Metastability and Dominant Eigenvalues of Transfer Operators

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Summary. Metastability is an important characteristic of molecular systems, e.g., when studying conformation dynamics, computing transition paths or speeding up Markov chain Monte Carlo sampling methods. In the context of Markovian (molecular) systems, metastability is closely linked to spectral properties of transfer operators associated with the dynamics. In this article, we prove upper and lower bounds for the metastability of a state-space decomposition for reversible Markov processes in terms of dominant eigenvalues and eigenvectors of the corresponding transfer operator. The bounds are explicitly computable, sharp, and do not rely on any asymptotic expansions in terms of some smallness parameter, but rather hold for arbitrary transfer operators satisfying a reasonable spectral condition.

Key words: Molecular dynamics, Markov processes, spectral properties, Rayleigh-trace, lower and upper bounds on metastability

1 Introduction

There are many problems in physics, chemistry, or biology where the length and time scales corresponding to the microscopic descriptions (given in terms of some stochastic or deterministic dynamical system) and the resulting macroscopic effects differ by many orders of magnitude. Rather than resolving all microscopic details one is often interested in characteristic features on a macroscopic level (e.g., phase transitions, conformational changes of molecules, climate changes, etc.). A typical mathematical example is the long-time limit behavior, where invariant measures or limit cycles are established characteristic objects (e.g., [LM94, MT93]). Metastability is another important characteristics which is related to the long time behavior of the dynamical system. It refers to the property that the dynamics is likely to remain within a certain part of the state space for a long period of time until it eventually exits and transits to some other part of the state space. There are well-established links of metastability to, e.g., exit times [BEGK02, FW84, Gar85], eigenvalues

of transfer operators or generators [BEGK02, DHFS00, DJ99, Dav82b, SH03], phase transitions [BEGK01, Dav82a], reduced Markovian approximations [SH03, HMS04, HSS03], averaging [SWHH04], and many other areas.

There exist several characterizations of metastability in the literature (see, e.g., [BEGK01, Dav82b, SH03, Sin84]). There are at least two different conceptual approaches to metastability. (1) A subset C is called metastable if the fraction of systems in C (measured w.r.t. some pre-specified probability measure) whose trajectory exits C during some pre-defined microscopic time span is significantly small. (2) A subset C is called metastable, if with high probability a typical trajectory stays within C longer than some macroscopic time span. Thus, in broad terms, you may either observe an ensemble of systems for a short time or a typical system for a long time to characterize metastability. We will restrict our attention to the ensemble approach, the use of which was motivated by a molecular application (conformation dynamics, see [DS04, SFHD99, SH03]) where the probability measure is given by the canonical ensemble or Boltzmann distribution while the observation time span is linked to the experimental setting.

We will assume that the dynamical system is given in terms of some reversible Markov chain with invariant measure μ. Equivalently, we may specify the dynamics in terms of the associated transfer operator P acting on $L^2(\mu)$ and being self-adjoint due to reversibility. There is a classical connection between invariant (stable) subsets and degeneracy of the maximal eigenvalue 1 of P. The degeneracy of 1 is just the number of invariant subsets of the state space (see e.g. [Doo53, Hui01]). Analogously, to each eigenvalue close to 1 there corresponds an almost invariant or metastable subset of the state space, see e.g. [Dav82c, DJ99, DHFS00].

Pursuing this analogy, there is a large amount of literature relating metastability to eigenvalues of transfer operators or generators corresponding to the underlying Markov process. However, the theoretical investigations are either restricted to the finite dimensional state space case (and thus related to stochastic matrices or Laplace matrices), e.g., [HH92, HM98, HL95, Mey89, Sin93] or stated asymptotically in terms of some smallness parameter, e.g., [FW84]. General state space non-asymptotic results are much more rare and may be found in the setting of exit times [BEGK04, BGK05] or in the setting of symmetric Markov semigroups [Dav82b, Dav82c, Sin84]. To our knowledge, even for the finite dimensional state space case, there are no lower bounds on the metastability (in the ensemble characterization) of a finite number of subsets in terms of eigenvalues known. It is our aim to derive an upper and in particular a lower bound on the metastability of an arbitrary decomposition from spectral properties of the transfer operator P. Such bounds are not only of theoretical interest but also of algorithmic relevance, e.g., in the context of dynamical clustering [DHFS00, DW04].

The paper is organized as follows: In section 2, we review stochastic models for molecular dynamics to motivate our study of metastability. In Section 3, we

introduce the set-up including the definition of metastability and its transfer operator formulation. In Section 4, a variational formula for the Rayleigh-trace of self-adjoint operators is reviewed, which is crucial in the proofs of our results. We prove upper and lower bounds for the metastability of arbitrary decompositions of the phase space under some quite general spectral assumption on P. Finally, in Section 5, we state some examples illustrating the sharpness and usefulness of the bounds.

