50° or more while the dark blue colour denotes the partition sets on which the angle discrepancy is low, i.e. the direction of the probability current is well approximated. Left: Discrepancies in angles between the probability current J_R^{MC} of Markov chains for lag time $\tau = 95\Delta t$ and the ground truth J_R^{FD}. Right: Angle discrepancies between the probability current $\tilde{J}_R$ obtained using our approach and the ground truth J_R^{FD}.

lying further away from the boundary of S align with the ground truth better than the directions of $J_R^{MC}(95)$. This corresponds to the larger dark blue area of the right figure figure showing angle discrepancies of $\tilde{J}_R$ compared to the figure in the left showing angle discrepancies of $J_R^{MC}(95)$. As before, we have used the lag time $\tau = 95\Delta t$ to obtain the transition probability matrix of the Markov chain. With a change in the lag time we noted no improvement in the pattern of the angle alignment between the probabilty current of TPT for Markov chains $J_R^{MC}(\ell)$ and the ground truth J_R^{FD}. However, increasing the lag time above $125\Delta t$ decreases the accuracy and angle discrepancies greater than 50° occur even in partition sets that are close to the centre of the state space.

We now investigate the second criterion - the approximation accuracy of the intensities of the vectors of J_R^{FD} by $\tilde{J}_R$ and $J_R^{MC}(\ell)$. Note that, even though the vectors of J_R^{FD} seem well approximated by the probability current of TPT for Markov chains, as shown in Figure 5.4, this is not the case because the presented vectors are rescaled. In particular, for all $\ell \in [1, 200]$ the intensities of vectors of the $J_R^{MC}(\ell)$ on any partition set are several orders of magnitude smaller than that of the J_R^{FD}.[3]

In order to be able to compare how well the relative intensities of the probability current calculated using the TPT for Markov chains and our approach approximate the relative intensities of the ground truth probability current we have scaled the length of vectors of probability current for all three approaches to lie in the unit interval $[0, 1]$. We denote the scaled probability currents by $J_R^{MC*}(\ell)$, J_R^{FD*}, and $\tilde{J}_R^*$ and analyse the

[3]This is not necessarily a problem for the following reason: The probability current of TPT for Markov chains is used to obtain the most probable paths using a recursive algorithm [36, Algorithm 2] which takes into account the relative intensities of the probability current only. The most probable path is found recursively as the path that has the maximal minimal flow among all other paths. Therefore, the scaling does not affect the relative transport conducted by each of the paths.

ratios $\left|J_R^{FD*}\right|_2 / \left|J_R^{MC*}(\ell)\right|_2$ and $\left|J_R^{FD*}\right|_2 / \left|\tilde{J}_R^*\right|_2$. Namely, if these ratios are close to 1, and differ only slightly and on the small number of partition sets, that would mean that the probability currents approximate the ground truth well. Values of ratio greater than 1, or smaller than 1 on the partition sets in $S \setminus (A \cup B)$ indicate the areas where the intensity of the rescaled probability current $J_R^{MC*}(\ell)$ or $\tilde{J}_R^*$ underestimates or overestimates the ground truth J_R^{FD*}, respectively. For better visibility, we have thresholded all the scaling factors greater than 2.5 and presented them as the ratio of 2.5.

In Figure 5.7 we present the ratio $\left|J_R^{FD*}\right|_2 / \left|J_R^{MC*}(\ell)\right|_2$ for the probability current of TPT for Markov chains computed for different values of lag time $\tau = \ell\Delta t$. The ratio is colour-coded according to the colourbar shown in the right of the figure. On the partition sets coloured in red and yellow the scaled probability current of transition path theory for Markov chains is underestimating the ground truth, while on the cells having a dark blue shade the probability current is overestimated. Ideally the entire figure should have the green-blue shade corresponding to 1 on the colourbar. Even though there was little effect of the change in the lag time parameter of the TPT for Markov chains when we compared the angle alignments between J_R^{FD} and $J_R^{MC}(\ell)$, the lag time parameter plays a more important role when comparing the intensities of the vectors J_R^{FD*} and $J_R^{MC*}(\ell)$. For the lag time $\tau = 15\Delta t$ a significant part of the upper and lower transition channel has the shade corresponding to the ratio value 1. For the same lag time the probability current in the regions close to the boundary of the state space are overestimated. We notice that by increasing the lag time, the region where the probability current is underestimated becomes larger. For the lag time $\tau = 95\Delta t$, which is the lag time for which the best approximation of the committor function is achieved, we observe that the probability current on the partition sets belonging to the lower transition channel is underestimated. This can be observed in Figure 5.4 as well, where the intensities of vectors corresponding to $J_R^{MC}(95)$ are smaller than the intensities of vectors corresponding to J_R^{FD}. According to Figure 5.7, smaller lag time, seems to yield better approximation of the probability current. This contradicts the behavior of the error of committor function that we observed in Figure 5.3 where increasing the lag time decreased the error. This unusual behavior occurs due to the fact that we used the net flow of reactive trajectories of TPT for Markov chains $f_{j,k}^+(\ell)$ in normal equations, to obtain the piecewise constant vector field $J_R^{MC}(\ell)$. However, as the lag time increases, the process is less likely to be found in the adjacent cells after ℓ time steps. Instead, the process spreads further, and therefore the flow of reactive trajectories to the immediate neighbours is not well presented by values of $f_{j,k}^+(\ell)$ for large ℓ.

In Figure 5.8 we compare the ratio between the rescaled probability current obtained using our approach $\tilde{J}_R^*$ and the rescaled ground truth probability current obtained using the finite differences approach J_R^{FD*}. We can see that the ratio on the central area of S is close to 1. This is a good sign, because this region contains the two transition channels. The accurate estimation on these channels is the most important for good prediction of the preferred transition paths. The probability current using our approach has the same problem of overestimating the length of the vectors close to the boundary of the state space. However, the overestimation is smaller than that of the TPT for Markov chains for $\ell = 15$. Namely, compare the shade of blue on the part of the state space close to the boundaries in Figures 5.8 and 5.7 for $\ell = 15$. Observe that the shade of blue is lighter in this region for Figure 5.8 compared to the shade of blue in this region for Figure 5.7. Furthermore,

