Pathwise estimates for effective dynamics: the case of nonlinear vectorial reaction coordinates

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Abstract

Effective dynamics using conditional expectation was proposed in [18] to approximate the essential dynamics of high-dimensional diffusion processes along a given reaction coordinate. The approximation error of the effective dynamics when it is used to approximate the behavior of the original dynamics has been considered in recent years. As a continuation of the previous work [19], in this paper we obtain pathwise estimates for effective dynamics when the reaction coordinate function is either nonlinear or vector-valued.

Keywords diffusion process, effective dynamics, reaction coordinate, time scale separation, pathwise estimates

1 Introduction

The evolution of many physical systems in biological molecular dynamics and material science can be often modelled by diffusion processes. The latter is a well-established mathematical model which allows us to rigorously study the dynamical behavior of many real-world complex systems. Assuming the system is in equilibrium, one often refers to the reversible diffusion process $x(s) \in \mathbb{R}^n$, which satisfies the stochastic differential equation (SDE)

$$dx(s) = -a(x(s))\nabla V(x(s)) \, ds + \frac{1}{\beta} (\nabla \cdot a)(x(s)) \, ds + \sqrt{2\beta^{-1}} \sigma(x(s)) \, dw(s) \,, \quad s \ge 0 \,, \quad (1)$$

where $\beta > 0$, $w(s) \in \mathbb{R}^{n'}$ is an *n'*-dimensional Brownian motion with $n' \geq n$, and both the potential $V : \mathbb{R}^n \to \mathbb{R}$ and the coefficient matrix $\sigma : \mathbb{R}^n \to \mathbb{R}^{n \times n'}$ are smooth functions. The symmetric matrix *a* is related to σ by $a = \sigma \sigma^T$ and in this work we always assume that *a* is uniformly positive definite, i.e.,

$$\sum_{1 \le i,j \le n} a_{ij}(x)\eta_i\eta_j \ge c_1|\eta|^2, \quad \forall x \in \mathbb{R}^n, \, \eta \in \mathbb{R}^n, \, (2)$$

for some constant $c_1 > 0$ and $|\cdot|$ denotes the usual Euclidean norm of vectors. The notation $\nabla \cdot a$ denotes the *n*-dimensional vector whose components are $(\nabla \cdot a)_i = \sum_{j=1}^n \frac{\partial a_{ij}}{\partial x_j}$, for $1 \le i \le n$.

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Under mild conditions on the potential V, it is well known [24] that dynamics (1) is ergodic with a unique invariant measure μ , whose probability density is given by

$$\frac{d\mu}{dx} = \frac{1}{Z} e^{-\beta V},\tag{3}$$

where $Z = \int_{\mathbb{R}^n} e^{-\beta V} dx$ denotes the normalization constant.

In view of real applications, one often encounters the situation where on the one hand the system is high-dimensional, i.e., $n \gg 1$, and on the other hand the essential behavior of the system can be characterized in a space whose dimension is much lower than n. To study the behavior of the system in this scenario, one often assumes that there is a (reaction coordinate) function $\xi : \mathbb{R}^n \to \mathbb{R}^m$, where

$$\boldsymbol{\xi} = (\xi_1, \xi_2, \cdots, \xi_m)^T, \qquad (4)$$

for some $1 \leq m < n$, such that the essential dynamics of x(s) can be captured by $\xi(x(s))$. Various coarse-graining or model-reduction techniques have been developed in order to study the behavior of the dynamics along the reaction coordinate ξ . We refer to [11, 29, 23, 12] for related work in the study of molecular dynamics.

Notice that, applying Ito's formula, we immediately know that $\xi(x(s))$ satisfies the SDE

$$d\xi(x(s)) = (\mathcal{L}\xi)(x(s))\,ds + \sqrt{2\beta^{-1}}(\nabla\xi\sigma)\big(x(s)\big)\,dw(s)\,,\tag{5}$$

where \mathcal{L} is the infinitesimal generator of (1) and $\nabla \xi$ denotes the $m \times n$ matrix whose entries are $(\nabla \xi)_{ij} = \frac{\partial \xi_i}{\partial x_j}$, for $1 \leq i \leq m, 1 \leq j \leq n$. However, (5) is of limited use in practice, due to the fact that it still depends on the original dynamics x(s). In another word, (5) is not in a closed form and does not correspond to a (Markovian) diffusion process in \mathbb{R}^m . Given a reaction coordinate function ξ , the search of a coarse-grained diffusion process in \mathbb{R}^m in order to approximate $\xi(x(s))$ has been studied in the past work [8, 18]. In particular, the authors in [18] proposed an effective dynamics by replacing the coefficients on the right hand side of (5) by their conditional expectations. In the following, we introduce several quantities in order to explain the conditional expectation suggested in [18].

Given $z \in \mathbb{R}^m$, we define the level set

$$\Sigma_z = \left\{ x \in \mathbb{R}^n \mid \xi(x) = z \right\}.$$
(6)

Assuming it is nonempty, under certain conditions (see Remark 1 in Subsection 2.2), Σ_z is an (n-m)-dimensional submanifold of \mathbb{R}^n . We denote by ν_z the surface measure of the submanifold Σ_z which is induced from the Euclidean metric on \mathbb{R}^n . The probability measure μ_z on Σ_z , which is defined by

$$d\mu_{z}(x) = \frac{1}{Q(z)} \frac{e^{-\beta V(x)}}{Z} \Big[\det(\nabla \xi \nabla \xi^{T})(x) \Big]^{-\frac{1}{2}} d\nu_{z}(x) , \qquad (7)$$

has been studied in the previous work [6, 18, 32, 31] and will play an important role in the current work. In (7), Q(z) is given by

$$Q(z) = \frac{1}{Z} \int_{\Sigma_z} e^{-\beta V(x)} \left[\det(\nabla \xi \nabla \xi^T)(x) \right]^{-\frac{1}{2}} d\nu_z(x)$$

$$= \frac{1}{Z} \int_{\mathbb{R}^n} \delta(\xi(x) - z) e^{-\beta V(x)} dx$$
(8)

and serves as the normalization constant. Clearly, we have $\int_{\mathbb{R}^m} Q(z) dz = 1$.

With the above preparations, we can introduce the effective dynamics proposed in [18]. Specifically, we consider the dynamics $z(s) \in \mathbb{R}^m$ which satisfies the SDE

$$dz(s) = \widetilde{b}(z(s)) \, ds + \sqrt{2\beta^{-1}} \widetilde{\sigma}(z(s)) \, d\widetilde{w}(s) \,, \quad s \ge 0 \,, \tag{9}$$

where $\widetilde{w}(s)$ is an *m*-dimensional Brownian motion, and the coefficients are given by

$$\widetilde{b}_{l}(z) = \int_{\Sigma_{z}} (\mathcal{L}\xi_{l})(x) d\mu_{z}(x) = \mathbf{E}_{\mu} \left[(\mathcal{L}\xi_{l})(x) \left| \xi(x) = z \right], \quad 1 \le l \le m,$$

$$\widetilde{\sigma}(z) = \left[\int_{\Sigma_{z}} \left(\nabla \xi a \nabla \xi^{T} \right)(x) d\mu_{z}(x) \right]^{\frac{1}{2}},$$
(10)

for $z \in \mathbb{R}^m$. We recall that, given a positive definite symmetric matrix X, $X^{\frac{1}{2}}$ denotes the unique positive definite symmetric matrix such that $X = X^{\frac{1}{2}}X^{\frac{1}{2}}$. And $\mathbf{E}_{\mu}[\cdot |\xi(x) = z]$ in (10) denotes the conditional expectation with respect to the probability measure μ . Furthermore, from [18, 32] we know that the effective dynamics (9) is again both reversible and ergodic with respect to the unique invariant measure $\tilde{\mu}$ on \mathbb{R}^m , whose probability density is Q(z), i.e.,

$$d\widetilde{\mu}(z) = Q(z) \, dz \,. \tag{11}$$

With the effective dynamics (9) at hand, it is natural to ask how good the SDE (9) is when z(s) is used to approximate the process $\xi(x(s))$. In literature, the approximation error of the effective dynamics has been studied using different criteria, such as entropy decay rate [18, 27], approximation of eigenvalues [32], and pathwise estimates [19]. As a continuation of the work [19], in the current paper we study pathwise estimates of the effective dynamics. While we are interested in the general case when the function ξ is nonlinear, we mention three concrete examples when the function

$$\xi(x) = (x_1, x_2, \cdots, x_m)^T, \quad \forall x \in \mathbb{R}^n$$
(12)

is a linear map, since they provide useful insights and strongly motivate our current study. For this purpose, let us denote by $I_{m\times m}$ the identity matrix of size m and write the state $x \in \mathbb{R}^n$ as $x = (z, y) \in \mathbb{R}^m \times \mathbb{R}^{n-m}$ where $y = (y_{m+1}, y_{m+2}, \cdots, y_n)^T$, i.e., the components are indexed from m+1 to n. Also let ϵ, δ denote two small parameters such that $0 < \epsilon, \delta \ll 1$. The following three cases are of particular interest.

1. Matrix $\sigma = I_{n \times n}$ and $V(z, y) = V_0(z, y) + \frac{1}{\epsilon}V_1(y)$, where V_0, V_1 are two potential functions and $0 < \epsilon \ll 1$. The SDE (1) becomes

$$dz_i(s) = -\frac{\partial V_0}{\partial z_i} (z(s), y(s)) ds + \sqrt{2\beta^{-1}} dw_i(s), \quad 1 \le i \le m,$$

$$dy_j(s) = -\frac{\partial V_0}{\partial y_j} (z(s), y(s)) ds - \frac{1}{\epsilon} \frac{\partial V_1}{\partial y_j} (y(s)) ds + \sqrt{2\beta^{-1}} dw_j(s), \quad m+1 \le j \le n.$$
(13)

2. Matrix σ is constant and is given by

$$\sigma \equiv \begin{pmatrix} I_{m \times m} & 0\\ 0 & \frac{1}{\sqrt{\delta}} I_{(n-m) \times (n-m)} \end{pmatrix}.$$
 (14)

The SDE (1) becomes

$$dz_i(s) = -\frac{\partial V}{\partial z_i}(z(s), y(s)) ds + \sqrt{2\beta^{-1}} dw_i(s), \quad 1 \le i \le m,$$

$$dy_j(s) = -\frac{1}{\delta} \frac{\partial V}{\partial y_j}(z(s), y(s)) ds + \sqrt{\frac{2\beta^{-1}}{\delta}} dw_j(s), \quad m+1 \le j \le n.$$
(15)

3. Matrix σ is given in (14) and $V(z, y) = V_0(z, y) + \frac{1}{\epsilon}V_1(y)$. The SDE (1) becomes

$$dz_{i}(s) = -\frac{\partial V_{0}}{\partial z_{i}} (z(s), y(s)) ds + \sqrt{2\beta^{-1}} dw_{i}(s), \quad 1 \le i \le m,$$

$$dy_{j}(s) = -\frac{1}{\delta} \frac{\partial V_{0}}{\partial y_{j}} (z(s), y(s)) ds - \frac{1}{\epsilon \delta} \frac{\partial V_{1}}{\partial y_{j}} (y(s)) ds + \sqrt{\frac{2\beta^{-1}}{\delta}} dw_{j}(s), \quad m+1 \le j \le n.$$
(16)

Among the above three cases, dynamics (15) in the second case is probably familiar, since it belongs to the typical slow-fast dynamics that has been widely studied using the standard averaging technique [26, 21, 28]. In this case, the probability measure μ_z in (7) is simply the invariant measure of the fast process y(s) in (15) when z(s) = z is fixed. Denoting by \mathcal{L}_0 the infinitesimal generator of the fast process in (15), we emphasize that the decomposition of the infinitesimal generator \mathcal{L} as

$$\mathcal{L} = \mathcal{L}_0 + \mathcal{L}_1 \tag{17}$$

plays an important role in order to derive convergence results of the system (15) when $\delta \rightarrow 0$ [26].

With the above observation on the concrete examples in mind, let us discuss three key ingredients of our approach, which enable us to obtain pathwise estimates of the effective dynamics for a general reaction coordinate function ξ , and in particular to provide a uniform treatment of the above three examples. Firstly, in analogy to the averaging technique in the study of SDE (15), given the SDE (1) and a nonlinear vectorial function ξ , we will make use of a similar decomposition of \mathcal{L} to (17), such that \mathcal{L}_0 corresponds to a diffusion process on Σ_z whose invariant measure is μ_z , for all $z \in \mathbb{R}^m$. Secondly, for each $z \in \mathbb{R}^m$, we introduce the Dirichlet form \mathcal{E}_z corresponding to \mathcal{L}_0 and μ_z on Σ_z . The separation of time scales in the dynamics (1) will be quantified by Poincaré inequality of the Dirichlet form \mathcal{E}_z . Thirdly, as the function ξ is assumed to be vector-valued, we apply Lieb's concavity theorem [20, 1] for positive definite symmetric matrices in order to get an estimate of the difference between two matrices in the noise term of SDEs. Combining these three ingredients together, we are able to generalize the pathwise estimates of [19] to the case when the reaction coordinate function ξ is either nonlinear or vector-valued. Since the time scale separation in the above three slow-fast examples can be characterized by the Poincaré inequality of \mathcal{E}_z in a uniform way, our pathwise estimate results can be applied to SDEs (13),(15), and (16).

The rest of the paper is organized as follows. In Section 2, after introducing necessary notations and assumptions, we state our main pathwise estimate results of this paper. In Section 3, we apply our pathwise estimate results to three different cases when there is a separation of time scales in the system (1). These cases are generalizations of the examples (13), (15), and (16), respectively. In Section 4, we prove a preliminary pathwise estimate result. Section 5 is devoted to the proof of pathwise estimates of effective dynamics, following the approach developed in [19]. In Appendix A, we consider the situation when there is a coordinate transformation such that the nonlinear reaction coordinate function can be locally reduced to a linear one. Appendix B contains the proof of Lemma 1 in Section 3. Finally, an error estimate of marginals under dissipative assumption is included in Appendix C.