2 Markovian molecular dynamics

This section introduces three popular Markovian models for molecular dynamics.

Hamiltonian System with Randomized Momenta. The Hamiltonian system with randomized momenta is a reduced dynamics defined on the position space and derived from the deterministic Hamiltonian system by "randomizing the momenta" and integrating for some fixed observation time span τ [Sch98]. Let Φ^t denote the flow corresponding to the deterministic Hamiltonian system

$$\dot{q} = p, \qquad \dot{p} \;=\; -\nabla_q V(q),$$

defined on the phase space Γ, and let $\Pi_q : \Gamma \to \Omega$ denote the projection onto the position space Ω. Then, the *Hamiltonian system with randomized momenta* is the discrete time Markov process $Q_n = \{Q_n\}_{n\in\mathbb{N}}$ satisfying

$$Q_{n+1} = \Pi_q \Phi^\tau(Q_n, P_n); \qquad n \in \mathbb{N},$$

where τ is some fixed observation time span, and $\{P_n\}$ is an i.i.d. sequence distributed according to the canonical distribution of momenta $\mathcal{P} \propto \exp(-\beta p^2/2)$ with inverse temperature $\beta = 1/(k_B T)$. As shown in [Sch98], the Markov process is reversible w.r.t. the positional canonical ensemble $\mu \propto \exp(-\beta V(q))$. For further details, in particular comments on τ, see [Sch98, SH03, SHD01]. We finally remark that the Hamiltonian system with randomized momenta is closely related to the hybrid Monte Carlo method.

Langevin Equation. The most popular model for an open system stochastically interacting with its environment is the *Langevin equation* (e.g., [Ris96])

$$\dot{q} \;=\; p, \qquad \dot{p} \;=\; -\nabla_q V(q) \;-\; \gamma\, p \;+\; \sigma\, \dot{W}$$

corresponding to some friction constant $\gamma > 0$ and external force $F_{\text{ext}} = \sigma\dot{W}$ defined in terms of a standard $3N$-dimensional Brownian motion W. The Langevin equation defines a continuous time Markov process on the phase space Γ whose invariant distribution is given by the canonical ensemble $\mu \propto \exp(-\beta H(q,p))$ with Hamiltonian H describing the internal energy of

the system. The inverse temperature β is via linked to the friction and the stochastic excitation $\beta = 2\gamma/\sigma^2$.

Smoluchowski Equation. As a reduced model of the Langevin equation, we introduce the Smoluchowski equation

$$\gamma\dot{q} = -\nabla_q V(q) + \sigma\dot{W}.$$

It is derived from the Langevin equation by considering the high friction limit $\gamma \to \infty$ [Nel67, Theorem 10.1]. In contrast to the Langevin equation, the Smoluchowski dynamics defines a reversible Markov process; its stationary distribution is given by $\mu \propto \exp(-\beta V(q))$ with $\beta = 2\gamma/\sigma^2$.

The above models describe the dynamics of a single system. On the contrary, the evolution of densities v_t w.r.t. μ is described by the action of the so-called semigroup of transfer operators $\{P_t\}$, i.e., $v_t = P_t v_0$ where v_0 denotes the initial density. For the Hamiltonian system with randomized momenta we obtain

$$Pv(q) = \int_{\mathbb{R}^d} v(\Pi_q \Phi^{-\tau}(q,p))\mathcal{P}(p)\mathrm{d}p,$$

while for the Langevin and Smoluchowski equation the semigroup is given by $P_t v = \exp(t\mathcal{L})v$ where $\mathcal{L}$ denotes the infinitesimal generator defined by the corresponding Fokker-Planck equation (e.g., [Hui01, SH03, Ris96]). In general, the spectrum $\sigma(P)$ of P is contained in the unit circle (the modulus of every eigenvalue is less or equal 1) and symmetric w.r.t. the real axis; moreover, $1 \in \sigma(P)$. Exploiting spectral properties of the transfer operators (eigenvalues close to 1 and their eigenvectors) we will be able to identify a decomposition of the state space into metastable subsets.