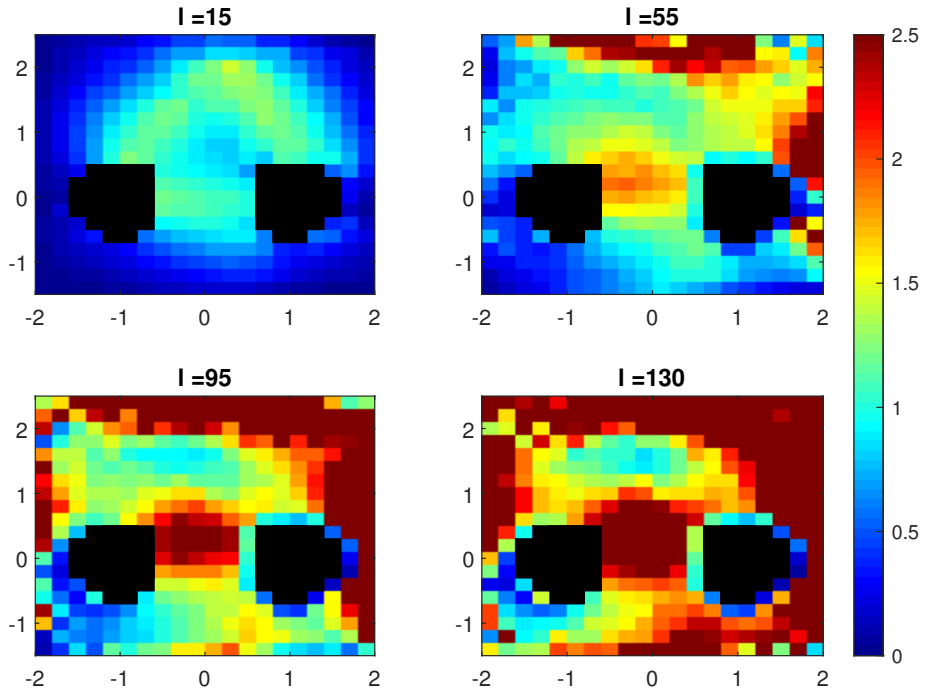


Figure 5.7: The value of ratio $\left|J_R^{FD*}\right|_2 / \left|J_R^{MC*}(\ell)\right|_2$ for $\ell \in \{15, 55, 95, 130\}$.

our approach does not underestimate the length of the probability current on the lower transition channel like TPT for Markov chains does for larger ℓ. Note however that in the area above and to the right side of the set B our approach systematically underestimates the true probability current. We believe this happens due to insufficient sampling. Namely, very few of the reactive trajectories actually populate these regions. Instead, the reactive trajectories get attracted to the minimum in the set B.

5.3 Streamlines

Finally, we use the obtained probability current for TPT for Markov chains $J_R^{MC}(\ell)$ and that that of our approach $\tilde{J}_R$ to show the corresponding streamlines.

In TPT for Markov chains usually the most probable paths are analysed instead of the streamlines. The most probable paths are obtained in a recursive procedure [36, Algoritm 2] using the net flow values $f_{j,k}^{+}(\ell)$. The most probable paths of TPT for Markov chains are ordered according to the flow that gets transported using each of them [36, Algoritm 2]. However, the most probable paths are sets, each consisting of partition sets that connect A and B. As such they do not show the exact location within a partition set but merely connect the neighbouring sets. On the other hand our discrete streamlines defined in (4.45) are piecewise linear functions whose relative position in a partition set depends on the point of entrance to the partition set. Therefore, the comparison of these two objects seems unfair, at least on the coarse discretisation mesh; we are not comparing the objects of the same type. Thus, we will compare the discrete streamlines obtained using the piecewise constant vector fields $J_R^{MC}(\ell)$ and $\tilde{J}_R$ with the discrete streamlines obtained using the finite

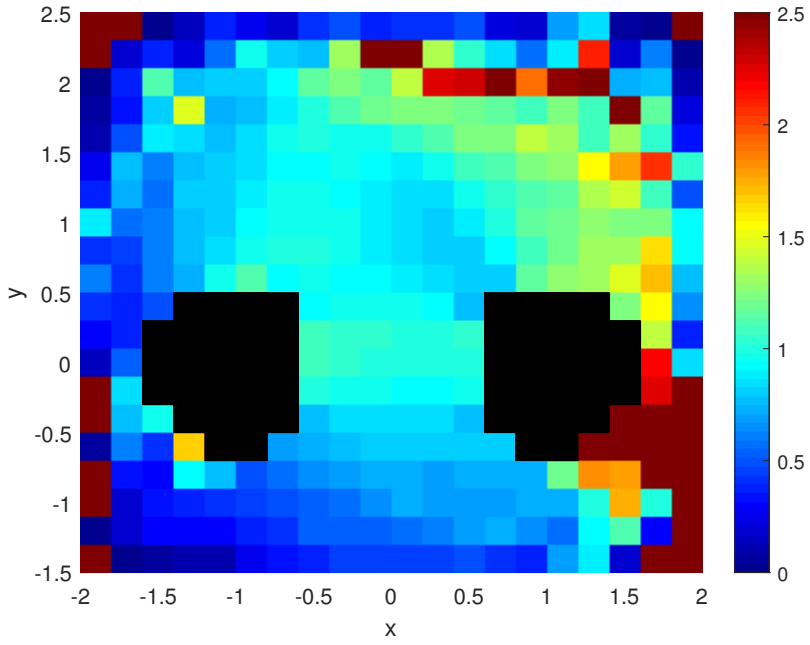


Figure 5.8: The value of ratio $\left|J_R^{FD*}\right|_2 / \left|\tilde{J}_R^*\right|_2$.

differences approximation J_R^{FD} of the probability current for diffusion processes TPT. We denote the respective streamlines by $s^{MC}(\ell)$, $\tilde{s}$ and s^{FD}. We show the results for two values of $\ell \in \{15, 95\}$ which were the two values that we determined to be optimal with respect to two different criteria – the error in the intensities of the probability current and the error of committor function respectively. The discrete streamlines we present are the integral lines of the corresponding discrete probability current.

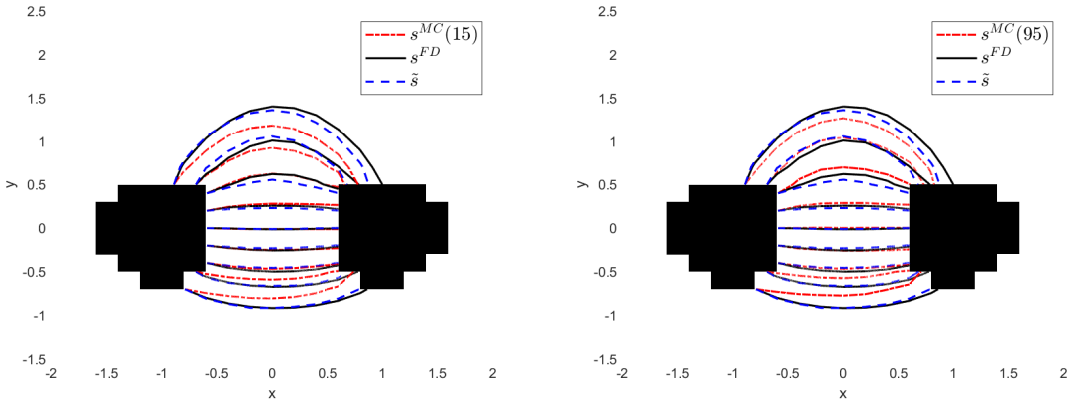
For each point on the boundary of the set A we obtain the streamline by following the discrete probabilty current until the set B is reached. We summarise this procedure in Algorithm 3.

