Uncertainty Quantification and Model Order Reduction Project: The adaptive biasing force method

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1 Theoretical background

1.1 Models of dynamics

In this subsection, we summarize mathematical models that have been used for describing evolution of dynamical systems, such as ensembles of molecules driven by forces arising from some modelled potential V.

Definition 1 (Hamiltonian dynamics)**.** [1] Let $N \in \mathbb{N}, n = 3N$ and $T \geq 0$. Let $\mathscr{D} \subset \mathbb{R}^n$ be an open domain and let

$$q : [0, T] \to \mathscr{D}, \quad p : [0, T] \to \mathbb{R}^n$$

be differentiable functions. The pair (q, p) is said to follow Hamiltonian dynamics with respect to a differentiable function $H : \mathscr{D} \times \mathbb{R}^n \to \mathbb{R}$ if it satisfies

$$\begin{cases} \frac{dp}{dt} = -\nabla_q H(q, p) \\ \frac{dq}{dt} = \nabla_p H(q, p) \end{cases} \tag{1}$$

Remark 2. *H is called the Hamiltonian. It is an invariant of the system in the sense that $\frac{d}{dt}H \equiv 0$. It can hence be interpreted as the energy of the system that is conserved.*

Remark 3. *In the following, we will restrict our discussion to the case of seperable Hamiltonians. That is, we will assume there exists a diagonal matrix $M \in \mathbb{R}^{n \times n}$ and a differentiable function $V : \mathscr{D} \to \mathbb{R}$ such that*

$$H(p, q) = \frac{1}{2} p^T M^{-1} p + V(q) \quad \forall q \in \mathscr{D}, p \in \mathbb{R}^n$$

The first term corresponds to kinetic energy due to particle movement. V is potential which encodes particle interactions. The choice of V depends on the particular modelling problem at hand.

For a canonical ensemble, one can emulate the exchange of heat of the system with a thermostat by introducing a noise term in form of a Wiener process. The resulting dynamics of the system is as follows.

Definition 4 (Classical Langevin dynamics)**.** [1] Let $(\Omega, \mathscr{F}, \mathbb{P})$ be a probability space and $T \geq 0$. Let

$$q : [0, T] \times \Omega \to \mathscr{D} \subset \mathbb{R}^n, \quad p : [0, T] \times \Omega \to \mathbb{R}^n$$

be stochastic processes. The pair (q, p) is said to follow Langevin dynamics driven by a Wiener process $(W_t)_{t \geq 0}$ if it satisfies

$$\begin{cases} dq_t = M^{-1} p_t dt \\ dp_t = -\nabla V(q_t)\, dt - \gamma M^{-1} p_t dt + \sigma dW_t \end{cases} \tag{2}$$

Remark 5. *Classical Langevin dynamics corresponds to choosing the Hamiltonian*

$$H(p,q) = \frac{1}{2}p_t^T M^{-1} p + \frac{1}{2}\gamma q_t^T q_t + V(q)$$

and adding the Wiener process. Indeed,

$$\nabla_p H = M^{-1}p_t, \quad \nabla_q H = \gamma \dot{q}_t + \nabla V(q_t) = \gamma M^{-1} p_t + \nabla V(q_t)$$

As a simplification of the dynamics (2), the following is often used in the context of molecular dynamics simulation and will be investigated in subsequent discussion.

Definition 6 (Overdamped Langevin dynamics)**.** [1] A stochastic process

$$q : [0,T] \times \Omega \to \mathscr{D} \subset \mathbb{R}^n$$

is said to follow the overdamped Langevin dynamics driven by a Wiener process $(W_t)_{t\geq 0}$ if it satisfies

$$dq_t = -\nabla V(q_t)dt + \sqrt{2\beta^{-1}}dW_t \tag{3}$$

Remark 7. *The overdamped Langevin dynamics can be derived (up to multiplication by constant) from the classical Langevin dynamics by substituting $dq_t = M^{-1}p_t dt$ from the first equation into the second equation and discarding the term dp_t.*

Remark 8. *Dynamics (3) is simply a gradient descent with respect to the potential V, with the presence of a noise term. The convergence to an invariant measure and its ergodicity will depend on the potential V and the parameter β.*

Proposition 9 (Boltzmann-Gibbs measure)**.** *[1] The invariant measure of the dynamics (3) is the measure on $\mathscr{D}$,*

$$\nu(dq) := Z_\nu^{-1} \mathrm{e}^{-\beta V(q)} dq$$

where $Z_\nu^{-1} := \int_{\mathscr{D}} \mathrm{e}^{-\beta V(q)} dq$. This measure is called the Boltzmann-Gibbs measure.

1.2 Reaction coordinates and free energy

Definition 10 (Reaction coordinate and its level sets)**.** [1] Let $\mathscr{D} \subset \mathbb{R}^{3N}$ be an open domain. A differentiable function $\xi : \mathscr{D} \to \mathscr{M} \subset \mathbb{R}^m$ for $m \leq 3N$ is called a reaction coordinate. Furthermore, for any $z \in \mathscr{M}$, denote by

$$\Sigma(z) := \{x \in \mathscr{D} : \xi(x) = z\}$$

the level sets of a reaction coordinate ξ.

