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Absolute Transition Rates for Rare Events from Dynamical Decoupling of Reaction Variables

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We introduce a new approach to evaluate transition rates for rare events in complex many-particle systems. Building on a path-integral representation of transition probabilities for Markov processes, the rate is first expressed in terms of a free energy in the transition-path ensemble. We then define an auxiliary process where a suitably defined reaction variable is dynamically decoupled from all the others, whose dynamics is left unchanged. For this system the transition rates coincide with those of a unidimensional process whose only coordinate is the reaction variable. The free-energy difference between the auxiliary and the physical transition-path ensembles is finally evaluated using standard techniques. The efficiency of this method is deemed to be optimal because the physical and auxiliary dynamics differ by one degree of freedom only at any system size. Our method is demonstrated numerically on a simple model of Lennard-Jones particles ruled by the overdamped Langevin equation.

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The calculation of rate constants for events that are rare on the molecular time scale, and more generally of transition probabilities for complex stochastic processes, has been an issue of paramount interest in the natural sciences ever since Kramers' work appeared in 1940 [1–3]. The main difficulty here stems from the fact that the relevant information, while determined by the details of the microscopic dynamics, can only be extracted from the statistical properties of trajectories in the (extremely) long-time limit. A particularly promising approach is transition path sampling [4] in which, building on the Markovian character of many relevant processes, the transition probabilities are expressed as path integrals of the exponential of a suitably defined functional, e.g., the Onsager-Machlup action, $\mathcal{S}[X(\cdot)]$, [5] over the set of reactive trajectories, $X(\cdot)$ (the transition-path ensemble, TPE) connecting microscopic configurations representative of the reactant and product macroscopic states, A and B, of the reaction of interest

$$P(B,t|A,0) = Z_A^{-1} \times \int \chi_A(X(0)) e^{-\beta V(X(0))} e^{-\mathcal{S}[X(\cdot)]} \chi_B(X(t)) \mathcal{D}[X(\cdot)], \tag{1}$$

where $\chi_{A/B}(X)$ is a characteristic function that is equal to one if $X \in A/B$ and zero otherwise and $Z_A = \int \chi_A(X) e^{-\beta V(X)} dX$. The path integral in Eq. (1) has the form of the exponential of the free energy of a generalized system whose configurations are reactive trajectories [4,6,7]. Free energies are notoriously difficult to evaluate numerically. In practice, the transition probability is first calculated for an auxiliary system, where this can be easily done. The ratio of the transition probabilities in the auxiliary and physical systems is then expressed as the exponential of the free-energy difference between the two TPEs: $P(B,t|A)/\bar{P}(B,t|A) = e^{-(\mathcal{F}-\bar{\mathcal{F}})}$. Such a difference can be evaluated via thermodynamic integration [8], or any equivalent technique. The freedom in the choice of the auxiliary system is pretty wide, the major differences between the various methods lying mainly in this choice. The auxiliary system can, for instance, differ from the physical one for a somehow different definition of initial and/or final states [4,9,10] or for the values of some physical parameters, such as temperature or pressure [11,12]. Some of these methods are affected by the usual difficulties that beset the numerical estimate of free energies: if the auxiliary and physical systems differ too much, the reversible transformation of one system into the other may require too slow a process to be efficiently simulated. This may become a major problem as the system size grows large, because the difference between the auxiliary and the real systems usually increases with the number of degrees of freedom.

In order to address this issue, we define an auxiliary system that differs from the physical one not by any physical property, nor by the definition of the reactant or product states, but by the dynamical process ruling its time evolution. The latter is designed so as to coincide with that of the physical process for all coordinates but one, which is a suitably defined reaction variable (RV) whose main property is the ability to discriminate reactant and product states. Furthermore, the evolution of this RV in the auxiliary process is dynamically decoupled from all the other degrees of freedom. In this way the reaction rate of the auxiliary system can be easily determined, as it coincides with that of a unidimensional system whose only coordinate is the RV. The efficiency of the free-energy difference evaluation should remain insensitive on system size, as the auxiliary and physical systems differ only along one degree of freedom at any size. As we will see, the choice of the RV is to a large extent arbitrary, as long as its serves to discriminate reactant and product states: a RV that hardly resembles the committor, which is considered to be the ideal reaction coordinate [7,13], may be just as good.