input : a point p on the boundary of A; discrete probability current J, small time step t
output: streamline s starting at p

$s_{old} \longleftarrow p$;
$s \longleftarrow [s_{old}]$;
while $s_{old} \notin B$ **do**
  $s_{new} \longleftarrow s_{old} + J(s_{old})t$;
  $s \longleftarrow [s, s_{new}]$;
  $s_{old} \longleftarrow s_{new}$;
end

Algorithm 3: Obtains the discrete streamline corresponding to a given discrete probability current and a point on the boundary of A.

In order to be able to compare the streamlines $s^{MC}(\ell)$, $\tilde{s}$ and s^{FD} we started them



(a) $\ell = 15$ (b) $\ell = 95$

Figure 5.9: The discrete streamlines corresponding to $J_R^{MC}(\ell)$, $\tilde{J}_R$ and J_R^{FD}, denoted by $s^{MC}(\ell)$, $\tilde{s}$, s^{FD} respectively for two different values of ℓ.

from the same initial point on the boundary of A. Figure 5.9 compares the streamlines for the three discrete probability currents started from 9 points on ∂A for two values of ℓ. For the chosen discretisation mesh it is difficult to see if either $s^{MC}(\ell)$ or $\tilde{s}$ approximate the ground truth s^{FD} better than the other one in the region of the high barrier of the energy landscape, i.e. in the region located between the sets A and B. However, in the regions above and below the high barrier, through which the top two and bottom two groups of streamlines pass, the discrepancies between $s^{MC}(\ell)$ and s^{FD} are larger than the discrepancies between $\tilde{s}$ and s^{FD}, for both values of ℓ. In particular, the error accumulates over time. This is a characteristic of Algorithm 3 for obtaining the streamlines. However, for our approach we have proven the upper bound on the discrepancy at any point, and as the mesh size decreases, so does the error. Contrarily, this has not been proven for the TPT approach for Markov Chains.

In the example presented above we observe that for the right choice of the lag time parameter the error of the discrete committor function of TPT for Markov chains is smaller than the error of the discrete committor function of our approach when compared to the committor function of TPT for diffusion processes. We have not tested if the performace of our approach would improve compared to that of the TPT for Markov chains on the meshes of finer width. We observe that the vectors of the discrete probability current obtained using TPT for Markov chains and the discrete probability current obtained using our approach approximate the probability current of the underlying diffusion process well. In particular, we compared the angle discrepancies between either of these two approaches and the ground truth as well as the intensities of the vectors of the respective probability currents. The intensities of the vectors of the discrete probability currents obtained by TPT for Markov chains and our approach differ by several orders of magnitude from the ground truth and therefore the results we show are qualitative rather than quantitative. This extends to the experiments involving the streamlines as well, because the streamlines are defined using the probability current. For quantitative results one would need to understand the source of the difference in scaling and perform the experiments on the

meshes of decreasing width. However, we believe that the presented experiments show the potential of our approach to approximate the ground truth in a more principled way compared to the results of the TPT for Markov chains obtained with roughly the same amount of data. This is because our approach does not depend on the choice of the lag time parameter.

Our experiments also show a drawback which results from the statistical nature of our approach and is not explicitly accounted for in the error bounds given in Chapter 4. Namely, in Section 4.5 we assume that the net flow of reactive trajectories is given. Since in practice we need to estimate the net flow of reactive trajectories by sampling the reactive trajectories, the accuracy on each discretisation set depends on the number of reactive trajectories going through that set. Since the reactive trajectories populate some regions very rarely, the statistics may be insufficient for accurate estimates.

Chapter 6

Conclusion

We aimed to develop an approach to analyse the statistics of a diffusion process on a bounded state space. In particular, for given two disjoint subsets A and B of the state space we aimed to describe the most probable path the diffusion process takes when going from set A to set B. This is exactly the same problem that transition path theory for diffusion processes was formulated to solve, with one key difference. Namely, we were motivated by applications where one can observe a diffusion process but the corresponding stochastic differential equation is either not available, or the state space is high dimensional and applying the transition path theory for diffusion processes is computationally difficult. The transition path theory for Markov jump processes (or for Markov chains) has been suggested for this purpose, however, we notice two drawbacks of using the transition path theory for Markov jump processes or Markov chains when aiming to describe the dynamics of the underlying diffusion process. First, the jump process that is obtained by projecting the diffusion process onto a discretised state space is not a Markov jump process, and second, there are no proofs that guarantee that in the limit of the partition width approaching zero that the results of the transition path theory for Markov jump processes approaches the results of transition path theory for diffusion processes. As in the applications one is interested in how well the results of any approach approximate the ground truth, we set out to develop a numerical approach that is proven to provide increasingly accurate approximations of the underlying diffusion process, in an appropriate limit.

We achieved this by defining some discrete transition path theory objects on Voronoi tessellations: the discrete forward committor, discrete isocommittor surfaces, the discrete probability current and discrete streamlines. These discrete objects are piecewise constant functions on the interiors of Voronoi cells that preserve certain key properties of the corresponding continuous objects of the transition path theory for diffusion processes. The discrete committor function, probability current and the discrete streamlines converge to their continuous couterparts, as we have shown in Section 4. Moreover, we have proven error bounds for the three objects. The convergence of all three objects is linear in the width of the partition, i.e. in the diameter of the largest partition set in the tessellation. To the best of our knowledge, this is the first discrete approach for computation of the transition path theory objects that provably converges to the continuous objects of transition path theory for diffusion processes.

Our approach is data driven and does not impose any additional assumptions on the model. In particular, unlike the existing approaches for the discrete transition path theory

[36] it does not assume the Markovianity of the jump process. Instead, we observe a non-Markovian jump process that occurs by projection of a diffusion process to the discrete state space. Furthermore, the definitions of the discrete objects we introduced do not require the estimation or a priori knowledge of the drift or diffusion coefficients of the stochastic differential equation that defines the underlying diffusion process. Therefore the definitions that we introduced can be applied to a wider spectrum of processes. However, the convergence results that we showed hold only for diffusion processes.