2 Notations, assumptions, and main results

2.1 Notations

Let us further introduce some useful notations and quantities. The infinitesimal generator of the diffusion process (1) is given by [25]

$$\mathcal{L} = -a\nabla V \cdot \nabla + \frac{1}{\beta} (\nabla \cdot a) \cdot \nabla + \frac{1}{\beta} a : \nabla^{2}$$
$$= \frac{e^{\beta V}}{\beta} \sum_{1 \le i, j \le n} \frac{\partial}{\partial x_{i}} \left(a_{ij} e^{-\beta V} \frac{\partial}{\partial x_{j}} \right),$$
(18)

with the notation $a: \nabla^2 = \sum_{1 \le i,j \le n} a_{ij} \frac{\partial^2}{\partial x_i \partial x_j}$. Given two functions $f, h: \mathbb{R}^n \to \mathbb{R}$, we define the weighted inner product

$$\langle f, h \rangle_{\mu} = \int_{\mathbb{R}^n} f(x) h(x) d\mu(x) , \qquad (19)$$

whenever the right hand side exists. Using integration by parts, it is easy to verify that \mathcal{L} is a self-adjoint operator with respect to the inner product (19). The Dirichlet form of \mathcal{L} is defined as [3, 30]

$$\mathcal{E}(f,h) := -\langle \mathcal{L}f,h\rangle_{\mu} = -\langle f,\mathcal{L}h\rangle_{\mu} = \frac{1}{\beta} \int_{\mathbb{R}^n} (a\nabla f) \cdot \nabla h \, d\mu \,, \tag{20}$$

for all functions $f, h \in \text{Dom}(\mathcal{L})$.

In this work, we assume that the reaction coordinate function $\xi : \mathbb{R}^n \to \mathbb{R}^m$ defined in (4) is C^3 smooth. Given $z \in \mathbb{R}^m$ and $x \in \Sigma_z$, we define the $m \times m$ matrix $\Phi = \nabla \xi a \nabla \xi^T$, i.e.,

$$\Phi_{ij} = \nabla \xi_i \cdot (a \nabla \xi_j), \quad \forall 1 \le i, j \le m.$$
(21)

With a slight abuse of notation, in (21) we have denoted by $\nabla \xi_i$ the usual gradient of the function ξ_i , for $1 \leq i \leq m$. Assuming the vectors $\nabla \xi_1, \nabla \xi_2, \dots, \nabla \xi_m$ are linearly independent (see Assumption 1 in Subsection 2.2), we have that Φ is positive definite and therefore invertible. In this case, we denote by A the positive definite symmetric matrix given by

$$A(x) = \left(\nabla \xi a \nabla \xi^T\right)^{\frac{1}{2}}(x) = \Phi^{\frac{1}{2}}(x), \quad \forall \ x \in \mathbb{R}^n,$$
(22)

and we introduce the $n \times n$ matrix

$$\Pi = I - \sum_{1 \le i,j \le m} (\Phi^{-1})_{ij} \nabla \xi_i \otimes (a \nabla \xi_j), \qquad (23)$$

where $I = I_{n \times n}$ is the identity matrix of size n and \otimes is the tensor product of two vectors. $T_x \Sigma_z$ denotes the tangent space of the submanifold Σ_z at x, and $P: T_x \mathbb{R}^n \to T_x \Sigma_z$ is the orthogonal projection operator. It is straightforward to verify that Π satisfies

$$\Pi^{2} = \Pi, \quad \Pi^{T} a = a \Pi, \quad \Pi P = \Pi, \Pi \nabla \xi_{i} = 0, \quad \Pi^{T} \eta = \eta, \quad |\Pi \eta| \ge |\eta|,$$
(24)

for $\forall \eta \in T_x \Sigma_z$ and $1 \leq i \leq m$, where the last inequality follows from the fact

$$|\Pi\eta| |\eta| \ge (\Pi\eta) \cdot \eta = \eta \cdot (\Pi^T \eta) = |\eta|^2, \qquad \forall \eta \in T_x \Sigma_z.$$
(25)

Therefore, Π^T defines a skew projection operator from $T_x \mathbb{R}^n$ to $T_x \Sigma_z$ and it coincides with P if and only if a = I.

With the matrix Π and the expression of \mathcal{L} in (18), we can observe that \mathcal{L} can be decomposed as

$$\mathcal{L} = \mathcal{L}_0 + \mathcal{L}_1 \,, \tag{26}$$

where

$$\mathcal{L}_{0} = \frac{e^{\beta V}}{\beta} \sum_{1 \le i,j \le n} \frac{\partial}{\partial x_{i}} \left(e^{-\beta V} (a\Pi)_{ij} \frac{\partial}{\partial x_{j}} \right),$$

$$\mathcal{L}_{1} = \frac{e^{\beta V}}{\beta} \sum_{1 \le i,j \le n} \frac{\partial}{\partial x_{i}} \left(e^{-\beta V} (a(I - \Pi))_{ij} \frac{\partial}{\partial x_{j}} \right).$$
(27)

As already mentioned in the Introduction, an important property of the decomposition (26)-(27) is that, for each $z \in \mathbb{R}^m$, the operator \mathcal{L}_0 defines a diffusion process on the submanifold Σ_z whose invariant measure is μ_z defined in (7). Furthermore, we have

$$\int_{\Sigma_z} \mathcal{L}_0(fh) \, d\mu_z = 0 \,, \quad \text{and} \quad \int_{\Sigma_z} (\mathcal{L}_0 f) h \, d\mu_z = \int_{\Sigma_z} f(\mathcal{L}_0 h) \, d\mu_z \tag{28}$$

for any two smooth and bounded functions $f, h: \Sigma_z \to \mathbb{R}$. Notice that, in the above and below, we will adopt the same notations for both functions on Σ_z and their smooth extensions to \mathbb{R}^n . We refer to [31] for more details. Corresponding to the Dirichlet form \mathcal{E} in (20), we denote by \mathcal{E}_z the Dirichlet form of the operator \mathcal{L}_0 on Σ_z , i.e.,

$$\mathcal{E}_z(f,h) = -\int_{\Sigma_z} (\mathcal{L}_0 f) h \, d\mu_z \,, \tag{29}$$

for all $f, h: \Sigma_z \to \mathbb{R}$ and $f, h \in \text{Dom}(\mathcal{L}_0)$. Then, (24), (27) and (28) imply that

$$\mathcal{E}_{z}(f,h) = -\int_{\Sigma_{z}} (\mathcal{L}_{0}f) h \, d\mu_{z} = -\int_{\Sigma_{z}} f(\mathcal{L}_{0}h) \, d\mu_{z} = \frac{1}{\beta} \int_{\Sigma_{z}} (a\Pi\nabla f) \cdot (\Pi\nabla h) \, d\mu_{z} \,, \tag{30}$$

where the last expression is independent of the extensions f, h we choose.

On a final note, $||X||_F = \sqrt{\operatorname{tr}(X^T X)}$ denotes the Frobenius norm of a matrix X. Notations \mathbf{E}_{μ} , \mathbf{E}_{μ_z} , $\mathbf{E}_{\tilde{\mu}}$ will denote the mathematical expectations on the spaces \mathbb{R}^n , Σ_z , and \mathbb{R}^m with respect to the probability measures μ , μ_z , and $\tilde{\mu}$, respectively. By contrast, \mathbf{E} is reserved for the mathematical expectation of paths of the dynamics (1) starting from $x(0) \sim \mu$.

2.2 Assumptions

The following assumptions will be used in the current work.

Assumption 1. The function $\xi : \mathbb{R}^n \to \mathbb{R}^m$ is onto, C^3 smooth, and satisfies that $rank(\nabla \xi) = m$ at each $x \in \mathbb{R}^n$.

Remark 1. Using the terminology of differential manifold, the map ξ satisfying the condition $rank(\nabla \xi) = m$ at each point is called a submersion from \mathbb{R}^n to \mathbb{R}^m . The assumption that ξ maps onto \mathbb{R}^m implies that the set Σ_z in (6) is nonempty for all $z \in \mathbb{R}^m$. Furthermore, according to the regular value theorem [4], Σ_z is an (n-m)-dimensional submanifold of \mathbb{R}^n .

Assumption 2. $\exists L_b, L_\sigma > 0$, such that

$$\left|\widetilde{b}(z) - \widetilde{b}(z')\right| \le L_b |z - z'|, \quad \left\|\widetilde{\sigma}(z) - \widetilde{\sigma}(z')\right\|_F \le L_\sigma |z - z'|, \quad \forall z, z' \in \mathbb{R}^m.$$
(31)

Assumption 3. For the matrix-valued functions Π and A defined in (23) and (22) respectively, we have

$$\kappa_1^2 := \sum_{i=1}^m \int_{\mathbb{R}^n} (\Pi \nabla \mathcal{L}\xi_i) \cdot (a \Pi \nabla \mathcal{L}\xi_i) \, d\mu < +\infty \,,$$

$$\kappa_2^2 := \sum_{1 \le i,j \le m} \int_{\mathbb{R}^n} (\Pi \nabla A_{ij}) \cdot (a \Pi \nabla A_{ij}) \, d\mu < +\infty \,.$$
(32)

Assumption 4. For all $z \in \mathbb{R}^m$, the probability measure μ_z and the Dirichlet form \mathcal{E}_z satisfy the Poincaré inequality with a uniform constant $\rho > 0$, i.e.,

$$Var_{\mu_z}(f) := \int_{\Sigma_z} f^2 d\mu_z - \left(\int_{\Sigma_z} f d\mu_z\right)^2 \le \frac{1}{\rho} \mathcal{E}_z(f, f), \qquad (33)$$

for all $f: \Sigma_z \to \mathbb{R}$ such that $\mathcal{E}_z(f, f) < +\infty$.

When studying the process (1) under fixed initial condition, we also assume the following assumption.

Assumption 5. The Dirichlet form \mathcal{E} satisfies the Poincaré inequality with constant $\alpha > 0$, *i.e.*,

$$Var_{\mu}(f) = \int_{\mathbb{R}^n} f^2 d\mu - \left(\int_{\mathbb{R}^n} f d\mu\right)^2 \le \frac{1}{\alpha} \mathcal{E}(f, f)$$
(34)

holds for all functions $f : \mathbb{R}^n \to \mathbb{R}$ such that $\mathcal{E}(f, f) < +\infty$.

2.3 Main results

In order to state our pathwise estimate results, we need to first construct a version of the effective dynamics z(s), such that the Brownian motion $\tilde{w}(s)$ in (9) is coupled to the Brownian

motion w(s) in the original dynamics (1). For this purpose, we introduce the process $\widetilde{w}(s)$ which satisfies

$$d\widetilde{w}(s) = \left(A^{-1}\nabla\xi\sigma\right)(x(s))\,dw(s) = \left[\left(\nabla\xi a\nabla\xi^T\right)^{-\frac{1}{2}}\nabla\xi\sigma\right](x(s))\,dw(s)\,,\quad s\ge 0\,.\tag{35}$$

Using Lévy's characterization of Brownian motion and the relation $a = \sigma \sigma^T$, it is straightforward to verify that (35) indeed defines an *m*-dimensional Brownian motion. With this choice of the driving noise, the effective dynamics (9) becomes

$$dz(s) = \widetilde{b}(z(s)) \, ds + \sqrt{2\beta^{-1}} \widetilde{\sigma}(z(s)) \, d\widetilde{w}(s) = \widetilde{b}(z(s)) \, ds + \sqrt{2\beta^{-1}} \widetilde{\sigma}(z(s)) \Big[\big(\nabla \xi a \nabla \xi^T \big)^{-\frac{1}{2}} \nabla \xi \sigma \Big] (x(s)) \, dw(s) \,.$$
(36)

Accordingly, the difference between z(s) and $\xi(x(s))$ satisfies

$$d\big(\xi(x(s)) - z(s)\big) = \Big[(\mathcal{L}\xi)(x(s)) - \widetilde{b}(z(s))\Big] \, ds + \sqrt{2\beta^{-1}} \Big[\big(\nabla\xi a\nabla\xi^T\big)^{\frac{1}{2}}(x(s)) - \widetilde{\sigma}(z(s))\Big] \, d\widetilde{w}(s) \\ = \varphi(x(s)) \, ds + \Big[\widetilde{b}\big(\xi(x(s))\big) - \widetilde{b}(z(s))\Big] \, ds + \sqrt{2\beta^{-1}} \Big[A(x(s)) - \widetilde{\sigma}(z(s))\Big] \, d\widetilde{w}(s) \,,$$

$$(37)$$

where we have introduced the function $\varphi : \mathbb{R}^n \to \mathbb{R}^m$, given by

$$\varphi(x) = (\mathcal{L}\xi)(x) - \hat{b}(\xi(x)), \quad \forall \ x \in \mathbb{R}^n.$$
(38)

Let us first consider the case when the dynamics x(s) starts from equilibrium, i.e., $x(0) \sim \mu$. Using relatively simple argument, in Section 4 we obtain our first pathwise estimate of the effective dynamics, which is stated below.

Proposition 1. Suppose that Assumptions 1-4 hold. x(s) satisfies the SDE (1) starting from $x(0) \sim \mu$, and z(s) is the effective dynamics (36) with $z(0) = \xi(x(0))$. For all $t \ge 0$, we have

$$\mathbf{E}\Big(\sup_{0\le s\le t} \left|\xi(x(s)) - z(s)\right|^2\Big) \le \frac{3t}{\beta\rho} \Big(\kappa_1^2 t + \frac{32\kappa_2^2}{\beta}\Big) e^{Lt},\tag{39}$$

where $L = 3L_b^2 + \frac{48L_{\sigma}^2}{\beta} + 1.$

Following the approach of [19] and applying the forward-backward martingale method [22, 14], in Section 5, we prove the following improved pathwise estimate of the effective dynamics.

Theorem 1. Suppose that Assumptions 1-4 hold. x(s) satisfies the SDE (1) starting from $x(0) \sim \mu$, and z(s) is the effective dynamics (36) with $z(0) = \xi(x(0))$. For all $t \ge 0$, we have

$$\mathbf{E}\Big(\sup_{0\le s\le t} \left|\xi(x(s)) - z(s)\right|^2\Big) \le \frac{3t}{\beta\rho} \Big(\frac{27\kappa_1^2}{2\rho} + \frac{32\kappa_2^2}{\beta}\Big)e^{Lt},\tag{40}$$

where $L = 3L_b^2 + \frac{48L_{\sigma}^2}{\beta} + 1$.

Remark 2. We make two remarks.

1. Theorem 1 replies on global Lipschitz conditions (Assumption 2) on the coefficients of the effective dynamics. Alternatively, in Appendix C we show that the dissipative assumption [21, 9] can be exploited as well, in order to obtain estimate of $\mathbf{E}|\xi(x(t)) - z(t)|^2$, i.e., the mean square error of the marginals between the two processes.

2. The setting of [19] corresponds to the case when $a = I_{n \times n}$ and the function ξ is linear. In this case, the constant $\kappa_2 = 0$ and the forward-backward martingale method indeed improves the pathwise estimate error from $\mathcal{O}(\frac{1}{\rho})$ to $\mathcal{O}(\frac{1}{\rho^2})$. However, in general cases when either ξ is nonlinear or the matrix a is non-identity, κ_2 is typically non-zero and the error bound (40) is still $\mathcal{O}(\frac{1}{\rho})$, i.e., the same as Proposition 1. This is partially due to the existence of the martingale term in (37). Nevertheless, the dependence of the error bound (40) on the parameter κ_2 seems necessary. And from Assumption 3 we can observe that κ_2 will be small when the matrix function A in (22) is close to a constant on each submanifold Σ_z .