3 Markov chains, transfer operators, and metastability

We now state the general setting in terms of which the above specified models of molecular dynamics are specific cases. Throughout let $X = (X_n)_{n\in\mathbb{N}}$ denote a homogeneous Markov chain on the state space $\mathcal{X}$ with transition kernel

$$p(x, A) = \mathbb{P}[X_1 \in A | X_0 = x] \tag{1}$$

for all $x \in \mathcal{X}$ and all subsets $A \subset \mathcal{X}$ contained in the σ–algebra $\mathcal{A}$. Consider a probability measure ν on $\mathcal{X}$, and assume that the Markov chain is initially distributed according to ν, i.e., $X_0 \sim \nu$ meaning

$$\mathbb{P}[X_0 \in A] = \nu(A) \tag{2}$$

for all $A \in \mathcal{A}$. Then, the Markov chain at time $k > 0$ is distributed according to

$$\mathbb{P}[X_k \in A | X_0 \sim \nu] = \mathbb{P}_\nu[X_k \in A] =: \nu_k(A).$$

The time-evolution of probability measures $\{\nu_k\}$ can be described by the transfer operator P acting on the space of bounded measures on $(\mathcal{X}, \mathcal{A})$ via

$$P\nu(A) = \mathbb{P}_\nu[X_1 \in A] = \int_{\mathcal{X}} p(x, A)\nu(dx). \tag{3}$$

Assume that the Markov chain exhibits a unique invariant probability measure μ, i.e., $P\mu = \mu$ and define the weighted Hilbert space of measurable functions

$$L^2(\mu) = \{f : \mathcal{X} \to \mathbb{R} : \|f\|^2 = \int_{\mathcal{X}} |f(x)|^2 \mu(dx) < \infty\}$$

with inner product given by

$$\langle f, g \rangle = \int_{\mathcal{X}} f(x)g(x)\mu(dx).$$

If μ is the invariant probability measure of P, then $\nu_0 \ll \mu$ implies $\nu_k \ll \mu$ [Rev75, Chapter 4]. Hence we may consider P as an operator on $L^2(\mu)$ acting on probability measures that are absolutely continuous w.r.t. μ according to

$$\int_A Pv(x)\mu(dx) = \int_{\mathcal{X}} p(x, A)v(x)\mu(dx).$$

In the sequel, we assume that the Markov chain X is reversible, hence the transition kernel satisfies

$$\mu(dx)p(x, dy) = \mu(dy)p(y, dx).$$

As a consequence, P is self-adjoint on $L^2(\mu)$.

We now introduce the notion of the transition probabilities between subsets (see [SH03, Hui01]) in terms of which metastability will be defined:

Definition 1. *Let $A, B \subset \mathcal{X}$ denote measurable subsets of the state space.*

1. *The transition probability from A to B is defined to be the conditional probability*

$$p(A, B) = \mathbb{P}_\mu[X_1 \in B | X_0 \in A] = \frac{1}{\mu(A)} \int_A p(x, B)\mu(dx),$$

   if $\mu(A) > 0$ and $p(A, B) = 0$ otherwise. In other words, the transition probability quantifies the dynamical fluctuations within the invariant distribution μ.
2. *A subset $A \in \mathcal{A}$ is called invariant if $p(A, A) = 1$.*
3. *A subset $A \in \mathcal{A}$ is called metastable if $p(A, A) \approx 1$.*

Hence, metastability is almost invariance. Requiring the transition probability to be "close to 1" is obviously a vague statement, however, in most applications, we are interested in a decomposition into the most metastable subsets, which eliminates the problem of interpreting "close to 1". Instead, we have to determine the number of subsets we are looking for. This is done by examining the spectrum of the transfer operator P. Alternatively, we could determine a cascade of decompositions with an increasing number of metastable subsets.

It is easy to see that the transition probability between subsets can be rewritten in terms of the inner product $\langle \cdot, \cdot \rangle$ according to

$$p(A, B) = \frac{\langle P\mathbf{1}_A, \mathbf{1}_B \rangle}{\langle \mathbf{1}_A, \mathbf{1}_A \rangle}, \tag{4}$$

where $\mathbf{1}_A$ denotes the characteristic function of the subset A.

Consider a decomposition of the state space $\mathcal{X}$ into mutually disjoint subsets $\mathcal{D} = \{A_1, \ldots, A_n\}$. Then,

$$m(\mathcal{D}) = p(A_1, A_1) + \ldots + p(A_n, A_n)$$

can be thought of as a measure of metastability of the decomposition $\mathcal{D}$. In general, $0 \leq m(\mathcal{D}) \leq n$ with $m(\mathcal{D}) = n$ if all subsets are invariant. It is our aim to get upper and lower bounds on the metastability of the decomposition in terms of eigenvalues and corresponding eigenvectors of the transfer operator.