The assumptions we use are fairly general. They include the global Lipschitz continuity of the committor function as well as the global Lipschitz continuity of the probability current of the transition path theory for diffusion processes. For convergence of the discrete probability current we make additional assumptions on the shape of the discrete partition sets. In particular, we assume that the number of neighbors of each partition set is bounded by a constant independently of the number of sets in the partition. Furthermore, we assume that all the partition sets in the partition retain the dimension of the state space, regardless of the partition width and number of cells in the partition. This assumption is motivated by a linear algebra result given in Theorem 4.4.5 which gives a relationship between the shape of the polytope and the smallest singular value of the matrix of the corresponding system of linear inequalities. We believe that this result is interesting in its own right.

Critique and future work

In our future work we would aim to weaken the assumptions. The first assumptions that we would seek to weaken would be the assumptions of global Lipschitz continuity of the committor function and of the probability current. Furthermore, we suspect that Assumption 4.5.4 is implied by Assumption 4.5.5, because if the partition sets behave nicely enough, and shrink uniformly in all directions as the partition width decreases, then the number of neighbors of each cell should stay unchanged and therefore bounded. We aim to prove this in future work.

Several open questions remain. The construction of the partition with partition sets satisfying Assumptions 4.5.4 and 4.5.5 is one of them. We believe that one solution is given by centroidal Voronoi tessellations [13] whose generators are the centres of the mass of corresponding Voronoi cells. We will investigate this in future, as finding methods for constructing suitable partitions will improve the applicability of our approach.

Another open question is the extension of our theory to include reaction rates. Recall that the reaction rate for the transition path theory for diffusion processes is defined as the integral of the probability current over any dividing surface (3.12). Naturally, we would observe a flow of reactive trajectories over some discrete dividing surface composed by a set of Voronoi cells. The problem arises when trying to approximate some dividing surface using a sequence of discrete dividing surfaces. If the discrete dividing surface converges to a continuous dividing surface of co-dimension 1, the convergence of the reaction rate should follow. However, the convergence of the surfaces is not a trivial matter. In particular, surface area cannot be defined as the limit of the area of inscribed polygonal surfaces in general. This was shown by Schwarz and Peano independently and is known as Schwarz's example or paradox [8,60]. Therefore, we would first have to ensure that using the partition sets described in this thesis we do not encounter this paradox.

On the one hand, when compared to transition path theory for diffusion processes our

approach might seem more applicable, as it does not require the knowledge of diffusion coefficients of the underlying diffusion process. On the other hand, when the diffusion coefficients are known, and the process is high dimensional our approach is not necessarily computationally more efficient than transition path theory for diffusion processes. We replaced the problem of solving the high dimensional backward Kolmogorov equation by the problem of computation of the facets of all the cells in the Voronoi partition. This is not easy in high dimension, as every d-dimensional polytope has at least $d+1$ facets. However, one could reduce the dimension of the state space if some prior knowledge of the system is available. In particular, if one has knowledge of the reaction coordinates which characterize the conformations of the system corresponding to some metastable states of the dynamics, one could observe the process in the lower dimensional space spanned by these coordinates, instead of the original state space. Once the dimensions is reduced, one could perform our approach on this reduced space.

Another weakness of our approach is that the constant in the error bound of the discrete probability current given in Proposition 4.5.6 depends on the dimension of the state space. Consequently the error bounds of the discrete streamlines given in Theorem 4.6.4 and Corollary 4.6.5 depend on the dimension of the state space as well. The dependence of the constant in the error bound on the dimension of the state space is problematic in the case of high-dimensional systems that often occur in the applications. While the convergence is still linear with respect to the diameter of the largest partition set, finer discretisations are required for higher dimensional state spaces than for lower-dimensionoal state spaces in order to achieve a certain approximation error, thus inducing higher computational costs. We aim to address this problem in our future work.

By being data-driven, the performance of our approach in estimating the objects of transition path theory for diffusion processes improves as the amount of data increases. However, this is at the same time the main weakness of our approach, because for computing the streamlines, we need to sample reactive trajectories, which is costly in the case of rare events. Future work would be to adapt our approach to work without the need for sampling reactive trajectories. We believe that this can be achieved by combining our definition for the discrete committor function given in Section 4.2 with the method presented in [31] for generating reactive trajectories of diffusion processes when the committor function is known. An alternative approach that could avoid sampling reactive trajectories is to define the streamlines using the discrete committor function or the discrete isocommittor surfaces. In particular, the presented definitions of the committor function and the isocommittor surfaces and the corresponding convergence result for the committor function are independent from the results concerning the probability current and the corresponding streamlines, i.e. our definition of the discrete probability current does not involve the committor function. However, note that, since the gradient of a function is orthogonal to its level sets, streamlines corresponding to the probability current (3.16) are orthogonal to the isocommittor surfaces for Smoluchowski diffusion in the case when all friction coefficients are equal. One could therefore try to generalise this property and define the discrete streamlines as sequences of cells that are orthogonal to each isocommittor surface they cross. This approach has already been exploited in [58] where isocommittor surfaces are used as reaction coordinates. However, our discrete isocommittor surfaces are not surfaces in mathematical sense and therefore it is not straightforward how to use them as reaction coordinates, because it is unclear how to define the orthogonality of a sequence of cells to

the discrete isocommittor surface.

Even if we managed to avoid sampling reactive trajectories, the problem of computing the discrete committor function still requires sampling of the process in order to estimate the conditional probabilities of reaching the set B before the set A when starting from a given state outside A and B. Therefore, an even more interesting open question is to develop a discrete transition path theory that uses short trajectories only, or no trajectory data. An approach for estimating the infinitesimal generator of a diffusion process without trajectory sampling which relies on the knowledge of the underlying stochastic differential equation is presented in [18]. Alternatively, the square root approximation approach [29] obtains the transition rate matrix of the Markov chain without sampling trajectories. Recently, the transition rate matrix obtained using the square root approximation was proven to converge in some sense to the infinitesimal generator of a diffusion process [12,20]. Combining the square root approximation approach [29] or the infinitesimal generator approach for estimating the long term behavior [18] with ours would improve the applicability of our approach by avoiding the sampling of trajectories. Additionally, the square root approximation approach does not suffer from the curse of dimensionality. Namely, the approach uses the Voronoi tessellation to partition the state space, but does not require computation of the vertices or facets of Voronoi cells; it solely uses the information on the adjacency of the cells. Since in our approach we used the Voronoi tessellation to discretise the space and compute the discrete objects on it, our approach is inherently meshless and therefore has the potential to alleviate the curse of dimensionality which often occurs in approaches that use regular grids. However, our approach requires the computation of the facets of Voronoi cells in order to obtain the probability current. This makes the computational cost of our approach scale poorly with the dimension of the problem. Therefore, the computational aspects of our approach could be improved by combining it with the square root approximation approach. This will be part of our future work.