The submanifolds $\Sigma(z)$ inherit the surface measures denoted $d\sigma_{\Sigma(z)}$ that are induced by the Lebesgue measure on the ambient space $\mathbb{R}^m$. Moreover, note that the differential of ξ is a mapping

$$\nabla \xi : \mathscr{D} \to \mathbb{R}^{n \times m}$$

Remark 11. *The purpose of a reaction coordinate is to capture meaningful directions in the configuration set $\mathscr{D}$, typically with m much smaller than $3N$, and thus reducing the dimensionality of the problem. Choosing a suitable reaction coordinate depends on the problem setting, in particular geometry of the configuration space and particle interaction potential. Picking the right reaction coordinate is largely a heuristic and in many cases an open problem.*

The definition of free energy associated with a reaction coordinate requires some prior geometric considerations, namely the notion of a Gram matrix and marginal distributions on submanifolds.

Definition 12 (The Gram matrix)**.** [1] The function

$$\begin{aligned} G : \mathscr{D} &\to \mathbb{R}^{m\times m} \\ q &\mapsto (\nabla\xi(q))^T(\nabla\xi(q)) \end{aligned}$$

is called the Gram matrix corresponding to the change of coordinates on $\mathbb{R}^m$ via ξ.

Lemma 13 (Co-area formula)**.** *[1] Let $\xi : \mathscr{D} \to \mathscr{M}$ be a reaction coordinate and G its corresponding Gram matrix. Then for all $f \in C^\infty(\mathscr{D})$,*

$$\int_{\mathscr{D}} f(q)(\det G)^{1/2}(q)dq = \int_{\mathscr{M}} \int_{\Sigma(z)} f d\sigma_{\Sigma(z)} dz \tag{4}$$

Definition 14 (A rescaled surface measure)**.** Define for every $z \in \mathscr{M}$,

$$\delta_{\xi(q)-z}(dq) := (\det G)^{-\frac{1}{2}} d\sigma_{\Sigma(z)}(q)$$

as a measure on $\Sigma(z)$.

Remark 15. *The definition of $\delta_{\xi(q)-z}(dq)$ is clearly motivated by Lemma 13 to take into account the geometry of $\Sigma(z)$ in $\mathbb{R}^m$ so that for all $f \in C^\infty(\mathscr{D})$,*

$$\int_{\mathscr{D}} f(q)dq = \int_{\mathscr{M}} \int_{\Sigma(z)} f(q)\delta_{\xi(q)-z}(dq)dz$$

Definition 16 (Free energy)**.** [1] Let $V : \mathscr{D} \to \mathbb{R}$ be a differentiable function and $\xi : \mathscr{D} \to \mathscr{M}$ a reaction coordinate. The free energy associated with potential V and reaction coordinate ξ is the mapping $F : \mathscr{M} \to \mathbb{R}$ defined as

$$F(z) := -\beta^{-1} \ln \left(\int_{\Sigma(z)} Z_\nu^{-1} \mathrm{e}^{-\beta V(q)} \delta_{\xi(q)-z}(dq) \right) \tag{5}$$

where

$$Z_\nu := \int_{\mathscr{D}} \mathrm{e}^{-\beta V(q)} dq$$

Remark 17. *[1] Note that expression (5) can be rearranged and integrated over measurable subsets of $\mathscr{M}$ to yield*

$$\exp(-\beta F(z))dz = \int_{\Sigma(z)} Z_\nu^{-1} \exp(-\beta V(q))\delta_{\xi(q)-z}(dq)dz$$

Hence the function $\exp(-\beta F(z))$ can be interpreted as relative mass of the submanifold $\Sigma(z)$ in the sense that

$$\nu^\xi(dq|z) := \int_{\Sigma(z)} Z_\nu^{-1} \exp(-\beta V(q))\delta_{\xi(q)-z}(dq) = \exp(-\beta F(z))dq$$

Note that $\nu^\xi(dq|z)$ is the marginal law on $\Sigma(z)$ of the Boltzmann-Gibbs measure for $z \in \mathscr{M}$.

1.3 An example of metastability

This section describes a toy example of metastable behaviour in particle dynamics simulation. In particular, we consider the case of a potential barrier between two regions of a bounded, two-dimensional container.

Example 18 (A particle in double well potential in 2D)**.** *[1] Suppose q_t follows the overdamped Langevin dynamics with potential*

$$V(x,y) = \tfrac{1}{6}\left[4\left(1-x^2-y^2\right)^2 + 2\left(x^2-2\right)^2 + \left((x+y)^2-1\right)^2 + \left((x-y)^2-1\right)^2\right] \tag{6}$$

This potential function and its gradient are plotted in Figure 1 and Figure 2, respectively. The graph of a sample trajectory is shown in Figure 3.

By definition of the dynamics (3), one expects the particle to be trapped near one of the two local minima for long periods of time. Indeed, this is the case as illustrated in Figure 3. This shows the particle stays in either of the wells for relatively many iterations before transitioning to the other part.

