

Some Remarks on Free Energy and Coarse-Graining

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Abstract We present recent results on coarse-graining techniques for thermodynamic quantities (canonical averages) and dynamical quantities (averages of path functionals over solutions of overdamped Langevin equations). The question is how to obtain reduced models to compute such quantities, in the specific case when the functional to be averaged only depends on a few degrees of freedom. We mainly review, numerically illustrate and extend results from (Blanc et al. *Journal of Nonlinear Science* 20(2):241–275, 2010; Legoll and Lelièvre *Nonlinearity* 23(9):2131–2163, 2010.), concerning the computation of the stress-strain relation for one-dimensional chains of atoms, and the construction of an effective dynamics for a scalar coarse-grained variable when the complete system evolves according to the overdamped Langevin equation.

1 Motivation

In molecular simulation, two types of quantities are typically of interest: averages with respect to the canonical ensemble (*thermodynamic quantities*, such as stress, root-mean-square distance, ...), and averages of functionals over paths (*dynamic quantities*, like viscosity, diffusion coefficients or rate constants). In both cases, the question of coarse-graining is relevant, in the sense that the considered functionals

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typically depend only on a few variables of the system (collective variables, or reaction coordinates). Therefore, it is essential to understand how to obtain coarse-grained models on these variables.

1.1 Coarse-Graining of Thermodynamic Quantities

Computing canonical averages is a standard task in molecular dynamics. For a molecular system whose atom positions are described by a vector $q \in \mathbb{R}^n$, these quantities read

$$\int_{\mathbb{R}^n} \Phi(q) d\mu,$$

where $\Phi : \mathbb{R}^n \rightarrow \mathbb{R}$ is the observable of interest and μ is the Boltzmann-Gibbs measure,

$$d\mu = Z^{-1} \exp(-\beta V(q)) dq, \quad (1)$$

where V is the potential energy of the system, β is proportional to the inverse of the system temperature, and

$$Z = \int_{\mathbb{R}^n} \exp(-\beta V(q)) dq$$

is a normalizing constant. Typically, q represents the position of N particles in dimension d , hence $q \in \mathbb{R}^n$ with $n = dN$.

As mentioned above, observables of interest are often functions of only part of the variable q . For example, q denotes the positions of *all* the atoms of a protein and of the solvent molecules around, and the quantity of interest is only a particular angle between some atoms in the protein, because this angle characterizes the conformation of the protein (and thus the potential energy well in which the system is, is completely determined by the knowledge of this quantity of interest). Another example is the case when $q = (q^1, \dots, q^n)$ denotes the positions of all the atoms of a one-dimensional chain, and quantities of interest are only a function of the total length $q^n - q^1$ of the chain.

We thus introduce the so-called *reaction coordinate*

$$\xi : \mathbb{R}^n \rightarrow \mathbb{R},$$

which contains all the information we are interested in. Throughout this article, we assume that it is a smooth function such that $|\nabla \xi|$ is bounded from below by a positive constant, so that the configurational space can be foliated by isosurfaces associated to ξ . A simple case that will be considered below is $\xi(q^1, \dots, q^n) = q^n$.

To this function ξ is naturally associated an effective energy A , called the *free energy*, such that

$$d(\xi \star \mu) = \exp(-\beta A(z)) dz,$$

where $\xi \star \mu$ denotes the image of the measure μ by ξ . In other words, for any test function $\Phi : \mathbb{R} \rightarrow \mathbb{R}$,

$$\int_{\mathbb{R}^n} \Phi(\xi(q)) Z^{-1} \exp(-\beta V(q)) dq = \int_{\mathbb{R}} \Phi(z) \exp(-\beta A(z)) dz. \quad (2)$$

Expressions of A and its derivative are given below (see Sect. 1.4).

The interpretation of (2) is that, when Q is a random variable distributed according to the Boltzmann measure (1), then $\xi(Q)$ is distributed according to the measure $\exp(-\beta A(z)) dz$. Hence, the free energy A is a relevant quantity for computing thermodynamic quantities, namely canonical averages.

In conclusion, the question of coarse-graining thermodynamic quantities amounts to computing the free energy, and there are several efficient methods to perform such calculations (see for example [6, 20]). In the sequel of this article, we address a particular case, motivated by materials science, where the system under consideration is a one-dimensional chain of atoms, and $\xi(q^1, \dots, q^n) = q^n - q^1$ is the length of the chain (see Fig. 1 below). We are interested in the free energy associated to this reaction coordinate, and its behaviour when the number n of particles goes to $+\infty$. Standard algorithms to compute the free energy then become prohibitively expensive, as the dimension of the system becomes larger and larger. Alternative strategies are needed, and we investigate analytical methods, based on large deviations principles, in Sect. 2.

1.2 Coarse-Graining of Dynamical Quantities

The second topic of this contribution is related to the *dynamics* of the system, and how to coarse-grain it. In short, we will show how to design a dynamics that approximates the path $t \mapsto \xi(Q_t)$, where ξ is the above reaction coordinate.

To make this question precise, we first have to *choose* the full dynamics, which will be the reference one. In the following, we consider the overdamped Langevin dynamics on state space \mathbb{R}^n :

$$dQ_t = -\nabla V(Q_t) dt + \sqrt{2\beta^{-1}} dW_t, \quad Q_{t=0} = Q_0, \quad (3)$$

where W_t is a standard n -dimensional Brownian motion. Under suitable assumptions on V , this dynamics is ergodic with respect to the Boltzmann-Gibbs measure (1) (see [5] and references therein). Hence, for μ -almost all initial conditions Q_0 ,

$$\lim_{T \rightarrow \infty} \frac{1}{T} \int_0^T \Phi(Q_t) dt = \int_{\mathbb{R}^n} \Phi(q) d\mu \quad (4)$$

almost surely. In practice, this convergence is often very slow, due to some metastabilities in the dynamics: Q_t samples a given well of the potential energy for a long time, before hopping to some other well of V .

An important dynamical quantity we will consider below is the average residence time, that is the mean time that the system spends in a given well, before hopping to another one, when it follows the dynamics (3). Typically, the wells are fully

described through ξ (q is in a given well if and only if $\xi(q)$ is in a given interval), so that these times can be obtained from the knowledge of the time evolution of $\xi(Q_t)$, which is expensive to compute since it means simulating the full system.

In Sect. 3 below, we will first present a one-dimensional dynamics of the form

$$d\bar{\eta}_t = b(\bar{\eta}_t) dt + \sqrt{2\beta^{-1}} \sigma(\bar{\eta}_t) dB_t, \quad (5)$$

where B_t is a standard one-dimensional Brownian motion and b and σ are scalar functions, such that $(\bar{\eta}_t)_{0 \leq t \leq T}$ is a good approximation (in a sense to be made precise below) of $(\xi(Q_t))_{0 \leq t \leq T}$. Hence, the dynamics (5) can be thought of as a coarse-grained, or *effective*, dynamics for the quantity of interest. A natural requirement is that (5) preserves equilibrium quantities, *i.e.* it is ergodic with respect to $\exp(-\beta A(z)) dz$, the equilibrium measure of $\xi(Q_t)$ when Q_t satisfies (3), but we typically ask for more than that. For example, we would like to be able to recover residence times in the wells from (5), hence bypassing the expensive simulation of $\xi(Q_t)$. We will show below that the effective dynamics we propose indeed fulfills these two requirements.

As a matter of fact, the coarse-grained dynamics

$$d\bar{z}_t = -A'(\bar{z}_t) dt + \sqrt{2\beta^{-1}} dB_t \quad (6)$$

is a one-dimensional dynamics that is ergodic with respect to $\exp(-\beta A(z)) dz$. It can thus be thought of as a natural candidate for a dynamics approximating $\xi(Q_t)$, all the more so as practitioners often look at the free energy profile (*i.e.* the function $z \mapsto A(z)$) to get an idea of the dynamics of transition (typically the transition time) between one region indexed by the reaction coordinate (say for example $\{q \in \mathbb{R}^n; \xi(q) \leq z_0\}$) and another one (for example $\{q \in \mathbb{R}^n; \xi(q) > z_0\}$). If $\xi(Q_t)$ follows a dynamics which is close to (6), then the Transition State Theory says that residence times are a function of the free energy barriers [17, 18], and then it makes sense to look at the free energy to compute some dynamical properties. It is thus often assumed that there is some dynamical information in the free energy A .

In the sequel, we will compare the accuracy (with respect to the original full dynamics) of both coarse-grained dynamics, an effective dynamics, an effective dynamics of type (5) (namely dynamics (67) below) and the dynamics (6) driven by the free energy. Their relation has been investigated from an analytical viewpoint in [19, Sect. 2.3] (see also [11, Sect. 10 and (89)] and [21]).

1.3 Outline of the Article

In this contribution, we mainly review, numerically illustrate and extend results from the two articles [3, 19]. Our aim is to present in a pedagogical and unified manner recent contributions on coarse-graining procedures concerning: (1) a static case inspired by material sciences, namely the computation of stress-

strain (namely force-elongation) relation for one-dimensional chains of atoms, in the thermodynamic limit (Sect. 2) and (2) a dynamic case inspired by molecular dynamics computations, namely the derivation of effective dynamics along the reaction coordinate, for overdamped Langevin equations (Sect. 3). Compared to the original articles [3, 19], we propose some extensions of the theoretical results (see *e.g.* Sect. 2.2), some simpler proofs in more restricted settings (in Sect. 3.3) and new numerical experiments (Sects. 2.2.4 and 3.4).

1.4 Notation

We gather here some useful notation and results. Let Σ_z be the submanifold of \mathbb{R}^n of positions at a fixed value of the reaction coordinate:

$$\Sigma_z = \{q \in \mathbb{R}^n; \xi(q) = z\}. \quad (7)$$

Let us introduce μ_{Σ_z} , which is the probability measure μ conditioned at a fixed value of the reaction coordinate:

$$d\mu_{\Sigma_z} = \frac{\exp(-\beta V) |\nabla \xi|^{-1} d\sigma_{\Sigma_z}}{\int_{\Sigma_z} \exp(-\beta V) |\nabla \xi|^{-1} d\sigma_{\Sigma_z}}, \quad (8)$$

where the measure σ_{Σ_z} is the Lebesgue measure on Σ_z induced by the Lebesgue measure in the ambient Euclidean space $\mathbb{R}^n \supset \Sigma_z$. By construction, if Q is distributed according to the Gibbs measure (1), then the law of Q conditioned to a fixed value z of $\xi(Q)$ is μ_{Σ_z} . The measure $|\nabla \xi|^{-1} d\sigma_{\Sigma_z}$ is sometimes denoted by $\delta_{\xi(q)=z}(dq)$ in the literature.

We recall the following expressions for the free energy A and its derivative A' , also called the *mean force* (see [7]):

$$A(z) = -\beta^{-1} \ln \left(\int_{\Sigma_z} Z^{-1} \exp(-\beta V) |\nabla \xi|^{-1} d\sigma_{\Sigma_z} \right), \quad (9)$$

$$A'(z) = \int_{\Sigma_z} F d\mu_{\Sigma_z}, \quad (10)$$

where F is the so-called *local mean force*:

$$F = \frac{\nabla V \cdot \nabla \xi}{|\nabla \xi|^2} - \beta^{-1} \operatorname{div} \left(\frac{\nabla \xi}{|\nabla \xi|^2} \right). \quad (11)$$

In the particular case when the reaction coordinate is just one of the cartesian coordinate, say $\xi(q) = q^n$, then

$$A(z) = -\beta^{-1} \ln \left(\int_{\mathbb{R}^{n-1}} Z^{-1} \exp(-\beta V(q^1, \dots, q^{n-1}, z)) dq^1 \dots dq^{n-1} \right)$$

and the local mean force is just $F = \partial_{q^n} V$, so that

$$A'(z) = \frac{\int_{\mathbb{R}^{n-1}} \partial_{q^n} V(q^1, \dots, q^{n-1}, z) \exp(-\beta V(q^1, \dots, q^{n-1}, z)) dq^1 \dots dq^{n-1}}{\int_{\mathbb{R}^{n-1}} \exp(-\beta V(q^1, \dots, q^{n-1}, z)) dq^1 \dots dq^{n-1}}.$$

2 Computing Macroscopic Stress-Strain Relations for One-Dimensional Chains of Atoms

In this section, we wish to compute the stress-strain relation of a one-dimensional chain of atoms, in the thermodynamic limit. More precisely, we consider a chain of $1 + N$ atoms, with its left-end atom fixed, and either submit the right-end atom to a force, and compute the average elongation, or prescribe the elongation, and compute the force. We will show that, in the limit $N \rightarrow \infty$, these two relations are identical, and that they can be computed in an extremely efficient manner. In short, passing to the limit $N \rightarrow \infty$ makes tractable a computation that is, for finite and large N , very expensive.

The relation between that question and the question of determining the free energy of the system, when the reaction coordinate is the length of the system, will also be discussed.

In the sequel, we first proceed with the nearest neighbour case (see Sect. 2.1). We next address the next-to-nearest neighbour case in Sect. 2.2, which is technically more involved.

2.1 The Nearest Neighbour (NN) Case

We consider a one-dimensional chain of atoms, with positions q^0, q^1, \dots, q^N . In this section, we only consider nearest neighbour interaction. In addition to this internal interaction, we assume that the atom at the right boundary of the chain is submitted to an external force f , and that the atom at the left boundary is fixed: $q^0 = 0$. The energy of the chain thus reads

$$\tilde{E}_f(q^1, \dots, q^N) = \sum_{i=1}^N W(q^i - q^{i-1}) - f q^N.$$

In the sequel, we will consider the limit when the number N of atoms goes to ∞ . We wish to make sure that, even when $N \rightarrow \infty$, the system occupies, on average, a finite length. To this aim, we introduce the rescaled positions $u^i = h q^i$, with $h = 1/N$. The energy now reads

$$E_f(u^1, \dots, u^N) = \sum_{i=1}^N W\left(\frac{u^i - u^{i-1}}{h}\right) - f \frac{u^N}{h}, \quad (12)$$

where again $u^0 = 0$.

For any observable Φ , depending on the variables u^1, \dots, u^N , we define the canonical average of Φ by

$$\langle \Phi \rangle_N^f = Z^{-1} \int_{\mathbb{R}^N} \Phi(u^1, \dots, u^N) \exp(-\beta E_f(u^1, \dots, u^N)) du^1 \dots du^N, \quad (13)$$

where the partition function Z reads

$$Z = \int_{\mathbb{R}^N} \exp(-\beta E_f(u^1, \dots, u^N)) du^1 \dots du^N.$$

We assume in the sequel that $W(r)$ grows fast enough to ∞ when $|r| \rightarrow \infty$, so that Z is well defined (it is for instance enough that $W(r) \sim_{|r| \rightarrow \infty} |r|^\alpha$ with $\alpha > 1$).

We will be interested in the limit of $\langle \Phi \rangle_N^f$, when $N \rightarrow \infty$, and when Φ only depends on u^N : $\Phi(u^1, \dots, u^N) = A(u^N)$ for a given function A .

Remark 1. In (13), we let the variables u^i vary on the whole real line. We do not constrain them to obey $u^{i-1} \leq u^i$, which would encode the fact that nearest neighbours remain nearest neighbours. The argument provided here carries through when this constraint is accounted for: we just need to replace the interaction potential W by

$$W_c(y) = \begin{cases} W(y) & \text{when } y \geq 0, \\ +\infty & \text{otherwise.} \end{cases}$$

2.1.1 Computing the Strain for a Given Stress

We first show a simple adaptation of [3, Theorem 1], which is useful to compute averages of general observables, in the thermodynamic limit, for the canonical ensemble at a fixed stress:

Lemma 1. *Assume that $A : \mathbb{R} \rightarrow \mathbb{R}$ is continuous, that for some $p \geq 1$, there exists a constant C such that*

$$\forall y \in \mathbb{R}, \quad |A(y)| \leq C(1 + |y|^p),$$

and that

$$\int_{\mathbb{R}} (1 + |y|^p) \exp(-\beta[W(y) - fy]) dy < +\infty.$$

Then

$$\lim_{N \rightarrow \infty} \langle A(u^N) \rangle_N^f = A(y^*(f)),$$

with

$$y^*(f) = \frac{\int_{\mathbb{R}} y \exp(-\beta[W(y) - fy]) dy}{\int_{\mathbb{R}} \exp(-\beta[W(y) - fy]) dy}. \quad (14)$$

Proof. We observe that

$$\begin{aligned}\langle A \rangle_N^f &= Z^{-1} \int_{\mathbb{R}^N} A(u^N) \exp(-\beta E_f(u^1, \dots, u^N)) du^1 \dots du^N \\ &= Z^{-1} \int_{\mathbb{R}^N} A(u^N) \exp\left(-\beta \sum_{i=1}^N W_f\left(\frac{u^i - u^{i-1}}{h}\right)\right) du^1 \dots du^N,\end{aligned}$$

where $W_f(x) = W(x) - fx$. Introducing $y^i = \frac{u^i - u^{i-1}}{h}$, a change of variables in the above integral yields

$$\langle A \rangle_N^f = Z^{-1} \int_{\mathbb{R}^N} A\left(\frac{1}{N} \sum_{i=1}^N y^i\right) \exp\left(-\beta \sum_{i=1}^N W_f(y^i)\right) dy^1 \dots dy^N,$$

where, with a slight abuse of notation,

$$Z = \int_{\mathbb{R}^N} \exp\left(-\beta \sum_{i=1}^N W_f(y^i)\right) dy^1 \dots dy^N.$$

Consider now a sequence $\{Y^i\}_{i=1}^N$ of independent random variables, sharing the same law $z^{-1} \exp(-\beta W_f(y)) dy$ with

$$z = \int_{\mathbb{R}} \exp(-\beta W_f(y)) dy.$$

It is clear that

$$\langle A \rangle_N^f = \mathbb{E} \left[A\left(\frac{1}{N} \sum_{i=1}^N Y^i\right) \right].$$

The law of large numbers readily yields that $\frac{1}{N} \sum_{i=1}^N Y^i$ converges almost surely to $y^*(f)$ defined by (14).