Appendix A

Divergence-free property of the probability current

In this section we show that probability current J_R [32], defined in Section 3.4 is divergence-free. The statement is proven in Theorem A.0.6 and it is preceded with technical Lemmas which we use for its proof.

First, let us introduce a shorhand notation $A : B$ for the Frobenius inner product of two matrices A and B of the same dimensions, i.e.

$$A : B := \sum_{i,j} a_{ij} b_{ij}.$$

Using this notation we can express the generator $\mathcal{A}$ given in (3.4) as

$$\mathcal{A}\psi = b \cdot \nabla\psi + \frac{1}{2} A : \nabla\nabla\psi, \tag{A.1}$$

where ∇ denotes the gradient and $\nabla\nabla$ the Hessian operator. Similarly, the generator of the reversed process given in (2.23) can be expressed by

$$\mathcal{A}^r\psi = -b \cdot \nabla\psi + \frac{1}{m}\mathrm{div}(A\rho) \cdot \nabla\psi + \frac{1}{2} A : \nabla\nabla\psi,$$

where ρ denotes the equilibrium probability density of the diffusion process corresponding to $\mathcal{A}$. Recall that the forward committor function solves the equation

$$\mathcal{A}q = 0, \tag{A.2}$$

while the backward committor function solves the equation

$$\mathcal{A}^r q_b = 0. \tag{A.3}$$

Let $M : \mathbb{R}^d \to \mathbb{R}^{d\times d}$ denote a matrix-valued function with (i,j)-th entry m_{ij} for $1 \le i, j \le d$. Divergence of the matrix valued function M is a d-dimensional vector with components

$$\left(\mathrm{div}(M)(x)\right)_i = \sum_{j=1}^{d} \frac{\partial m_{ij}(x)}{\partial x_j}. \tag{A.4}$$

Given a vector-valued function $V : \mathbb{R}^d \to \mathbb{R}^d$ its divergence is defined in the usual way:

$$\operatorname{div}(V) = \nabla \cdot V = \sum_{i=1}^{d} \frac{\partial V_i(x)}{\partial x_i}. \tag{A.5}$$

This yields the following identity. For a matrix-valued function $M : \mathbb{R}^d \to \mathbb{R}^{d\times d}$ and a scalar-valued function $h : \mathbb{R}^d \to \mathbb{R}$,

$$\operatorname{div}(\operatorname{div}(Mh)) = \sum_{i,j} \frac{\partial^2 (m_{ij}(x)h(x))}{\partial x_i \partial x_j} = E : \nabla\nabla(Mh),$$

where $E \in \mathbb{R}^{d\times d}$ with all elements equal to 1, i.e. $e_{ij} = 1$ for all $i, j \in \{1, \dots, n\}$.

According to equation (2.18), adjoint operator of generator is given by

$$\begin{aligned}\mathcal{A}^*\psi &= \frac{1}{2}\sum_{i,j=1}^{d} \frac{\partial^2 (a_{ij}(t,x)\psi)}{\partial x_i \partial x_j} - \sum_{i=1}^{d} \frac{\partial \left(b_i(t,x)\psi\right)}{\partial x_i} \\ &= \frac{1}{2} E : \nabla\nabla(A\psi) - \nabla \cdot (b\psi).\end{aligned}$$

Notice that by (A.4) and (A.5) $\mathcal{A}^*$ is a divergence-form operator, i.e.

$$\begin{aligned}\mathcal{A}^*\psi &= \sum_{i=1}^{d} \frac{\partial}{\partial x_i}\left(\frac{1}{2}\sum_{j=1}^{d} \frac{\partial (a_{ij}\psi)}{\partial x_j} - b_i\psi\right) \\ &= \operatorname{div}(\frac{1}{2}\operatorname{div}(A\psi) - b\psi).\end{aligned} \tag{A.6}$$

Recall that for the unique equilibrium density ρ of the diffusion process corresponding to generator $\mathcal{A}$ we have

$$\mathcal{A}^*\rho = 0. \tag{A.7}$$

Let V as before, be a vector-valued function and let f, g be scalar-valued functions. By applying the definition of the divergence of a vector valued function given in (A.5) and the product rule we have

$$\operatorname{div}(Vfg) = g\ \operatorname{div}(Vf) + Vf \cdot \nabla g. \tag{A.8}$$

Lemma A.0.1. *Let $M \in C^1(\mathbb{R}^d; \mathbb{R}^{d\times d})$ be such that $m_{ij}(x) = m_{ji}(x)$ for all $x \in \mathbb{R}^d$ and all $i, j \in \{1, \dots, d\}$ and let $f, g \in C^1(\mathbb{R}^d; \mathbb{R})$ be arbitrary. Then*

$$\operatorname{div}(\operatorname{div}(Mfg)) = g\ \operatorname{div}(\operatorname{div}(Mf)) + 2\ \operatorname{div}(Mf) \cdot \nabla g + fM : \nabla\nabla g.$$

Proof. Observe first that

$$\begin{aligned}(\operatorname{div}(Mfg))_i &= \sum_{j=1}^{d} \frac{\partial \left(m_{ij}(x)f(x)g(x)\right)}{\partial x_j} \\ &= \sum_{j=1}^{d} g(x)\frac{\partial (m_{ij}(x)f(x))}{\partial x_j} + \sum_{j=1}^{d} m_{ij}(x)f(x)\frac{\partial g(x)}{\partial x_j} \\ &= g(\operatorname{div}(Mf))_i + \nabla g \cdot m_i f,\end{aligned}$$

where $m_i^\top = (m_i(x))^\top$ denotes the i-th row of matrix $M(x)$. This follows by using the definition of the divergence of the matrix valued function (A.4) to obtain the first and the third equality and the product rule to obtain the second equality. Using the previous equation, the definition of divergence of a vector valued function (A.5) and the product rule yields

$$\begin{aligned}\operatorname{div}(\operatorname{div}(Mfg)) &= \sum_{i=1}^{d} \frac{\partial \left[g(\operatorname{div}(Mf))_i + \nabla g \cdot m_i f\right]}{\partial x_i} \\ &= \sum_{i=1}^{d} \left[\frac{\partial g}{\partial x_i}(\operatorname{div}(Mf))_i + g\frac{\partial(\operatorname{div}(Mf)_i)}{\partial x_i} + \frac{\partial}{\partial x_i}\left(\nabla g \cdot m_i f\right)\right].\end{aligned} \tag{A.9}$$