In the following we specialize the derivation to the case where the microscopic dynamics of the system is described by an overdamped Langevin process

$$dx_i = dt f_i(X) + \sqrt{2D} dW_i, \tag{2}$$

where dW_i is a multivariate Wiener process of covariance $\langle dW_i dW_j \rangle = dt\delta_{ij}$, D is a diffusion coefficient related to the friction γ through the relation $\gamma^{-1} = \beta D$, $f_i = -\gamma^{-1}\partial_i V(X)$, and $V(X)$ a potential function. For this system, we define a RV, $S(X)$, which we assume to take different values for the reactants (state A) and products (state B). In order to compute the conditional probability $P(B, t|A)$ that the system undergoes a transition from A to B in a time t, we introduce an auxiliary stochastic process in configuration space that is as similar as possible to the original dynamics (2), but such that the RV is decoupled from the other variables, namely, its dynamics is described by a one-dimensional process, for which transition rates can be easily calculated. We assume the auxiliary process to have the form

$$dx_i = dt\bar{f}_i(X) + (2\bar{D})^{1/2}_{ij}(X) dW_j, \tag{3}$$

where summation over repeated indices is implied throughout, the Itō convention for stochastic differential equations is assumed [14], and $\bar{f}_i(X)$ and $\bar{D}_{ij}(X)$ are a vector and a matrix field, respectively. The latter are determined by the following conditions:

Dynamical decoupling.—The motion perpendicular to the hypersurface in configuration space determined by the equation $S(X) = s$ is decoupled from the dynamics on the surface. For this to be the case, it is sufficient that the first and second moments of the variation of S in the stochastic process (3) only depend on the value of s, and not on the specific point on the hypersurface:

$$\langle dS \rangle_X = \varphi(S(X)) dt, \tag{4}$$

$$\langle dS^2 \rangle_X = 2\Delta(S(X)) dt, \tag{5}$$

where $\varphi(s)$ and $\Delta(s)$ are as of yet unspecified functions of the RV. Using Itō calculus, these conditions imply

$$\bar{f}_i(X)\partial_i S(X) + \bar{D}_{ij}(X)\partial^2_{ij} S(X) = \varphi(S(X)), \tag{6}$$

$$\bar{D}_{ij}(X)\partial_i S(X)\partial_j S(X) = \Delta(S(X)). \tag{7}$$

Minimal variance.—The dynamical properties of the two processes, Eqs. (3) and (2), are as close as possible. This is enforced by requiring that the two residui, $R_1 = \sum_{ij}(\bar{D}_{ij} - D\delta_{ij})^2$ and $R_2 = \sum_i(\bar{f}_i(X) - f_i(X))^2$ are as small as possible. These conditions can be satisfied by first minimizing R_1 under the constraint (7), then R_2 under the constraints (6). This gives

$$\bar{D}_{ij}(X) = D P^{\|}_{ij}(X) + \tilde{D}(X) P^{\perp}_{ij}(X), \tag{8}$$

$$\bar{f}_i(X) = P^{\|}_{ij}(X) f_j(X) + n_i(X) f^{\perp}(X), \tag{9}$$

where $n_i(X) = \partial_i S(X)/\|\partial S(X)\|$ is the versor normal to the $S(X) = s$ hypersurface at point X, $P^{\perp}_{ij}(X)$ is the projector along the n direction, $P^{\|}_{ij}(X) = \delta_{ij} - P^{\perp}_{ij}(X)$, and $f^{\perp}(X) = [\varphi(S(X)) - \bar{D}_{kl}(X)\partial^2_{kl} S(X)]/\|\partial S(X)\|$ is the effective force acting perpendicularly to the iso-S hypersurface. Finally, $\tilde{D}(X) = \Delta(S(X))/\|\partial S(X)\|^2$. It can be easily checked that the transition probabilities for any displacement dX orthogonal to ∂S are identical for the two processes, (2) and (3): thus, the two processes differ only by one degree of freedom, namely, the RV. Due to the conditions (6) and (7), in the stochastic process (3) the evolution of the RV is dynamically decoupled from that on the hypersurface $S(X) = s$ and is ruled by the stochastic differential equation: $ds = \varphi(s)dt + \sqrt{2\Delta(s)} dW$. Thanks to this property, the probability $\bar{P}(B, t|A)$ to observe a transition between A and B in a time t for the auxiliary process (3) can be easily computed, either by direct simulation or by solving numerically the corresponding Fokker-Planck equation.