Now we turn to more general initial conditions. Applying Theorem 1, in Section 5 we will prove the following pathwise estimate result.

Theorem 2. Suppose that Assumptions 1-4 hold. x(s) satisfies the SDE (1) and z(s) is the effective dynamics (36) with $z(0) = \xi(x(0))$.

1. Suppose $x(0) \sim \bar{\mu}$, where the probability measure $\bar{\mu}$ is absolutely continuous with respect to μ such that

$$\int_{\mathbb{R}^n} \left(\frac{d\bar{\mu}}{d\mu}\right)^2 d\mu < +\infty \,.$$

Then, for all $t \ge 0$, we have

$$\mathbf{E}\bigg(\sup_{0\leq s\leq t} \left|\xi(x(s)) - z(s)\right| \left| x(0) \sim \bar{\mu}\right) \leq \sqrt{t} \bigg(\frac{9\kappa_1}{\sqrt{2\beta\rho}} + \frac{12\kappa_2}{\beta\sqrt{\rho}}\bigg) \bigg[\int_{\mathbb{R}^n} \bigg(\frac{d\bar{\mu}}{d\mu}\bigg)^2 d\mu\bigg]^{\frac{1}{2}} e^{Lt}, \quad (41)$$

where $L = \frac{3}{2}L_b^2 + \frac{24L_{\sigma}^2}{\beta} + \frac{1}{2}.$

Suppose x(0) = x' ∈ ℝⁿ is fixed and that Assumption 5 holds. Both the function φ in (38) and the matrix A in (22) are bounded on ℝⁿ, i.e., |φ(x)| ≤ C₁ and ||A(x)||_F ≤ C₂, ∀x ∈ ℝⁿ, for some C₁, C₂ > 0. Let μ_s be the probability measure of x(s) for s ≥ 0 and denote p_s = dμ_s/dμ when s > 0. Given any 0 < t₀ ≤ t₁ ≤ t, we have

$$\mathbf{E}\left(\sup_{0\leq s\leq t}\left|\xi(x(s))-z(s)\right| \mid x(0)=x'\right) \\
\leq \left\{\sqrt{t}\left(\frac{9\kappa_1}{\sqrt{2\beta\rho}}+\frac{12\kappa_2}{\beta\sqrt{\rho}}\right)\left[1+e^{-\alpha(t_1-t_0)}\left(\int_{\mathbb{R}^n}p_{t_0}^2d\mu\right)^{\frac{1}{2}}\right]+\sqrt{t_1}\left(3C_1\sqrt{t_1}+\frac{18C_2}{\sqrt{\beta}}\right)\right\}e^{Lt},$$
(42)

where $L = \frac{3}{2}L_b^2 + \frac{24L_{\sigma}^2}{\beta} + \frac{1}{2}$ and α is the Poincaré constant in (34).

Remark 3. Notice that μ_0 in Theorem 2 will be a delta measure when x(s) starts from a fixed initial condition x(0) = x'. The time $t_0 > 0$ is introduced to make sure that $\int_{\mathbb{R}^n} p_{t_0}^2 d\mu < +\infty$. We point out that Assumption 5 is not needed when $t_1 = t_0$, and in this case (42) becomes

$$\mathbf{E}\left(\sup_{0\leq s\leq t} \left|\xi(x(s)) - z(s)\right| \mid x(0) = x'\right) \\
\leq \left\{\sqrt{t}\left(\frac{9\kappa_1}{\sqrt{2\beta\rho}} + \frac{12\kappa_2}{\beta\sqrt{\rho}}\right) \left[1 + \left(\int_{\mathbb{R}^n} p_{t_0}^2 d\mu\right)^{\frac{1}{2}}\right] + \sqrt{t_0}\left(3C_1\sqrt{t_0} + \frac{18C_2}{\sqrt{\beta}}\right)\right\} e^{Lt}.$$
(43)

Comparing to (43), the estimate (42) allows us to further optimize the upper bound of the error estimate by varying $t_1 \in [t_0, t]$, under Assumption 5.

In the next section, we will apply Theorem 1 to three different scenarios when there is time scale separation in the system. We refer to Corollary 1-3 in Section 3 for the pathwise estimate result in each case.

3 Separation of time scales in diffusion processes

Our pathwise estimates of the effective dynamics rely on Assumption 4, which characterizes the existence of the time scale separation in the system (1). In this section, we consider the relation between the structure of the SDE (1) and the emergence of the time scale separation phenomena in the process x(x). We apply our pathwise estimates to different scenarios, and in particular we obtain pathwise estimates of the effective dynamics for the SDEs (13), (15), and (16) in the Introduction.

Roughly speaking, the time scales of the dynamics (1) are related to the magnitudes of coefficients in the infinitesimal generator \mathcal{L} . With the choice of the reaction coordinate function ξ in (4) and the corresponding decomposition (26)-(27) of the infinitesimal generator \mathcal{L} , we are interested in cases when

operator
$$\mathcal{L}_0$$
 contains large coefficients, while \mathcal{L}_1 does not. (44)

As we will see, condition (44) often implies that the operator \mathcal{L}_0 has a large spectral gap while the process $\xi(x(s))$ evolves relatively slowly. From the expression of \mathcal{L}_0 in (27), we can observe that large coefficients in \mathcal{L}_0 may come from either the potential V or the (eigenvalues of) matrix a. Motivated by the concrete examples (13), (15), and (16) in the Introduction, in the following we consider three different cases. For simplicity, we will assume the existence of small parameters ϵ or δ whose specific values are not necessarily known, such that the magnitudes of small and large quantities correspond to $\mathcal{O}(1)$ and $\mathcal{O}(\frac{1}{\epsilon})$ (or $\mathcal{O}(\frac{1}{\delta})$), respectively.

Case 1. In the first case, let us assume that the potential V contains stiff components of $\mathcal{O}(\frac{1}{\epsilon})$, while the eigenvalues of matrix a are $\mathcal{O}(1)$. From expressions in (27), we see that the condition (44) holds if

$$\Pi^{T} a \nabla V = \mathcal{O}\left(\frac{1}{\epsilon}\right), \quad \text{and} \quad (I - \Pi^{T}) a \nabla V = \mathcal{O}(1).$$
(45)

Since Π^T is a skew projection operator from $T_x \mathbb{R}^n$ to $T_x \Sigma_z$ at each $x \in \mathbb{R}^n$, (45) is equivalent to that the stiff component of $a \nabla V$ lies in the subspace $T_x \Sigma_z$ at each x. As a concrete example, assume that the potential V takes the form

$$V(x) = V_0(x) + \frac{1}{\epsilon} V_1(x),$$
(46)

where $V_0, V_1 : \mathbb{R}^n \to \mathbb{R}$ are two potential functions, $\epsilon > 0$ is a small parameter and that the condition

$$(I - \Pi)^T a \nabla V_1 \equiv 0 \tag{47}$$

is satisfied at each x. Clearly, in this case we have

$$\Pi^T a \nabla V = \Pi^T a \nabla V_0 + \frac{1}{\epsilon} a \nabla V_1$$

$$(I - \Pi)^T a \nabla V = (I - \Pi)^T a \nabla V_0 ,$$
(48)

which implies that the condition (44) holds. In fact, corresponding to the potential V in (46), the probability measure μ_z in (7) becomes

$$d\mu_z(x) = \frac{1}{Z Q(z)} \exp\left[-\beta \left(V_0(x) + \frac{1}{\epsilon} V_1(x)\right)\right] \left[\det(\nabla \xi \nabla \xi^T)(x)\right]^{-\frac{1}{2}} d\nu_z(x), \qquad (49)$$

for each $z \in \mathbb{R}^m$. This measure indeed satisfies a Poincaré inequality with a large spectral gap if the potential V_1 is convex on Σ_z . Precisely, we have the following result.

Lemma 1. Suppose the function V_0 in (46) is bounded on Σ_z . V_1 is both C^2 smooth and Kconvex on Σ_z for some K > 0. Matrix a satisfies the uniform elliptic condition (2) with some constant $c_1 > 0$, and the function ξ has bounded derivatives up to order 3. Then $\exists \epsilon_0, C \geq 0$, which may depend on V_0 , a, ξ and β , such that when $\epsilon \leq \epsilon_0$, the Poincaré inequality

$$Var_{\mu_z}(f) = \int_{\Sigma_z} f^2 d\mu_z - \left(\int_{\Sigma_z} f d\mu_z\right)^2 \le \frac{C\epsilon}{c_1 K} \mathcal{E}_z(f, f)$$
(50)

holds for all functions $f: \Sigma_z \to \mathbb{R}$ which satisfy $\mathcal{E}_z(f, f) < +\infty$.

The proof of Lemma 1 can be found in Appendix B. Applying Theorem 1 and Lemma 1, we can obtain the pathwise estimate of the effective dynamics in this case.

Corollary 1. Assume Assumptions 1-2 hold. Let the potential V be given in (46), where $\epsilon > 0$ is a small parameter, such that the assumptions of Lemma 1 hold uniformly for $z \in \mathbb{R}^m$. Further suppose that the condition (47) is satisfied. Let x(s) satisfy the SDE (1) starting from $x(0) \sim \mu$, and z(s) be the effective dynamics (36) with $z(0) = \xi(x(0))$. Define $L = 3L_b^2 + \frac{48L_{\sigma}^2}{\beta} + 1$. Then $\exists \epsilon_0 \geq 0$, such that when $\epsilon \leq \epsilon_0$, we have

$$\mathbf{E}\Big(\sup_{0\leq s\leq t}\left|\xi(x(s))-z(s)\right|^2\Big)\leq t\Big(\frac{C_1\epsilon}{K}+\frac{C_2\epsilon^2}{K^2}\Big)e^{Lt}\,,\tag{51}$$

for some constants $C_1, C_2 > 0$ which are independent of ϵ and K.

Proof. From the definition of \mathcal{L} in (18), the condition (47), as well as the boundedness of both the matrix a and $\nabla \xi$, we know that Assumption 3 holds with constants κ_1, κ_2 which are independent of ϵ . Lemma 1 implies that Assumption 4 is met with $\rho = \frac{c_1 K}{C \epsilon}$. Therefore, the estimate (51) follows by applying Theorem 1.

Remark 4. Given $x \in \mathbb{R}^n$, in Appendix A we will study the condition under which there exists a function $\phi : \mathbb{R}^n \to \mathbb{R}^{n-m}$ and a coordinate transformation $G(x) = (\xi(x), \phi(x))$, such that G is one to one in a neighborhood of x and that

$$\nabla \xi a \nabla \phi^T \equiv 0 \tag{52}$$

is satisfied. See the condition (109) in Appendix A. For simplicity, let us assume that the map ϕ exists globally such that G is one to one from \mathbb{R}^n to itself. In this case, Assuming the potential V is given in (46) with $V_1(x) = \widetilde{V}_1(\phi(x))$ for some function $\widetilde{V}_1 : \mathbb{R}^{n-m} \to \mathbb{R}$, then (47) holds because of (52), and the SDE of $\overline{y}(s) = \phi(x(s))$ has a large drift term which involves the small parameter ϵ , while the SDE of $\overline{z}(s) = \xi(x(s))$ is independent of ϵ . See (110) in Appendix A for details. According to Proposition 4 in Appendix A and Lemma 1 above, the invariant measure of

the dynamics $\bar{x}(s) = G^{-1}(z, \bar{y}(s)) \in \Sigma_z$ with $\bar{z}(s) = z$ being fixed (see (117)) is μ_z and satisfies the Poincaré inequality (50). As a concrete example, consider the linear reaction coordinate case when

$$\xi = (x_1, x_2, \cdots, x_m)^T, \quad \phi = (x_{m+1}, \cdots, x_n)^T,$$
(53)

and $a \equiv I_{n \times n}$, where the potential function $V_1(x) = V_1(x_{m+1}, \dots, x_n)$ is independent of the first m components of x. In this case, we have

$$\Phi = I_{m \times m}, \quad \Pi = \begin{pmatrix} 0 & 0 \\ 0 & I_{(n-m) \times (n-m)} \end{pmatrix}, \tag{54}$$

and the dynamics (1) reduces to the SDE (13) in the Introduction. Correspondingly, the constant $C_1 = 0$ in (51), since $\kappa_2 = 0$ in Assumption 3. Therefore, we have the pathwise estimate

$$\mathbf{E}\left(\sup_{0\le s\le t}\left|\xi(x(s)) - z(s)\right|^{2}\right) \le \frac{C_{2}\epsilon^{2}t}{K^{2}}e^{Lt}.$$
(55)

Case 2. In the second case, let us assume that the potential function V is $\mathcal{O}(1)$, but the matrix a has widely spread eigenvalues at two different orders of magnitude. Specifically, suppose that the eigenvalues λ_i of a satisfy that $\lambda_i = \mathcal{O}(1)$ for $1 \leq i \leq m$, and $\lambda_i = \mathcal{O}(\frac{1}{\delta})$ for $m+1 \leq i \leq n$. Furthermore, the reaction coordinate function ξ is chosen in a way such that at each state x the linear subspace

$$\operatorname{span}\left\{\nabla\xi_1, \nabla\xi_2, \cdots, \nabla\xi_m\right\}$$
(56)

coincides with the subspace spanned by the eigenvectors of matrix a which correspond to the (small) eigenvalues $\lambda_1, \lambda_2, \dots, \lambda_m$. Since the projection matrix Π^T satisfies (24), in this case we have

$$\Pi^{T} a = a\Pi = \mathcal{O}\left(\frac{1}{\delta}\right), \quad \text{and} \quad (I - \Pi^{T})a = a(I - \Pi) = \mathcal{O}(1).$$
(57)

Therefore, from expressions in (27) we can conclude that the condition (44) is satisfied. Notice that, different from the previous case, now the probability measure μ_z in (7) does not depend on δ , while the Dirichlet form \mathcal{E}_z in (30) does. Concerning the Poincaré inequality, we have the following straightforward result.

Lemma 2. Given $\rho_0, \delta > 0$. Recall that P is the orthogonal projection operator from $T_x \mathbb{R}^n$ to $T_x \Sigma_z$. Assume that the probability measure μ_z satisfies

$$Var_{\mu_z}(f) = \int_{\Sigma_z} f^2 d\mu_z - \left(\int_{\Sigma_z} f d\mu_z\right)^2 \le \frac{1}{\beta\rho_0} \int_{\Sigma_z} |P\nabla f|^2 d\mu_z , \qquad (58)$$

for all functions $f: \Sigma_z \to \mathbb{R}$ such that $\int_{\Sigma_z} |P\nabla f|^2 d\mu_z < +\infty$ (after being extended to a function on \mathbb{R}^n). Also assume the matrices a and Π satisfy

$$(a\Pi\eta) \cdot \eta \ge \frac{c_2}{\delta} |\eta|^2 \,, \quad \forall \eta \in T_x \Sigma_z \,, \, \forall x \in \Sigma_z \,, \tag{59}$$

for some $c_2 > 0$, which is independent of δ . Then we have the Poincaré inequality

$$Var_{\mu_z}(f) = \int_{\Sigma_z} f^2 d\mu_z - \left(\int_{\Sigma_z} f d\mu_z\right)^2 \le \frac{\delta}{c_2 \rho_0} \mathcal{E}_z(f, f), \qquad (60)$$

for all functions $f: \Sigma_z \to \mathbb{R}$ such that $\mathcal{E}_z(f, f) < +\infty$.