The second term of (A.9) can be written as

$$\sum_{i=1}^{d} g\frac{\partial(\operatorname{div}(Mf)_i)}{\partial x_i} = g\sum_{i=1}^{d}\frac{\partial}{\partial x_i}\sum_{j=1}^{d}\frac{\partial(m_{ij}(x)f(x))}{x_j} = g\ \operatorname{div}(\operatorname{div}(Mf)), \tag{A.10}$$

where we used the definition of the divergence of the matrix valued function (A.4). The third summand of (A.9) can be expressed as

$$\begin{aligned}\sum_{i=1}^{d}\frac{\partial}{\partial x_i}\left(\nabla g \cdot m_i f\right) &= \sum_{i=1}^{d}\frac{\partial}{\partial x_i}\left(\sum_{j=1}^{d}\frac{\partial g}{\partial x_j}m_{ij}f\right) = \sum_{i,j=1}^{d}\frac{\partial}{\partial x_i}\left(\frac{\partial g}{\partial x_j}m_{ij}f\right) \\ &= \sum_{i,j=1}^{d}\frac{\partial^2 g}{\partial x_i x_j}m_{ij}f + \sum_{i,j=1}^{d}\frac{\partial g}{\partial x_j}\frac{\partial(m_{ij}f)}{\partial x_i} \\ &= fM : \nabla\nabla g + \sum_{j=1}^{d}\frac{\partial g}{\partial x_j}\sum_{i=1}^{d}\frac{\partial(m_{ji})f}{\partial x_i} \\ &= fM : \nabla\nabla g + \nabla g \cdot \operatorname{div}(Mf),\end{aligned} \tag{A.11}$$

where we used the product rule to obtain the third equality, the fact that M is symmetric in the fourth and (A.5) in the last equality. By substituting equations (A.10) and (A.11) into (A.9) we obtain

$$\operatorname{div}(\operatorname{div}(Mfg)) = \nabla g \cdot \operatorname{div}(Mf) + g\operatorname{div}(\operatorname{div}(Mf)) + fM : \nabla\nabla g + \nabla g \cdot \operatorname{div}(Mf)$$

which completes the proof. □

Let J be a vector valued function $J : \mathbb{R}^d \to \mathbb{R}^d$ defined by

$$J = b\rho q_b - \operatorname{div}(\frac{1}{2}A\rho q_b), \tag{A.12}$$

where $A : \mathbb{R}^d \to \mathbb{R}^{d\times d}$ and $b : \mathbb{R}^d \to \mathbb{R}^d$ are the diffusion coefficients corresponding to the generator $\mathcal{A}$ and ρ is its equilibrium density.

Corollary A.0.2. *It holds that*

$$\operatorname{div}(J) = q_b(-\mathcal{A}^*\rho) + \rho(-\mathcal{A}^r q_b) = 0,$$

i.e. J is a divergence-free vector field.

Proof. Since divergence $\mathrm{div}(\cdot)$ is a liner operator, applying $\mathrm{div}(\cdot)$ individually to the terms of (A.12), using Lemma A.0.1 with $M = A$, $V = b$, $f = m$ and $g = q_b$, (A.8), (A.6) yields

$$\begin{aligned}
\mathrm{div}(J) &= \mathrm{div}(b\rho q_b) - \frac{1}{2}\mathrm{div}(\mathrm{div}(A\rho q_b)) \\
&= \mathrm{div}(b\rho q_b) - \frac{1}{2}\left[q_b \mathrm{div}(\mathrm{div}(A\rho)) + 2\mathrm{div}(A\rho)\cdot\nabla q_b + \rho A : \nabla\nabla q_b\right] \\
&= q_b \mathrm{div}(b\rho) + b\rho\cdot\nabla q_b - \frac{1}{2}\left[q_b \mathrm{div}(\mathrm{div}(A\rho)) + 2\mathrm{div}(A\rho)\cdot\nabla q_b + \rho A : \nabla\nabla q_b\right] \\
&= q_b\left(-\mathcal{A}^*\rho\right) + b\rho\cdot\nabla q_b - \mathrm{div}(A\rho)\cdot\nabla q_b - \frac{1}{2}\rho A : \nabla\nabla q_b \\
&= q_b(-\mathcal{A}^*\rho) + \rho\left(b\cdot\nabla q_b - \frac{1}{\rho}\mathrm{div}(A\rho)\cdot\nabla q_b - \frac{1}{2}A : \nabla\nabla q_b\right) \\
&= q_b(-\mathcal{A}^*\rho) + \rho(-\mathcal{A}^r q_b) = 0
\end{aligned}$$

where the last equality follows from (A.7) and (A.3). □

Remark A.0.3. *By Proposition 5 of [14], J in equation* (A.12) *is equivalent to the probability current of [14] given in 3.11. Therefore, by Corollary A.0.2, the probability current of [14] is divergence-free.*

Lemma A.0.4. *Let $M \in C^1(\mathbb{R}^d;\mathbb{R}^{d\times d})$ be such that $m_{ij}(x) = m_{ji}(x)$ for all $x \in \mathbb{R}^d$ and all $i, j \in \{1,\dots,d\}$ and let $f, g \in C^1(\mathbb{R}^d;\mathbb{R})$. Then*

$$\mathrm{div}(fM\nabla g) = \nabla g\cdot\mathrm{div}(fM) + fM : \nabla\nabla g.$$

Proof. By product rule we have

$$\begin{aligned}
\mathrm{div}(fM\nabla g) &= \sum_{i=1}^{d}\frac{\partial\left(fM\nabla g\right)_i}{\partial x_i} = \sum_{i=1}^{d}\frac{\partial}{\partial x_i}\left(f\sum_{j=1}^{d} m_{ij}\frac{\partial g}{\partial x_j}\right) \\
&= \sum_{i=1}^{d}\left(\frac{\partial f}{\partial x_i}\sum_{j=1}^{d} m_{ij}\frac{\partial g}{\partial x_j} + f\sum_{j=1}^{d}\frac{\partial}{\partial x_i}\left(m_{ij}\frac{\partial g}{\partial x_j}\right)\right) \\
&= \sum_{i=1}^{d}\left(\frac{\partial f}{\partial x_i}\sum_{j=1}^{d} m_{ij}\frac{\partial g}{\partial x_j} + f\sum_{j=1}^{d}\frac{\partial m_{ij}}{\partial x_i}\frac{\partial g}{\partial x_j} + f\sum_{j=1}^{d} m_{ij}\frac{\partial^2 g}{\partial x_i\partial x_j}\right) \\
&= \sum_{j=1}^{d}\frac{\partial g}{\partial x_j}\sum_{i=1}^{d}\frac{\partial\left(fm_{ij}\right)}{\partial x_i} + fM : \nabla\nabla g = \nabla g\cdot\mathrm{div}(fM) + fM : \nabla\nabla g.
\end{aligned}$$