We infer from [3, Theorem 1] that, for any force f , and for any observable A sufficiently smooth, the limit when $N \rightarrow \infty$ of $\langle A \rangle_N^f$ is

$$\lim_{N \rightarrow \infty} \langle A \rangle_N^f = A(y^*(f)).$$

Rates of convergence are also provided in the same theorem. □

Numerical simulations illustrating this result are reported in [3, Sect. 2.3].

In the specific case of interest here, namely computing the stress-strain relation, we take $A(u^N) = u^N$, thus $\epsilon_N(f) := \langle A \rangle_N^f$ represents the average length of the chain, for a prescribed force f . We infer from the previous result that

$$\lim_{N \rightarrow \infty} \epsilon_N(f) = y^*(f).$$

We hence have determined the macroscopic elongation, namely $y^*(f)$, for a prescribed microscopic force f in the chain.

Notice that, in this specific case, A is a linear function, so we actually have $\epsilon_N(f) = y^*(f)$ for any N . The result of Lemma 1 remains interesting for computing standard deviation of the average length, for example.

Remark 2. The force between atoms j and $j - 1$ is $W'\left(\frac{u^j - u^{j-1}}{h}\right)$. Its canonical average, defined by (13), is

$$\begin{aligned} \sigma_N^j &= Z^{-1} \int_{\mathbb{R}^N} W'\left(\frac{u^j - u^{j-1}}{h}\right) \exp\left(-\beta E_f(u^1, \dots, u^N)\right) du^1 \dots du^N \\ &= Z^{-1} \int_{\mathbb{R}^N} W'(y^j) \exp\left(-\beta \sum_{i=1}^N [W(y^i) - f y^i]\right) dy^1 \dots dy^N \\ &= \frac{\int_{\mathbb{R}} W'(y^j) \exp(-\beta [W(y^j) - f y^j]) dy^j}{\int_{\mathbb{R}} \exp(-\beta [W(y^j) - f y^j]) dy^j} \\ &= f + \frac{\int_{\mathbb{R}} [W'(y^j) - f] \exp(-\beta [W(y^j) - f y^j]) dy^j}{\int_{\mathbb{R}} \exp(-\beta [W(y^j) - f y^j]) dy^j}, \end{aligned}$$

where $y^j = \frac{u^j - u^{j-1}}{h}$. Integrating by parts, we see that the second term of the last line vanishes. We hence obtain that the average force between two consecutive atoms is independent of j (the stress is homogeneous in the material), and is equal to its prescribed microscopic value f :

$$\forall j, \forall N, \quad \sigma_N^j = f.$$

Imposing a force f on the right boundary atom hence implies that the average force between any two consecutive atoms is equal to f . \diamond

2.1.2 Computing the Stress for a Given Strain

In the previous section, we have prescribed a force, and computed an average elongation. We now prescribe the length of the material, by imposing $u^0 = 0$ and $u^N = x$ (see Fig. 1).

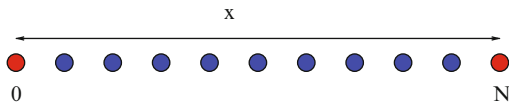


Fig. 1 One-dimensional chain of $1 + N$ atoms, where the total length of the system is prescribed at the value x

As we fix the position of atom N , the system is insensitive to any force f imposed on that atom. We hence set $f = 0$. Our aim is to compute the force in the chain,

$$\mathcal{T}_N(x) = \frac{\int_{\mathbb{R}^{N-1}} W' \left(\frac{x - u^{N-1}}{h} \right) \exp(-\beta E_0(u^1, \dots, u^{N-1}, x)) du^1 \dots du^{N-1}}{\int_{\mathbb{R}^{N-1}} \exp(-\beta E_0(u^1, \dots, u^{N-1}, x)) du^1 \dots du^{N-1}}, \quad (15)$$

or, more precisely, its limit when $N \rightarrow \infty$. Note that, as all the $(u^i - u^{i-1})/h$ play the same role in the above expression, we also have, for any $1 \leq i \leq N-1$,

$$\mathcal{T}_N(x) = \frac{\int_{\mathbb{R}^{N-1}} W' \left(\frac{u^i - u^{i-1}}{h} \right) \exp(-\beta E_0(u^1, \dots, u^{N-1}, x)) du^1 \dots du^{N-1}}{\int_{\mathbb{R}^{N-1}} \exp(-\beta E_0(u^1, \dots, u^{N-1}, x)) du^1 \dots du^{N-1}}.$$

The force between atom N and $N-1$ is thus equal to the force between any two consecutive atoms.

We infer from (15) that $\mathcal{T}_N(x) = F'_N(x)$, where

$$F_N(x) = -\frac{1}{\beta N} \ln \left[\int_{\mathbb{R}^{N-1}} \exp(-\beta E_0(u^1, \dots, u^{N-1}, x)) du^1 \dots du^{N-1} \right].$$

Hence NF_N is the free energy of the material associated to the reaction coordinate $\xi(u^1, \dots, u^N) = u^N$, and F_N is a rescaled free energy (free energy per integrated out particle). Using the variables $y^i = (u^i - u^{i-1})/h$, we also see that $\exp(-\beta NF_N(x)) dx$ is (up to a normalizing multiplicative constant) the probability distribution of the random variable $\frac{1}{N} \sum_{i=1}^N Y^i$, when $\{Y^i\}_{i=1}^N$ is a sequence of independent random variables, sharing the same law $z^{-1} \exp(-\beta W(y)) dy$, with

$$z = \int_{\mathbb{R}} \exp(-\beta W(y)) dy.$$

In the case $W(y) = (y-a)^2/2$, it is possible to analytically compute $F_N(x)$, and to observe that there exists a constant C_N , independent of x , such that $F_N(x) + C_N$ has a finite limit when $N \rightarrow \infty$. In the general case, the limit of F_N is given by the following result, which relies on a large deviations result for i.i.d. random variables:

Lemma 2 ([3], Theorem 2). *Assume that the potential W satisfies*

$$\forall \xi \in \mathbb{R}, \quad \int_{\mathbb{R}} \exp(\xi y - \beta W(y)) dy < +\infty,$$

and $\exp(-\beta W) \in H^1(\mathbb{R})$. Then

$$\lim_{N \rightarrow +\infty} \left(F_N(x) + \frac{1}{\beta} \ln \frac{z}{N} \right) = F_\infty(x), \quad (16)$$

with

$$F_\infty(x) := \frac{1}{\beta} \sup_{\xi \in \mathbb{R}} \left(\xi x - \ln \left[z^{-1} \int_{\mathbb{R}} \exp(\xi y - \beta W(y)) dy \right] \right) \quad (17)$$

and

$$z = \int_{\mathbb{R}} \exp(-\beta W(y)) dy.$$

This convergence holds pointwise in x , and also in L_{loc}^p for any $1 \leq p < \infty$. As a consequence, F'_N converges to F'_∞ in $W_{\text{loc}}^{-1,p}$.

We hence obtain the macroscopic force $F'_\infty(x)$ for a prescribed elongation x . Numerical simulations that illustrate this result are reported in [3, Sect. 2.3].

Remark 3. The additive term $\beta^{-1} \ln(z/N)$ in (16) can be seen as a normalizing constant. Indeed, as mentioned above, NF_N is a free energy, and the correct normalization for $\exp(-\beta NF_N)$ to be a probability density function is:

$$\int_{\mathbb{R}} \exp \left[-\beta N \left(F_N(x) + \frac{1}{\beta} \ln \frac{z}{N} \right) \right] dx = 1.$$

◇

Remark 4. F_N is a challenging quantity to compute. One possible method is to compute, for each x , its derivative $F'_N(x)$, and deduce F_N (this is the so-called thermodynamic integration method). Note that $F'_N(x) = \mathcal{T}_N(x)$ is given by (15): it is a canonical average of some observable, in a space of dimension $N - 1 \gg 1$. In contrast, F_∞ is easier to compute, since it only involves one-dimensional integrals or optimization problems. ◇

2.1.3 Equivalence of Stress-Strain Relations in the Thermodynamic Limit

The function we maximize in (17) is concave, so there exists a unique maximizer $\xi(x)$ in (17), that satisfies the Euler-Lagrange equation

$$x = \frac{\int_{\mathbb{R}} y \exp(\xi(x)y - \beta W(y)) dy}{\int_{\mathbb{R}} \exp(\xi(x)y - \beta W(y)) dy}. \quad (18)$$

We observe that

$$F'_\infty(x) = \frac{\xi(x)}{\beta}.$$

On the other hand, recall the definition (14) of $y^*(f)$:

$$y^*(f) = \frac{\int_{\mathbb{R}} y \exp(-\beta [W(y) - fy]) dy}{\int_{\mathbb{R}} \exp(-\beta [W(y) - fy]) dy}.$$

Comparing (18) and (14), we see that $y^*(\beta^{-1}\xi(x)) = y^*(F'_\infty(x)) = x$. The function $f \mapsto y^*(f)$ is increasing (because its derivative is positive), thus it is injective, and we also get the converse relation: $F'_\infty(y^*(f)) = f$.

Otherwise stated, the relation $f \mapsto y^*(f)$ and $x \mapsto F'_\infty(x)$ are inverse one to each other. So, prescribing a microscopic force f and computing the macroscopic elongation is equivalent to prescribing an elongation and computing the macroscopic force, *in the thermodynamic limit* (namely in the limit $N \rightarrow \infty$).

2.2 The Next-to-Nearest Neighbour (NNN) Case

We now consider next-to-nearest neighbour interactions in the chain. Again, the first atom is fixed: $u^0 = 0$, whereas the last one is submitted to an external force f . The (rescaled) energy reads

$$E_f(u^1, \dots, u^N) = \sum_{i=1}^N W_1\left(\frac{u^i - u^{i-1}}{h}\right) + \sum_{i=1}^{N-1} W_2\left(\frac{u^{i+1} - u^{i-1}}{h}\right) - f \frac{u^N}{h}. \quad (19)$$

If $W_2 \equiv 0$, this energy reduces to (12). Averages of observables are again defined by (13).

2.2.1 Computing the Strain for a Given Stress

Our aim, as in Sect. 2.1.1, is to compute the macroscopic strain, which is the average length of the material, that is

$$\epsilon_N(f) = \langle u^N \rangle_N^f,$$

where $\langle \cdot \rangle_N^f$ is the average with respect to the canonical measure associated to E_f . We introduce the notation

$$W_{1f}(x) = W_1(x) - fx,$$

which will be useful in the sequel. A simple adaptation of [3, Theorem 3] yields the following general result:

Lemma 3. *Assume that $A : \mathbb{R} \mapsto \mathbb{R}$ is continuous, and that there exists $p \geq 1$ and $C > 0$ such that*

$$|A(x)| \leq C(1 + |x|^p).$$

Assume also that W_{1f} and W_2 both belong to $L^1_{\text{loc}}(\mathbb{R})$, that they are bounded from below, and that, for any $x \in \mathbb{R}$, we have $|W_{1f}(x)| < \infty$ and $|W_2(x)| < \infty$. In addition, we assume that $e^{-\beta W_{1f}}$ and $e^{-\beta W_2}$ both belong to $W^{1,1}_{\text{loc}}(\mathbb{R})$, with

$$\int_{\mathbb{R}} (1 + |x|^p) e^{-\beta W_{1f}(x)} dx < +\infty \quad \text{and} \quad \int_{\mathbb{R}} (1 + |x|^p) e^{-\beta W_2(x)} dx < +\infty.$$

Then

$$\lim_{N \rightarrow \infty} \langle A(u^N) \rangle_N^f = A(y^*(f)), \quad (20)$$

with

$$y^*(f) = \int_{\mathbb{R}} y \psi_f^2(y) dy, \quad (21)$$

where ψ_f solves the variational problem

$$\lambda_f = \max_{\psi \in L^2(\mathbb{R})} \left\{ \int_{\mathbb{R}^2} \psi(y) \psi(z) K_f(y, z) dy dz; \int_{\mathbb{R}} \psi^2(y) dy = 1 \right\}, \quad (22)$$

with

$$K_f(x, y) := \exp \left[-\beta W_2(x + y) - \frac{\beta}{2} W_{1f}(x) - \frac{\beta}{2} W_{1f}(y) \right]. \quad (23)$$

We only provide here the main arguments to prove this result (see [3, Sec. 3.1.1 and Theorem 3] for details). They will be useful in the sequel. The observable $A(u^N)$ only depends on u^N , thus

$$\begin{aligned} \langle A(u^N) \rangle_N^f &= Z^{-1} \int_{\mathbb{R}^N} A(u^N) \exp(-\beta E_f(u^1, \dots, u^N)) du^1 \dots du^N \\ &= Z^{-1} \int_{\mathbb{R}^N} A(u^N) \exp \left(-\beta \sum_{i=1}^N W_{1f} \left(\frac{u^i - u^{i-1}}{h} \right) \right. \\ &\quad \left. - \beta \sum_{i=1}^{N-1} W_2 \left(\frac{u^{i+1} - u^{i-1}}{h} \right) \right) du^1 \dots du^N. \end{aligned}$$

Introducing again the variables $y^i = \frac{u^i - u^{i-1}}{h}$, we see that

$$\langle A(u^N) \rangle_N^f = Z^{-1} \int_{\mathbb{R}^N} A \left(\frac{1}{N} \sum_{i=1}^N y^i \right) \exp(-\beta W_{1f}(y^1)) \prod_{i=2}^N k_f(y^{i-1}, y^i) dy^1 \dots dy^N, \quad (24)$$

with

$$k_f(y^{i-1}, y^i) = \exp(-\beta W_{1f}(y^i) - \beta W_2(y^{i-1} + y^i)).$$

Assume for a moment that $\int_{\mathbb{R}} k_f(a, b) db = 1$. Then we see that

$$\langle A(u^N) \rangle_N^f = \mathbb{E} \left[A \left(\frac{1}{N} \sum_{i=1}^N Y^i \right) \right],$$

where $\{Y^i\}_{i=1}^N$ is a realization of a Markov chain of transition kernel k_f , and where Y^1 has the initial law (up to a normalization constant) $\exp(-\beta W_{1f}(y^1)) dy^1$. A law of large numbers argument, now for Markov chains, yields the large N limit

of $\langle A(u^N) \rangle_N^f$ (recall that, in the case of the NN model considered in Sect. 2.1.1, this limit is given by a law of large numbers argument for i.i.d. sequences).

In general, of course, $\int_{\mathbb{R}} k_f(a, b) db \neq 1$. There is thus a slight technical difficulty in identifying a Markov chain structure in (24). It yet turns out that the above argument can be made rigorous as follows. Consider the variational problem (22), with K_f defined by (23). Under our assumptions, $K_f \in L^2(\mathbb{R} \times \mathbb{R})$. Using standard tools of spectral theory of self-adjoint operators (see e.g. [10]), one can prove that this problem has a maximizer (denoted ψ_f), and that, up to changing ψ_f in $-\psi_f$, the maximizer is unique. In addition, one can choose it such that $\psi_f > 0$. We can next define

$$g_f(x, y) := \frac{\psi_f(y)}{\lambda_f \psi_f(x)} K_f(x, y), \quad (25)$$

which satisfies

$$\int_{\mathbb{R}} g_f(y, z) dz = 1, \quad \int_{\mathbb{R}} \psi_f^2(y) g_f(y, z) dy = \psi_f^2(z).$$

The average (24) now reads

$$\begin{aligned} \langle A(u^N) \rangle_N^f &= Z_g^{-1} \int_{\mathbb{R}^N} A\left(\frac{1}{N} \sum_{i=1}^N y^i\right) \psi_f(y^1) e^{-\frac{\beta}{2} W_{1f}(y^1)} \\ &\quad \times g_f(y^1, y^2) \dots g_f(y^{N-1}, y^N) \frac{e^{-\frac{\beta}{2} W_{1f}(y^N)}}{\psi_f(y^N)} dy^1 \dots dy^N, \end{aligned} \quad (26)$$

with

$$Z_g = \int_{\mathbb{R}^N} \psi_f(y^1) e^{-\frac{\beta}{2} W_{1f}(y^1)} g_f(y^1, y^2) \dots g_f(y^{N-1}, y^N) \frac{e^{-\frac{\beta}{2} W_{1f}(y^N)}}{\psi_f(y^N)} dy^1 \dots dy^N.$$

Thus

$$\langle A(u^N) \rangle_N^f = \mathbb{E} \left[A\left(\frac{1}{N} \sum_{i=1}^N Y^i\right) \right],$$

where (Y^1, \dots, Y^N) may now be seen as a realization of a *normalized* Markov chain of kernel g_f , with invariant probability measure ψ_f^2 .