Proof. Notice that (24) implies $\Pi P = \Pi$ and $\Pi^T a \Pi = a \Pi^2 = a \Pi$. Since $P \nabla f \in T_x \Sigma_z$, using (59) we can deduce

$$|P\nabla f|^2 \leq \frac{\delta}{c_2} (a \Pi P \nabla f) \cdot (P \nabla f) = \frac{\delta}{c_2} (\Pi^T a \Pi \nabla f) \cdot (P \nabla f) = \frac{\delta}{c_2} (a \Pi \nabla f) \cdot (\Pi \nabla f) \,.$$

The conclusion (60) follows by recalling the definition of \mathcal{E}_z in (30).

Applying Theorem 1 and Lemma 2, we can obtain the pathwise estimate of the effective dynamics in this case.

Corollary 2. Assume Assumptions 1-2 hold. Suppose that the matrix a satisfies the uniform elliptic condition (2) with some constant $c_1 > 0$, and the function ξ has bounded derivatives up to order 2. Furthermore, the matrices a and Π satisfy

$$\frac{c_2}{\delta}|\eta|^2 \le (a\Pi\eta) \cdot \eta \le \frac{c_2'}{\delta}|\eta|^2, \quad \forall \eta \in T_x \Sigma_z, \ \forall x \in \Sigma_z, \ z \in \mathbb{R}^m,$$
(61)

for some $0 < c_2 \leq c'_2$, which are independent of $\delta > 0$. Suppose μ_z satisfies the Poincaré inequality (58) with the constant $\rho_0 > 0$, uniformly for $z \in \mathbb{R}^m$. The matrix A in (22) is bounded with bounded derivatives up to order 2. Let x(s) satisfy the SDE (1) starting from $x(0) \sim \mu$, and z(s) be the effective dynamics (36) with $z(0) = \xi(x(0))$. Define $L = 3L_b^2 + \frac{48L_a^2}{\beta} + 1$. We have

$$\mathbf{E}\left(\sup_{0\leq s\leq t}\left|\xi(x(s))-z(s)\right|^{2}\right)\leq t\left(\frac{C_{1}}{\rho_{0}}+\frac{C_{2}\delta}{\rho_{0}^{2}}\right)e^{Lt},$$
(62)

for some constants $C_1, C_2 > 0$ which are independent of δ and ρ_0 .

Proof. Condition (61) implies that Assumption 3 holds but the constants κ_1, κ_2 may depend on δ such that $\kappa_1^2, \kappa_2^2 \leq \frac{C}{\delta}$, for some C > 0. Assumption 4 is met with $\rho = \frac{c_2\rho_0}{\delta}$ as a consequence of Lemma 2. Therefore, the estimate (62) follows by applying Theorem 1.

Remark 5. Consider the function ϕ in Appendix A which satisfies the condition $\nabla \xi a \nabla \phi^T \equiv 0$. In this case, the subspace span $\{\nabla \phi_1, \nabla \phi_2, \dots, \nabla \phi_{n-m}\}$ coincides with the subspace spanned by the eigenvectors of matrix a which correspond to the large eigenvalues $\lambda_{m+1}, \lambda_{m+2}, \dots, \lambda_n$. And we have

$$\begin{pmatrix} \nabla \xi \\ \nabla \phi \end{pmatrix} a \begin{pmatrix} \nabla \xi^T & \nabla \phi^T \end{pmatrix} = \begin{pmatrix} \nabla \xi a \nabla \xi^T & 0 \\ 0 & \nabla \phi a \nabla \phi^T \end{pmatrix} = \begin{pmatrix} \mathcal{O}(1) & 0 \\ 0 & \mathcal{O}(\frac{1}{\delta}) \end{pmatrix}.$$
 (63)

Therefore, we can observe that the dynamics of $\phi(x(s))$ will be fast, while the dynamics of $\xi(x(s))$ is relatively slow. See the equation (110) in Appendix A. As a concrete example, consider the linear case in (53) with the matrix

$$a \equiv \begin{pmatrix} I_{m \times m} & 0\\ 0 & \frac{1}{\delta} I_{(n-m) \times (n-m)} \end{pmatrix}, \tag{64}$$

where we have recovered the SDE (15) in the Introduction. In this case, in analogy to Remark 4, we have $C_1 = 0$ in (62) and the pathwise estimate becomes

$$\mathbf{E}\left(\sup_{0\leq s\leq t}\left|\xi(x(s))-z(s)\right|^{2}\right)\leq \frac{C_{2}\delta t}{\rho_{0}^{2}}e^{Lt}.$$
(65)

In the general case, however, it is important to point out that the error bound (62) can still be large even when the time scale separation parameter δ is small. We refer to Remark 2, as well as the previous work [21] for relevant discussions when ξ is linear and a is non-identity matrix.

Case 3. In the third case, we consider the combination of the above two cases, i.e., the potential V is given in (46) and the matrix a has large eigenvalues such that (57) is satisfied. The following lemma is a direct application of Lemma 1 and Lemma 2.

Lemma 3. Given $\epsilon, \delta > 0$. Under the assumptions of Lemma 1 and assume the matrices a and Π satisfy (59) for some $c_2 > 0$, which is independent of ϵ, δ . Then $\exists \epsilon_0, C \geq 0$, which may depend on V_0 , a, ξ and β , such that when $\epsilon \leq \epsilon_0$, we have the Poincaré inequality

$$Var_{\mu_z}(f) = \int_{\Sigma_z} f^2 d\mu_z - \left(\int_{\Sigma_z} f d\mu_z\right)^2 \le \frac{C\epsilon\delta}{c_2 K} \mathcal{E}_z(f, f),$$
(66)

for all functions $f: \Sigma_z \to \mathbb{R}$ which satisfy $\mathcal{E}_z(f, f) < +\infty$.

Proof. In the proof of Lemma 1 in Appendix B, we have actually proved that (58) is satisfied with $\rho_0 = \frac{K}{C\epsilon}$, for some constant C > 0. See (138) for details. Therefore, the Poincaré inequality (66) follows as a direct consequence of Lemma 2.

Applying Theorem 1 and Lemma 3, we can obtain the pathwise estimate of the effective dynamics in this case.

Corollary 3. Assume Assumptions 1-2 hold. Let the potential V be given in (46), where $\epsilon > 0$ is a small parameter, and suppose that the condition (47) is satisfied. Assume the assumptions of Lemma 1 hold uniformly for $z \in \mathbb{R}^m$. Matrices a and Π satisfy (61) for some $0 < c_2 \le c'_2$, which are independent of ϵ, δ . x(s) satisfies the SDE (1) starting from $x(0) \sim \mu$, and z(s) is the effective dynamics (36) with $z(0) = \xi(x(0))$. Define $L = 3L_b^2 + \frac{48L_{\sigma}^2}{\beta} + 1$. Then $\exists \epsilon_0 \ge 0$, such that when $\epsilon \le \epsilon_0$, we have

$$\mathbf{E}\left(\sup_{0\le s\le t}\left|\xi(x(s)) - z(s)\right|^{2}\right) \le t\left(\frac{C_{1}\epsilon}{K} + \frac{C_{2}\epsilon^{2}\delta}{K^{2}}\right)e^{Lt},\tag{67}$$

for some constants $C_1, C_2 > 0$ which are independent of ϵ , δ and K.

Proof. The proof is similar to that of Corollary 2, by noticing that $\kappa_1^2, \kappa_2^2 \leq \frac{C}{\delta}$ and Assumption 4 holds with $\rho = \frac{CK}{\epsilon\delta}$, for some C > 0.

Remark 6. Consider the linear case (53) in Remark 4 and assume the potential V is given in (46) with $V_1(x) = V_1(x_{m+1}, \dots, x_n)$. Also let the matrix a be given in (64), then we recover the SDE (16) in the Introduction. Correspondingly, in this case $C_1 = 0$ in (67) and therefore we have the pathwise estimate

$$\mathbf{E}\left(\sup_{0\le s\le t}\left|\xi(x(s))-z(s)\right|^{2}\right)\le \frac{C_{2}\epsilon^{2}\delta t}{K^{2}}e^{Lt}.$$
(68)

4 Preliminary pathwise estimates : Proof of Proposition 1

In this section, after deriving two useful lemmas, we prove our first version of pathwise estimate of the effective dynamics.

Lemma 4. Recall that μ is the invariant measure in (3) and let φ be the function defined in (38). Under Assumption 1, Assumption 3 and Assumption 4, we have

$$\mathbf{E}_{\mu}|\varphi|^{2} = \int_{\mathbb{R}^{n}} |\varphi|^{2} d\mu \leq \frac{\kappa_{1}^{2}}{\beta\rho}.$$
(69)

Proof. From the definition of the function \tilde{b} in (10), we have $\int_{\Sigma_z} \varphi(x) d\mu_z(x) = 0, \forall z \in \mathbb{R}^m$. Furthermore, (24) and (38) imply that $\Pi \nabla \varphi_i = \Pi \nabla \mathcal{L} \xi_i$, for $1 \leq i \leq m$. Therefore, applying Assumptions 3-4 and using the expression of the Dirichlet form \mathcal{E}_z in (30), we can derive

$$\begin{split} \int_{\mathbb{R}^n} |\varphi|^2 \, d\mu &= \sum_{i=1}^m \int_{\mathbb{R}^m} \left(\int_{\Sigma_z} |\varphi_i|^2 \, d\mu_z \right) Q(z) \, dz \\ &\leq \sum_{i=1}^m \frac{1}{\rho} \int_{\mathbb{R}^m} \mathcal{E}_z(\varphi_i, \varphi_i) \, Q(z) \, dz \\ &= \sum_{i=1}^m \frac{1}{\beta\rho} \int_{\mathbb{R}^n} (\Pi \nabla \varphi_i) \cdot (a \Pi \nabla \varphi_i) \, d\mu \\ &= \sum_{i=1}^m \frac{1}{\beta\rho} \int_{\mathbb{R}^n} (\Pi \nabla \mathcal{L}\xi_i) \cdot (a \Pi \nabla \mathcal{L}\xi_i) \, d\mu = \frac{\kappa_1^2}{\beta\rho} \, . \end{split}$$

We also need to estimate the Frobenius norm of the difference of the two matrices which appeared in the noise term of the equation (37).

Lemma 5. Assume Assumption 1 holds. Recall the positive definite symmetric matrix functions $\tilde{\sigma}$, A defined in (10) and (22), respectively. We have

$$\mathbf{E}_{\mu} \| A - \widetilde{\sigma} \circ \xi \|_{F}^{2} = \mathbf{E}_{\mu} \| A - (\mathbf{E}_{\mu_{z}} A) \circ \xi \|_{F}^{2} + \mathbf{E}_{\mu} \| (\widetilde{\sigma} - \mathbf{E}_{\mu_{z}} A) \circ \xi \|_{F}^{2},$$
(70)

and

$$\mathbf{E}_{\mu} \left\| A - (\mathbf{E}_{\mu_{z}} A) \circ \xi \right\|_{F}^{2} \leq \mathbf{E}_{\mu} \left\| A - \widetilde{\sigma} \circ \xi \right\|_{F}^{2} \leq 2 \mathbf{E}_{\mu} \left\| A - (\mathbf{E}_{\mu_{z}} A) \circ \xi \right\|_{F}^{2}.$$
(71)

Further suppose that Assumption 3 and Assumption 4 hold, then we have

$$\mathbf{E}_{\mu} \left\| A - \widetilde{\sigma} \circ \xi \right\|_{F}^{2} \leq \frac{2\kappa_{2}^{2}}{\beta\rho}.$$
(72)

Proof. From the definitions (10) and (22), we have $\tilde{\sigma}(z) = (\mathbf{E}_{\mu_z} A^2)^{\frac{1}{2}}, \forall z \in \mathbb{R}^m$. Direct calculation shows that

$$\begin{aligned} \mathbf{E}_{\mu} \left\| A - \widetilde{\sigma} \circ \xi \right\|_{F}^{2} \\ &= \int_{\mathbb{R}^{m}} \left(\mathbf{E}_{\mu_{z}} \left\| A - (\mathbf{E}_{\mu_{z}} A^{2})^{\frac{1}{2}} \right\|_{F}^{2} \right) Q(z) \, dz \\ &= \int_{\mathbb{R}^{m}} \left[2 \operatorname{tr}(\mathbf{E}_{\mu_{z}} A^{2}) - 2 \operatorname{tr}\left((\mathbf{E}_{\mu_{z}} A) \left(\mathbf{E}_{\mu_{z}} A^{2} \right)^{\frac{1}{2}} \right) \right] Q(z) \, dz \\ &= \int_{\mathbb{R}^{m}} \left[\mathbf{E}_{\mu_{z}} \left(\operatorname{tr} \left(A - \mathbf{E}_{\mu_{z}} A \right)^{2} \right) + \operatorname{tr} \left(\left((\mathbf{E}_{\mu_{z}} A^{2})^{\frac{1}{2}} - \mathbf{E}_{\mu_{z}} A \right)^{2} \right) \right] Q(z) \, dz \\ &= \mathbf{E}_{\mu} \left\| A - \left(\mathbf{E}_{\mu_{z}} A \right) \circ \xi \right\|_{F}^{2} + \mathbf{E}_{\mu} \left\| \left(\widetilde{\sigma} - \mathbf{E}_{\mu_{z}} A \right) \circ \xi \right\|_{F}^{2}, \end{aligned}$$

$$(73)$$

from which the equality (70) and the lower bound in (71) follow. For the upper bound in (71), applying Lieb's concavity theorem [20, 1], we can estimate

$$\operatorname{tr}\left((\mathbf{E}_{\mu_{z}}A)(\mathbf{E}_{\mu_{z}}A^{2})^{\frac{1}{2}}\right) \geq \mathbf{E}_{\mu_{z}}\operatorname{tr}\left((\mathbf{E}_{\mu_{z}}A)A(\cdot)\right) = \operatorname{tr}\left(\left(\mathbf{E}_{\mu_{z}}A\right)^{2}\right),\tag{74}$$

and therefore (73) implies

$$\mathbf{E}_{\mu} \| A - \widetilde{\sigma} \circ \xi \|_{F}^{2} \\
\leq 2 \int_{\mathbb{R}^{m}} \left[\operatorname{tr} (\mathbf{E}_{\mu_{z}} A^{2}) - \operatorname{tr} \left((\mathbf{E}_{\mu_{z}} A)^{2} \right) \right] Q(z) \, dz \\
= 2 \int_{\mathbb{R}^{m}} \left[\operatorname{tr} \left(\mathbf{E}_{\mu_{z}} \left(A - \mathbf{E}_{\mu_{z}} A \right)^{2} \right) \right] Q(z) \, dz \\
= 2 \, \mathbf{E}_{\mu} \| A - (\mathbf{E}_{\mu_{z}} A) \circ \xi \|_{F}^{2}.$$
(75)

Finally, under Assumption 3 and Assumption 4, applying Poincaré inequality, we obtain

$$\begin{aligned} \mathbf{E}_{\mu} \| A - \widetilde{\sigma} \circ \xi \|_{F}^{2} \\ &\leq 2 \int_{\mathbb{R}^{m}} \left[\operatorname{tr} \left(\mathbf{E}_{\mu_{z}} \left(A - \mathbf{E}_{\mu_{z}} A \right)^{2} \right) \right] Q(z) \, dz \\ &= 2 \sum_{1 \leq i, j \leq m} \int_{\mathbb{R}^{m}} \left[\mathbf{E}_{\mu_{z}} \left(A_{ij} - \mathbf{E}_{\mu_{z}} A_{ij} \right)^{2} \right] Q(z) \, dz \\ &\leq \frac{2}{\rho} \sum_{1 \leq i, j \leq m} \int_{\mathbb{R}^{m}} \mathcal{E}_{z}(A_{ij}, A_{ij}) \, Q(z) \, dz = \frac{2\kappa_{2}^{2}}{\beta \rho} \,. \end{aligned}$$

Applying the above two lemmas, we are ready to prove the first pathwise estimate Proposition 1.