□

Lemma A.0.5. *Let $M \in C^1(\mathbb{R}^d;\mathbb{R}^{d\times d})$ be such that $m_{ij}(x) = m_{ji}(x)$ for all $x \in \mathbb{R}^d$ and all $i, j \in \{1,\dots,d\}$ and let $f_1, f_2, h \in C^1(\mathbb{R}^d;\mathbb{R})$. Then*

$$\begin{aligned}
\mathrm{div}(f_1 hM\nabla f_2) - \mathrm{div}(f_2 hM\nabla f_1) &= \mathrm{div}(hM)\cdot(f_1\nabla f_2 - f_2\nabla f_1) \\
&\quad + hf_1 M : \nabla\nabla f_2 - hf_2 M : \nabla\nabla f_1.
\end{aligned} \tag{A.13}$$

Proof. Applying (A.8) for $V = M\nabla f_2$, $f = h$ and $g = f_1$ we have

$$\mathrm{div}(hf_1M\nabla f_2) = f_1\mathrm{div}(hM\nabla f_2) + hM\nabla f_2 \cdot \nabla f_1.$$

Using the previous equation and Lemma A.0.4 it follows that

$$\mathrm{div}(hf_1M\nabla f_2) = f_1\left(\nabla f_2 \cdot \mathrm{div}(hM) + hM : \nabla\nabla f_2\right) + hM\nabla f_2 \cdot \nabla f_1.$$

Since the last term is symmetric with respect to f_1 and f_2, it cancels out when taking the difference on the left-hand side of (A.13).

$$\begin{aligned}\mathrm{div}(f_1hM\nabla f_2) - \mathrm{div}(f_2hM\nabla f_1) = f_1(\nabla f_2 \cdot \mathrm{div}(hM) + hM : \nabla\nabla f_2)\\ - f_2(\nabla f_1 \cdot \mathrm{div}(hM) + hM : \nabla\nabla f_1).\end{aligned}$$

Collecting the remaining terms yields the desired conclusion. □

In the following theorem we show that the probability current J_R defined in (3.10) is divergence-free.

Theorem A.0.6. *Let J_R be defined as in* (3.10)*, then*

$$\mathrm{div}(J_R) = q\mathrm{div}(J) + q_b\rho\mathcal{A}q = 0.$$

Proof. According to Theorem 3.4.1, the probability current (3.10) can be expressed in vector form

$$J_R = qq_bK + \frac{1}{2}q_b\rho A\nabla q - \frac{1}{2}q\rho A\nabla q_b,$$

where

$$K = b\rho - \frac{1}{2}\,\mathrm{div}(A\rho). \tag{A.14}$$

Since divergence is a linear operator,

$$\mathrm{div}(J_R) = \mathrm{div}(qq_bK) + \frac{1}{2}\mathrm{div}(q_b\rho A\nabla q) - \frac{1}{2}\mathrm{div}(q\rho A\nabla q_b). \tag{A.15}$$

By (A.8) with $V = K$ and $g = q$ and the definition (A.14) of the vector field K it follows that

$$\begin{aligned}\mathrm{div}(qq_bK) &= q\mathrm{div}(Kq_b) + Kq_b \cdot \nabla q\\ &= q\mathrm{div}(q_b\left(b\rho - \frac{1}{2}\mathrm{div}(A\rho)\right)) + q_b\left(b\rho - \frac{1}{2}\mathrm{div}(A\rho)\right) \cdot \nabla q\\ &= q\left(\mathrm{div}(q_bb\rho) - \frac{1}{2}\mathrm{div}(q_b\mathrm{div}(A\rho))\right) + q_b\left(b\rho - \frac{1}{2}\mathrm{div}(A\rho)\right) \cdot \nabla q.\end{aligned} \tag{A.16}$$

Another application of (A.8) with $V = \mathrm{div}(A\rho)$, $g = q_b$ and $f = 1$ yields

$$\mathrm{div}(q_b\mathrm{div}(A\rho)) = q_b\mathrm{div}(\mathrm{div}(A\rho)) + \mathrm{div}(A\rho) \cdot q_b. \tag{A.17}$$

Lemma A.0.1 with $M = A$, $f = \rho$ and $g = q_b$ yields

$$\mathrm{div}(\mathrm{div}(A\rho q_b)) = q_b\mathrm{div}(\mathrm{div}(A\rho)) + 2\mathrm{div}(A\rho) \cdot \nabla q_b + \rho A : \nabla\nabla q_b,$$

and therefore

$$q_b \mathrm{div}(\mathrm{div}(A\rho)) = \mathrm{div}(\mathrm{div}(A\rho q_b)) - 2\mathrm{div}(A\rho)\cdot\nabla q_b - \rho A : \nabla\nabla q_b.$$

By substituting the last equation into (A.17) we obtain

$$\mathrm{div}(q_b \mathrm{div}(A\rho)) = \mathrm{div}(\mathrm{div}(A\rho q_b)) - \mathrm{div}(A\rho)\cdot\nabla q_b - \rho A : \nabla\nabla q_b.$$

Now by supplementing the last expression into (A.16) we have

$$\begin{aligned}
\mathrm{div}(qq_bK) &= q\left(\mathrm{div}(q_b b\rho) - \frac{1}{2}\left(\mathrm{div}(\mathrm{div}(A\rho q_b)) - \mathrm{div}(A\rho)\cdot\nabla q_b - \rho A : \nabla\nabla q_b\right)\right) \\
&\qquad + q_b\left(b\rho - \frac{1}{2}\mathrm{div}(A\rho)\right)\cdot\nabla q \\
&= q\left(\mathrm{div}(q_b b\rho) - \frac{1}{2}\mathrm{div}(\mathrm{div}(A\rho q_b))\right) + \frac{1}{2}q\left(\mathrm{div}(A\rho)\cdot\nabla q_b + \rho A : \nabla\nabla q_b\right) \\
&\qquad + q_b\left(b\rho - \frac{1}{2}\mathrm{div}(A\rho)\right)\cdot\nabla q \\
&= q\mathrm{div}(J) + \frac{1}{2}q\left(\mathrm{div}(A\rho)\cdot\nabla q_b + \rho A : \nabla\nabla q_b\right) + q_b\left(b\rho - \frac{1}{2}\mathrm{div}(A\rho)\right)\cdot\nabla q,
\end{aligned}$$

where J is given by (A.12). Since $\mathrm{div}(J) = 0$ by Corollary A.0.2, we have

$$\begin{aligned}
\mathrm{div}(qq_bK) &= \frac{1}{2}q\left(\mathrm{div}(A\rho)\cdot\nabla q_b + \rho A : \nabla\nabla q_b\right) + q_b\left(b\rho - \frac{1}{2}\mathrm{div}(A\rho)\right)\cdot\nabla q \\
&= \frac{1}{2}\mathrm{div}(A\rho)\cdot(q\nabla q_b - q_b\nabla q) + q_b b\rho\cdot\nabla q + \frac{1}{2}q\rho A : \nabla\nabla q_b.
\end{aligned} \tag{A.18}$$