Under our assumptions, the Markov chain has a unique invariant measure, and satisfies a law of large numbers with respect to it. This yields the convergence (20). Numerical simulations illustrating this result are reported in [3, Sect. 3.1.3].

In the specific case of interest here, namely computing the stress-strain relation, we take $A(u^N) = u^N$, thus $\epsilon_N(f) := \langle A \rangle_N^f$ represents the average length of the chain, for a prescribed force f . We infer from the previous result that

$$\lim_{N \rightarrow \infty} \epsilon_N(f) = y^*(f).$$

We hence have determined the macroscopic elongation, namely $y^*(f)$, for a prescribed microscopic force f in the chain.

We conclude this section by showing the following result, which will be useful in the sequel.

Lemma 4. *Under the assumptions of Lemma 3, introduce the asymptotic variance $\sigma^2(f)$ defined by*

$$\sigma^2(f) = \int_{\mathbb{R}} (x - y^*(f))^2 \psi_f^2(x) dx + 2 \sum_{i \geq 2} \mathbb{E}((\tilde{Y}_i - y^*(f))(\tilde{Y}_1 - y^*(f))), \quad (27)$$

where $(\tilde{Y}_i)_{i \geq 1}$ is a Markov chain of transition kernel g_f , and of initial law ψ_f^2 , the invariant measure.

Assume that $\sigma^2(f) \neq 0$ almost everywhere. Then the function $f \mapsto y^*(f)$ is increasing.

Note that the right-hand side of (27) is exactly the variance appearing in the Central Limit Theorem for Markov chains [23, Theorem 17.0.1]. It is thus non-negative. More precisely, we have that

$$\lim_{N \rightarrow \infty} N \text{Var} \left(\frac{1}{N} \sum_{i=1}^N \tilde{Y}_i \right) = \sigma^2(f),$$

where $(\tilde{Y}_i)_{i \geq 1}$ is the Markov chain defined in the above lemma.

Proof. Let $\epsilon_N(f) := \langle u^N \rangle_N^f$. An analytical computation shows that

$$D_N(f) := \frac{d\epsilon_N}{df}(f) = N\beta \left[\langle (u^N)^2 \rangle_N^f - \left(\langle u^N \rangle_N^f \right)^2 \right].$$

Thus the function $f \mapsto \epsilon_N(f)$ is non-decreasing. By Lemma 3, $y^*(f)$ is the pointwise limit of $\epsilon_N(f)$: it is thus non-decreasing. It remains to prove that it is increasing.

Let us now compute the limit when $N \rightarrow \infty$ of $D_N(f)$. Using [3, Theorem 4], we see that

$$\lim_{N \rightarrow \infty} D_N(f) = \beta \sigma^2(f),$$

where $\sigma^2(f)$ is defined by (27).

Let us now fix τ and $\bar{\tau} \geq \tau$. Since $D_N(f) \geq 0$, we can use Fatou lemma, which yields that

$$\beta \int_{\tau}^{\bar{\tau}} \sigma^2(f) df = \int_{\tau}^{\bar{\tau}} \liminf D_N(f) df \leq \liminf \int_{\tau}^{\bar{\tau}} D_N(f) df = y^*(\bar{\tau}) - y^*(\tau).$$

As $\sigma^2(f) > 0$ almost everywhere, we thus obtain that $\tau \mapsto y^\star(\tau)$ is an increasing function. \square

2.2.2 Computing the Stress for a Given Strain

We now prescribe the length of the material, by imposing $u^0 = 0$ and $u^N = x$. Our aim is to compute the average force in the chain,

$$\mathcal{T}_N(x) = \frac{\int_{\mathbb{R}^{N-1}} A_h(u^{N-1}, u^{N-2}; x) \exp(-\beta E_0(u^1, \dots, u^{N-1}, x)) du^1 \dots du^{N-1}}{\int_{\mathbb{R}^{N-1}} \exp(-\beta E_0(u^1, \dots, u^{N-1}, x)) du^1 \dots du^{N-1}}, \quad (28)$$

where E_0 is the energy (19) with $f = 0$, and where the observable A_h is the force at the end of the chain, which reads

$$A_h(u^{N-1}, u^{N-2}; x) = W_1' \left(\frac{x - u^{N-1}}{h} \right) + W_2' \left(\frac{x - u^{N-2}}{h} \right).$$

More precisely, we are interested in $\lim_{N \rightarrow \infty} \mathcal{T}_N(x)$.

As in Sect. 2.1.2, we see that $\mathcal{T}_N(x) = F_N'(x)$, with

$$F_N(x) = -\frac{1}{\beta N} \ln \left[\int_{\mathbb{R}^{N-1}} \exp(-\beta E_0(u^1, \dots, u^{N-1}, x)) du^1 \dots du^{N-1} \right]. \quad (29)$$

Again, NF_N is the free energy associated to the reaction coordinate $\xi(u^1, \dots, u^N) = u^N$, and F_N is a rescaled free energy (free energy per integrated out particle). In the NN case, we have computed the large N limit of $F_N(x)$ using a large deviations result for i.i.d. random variables. Comparing Sects. 2.1.1 and 2.2.1, we also see that moving from a NN setting to a NNN setting implies moving from a framework where random variables are i.i.d. to a framework where they are a realization of a Markov chain. It is hence natural to try and use a large deviations result for Markov chains to compute the large N limit of (29).

We now assume that the underlying Markov chain satisfies the following *pointwise large deviations* result:

Assumption 1 Consider the Markov chain $\{Y^i\}_{i \geq 1}$ of kernel $k \in L^2(\mathbb{R} \times \mathbb{R})$. Assume that, for any $\xi \in \mathbb{R}$, the function $\exp(\xi y) k(x, y) \in L^2(\mathbb{R} \times \mathbb{R})$.

Introduce the operator (on $L^2(\mathbb{R})$)

$$(Q_\xi \varphi)(y) = \int_{\mathbb{R}} \varphi(x) \exp(\xi y) k(x, y) dx$$

and assume that it has a simple and isolated largest eigenvalue $\Lambda(\xi)$, and that $\xi \mapsto \ln \Lambda(\xi)$ is convex.

Let $\exp(-N\overline{F}_N(x))dx$ be the law of the random variable $\frac{1}{N}\sum_{i=1}^N Y^i$. We assume the large deviations principle

$$\lim_{N \rightarrow +\infty} \overline{F}_N(x) = \overline{F}_\infty(x), \quad (30)$$

where

$$\overline{F}_\infty(x) := \sup_{\xi \in \mathbb{R}} (\xi x - \ln \Lambda(\xi)). \quad (31)$$

We moreover assume that the convergence (30) holds pointwise in x , and also in L^p_{loc} , for any $1 \leq p < \infty$. As a consequence, \overline{F}'_N converges to \overline{F}'_∞ in $W^{-1,p}_{\text{loc}}$.

Note that similar results in a finite state Markov chain setting are reviewed in [9, pages 60–61] or [8, Sec. 3.1.1] (the continuous state case is addressed in e.g. [8, Secs. 6.3 and 6.5]). In the discrete state case, one can prove that $\xi \mapsto \ln \Lambda(\xi)$ is convex (see [9, Exercise V.14]). We will numerically check in the sequel that this assumption is indeed satisfied in the example we consider (see Fig. 2).

Remark 5. We have assumed that the operator Q_ξ has a simple and isolated largest eigenvalue. This can be proved for many kernels k , using for instance Krein-Rutman theorem [28]. In the case of interest in this contribution, we will use the specific expression of the kernel to transform the operator Q_ξ into a self-adjoint Hilbert-Schmidt operator on $L^2(\mathbb{R})$ (see Remark 7 below). We will thus be in position to work with self-adjoint compact operators. \diamond

Remark 6. In the NN case, when $k(x, y) = \theta(y) = z^{-1} \exp(-\beta W(y))$, the sequence $\{Y^i\}_{i \geq 1}$ is a sequence of i.i.d. variables sharing the same law $\theta(y) dy$. The operator Q_ξ has a unique eigenvalue

$$\Lambda(\xi) = \int_{\mathbb{R}} \exp(\xi y) \theta(y) dy.$$

We then recover the large deviations result of i.i.d. sequence given in Lemma 2 (see also [12–14, 29]). \diamond

We now wish to use Assumption 1 to compute the large N limit of (29). As pointed out in Sect. 2.2.1, there is a slight technical difficulty in identifying a Markov chain structure in the NNN setting, related to the normalization of the Markov chain kernel. We thus cannot readily use Assumption 1. We now detail how to overcome this difficulty.

Consider an observable A that depends only on u_N . In view of (29) and (26), its canonical average reads

$$\begin{aligned}
\langle A \rangle_N &= Z^{-1} \int_{\mathbb{R}^N} A(u^N) \exp(-\beta E_0(u^1, \dots, u^{N-1}, u^N)) du^1 \dots du^{N-1} du^N \\
&= Z^{-1} \int_{\mathbb{R}} A(x) \exp(-\beta N F_N(x)) dx \\
&= Z_g^{-1} \int_{\mathbb{R}^N} A\left(\frac{1}{N} \sum_{i=1}^N y^i\right) \psi_0(y^1) e^{-\frac{\beta}{2} W_1(y^1)} \\
&\quad \times g_0(y^1, y^2) \dots g_0(y^{N-1}, y^N) \frac{e^{-\frac{\beta}{2} W_1(y^N)}}{\psi_0(y^N)} dy^1 \dots dy^N,
\end{aligned}$$

where g_0 is defined by (25) and ψ_0 is the maximizer in (22), when the body force $f = 0$. Let $\mathcal{P}(y^1, \dots, y^N)$ be the probability density of a Markov chain $\{Y^i\}_{i=1}^N$ of kernel g_0 , where the law of Y^1 is (up to a normalization constant) $\psi_0(y^1) \exp(-\beta W_1(y^1)/2) dy^1$. Then

$$\int_{\mathbb{R}} A(x) \exp(-\beta N F_N(x)) dx = C_N \int_{\mathbb{R}^N} A\left(\frac{1}{N} \sum_{i=1}^N y^i\right) \mathcal{P}(y^1, \dots, y^N) r(y^N) dy^1 \dots dy^N, \quad (32)$$

where C_N is a constant that does not depend on the observable A , and

$$r(y^N) = \frac{e^{-\frac{\beta}{2} W_1(y^N)}}{\psi_0(y^N)}.$$

Let now $\alpha_N(x, y^N) dx dy^N$ be the law of the couple $\left(\frac{1}{N} \sum_{i=1}^N Y^i, Y^N\right)$. We recast (32) as

$$\int_{\mathbb{R}} A(x) \exp(-\beta N F_N(x)) dx = C_N \int_{\mathbb{R}^2} A(x) \alpha_N(x, y^N) r(y^N) dx dy^N.$$

As this relation holds for any observable A , with a constant C_N independent of A , we obtain

$$\exp(-\beta N F_N(x)) = C_N \int_{\mathbb{R}} \alpha_N(x, y^N) r(y^N) dy^N.$$

Assuming that r and $1/r$ are in $L^\infty(\mathbb{R})$, we have

$$C_N \|1/r\|_{L^\infty}^{-1} \int_{\mathbb{R}} \alpha_N(x, y^N) dy^N \leq \exp(-\beta N F_N(x)) \leq C_N \|r\|_{L^\infty} \int_{\mathbb{R}} \alpha_N(x, y^N) dy^N.$$

As a consequence, since the function r is independent of N ,

$$\lim_{N \rightarrow \infty} (F_N(x) + D_N) = \lim_{N \rightarrow \infty} \left[-\frac{1}{\beta N} \ln \int_{\mathbb{R}} \alpha_N(x, y^N) dy^N \right], \quad (33)$$

where $D_N = \frac{1}{\beta N} \ln C_N$. Recall now that

$$\gamma_N(x) = \int_{\mathbb{R}} \alpha_N(x, y^N) dy^N$$

is the density of $\frac{1}{N} \sum_{i=1}^N Y^i$, where $\{Y^i\}_{i=1}^N$ is a realization of the Markov chain of kernel g_0 . The behaviour of γ_N when $N \rightarrow \infty$ is given by Assumption 1:

$$\lim_{N \rightarrow +\infty} -\frac{1}{N} \ln \gamma_N(x) = \overline{F}_\infty(x), \quad (34)$$

where \overline{F}_∞ is given by (31). Collecting (33) and (34), we hence obtain that

$$\lim_{N \rightarrow \infty} (F_N(x) + D_N) = \frac{1}{\beta} \overline{F}_\infty(x).$$

We thus have the following result:

Lemma 5. *Assume that W_1 and W_2 both belong to $L^1_{\text{loc}}(\mathbb{R})$, that they are bounded from below, and that, for any $x \in \mathbb{R}$, we have $|W_1(x)| < \infty$ and $|W_2(x)| < \infty$. In addition, we assume that $e^{-\beta W_1}$ and $e^{-\beta W_2}$ both belong to $W^{1,1}_{\text{loc}}(\mathbb{R})$, with*

$$\int_{\mathbb{R}} e^{-\beta W_1(x)} dx < +\infty \quad \text{and} \quad \int_{\mathbb{R}} e^{-\beta W_2(x)} dx < +\infty,$$

and that, for any $\xi \in \mathbb{R}$, we have $\exp(\xi x - \beta W_1(x)) \in L^1(\mathbb{R})$.

Under Assumption 1 for the kernel g_0 defined by (25), we have that

$$\lim_{N \rightarrow +\infty} (F_N(x) + C_N) = F_\infty(x), \quad (35)$$

where F_N is defined by (29), C_N is a constant that does not depend on x , and F_∞ is given by the Legendre transform

$$F_\infty(x) := \frac{1}{\beta} \sup_{\xi \in \mathbb{R}} (\xi x - \ln \Lambda(\xi)), \quad (36)$$

where $\Lambda(\xi)$ is the largest eigenvalue of the operator (defined on $L^2(\mathbb{R})$)

$$(Q_\xi \varphi)(y) = \int_{\mathbb{R}} \varphi(x) \exp(\xi y) g_0(x, y) dx. \quad (37)$$

The convergence (35) holds pointwise in x , and also in L^p_{loc} , for any $1 \leq p < \infty$. As a consequence, the macroscopic force in the chain $\mathcal{T}_N(x) = F'_N(x)$ converges to F'_∞ in $W^{-1,p}_{\text{loc}}$.

We hence obtain the macroscopic force $F'_\infty(x)$ for a prescribed elongation x . Note that, under our assumptions, in view of its definition (36), F_∞ is (up to the

factor β) the Legendre transform of some function. It is hence always a convex function. Thus, as in the zero temperature case, we observe, in this one-dimensional setting, that the macroscopic constitutive law $x \mapsto F_\infty(x)$ is a convex function.

Remark 7. In view of the definitions (25) of g_0 and (23) of K_0 , we see that

$$\frac{(Q_\xi \varphi)(y)}{\psi_0(y)} = \frac{1}{\lambda_0} \int_{\mathbb{R}} \frac{\varphi(x)}{\psi_0(x)} \exp(\xi y) K_0(x, y) dx.$$

Thus $\Lambda(\xi)$ is also the largest eigenvalue of the operator

$$(\tilde{Q}_\xi \varphi)(y) = \frac{1}{\lambda_0} \int_{\mathbb{R}} \varphi(x) \exp(\xi y) K_0(x, y) dx.$$

Furthermore, if λ is an eigenvalue of \tilde{Q}_ξ , then

$$\int_{\mathbb{R}} \varphi(x) \exp(\xi y) K_0(x, y) dx = \lambda_0 \lambda \varphi(y),$$

where φ is an associated eigenfunction. Thus

$$\int_{\mathbb{R}} \frac{\varphi(x)}{\exp(\xi x/2)} \exp(\xi y/2) \exp(\xi x/2) K_0(x, y) dx = \lambda_0 \lambda \frac{\varphi(y)}{\exp(\xi y/2)}$$

and $\lambda_0 \lambda$ is an eigenvalue of the operator

$$(\overline{Q}_\xi \varphi)(y) = \int_{\mathbb{R}} \varphi(x) \exp(\xi y/2) \exp(\xi x/2) K_0(x, y) dx.$$

The converse is also true. As $\Lambda(\xi)$ is the largest eigenvalue of the operator \tilde{Q}_ξ , we have that $\lambda_0 \Lambda(\xi)$ is the largest eigenvalue of the operator \overline{Q}_ξ .

As W_2 is bounded from below and $\exp(\xi x - \beta W_1(x)) \in L^1(\mathbb{R})$ for any ξ , we have that $\exp(\xi x/2) \exp(\xi y/2) K_0(x, y) \in L^2(\mathbb{R} \times \mathbb{R})$. Hence \overline{Q}_ξ is a self-adjoint compact operator on $L^2(\mathbb{R})$, which is thus easier to manipulate theoretically and numerically than Q_ξ . In particular, using standard tools of spectral theory of self-adjoint operators (see *e.g.* [10]), one can prove that the largest eigenvalue of \overline{Q}_ξ is simple, and that the associated eigenvector Ψ_ξ (which is unique up to a multiplicative constant) can be chosen such that $\Psi_\xi > 0$. \diamond

2.2.3 Equivalence of Stress-Strain Relations in the Thermodynamic Limit

In Sect. 2.2.1, we have identified the function $f \mapsto y^*(f)$, that associates to a prescribed force f the macroscopic elongation $y^*(f)$. Next, in Sect. 2.2.2, we have identified the function $x \mapsto F'_\infty(x)$, that associates to a prescribed elongation x the macroscopic force $F'_\infty(x)$. We show now that these functions are reciprocal one to each other.