Proof of Proposition 1. Recall the function φ defined in (38). From (37), we have

$$\xi(x(t)) - z(t) = \int_0^t \varphi(x(s)) \, ds + \int_0^t \left(\tilde{b}(\xi(x(s))) - \tilde{b}(z(s)) \right) \, ds + \sqrt{2\beta^{-1}} M(t) \,, \tag{76}$$

where M(t) denotes the martingale term

$$M(t) = \int_0^t \left(A(x(s)) - \widetilde{\sigma}(z(s)) \right) d\widetilde{w}(s) , \qquad (77)$$

with the matrix-valued function A defined in (22). Therefore, squaring both sides of (76), using Assumption 2 and the elementary inequality $(a+b+c)^2 \leq 3(a^2+b^2+c^2), \forall a, b, c \in \mathbb{R}$, we obtain

$$\left|\xi(x(t)) - z(t)\right|^{2} \leq 3 \left| \int_{0}^{t} \varphi(x(s)) \, ds \right|^{2} + 3L_{b}^{2} \left(\int_{0}^{t} \left|\xi(x(s)) - z(s)\right| \, ds \right)^{2} + \frac{6}{\beta} \left|M(t)\right|^{2}.$$

Taking supremum followed by mathematical expectation in the above inequality, we get

$$\mathbf{E} \Big(\sup_{0 \le t' \le t} \left| \xi(x(t')) - z(t') \right|^2 \Big) \\
\le 3 \mathbf{E} \Big[\sup_{0 \le t' \le t} \left| \int_0^{t'} \varphi(x(s)) \, ds \right|^2 \Big] + 3 L_b^2 \, \mathbf{E} \Big(\int_0^t \left| \xi(x(s)) - z(s) \right| \, ds \Big)^2 + \frac{6}{\beta} \mathbf{E} \sup_{0 \le s \le t} \left| M(s) \right|^2.$$
(78)

To estimate the right hand side of (78), we notice that $x(s) \sim \mu$ for $s \geq 0$, since μ is the invariant measure and $x(0) \sim \mu$. For the first term in (78), using Cauchy-Schwarz inequality and Lemma 4, we have

$$\mathbf{E}\left[\sup_{0\leq t'\leq t}\left|\int_{0}^{t'}\varphi(x(s))\,ds\right|^{2}\right] \\
\leq \mathbf{E}\left[\sup_{0\leq t'\leq t}\left(t'\int_{0}^{t'}\left|\varphi(x(s))\right|^{2}\,ds\right)\right] \\
\leq t\,\mathbf{E}\left[\int_{0}^{t}\left|\varphi(x(s))\right|^{2}\,ds\right] \\
= t^{2}\int_{\mathbb{R}^{n}}|\varphi|^{2}d\mu\leq\frac{\kappa_{1}^{2}\,t^{2}}{\beta\rho}.$$
(79)

The last term in (78) can be estimated by applying Doob's martingale inequality as

$$\mathbf{E} \sup_{0 \le s \le t} |M(s)|^{2} \le 4\mathbf{E}|M(t)|^{2}
= 4\mathbf{E} \int_{0}^{t} ||A(x(s)) - \widetilde{\sigma}(z(s))||_{F}^{2} ds
\le 8 \int_{0}^{t} \mathbf{E} ||A(x(s)) - \widetilde{\sigma}(\xi(x(s)))||_{F}^{2} ds + 8 \int_{0}^{t} \mathbf{E} ||\widetilde{\sigma}(\xi(x(s))) - \widetilde{\sigma}(z(s))||_{F}^{2} ds
\le \frac{16\kappa_{2}^{2}t}{\beta\rho} + 8L_{\sigma}^{2} \int_{0}^{t} \mathbf{E} |\xi(x(s)) - z(s)|^{2} ds,$$
(80)

where we have used Assumption 2, Lemma 5, together with the fact that $x(s) \sim \mu$. Combining (78), (79), and (80), we get

$$\mathbf{E} \Big(\sup_{0 \le t' \le t} \left| \xi(x(t')) - z(t') \right|^2 \Big) \\
\le \Big(\frac{3\kappa_1^2 t^2}{\beta \rho} + \frac{96\kappa_2^2 t}{\beta^2 \rho} \Big) + 3L_b^2 \mathbf{E} \Big(\int_0^t \sup_{0 \le t' \le s} \left| \xi(x(t')) - z(t') \right| ds \Big)^2 + \frac{48L_\sigma^2}{\beta} \int_0^t \Big(\mathbf{E} \sup_{0 \le t' \le s} \left| \xi(x(t')) - z(t') \right|^2 \Big) ds \,. \tag{81}$$

The conclusion follows by applying Lemma 6 below.

Remark 7. Applying Cauchy-Schwarz inequality to the right hand side of (81), we can get

$$\mathbf{E} \Big(\sup_{0 \le t' \le t} \left| \xi(x(t')) - z(t') \right|^2 \Big) \\
\le \Big(\frac{3\kappa_1^2 t^2}{\beta \rho} + \frac{96\kappa_2^2 t}{\beta^2 \rho} \Big) + \Big(3L_b^2 t + \frac{48L_\sigma^2}{\beta} \Big) \int_0^t \Big(\mathbf{E} \sup_{0 \le t' \le s} \left| \xi(x(t')) - z(t') \right|^2 \Big) ds , \tag{82}$$

and therefore Gronwall's inequality directly implies

$$\mathbf{E}\Big(\sup_{0\leq t'\leq t}\left|\xi(x(t'))-z(t')\right|^2\Big)\leq \Big(\frac{3\kappa_1^2t^2}{\beta\rho}+\frac{96\kappa_2^2t}{\beta^2\rho}\Big)e^{Lt}\,,$$

with $L = 3L_b^2 t + \frac{48L_{\sigma}^2}{\beta}$. Notice that, however, using this argument the constant L will depend on the time t. Instead, Lemma 6 below allows us to obtain an upper bound where the constant $L = 3L_b^2 + \frac{48L_{\sigma}^2}{\beta} + 1$, which is independent of t.

Lemma 6. Let $f(t) \in \mathbb{R}$ be a function on $t \in [0, +\infty)$ taking random values, such that $\mathbf{E}(f(t))^2 < +\infty$ for all $t \ge 0$. Further assume that f satisfies the inequality

$$\mathbf{E}(f(t))^2 \le g(t) + C_1 \mathbf{E}\left(\int_0^t f(s)ds\right)^2 + C_2 \int_0^t \mathbf{E}(f(s))^2 ds \,, \quad \forall t \ge 0 \,, \tag{83}$$

where the constants $C_1, C_2 \ge 0$, and $g \ge 0$ is a function of $t \in [0, +\infty)$. We have

$$\mathbf{E}(f(t))^{2} \leq g(t) + (C_{1} + C_{2}) \int_{0}^{t} e^{(C_{1} + C_{2} + 1)(t-s)} g(s) \, ds \,, \quad \forall t \geq 0 \,. \tag{84}$$

In particular, when the function g is non-decreasing, we have

$$\mathbf{E}(f(t))^{2} \le g(t) e^{(C_{1}+C_{2}+1)t}, \quad \forall t \ge 0.$$
(85)

Proof. For $t \ge 0$, we define the function

$$F(t) = C_1 \mathbf{E} \left(\int_0^t f(s) ds \right)^2 + C_2 \int_0^t \mathbf{E} (f(s))^2 ds \,.$$
(86)

From (83) and (86), we can compute

$$\frac{dF}{dt} = 2C_1 \mathbf{E} \left(f(t) \int_0^t f(s) ds \right) + C_2 \mathbf{E} \left(f(t) \right)^2$$

$$\leq C_1 \mathbf{E} \left(\int_0^t f(s) ds \right)^2 + (C_1 + C_2) \mathbf{E} \left(f(t) \right)^2$$

$$\leq F(t) + (C_1 + C_2) \left(g(t) + F(t) \right)$$

$$= (C_1 + C_2 + 1) F(t) + (C_1 + C_2) g(t) .$$

Since F(0) = 0, after integration we obtain

$$F(t) \le (C_1 + C_2) \int_0^t e^{(C_1 + C_2 + 1)(t-s)} g(s) \, ds \,. \tag{87}$$

The inequalities (84) and (85) follow by substituting (87) into (83).

5 Pathwise estimates of effective dynamics: Proof of Theorem 1 and Theorem 2

In this section, we prove the Theorem 1 and Theorem 2, which improve the pathwise estimate result in Proposition 1. The main tool we will use is the forward-backward martingale approach developed in [22, 14].

Following the argument in [19], we first establish a technique result. Given $\Psi \in C^2(\mathbb{R}^n, \mathbb{R}^n)$, we denote by

$$\nabla^* \Psi = \beta \nabla V \cdot \Psi - \operatorname{div} \Psi \tag{88}$$

the adjoint of the gradient operator ∇ with respect to the probability measure μ , i.e.,

$$\int_{\mathbb{R}^n} h\nabla^* \Psi \, d\mu = \int_{\mathbb{R}^n} \Psi \cdot \nabla h \, d\mu \tag{89}$$

holds for any C^1 function $h : \mathbb{R}^n \to \mathbb{R}$. We have the following estimate.

Proposition 2. Recall that μ is the invariant measure in (3) and the matrix a satisfies the uniform elliptic condition (2). Let $\Psi \in C^2(\mathbb{R}^n, \mathbb{R}^n)$ and x(s) be the dynamics in (1) starting from $x(0) \sim \mu$. For all $t \geq 0$, we have

$$\mathbf{E}\left[\sup_{0\leq t'\leq t}\left|\int_{0}^{t'}\nabla^{*}\Psi(x(s))\,ds\right|^{2}\right]\leq\frac{27\beta t}{2}\int_{\mathbb{R}^{n}}\Psi\cdot\left(a^{-1}\Psi\right)d\mu\,.$$
(90)

Proof. We will only sketch the proof since the argument resembles the one in [19], with minor modifications due to the appearance of the matrix a. First of all, condition (2) implies that the matrix a is positive definite and therefore invertible. Given $\eta > 0$, we consider the function $\omega_{\eta} : \mathbb{R}^n \to \mathbb{R}$ which solves the PDE

$$\eta \omega_{\eta} - \mathcal{L} \omega_{\eta} = -\nabla^* \Psi \,. \tag{91}$$

Multiplying both sides of (91) by ω_{η} and integrating with respect to μ , we obtain

$$\eta \int_{\mathbb{R}^n} \omega_\eta^2 \, d\mu + \mathcal{E}(\omega_\eta, \omega_\eta) = - \int_{\mathbb{R}^n} \Psi \cdot \nabla \omega_\eta \, d\mu$$

where \mathcal{E} is the Dirichlet form in (20). Applying Cauchy-Schwarz inequality to the right hand side of the above equality, we can estimate

$$\eta \int_{\mathbb{R}^{n}} \omega_{\eta}^{2} d\mu + \mathcal{E}(\omega_{\eta}, \omega_{\eta})$$

$$\leq \left(\int_{\mathbb{R}^{n}} \Psi \cdot (a^{-1}\Psi) d\mu\right)^{\frac{1}{2}} \left(\int_{\mathbb{R}^{n}} \nabla \omega_{\eta} \cdot (a\nabla \omega_{\eta}) d\mu\right)^{\frac{1}{2}}$$

$$= \left(\int_{\mathbb{R}^{n}} \Psi \cdot (a^{-1}\Psi) d\mu\right)^{\frac{1}{2}} \left(\beta \mathcal{E}(\omega_{\eta}, \omega_{\eta})\right)^{\frac{1}{2}},$$

from which we can deduce that

$$\mathcal{E}(\omega_{\eta}, \omega_{\eta}) \leq \beta \int_{\mathbb{R}^{n}} \Psi \cdot (a^{-1}\Psi) \, d\mu \,,$$

$$\lim_{\eta \to 0} \left(\eta^{2} \int_{\mathbb{R}^{n}} \omega_{\eta}^{2} \, d\mu \right) = 0 \,.$$
(92)

Now let us define the process y(t') := x(t - t') for $t' \in [0, t]$. Since x(s) is both reversible and in stationary, the process $(y(s))_{\{0 \le s \le t\}}$ satisfies the same law as $(x(s))_{\{0 \le s \le t\}}$. And we can assume that there is another n'-dimensional Brownian motion \overline{w} , such that

$$dy(s) = -a(y(s))\nabla V(y(s)) \, ds + \frac{1}{\beta} (\nabla \cdot a)(y(s)) \, ds + \sqrt{2\beta^{-1}} \sigma(y(s)) \, d\bar{w}(s) \,, \quad s \in [0, t] \,. \tag{93}$$

Applying Ito's formula, we have

$$\omega_{\eta}(x(t')) - \omega_{\eta}(x(0)) = \int_{0}^{t'} (\mathcal{L}\omega_{\eta})(x(s)) \, ds + \sqrt{2\beta^{-1}} \int_{0}^{t'} \left[(\nabla \omega_{\eta})^{T} \sigma \right](x(s)) \, dw(s) \,, \tag{94}$$

and similarly,

$$\omega_{\eta}(y(t)) - \omega_{\eta}(y(t-t')) = \int_{t-t'}^{t} (\mathcal{L}\omega_{\eta})(y(s)) \, ds + \sqrt{2\beta^{-1}} \int_{t-t'}^{t} \left[(\nabla \omega_{\eta})^T \sigma \right](y(s)) \, d\bar{w}(s) \,. \tag{95}$$