We are interested in situations where the spectrum of the transfer operator satisfies the following

Assumption S: The transfer operator $P : L^2(\mu) \to L^2(\mu)$ is self–adjoint and exhibits n eigenvalues

$$\lambda_n \leq \ldots \leq \lambda_2 < \lambda_1 = 1$$

counted according to their multiplicity. The corresponding set of μ–orthonormal eigenvectors will be denoted by $\{v_n, \ldots, v_1\}$. Furthermore, the spectrum $\sigma(P)$ of P satisfies

$$\sigma(P) \subset [a, b] \cup \{\lambda_n, \ldots, \lambda_2, 1\}$$

for some constants $a, b \in (-1, +1)$ satisfying $-1 < a \leq b < \lambda_n$. In this sense, the eigenvalues $\lambda_1, \ldots, \lambda_n$ are called dominant.

In particular, Assumption S is satisfied if the underlying Markov chain is reversible and geometrically or V-uniformly ergodic (see, e.g., [Hui01, Thm. 4.31]) which is always the case if the state space is finite dimensional (and the Markov chain reversible). Moreover, fixing some time span $\tau > 0$ the Assumption S is satisfied for (i) the Hamiltonian system with randomized momenta with periodic boundary conditions and some smooth potential, (ii) the

Smoluchowski equation with periodic boundary conditions and some smooth potential, or for so-called bounded systems with smooth potentials satisfying a suitable growth condition at infinity. For further details, also regarding the Langevin equation, see [Hui01, Sch98]. Note that reversibility and "simple" ergodicity (space and time average coincide) is not sufficient to guarantee Assumption S.

4 Upper and Lower Bounds

This section proves upper and lower bounds on the metastability of an arbitrary decomposition of the state space in terms of dominant eigenvalues and eigenvectors of the transfer operator corresponding to the dynamics of the Markov process.

Recall that by Rayleigh's Principle the kth largest eigenvalue λ_k for $1 \leq k \leq n$, is given by the variational formula

$$\lambda_k = \max\{\langle Pw, w\rangle : w \in L^2(\mu), \|w\|_2 = 1, w \perp v_1 \ldots, v_{k-1}\},$$

where $\perp$ denotes orthogonality w.r.t. the inner product $\langle\cdot,\cdot\rangle$, and v_i is the eigenvector corresponding to λ_i. The above variational formula can be generalized (for our purpose) in the following way: Consider a finite dimensional subspace U of $L^2(\mu)$ with orthonormal basis $(\varphi_1, \ldots, \varphi_n)$. Then, for a self-adjoint operator P on $L^2(\mu)$ the Rayleigh-trace w.r.t. U is defined as

$$\mathrm{Tr}_U P = \sum_{i=1}^{n} \langle P\varphi_i, \varphi_i\rangle.$$

Note that this definition is independent of the particular choice of the orthonormal basis (see, e.g., [Ban80]).

Theorem 1. *Assume that $P : L^2(\mu) \to L^2(\mu)$ is a self adjoint transfer operator satisfying Assumption S. Then*

$$\begin{aligned}
&\lambda_n + \ldots + \lambda_1 \\
&= \max\{\mathit{Tr}_U P : U \textit{ is } n\textit{-dimensional subspace}\} \\
&= \max\left\{\sum_{i=1}^{n}\langle P\varphi_i, \varphi_i\rangle : (\varphi_1, \ldots, \varphi_n) \textit{ is orthonormal system.}\right\}
\end{aligned}$$

The above proposition is actually known to hold for every self-adjoint bounded operator P on a Hilbert space H [Ban80]. The generalized Rayleigh Principle can be exploited to prove upper bounds on the metastability of some (arbitrary) partition $A_1, \ldots, A_n$ of the state space $\mathcal{X}$ that satisfies $\mu(A_k) > 0$ for $k = 1, \ldots n$. Recall that the orthogonal projection $Q : L^2(\mu) \to L^2(\mu)$ onto $\mathrm{span}\{\mathbf{1}_{A_1}, \ldots, \mathbf{1}_{A_n}\}$ is defined as

$$Q\,v = \sum_{k=1}^{n} \frac{\langle v, \mathbf{1}_{A_k}\rangle}{\langle \mathbf{1}_{A_k}, \mathbf{1}_{A_k}\rangle} \mathbf{1}_{A_k} \;=\; \sum_{k=1}^{n} \langle v, \chi_{A_k}\rangle \chi_{A_k}$$

with

$$\chi_{A_k} = \frac{\mathbf{1}_{A_k}}{\sqrt{\langle \mathbf{1}_{A_k}, \mathbf{1}_{A_k}\rangle}}$$

for $k = 1, \ldots, n$ and for every $v \in L^2(\mu)$. Our central result is

Theorem 2. *Consider some transfer operator $P : L^2(\mu) \to L^2(\mu)$ satisfying Assumption S. Then the metastability of an arbitrary decomposition $\mathcal{D} = \{A_1, \ldots, A_n\}$ of the state space can be bounded from above by*