Consider the optimization problem (36). Since the function $\xi \mapsto \ln \Lambda(\xi)$ is convex (see Assumption 1), there exists a unique maximizer $\xi(x)$ in (36), which satisfies the Euler-Lagrange equation

$$x = \frac{\Lambda'(\xi(x))}{\Lambda(\xi(x))}. \quad (38)$$

We also observe that

$$F'_\infty(x) = \frac{\xi(x)}{\beta}.$$

We see from (38) that we need to compute $\Lambda'(\xi)$. Recall that $\Lambda(\xi)$ is the largest eigenvalue of the operator (37). In view of Remark 7, $\lambda_0 \Lambda(\xi)$ is also the largest eigenvalue of \overline{Q}_ξ . Denoting Ψ_ξ the associated eigenfunction satisfying $\|\Psi_\xi\|_{L^2} = 1$ and $\Psi_\xi > 0$, we thus have

$$(\overline{Q}_\xi \Psi_\xi)(y) = \int_{\mathbb{R}} \Psi_\xi(t) K_0^\xi(t, y) dt = \lambda_0 \Lambda(\xi) \Psi_\xi(y),$$

where

$$K_0^\xi(t, y) = \exp(\xi y/2) \exp(\xi t/2) K_0(t, y). \quad (39)$$

Multiplying by $\Psi_\xi(y)$ and integrating, we obtain

$$\int_{\mathbb{R}^2} \Psi_\xi(y) \Psi_\xi(t) K_0^\xi(t, y) dt dy = \lambda_0 \Lambda(\xi). \quad (40)$$

We thus have, using that $K_0^\xi(t, y) = K_0^\xi(y, t)$, that

$$\begin{aligned} \lambda_0 \Lambda'(\xi) &= \int_{\mathbb{R}^2} \frac{d\Psi_\xi}{d\xi}(y) \Psi_\xi(t) K_0^\xi(t, y) dt dy + \int_{\mathbb{R}^2} \Psi_\xi(y) \frac{d\Psi_\xi}{d\xi}(t) K_0^\xi(t, y) dt dy \\ &\quad + \int_{\mathbb{R}^2} \Psi_\xi(y) \Psi_\xi(t) \frac{dK_0^\xi}{d\xi}(t, y) dt dy \\ &= 2\lambda_0 \Lambda(\xi) \int_{\mathbb{R}} \frac{d\Psi_\xi}{d\xi}(y) \Psi_\xi(y) dy + \int_{\mathbb{R}^2} \Psi_\xi(y) \Psi_\xi(t) \frac{dK_0^\xi}{d\xi}(t, y) dt dy. \end{aligned}$$

In the above expression, the first term vanishes, since, for any ξ , $\int_{\mathbb{R}} \Psi_\xi^2(y) dy = 1$.

We thus obtain

$$\lambda_0 \Lambda'(\xi) = \int_{\mathbb{R}^2} \Psi_\xi(y) \Psi_\xi(t) \frac{t+y}{2} K_0^\xi(t, y) dt dy. \quad (41)$$

Collecting (38), (40) and (41), we see that

$$\begin{aligned}
x &= \frac{\int_{\mathbb{R}^2} \Psi_{\xi(x)}(y) \Psi_{\xi(x)}(t) \frac{t+y}{2} K_0^{\xi(x)}(t, y) dt dy}{\int_{\mathbb{R}^2} \Psi_{\xi(x)}(y) \Psi_{\xi(x)}(t) K_0^{\xi(x)}(t, y) dt dy} \\
&= \frac{\int_{\mathbb{R}^2} y \Psi_{\xi(x)}(y) \Psi_{\xi(x)}(t) K_0^{\xi(x)}(t, y) dt dy}{\int_{\mathbb{R}^2} \Psi_{\xi(x)}(y) \Psi_{\xi(x)}(t) K_0^{\xi(x)}(t, y) dt dy} \\
&= \frac{\int_{\mathbb{R}} y \Psi_{\xi(x)}^2(y) dy}{\int_{\mathbb{R}} \Psi_{\xi(x)}^2(y) dy} \\
&= \int_{\mathbb{R}} y \Psi_{\xi(x)}^2(y) dy,
\end{aligned} \tag{42}$$

where we have used, at the second line, that $K_0^{\xi(x)}(t, y) = K_0^{\xi(x)}(y, t)$.

On the other hand, we have obtained that the macroscopic elongation $y^*(f)$, for a prescribed force f , is given by (21), namely

$$y^*(f) = \int_{\mathbb{R}} y \psi_f^2(y) dy, \tag{43}$$

where ψ_f is the maximizer of the variational problem (22). As K_f is symmetric, the Euler-Lagrange equation of (22) reads

$$\begin{aligned}
\lambda_f \psi_f(y) &= \int_{\mathbb{R}} \psi_f(t) K_f(t, y) dt \\
&= \int_{\mathbb{R}} \psi_f(t) K_0(t, y) \exp\left(\beta f \frac{x+y}{2}\right) dt \\
&= \int_{\mathbb{R}} \psi_f(t) K_0^{\beta f}(t, y) dt,
\end{aligned}$$

where $K_0^{\beta f}$ is defined by (39). Thus ψ_f is an eigenfunction associated to the largest eigenvalue λ_f of the Hilbert-Schmidt operator $\overline{Q}_{\beta f}$ of kernel $K_0^{\beta f}$. By definition of $\Psi_{\beta f}$, and using the fact that the largest eigenvalue of $\overline{Q}_{\beta f}$ is simple, we obtain

$$\Psi_{\beta f} = \pm \psi_f \quad \text{and} \quad \Lambda(\beta f) = \frac{\lambda_f}{\lambda_0}.$$

We thus recast (43) as

$$y^*(f) = \int_{\mathbb{R}} y \Psi_{\beta f}^2(y) dy. \tag{44}$$

We deduce from the comparison of (42) and (44) that $y^*(\beta^{-1}\xi(x)) = y^*(F'_\infty(x)) = x$. Recall now that the function $f \mapsto y^*(f)$ is increasing, as shown by Lemma 4. It is thus injective, and we also get the converse relation $F'_\infty(y^*(f)) = f$.

As a consequence, as in the NN setting considered in Sect. 2.1.3, the relation $f \mapsto y^*(f)$ and $x \mapsto F'_\infty(x)$ are inverse one to each other. Prescribing a microscopic force f and computing the macroscopic elongation is equivalent to prescribing an elongation and computing the macroscopic force, *in the thermodynamic limit*.

2.2.4 Numerical Computation of F'_∞ and Comparison with the Zero Temperature Model

For our numerical tests, we follow the choices made in [3], for the sake of comparison. We thus take the pair interaction potentials

$$W_1(x) = \frac{1}{2}(x-1)^4 + \frac{1}{2}x^2 \quad \text{and} \quad W_2(x) = \frac{1}{4}(x-2.1)^4.$$

Note that these potentials satisfy all the assumptions that we have made above.

We are going to compare the free energy derivative $\mathcal{T}_N(x) = F'_N(x)$ with its thermodynamic limit approximation $F'_\infty(x)$. The reference value $F'_N(x)$ is computed as the ensemble average (28), which is in turn computed as a long-time average along the lines of (3)–(4). To compute $F'_\infty(x)$, we proceed as follows:

- (i) We first compute the largest eigenvalue $\Lambda(\xi)$ of the operator (37), for all ξ in some prescribed interval.
- (ii) For any fixed x in a prescribed interval, we next consider the variational problem (36), compute its maximizer $\xi(x)$, and obtain $F'_\infty(x)$ using $F'_\infty(x) = \xi(x)/\beta$.

In practice, using Remark 7, we work with the operator \overline{Q}_ξ , which is easier to manipulate since it is self-adjoint and we do not need to first solve (22). We thus first compute the largest eigenvalue $\lambda_0 \Lambda(\xi)$ of \overline{Q}_ξ , and next compute the Legendre transform of the function $\xi \mapsto \ln(\lambda_0 \Lambda(\xi))$. The maximizer is the same as that for $F_\infty(x)$. On Fig. 2, we plot the function $\xi \mapsto \ln(\lambda_0 \Lambda(\xi))$, and observe that it is convex, in agreement with Assumption 1.

We first study the convergence of $F'_N(x)$ to $F'_\infty(x)$ as N increases, for a fixed chain length $x = 1.4$ and a fixed temperature $1/\beta = 1$. Results are shown on Fig. 3. We indeed observe that $F'_N(x) \rightarrow F'_\infty(x)$ when $N \rightarrow +\infty$.

We now compare $F'_N(x)$ with its approximation $F'_\infty(x)$, for $N = 100$ and $1/\beta = 1$. Results are shown on Fig. 4. We observe that $F'_\infty(x)$ is a very good approximation of $F'_N(x)$, for any x in the considered interval.

For the sake of comparison, we now identify the zero temperature behaviour of the system, in the thermodynamic limit. At zero temperature, for a finite N , we model the system by minimizing the energy E_0 , with prescribed Dirichlet boundary conditions (this corresponds to prescribing the elongation, and computing the force;

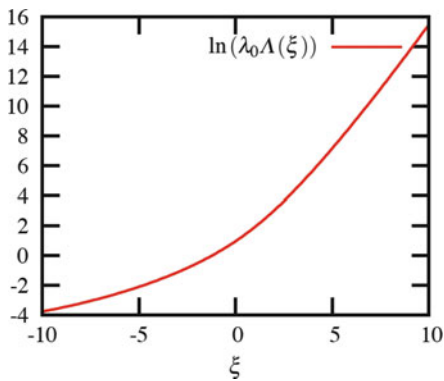


Fig. 2 Plot of $\ln(\lambda_0 \Lambda(\xi))$ as a function of ξ (temperature $1/\beta = 1$)

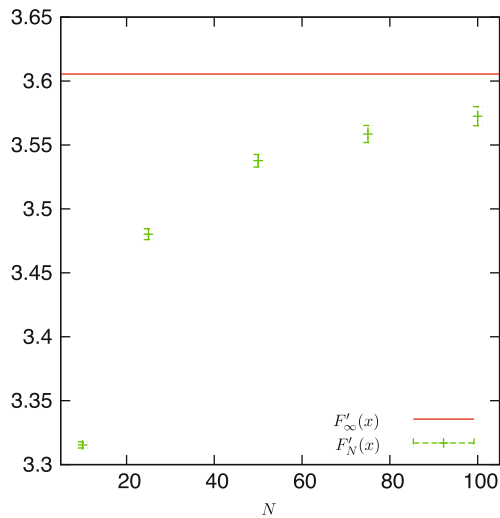


Fig. 3 Convergence of $F'_N(x)$ (shown with error bars computed from 40 independent realizations) to $F'_\infty(x)$ as N increases (temperature $1/\beta = 1$, fixed chain length $x = 1.4$)

alternatively, one could impose Neumann boundary conditions, *i.e.* prescribe a force and compute an elongation):

$$J_N(x) = \frac{1}{N} \inf \left\{ E_0(u^0, u^1, \dots, u^{N-1}, u^N), u^0 = 0, u^N = x \right\}. \quad (45)$$

We have the following result, which proof will be given below:

Lemma 6. *Let us introduce ϕ defined by*

$$\phi(x) = W_1(x) + W_2(2x). \quad (46)$$

Assume that there exists $\alpha > 0$ such that

$$W_1(x) \geq \alpha x^2, \quad (47)$$

and that W_1 and ϕ are non-negative and strictly convex functions. Then we have the pointwise convergence

$$\lim_{N \rightarrow \infty} J_N(x) = \phi(x).$$

Assume in addition that $\phi \in L^p_{\text{loc}}$ for some $1 \leq p < \infty$ and that W_2 is non-negative. Then the above convergence also holds in L^p_{loc} . As a consequence, $J'_N(x)$ converges to $\phi'(x)$ in $W^{-1,p}_{\text{loc}}$.

When the temperature is set to zero, the energy thus converges, in the thermodynamic limit, to $\phi(x)$, and the force (*i.e.* the derivative of the energy with respect to the prescribed Dirichlet boundary condition) converges to $\phi'(x)$. We plot on Fig. 4 the function $x \mapsto \phi'(x)$. We clearly observe the effect of temperature, as $F'_\infty(x)$ for $\beta = 1$ significantly differs from $\phi'(x)$.

Proof (Lemma 6). Let

$$X_N(x) = \left\{ (u^0, u^1, \dots, u^{N-1}, u^N) \in \mathbb{R}^{1+N}, u^0 = 0, u^N = x \right\}$$

be the variational ensemble for the problem (45). The configuration $u^i = ix/N$ clearly belongs to that ensemble. We thus obtain the upper-bound

$$J_N(x) \leq W_1(x) + \frac{N-1}{N} W_2(2x). \quad (48)$$

In the sequel, we first show a lower-bound for $J_N(x)$, and next study its behaviour when $N \rightarrow \infty$.

Let us first build a lower bound for $J_N(x)$. Assuming for the sake of simplicity that N is even, and using the short-hand notation $y^i = (u^i - u^{i-1})/h$, we have

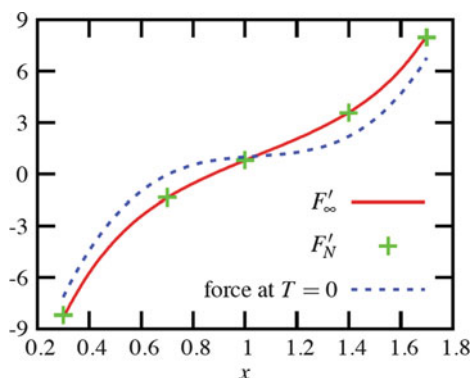


Fig. 4 We plot $F'_N(x)$ and $F'_\infty(x)$ for the temperature $1/\beta = 1$ and $N = 100$. On the scale of the figure, $F'_N(x)$ and $F'_\infty(x)$ are on top of each other. We also plot the zero temperature response $\phi'(x)$

$$\begin{aligned}
 \frac{1}{N} \sum_{i=1}^N W_1 \left(\frac{u^i - u^{i-1}}{h} \right) &= \frac{1}{N} \sum_{i=1}^N W_1(y^i) \\
 &= \frac{1}{2N} W_1(y^1) + \frac{1}{2N} W_1(y^N) \\
 &\quad + \frac{1}{2N} \sum_{i=1}^{N/2} [W_1(y^{2i-1}) + W_1(y^{2i})] \\
 &\quad + \frac{1}{2N} \sum_{i=1}^{N/2-1} [W_1(y^{2i}) + W_1(y^{2i+1})].
 \end{aligned}$$

By convexity of W_1 , we obtain

$$\begin{aligned}
 \frac{1}{N} \sum_{i=1}^N W_1 \left(\frac{u^i - u^{i-1}}{h} \right) &\geq \frac{1}{2N} W_1(y^1) + \frac{1}{2N} W_1(y^N) \\
 &\quad + \frac{1}{N} \sum_{i=1}^{N/2} W_1 \left[\frac{1}{2} (y^{2i-1} + y^{2i}) \right] \\
 &\quad + \frac{1}{N} \sum_{i=1}^{N/2-1} W_1 \left[\frac{1}{2} (y^{2i} + y^{2i+1}) \right].
 \end{aligned}$$

Taking into account the next-to-nearest interactions, we thus obtain that, for any $(u^0, u^1, \dots, u^{N-1}, u^N) \in \mathbb{R}^{1+N}$,

$$\begin{aligned}
\frac{1}{N} E_0(u^0, u^1, \dots, u^{N-1}, u^N) &\geq \frac{1}{2N} W_1(y^1) + \frac{1}{2N} W_1(y^N) \\
&\quad + \frac{1}{N} \sum_{i=1}^{N/2} \phi \left[\frac{1}{2} (y^{2i-1} + y^{2i}) \right] \\
&\quad + \frac{1}{N} \sum_{i=1}^{N/2-1} \phi \left[\frac{1}{2} (y^{2i} + y^{2i+1}) \right],
\end{aligned}$$

where ϕ is defined by (46). As ϕ is convex, we deduce that

$$\begin{aligned}
\frac{1}{N} E_0(u) &\geq \frac{1}{2N} W_1(y^1) + \frac{1}{2N} W_1(y^N) + \frac{1}{2} \phi \left(\frac{1}{N} \sum_{i=1}^{N/2} [y^{2i-1} + y^{2i}] \right) \\
&\quad + \frac{N-2}{2N} \phi \left(\frac{1}{N-2} \sum_{i=1}^{N/2-1} [y^{2i} + y^{2i+1}] \right) \\
&= \frac{1}{2N} W_1(y^1) + \frac{1}{2N} W_1(y^N) + \frac{1}{2} \phi(u^N - u^0) \\
&\quad + \frac{N-2}{2N} \phi \left(\frac{N}{N-2} (u^{N-1} - u^1) \right).
\end{aligned}$$

As a consequence, for any configuration $u \in X_N(x)$, we have

$$\frac{1}{N} E_0(u^0, u^1, \dots, u^{N-1}, u^N) \geq \bar{E}_N(u^1, u^{N-1}; x), \quad (49)$$

with

$$\begin{aligned}
\bar{E}_N(u^1, u^{N-1}; x) &= \frac{1}{2N} W_1(Nu^1) + \frac{1}{2N} W_1(N(x - u^{N-1})) + \frac{1}{2} \phi(x) \\
&\quad + \frac{N-2}{2N} \phi \left(\frac{N}{N-2} (u^{N-1} - u^1) \right). \quad (50)
\end{aligned}$$

We infer from (49) the lower bound

$$J_N(x) \geq \bar{J}_N(x), \quad (51)$$

with

$$\bar{J}_N(x) = \inf \left\{ \bar{E}_N(u^1, u^{N-1}; x); u^1 \in \mathbb{R}, u^{N-1} \in \mathbb{R} \right\}. \quad (52)$$

We now study the auxiliary variational problem (52) to determine the limit of $\bar{J}_N(x)$ when $N \rightarrow \infty$. Since ϕ is non-negative, and using (47), we have that

$$\bar{E}_N(u^1, u^{N-1}; x) \geq \frac{\alpha N}{2} \left[(u^1)^2 + (x - u^{N-1})^2 \right] \geq 0.$$

As a consequence, $\bar{J}_N(x) \geq 0$, and any minimizing sequence is bounded (by a constant possibly depending on N). Up to extraction, it thus converges to a minimizer,

that we denote $(\bar{u}^1, \bar{u}^{N-1})$. As W_1 and ϕ are strictly convex, it is easy to see that the hessian matrix of \bar{E}_N is positive definite, hence \bar{E}_N is also strictly convex, hence it has a unique minimizer. The problem (52) is thus well-posed. To underline the dependency of its minimizer with N , we denote it $(\bar{u}^1(N), \bar{u}^{N-1}(N))$ in the sequel.