Let us denote

$$M(t') = \int_0^{t'} \left[(\nabla \omega_\eta)^T \sigma \right](x(s)) \, dw(s) \,, \quad \text{and} \quad \overline{M}(t') = \int_0^{t'} \left[(\nabla \omega_\eta)^T \sigma \right](y(s)) \, d\overline{w}(s) \,.$$

Adding up (94) and (95), we obtain

$$2\int_0^{t'} (\mathcal{L}\omega_\eta)(x(s))\,ds + \sqrt{2\beta^{-1}} \Big[M(t') + \overline{M}(t) - \overline{M}(t-t') \Big] = 0\,,\tag{96}$$

where the terms M(t'), $\overline{M}(t)$ and $\overline{M}(t-t')$ can be bounded using Doob's martingale inequality. We refer to [19] for details. Combining these upper bounds with (96) and (92), we can obtain

$$\mathbf{E}\left[\sup_{0\leq t'\leq t}\left|\int_{0}^{t'} (\mathcal{L}\omega_{\eta})(x(s))\,ds\right|^{2}\right] \leq \frac{27t}{2}\mathcal{E}(\omega_{\eta},\omega_{\eta}) \leq \frac{27\beta t}{2}\int_{\mathbb{R}^{n}}\Psi\cdot(a^{-1}\Psi)\,d\mu\,.$$
(97)

Letting $\eta \to 0$, using (91), (92) and the estimate (97), we conclude that

$$\mathbf{E}\left[\sup_{0\leq t'\leq t}\left|\int_{0}^{t'} (\nabla^{*}\Psi)(x(s))\,ds\right|^{2}\right] \leq \frac{27\beta t}{2}\int_{\mathbb{R}^{n}}\Psi\cdot\left(a^{-1}\Psi\right)d\mu\,.$$

To proceed, we consider the equation

$$\mathcal{L}_0 u = \varphi \,, \tag{98}$$

where $u : \mathbb{R}^n \to \mathbb{R}^m$, \mathcal{L}_0 is the operator in (27) and φ is the function introduced in (38). For each $z \in \mathbb{R}^m$, (98) can be viewed as a Poisson equation on the submanifold Σ_z for the components of u. Applying Proposition 2, we can obtain the following result.

Lemma 7. Assume Assumption 1, Assumption 3 and Assumption 4 hold. Let x(s) be the dynamics in (1) starting from $x(0) \sim \mu$. For all $t \geq 0$, we have

$$\mathbf{E}\left[\sup_{0 \le t' \le t} \left| \int_0^{t'} \varphi(x(s)) \, ds \right|^2 \right] \le \frac{27\kappa_1^2 t}{2\beta \rho^2} \, .$$

Proof. Using the equation (98) and the fact that \mathcal{E}_z satisfies Poincaré inequality (Assumption 4), we can deduce that

$$\mathcal{E}_z(u_i, u_i) \le \frac{1}{\rho} \int_{\Sigma_z} \varphi_i^2 \, d\mu_z \,, \tag{99}$$

for $1 \leq i \leq m$ and for all $z \in \mathbb{R}^m$. We refer to [19, Lemma 9] for details. Recalling the matrix Π in (23) and (24), let us define $\Psi^{(i)} = a \Pi \nabla u_i \in \mathbb{R}^n$, for $1 \leq i \leq m$. From (88) and the expression of \mathcal{L}_0 in (27), direct calculation shows that

$$\nabla^* \Psi^{(i)} = \beta \nabla V \cdot \Psi^{(i)} - \operatorname{div} \Psi^{(i)} = \beta \nabla V \cdot (a \Pi \nabla u_i) - \operatorname{div}(a \Pi \nabla u_i) = -\beta \mathcal{L}_0 u_i.$$
(100)

Therefore, applying Proposition 2, Lemma 4 and the expression in (30), we can derive

$$\begin{split} & \mathbf{E} \bigg[\sup_{0 \leq t' \leq t} \bigg| \int_{0}^{t'} \varphi(x(s)) \, ds \bigg|^2 \bigg] \\ &= \mathbf{E} \bigg[\sup_{0 \leq t' \leq t} \sum_{i=1}^{m} \bigg| \int_{0}^{t'} \varphi_i(x(s)) \, ds \bigg|^2 \bigg] \\ &\leq \sum_{i=1}^{m} \mathbf{E} \bigg[\sup_{0 \leq t' \leq t} \bigg| \int_{0}^{t'} \varphi_i(x(s)) \, ds \bigg|^2 \bigg] \\ &= \sum_{i=1}^{m} \mathbf{E} \bigg[\sup_{0 \leq t' \leq t} \bigg| \int_{0}^{t'} (\mathcal{L}_0 u_i)(x(s)) \, ds \bigg|^2 \bigg] \\ &\leq \frac{27t}{2\beta} \sum_{i=1}^{m} \int_{\mathbb{R}^n} (a \Pi \nabla u_i) \cdot \bigg[a^{-1} (a \Pi \nabla u_i) \bigg] \, d\mu \\ &= \frac{27t}{2\beta} \sum_{i=1}^{m} \int_{\mathbb{R}^m} \bigg[\int_{\Sigma_z} (a \Pi \nabla u_i) \cdot (\Pi \nabla u_i) \, d\mu_z \bigg] Q(z) \, dz \\ &= \frac{27t}{2} \sum_{i=1}^{m} \int_{\mathbb{R}^m} \mathcal{E}_z(u_i, u_i) \, Q(z) \, dz \\ &\leq \frac{27t}{2\rho} \sum_{i=1}^{m} \int_{\mathbb{R}^m} \bigg(\int_{\Sigma_z} \varphi_i^2 \, d\mu_z \bigg) Q(z) \, dz \leq \frac{27\kappa_1^2 t}{2\beta\rho^2} \,, \end{split}$$

where the inequality (99) has been used.

We are ready to prove Theorem 1.

Proof of Theorem 1. The proof is similar to that of Proposition 1 in Section 4, with a few modifications. Specifically, in analogy to the inequalities (78) and (80), we have

$$\mathbf{E} \Big(\sup_{0 \le t' \le t} |\xi(x(t')) - z(t')|^2 \Big) \\
\le 3 \mathbf{E} \Big[\sup_{0 \le t' \le t} \left| \int_0^{t'} \varphi(x(s)) \, ds \right|^2 \Big] + 3 L_b^2 \, \mathbf{E} \Big(\int_0^t |\xi(x(s)) - z(s)| \, ds \Big)^2 + \frac{6}{\beta} \mathbf{E} \sup_{0 \le s \le t} |M(s)|^2 . \tag{101}$$

where the last term can be estimated using Doob's martingale inequality as

$$\mathbf{E} \sup_{0 \le s \le t} |M(s)|^2 \le \frac{16\kappa_2^2 t}{\beta \rho} + 8L_{\sigma}^2 \int_0^t \mathbf{E} |\xi(x(s)) - z(s)|^2 \, ds \,. \tag{102}$$

Now, the main different step from Proposition 1 is that we will estimate the first term on the right hand side of (101) by applying Lemma 7. Combining (101), (102) and Lemma 7, we get

$$\mathbf{E}\left(\sup_{0\leq t'\leq t}\left|\xi(x(t'))-z(t')\right|^{2}\right)$$

$$\leq \left(\frac{81\kappa_1^2}{2\beta\rho^2} + \frac{96\kappa_2^2}{\beta^2\rho}\right)t + 3L_b^2 \mathbf{E}\left(\int_0^t \sup_{0 \leq t' \leq s} \left|\xi(x(t')) - z(t')\right| ds\right)^2 \\ + \frac{48L_\sigma^2}{\beta}\int_0^t \mathbf{E}\left(\sup_{0 \leq t' \leq s} \left|\xi(x(t')) - z(t')\right|^2\right) ds \,.$$

The conclusion follows by applying Lemma 6.

Finally, we apply Theorem 1 to prove Theorem 2 for more general initial conditions.

Proof of Theorem 2. Let us denote by \mathbf{E} and $\mathbf{E}_{x'}$ the shorthands of $\mathbf{E}(\cdot | x(0) \sim \mu)$, $\mathbf{E}(\cdot | x(0) = x')$, i.e., the expectations with respect to the trajectories $(x(s))_{s\geq 0}$ starting from the invariant distribution μ and the state x', respectively. We will frequently use the elementary inequality $\sqrt{a+b} \leq \sqrt{a} + \sqrt{b}$, $\forall a, b \geq 0$.

1. Applying Theorem 1 and Cauchy-Schwarz inequality, we can compute

$$\begin{split} \mathbf{E} & \left(\sup_{0 \le s \le t} \left| \xi(x(s)) - z(s) \right| \, \left| \, x(0) \sim \bar{\mu} \right) \right. \\ &= \mathbf{E} \left[\left(\sup_{0 \le s \le t} \left| \xi(x(s)) - z(s) \right| \right) \frac{d\bar{\mu}}{d\mu} \right] \\ &\leq & \left[\mathbf{E} \left(\sup_{0 \le s \le t} \left| \xi(x(s)) - z(s) \right|^2 \right) \right]^{\frac{1}{2}} \left[\int_{\mathbb{R}^n} \left(\frac{d\bar{\mu}}{d\mu} \right)^2 d\mu \right]^{\frac{1}{2}} \\ &\leq & \sqrt{t} \left(\frac{9\kappa_1}{\sqrt{2\beta\rho}} + \frac{12\kappa_2}{\beta\sqrt{\rho}} \right) \left[\int_{\mathbb{R}^n} \left(\frac{d\bar{\mu}}{d\mu} \right)^2 d\mu \right]^{\frac{1}{2}} e^{Lt} \,, \end{split}$$

where $L = \frac{3}{2}L_b^2 + \frac{24L_{\sigma}^2}{\beta} + \frac{1}{2}$.

2. Let us define $h(s) = \int_{\mathbb{R}^n} (p_s - 1)^2 d\mu$ for s > 0. From the study of the heat kernel estimate [7, 2], it is known that h(s) is finite for $\forall s > 0$. Since $\int_{\mathbb{R}^n} p_s d\mu = 1$, we have $h(s) = \int_{\mathbb{R}^n} p_s^2 d\mu - 1$. Using the Poincaré inequality (34) and noticing that p_s satisfies the Kolmogorov equation, we can calculate

$$h'(s) = 2 \int_{\mathbb{R}^n} p_s \mathcal{L} p_s \, d\mu = -2\mathcal{E}(p_s, p_s) \le -2\alpha h(s) \,,$$

which implies

$$\int_{\mathbb{R}^n} p_{t_1}^2 \, d\mu \le 1 + \Big(\int_{\mathbb{R}^n} p_{t_0}^2 \, d\mu - 1 \Big) e^{-2\alpha(t_1 - t_0)} < 1 + e^{-2\alpha(t_1 - t_0)} \int_{\mathbb{R}^n} p_{t_0}^2 \, d\mu \,, \tag{103}$$

for any $0 < t_0 \le t_1 \le t$. We also introduce the auxiliary process $\bar{z}(s)$, which is the effective dynamics (36) on $s \in [t_1, t]$, starting from $\bar{z}(t_1) = \xi(x(t_1))$. Clearly, we have

$$\mathbf{E}_{x'} \left(\sup_{0 \le s \le t} \left| \xi(x(s)) - z(s) \right| \right)$$

$$\le \max \left\{ \mathbf{E}_{x'} \left(\sup_{0 \le s \le t_1} \left| \xi(x(s)) - z(s) \right| \right), \mathbf{E}_{x'} \left(\sup_{t_1 \le s \le t} \left| \xi(x(s)) - \bar{z}(s) \right| \right) + \mathbf{E}_{x'} \left(\sup_{t_1 \le s \le t} \left| z(s) - \bar{z}(s) \right| \right) \right\}$$

On the time interval $[t_1, t]$, from the estimate (41) in the previous conclusion and the estimate (103), we know

$$\mathbf{E}_{x'} \left(\sup_{\substack{t_1 \le s \le t}} \left| \xi(x(s)) - \bar{z}(s) \right| \right) \\
= \mathbf{E} \left(\sup_{\substack{t_1 \le s \le t}} \left| \xi(x(s)) - \bar{z}(s) \right| \left| x(t_1) \sim \mu_{t_1} \right) \\
\leq \sqrt{t - t_1} \left(\frac{9\kappa_1}{\sqrt{2\beta\rho}} + \frac{12\kappa_2}{\beta\sqrt{\rho}} \right) \left[1 + e^{-\alpha(t_1 - t_0)} \left(\int_{\mathbb{R}^n} p_{t_0}^2 d\mu \right)^{\frac{1}{2}} \right] e^{L(t - t_1)},$$
(104)

where $L = \frac{3}{2}L_b^2 + \frac{24L_{\sigma}^2}{\beta} + \frac{1}{2}$. Meanwhile, using the same argument as in Proposition 1 and Theorem 1, we can obtain the estimate

$$\mathbf{E}_{x'} \left(\sup_{t_1 \le s \le t} \left| z(s) - \bar{z}(s) \right|^2 \right) \le 3 \mathbf{E}_{x'} \left(\left| z(t_1) - \bar{z}(t_1) \right|^2 \right) e^{L_1(t-t_1)} \\
\le 3 \mathbf{E}_{x'} \left(\sup_{0 \le s \le t_1} \left| \xi(x(s)) - z(s) \right|^2 \right) e^{L_1(t-t_1)},$$
(105)

where $L_1 = 3L_b^2 + \frac{24L_{\sigma}^2}{\beta} + 1$, and we have used the fact that $\bar{z}(t_1) = \xi(x(t_1))$. On the time interval $s \in [0, t_1]$, in analogy to (78) in the proof of Proposition 1, we can

$$\mathbf{E}_{x'} \left(\sup_{0 \le t' \le s} \left| \xi(x(t')) - z(t') \right|^2 \right) \\
\le 3 \mathbf{E}_{x'} \left[\sup_{0 \le t' \le s} \left| \int_0^{t'} \varphi(x(r)) \, dr \right|^2 \right] + 3 L_b^2 \, \mathbf{E}_{x'} \left(\int_0^s \sup_{0 \le t' \le r} \left| \xi(x(t')) - z(t') \right| \, dr \right)^2 \quad (106) \\
+ \frac{6}{\beta} \mathbf{E}_{x'} \left(\sup_{0 \le t' \le s} \left| M(t') \right|^2 \right),$$

where M(t') is the martingale given in (77). Since both φ and A are bounded, applying Doob's martingale inequality, it follows that

$$\mathbf{E}_{x'} \Big(\sup_{0 \le t' \le s} \left| \xi(x(t')) - z(t') \right|^2 \Big) \\ \le 3C_1^2 s^2 + \frac{96}{\beta} C_2^2 s + 3L_b^2 \mathbf{E}_{x'} \left(\int_0^s \sup_{0 \le t' \le r} \left| \xi(x(t')) - z(t') \right| dr \right)^2,$$

which, from Lemma 6, implies

obtain

$$\mathbf{E}_{x'}\left(\sup_{0 \le t' \le t_1} \left|\xi(x(t')) - z(t')\right|^2\right) \le \left(3C_1^2 t_1^2 + \frac{96}{\beta}C_2^2 t_1\right)e^{(3L_b^2 + 1)t_1}.$$
(107)