This simulation of dynamics serves to illustrate the metastability phenomenon. Nonetheless, it is computationally undemanding, since we only consider a single particle in a given potential field that is only dependent on the single particle's position. Therefore, the long exploration times of the potential landscape do not pose a problem. However, in more complex settings with pairwise particle interactions between many particles, the mixing time for the process q_t may be too large for the sampling of the entire configuration space to be feasible and some regions may remain unexplored.

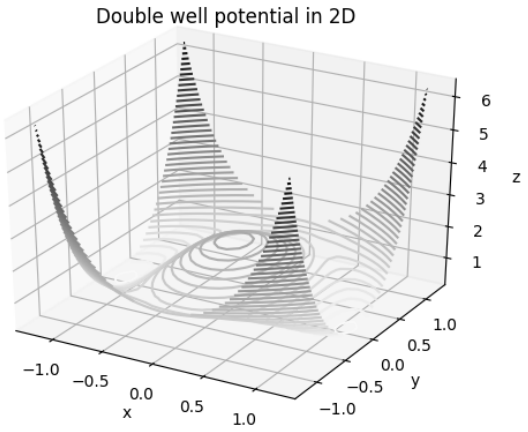

Figure 1: Double well potential stated in equation (6).

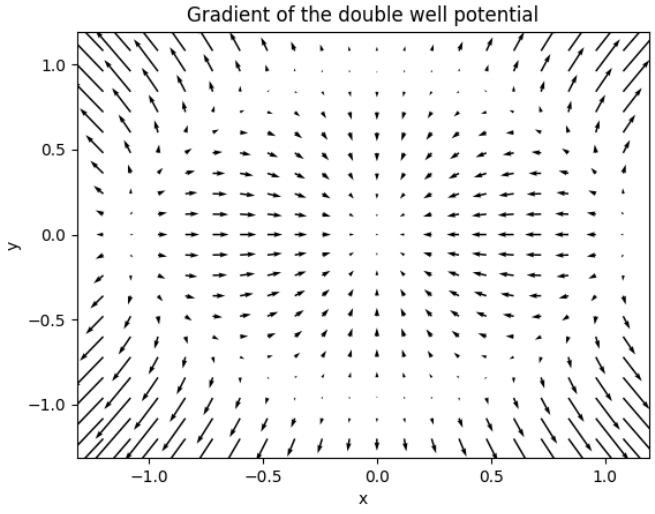

Figure 2: Gradient of the double well potential stated in equation (6).

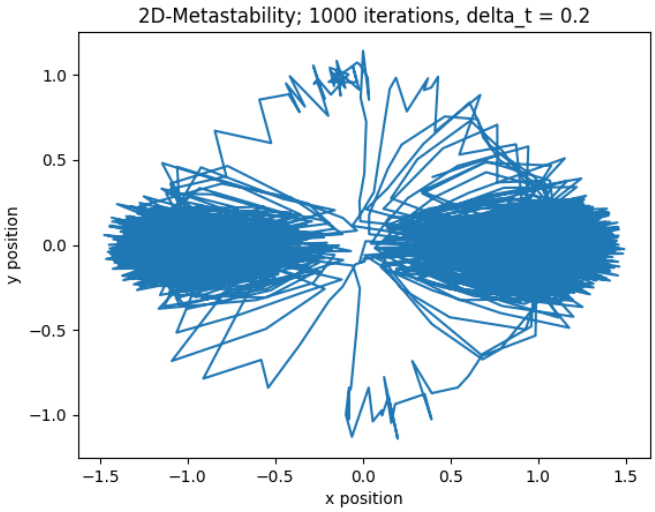

Figure 3: Simulated trajectory of a particle subject to an overdamped Langevin dynamics for the potential (6) starting at $x_0 = (0.1, 0.1)$; one can observe that the particle spent most of the time in the two wells with some short transitions from one to another. The simulation was run for 1000 iterations with time step increments of size 0.2.

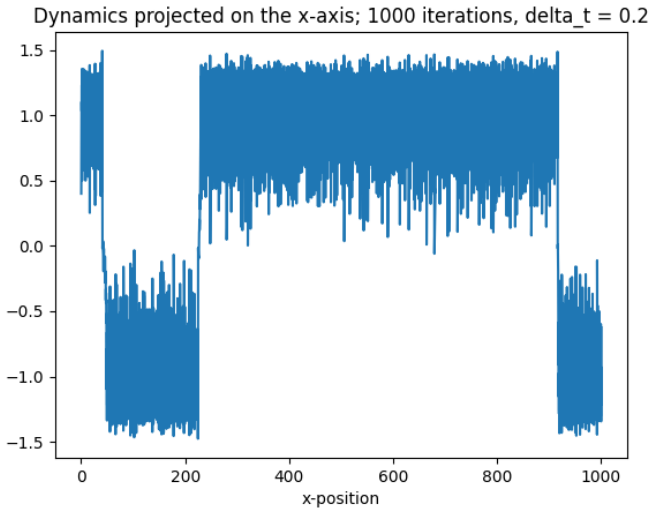

Figure 4: x-axis projection of the 2D-simulation time for the Langevin dynamics (3) starting at $x_0 = (0.1, 0.1)$. This shows oscillations on different time scales are present. This means the particle tends to stay in one of the wells for a long time before abruptly transitioning.