The free energy difference between the physical and auxiliary TPEs, $\mathcal{F} - \bar{\mathcal{F}}$, can be calculated by introducing a family of stochastic processes, labeled by a real number $0 \leq \lambda \leq 1$, which interpolate between the auxiliary and the physical ones, Eqs. (2) and (3)

$$dx_i = dt f^{\lambda}_i(X) + (2D^{\lambda})^{1/2}_{ij}(X) dW_j, \tag{10}$$

where

$$f^{\lambda}_i(X) = (1 - \lambda)\bar{f}_i(X) + \lambda f_i(X), \tag{11}$$

$$D^{\lambda}_{ij}(X) = (1 - \lambda)\bar{D}_{ij}(X) + \lambda D\delta_{ij}. \tag{12}$$

The corresponding TPE has probability density

$$\begin{aligned} P^{\lambda}[X(\cdot)] = {}& Z_A^{-1} e^{-\beta V(X(0))} \chi_A(X(0)) \\ & e^{-\mathcal{S}^{\lambda}_{\text{eff}}[X(\cdot)]} \chi_B(X(t)) \end{aligned} \tag{13}$$

In the above equation, $\mathcal{S}^{\lambda}_{\text{eff}}[X(\cdot)]$ is an effective action incorporating the effect of the position-dependent diffusion matrix, Eq. (12), on the measure of the integral in Eq. (1) (see Supplemental Material [15]). Such a TPE can be generated either by transition path sampling [6] or by a stochastic process in path space that directly samples this distribution. Note also that, in Eq. (13), the statistical weight of the initial configuration is the canonical distribution of the physical system for every λ. Using Eq. (13), the free energy difference reads [8]

$$\mathcal{F} - \bar{\mathcal{F}} = \int_0^1 \langle -\partial_{\lambda} \mathcal{S}^{\lambda}_{\text{eff}}[X(\cdot)] \rangle_{\lambda} d\lambda, \tag{14}$$

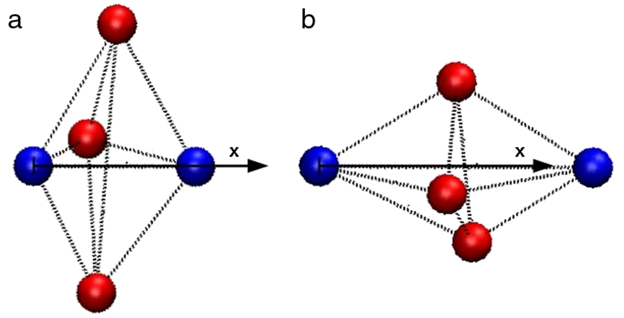

FIG. 1 (color online). Reactant (a) and Product (b) states of our system. The RV is the distance between the two blue particles.

where $\langle\rangle_\lambda$ indicates an equilibrium average in the space of reactive trajectories, performed with respect to the probability density (13).

In order to demonstrate our approach, we calculate the transition probability between two stable configurations of a system of 5 Lennard-Jones (LJ) particles. The typical configuration of the system is a double tetrahedron with three particles forming the common base, and the remaining two symmetrically placed above and under it (see Fig. 1). This system is so simple that, at an appropriate temperature, it is possible to compute transition probabilities directly and thus benchmark our method. However, we will show that our approach allows one to compute the transition probability in conditions where direct simulation would be hopeless. The configurations of the system are identified in the present case by the Cartesian coordinates of the 5 atoms: $X = \{r_{i,\alpha}; i = 1, \ldots 5; \alpha = 1, 2, 3\}$. The stochastic process (2) reads $dr_{i,\alpha} = -dt\beta\partial_{i,\alpha}V(X) + \sqrt{2}dW_{i,\alpha}$, where $V(X) = \frac{1}{2}\sum_{i\neq j} v_{LJ}(|\mathbf{r}_i - \mathbf{r}_j|)$ is a sum of pairwise Lennard-Jones potentials, $v_{\mathrm{LJ}}(r)$ and units are chosen so as to make $D = 1$.