Combining (104), (105), and (107), we conclude that

$$\begin{split} \mathbf{E}_{x'} \Big(\sup_{0 \le s \le t} \left| \xi(x(s)) - z(s) \right| \Big) \\ \leq & \sqrt{t} \Big(\frac{9\kappa_1}{\sqrt{2\beta\rho}} + \frac{12\kappa_2}{\beta\sqrt{\rho}} \Big) \left[1 + e^{-\alpha(t_1 - t_0)} \Big(\int_{\mathbb{R}^n} p_{t_0}^2 d\mu \Big)^{\frac{1}{2}} \right] e^{L(t - t_1)} \\ & + \sqrt{t_1} \Big(3C_1 \sqrt{t_1} + \frac{18C_2}{\sqrt{\beta}} \Big) e^{(\frac{3}{2}L_b^2 + \frac{1}{2})t_1 + \frac{1}{2}L_1(t - t_1)} \\ \leq & \left\{ \sqrt{t} \Big(\frac{9\kappa_1}{\sqrt{2\beta\rho}} + \frac{12\kappa_2}{\beta\sqrt{\rho}} \Big) \Big[1 + e^{-\alpha(t_1 - t_0)} \Big(\int_{\mathbb{R}^n} p_{t_0}^2 d\mu \Big)^{\frac{1}{2}} \Big] + \sqrt{t_1} \Big(3C_1 \sqrt{t_1} + \frac{18C_2}{\sqrt{\beta}} \Big) \Big\} e^{Lt} \,. \end{split}$$

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A Coordinate transformation : from nonlinear to linear reaction coordinate

In this appendix, given a (nonlinear) reaction coordinate function $\xi : \mathbb{R}^n \to \mathbb{R}^m$, we study the coordinate transformation under which the original reaction coordinate becomes the mapping onto the first *m* components of system's state, i.e., the linear reaction coordinate. Specifically, given $x \in \mathbb{R}^n$, we consider the existence of a function $\phi : \Omega_x \to \mathbb{R}^{n-m}$, where $\Omega_x \subseteq \mathbb{R}^n$ is a neighborhood of *x*, such that the map

$$G(x) = (\xi(x), \phi(x)) \tag{108}$$

is one to one from Ω_x to Im(G). We further impose that

$$(\nabla \xi a \nabla \phi^T) \equiv 0, \quad \Longleftrightarrow \quad (a \nabla \xi_i)_l \frac{\partial \phi_j}{\partial x_l} = 0, \qquad \forall \ 1 \le i \le m, \quad 1 \le j \le n - m.$$
(109)

Notice that, in this appendix we will adopt the Einstein summation convention, i.e., repeated indices indicate summation over a set of indexed terms. Recalling the dynamics x(s) in (1) and applying Ito's formula, we know that the dynamics of $\bar{z}(s) = \xi(x(s))$ and $\bar{y}(s) = \phi(x(s))$ are given by

$$d\bar{z}_{i}(s) = (\mathcal{L}\xi_{i}) (G^{-1}(\bar{z}(s), \bar{y}(s))) ds + \sqrt{2\beta^{-1}} (\nabla \xi \sigma)_{il} (G^{-1}(\bar{z}(s), \bar{y}(s))) dw_{l}(s), d\bar{y}_{j}(s) = (\mathcal{L}\phi_{j}) (G^{-1}(\bar{z}(s), \bar{y}(s))) ds + \sqrt{2\beta^{-1}} (\nabla \phi \sigma)_{jl} (G^{-1}(\bar{z}(s), \bar{y}(s))) dw_{l}(s),$$
(110)

for $1 \le i \le m$ and $1 \le j \le n-m$, which can be considered as the equation of the dynamics x(s) under the new coordinate (ξ, ϕ) . Furthermore, the condition (109) implies that the noise terms driving the dynamics $\bar{z}(s)$ and $\bar{y}(s)$ in (110) are independent of each other.

The following result concerns the local existence of the function ϕ .

Proposition 3. Suppose Assumption 1 holds. The matrix a is C^2 smooth and satisfies the condition (2) for some constant $c_1 > 0$. The following two statements are equivalent.

- (1) There exists a neighborhood Ω_x of x, such that the map G in (108) is one to one from Ω_x to Im(G), and that the condition (109) is satisfied.
- (2) There exists a neighborhood Ω_x of x, such that $\Pi^T B_{ij} \equiv 0$ on Ω_x , for $1 \leq i, j \leq m$, where Π is defined in (24) and $B_{ij} \in \mathbb{R}^n$ is given by

$$B_{ij,l'} = (a\nabla\xi_i)_l \frac{\partial (a\nabla\xi_j)_{l'}}{\partial x_l} - (a\nabla\xi_j)_l \frac{\partial (a\nabla\xi_i)_{l'}}{\partial x_l}, \quad 1 \le l' \le n.$$
(111)

Proof. Let $u : \mathbb{R}^n \to \mathbb{R}$ be a C^2 smooth function. For $1 \leq i \leq m$, we define the differential operator L_i by

$$L_i u = (a \nabla \xi_i)_l \frac{\partial u}{\partial x_l} \,. \tag{112}$$

By inverse mapping theorem, it is sufficient to find functions $\phi_1, \phi_2, \cdots, \phi_{n-m}$, which solve the PDE system

$$L_i \phi_j = 0, \quad \text{for } 1 \le i \le m, \tag{113}$$

where $1 \leq j \leq n-m$, such that $\nabla \phi_1, \nabla \phi_2, \cdots, \nabla \phi_{n-m}$ are linearly independent. From Frobenius theorem [15], such linearly independent solutions of the PDE system (113) exist if and only if there are functions $c_{ij}^k : \mathbb{R}^n \to \mathbb{R}$, such that

$$L_i L_j u - L_j L_i u = c_{ij}^k L_k u = c_{ij}^k (a \nabla \xi_k)_{l'} \frac{\partial u}{\partial x_{l'}}, \qquad (114)$$

holds for all $1 \le i, j \le m$, and for any C^2 function u. From (112), we can directly compute

$$L_i L_j u - L_j L_i u = \left[(a \nabla \xi_i)_l \frac{\partial (a \nabla \xi_j)_{l'}}{\partial x_l} - (a \nabla \xi_j)_l \frac{\partial (a \nabla \xi_i)_{l'}}{\partial x_l} \right] \frac{\partial u}{\partial x_{l'}} = B_{ij,l'} \frac{\partial u}{\partial x_{l'}}, \quad (115)$$

for $1 \leq i, j \leq m$. Now we prove the equivalence of the statements (1) and (2).

 $(1) \Rightarrow (2)$. Suppose (114) holds for some functions c_{ij}^k , then from (115) we have $B_{ij} = c_{ij}^k (a \nabla \xi_k)$. Since the matrix Π satisfies $\Pi^T a = a \Pi$ and $\Pi \nabla \xi_k = 0$ in (24), we conclude that

$$\Pi^T B_{ij} = c_{ij}^k (\Pi^T a) \nabla \xi_k = c_{ij}^k a \Pi \nabla \xi_k = 0.$$

 $(2) \Rightarrow (1)$. Suppose $\Pi^T B_{ij} \equiv 0$. Then from the definition of Π in (23), we have

$$B_{ij} = (\Phi^{-1})_{kk'} \frac{\partial \xi_{k'}}{\partial x_{l'}} B_{ij,l'}(a\nabla\xi_k), \quad 1 \le i,j \le m,$$
(116)

which implies that (114) holds if we choose $c_{ij}^k = (\Phi^{-1})_{kk'} \frac{\partial \xi_{k'}}{\partial x_{l'}} B_{ij,l'}$. Therefore the statement (1) is true by Frobenius theorem.

Remark 8. Proposition 3 provides conditions under which we can reduce the case of a nonlinear reaction coordinate to the linear reaction coordinate case in (110), locally in a neighborhood of a given state. The latter has been extensively investigated in literature in the study of slow-fast stochastic dynamical systems [26, 21, 5, 13]. Although it seems impossible to solve ϕ for a general ξ and matrix a provided that it exists, it is interesting to mention the following special cases when ϕ exists or can be explicitly constructed.

- 1. When the reaction coordinate ξ is scalar (m = 1), the statements of Proposition 3 are always true, i.e., the function ϕ always exists in this case.
- 2. Consider $\xi(x) = (x_1, x_2, \cdots, x_m)^T$ is linear and the matrix $a = diag\{\sigma_1 \sigma_1^T, \sigma_2 \sigma_2^T\}$ is block diagonal, where $\sigma_1 \sigma_1^T \in \mathbb{R}^{m \times m}$ and $\sigma_2 \sigma_2^T \in \mathbb{R}^{(n-m) \times (n-m)}$. In this case, we can simply choose $\phi(x) = (x_{m+1}, \cdots, x_n)^T$.

3. Let $x = (x_1, x_2)^T$ be the state of a particle in \mathbb{R}^2 and (r, θ) denotes the coordinate of x in the polar coordinate system. Assuming $a = I_{2\times 2}$ and $\xi(x) = r = (x_1^2 + x_2^2)^{\frac{1}{2}}$, we can verify that condition (109) is satisfied with the function $\phi(x) = \theta(x)$. Furthermore, we note that this example can be generalized to the case of multiple particles where ξ consists of radius or angles of different particles.

In the following, let us assume that ϕ exists globally such that the map G in (108) is one to one from \mathbb{R}^n to itself. Given $z \in \mathbb{R}^m$, we consider the dynamics

$$\bar{x}(s) = G^{-1}(z, \bar{y}(s)),$$
(117)

where $\bar{y}(s)$ satisfies the second equation in (110) with $\bar{z}(s) = z$ fixed. The following result states that the invariant measure of (117) coincides with μ_z .

Proposition 4. Given $z \in \mathbb{R}^m$, the dynamics $\bar{x}(s)$ in (117) satisfies the SDE

$$d\bar{x}_i(s) = -(\Pi^T a)_{ij} \frac{\partial V}{\partial x_j} ds + \frac{1}{\beta} \frac{\partial (\Pi^T a)_{ij}}{\partial x_j} ds + \sqrt{2\beta^{-1}} (\Pi^T \sigma)_{ij} dw_j(s), \quad 1 \le i \le n.$$
(118)

In particular, $\bar{x}(s) \in \Sigma_z$ for $s \ge 0$ and it has a unique invariant measure μ_z , which is defined in (7).

Proof. Clearly, (117) implies $\bar{x}(s) \in \Sigma_z$, for $\forall s \ge 0$. Applying Ito's formula to (117), we get

$$d\bar{x}_{i}(s) = \frac{\partial (G^{-1})_{i}}{\partial \phi_{j}} \mathcal{L}\phi_{j} \, ds + \frac{1}{\beta} (\nabla \phi a \nabla \phi^{T})_{jl} \frac{\partial^{2} (G^{-1})_{i}}{\partial \phi_{j} \partial \phi_{l}} ds + \sqrt{2\beta^{-1}} \frac{\partial (G^{-1})_{i}}{\partial \phi_{j}} (\nabla \phi \, \sigma)_{jl} \, dw_{l}(s) \,,$$

$$(119)$$

where derivatives of G^{-1} are evaluated at $(z, \phi(\bar{x}(s)))$, while functions $\mathcal{L}\phi_j$, $\nabla\phi a\nabla\phi^T$, and $\nabla\phi\sigma$ are evaluated at $\bar{x}(s)$.

Based on the discussions in Subsection 2.1, we know that, in order to prove the conclusion, it suffices to show the infinitesimal generator of (119) coincides with the operator \mathcal{L}_0 which is defined in (27). For this purpose, taking derivatives in the identity

$$G^{-1}(\xi(x),\phi(x)) = x, \quad \forall x \in \mathbb{R}^n,$$
(120)

we have

$$\frac{\partial (G^{-1})_i}{\partial \xi_l} \frac{\partial \xi_l}{\partial x_j} + \frac{\partial (G^{-1})_i}{\partial \phi_l} \frac{\partial \phi_l}{\partial x_j} = \delta_{ij}, \qquad \forall \ 1 \le i, j \le n.$$
(121)

Together with (23) and the condition (109), we can obtain

$$\frac{\partial (G^{-1})_i}{\partial \xi_l} = (\Phi^{-1})_{ll'} (a\nabla \xi_{l'})_i , \qquad (122)$$

as well as

$$\frac{\partial (G^{-1})_i}{\partial \phi_l} \frac{\partial \phi_l}{\partial x_j} = \delta_{ij} - \frac{\partial (G^{-1})_i}{\partial \xi_l} \frac{\partial \xi_l}{\partial x_j} = \delta_{ij} - (\Phi^{-1})_{ll'} (a\nabla \xi_{l'})_i \frac{\partial \xi_l}{\partial x_j} = \Pi_{ji} \,. \tag{123}$$

For the first term on the right hand side of (119), using the expression (18) of \mathcal{L} and noticing that the first argument of G^{-1} is fixed, we can compute

$$\frac{\partial (G^{-1})_{i}}{\partial \phi_{j}} \mathcal{L}\phi_{j} = \frac{e^{\beta V}}{\beta} \frac{\partial (G^{-1})_{i}}{\partial \phi_{j}} \frac{\partial}{\partial x_{i'}} \left(a_{i'j'} e^{-\beta V} \frac{\partial \phi_{j}}{\partial x_{j'}} \right)
= \frac{e^{\beta V}}{\beta} \frac{\partial}{\partial x_{i'}} \left[\frac{\partial (G^{-1})_{i}}{\partial \phi_{j}} a_{i'j'} e^{-\beta V} \frac{\partial \phi_{j}}{\partial x_{j'}} \right] - \frac{1}{\beta} a_{i'j'} \frac{\partial^{2} (G^{-1})_{i}}{\partial \phi_{j} \partial \phi_{l}} \frac{\partial \phi_{j}}{\partial x_{j'}} \frac{\partial \phi_{l}}{\partial x_{i'}} \qquad (124)
= \frac{e^{\beta V}}{\beta} \frac{\partial}{\partial x_{i'}} \left[(\Pi^{T} a)_{ii'} e^{-\beta V} \right] - \frac{1}{\beta} a_{i'j'} \frac{\partial^{2} (G^{-1})_{i}}{\partial \phi_{j} \partial \phi_{l}} \frac{\partial \phi_{j}}{\partial x_{j'}} \frac{\partial \phi_{l}}{\partial x_{i'}} .$$

With the above computation, we know that the infinitesimal generator of $\bar{x}(s)$ in (119) is indeed \mathcal{L}_0 , and the SDE (119) can be simplified as

$$d\bar{x}_i(s) = -(\Pi^T a)_{ij} \frac{\partial V}{\partial x_j} ds + \frac{1}{\beta} \frac{\partial (\Pi^T a)_{ij}}{\partial x_j} ds + \sqrt{2\beta^{-1}} (\Pi^T \sigma)_{ij} dw_j(s).$$
(125)

Applying the result of [31, Theorem 4], we conclude that the invariant measure of the dynamics $\bar{x}(s)$ is given by μ_z .