2 Adaptive biasing potential and force

We will study the problem of sampling the gradient of free energy in the context of overdamped Langevin dynamics (3) for q_t with an important modification. Instead of following the dynamics with simply the potential V, we use dynamics driven by a biasing force that furthermore changes as q_t evolves.

The purpose of sampling the gradient of the free energy is to overcome the problems of metastability discussed in the previous section by driving the evolution of q_t away from regions already visited. [1]

Definition 19 (Adaptive biased dynamics)**.** [1] Let $(\Omega, \mathscr{F}, \mathbb{P})$ be a probability space and $T \geq 0$. A stochastic process

$$q : [0, T] \times \Omega \to \mathscr{D}$$

is said to follow adaptive biased dynamics with respect to a biasing potential $F_\cdot : [0, T] \times \mathscr{M} \to \mathbb{R}$ and a Wiener process $(W_t)_{t \geq 0}$ if it satisfies

$$dq_t = \left(-\nabla V(q_t) + \sum_{\alpha=1}^{m} \nabla_\alpha F_t(\xi(q_t)) \nabla \xi_\alpha(q_t) \right) dt + \sqrt{\frac{2}{\beta}} dW_t \tag{7}$$

Alternatively, the process q is said to follow adaptive biased dynamics with respect to a biasing force $\Gamma_t : [0, T] \times \mathscr{M} \to \mathbb{R}^{m \times n}$ defined by

$$\Gamma_t(z) := \nabla F_t(z) \quad \forall z \in \mathscr{M}$$

if it holds that

$$dq_t = \left(-\nabla V\left(q_t\right) + \sum_{\alpha=1}^{m} \left[\Gamma_t\left(\xi\left(q_t\right)\right)\right]_\alpha \nabla \xi_\alpha\left(q_t\right) \right) dt + \sqrt{\frac{2}{\beta}} dW_t \tag{8}$$

Furthermore, denote by $\psi(t,\cdot)$ the density with respect to Lebesgue measure on $\mathscr{D}$ of the law of q_t satisfying (7) or equivalently (8).

Remark 20. *Note that $\Gamma_t = \nabla F_t$ is dependent on time. Since the free energy F is not known, the question is how to choose F_t so that it approximates F well and converges to it in the long time limit. In numerical simulation, it is also necessary to have an updating algorithm for F_t or Γ_t.*

Remark 21. *The motivation to bias the potential via free energy or its gradient is that with a suitable choice of a reaction coordinate, the biasing potential Γ_t will act against the potential gradient ∇V in a way that will lower the potential barriers between different parts of the configuration space $\mathscr{D}$. An example thereof is presented in Section*

Remark 22. *In all of the following, the process q_t will be assumed to follow the adaptive biased dynamics with respect to a biasing force Γ_t, which is to be specified.*

Since the free energy and associated mean force are unknown at the outset, *observed* free energy and its corresponding *observed* mean force will be used as a surrogate. To define these, several preliminary definitions are necessary.

First, the observed free energy and observed mean force will be dependent on the choice of reaction coordinate $\xi : \mathscr{D} \to \mathscr{M}$ and its induced conditional laws on its preimages $\{\Sigma(z)\}_{z\in\mathscr{M}}$ as submanifolds of $\mathscr{D}$.

Definition 23 (Instantaneous conditional law)**.** [1] Suppose the law of q_t has density $\psi(t,\cdot)$ with respect to the Lebesgue measure on $\mathscr{D}$ for each instant $t \geq 0$ and let

$$\begin{aligned} G : \mathscr{D} &\to \mathbb{R}^{m\times m} \\ q &\mapsto (\nabla\xi(q))^T(\nabla\xi(q)) \end{aligned}$$

be the Gram matrix. For every $t \geq 0$ and $z \in \mathscr{M}$, the instantaneous conditional law of q_t is the marginal density

$$\nu^\xi(t, dq|z) = \frac{\psi(t,q)|\det G(q)|^{-1/2}\sigma_{\Sigma(z)}(dq)}{\int_{\Sigma(z)} \psi(t,q)|\det G|^{-1/2} d\sigma_{\Sigma(z)}}(dq) \tag{9}$$

on the submanifold $\Sigma(z)$ of $\mathscr{D}$. Note that these conditional laws are precisely the marginals of the pushforward measure of q_t via the reaction coordinate ξ.

Remark 24. *[1] The fact that this is the correct form of the marginals on $\Sigma(z)$ for the law of q_t follows again from the co-area formula (4) in Lemma 13 which suggests that the marginal law of q_t on $\Sigma(z)$ for every $z \in \mathscr{M}$ is*

$$|\det G(q)|^{-\frac{1}{2}} d\sigma_{\Sigma(z)}(dq)$$

Setting $f(q) := \psi(t,q)$ then yields formula (9).