$$p(A_1, A_1) + \ldots + p(A_n, A_n) \leq 1 + \lambda_2 + \ldots + \lambda_n,$$

while it is bounded from below by

$$1 + \rho_2\lambda_2 + \ldots + \rho_n\lambda_n + c \leq p(A_1, A_1) + \ldots + p(A_n, A_n)$$

where $\rho_j = \|Qv_j\|^2 = \langle Qv_j, Qv_j\rangle \in [0, 1]$ and

$$c = a\,\big(1 - \rho_2 + \ldots + 1 - \rho_n\big).$$

In particular, we have $c \geq 0$ if $\sigma(P) \subset [0, 1]$.

The coefficients ρ_j in Theorem 2 measure how close the eigenfunctions v_j restricted to each of the subsets of the decomposition are to the constant function. The more constant the eigenfunctions are on the subsets, the larger the ρ_j are and thus the larger the lower bound is. Hence, one can try to maximize the lower bound in seeking for a decomposition such that the eigenfunctions, restricted to each subset, are as constant as possible. This strategy is used algorithmically to identify a decomposition into metastable subsets ([DHFS00, DW04, SHD01]).

Proof. Upper bound: Since $p(A_k, A_k) = \langle P\chi_{A_k}, \chi_{A_k}\rangle$ using (4) and the definition of χ_{A_k} we have

$$\sum_{k=1}^{n} p(A_k, A_k) = \sum_{k=1}^{n} \langle P\chi_{A_j}, \chi_{A_j}\rangle. \tag{5}$$

By Theorem 1, the right hand side of (5) is less than or equal to $\lambda_1 + \ldots + \lambda_n$ since $\{\chi_{A_1}, \ldots, \chi_{A_n}\}$ is an orthonormal basis of $\operatorname{span}\{\mathbf{1}_{A_1}, \ldots, \mathbf{1}_{A_n}\}$.

Lower bound: Denote by $\Pi : L^2(\mu) \to \operatorname{span}\{v_1, \ldots, v_n\}$ the orthogonal projection onto the subspace spanned by the maximal eigenvectors, and set $\Pi^\perp = \mathrm{Id} - \Pi$. Then

$$\begin{aligned}\sum_{j=1}^{n} p(A_j, A_j) &= \sum_{j=1}^{n} \left\langle (P - a\mathrm{Id})\chi_{A_j}, \chi_{A_j} \right\rangle + \sum_{j=1}^{n} a \left\langle \chi_{A_j}, \chi_{A_j} \right\rangle \\ &= \sum_{j=1}^{n} \left\langle ((P - a\mathrm{Id})\Pi + (P - a\mathrm{Id})\Pi^{\perp})\chi_{A_j}, (\Pi + \Pi^{\perp})\chi_{A_j} \right\rangle \\ &\quad + an \\ &= \sum_{j=1}^{n} \left\langle (P - a\mathrm{Id})\Pi\chi_{A_j}, \Pi\chi_{A_j} \right\rangle \\ &\quad + \sum_{j=1}^{n} \left\langle (P - a\mathrm{Id})\Pi^{\perp}\chi_{A_j}, \Pi^{\perp}\chi_{A_j} \right\rangle + an.\end{aligned}$$

The first two terms of the right hand side can be further analyzed:

$$\begin{aligned}\sum_{j=1}^{n} \left\langle (P - a\mathrm{Id})\Pi\chi_{A_j}, \Pi\chi_{A_j} \right\rangle &= \sum_{j=1}^{n} \left\langle \sum_{k=1}^{n} (\lambda_k - a)\langle \chi_{A_j}, v_k \rangle v_k, \sum_{l=1}^{n} \langle \chi_{A_j}, v_l \rangle v_l \right\rangle \\ &= \sum_{j=1}^{n} \sum_{k=1}^{n} (\lambda_k - a)\langle \chi_{A_j}, v_k \rangle^2 \\ &= \sum_{k=1}^{n} (\lambda_k - a)\langle Qv_k, Qv_k \rangle.\end{aligned}$$

Now $\left\langle (P - a\mathrm{Id})\Pi^{\perp}\chi_{A_j}, \Pi^{\perp}\chi_{A_j} \right\rangle$ is non–negative since $P - a\mathrm{Id}$ is non-negative definite according to the assumptions made. Hence,

$$\sum_{j=1}^{n} p(A_j, A_j) \geq \sum_{k=1}^{n} \lambda_k \rho_k + a \sum_{k=1}^{n} (1 - \rho_k),$$

which completes the proof since invariance of μ implies $v_1 = \mathbf{1}_{\mathcal{X}}$ and thus $\rho_1 = \|Qv_1\|^2 = 1$.