The Euler-Lagrange equation associated to (52) reads

$$W_1'(N\bar{u}^1(N)) = \phi' \left(\frac{N}{N-2} (\bar{u}^{N-1}(N) - \bar{u}^1(N)) \right) = W_1'(N(x - \bar{u}^{N-1}(N))).$$

As W_1 is strictly convex, this implies that

$$\begin{cases} \bar{u}^1(N) = x - \bar{u}^{N-1}(N), \\ N\bar{u}^1(N) = \chi \left(\frac{N}{N-2} (x - 2\bar{u}^1(N)) \right), \end{cases} \quad (53)$$

where the function $\chi = (W_1')^{-1} \circ \phi'$ is independent of N , and increasing.

Let us now show that $\bar{u}^1(N)$ is bounded with respect to N . If this is not the case, then, without loss of generality, it is possible to find a subsequence $\varphi(N)$ such that $\lim_{N \rightarrow \infty} \bar{u}^1(\varphi(N)) = +\infty$. Passing to the limit in the second line of (53), one obtains a contradiction. Thus $\bar{u}^1(N)$ is bounded.

In view of the first line of (53), $\bar{u}^{N-1}(N)$ is also bounded. Up to a subsequence extraction, $(\bar{u}^1(N), \bar{u}^{N-1}(N))$ converges when $N \rightarrow \infty$ to some (a, b) . We infer from (53) that $a = 0$ and $b = x$, thus the limit is unique, and the whole sequence converges:

$$\lim_{N \rightarrow \infty} \bar{u}^1(N) = 0, \quad \lim_{N \rightarrow \infty} \bar{u}^{N-1}(N) = x. \quad (54)$$

We next infer from the above limits and (53) that

$$\lim_{N \rightarrow \infty} N\bar{u}^1(N) = \lim_{N \rightarrow \infty} N(x - \bar{u}^{N-1}(N)) = \chi(x). \quad (55)$$

By definition, we have

$$\bar{J}_N(x) = \inf \left\{ \bar{E}_N(u^1, u^{N-1}; x); u^1 \in \mathbb{R}, u^{N-1} \in \mathbb{R} \right\} = \bar{E}_N(\bar{u}^1(N), \bar{u}^{N-1}(N); x).$$

In view of (50), (54) and (55), we obtain

$$\lim_{N \rightarrow \infty} \bar{J}_N(x) = \lim_{N \rightarrow \infty} \bar{E}_N(\bar{u}^1(N), \bar{u}^{N-1}(N); x) = \phi(x). \quad (56)$$

Collecting (48), (51) and (56), we obtain the claimed pointwise convergence of $J_N(x)$ to $\phi(x)$.

We now turn to the second assertion of Lemma 6. Under the additional assumption that W_2 is non-negative, we deduce from (48) that, for any N and any x ,

$$0 \leq J_N(x) \leq W_1(x) + W_2(2x) = \phi(x).$$

As $\phi \in L_{\text{loc}}^p$, we obtain the convergence of J_N to ϕ in L_{loc}^p . \square

3 A Coarse-Graining Procedure in the Dynamical Setting

In this section, we present a procedure for coarse-graining a dynamics. More precisely, we consider $Q_t \in \mathbb{R}^n$ solution to the overdamped dynamics (3), and a reaction coordinate $\xi : \mathbb{R}^n \mapsto \mathbb{R}$. Our aim is to find a closed one-dimensional dynamics of type (5) on a process $\bar{\eta}_t$, such that $\bar{\eta}_t$ is a good approximation of $\xi(Q_t)$. In Sects. 3.2 and 3.3, we build such a process (see (67) below), and present an analytical estimation of its accuracy (the obtained estimate is an upper-bound on the “distance” between the laws of $\xi(Q_t)$ and $\bar{\eta}_t$ at any time t). We will next report on some numerical experiments that somewhat check the accuracy of $\bar{\eta}_t$ in a stronger sense (Sect. 3.4).

3.1 Measuring Distances Between Probability Measures

We introduce here some tools that will be useful in the sequel, to measure how close two probability measures are. Consider two probability measures $\nu(dq)$ and $\eta(dq)$. The distance between the two can be measured by the total variation norm $\|\nu - \eta\|_{\text{TV}}$, which amounts to the L^1 -norm $\int |\psi_\nu(q) - \psi_\eta(q)| dq$ in case ν and η have respectively the densities ψ_ν and ψ_η with respect to the Lebesgue measure.

When studying the long-time behaviour of solutions to PDEs (such as long time convergence of the solution of a Fokker-Planck equation to the stationary measure of the corresponding SDE), the notion of relative entropy turns out to be more useful. Under the assumption that ν is absolutely continuous with respect to η (denoted $\nu \ll \eta$ in the sequel), it is defined by

$$H(\nu|\eta) = \int \ln\left(\frac{d\nu}{d\eta}\right) d\nu.$$

The relative entropy provides an upper-bound on the total variation norm, by the Csiszár-Kullback inequality [1]:

$$\|\nu - \eta\|_{\text{TV}} \leq \sqrt{2H(\nu|\eta)}.$$

In the sequel, we will also use the Wasserstein distance with quadratic cost, which is another way to measure distances between probability measures. It is defined, for any two probability measures ν and η with support on a Riemannian manifold Σ , by

$$W(\nu, \eta) = \sqrt{\inf_{\pi \in \Pi(\nu, \eta)} \int_{\Sigma \times \Sigma} d_\Sigma(x, y)^2 \pi(dx, dy)}. \quad (57)$$

In the above expression, $d_\Sigma(x, y)$ denotes the geodesic distance between x and y on Σ ,

$$d_{\Sigma}(x, y) = \inf \left\{ \sqrt{\int_0^1 |\dot{\alpha}(t)|^2 dt}; \alpha \in C^1([0, 1], \Sigma), \alpha(0) = x, \alpha(1) = y \right\},$$

and $\Pi(\nu, \eta)$ denotes the set of coupling probability measures, that is probability measures π on $\Sigma \times \Sigma$ such that their marginals are ν and η : for any test function Φ ,

$$\int_{\Sigma \times \Sigma} \Phi(x) \pi(dx, dy) = \int_{\Sigma} \Phi(x) \nu(dx) \text{ and } \int_{\Sigma \times \Sigma} \Phi(y) \pi(dx, dy) = \int_{\Sigma} \Phi(y) \eta(dy).$$

In the sequel, we will need two functional inequalities, that we now recall [1]:

Definition 1. A probability measure η satisfies a logarithmic Sobolev inequality with a constant $\rho > 0$ if, for any probability measure ν such that $\nu \ll \eta$,

$$H(\nu|\eta) \leq \frac{1}{2\rho} I(\nu|\eta),$$

where the Fisher information $I(\nu|\eta)$ is defined by

$$I(\nu|\eta) = \int \left| \nabla \ln \left(\frac{d\nu}{d\eta} \right) \right|^2 d\nu.$$

Definition 2. A probability measure η satisfies a Talagrand inequality with a constant $\rho > 0$ if, for any probability measure ν ,

$$W(\nu, \eta) \leq \sqrt{\frac{2}{\rho} H(\nu|\eta)}.$$

We will also need the following important result (see [24, Theorem 1] and [4]):

Lemma 7. If η satisfies a logarithmic Sobolev inequality with a constant $\rho > 0$, then η satisfies a Talagrand inequality with the same constant $\rho > 0$.

The following standard result illustrates the usefulness of logarithmic Sobolev inequalities (we refer to [1, 2, 30] for more details on this subject).

Theorem 1. Consider Q_t solution to the overdamped Langevin equation (3), and assume the stationary measure $\psi_{\infty}(q) dq = Z^{-1} \exp(-\beta V(q)) dq$ satisfies a logarithmic Sobolev inequality with a constant $\rho > 0$. Then the probability distribution $\psi(t, \cdot)$ of Q_t converges to ψ_{∞} exponentially fast, in the sense:

$$\forall t \geq 0, \quad H(\psi(t, \cdot) | \psi_{\infty}) \leq H(\psi(0, \cdot) | \psi_{\infty}) \exp(-2\rho\beta^{-1}t). \quad (58)$$

Conversely, if (58) holds for any initial condition $\psi(0, \cdot)$, then the stationary measure $\psi_{\infty}(q) dq$ satisfies a logarithmic Sobolev inequality with a constant $\rho > 0$.

Proof. The probability distribution function $\psi(t, q)$ of Q_t satisfies the Fokker-Planck equation

$$\partial_t \psi = \operatorname{div}(\psi \nabla V) + \beta^{-1} \Delta \psi. \quad (59)$$

As $\nabla \psi_\infty = -\beta \psi_\infty \nabla V$, we recast the above equation as

$$\partial_t \psi = \beta^{-1} \operatorname{div} \left[\psi_\infty \nabla \left(\frac{\psi}{\psi_\infty} \right) \right].$$

Note that this equation implies that $\int_{\mathbb{R}^n} \psi(t, q) dq$ is a constant. Introduce now the relative entropy

$$\mathcal{E}(t) = H(\psi(t, \cdot) | \psi_\infty) = \int_{\mathbb{R}^n} \ln \left(\frac{\psi(t, q)}{\psi_\infty(q)} \right) \psi(t, q) dq.$$

Then

$$\begin{aligned} \frac{d\mathcal{E}}{dt} &= \int_{\mathbb{R}^n} \ln \left(\frac{\psi}{\psi_\infty} \right) \partial_t \psi + \frac{\psi_\infty}{\psi} \frac{\partial_t \psi}{\psi_\infty} \psi \\ &= \int_{\mathbb{R}^n} \ln \left(\frac{\psi}{\psi_\infty} \right) \beta^{-1} \operatorname{div} \left[\psi_\infty \nabla \left(\frac{\psi}{\psi_\infty} \right) \right] \\ &= -\beta^{-1} \int_{\mathbb{R}^n} \nabla \left[\ln \left(\frac{\psi}{\psi_\infty} \right) \right] \psi_\infty \nabla \left(\frac{\psi}{\psi_\infty} \right) \\ &= -\beta^{-1} \int_{\mathbb{R}^n} \left| \nabla \left[\ln \left(\frac{\psi}{\psi_\infty} \right) \right] \right|^2 \psi \\ &= -\beta^{-1} I(\psi(t, \cdot) | \psi_\infty). \end{aligned} \quad (60)$$

As ψ_∞ satisfies a logarithmic Sobolev inequality with the constant $\rho > 0$, we have that, for any time $t \geq 0$,

$$H(\psi(t, \cdot) | \psi_\infty) \leq (2\rho)^{-1} I(\psi(t, \cdot) | \psi_\infty). \quad (61)$$

We infer from (60) and (61) that

$$\frac{d\mathcal{E}}{dt} \leq -2\rho\beta^{-1} \mathcal{E}.$$

Using the Gronwall lemma, we obtain the claimed result.

Conversely, if

$$\forall t \geq 0, \quad \mathcal{E}(t) \leq \mathcal{E}(0) \exp(-2\rho\beta^{-1}t),$$

we also have

$$\forall t > 0, \quad \frac{\mathcal{E}(t) - \mathcal{E}(0)}{t} \leq \mathcal{E}(0) \frac{\exp(-2\rho\beta^{-1}t) - 1}{t}.$$

By letting t go to 0 and using (60), one obtains the logarithmic Sobolev inequality $I(\psi(0, \cdot) | \psi_\infty) \geq 2\rho H(\psi(0, \cdot) | \psi_\infty)$. \square

3.2 Effective Dynamics

Consider Q_t that solves (3). By a simple Itô computation, we have

$$d\xi(Q_t) = (-\nabla V \cdot \nabla \xi + \beta^{-1} \Delta \xi)(Q_t) dt + \sqrt{2\beta^{-1}} |\nabla \xi|(Q_t) dB_t, \quad (62)$$

where B_t is the one-dimensional Brownian motion

$$dB_t = \frac{\nabla \xi}{|\nabla \xi|}(Q_t) \cdot dW_t.$$

Of course, (62) is not closed. Following Gyöngy [16], a simple closing procedure is to consider $\widetilde{\eta}_t$ solution to

$$d\widetilde{\eta}_t = \widetilde{b}(t, \widetilde{\eta}_t) dt + \sqrt{2\beta^{-1}} \widetilde{\sigma}(t, \widetilde{\eta}_t) dB_t, \quad (63)$$

where

$$\widetilde{b}(t, z) = \mathbb{E} [(-\nabla V \cdot \nabla \xi + \beta^{-1} \Delta \xi)(Q_t) \mid \xi(Q_t) = z], \quad (64)$$

$$\widetilde{\sigma}^2(t, z) = \mathbb{E} [|\nabla \xi|^2(Q_t) \mid \xi(Q_t) = z]. \quad (65)$$

Note that \widetilde{b} and $\widetilde{\sigma}$ depend on t , since these are expected values conditioned on the fact that $\xi(Q_t) = z$, and the probability distribution function of Q_t of course depends on t .

As shown in [16], this procedure is exact from the point of view of time marginals: at any time t , the random variables $\widetilde{\eta}_t$ and $\xi(Q_t)$ have the same law. This is stated in the following lemma.

Lemma 8 ([19], Lemma 2.3). *The probability distribution function ψ^ξ of $\xi(Q_t)$, where Q_t satisfies (3), satisfies the Fokker-Planck equation associated to (63):*

$$\partial_t \psi^\xi = \partial_z \left(-\widetilde{b} \psi^\xi + \beta^{-1} \partial_z (\widetilde{\sigma}^2 \psi^\xi) \right).$$

The problem with equation (63) is that the functions \widetilde{b} and $\widetilde{\sigma}$ are very complicated to compute, since they involve the full knowledge of ψ . Therefore, one cannot consider (63) as a reasonable closure. A natural simplification is to consider a time-independent approximation of the functions \widetilde{b} and $\widetilde{\sigma}$. Considering (64) and (65), we introduce $(\mathbb{E}_\mu$ denoting a mean with respect to the measure μ)

$$\begin{aligned} b(z) &= \mathbb{E}_\mu [(-\nabla V \cdot \nabla \xi + \beta^{-1} \Delta \xi)(Q) \mid \xi(Q) = z] \\ &= \int_{\Sigma_z} (-\nabla V \cdot \nabla \xi + \beta^{-1} \Delta \xi) d\mu_{\Sigma_z}, \end{aligned} \quad (66)$$

and

$$\sigma^2(z) = \mathbb{E}_\mu (|\nabla \xi|^2(Q) \mid \xi(Q) = z) = \int_{\Sigma_z} |\nabla \xi|^2 d\mu_{\Sigma_z},$$

where μ_{Σ_z} is defined by (8). This amounts to replacing the measure $\psi(t, x)$ in (64) (conditioned at the value $\xi(x) = z$) by the equilibrium measure $\psi_\infty(x)$ (conditioned at the value $\xi(x) = z$), and likewise for (65). This simplification especially makes sense if $\xi(Q_t)$ is a slow variable, that is if the characteristic evolution time of $\xi(Q_t)$ is much larger than the characteristic time needed by Q_t to sample the manifold Σ_z . This is quantified in the sequel.

In the spirit of (63), we next introduce the coarse-grained dynamics

$$d\bar{\eta}_t = b(\bar{\eta}_t) dt + \sqrt{2\beta^{-1}} \sigma(\bar{\eta}_t) dB_t, \quad \bar{\eta}_{t=0} = \xi(Q_0). \quad (67)$$

We have proved in [19] that the effective dynamics (67) is ergodic for the equilibrium measure $\xi \star \mu$, that is $\exp(-\beta A(z)) dz$. In addition, this measure satisfies a detailed balance condition. We have also proved the following error bound, that quantifies the “distance” between the probability distribution function of $\xi(Q_t)$ (at any given time t) and that of $\bar{\eta}_t$.