The following lemma will be essential for computing the gradient of the free energy for adaptive biased forcing methods.

Lemma 25. *[1] The gradient of free energy can be written as*

$$\nabla F(z) = \int_{\Sigma(z)} f d\nu^{\xi}(\cdot|z)$$

where $f : \mathscr{D} \to \mathbb{R}^m$ is defined as

$$f_\alpha = \sum_{\gamma=1}^{m} G^{-1}_{\alpha,\gamma} \nabla \xi_\gamma \cdot \nabla V - \beta^{-1} \operatorname{div} \left(\sum_{\gamma=1}^{m} G^{-1}_{\alpha,\gamma} \nabla \xi_\gamma \right)$$

Remark 26. *The function f is called the local mean force associated to the reaction coordinate ξ.*

Definition 27 (Observed mean force)**.** [1] Define the observed mean force with respect to a reaction coordinate $\xi : \mathscr{D} \to \mathbb{R}^m$ at time $t \geq 0$ as

$$\Gamma_{\text{obs}}(t, z) := \int_{\Sigma(z)} f(q) \nu^{\xi}(t, dq|z)$$

Definition 28 (Density at instantaneous equilibrium)**.** [1] For any $t \geq 0$, define the instantaneous equilibrium density of q_t as

$$\psi^{\text{eq}}(t, q) := Z_t^{-1} \mathrm{e}^{-\beta[V(q) - F_t(\xi(q))]}. \tag{10}$$

with $Z_t = \int_{\mathscr{D}} \exp\left(-\beta \left(V(q) - F_t \circ \xi(q)\right)\right) dq$

Remark 29. *The intuition here is that the invariant measure of overdamped Langevin dynamics is the Boltzmann-Gibbs measure. Hence, at an instant $t \geq 0$, the law of q_t appears at small time scale to be in equilibrium if precisely $q_t \sim \psi^{eq}(t, \cdot)$, where ψ^{eq} is defined above.*

One needs to choose the form of Γ_t that can be estimated numerically. Lemma 25 suggests to integrate the local mean force with respect to the marginal law of q_t via ξ. Concretely, this yields the following dynamics:

Definition 30 (Dynamics biased by mean force)**.** [1] The stochastic process q_t is said to follow overdamped Langevin dynamics biased by the mean force Γ_t if it satisfies

$$\begin{cases} dq_t = \left(-\nabla V\left(q_t\right) + \sum_{\alpha=1}^{m} \left[\Gamma_t\left(\xi\left(q_t\right)\right)\right]_\alpha \nabla \xi_\alpha\left(q_t\right)\right) dt + \sqrt{\frac{2}{\beta}} dW_t \\ \Gamma_t(z) = \int_{\Sigma(z)} f(q) \nu^{\xi}(t, dq|z) \end{cases} \tag{11}$$

where f is the local mean force from Lemma 25.

This formulation will be particularly suitable for formulation of numerical schemes for the adaptive biased dynamics.

Remark 31. *Since we took the liberty of defining the dynamics of Γ_t in (11) and thus somewhat diverged from (8) where it corresponded to ∇F_t, in the new dynamics Γ_t may no longer be a gradient of a function.*

Remark 32. *[1] The formula for adaptive biased dynamics increases the potential of regions already visited.*

2.1 Implementing the ABF method

In the following, we have considered metastable behaviour of the overdamped Langevin dynamics for a single particle in two dimensions with double well potential, with the extension that the dynamics is additionally driven by the biasing force Γ_t as in Definition 30.

First, we present the sampling algorithm which is based on the dynamics given in Definition 30. We limit ourselves here to the case of one-dimensional reaction coordinate, but the generalization to subsets of higher dimensional Euclidean spaces is straightforward.

Algorithm 33 (Adaptive biased forcing)**.** The adaptive biased forcing algorithm $\mathrm{ABF}(N, T, n, m, \xi : \mathscr{D} \to [a, b], u, f, q_0)$ is an iterative algorithm with inputs

- N the number of simulated paths
- T terminal time of the simulation
- n the number of discrete time steps
- biasing force updating factor m: the biasing force is updated every m steps of the Euler-Maruyama scheme for the dynamics of the process q
- $\xi : \mathscr{D} \to [a, b]$ the reaction coordinate mapping from the configuration set $\mathscr{D}$ to the interval $[a, b]$
- u the discretization factor for the interval $[a, b]$: it is partitioned into u subintervals (bins)
- $f : \mathscr{D} \to \mathbb{R}$ the local mean force, note that by its definition in Lemma 25 this also incorporates the potential function V
- q_0 the initial state of the system

These inputs then define the time step $\Delta t := \frac{T}{n}$ for the Euler-Maruyama scheme and the time step $\Delta s := m\Delta t$ for updating the biasing force. Hence there will be $\bar{m} := \frac{T}{\Delta s}$ number of updates of the biasing force in the procedure.