B Proof of Lemma 1

This appendix is devoted to proving Lemma 1. We will only sketch the proof, since we essentially follow the argument in [3] (also see [30, Chap. 14]) with some technical modifications. Before entering the proof, we need to first introduce some notations.

In the following, for fixed $z \in \mathbb{R}^m$, we will denote by N the Riemannian submanifold Σ_z where the metric is induced from the Euclidean distance on \mathbb{R}^n . Let ∇^N , Δ^N be the gradient operator and the Laplacian operator on N, respectively. Recalling the parameter $\epsilon \ll 1$ and the potential function V_1 in (46), we consider the operator

$$\mathcal{L}^{N} = -\frac{1}{\epsilon} \nabla^{N} V_{1} \cdot \nabla^{N} + \frac{1}{\beta} \Delta^{N}$$
(126)

on N and denote by $(T_t)_{t\geq 0}$ the corresponding semigroup. It is straightforward to verify that T_t is invariant with respect to the probability measure $\bar{\nu}$ which is given by

$$d\bar{\nu} = \frac{1}{Z} e^{-\frac{\beta}{\epsilon} V_1} d\nu_z , \qquad (127)$$

where Z is the normalization constant and ν_z denotes the surface measure on N.

Given two smooth functions $f, h : N \to \mathbb{R}$, the associated Γ operator (*carré du champ*) and Γ_2 operator of \mathcal{L}^N are defined as

$$\Gamma(f,h) = \frac{1}{2} \left[\mathcal{L}^{N}(fh) - f\mathcal{L}^{N}h - h\mathcal{L}^{N}f \right] = \frac{1}{\beta} \nabla^{N}f \cdot \nabla^{N}h,$$

$$\Gamma_{2}(f,h) = \frac{1}{2} \left[\mathcal{L}^{N}\Gamma(f,h) - \Gamma(f,\mathcal{L}^{N}h) - \Gamma(\mathcal{L}^{N}f,h) \right].$$
(128)

Let us consider the (smooth) extensions of f, h from N to \mathbb{R}^n , which we again denote by f and h, respectively. Recall that P is the orthogonal projection operator from $T_x\mathbb{R}^n$ to T_xN introduced in Subsection 2.1. We can check that $\nabla^N f = P\nabla f, \nabla^N h = P\nabla h$, and therefore from (128) we have

$$\Gamma(f,h) = \frac{1}{\beta} (P\nabla f) \cdot (P\nabla h) \,. \tag{129}$$

Clearly, the above expression of Γ does not depend on the extensions of f and h we choose.

For the Γ_2 operator in (128), applying the Bochner-Lichnerowicz formula [3, Theorem C.3.3], we can compute

$$\Gamma_{2}(f,f) = \frac{1}{2} \mathcal{L}^{N} \Gamma(f,f) - \Gamma(f,\mathcal{L}^{N}f)$$

$$= \frac{1}{\beta^{2}} \|\operatorname{Hess}^{N}f\|_{HS}^{2} + \left(\frac{1}{\beta^{2}} \operatorname{Ric}^{N} + \frac{1}{\epsilon\beta} \operatorname{Hess}^{N}V_{1}\right) (\nabla^{N}f,\nabla^{N}f) \qquad (130)$$

$$\geq \left(\frac{1}{\beta^{2}} \operatorname{Ric}^{N} + \frac{1}{\epsilon\beta} \operatorname{Hess}^{N}V_{1}\right) (\nabla^{N}f,\nabla^{N}f) .$$

In the above, $\|\text{Hess}^N f\|_{HS}$ is the Hilbert-Schmidt norm of the Hessian of the function f, and Ric^N denotes the Ricci tensor on N.

After the above preparations, we are ready to prove Lemma 1.

Proof of Lemma 1. We divide the proof into two steps.

1. Firstly, let us prove the Poincaré inequality for the invariant measure $\bar{\nu}$, i.e.,

$$\int_{N} f^{2} d\bar{\nu} - \left(\int_{N} f d\bar{\nu}\right)^{2} \leq \frac{2\epsilon}{K} \int_{N} \Gamma(f, f) d\bar{\nu}, \qquad (131)$$

for all smooth functions $f: N \to \mathbb{R}$, when ϵ is small enough. According to [3, Proposition 4.8.1], it is sufficient to prove the curvature condition $CD(\frac{K}{2\epsilon}, \infty)$, i.e.,

$$\Gamma_2(f,f) \ge \frac{K}{2\epsilon} \Gamma(f,f) \,, \tag{132}$$

for all smooth functions $f: N \to \mathbb{R}$. Notice that, the K-convexity and C^2 smoothness of V_1 imply

$$\operatorname{Hess}^{N} V_{1}(\nabla^{N} f, \nabla^{N} f) \geq K |\nabla^{N} f|^{2}.$$
(133)

Denote by \mathbb{R}^N , H the Riemannian curvature tensor and the mean curvature vector of N, respectively. Given $x \in N$, let $e_i \in T_x N$, $1 \leq i \leq n-m$, be an orthonormal basis of $T_x N$. Applying the Gauss equation [17, Theorem 8.4] and using the relation $H = (I-P)\sum_{i=1}^{n-m} \nabla_{e_i} e_i$ [31, Proposition 1], we can compute

$$\operatorname{Ric}^{N}(X, X) = \sum_{i=1}^{n-m} \left[R^{N}(X, \boldsymbol{e}_{i})\boldsymbol{e}_{i} \right] \cdot X$$
$$= \sum_{i=1}^{n-m} \left[-\left((I-P)\nabla_{X}\boldsymbol{e}_{i} \right) \cdot \left((I-P)\nabla_{\boldsymbol{e}_{i}} X \right) + \left((I-P)\nabla_{\boldsymbol{e}_{i}} \boldsymbol{e}_{i} \right) \cdot \left((I-P)\nabla_{X} X \right) \right]^{(134)}$$
$$= -\sum_{i=1}^{n-m} \left((I-P)\nabla_{X}\boldsymbol{e}_{i} \right) \cdot \left((I-P)\nabla_{X}\boldsymbol{e}_{i} \right) - (\nabla_{X}H) \cdot X,$$

for all $X \in T_x N$. In the above, we have used the fact that the Riemannian curvature tensor of the Euclidean space \mathbb{R}^n vanishes, as well as

$$(I-P)(\nabla_{\boldsymbol{e}_i}X-\nabla_X\boldsymbol{e}_i)=(I-P)[\boldsymbol{e}_i,X]=0,$$

and $X \cdot H = 0$, since $e_i, X \in T_x N$ and $H \in (T_x N)^{\perp}$. From the last expression in (134) and the assumptions in Lemma 1, it is not difficult to conclude that $\exists C \in \mathbb{R}$, such that

$$\operatorname{Ric}^{N}(X, X) \ge C|X|^{2}, \quad \forall \ X \in T_{x}N.$$
(135)

Combining (130), (133), and (135), we obtain

$$\Gamma_2(f,f) \ge \frac{1}{\beta} \left(\frac{C}{\beta} + \frac{K}{\epsilon}\right) |\nabla^N f|^2 \ge \frac{K}{2\epsilon} \Gamma(f,f), \qquad (136)$$

when ϵ is small enough. Therefore, the curvature condition (132) is satisfied and the Poincaré inequality (131) follows.

2. Secondly, we derive the Poincaré inequality for the measure μ_z using Holley-Stroock perturbation lemma [10, 16]. For this purpose, from (7) and (127), we know that the probability measure μ_z is related to $\bar{\nu}$ by

$$d\mu_z = \frac{1}{Z} e^{-\beta V_0} \left[\det(\nabla \xi \nabla \xi^T) \right]^{-\frac{1}{2}} d\bar{\nu} , \qquad (137)$$

where Z is the normalization constant. And our assumptions imply that both $\frac{d\mu_z}{d\bar{\nu}}$ and $\frac{d\bar{\nu}}{d\mu_z}$ are bounded on N by some constant C > 0. Therefore, applying [3, Proposition 4.2.7], we have

$$\int_{\Sigma_z} f^2 d\mu_z - \left(\int_{\Sigma_z} f d\mu_z\right)^2 \le \frac{2\epsilon C}{K} \int_{\Sigma_z} \Gamma(f, f) d\mu_z = \frac{2\epsilon C}{\beta K} \int_{\Sigma_z} |P\nabla f|^2 d\mu_z , \qquad (138)$$

where the constant C may differ from the upper bound of $\frac{d\bar{\nu}}{d\mu_z}$ and $\frac{d\mu_z}{d\bar{\nu}}$. Assuming that f has been extended from N to \mathbb{R}^n , (2) and (24) imply

$$|P\nabla f|^2 \le |\Pi P\nabla f|^2 = |\Pi \nabla f|^2 \le \frac{1}{c_1} (a\Pi \nabla f) \cdot (\Pi \nabla f) .$$
(139)

Therefore, the inequality (50) follows readily from (138) and the expression of the Dirichlet form \mathcal{E}_z in (30).

C Mean square error estimate of marginals

In this appendix, instead of assuming the Lipschitz condition on \tilde{b} (Assumption 2), we provide a mean square error estimate of the marginals for the effective dynamics and the process $\xi(x(s))$, under the following dissipative assumption.

Assumption 6. $\exists L_d, L_\sigma > 0$, such that $\forall z, z' \in \mathbb{R}^m$, we have

$$\left(\widetilde{b}(z) - \widetilde{b}(z')\right) \cdot (z - z') \le -L_d |z - z'|^2, \qquad \left\|\widetilde{\sigma}(z) - \widetilde{\sigma}(z')\right\|_F \le L_\sigma |z - z'|.$$
(140)

Proposition 5. Suppose that Assumptions 1, 3, 4 and 6 hold. x(s) satisfies the SDE (1) starting from $x(0) \sim \mu$, and z(s) is the effective dynamics (36) with $z(0) = \xi(x(0))$.

1. Assume $L_d > \frac{L_a^2}{\beta}$. Choose $v_1, v_2 > 0$ such that

$$C_1 = L_d - \frac{L_{\sigma}^2(1+v_2)}{\beta} - \frac{v_1}{2} > 0.$$

 $We \ have$

$$\mathbf{E} \left| \xi(x(t)) - z(t) \right|^2 \le \frac{C_1^{-1}}{\beta \rho} \left[\frac{\kappa_1^2}{2v_1} + \frac{2\kappa_2^2}{\beta} \left(1 + \frac{1}{v_2} \right) \right] \left(1 - e^{-2C_1 t} \right), \quad \forall t \ge 0.$$
(141)

2. Assume $L_d \leq \frac{L_{\sigma}^2}{\beta}$. For any $v_1, v_2 > 0$, we define

$$C_2 = \frac{L_{\sigma}^2(1+v_2)}{\beta} - L_d + \frac{v_1}{2} > 0.$$

 $We\ have$

$$\mathbf{E} \left| \xi(x(t)) - z(t) \right|^2 \le \frac{C_2^{-1}}{\beta \rho} \left[\frac{\kappa_1^2}{2v_1} + \frac{2\kappa_2^2}{\beta} \left(1 + \frac{1}{v_2} \right) \right] \left(e^{2C_2 t} - 1 \right), \quad \forall t \ge 0.$$
 (142)

Proof. Recall the function φ defined in (38). Using (37) and applying Ito's formula, we obtain

$$\frac{1}{2} |\xi(x(t)) - z(t)|^2 = \int_0^t \varphi(x(s)) \cdot (\xi(x(s)) - z(s)) \, ds + \int_0^t \left(\tilde{b}(\xi(x(s))) - \tilde{b}(z(s)) \right) \cdot (\xi(x(s)) - z(s)) \, ds \\ + \frac{1}{\beta} \int_0^t \left\| A(x(s)) - \tilde{\sigma}(z(s)) \right\|_F^2 \, ds + \sqrt{2\beta^{-1}} M(t) \,,$$
(143)

where

$$M(t) = \int_0^t \left(\xi(x(s)) - z(s)\right)^T \left(A(x(s)) - \widetilde{\sigma}(z(s))\right) d\widetilde{w}_s$$

is the martingale term. Taking expectation in (143) and differentiating with respect to time t, we get

$$\frac{1}{2}\frac{d}{dt}\mathbf{E}\left|\xi(x(t)) - z(t)\right|^{2} = \mathbf{E}\left[\varphi(x(t)) \cdot \left(\xi(x(t)) - z(t)\right)\right] + \mathbf{E}\left[\left(\widetilde{b}\left(\xi(x(t))\right) - \widetilde{b}(z(t))\right) \cdot \left(\xi(x(t)) - z(t)\right)\right] \\ + \frac{1}{\beta}\mathbf{E}\left\|A(x(t)) - \widetilde{\sigma}(z(t))\right\|_{F}^{2}.$$
(144)

Applying Assumption 6, Lemmas 4–5, together with Young's inequality, we can estimate the right hand side of (144) and obtain

$$\frac{1}{2}\frac{d}{dt}\mathbf{E}|\xi(x(t)) - z(t)|^{2} \\
\leq \frac{1}{2v_{1}}\mathbf{E}_{\mu}|\varphi|^{2} - \left(L_{d} - \frac{v_{1}}{2}\right)\mathbf{E}|\xi(x(t)) - z(t)|^{2} + \frac{2\kappa_{2}^{2}(1+\frac{1}{v_{2}})}{\beta^{2}\rho} + \frac{L_{\sigma}^{2}(1+v_{2})}{\beta}\mathbf{E}|\xi(x(t)) - z(t)|^{2} \\
\leq \frac{1}{\beta\rho}\left[\frac{\kappa_{1}^{2}}{2v_{1}} + \frac{2\kappa_{2}^{2}}{\beta}\left(1+\frac{1}{v_{2}}\right)\right] + \left(\frac{L_{\sigma}^{2}(1+v_{2})}{\beta} - L_{d} + \frac{v_{1}}{2}\right)\mathbf{E}|\xi(x(t)) - z(t)|^{2},$$

for any $v_1, v_2 > 0$. The conclusions follow by applying Gronwall's inequality.

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