We consider the transition from a state where two particles lie in the base of the two tetrahedra to one where they are placed at the two opposite vertices (see Fig. 1). The distance between these two particles can therefore be conveniently taken as the RV: $S(X) = |\mathbf{r}_2 - \mathbf{r}_1|$. In order to highlight our central idea, while keeping the presentation as simple as possible, we constrain the first particle to stay at the origin ($\mathbf{r}_1 = 0$) and the second to move along the x axis only ($r_{2,2} = r_{2,3} = 0$). Hence, we simply have $S(X) = r_{2,1}$. Explicit expression of $\bar{f}$ and $\bar{D}$ for the general unconstrained case are reported in the Supplemental Material [15]. $r_{2,1}$ is a really poor reaction coordinate (see the committor distribution in Fig. 2). The motion of the RV in the auxiliary dynamics is chosen to be free Brownian, $\varphi(s) = 0$, and we take $\Delta(s) = 1$. With these choices, Eq. (10) becomes

$$\begin{aligned} dr_{i,\alpha} &= -dt\beta\partial_{i,\alpha}V(X) + \sqrt{2}dW_{i,\alpha}, \quad \text{for } i > 2 \\ dr_{2,1} &= -dt\beta\lambda\partial_{2,1}V(X) + \sqrt{2}dW_{2,1}. \end{aligned} \tag{15}$$

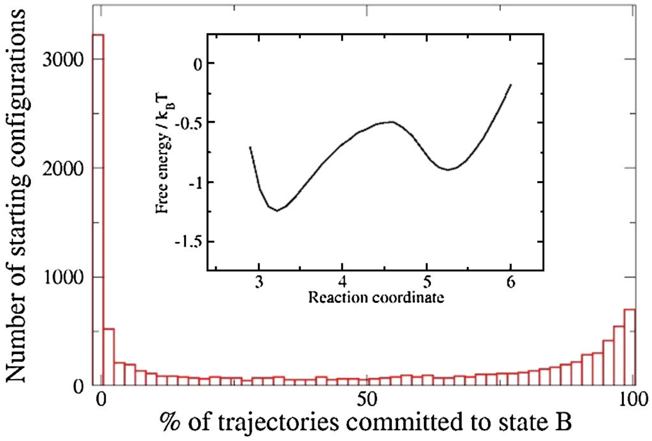

FIG. 2 (color online). Committor distribution for trajectories departing from the top of the barrier of the free energy profile (shown in the inset) of the chosen RV, $S(X) = r_{2,1}$. A number of 10^4 different initial configurations have been sampled. From each of these, 10^2 trajectories have been run until they committed either to the product or the reactant basin. The x axis reports the fraction of trajectories committed to the product basin, while the y axis reports the number of initial configurations with a certain degree of commitment [13].

As anticipated, the auxiliary process coincides with the original one for all the degrees of freedom, but the RV, $r_{2,1}$. In fact, for $\lambda = 0$ the dynamics along $r_{2,1}$ is a one-dimensional Brownian motion, uncorrelated with the other degrees of freedom. It should also be noted that for $\lambda \neq 1$ the canonical distribution $e^{-\beta V(X)}$ is not a stationary distribution for the process (15), as the uncorrelated motion of the system along $r_{2,1}$ prevents its equilibration, nor does the auxiliary dynamics satisfy detailed balance.

For the system in Fig. 1 we aim at estimating the transition probability from state A to state B in 10^3 time steps ($dt = 0.00096$ in units where the position of the LJ minimum is $\sigma_{\mathrm{LJ}} = 3.16$) at a temperature $k_B T_1 = \epsilon_{\mathrm{LJ}}/10$, k_B being the Boltzmann constant and ϵ_{LJ} the depth of the LJ well. Direct inspection of the dynamics of the system shows that a typical transition takes place in no more than a couple of hundred time steps so that sampling trajectories of 10^3 time steps is enough to capture the transition mechanism. The transition rate can then be obtained from the slope of the transition probability as a function of time [4]. The transition probability, P, is first evaluated directly, by letting the system evolve by Eq. (2) for 8×10^8 steps. This gives $P = 2.66 \times 10^{-5}$. We then apply the algorithm described in this work. The transition probability $\bar{P}$ of the auxiliary process is estimated by drawing a canonical ensemble of configurations belonging to the reactant state, A. Each of these configurations is then let to evolve for 10^3 time steps by the auxiliary dynamics. $\bar{P}$ is estimated as the fraction of these trajectories whose end point belongs to the product state, B. This gives $\bar{P} = 3.98 \times 10^{-3}$. Estimating the free energy difference in Eq. (14) requires performing an integral in a $(m \times n + 1)$-dimensional space, m and n