Our main result, Theorem 2, does hold for an arbitrary transfer operator satisfying Assumption S. Note that for the finite state space case Assumption S is trivially satisfied (and to the best of our knowledge even for finite stochastic matrices the lower bound is new). We did not need to introduce any asymptotic smallness parameter κ, say, in order to prove asymptotic results for $\kappa \to 0$. This is a remarkable difference to other approaches. Moreover, the lower bound is computable explicitly given some decomposition of the state space. Hence, comparing the lower and upper bound one is able to "judge" the quality of the decomposition. Moreover, we remark that if $\{\varphi_1, \ldots, \varphi_n\}$ is an arbitrary orthonormal basis of $\mathrm{span}\{\mathbf{1}_{A_1}, \ldots, \mathbf{1}_{A_n}\}$, then

$$\kappa_1\lambda_1 + \ldots + \kappa_n\lambda_n + c \leq p(A_1, A_1) + \ldots + p(A_n, A_n), \tag{6}$$

where $\kappa_j = |\langle v_j, \varphi_j \rangle|^2 \in [0, 1]$ which follows from

$$\rho_j \;=\; \langle Qv_j, Qv_j\rangle \;=\; \sum_{k=1}^{n} |\langle v_j, \varphi_k\rangle|^2 \geq |\langle v_j, \varphi_j\rangle|^2 \;=\; \kappa_j.$$

In some situations, we additionally know that P is positive, for instance, if we consider the case of $P = P_\tau$, where $(P_t)_{t\geq 0}$ is a semigroup of transfer operators, and τ is some fixed time. (This is the case, e.g., for the Langevin and Smoluchowski dynamics discussed in section 2 but not for the Hamiltonian system with randomized momenta.) Then, we can state:

Corollary 3 *Consider a reversible homogeneous continuous-time Markov process $X = (X_t)_{t\in[0,\infty)}$ and its corresponding semigroup of transfer operators $P_t : L^2(\mu) \to L^2(\mu)$. If $P = P_\tau$ satisfies Assumption S for some fixed $\tau > 0$, then*

$$1 + \rho_2\lambda_2 + \ldots + \rho_n\lambda_n \leq p(A_1, A_1) + \ldots + p(A_n, A_n) \leq \lambda_1 + \ldots + \lambda_n, \quad (7)$$

where λ_k denote eigenvalues of the operator P_τ.

Proof. Simply note that $P = P_\tau$ is positive since $P = P_{\tau/2}P_{\tau/2}$, and apply Theorem 2 (with $a = 0$).

5 Illustrative Examples

The first example proves that both the lower and the upper bound of Theorem 2 are sharp.

Example 1. Let $\mathcal{X} = \{0, 1, 2\}$ and the transition probability P be given by

$$P = \begin{pmatrix} 0.90 & 0.05 & 0.05 \\ 0.05 & 0.05 & 0.90 \\ 0.05 & 0.90 & 0.05 \end{pmatrix}.$$

Clearly P is ergodic, and since it is symmetric, the measure μ given by $\mu(\{0\}) = \mu(\{1\}) = \mu(\{2\}) = 1/3$ is invariant. The eigenvalues λ_j and corresponding eigenvectors v_j are calculated to be

$$\lambda_1 = 1, \quad \lambda_2 = 0.85, \quad \lambda_3 = -0.85$$

and (we do not need v_3)

$$v_1 = \begin{pmatrix} 1 \\ 1 \\ 1 \end{pmatrix}, \quad v_2 = \frac{1}{\sqrt{2}} \begin{pmatrix} 2 \\ -1 \\ -1 \end{pmatrix}.$$

Consider the partition $(A_1, A_2) = (\{0, 1\}, \{2\})$. The resulting metastability is given by $p(A_1, A_1) + p(A_2, A_2) = 0.525 + 0.05 = 0.575$, which is bounded from

above by $1 + \lambda_2 = 1.85$. Calculating the lower bound from Theorem 2, we obtain (here the correction term is $c = -0.6375$)

$$0.575 = 1 + \rho_2\lambda_2 + c \leq p(A_1, A_1) + p(A_2, A_2) = 0.575$$

which furthermore proves that the lower bound is sharp.