Proposition 1 ([19], Proposition 3.1). *Assume that ξ is a smooth scalar function such that*

$$\text{for all } q \in \mathbb{R}^n, \quad 0 < m \leq |\nabla \xi(q)| \leq M < \infty, \quad (68)$$

and that the conditioned probability measures μ_{Σ_z} , defined by (8), satisfy a logarithmic Sobolev inequality with a constant ρ uniform in z : for any probability measure ν on Σ_z which is absolutely continuous with respect to the measure μ_{Σ_z} , we have

$$H(\nu | \mu_{\Sigma_z}) \leq \frac{1}{2\rho} I(\nu | \mu_{\Sigma_z}). \quad (69)$$

Let us also assume that the coupling is bounded in the following sense:

$$\kappa = \|\nabla_{\Sigma_z} F\|_{L^\infty} < \infty, \quad (70)$$

where F is the local mean force defined by (11).

Finally, let us assume that $|\nabla \xi|$ is close to a constant on the manifold Σ_z in the following sense:

$$\lambda = \left\| \frac{|\nabla \xi|^2 - \sigma^2 \circ \xi}{\sigma^2 \circ \xi} \right\|_{L^\infty} < \infty. \quad (71)$$

Assume that, at time $t = 0$, the distribution of the initial conditions of (3) and (67) are consistent one with each other: $\psi^\xi(t = 0, \cdot) = \phi(t = 0, \cdot)$. Then we have the following estimate: for any time $t \geq 0$,

$$E(t) \leq \frac{M^2}{4m^2} \left(\lambda^2 + \frac{m^2 \beta^2 \kappa^2}{\rho^2} \right) (H(\psi(0, \cdot) | \mu) - H(\psi(t, \cdot) | \mu)), \quad (72)$$

where $E(t)$ is the relative entropy of the probability distribution function ψ^ξ of $\xi(Q_t)$, where Q_t follows (3), with respect to the probability distribution function ϕ of the solution $\bar{\eta}_t$ to (67):

$$E(t) = H\left(\psi^\xi(t, \cdot) | \phi(t, \cdot)\right) = \int_{\mathbb{R}} \ln\left(\frac{\psi^\xi(t, z)}{\phi(t, z)}\right) \psi^\xi(t, z) dz.$$

The above proposition thus yields a uniform-in-time bound on the relative entropy between ψ^ξ and ϕ . In addition, we also know that the effective dynamics is ergodic for $\exp(-\beta A(z)) dz$, which is the equilibrium measure of $\xi(Q_t)$, in the long-time limit. We thus expect the two probability densities to converge one to each other, in the long-time limit. This is indeed the case, as it is shown in [19, Corollary 3.1]: under some mild assumptions, the L^1 distance between $\psi^\xi(t, \cdot)$ and $\phi(t, \cdot)$ vanishes at an exponential rate in the long-time limit.

The difficulty of the question we address stems from the fact that, in general, $t \rightarrow \xi(Q_t)$ is not a Markov process: this is a closure problem. If an appropriate time-scale separation is present in the system (between $\xi(Q_t)$ and the complementary degrees of freedom), then memory effects may be neglected, and $\xi(Q_t)$ be approximated by a Markov process such as (67).

One interest of our approach is to get the error estimate (72), which is not an asymptotic result, and holds for any coarse-grained variable. Of course, this error estimate certainly yields a large error bound in some cases, in particular if ξ is not well-chosen, or when no time-scale separation is present in the dynamics. If bounds (69) and (70) encode a time-scale separation, namely if $\kappa \ll 1$ and $\rho \gg 1$, then the right-hand side of (72) is small, and $\bar{\eta}_t$ solution to (67) is indeed a good approximation of $\xi(Q_t)$.

We would like to emphasize that the effective dynamics (67) may also be obtained using different arguments, such as the Mori-Zwanzig projection approach [15]. In the case when a small parameter is present in the system, one can alternatively use asymptotic expansions of the generator (see [11, 25, 26]).

3.3 The Proof in a Simple Two-Dimensional Case

For the purpose of illustration, we consider in this section an extremely simple case: starting from the overdamped dynamics (3) in *two dimensions* (we write $q = (x, y) \in \mathbb{R}^2$), we want to derive an effective dynamics for the coarse-grained variable $\xi(q) = \xi(x, y) = x$. Although this case is over-simplified, it turns out that the main arguments of our derivation, as well as the proof arguments, can be well understood here.

In that context, the complete dynamics (3) reads

$$\begin{cases} dX_t = -\partial_x V(X_t, Y_t) dt + \sqrt{2\beta^{-1}} dW_t^x, \\ dY_t = -\partial_y V(X_t, Y_t) dt + \sqrt{2\beta^{-1}} dW_t^y, \end{cases} \quad (73)$$

with the initial condition $Q_0 = (X_0, Y_0)$. The manifold Σ_z defined by (7) is

$$\Sigma_z = \{(z, y); y \in \mathbb{R}\}$$

and the probability measure $d\mu_{\Sigma_z}$ defined by (8) reads

$$d\mu_{\Sigma_z} = \frac{\exp(-\beta V(z, y)) dy}{\int_{\mathbb{R}} \exp(-\beta V(z, y)) dy} = \frac{\psi_{\infty}(z, y) dy}{\int_{\mathbb{R}} \psi_{\infty}(z, y) dy}. \quad (74)$$

We focus on the dynamics of $\xi(X_t, Y_t) = X_t$. In that case, the equation (62) is just the first line of (73), which is obviously not closed in X_t , since Y_t appears. At time t , Q_t is distributed according to the measure $\psi(t, q)$. Hence, the probability distribution function of Y_t , conditioned to the fact that $\xi(Q_t) = X_t = x$, is given by

$$\psi_{\text{cond}}^x(t, y) = \frac{\psi(t, x, y)}{\int_{\mathbb{R}} \psi(t, x, y) dy}.$$

Following Gyöngy [16], we introduce the function $\tilde{b}(t, x)$ defined by (64), which reads in the present context as

$$\tilde{b}(t, x) = \int_{\mathbb{R}} [-\partial_x V(x, y)] \psi_{\text{cond}}^x(t, y) dy = - \frac{\int_{\mathbb{R}} \partial_x V(x, y) \psi(t, x, y) dy}{\int_{\mathbb{R}} \psi(t, x, y) dy}. \quad (75)$$

The resulting dynamics (63) reads

$$d\tilde{X}_t = \tilde{b}(t, \tilde{X}_t) dt + \sqrt{2\beta^{-1}} dW_t^x. \quad (76)$$

We now prove Lemma 8 in that specific context and show that, at any time t , the probability distribution function of \tilde{X}_t is equal to that of $\xi(Q_t) = X_t$.

Proof (Lemma 8, case $\xi(x, y) = x$). The probability density function $\psi(t, x, y)$ of $Q_t = (X_t, Y_t)$ satisfies the Fokker-Planck (59):

$$\begin{aligned} \partial_t \psi &= \text{div}(\psi \nabla V) + \beta^{-1} \Delta \psi \\ &= \partial_x (\psi \partial_x V) + \partial_y (\psi \partial_y V) + \beta^{-1} \partial_{xx} \psi + \beta^{-1} \partial_{yy} \psi. \end{aligned} \quad (77)$$

The probability distribution function of $\xi(Q_t) = X_t$ is

$$\psi^{\xi}(t, x) = \int_{\mathbb{R}} \psi(t, x, y) dy.$$

Integrating (77) with respect to y , we obtain

$$\begin{aligned}
\partial_t \psi^\xi &= \partial_x \left(\int \psi \partial_x V dy \right) + \beta^{-1} \partial_{xx} \psi^\xi \\
&= -\partial_x \left(\psi^\xi \widetilde{b} \right) + \beta^{-1} \partial_{xx} \psi^\xi,
\end{aligned} \tag{78}$$

where $\widetilde{b}(t, x)$ is given by (75). We recognize the Fokker-Planck equation associated to the (76). \square

As pointed out above, (63) (i.e. (76) here) cannot be considered as a reasonable closure, since it involves the function \widetilde{b} , which is defined using $\underline{\psi}(t, x, y)$ (see (75)), which in practice is hardly computable. We thus approximate \widetilde{b} by the function b defined by (66), which amounts to replacing $\psi(t, x, y)$ in (75) by the equilibrium measure $\psi_\infty(x, y)$:

$$b(x) = - \frac{\int_{\mathbb{R}} \partial_x V(x, y) \psi_\infty(x, y) dy}{\int_{\mathbb{R}} \psi_\infty(x, y) dy}.$$

In the spirit of (76), we thus introduce the effective dynamics

$$d\overline{X}_t = b(\overline{X}_t) dt + \sqrt{2\beta^{-1}} dW_t^x. \tag{79}$$

We now prove Proposition 1 (error estimator on the effective dynamics), in the specific case at hand here. The assumption (69) means that the measure (74) satisfies, for any z , a logarithmic Sobolev inequality with a constant ρ independent of z . The assumption (70) reads $\kappa = \|\partial_{xy} V\|_{L^\infty} < \infty$, and the assumption (71) is satisfied with $\lambda = 0$ since $\nabla \xi = (1, 0)^T$ is a constant vector.

Proof (Proposition 1, case $\xi(x, y) = x$). By definition (see (9)), the free energy A associated to the reaction coordinate ξ satisfies

$$\exp(-\beta A(x)) = \int_{\mathbb{R}} \psi_\infty(x, y) dy = Z^{-1} \int_{\mathbb{R}} \exp(-\beta V(x, y)) dy,$$

hence

$$A'(x) = \frac{\int \partial_x V(x, y) \psi_\infty(x, y) dy}{\int_{\mathbb{R}} \psi_\infty(x, y) dy} = -b(x). \tag{80}$$

The effective dynamics (79) thus reads

$$d\overline{X}_t = -A'(\overline{X}_t) dt + \sqrt{2/\beta} dW_t^x.$$

Note that, in this specific context, the effective dynamics is of the form (6) (see [19, Sect. 2.3] for a comprehensive discussion of the relation between the effective dynamics and (6)). The probability distribution $\phi(t, x)$ of \overline{X}_t satisfies the

Fokker-Planck equation associated to the above stochastic differential equation, that reads

$$\partial_t \phi = \partial_x (\phi A') + \beta^{-1} \partial_{xx} \phi. \quad (81)$$

Consider now the relative entropy

$$E(t) = H(\psi^\xi | \phi) = \int_{\mathbb{R}} \ln \left(\frac{\psi^\xi(t, x)}{\phi(t, x)} \right) \psi^\xi(t, x) dx.$$

We compute, using (81) and (78), that

$$\begin{aligned} \frac{dE}{dt} &= \int_{\mathbb{R}} \ln \left(\frac{\psi^\xi}{\phi} \right) \partial_t \psi^\xi - \int_{\mathbb{R}} \frac{\psi^\xi}{\phi} \partial_t \phi \\ &= \int_{\mathbb{R}} \ln \left(\frac{\psi^\xi}{\phi} \right) \left[-\partial_x (\psi^\xi \tilde{b}) + \beta^{-1} \partial_{xx} \psi^\xi \right] - \int_{\mathbb{R}} \frac{\psi^\xi}{\phi} [\partial_x (\phi A') + \beta^{-1} \partial_{xx} \phi] \\ &= -\beta^{-1} \int_{\mathbb{R}} \partial_x \left[\ln \left(\frac{\psi^\xi}{\phi} \right) \right] \partial_x \psi^\xi + \beta^{-1} \int_{\mathbb{R}} \partial_x \left(\frac{\psi^\xi}{\phi} \right) \partial_x \phi \\ &\quad + \int_{\mathbb{R}} \psi^\xi \partial_x \left(\ln \frac{\psi^\xi}{\phi} \right) (\tilde{b} + A') \\ &= -\beta^{-1} \int_{\mathbb{R}} \partial_x \left[\ln \left(\frac{\psi^\xi}{\phi} \right) \right] \left[\partial_x \psi^\xi - \frac{\psi^\xi \partial_x \phi}{\phi} \right] + \int_{\mathbb{R}} \psi^\xi \partial_x \left(\ln \frac{\psi^\xi}{\phi} \right) (\tilde{b} + A') \\ &= -\beta^{-1} \int_{\mathbb{R}} \partial_x \left[\ln \left(\frac{\psi^\xi}{\phi} \right) \right] \phi \partial_x \left(\frac{\psi^\xi}{\phi} \right) + \int_{\mathbb{R}} \psi^\xi \partial_x \left(\ln \frac{\psi^\xi}{\phi} \right) (\tilde{b} + A') \\ &= -\beta^{-1} I(\psi^\xi | \phi) + \int_{\mathbb{R}} \psi^\xi \partial_x \left(\ln \frac{\psi^\xi}{\phi} \right) (\tilde{b} + A'). \end{aligned}$$

Using a Young inequality with a parameter $\alpha > 0$ to be fixed later, we obtain

$$\begin{aligned} \frac{dE}{dt} &\leq -\beta^{-1} I(\psi^\xi | \phi) + \frac{1}{2\alpha} \int_{\mathbb{R}} \psi^\xi \left(\partial_x \left(\ln \frac{\psi^\xi}{\phi} \right) \right)^2 + \frac{\alpha}{2} \int_{\mathbb{R}} \psi^\xi (A' + \tilde{b})^2 \\ &= \left(\frac{1}{2\alpha} - \beta^{-1} \right) I(\psi^\xi | \phi) + \frac{\alpha}{2} \int_{\mathbb{R}} \psi^\xi (A' + \tilde{b})^2. \end{aligned} \quad (82)$$

We now observe that, in view of (75) and (80), A' and $-\tilde{b}$ are averages of the *same* quantity with respect to different probability measures:

$$-\tilde{b}(t, x) = \int_{\mathbb{R}} \partial_x V(x, y) v_1^{t, x}(y) dy \quad \text{and} \quad A'(x) = \int_{\mathbb{R}} \partial_x V(x, y) v_2^x(y) dy$$

with

$$v_1^{t,x}(y) = \frac{\psi(t, x, y)}{\int_{\mathbb{R}} \psi(t, x, y) dy} \quad \text{and} \quad v_2^x(y) = \frac{\psi_{\infty}(x, y)}{\int_{\mathbb{R}} \psi_{\infty}(x, y) dy}. \quad (83)$$

We write

$$\begin{aligned} A'(x) + \widetilde{b}(t, x) &= \int_{\mathbb{R}} \partial_x V(x, y) v_2^x(y) dy - \int_{\mathbb{R}} \partial_x V(x, y) v_1^{t,x}(y) dy \\ &= \int_{\mathbb{R}^2} (\partial_x V(x, y_1) - \partial_x V(x, y_2)) k^{t,x}(y_1, y_2) dy_1 dy_2 \end{aligned}$$

for any probability measure $k^{t,x}$ such that

$$\int_{\mathbb{R}} k^{t,x}(y_1, y_2) dy_2 = v_2^x(y_1) \quad \text{and} \quad \int_{\mathbb{R}} k^{t,x}(y_1, y_2) dy_1 = v_1^{t,x}(y_2).$$

Hence,

$$\begin{aligned} \left| A'(x) + \widetilde{b}(t, x) \right| &\leq \|\partial_{xy} V\|_{L^\infty} \int_{\mathbb{R}^2} |y_1 - y_2| k^{t,x}(y_1, y_2) dy_1 dy_2 \\ &\leq \|\partial_{xy} V\|_{L^\infty} \left(\int_{\mathbb{R}^2} |y_1 - y_2|^2 k^{t,x}(y_1, y_2) dy_1 dy_2 \right)^{1/2}. \end{aligned}$$

We now optimize on $k^{t,x}$. Introducing the Wasserstein distance $W(v_1^{t,x}, v_2^x)$ between $v_1^{t,x}$ and v_2^x (see (57)), we obtain

$$\left| A'(x) + \widetilde{b}(t, x) \right| \leq \|\partial_{xy} V\|_{L^\infty} W(v_1^{t,x}, v_2^x).$$

As recalled above, assumption (69) means that v_2^x satisfies a logarithmic Sobolev inequality. Thus, it also satisfies a Talagrand inequality (see Lemma 7), hence

$$W(v_1^{t,x}, v_2^x) \leq \sqrt{\frac{2}{\rho} H(v_1^{t,x} | v_2^x)} \leq \frac{1}{\rho} \sqrt{I(v_1^{t,x} | v_2^x)}.$$

As a consequence,

$$\left| A'(x) + \widetilde{b}(t, x) \right| \leq \frac{\|\partial_{xy} V\|_{L^\infty}}{\rho} \sqrt{I(v_1^{t,x} | v_2^x)}.$$

Using (83), we obtain

$$\begin{aligned}
\int_{\mathbb{R}} \psi^\xi (A' + \widetilde{b})^2 dx &\leq \frac{\|\partial_{xy} V\|_{L^\infty}^2}{\rho^2} \int_{\mathbb{R}} \psi^\xi(t, x) I(v_1^{t,x} | v_2^x) dx \\
&\leq \frac{\|\partial_{xy} V\|_{L^\infty}^2}{\rho^2} \int_{\mathbb{R}} \psi^\xi(t, x) \left[\int_{\mathbb{R}} \left| \partial_y \ln \frac{\psi(t, x, y)}{\psi_\infty(x, y)} \right|^2 \frac{\psi(t, x, y)}{\psi^\xi(t, x)} dy \right] dx \\
&\leq \frac{\|\partial_{xy} V\|_{L^\infty}^2}{\rho^2} I(\psi | \psi_\infty).
\end{aligned}$$

Returning to (82), and using (60), we thus deduce that

$$\begin{aligned}
\frac{dE}{dt} &\leq \left(\frac{1}{2\alpha} - \beta^{-1} \right) I(\psi^\xi | \phi) + \frac{\alpha}{2} \frac{\|\partial_{xy} V\|_{L^\infty}^2}{\rho^2} I(\psi | \psi_\infty) \\
&= \left(\frac{1}{2\alpha} - \beta^{-1} \right) I(\psi^\xi | \phi) - \frac{\alpha\beta \|\partial_{xy} V\|_{L^\infty}^2}{2\rho^2} \partial_t H(\psi | \psi_\infty).
\end{aligned}$$

We take $2\alpha = \beta$, so that the first term vanishes, and we are left with

$$\frac{dE}{dt} \leq - \frac{\beta^2 \|\partial_{xy} V\|_{L^\infty}^2}{4\rho^2} \partial_t H(\psi | \psi_\infty).$$

Integrating this inequality between the times 0 and t , and using that $E(0) = 0$, we obtain

$$E(t) \leq \frac{\beta^2 \|\partial_{xy} V\|_{L^\infty}^2}{4\rho^2} (H(\psi(t=0) | \psi_\infty) - H(\psi(t, \cdot) | \psi_\infty)).$$

As recalled above, assumption (70) reads $\kappa = \|\partial_{xy} V\|_{L^\infty} < \infty$. The above bound is thus exactly the bound (72) in the present context. \square

3.4 Numerical Results

In this section, we check the accuracy of the effective dynamics (67) in terms of residence times, and also compare this effective dynamics with the coarse-grained dynamics (6) based on the free energy. We perform such comparison on two test-cases, and evaluate the influence of the temperature on the results. We also provide some analytical explanations for the observed numerical results.