Since the biasing force is a function of the reaction coordinate, it is also necessary to divide the interval $[a, b]$ into bins $[z_l, z_{l+1})$ where $z_l := a + l \cdot \frac{b-a}{u}$. The sample at time $k\Delta s$, $\{q^{(i)}_{k\Delta s}\}_{i=1}^N$, can then be partitioned into subsamples

$$S(k, l) := \{q_t^{(i)} : i = 1, \ldots, N, q_t^{(i)} \in [z_l, z_{l+1})\}$$

for $l = 0, \ldots, u - 1$

In the following, $q_t^{(i)}$ will denote the i-th sample path of the process q at time t computed by the Euler-Maruyama scheme and $\hat{\Gamma}_t(z_l)$ will denote the estimate of the mean force at time t in bin $[z_l, z_{l+1})$ given by the empirical mean of f with respect to the conditional measure $\nu^{\xi}(t, dq|z)$. Concretely, the measure

$\nu^{\xi}(t, dq|z_l)$ will be approximated by the corresponding empirical measure arising from sampling up until time $k\Delta s$,

$$\frac{1}{N_{kl}} \sum_{q^{(i)}_{k\Delta s} \in S(k,l)} \delta_{q^{(i)}_{k\Delta s}}(dq)$$

and the empirical mean of $\Gamma_{k\Delta s}(z)$ for $z \in [z_l, z_{l+1}), l = 0, \ldots, u-1$ will be

$$\hat{\Gamma}_{k\Delta s}(z_l) := \frac{1}{N_{kl}} \sum_{q^{(i)}_{k\Delta s} \in S(k,l)} f(q^{(i)}_{k\Delta s})$$

Given a deterministic initial point q_0, initialize $q^{(i)}_0 := q_0$ and the biasing force can be initialized as $\hat{\Gamma}_0 := f(q_0)$ which is in alignment with Lemma 25.

Given $\hat{\Gamma}_{k\Delta s}$ and $\{q^{(i)}_{k\Delta s}\}_{i=1}^N$, compute $\hat{\Gamma}_{(k+1)\Delta s}$ and $\{q^{(i)}_{(k+1)\Delta s}\}_{i=1}^N$ as follows:

1. for every $i = 1, \ldots, N$, apply the Euler-Maruyama scheme with $\hat{\Gamma}_{k\Delta s}(z_l)$ in place of $\Gamma_{k\Delta s}(z)$ with time step Δt to compute $\{q^{(i)}_{k\Delta s + j\Delta t} : j = 1, \ldots, m\}_{i=1}^N$. Concretely, compute

   $$q^{(i)}_{k\Delta s + (j+1)\Delta t} := -\nabla V(q^{(i)}_{k\Delta s + j\Delta t})\Delta t + \hat{\Gamma}_{k\Delta s}(z_l)\nabla\xi(q^{(i)}_{k\Delta s + j\Delta t})\Delta t + \sqrt{\Delta t}W$$

   where z_l is such that $q^{(i)}_{k\Delta s} \in [z_l, z_{l+1})$ (that is $q^{(i)}_{k\Delta s} \in S(k,l)$ where $S(k,l)$ is the partition of the sample paths as defined above).

2. find the subsamples $S(k+1, l)$ for $l = 0, \ldots, u-1$

3. for $l = 0, \ldots, u-1$ compute

   $$\hat{\Gamma}_{(k+1)\Delta s}(z_l) := \frac{1}{N_{(k+1)l}} \sum_{q^{(i)}_{(k+1)\Delta s} \in S(k+1,l)} f(q^{(i)}_{(k+1)\Delta s})$$

The above steps are repeated for $k = 0, \ldots \bar{m} - 1$. Note that this yields the sample paths on the scale Δt, that is $\{q^{(i)}_{j\Delta t} : j = 0, \ldots, n\}_{i=1}^N$.

For step-by-step summary description of the procedure for the particular case $\xi : \mathbb{R}^2 \supset \mathscr{D} \to [a, b], \xi(x, y) = x$, assuming that $\mathscr{D}$ can be projected surjectively onto $[a, b]$, see Algorithm 1 in the table below.

Remark 34 (On the empirical mean)**.** *The justification to use*

$$\nu^{\xi}(k\Delta s, dq|z) \approx \frac{1}{N_{kl}} \sum_{q^{(i)}_{k\Delta s} \in S(k,l)} \delta_{q^{(i)}_{k\Delta s}}(dq)$$

for $z \in [z_l, z_{l+1})$ is that if the system is assumed to be in instantaneous equilibrium at each instant $k\Delta s$, then we would expect the subsample $S(k,l)$ to be representative of the conditional distribution $\nu^{\xi}(k\Delta s, dq|z)$ for $z \in [z_l, z_{l+1})$.

2.2 Application: the 2D double well potential

Example 35 (A particle in double well potential in 2D - continued)**.** *[1] Consider again Example 18 with potential*

$$V(x,y) = \tfrac{1}{6}\left[4\left(1-x^2-y^2\right)^2 + 2\left(x^2-2\right)^2 + \left((x+y)^2-1\right)^2 + \left((x-y)^2-1\right)^2\right] \tag{12}$$

The main idea of the computation will be to use a $\mathbb{P}_0$-finite element approximation type on the mean force coupled with an Euler-Maruyama method for the dynamics. In the rest of this section, we will first motivate a choice of reaction coordinate before clearly exposing the computational scheme for the dynamics (11).