Applying (A.13) of Lemma A.0.5 with $M = A$, $h = \rho$, $f_1 = q_b$, $f_2 = q$, yields

$$\begin{aligned}
\mathrm{div}(q_b\rho A\nabla q) - \mathrm{div}(q\rho A\nabla q_b) &= \mathrm{div}(\rho A)\cdot(q_b\nabla q - q\nabla q_b) \\
&\qquad + q_b A\rho : \nabla\nabla q - qA\rho : \nabla\nabla q_b.
\end{aligned} \tag{A.19}$$

By substituting (A.19) and (A.18) into (A.15) we obtain

$$\begin{aligned}
\mathrm{div}(J_R) &= \frac{1}{2}q_b\rho A : \nabla\nabla q + q_b b\rho\cdot\nabla q \\
&= q_b\rho\mathcal{A}q = 0,
\end{aligned}$$

where we used (A.1) and (A.2). □

Summary

Many applications involve analysing dynamical systems that undergo rare transitions between two metastable subsets A and B of state space. For example, in clinical disease modelling, one can model a patient's state as a metastable stochastic process that occasionally transits from a 'healthy' subset A to a 'diseased' subset B. We develop a numerical method for analysing the statistics of transitions of a diffusion process between the two disjoint subsets of the bounded state space.

Transition path theory (TPT) was first formulated to solve this problem for ergodic diffusion processes. The main object of this theory is a committor function, which at any state of the state space is defined as the probability of reaching the set B before reaching the set A, conditioned on starting from the given state. The computation of the committor function requires solving a second order partial differential equation involving the generator of the process. Therefore, TPT for diffusion processes requires the knowledge of the stochastic differential equation governing the process. Furthermore, the high dimensional nature of many problems makes solving such partial differential equations difficult in practice. In order to perform computations, a discretisation method is needed. TPT for Markov jump processes has been developed for this reason. However, space discretisation results in a loss of the Markov property.

We discretise the state space using Voronoi tessellations and model the underlying diffusion process by a non-Markovian jump process on the associated Delaunay graph. To this process we associate the analogues of the committor function, isocommittor surfaces, the probability current and streamlines. These objects are the key objects in both TPT for diffusion processes and TPT for Markov jump processes. In this thesis, we define these objects for the non-Markovian jump process described above. All of the objects we define can be computed using sampled trajectories, thus our approach is completely data-driven and does not rely on the knowledge of the stochastic differential equation governing the underlying process. This differentiates our approach from TPT for diffusion processes. Furthermore, we do not assume Markovianity which differentiates our approach from TPT for Markov jump processes.

We prove the convergence of three of our objects to their analogues in TPT for diffusion processes, in the limit of infinitely fine discretisation. This validates the discrete approach we suggest. Moreover, we prove error bounds for the committor function, the probability current and the associated streamlines. To the best of our knowledge this is the first discrete TPT approach that comes with rigorous proofs of convergence.

Zusammenfassung

Viele Anwendungen beinhalten die Analyse dynamischer Systeme, die seltene Übergänge zwischen zwei metastabilen Teilmengen A und B des Zustandsraums durchlaufen. Beispielsweise kann der Zustand eines Patienten als metastabiler stochastischer Prozess modelliert werden, der gelegentlich von einer "gesunden" Teilmenge A zu einer "krankhaften" Teilmenge B übergeht. Wir entwickeln ein numerisches Verfahren zur Analyse der Statistik der Übergänge eines Diffusionsprozesses zwischen den beiden disjunkten Teilmengen des begrenzten Zustandsraums.

Transition Path Theory (TPT) wurde zunächst formuliert, um dieses Problem für ergodische Diffusionsprozesse zu lösen. Das Hauptobjekt dieser Theorie ist eine Committor-Funktion, die in jedem Zustand des Zustandsraums definiert ist als die Wahrscheinlichkeit, die Menge B zu erreichen, bevor die Menge A erreicht wird, bedingt auf das Starten aus dem gegebenen Zustand. Die Berechnung der Committor-Funktion erfordert das Lösen einer partiellen Differentialgleichung zweiter Ordnung, an welcher der Generator des Prozesses beteiligt ist. Daher erfordert TPT für Diffusionsprozesse die Kenntnis der stochastischen Differentialgleichung, die den Prozess steuert. Darüber hinaus erschwert die hohe Dimensionalität vieler Probleme die Lösung solcher partiellen Differentialgleichungen in der Praxis. Um Berechnungen durchführen zu können, ist eine Diskretisierungsmethode erforderlich. Aus diesem Grund wurde TPT für Markow-Sprungprozesse entwickelt. Die Diskretisierung des Raumes führt jedoch zum Verlust der Markow-Eigenschaft.

Wir diskretisieren den Zustandsraum mit Hilfe von Voronoi-Diagrammen und modellieren den zugrunde liegenden Diffusionsprozess durch einen nicht-Markowschen Sprungprozess auf dem zugehörigen Delaunay-Diagramm. Diesem Prozess ordnen wir die Analoga der Committor-Funktion, die Isocommittor-Oberflächen, den Wahrscheinlichkeitsstrom und die Stromlinien zu. Diese Objekte sind die Schlüsselobjekte sowohl in TPT für Diffusionsprozesse als auch in TPT für Markow-Sprungprozesse. In dieser Arbeit definieren wir diese Objekte für den oben beschriebenen nicht-Markowschen Sprungprozess. Alle von uns definierten Objekte können mit simulierten Trajektorien berechnet werden, sodass unser Ansatz vollständig datenbasiert ist und sich nicht auf das Wissen der stochastischen Differentialgleichung stützt, die den zugrunde liegenden Prozess steuert. Dies unterscheidet unseren Ansatz von TPT für Diffusionsprozesse. Darüber hinaus setzen wir keine Markow-Eigenschaft voraus, was unseren Ansatz von TPT für Markow-Sprungprozesse unterscheidet.

Wir beweisen die Konvergenz von drei unserer Objekte zu ihren Analoga in TPT für Diffusionsprozesse, im Limes der unendlich feinen Diskretisierung. Dies bestätigt den von uns vorgeschlagenen diskreten Ansatz. Darüber hinaus beweisen wir Fehlerabschätzungen für die Committor-Funktion, den Wahrscheinlichkeitsstrom und die damit verbundenen Stromlinien. Nach unserem besten Wissen ist dies der erste diskrete TPT-Ansatz, der mit rigorosen Konvergenznachweisen einhergeht.

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