Now consider the partition $(A_1, A_2) = (\{0\}, \{1, 2\})$. The resulting metastability is given by

$$p(A_1, A_1) + p(A_2, A_2) = 0.90 + 0.95 = 1.85$$

which in this case is equal to both the upper and lower bound

$$1 + \lambda_2 = 1.85 \text{ and } 1 + \rho_2\lambda_2 + c = 1.85$$

since $\rho_1 = \rho_2 = 1$ and $c = 0$. This additionally proves that the upper bound is sharp, too. Note that although $\lambda_3 = -0.85$ is large negative, the correction term c does not necessarily result in some lower bound that underestimates the metastability of the decomposition. The above example particularly demonstrates the need for a correction of the sum $1 + \rho_2\lambda_2 + \ldots + \rho_n\lambda_n$ by c in order to get a correct lower bound stated in Theorem 2.

We next illustrate for a more advanced system that the lower bound mimics the behavior of the metastability for different decompositions of the state space.

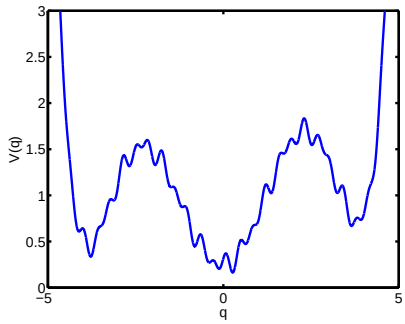

Fig. 1. Graph of the perturbed three well potential V defined in (8).

Example 2. Consider the Smoluchowski dynamics

$$\gamma\dot{q} = -\text{grad}V(q)t + \sigma\dot{W}_t$$

within a "perturbed" three well potential (see Fig. 1)

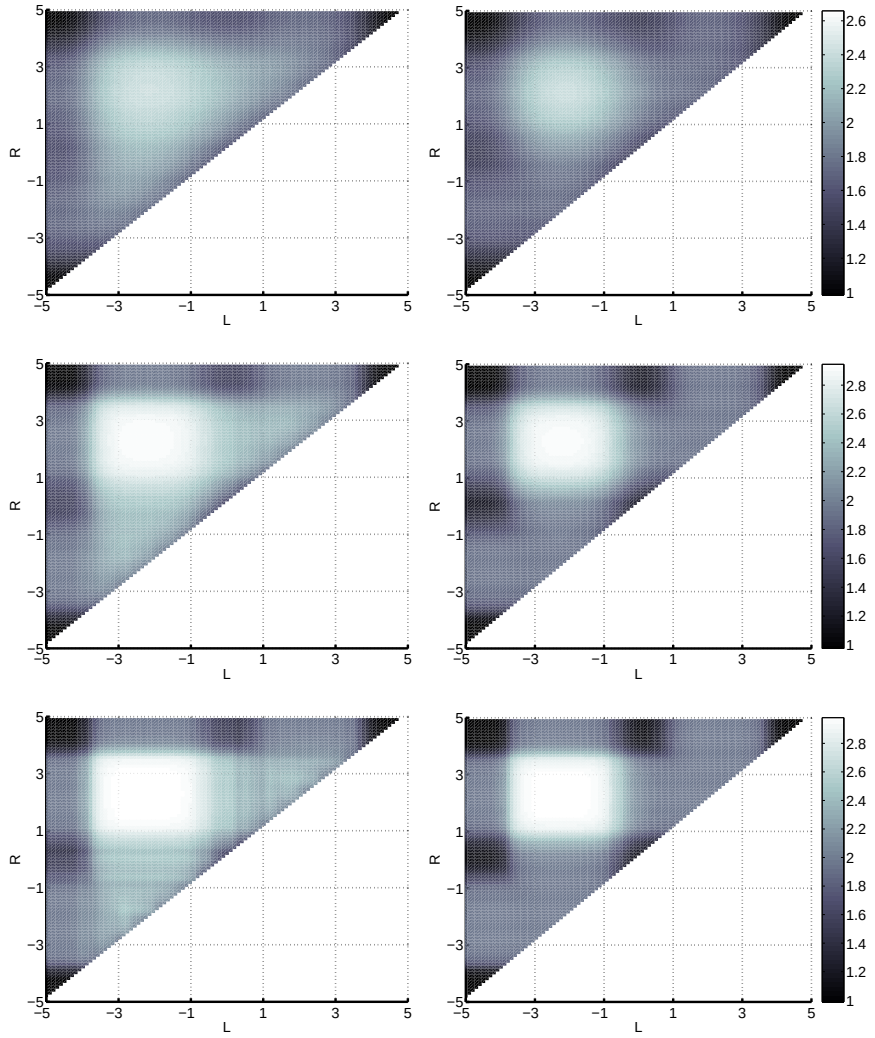

Fig. 2. Metastability (left column) and lower bound (right column) corresponding to the perturbed three–well potential. From top to bottom increasing metastability due to increasing inverse temperature $\beta = 1$ (top), $\beta = 3$ (middle) and $\beta = 5$ (bottom).