First, to remedy metastability, we tested the adaptive biased forcing method described in the previous section. The form of potential and Figure 2 suggest choosing

$$\begin{aligned} \xi : \mathbb{R}^2 &\to I \\ (x,y) &\mapsto x \end{aligned}$$

where $I \subset \mathbb{R}$ is a bounded interval, as a reaction coordinate to surpass the potential barrier that lies in the direction of the x-axis.

For this coordinate, the biased dynamics takes first the following form

$$\begin{cases} dq_t = \left(-\nabla V\left(q_t\right) + \sum_{\alpha=1}^{2}\left[\Gamma_t\left(\xi\left(q_t\right)\right)\right]_\alpha e_x\right)dt + \sqrt{\frac{2}{\beta}}dW_t \\ \Gamma_t(z) = \int_{\Sigma(z)} f(q)\nu^\xi(t,dq|z) = \int_{\{z\}\times\mathbb{R}} f(q)\nu^\xi(t,dq|z) \end{cases} \tag{13}$$

as $\Sigma(z) := \xi^{-1}(z) = \{(x,y) \in \mathbb{R}^2 \,|x = z\} = \{z\} \times \mathbb{R}$ for $z \in \mathbb{R}$ and where $e_x := (1,0) \in \mathbb{R}^2$.

Second, as $G(q) = x^2$ for $q := (x,y) \in \mathbb{R}^2$, the instantaneous conditional law of q_t can in our case be written as

$$\nu^\xi(t,dq|z) = \frac{\psi(t,q)|x|\sigma_{\Sigma(z)}(dq)}{\int_{\Sigma(z)}\psi(t,q)|x|d\sigma_{\Sigma(z)}}(dq) \tag{14}$$

Finally, motivated by Remark 29, one can also consider the particle's density at instantaneous equilibrium $\psi^{\mathrm{eq}}(t,q)$ prescribed by equation (10) to obtain the following form

$$\nu^\xi(t,dq|z) = \frac{Z_t^{-1}e^{-\beta[V(q)-F_t(x)]}\cdot|x|\cdot\sigma_{\Sigma(z)}(dq)}{\int_{\mathbb{R}} Z_t^{-1}e^{-\beta[V((z,y))-F_t(z)]}|z|dy} \tag{15}$$

$$=: \alpha(q,t,z)\cdot\mathbb{1}_{\{(\cdot)=z\}}(\cdot)\times dy \tag{16}$$

where we used the fact that

$$\sigma_{\Sigma(z)}(dq) = \mathbb{1}_{\{z\}}(\cdot)\times dy \tag{17}$$

and where

$$Z_t = \int_{\mathbb{R}^2}\exp\left(-\beta\left(V((x,y)) - F_t(x)\right)\right)dx\,dy, \tag{18}$$

2.3 Approximating Γ_t

On the other side, Γ_t will be approximated following a $\mathbb{P}_0$-finite element scheme [2], i.e.

$$\Gamma_t(z) = \nabla F_t(z) \tag{19}$$

$$\simeq \Gamma_t^{\Delta z}\left(\lfloor \frac{z - z_{\min}}{\Delta z} \rfloor\right) \tag{20}$$

$$:= \frac{\sum_{j=0}^{M} f(q_t^j)\mathbb{1}_{\hat{\Sigma}^n}(q_t^j)}{\sum_{j=1}^{M} \mathbb{1}_{\hat{\Sigma}^n}(q_t^j)} \tag{21}$$

where $\hat{\Sigma}^n := \xi^{-1}([z_n;\, z_{n+1}])$

where we use the following local mean force expression for $\xi(x, y) = x$

$$f(x,y) = \sum_{\gamma=1}^{m} \frac{1}{x^2}\frac{\partial}{\partial x}V(x,y) - \beta^{-1}\,\mathrm{div}\left(\sum_{\gamma=1}^{m}\frac{1}{x^2}\delta_1(\gamma)e_x\right) \tag{22}$$

$$= \frac{2}{x^2}\frac{\partial}{\partial x}V(x,y) + \frac{2}{\beta\, x^3} \tag{23}$$

The derivative involves the potential prescribed by equation (12) and has the explicit form

$$\frac{\partial}{\partial x}V(x,y) = \frac{4}{3}x\big(4x^2 + 5y^2 - 5\big) \tag{24}$$

Substituting the latter in the former gives

$$f(x,y) = \frac{2}{\beta x^3} - \frac{8x}{3}\,\frac{4x^2 + 5y^2 - 5}{3x^2} \tag{25}$$

2.4 Computational scheme

Wrapping up all the above results and remarks allow one to obtain the following computational scheme for the computation of the ABF method in the case of the double well potential. The corresponding implementation is hosted in the following repository: `https://github.com/benediktpetko/uncertaintyQuantification`.