In the following numerical tests, we focus on residence times. We have indeed already underlined that the characteristic behaviour of the dynamics (3) is to sample a given well of the potential energy, then suddenly jump to another basin, and start over. Consequently, an important quantity is the residence time that the system spends in the well, before going to another one.

For all the numerical tests reported in this section, the complete dynamics (3) has been integrated with the Euler-Maruyama scheme

$$Q_{j+1} = Q_j - \Delta t \nabla V(Q_j) + \sqrt{2 \Delta t \beta^{-1}} G_j,$$

where, for any j , G_j is a n -dimensional vector, whose coordinates are independent and identically distributed (i.i.d.) random variables, distributed according to a normal Gaussian law.

For the simulation of the dynamics (67) and (6), we need to have an expression for the free energy derivative A' and the functions b and σ . These have been computed using the algorithm proposed in [7], on a regular grid of some bounded interval. Values of the functions for points that do not belong to that grid were obtained by linear interpolation. We have again used the Euler-Maruyama scheme to numerically integrate the dynamics (67) and (6).

To compute residence times in a well, we have proceeded as follows (for the sake of clarity, we assume in the following that there are only two wells in the test case at hand). First, the left and the right wells are defined as the sets $\{q \in \mathbb{R}^n; \xi(q) \leq \xi_{\text{left}}^{\text{th}}\}$ and $\{q \in \mathbb{R}^n; \xi(q) \geq \xi_{\text{right}}^{\text{th}}\}$ respectively, with $\xi_{\text{right}}^{\text{th}} > \xi_{\text{left}}^{\text{th}}$. Next, we perform the following computations:

1. We first generate a large number \mathcal{N} of configurations $\{q_i \in \mathbb{R}^n\}_{1 \leq i \leq \mathcal{N}}$, distributed according to the measure μ restricted to the right well: as a consequence, $\xi(q_i) > \xi_{\text{right}}^{\text{th}}$.
2. We next run the dynamics (3) from the initial condition q_i , and monitor the first time τ_i at which the system reaches a point $q(\tau_i)$ in the left well: $\tau_i = \inf\{t; \xi(q_t) < \xi_{\text{left}}^{\text{th}}\}$.
3. From these $(\tau_i)_{1 \leq i \leq \mathcal{N}}$, we compute an average residence time and a confidence interval. These figures are the reference figures.
4. We next consider the initial conditions $\{\xi(q_i) \in \mathbb{R}\}_{1 \leq i \leq \mathcal{N}}$ for the effective dynamics. By construction, these configurations are distributed according to the equilibrium measure $\xi \star \mu$ (that is $\exp(-\beta A(z)) dz$) restricted to the right well.
5. From these initial conditions, we run the dynamics (67) or (6) until the left well is reached, and compute, as for the complete description, a residence time and its confidence interval.

3.4.1 A Three Atom Molecule

Our aim in this section is to show that different reaction coordinates, although similar at first sight, can lead to very different results. As explained in [19], the error estimate (72) can then help discriminating between these reaction coordinates.

We consider here a molecule made of three two-dimensional particles, whose positions are q_A , q_B and q_C . The potential energy of the system is

$$V(q) = \frac{1}{2\epsilon} (r_{AB} - \ell_{\text{eq}})^2 + \frac{1}{2\epsilon} (r_{BC} - \ell_{\text{eq}})^2 + W_3(\theta_{ABC}), \quad (84)$$

where $r_{AB} = \|q_A - q_B\|$ is the distance between atoms A and B, ℓ_{eq} is an equilibrium distance, θ_{ABC} is the angle formed by the three atoms, and $W_3(\theta)$ is a three-body potential, that we choose here to be a double-well potential:

$$W_3(\theta) = \frac{1}{2}k_\theta ((\theta - \theta_{\text{saddle}})^2 - \delta\theta^2)^2.$$

Wells of W_3 are located at $\theta = \theta_{\text{saddle}} \pm \delta\theta$. The potential (84) represents stiff bonds between particles A and B on the one hand, and B and C on the other hand, with a softer term depending on the angle θ_{ABC} . To remove rigid body motion invariance, we set $q_B = 0$ and $q_A \cdot e_y = 0$. In the following, we work with the parameters $\epsilon = 10^{-3}$, $k_\theta = 208$, $\ell_{\text{eq}} = 1$, $\theta_{\text{saddle}} = \pi/2$ and $\delta\theta = \theta_{\text{saddle}} - 1.187$. All dynamics are integrated with the time step $\Delta t = 10^{-3}$.

We consider two reaction coordinates, that both indicate in which well the system is:

- The angle formed by the three atoms:

$$\xi_1 = \theta_{ABC}.$$

In that case, wells are defined by $\{q \in \mathbb{R}^n; \xi_1(q) \leq \xi_{\text{left}}^{\text{th}} = \theta_{\text{saddle}} - 0.15\}$ and $\{q \in \mathbb{R}^n; \xi_1(q) \geq \xi_{\text{right}}^{\text{th}} = \theta_{\text{saddle}} + 0.15\}$.

- The square of the distance between A and C:

$$\xi_2 = \|q_A - q_C\|^2.$$

In that case, wells are defined by $\{q \in \mathbb{R}^n; \xi_2(q) \leq \xi_{\text{left}}^{\text{th}} = 1.6\ell_{\text{eq}}^2\}$ and $\{q \in \mathbb{R}^n; \xi_2(q) \geq \xi_{\text{right}}^{\text{th}} = 2.4\ell_{\text{eq}}^2\}$.

Note that there is a region of state space that does not belong to any well. This choice allows to circumvent the so-called recrossing problem.

Remark 8. Note that (84) reads

$$V(q) = \frac{1}{2\epsilon} (U_{AB}(q)^2 + U_{BC}(q)^2) + W_3(\theta_{ABC})$$

with $U_{AB}(q) = r_{AB} - \ell_{\text{eq}}$ and $U_{BC}(q) = r_{BC} - \ell_{\text{eq}}$. The two first terms in V are much stiffer than the last one. We observe that $\nabla\theta_{ABC} \cdot \nabla U_{AB} = \nabla\theta_{ABC} \cdot \nabla U_{BC} = 0$. Hence, the reaction coordinate ξ_1 is orthogonal to the stiff terms of the potential energy, in contrast to ξ_2 .

For potentials of the above type, we have shown in [19, Sect. 3.2] that the coupling constant κ defined by (70) is of the order of ϵ when the reaction coordinate is orthogonal to the stiff terms of the potential energy, and of order 1 otherwise. In turn, the constant ρ defined by (69) typically remains bounded away from 0 when ϵ goes to zero. Ignoring the effect of the constant λ , we hence see that the right-hand side of the error bound (72) is much smaller (and so the effective dynamics is more accurate) when the reaction coordinate is orthogonal to the stiff terms of the potential energy.

Consequently, in the case at hand here, we expect to obtain accurate results with ξ_1 , in contrast to ξ_2 . This is indeed the case, as shown in the sequel of this section. \diamond

We compute the residence time in a given well following the complete description, and compare it with the result given by a reduced description, based either on (67) or (6). Results are gathered in Table 1, for the temperatures $\beta^{-1} = 1$ and $\beta^{-1} = 0.2$. We observe that working with ξ_1 (and either (67) or (6)) leads to very accurate results, independently of the temperature. On the other hand, when working with ξ_2 , the reaction coordinate is not orthogonal to the stiff terms of the potential, and both coarse-grained dynamics turn out to be not accurate.

Remark 9. In the case at hand here, $\|\nabla \xi_1\|^2 = \|\nabla \theta_{ABC}\|^2 = r_{BC}^{-2}$. This quantity is almost a constant, since the bond length potential is stiff and the temperature is small. Hence, along the trajectory, we have that $\|\nabla \xi_1\|^2 \approx \ell_{\text{eq}}^{-2} = 1$. We pointed out in [19, Sect. 2.3] that, when the reaction coordinate satisfies $\|\nabla \xi\| = 1$, then both coarse-grained dynamics (67) and (6) are identical. This explains why, in the present case, when choosing the reaction coordinate ξ_1 , dynamics (67) and (6) give similar results. \diamond

Table 1 Three-atom molecule: residence times obtained from the complete description (third column) and from the reduced descriptions (two last columns), for both reaction coordinates (confidence intervals have been computed on the basis of $\mathcal{N} = 15,000$ realizations)

Temperature	Reaction coordinate	Reference residence time	Residence time using (67)	Residence time using (6)
$\beta^{-1} = 1$	$\xi_1 = \theta_{ABC}$	0.700 ± 0.011	0.704 ± 0.011	0.710 ± 0.011
$\beta^{-1} = 1$	$\xi_2 = r_{AC}^2$	0.709 ± 0.015	0.219 ± 0.004	2.744 ± 0.056
$\beta^{-1} = 0.2$	$\xi_1 = \theta_{ABC}$	5784 ± 101	5836 ± 100	5752 ± 101
$\beta^{-1} = 0.2$	$\xi_2 = r_{AC}^2$	5833 ± 88	1373 ± 20	2135 ± 319

We now study how results depend on temperature. Let us first consider the reaction coordinate $\xi_1 = \theta_{ABC}$. Results are shown on Fig. 5. Both coarse-grained dynamics provide extremely accurate results, independently of the temperature. We also observe that we can fit the residence time τ_{res} according to the relation

$$\tau_{\text{res}} \approx \tau_{\text{res}}^0 \exp(s\beta) \quad (85)$$

with $\tau_{\text{res}}^0 = 0.07521$ and $s = 2.25031$.

By analytical considerations, we now explain why the residence times computed from both coarse-grained dynamics (6) and (67) satisfy the relation (85), with the numerical values of s and τ_{res}^0 reported above.

We first consider the coarse-grained dynamics (6) driven by the free energy. In the case at hand here, it is possible to compute analytically the free energy. Using the internal coordinates r_{AB} , r_{BC} and θ_{ABC} , we indeed infer from (2) that the free energy A_1 does not depend on the temperature and satisfies

$$A_1(\theta_{ABC}) = W_3(\theta_{ABC}).$$

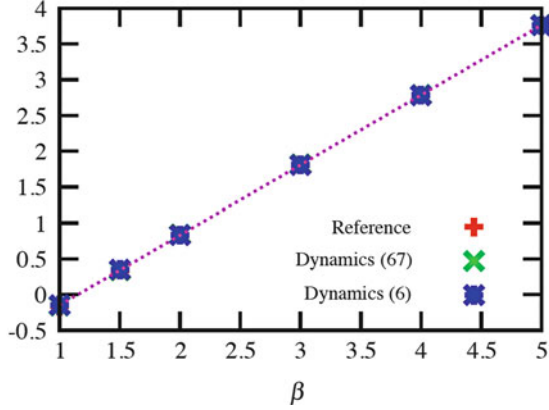


Fig. 5 $\log_{10}(\text{residence time})$ as a function of β , for the reaction coordinate $\xi_1 = \theta_{ABC}$

Thus A_1 has two global minimizers, separated by a barrier

$$\Delta A_1 = \frac{1}{2} k_\theta (\delta\theta)^4 \approx 2.25648.$$

The large deviations theory can be used to understand the behaviour of the dynamics (6), in the low temperature regime. It yields the fact that, when $\beta \gg 1$, residence times are given by

$$\tau_{\text{res}}^{\text{LD}} \approx \tau_{\text{res}}^{0,\text{LD}} \exp(\beta \Delta A_1) \quad \text{with} \quad \tau_{\text{res}}^{0,\text{LD}} = \frac{2\pi}{\omega_{\text{SP}} \omega_{\text{W}}}, \quad (86)$$

where $\omega_{\text{SP}}^2 = -A_1''(\xi_{\text{SP}})$ is the pulsation at the saddle-point $\xi_{\text{SP}} = \theta_{\text{saddle}}$, and $\omega_{\text{W}}^2 = A_1''(\xi_{\text{W}})$ is the pulsation at the local minimizer $\xi_{\text{W}} = \theta_{\text{saddle}} \pm \delta\theta$ (see also [17, (7.9) and (7.10)]). In the present case, we compute that $\omega_{\text{SP}} \approx 7.828$ and $\omega_{\text{W}} \approx 11.07$, thus $\tau_{\text{res}}^{0,\text{LD}} \approx 0.0725$, and we find that

$$s \approx \Delta A_1 \quad \text{and} \quad \tau_{\text{res}}^0 \approx \tau_{\text{res}}^{0,\text{LD}}.$$

We thus obtain a good agreement between (85) and (86), as observed on Fig. 5. Note that this agreement holds even up to temperature $\beta^{-1} = 1$.

We now turn to the dynamics (67). We pointed out in Remark 9 that dynamics (67) and (6) are identical in the limit of low temperature, for the reaction coordinate ξ_1 . The functions b and σ are plotted for the temperature $\beta^{-1} = 1$ on Fig. 6. We observe that, even though the temperature is not very small, we already have $b \approx -W_3' = -A_1'$ and $\sigma \approx 1$. The agreement is even better when the

temperature is smaller. This thus explains why results given by both coarse-grained dynamics (67) and (6) can be fitted by the same relation (85), on the whole range of temperature.

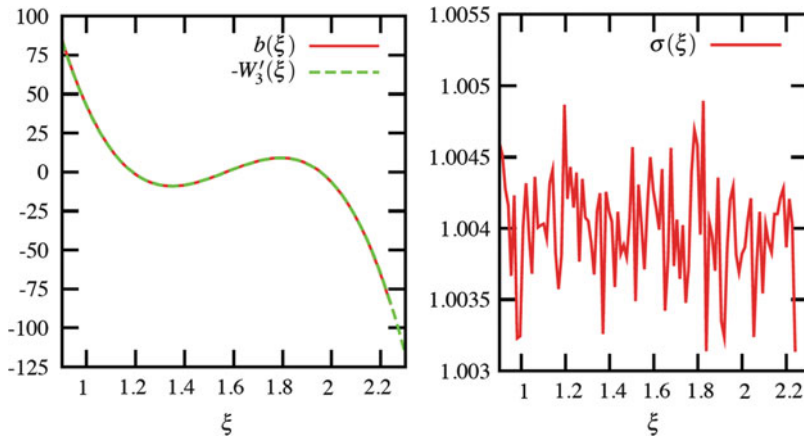


Fig. 6 Plot of the functions b and σ , for the reaction coordinate $\xi_1 = \theta_{ABC}$, at the temperature $\beta^{-1} = 1$

We now consider the reaction coordinate $\xi_2 = r_{AC}^2$. Residence times as a function of the inverse temperature β are shown on Fig. 7. We observe that neither the dynamics (6) nor the dynamics (67) provide accurate results. More precisely, the reference results, the results given by (67) and the results given by (6) can be fitted by

$$\tau_{\text{res}}^{\text{ref}} \approx \tau_{\text{res}}^{0,\text{ref}} \exp(s\beta),$$

$$\tau_{\text{res}}^{\text{eff}} \approx \tau_{\text{res}}^{0,\text{eff}} \exp(s\beta), \quad (87)$$

$$\tau_{\text{res}}^{\text{free}} \approx \tau_{\text{res}}^{0,\text{free}} \exp(s\beta), \quad (88)$$

respectively, with the same parameter $s = 2.21 \pm 0.03$ and

$$\tau_{\text{res}}^{0,\text{ref}} \approx 0.0768, \quad \tau_{\text{res}}^{0,\text{eff}} \approx 0.0241, \quad \tau_{\text{res}}^{0,\text{free}} \approx 0.293.$$

The dependency with respect to the temperature is thus accurately reproduced by both coarse-grained dynamics. The inaccuracy comes from the fact that the prefactor $\tau_{\text{res}}^{0,\text{ref}}$ is ill-approximated.