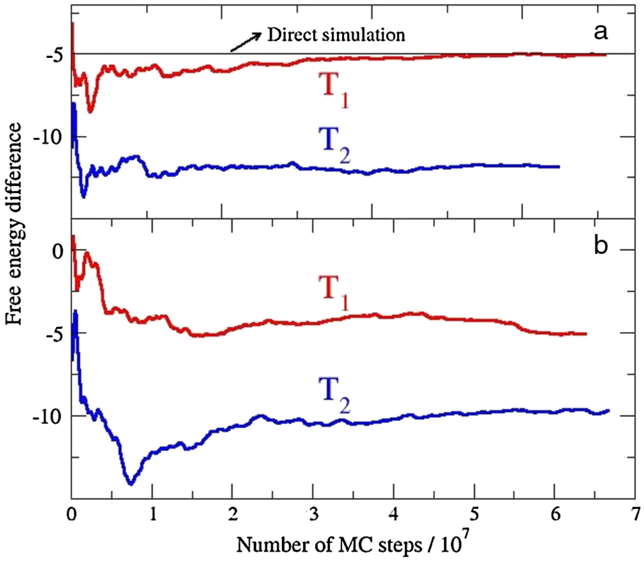

FIG. 3 (color online). (a): Convergence of the free energy difference evaluated for the 5-particle system at high (T_1, red) and low (T_2, blue) temperature (see text). For $T = T_1$, the value corresponding to the transition probability obtained from direct simulation is also shown as a thin line. (b): Same as (a) for the 100-particle system. The estimated transition probabilities for T_1 and T_2 are $2.28(\pm 1.43) \times 10^{-5}$ and $6.29(\pm 3.65) \times 10^{-7}$, respectively.

being the number of degrees of freedom of the system and the number of time steps of reactive trajectories, and λ the $(m \times n + 1)$th coordinate. In practice, this integral is performed by Monte Carlo (MC) sampling in trajectory space. The trial moves are generated via an overdamped Langevin process whose drift is derived from the action $\mathcal{S}^\lambda[X(\cdot)]$. This approach is not based on any particular property of the dynamics (e.g., detailed balance, like in Ref. [16]), but the evaluation of the first derivatives of the action requires the second derivatives of the potential, $V(X)$. In order to efficiently estimate $\mathcal{F} - \bar{\mathcal{F}}$ we bias the MC sampling with a metadynamics history-dependent potential, as in Ref. [17] (See Supplemental Material for details [15]). This procedure gives $\mathcal{F} - \bar{\mathcal{F}} = -5.04 \pm 0.27$, and $P = 2.58(\pm 0.70) \times 10^{-5}$, consistently with the direct evaluation (see Fig. 3).

Clearly, the same approach can be applied also in those cases where the reaction barrier is so high as to hinder any transition in any reasonable time. This would be the case, for instance, by lowering the temperature to $T_2 = T_1/2$, thus making a direct estimate of the transition probability impossible. Nevertheless, we can easily estimate the rate for the auxiliary process and evaluate the ratio in the prescribed manner, obtaining a value of $1.01(\pm 0.30) \times 10^{-7}$ for the transition probability.

Another major advantage of our approach is the insensitivity of its efficiency on system size: whether applied to an isolated molecule or to an extended system, the dynamical decoupling only affects one degree of freedom, the RV. Thus, the similarity between the two TPEs is significant even in the condensed phase, making the free-energy difference calculation affordable also in this case. In order to demonstrate this point, we have considered a system where the five particles are surrounded by 95 other particles interacting with each other and with the five original ones via a LJ potential rescaled by a proper factor, in such a way that the 95 "solvent" particles are approximately at the triple point, thus displaying a slow relaxation dynamics and further challenging the efficiency of our method. Fig. 3(b) shows that the number of MC steps necessary to estimate the rate does not depend sensitively on the presence of the solvent.

We have introduced a dynamical decoupling scheme that allows one to evaluate absolute transition rates for processes that are (extremely) slow on the molecular time scale, while maintaining the full accuracy of an atomistic description of the process. The scheme does not assume the existence of a dominant transition pathway and its efficiency is deemed to be roughly independent of the system size. This opens the way to the simulation of complex processes in condensed phase, where entropic effects may play a dominant role. The presentation is specialized to processes ruled by the overdamped Langevin dynamics, but our approach appears naturally applicable to any Markov processes characterized by a regular propagator, such as Langevin dynamics with inertia, while extension to processes with a singular propagator, such as Newtonian dynamics, appears to be less straightforward. The freedom in the choice of the reaction variable being decoupled and of its dynamics leaves ample space for optimizing the efficiency of the method, while the formal analogies existing between the overdamped Langevin dynamics and Euclidean quantum mechanics make us believe that a similar approach can be used to evaluate tunneling splitting in quantum systems.

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