Algorithm 1 Adaptive biased forcing algorithm for $\xi(x, y) = x$ [1]

procedure ABF(N, T, n, m, u, f, q_0)
  $\Delta t := \frac{T}{n}, \quad \Delta s := m\Delta t, \quad \bar{m} := \frac{T}{\Delta s}$
  Discretize $[a, b]$ via partition $z_l := a + l\frac{b-a}{u}, \quad l = 0, \dots u$
  Initialize $q_0^{(i)} := q_0, \quad i = 1, \dots N$
  Initialize $\hat{\Gamma}_0(z_l) := f(q_0), \quad l = 0, \dots, u$
  Generate $W \sim N(0, 1)$ iid as needed
  for $k = 0, \dots, \bar{m} - 1$ **do**
    for $j = 0, \dots, m - 1$ **do**
      for $i = 1, \dots, N$ **do**
        $z^{ijk} := z_l$ such that $\xi(q^{(i)}_{k\Delta s + j\Delta t}) \in [z_l, z_{l+1})$
        $q^{(i)}_{k\Delta s+(j+1)\Delta t} = q^{(i)}_{k\Delta s+j\Delta t} - \nabla V(q^{(i)}_{k\Delta s+j\Delta t})\Delta t$
                $+\hat{\Gamma}_{k\Delta s}(z^{ijk})\Delta t \cdot e_x$
                $+\sqrt{\Delta t}W$
    $N_{kl} := \#\{i | 1 \le i \le N, \xi(q^{(i)}_{(k+1)\Delta s}) \in [z_l, z_{l+1})\}, \quad l = 0, \dots, u - 1$
    if $N_{kl}! = 0$ **then**
        $\hat{\Gamma}_{(k+1)\Delta s}(z_l) := \frac{1}{N_{kl}} \sum_{i=1}^{N} f(q^{(i)}_{(k+1)\Delta s}), \quad l = 0, \dots, u - 1$
    else do
        $\hat{\Gamma}_{(k+1)\Delta s}(z_l) := 0$

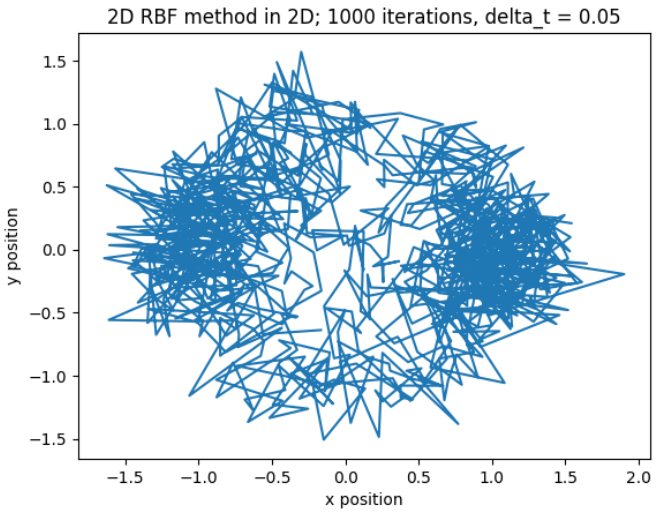

Figure 5: 2D-simulation time using the ABF method for a particle starting at $x_0 = (0.1, 0.1)$. After comparing this graph with the above figure 3 ran with the standard Langevin dynamics, one can observe that the particle spent less of its time stuck in the wells and explores the space more effectively.

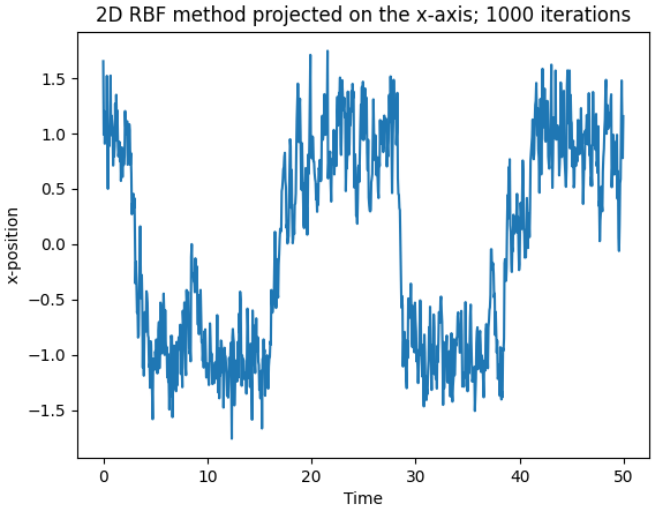

Figure 6: x-axis projection of a 2D-simulation using the ABF method with initial condition $x_0 = (0.1, 0.1)$. Compared to the simulation run with the non-biased Langevin dynamics (cf. figure 4), transitions between the two wells are done in a smoother manner, i.e. more time is spent inbetween the wells.

References

[1] T. Lelièvre, M. Rousset, and G. Stoltz. *Free Energy Computations: A Mathematical Perspective*. Imperial College Press, 2010.

[2] Olgierd Cecil Zienkiewicz et al. *The finite element method*. Vol. 3. McGraw-hill London, 1977.