Again, these numerical observations are in agreement with analytical computations based on the large deviations theory. More precisely, we explain in the sequel why the residence times computed from both coarse-grained dynamics (67) and (6)

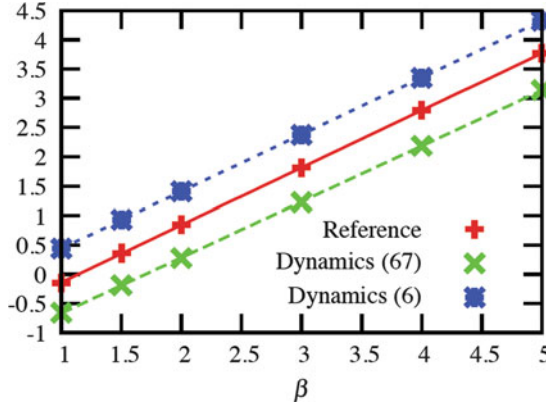


Fig. 7 $\log_{10}(\text{residence time})$ as a function of β , for the reaction coordinate $\xi_2 = r_{AC}^2$

satisfy (87) and (88), with the same s , and for the numerical values of s , $\tau_{\text{res}}^{0,\text{eff}}$ and $\tau_{\text{res}}^{0,\text{free}}$ reported above.

The functions A'_2 , b and σ are plotted for two different temperatures on Fig. 8. Although A_2 a priori depends on β (as expected), it turns out this dependency becomes quite weak when $\beta \geq 1$. It turns out that we can fit A'_2 by

$$A'_2(\xi) \approx c_5(x-2)^5 + c_4(x-2)^4 + c_3(x-2)^3 + c_2(x-2)^2 + c_1(x-2),$$

with $c_1 = -16.4433$, $c_2 = 3.87398$, $c_3 = 34.2171$, $c_4 = -6.36938$ and $c_5 = -7.89431$. The free energy has thus two local minimizers, $\xi_{W,r} \approx 2.73$ and $\xi_{W,l} \approx 1.25$ and a saddle point, $\xi_{SP} \approx 2$, with

$$A_2(\xi_{SP}) \approx 0, \quad A_2(\xi_{W,r}) \approx -2.1, \quad A_2(\xi_{W,l}) \approx -2.37.$$

We introduce the barriers to go from the right well to the left well ($r \rightarrow l$) and *vice-versa*:

$$\Delta A_2^{r \rightarrow l} = A_2(\xi_{SP}) - A_2(\xi_{W,r}) \quad \text{and} \quad \Delta A_2^{l \rightarrow r} = A_2(\xi_{SP}) - A_2(\xi_{W,l}).$$

In the case of the dynamics (6) driven by the free energy, and under the assumption that the temperature is low enough so that A_2 becomes independent of β , the large deviations theory can again be used, and yields the fact that residence times are given by

$$\tau_{\text{res,free}}^{\text{LD},r \rightarrow l} \approx \frac{2\pi}{\omega_{SP} \omega_{W,r}} \exp(\beta \Delta A_2^{r \rightarrow l}), \quad \tau_{\text{res,free}}^{\text{LD},l \rightarrow r} \approx \frac{2\pi}{\omega_{SP} \omega_{W,l}} \exp(\beta \Delta A_2^{l \rightarrow r}),$$

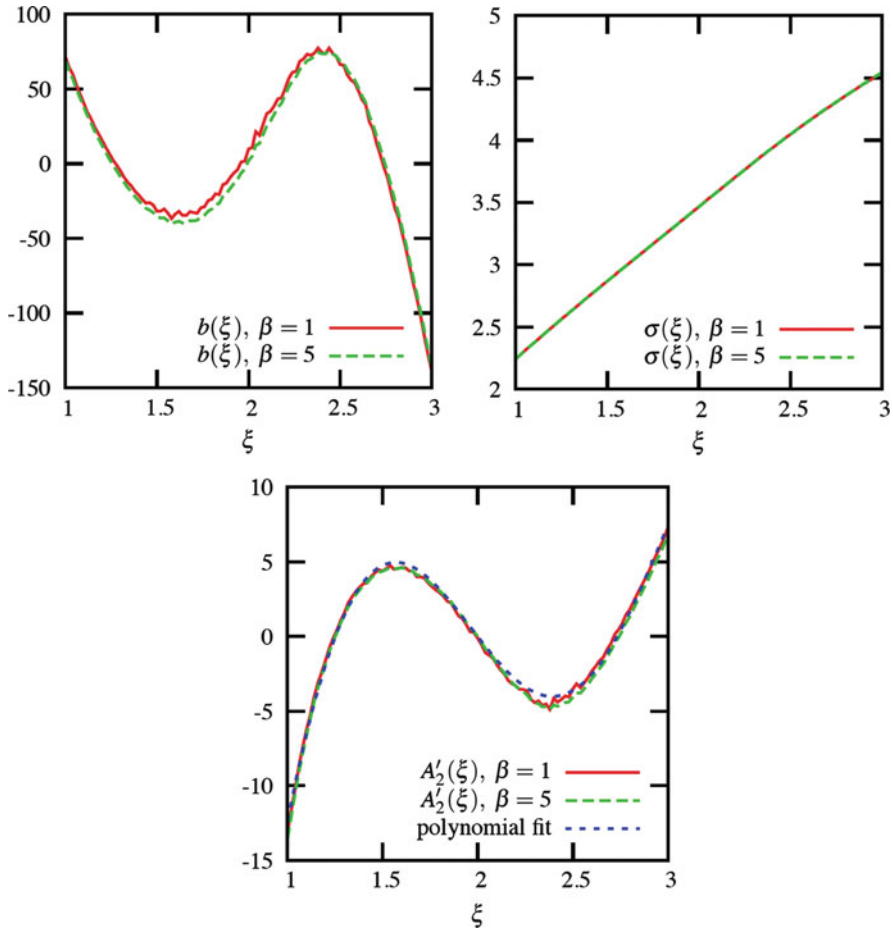


Fig. 8 Plot of the functions b , σ and A'_2 , for the reaction coordinate $\xi_2 = r_{AC}^2$, at two different temperatures

where ω_{SP}^2 , $\omega_{W,l}^2$ and $\omega_{W,r}^2$ are the pulsations at the saddle-point, the left well and the right well, respectively. In the present case, we compute that $\omega_{SP} \approx \sqrt{-c_1} \approx 4.055$, $\omega_{W,l} \approx 5.809$ and $\omega_{W,r} \approx 4.774$.

The left well is deeper than the right well. Hence, in the low temperature limit, the residence time in the left well is much larger than the residence time in the right well, and the probability to be in the left well is higher than the probability to be in the right well. Hence,

$$\tau_{res,free}^{LD} \approx \tau_{res,free}^{LD,l \rightarrow r} \approx \tau_{res,free}^{0,LD,l \rightarrow r} \exp(\beta \Delta A_2^{l \rightarrow r}) \quad \text{with} \quad \tau_{res,free}^{0,LD,l \rightarrow r} = \frac{2\pi}{\omega_{SP} \omega_{W,l}}. \quad (89)$$

With the parameters that we used, we compute $\tau_{res,free}^{0,LD,l \rightarrow r} \approx 0.267$, hence

$$s \approx \Delta A_2^{l \rightarrow r} \quad \text{and} \quad \tau_{\text{res}}^{0, \text{free}} \approx \tau_{\text{res}, \text{free}}^{0, \text{LD}, l \rightarrow r},$$

and we obtain a good agreement between (88) and (89).

We now turn to the dynamics (67). The functions b and σ plotted on Fig. 8 seem to be almost independent of the temperature when $\beta \geq 1$. Following [19, Sect. 2.3] and [11, Sect. 10 and (89)], we introduce the one-to-one function

$$h(\xi) = \int_0^\xi \sigma^{-1}(y) dy$$

and the coordinate $\zeta = h(\xi_2)$. We next change of variable in the effective dynamics (67) on the reaction coordinate ξ and recast it as

$$d\zeta_t = -\tilde{A}'(\zeta_t) dt + \sqrt{2\beta^{-1}} dB_t,$$

where \tilde{A} turns out to be the free energy associated to the reaction coordinate $\zeta(q) = h(\xi_2(q))$. The residence time to exit the left well is hence given by

$$\tau_{\text{res}, \text{eff}}^{\text{LD}, l \rightarrow r} \approx \frac{2\pi}{\tilde{\omega}_{\text{SP}} \tilde{\omega}_{\text{W}, l}} \exp(\beta \Delta \tilde{A}^{l \rightarrow r}).$$

In the regime of low temperature, the second term of (11) is negligible, and we deduce from (10) that $\tilde{A}(h(\xi)) = A_2(\xi)$, where A_2 is the free energy associated with the reaction coordinate ξ_2 . As a consequence,

$$\Delta \tilde{A}^{l \rightarrow r} = \Delta A^{l \rightarrow r}, \quad \tilde{\omega}_{\text{SP}} = \omega_{\text{SP}} \sigma(\xi_{\text{SP}}), \quad \tilde{\omega}_{\text{W}, l} = \omega_{\text{W}, l} \sigma(\xi_{\text{W}, l}).$$

Hence,

$$\tau_{\text{res}, \text{eff}}^{\text{LD}, l \rightarrow r} \approx \tau_{\text{res}, \text{eff}}^{0, \text{LD}, l \rightarrow r} \exp(\beta \Delta A_2^{l \rightarrow r}), \quad (90)$$

with

$$\tau_{\text{res}, \text{eff}}^{0, \text{LD}, l \rightarrow r} = \frac{2\pi}{\omega_{\text{SP}} \omega_{\text{W}, l} \sigma(\xi_{\text{SP}}) \sigma(\xi_{\text{W}, l})}.$$

We thus recover that the dependency of the residence times with temperature is identical between the residence times predicted by the effective dynamics (67) and the residence times predicted by (6): this dependency is exponential, with the same prefactor $\Delta A_2^{l \rightarrow r}$.

We also compute $\sigma(\xi_{\text{SP}}) \approx 3.465$ and $\sigma(\xi_{\text{W}, l}) \approx 2.563$, so $\tau_{\text{res}, \text{eff}}^{0, \text{LD}, l \rightarrow r} \approx 0.03$. Thus the values $\tau_{\text{res}}^{0, \text{eff}}$ and $\tau_{\text{res}, \text{eff}}^{0, \text{LD}, l \rightarrow r}$ qualitatively agree, and we obtain a good agreement between (87) and (90).

3.4.2 The Butane Molecule Case

We now consider a system in higher dimension, namely a butane molecule, in the united atom model [22, 27]. We hence only simulate four particles, whose positions

are $q^i \in \mathbb{R}^3$, for $1 \leq i \leq 4$. The potential energy reads

$$V(q) = \sum_{i=1}^3 V_{\text{bond}}(\|q^{i+1} - q^i\|) + V_{\text{bond-angle}}(\theta_1) + V_{\text{bond-angle}}(\theta_2) + V_{\text{torsion}}(\phi),$$

where θ_1 is the angle formed by the three first particles, θ_2 is the angle formed by the three last particles, and ϕ is the dihedral angle, namely the angle between the plane on which the three first particles lay and the plane on which the three last particles lay, with the convention $\phi \in (-\pi, \pi)$. We work with

$$V_{\text{bond}}(\ell) = \frac{k_2}{2}(\ell - \ell_{eq})^2, \quad V_{\text{bond-angle}}(\theta) = \frac{k_3}{2}(\theta - \theta_{eq})^2$$

and

$$V_{\text{torsion}}(\phi) = c_1(1 - \cos \phi) + 2c_2(1 - \cos^2 \phi) + c_3(1 + 3\cos \phi - 4\cos^3 \phi).$$

Rigid body motion invariance is removed by setting $q^2 = 0$, $q^1 \cdot e_z = 0$ and $q^3 \cdot e_x = q^3 \cdot e_z = 0$.

In the system of units where the length unit is $\ell_0 = 1.53 \cdot 10^{-10}$ m and the energy unit is such that $k_B T = 1$ at $T = 300$ K, the time unit is $\bar{t} = 364$ fs, and the numerical values of the parameters are $\ell_{eq} = 1$, $k_3 = 208$, $\theta_{eq} = 1.187$, $c_1 = 1.18$, $c_2 = -0.23$, and $c_3 = 2.64$. We will work in the sequel with $k_2 = 1,000$. We set the unit of mass such that the mass of each particle is equal to 1.

For these values of the parameters c_i , the function V_{torsion} has a unique global minimum (at $\phi = 0$) and two local non-global minima (see Fig. 9). It is hence a metastable potential. We choose to work with the dihedral angle as reaction coordinate:

$$\xi(q) = \phi.$$

We are interested in the residence time in the main well (around the global minimizer $\phi_0 = 0$) before hopping to any of the two wells around the local minimizers $\phi_{\pm 1} = \pm 2\pi/3$. For each minimizer ϕ_0 , ϕ_1 and ϕ_{-1} , the associated well is defined by $\{q; |\xi(q) - \phi_i| \leq \xi^{\text{th}}\}$, $i = -1, 0, 1$, with $\xi^{\text{th}} = 0.5$.

Remark 10. We observe that

$$\nabla V_{\text{stiff}} \cdot \nabla \xi = 0,$$

where $V_{\text{stiff}}(q) = \sum_{i=1}^3 V_{\text{bond}}(\|q^{i+1} - q^i\|) + V_{\text{bond-angle}}(\theta_1) + V_{\text{bond-angle}}(\theta_2)$. In view of [19, Sect. 3.2], we hence expect to obtain accurate results with this choice of reaction coordinate, as it is indeed the case. \diamond

As in the previous section, we compute reference residence times by integrating the complete dynamics, and we then consider both coarse-grained dynamics (67) and (6). All computations have been done with the time step $\Delta t = 10^{-3}$. Results are reported in Table 2. We observe that the effective dynamics (67) again yields extremely accurate results. The results obtained by the dynamics (6), although

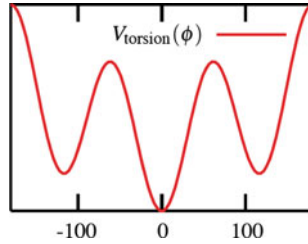


Fig. 9 Torsion angle potential $V_{\text{torsion}}(\phi)$

qualitatively correct, are less accurate. This conclusion holds for all the temperatures we considered.

As in the previous section, residence times depend on the temperature following

$$\tau_{\text{res}} \approx \tau_{\text{res}}^0 \exp(s\beta).$$

For both coarse-grained dynamics, the values found for s and τ_{res}^0 agree with predictions based on the large deviations theory. In the case at hand here, it turns out that the free energy associated to the reaction coordinate $\xi(q) = \phi$ is simply $A(\xi) = V_{\text{torsion}}(\xi)$. On Fig. 10, we plot the functions b and σ . We observe that they are almost independent of the temperature (as soon as $\beta \geq 1$), and that σ is almost a constant. Hence, up to the time rescaling $t_{\text{rescale}} = \sigma t$, the effective dynamics reads as the dynamics (6) governed by the free energy. As $\sigma = 1.086 \approx 1$ (see Fig. 10), the dynamics (6) yields qualitatively correct results.

Table 2 Butane molecule: residence times obtained from the complete description (second column) and from the reduced descriptions (two last columns), at different temperatures (confidence intervals have been computed on the basis of $\mathcal{N} = 13,000$ realizations)

Temperature	Reference residence time	Residence time using (67)	Residence time using (6)
$\beta^{-1} = 1$	31.9 ± 0.56	32.0 ± 0.56	37.1 ± 0.64
$\beta^{-1} = 0.67$	493 ± 8	490 ± 8	581 ± 9
$\beta^{-1} = 0.5$	7624 ± 113	7794 ± 115	9046 ± 133

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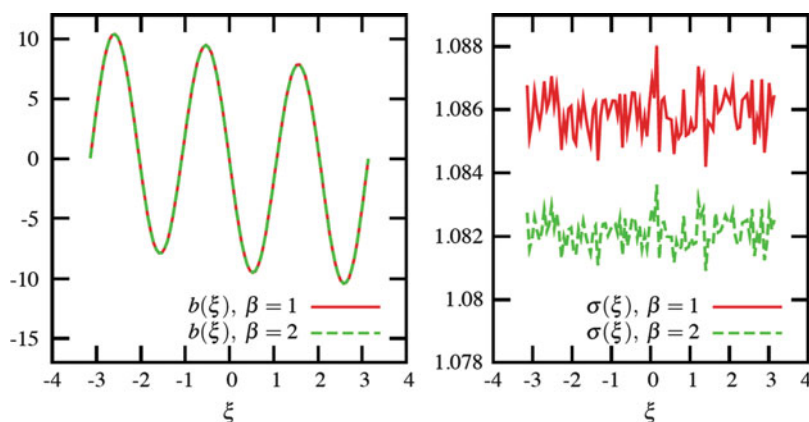


Fig. 10 Plot of the functions b and σ , for the reaction coordinate $\xi = \phi$, at different temperatures

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