$$V(q) = 0.01\Big(q^6 - 30q^4 + 234q^2 + 14q + 100 + \\ 30\sin(17q) + 26\cos(11q)\Big) \tag{8}$$

for given parameters $\gamma = 2$ and $\sigma^2 = 2\gamma/\beta$ with inverse temperature β. For a fixed observation time span $\tau = 1$ we discretize the transfer operator P_τ

(for details or the discretization see [SH03, Hui01]). In view of the potential function V shown in Fig. 1, we would expect to exist three metastable subsets, each corresponding to one of the wells, if the inverse temperature is not too small. Hence, we choose $L < R \in \mathbb{R}$ and decompose the state space into the subsets

$$A_1 = (-\infty, L], A_2 = (L, R], A_3 = (R, \infty)$$

The purpose of this example is to illustrate the dependence of the metastability $m(\mathcal{D})$ of the decomposition $\mathcal{D} = \{A_1, A_2, A_3\}$ on the location of the boundaries L and R and, moreover, to show that the lower bound (in this case) behaves similar to the true metastability of the decomposition for different choices of L, R.

Figure 2 shows the calculated metastability $m(\mathcal{D})$ and the lower bound according to Theorem 2 for three different values of inverse temperature. The case $\beta = 1$ mimics the situation of moderate metastability, while the case $\beta = 7$ corresponds to high metastability. As can be seen from Fig. 2, the lower bound is a good indicator for the actual metastability of the decomposition. Moreover, the shape of the "metastability landscape" gets more plateau-like for larger β, in particular, the identification of the optimal decomposition becomes more and more difficult (and numerically ill-conditioned) for larger β.

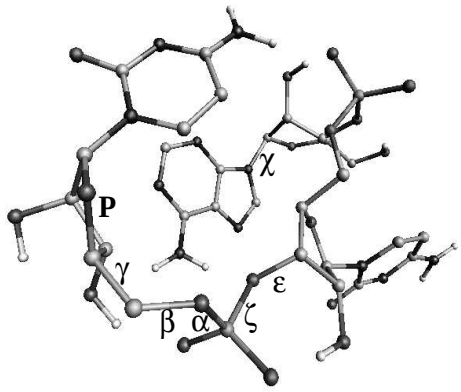

Fig. 3. Configuration of the trinucleotide $r(ACC)$ in a ball–and–stick representation. The Greek symbols indicate some of the important dihedral angles of the molecule.

The third example demonstrates the application to a small biomolecule.

Example 3. Consider the triribonucleotide adenylyl(3'-5')cytidylyl(3'-5')cytidin (r(ACC)) model system in vacuum (see Fig. 3). Its physical representa-

tion ($N = 70$ atoms) is based on the GROMOS96 extended atom force field [vGBE$^+$96]. In the first step, the canonical ensemble has been sampled by means of the Hamiltonian system with randomized momenta [SHD01, HBR$^+$99]. Then, based on some coarse-grained clustering of the resulting sampling point, the transfer operator has be discretized. Solving the eigenvalue problem for the discretized transfer operator, a cluster of eight eigenvalues with a significant gap to the remaining part of the spectrum showed up:

k	1	2	3	4	5	6	7	8	9	...
λ_k	1.000	0.999	0.989	0.974	0.963	0.946	0.933	0.904	0.805	...

Then, the almost constant level structure of eigenvectors corresponding to a cluster of eigenvalues near 1 was exploited and eight conformations characterized by their statistical weight within the canonical ensemble (the probability of the conformation) and metastability were identified (see [SHD01, HBR$^+$99] for details):

conformation	1	2	3	4	5	6	7	8
statistical weight	0.107	0.011	0.116	0.028	0.320	0.038	0.285	0.095
metastability	0.986	0.938	0.961	0.888	0.991	0.949	0.981	0.962

The above table clearly illustrates that metastability and the statistical weight within the stationary ensemble are two independent properties. Of course, in most bio-chemical applications one likely is interested to identify metastable conformations with a relevant statistical weight.

6 Outlook

The detection and identification of metastability in dynamical systems is an active field of research. The existence of metastability is exploited to avoid so-called trapping problems in Markov chain Monte Carlo simulations (e.g., Uncoupling-Coupling techniques [Fis03]) to identify molecular conformations (e.g., [SH03]) or to extend standard averaging schemes [HSS03]. Recent studies indicate a relation between metastable subsets and hidden states in so-called Hidden Markov models [HDFS05]. The concept of metastability is also exploited to identify multiple transition paths between different metastable conformations. Besides molecular applications, the concept of metastability is applied, e.g., to economics [Sta03], climate modelling [IM02], or astronomy [DJK$^+$05].

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