Efficient Exploration of Reactive Potential Energy Surfaces Using Car-Parrinello Molecular Dynamics

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The possibility of observing chemical reactions in *ab initio* molecular dynamics runs is severely hindered by the short simulation time accessible. We propose a new method for accelerating the reaction process, based on the ideas of the extended Lagrangian and coarse-grained non-Markovian metadynamics. We demonstrate that by this method it is possible to simulate reactions involving complex atomic rearrangements and very large energy barriers in runs of a few picoseconds.

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One of the main benefits of *ab initio* molecular dynamics (MD) is its ability to simulate complex chemical reactions. However, this potentiality is often frustrated by the long time scale needed for chemical processes to take place. Indeed, chemical reactions occur when the system migrates from one local equilibrium minimum to another, overcoming the usually large energy barriers that separate reagents from products. The probability of such an event occurring spontaneously depends exponentially on the energy barrier and easily exceeds the 10 ps regime that present-day computer technology can afford.

The classical approach of quantum chemistry to this problem is to determine local minima and saddle points on the potential energy surface (PES). The minima determine the possible equilibrium configuration, while saddle points determine reaction pathways. Many theoretical papers that deal with chemical reactions follow the scheme: optimization of the structure and determination of the transition state followed, at times, by the application of transition state theory [1–7]. The location of saddle points, however, is far from trivial, and a large variety of methods has been devised, many of which have made their way into commercially available and widely diffused software packages [8–10]. Yet the determination of transition states is very difficult and requires much insight and computational labor. Furthermore this strategy fails when entropic effects are important and the free energy surface (FES) needs to be explored.

Here we present a method based on the ideas of the extended Lagrangian [11–13] and coarse-grained non-Markovian dynamics [14]; it is able to clear large energy barriers in short *ab initio* MD runs. It is suitable for implementation within the Car-Parrinello model [11] or other *ab initio* MD schemes, but it can be more generally applied to explore any PES (i.e., empirical potential). The basic assumption of this method is that one can select a manifold of collective coordinates S_α that are able to characterize the reaction process. The collective coordinates are functions of the ionic coordinates R_I and must be able to discriminate between reactants and products. Moreover, they must include the relevant modes that cannot be sampled within the typical time scale of the simulation (for *ab initio* MD, of the order of 10 ps). The method will not sample motions along slow modes that are not included in the collective coordinates. Examples of collective variables are distances between atoms, dihedral angles, coordination numbers, or any other function of the ionic coordinates R_I.

The aim of the method is to explore the FES $F(\mathbf{s})$, where $\mathbf{s}$ is the vector of the collective variables, denoted by s_α's. In our approach, the collective variables are treated as new dynamical variables, and the extended system is described by a Lagrangian of the form

$$\mathcal{L} = \mathcal{L}_0 + \sum_\alpha \frac{1}{2} M_\alpha \dot{s}_\alpha^2 - \sum_\alpha \frac{1}{2} k_\alpha [S_\alpha(R_I) - s_\alpha]^2 + V(t, \mathbf{s}), \tag{1}$$

where $\mathcal{L}_0$ is the usual Lagrangian that drives the electronic and ionic dynamics, which, in our specific case, is the Car-Parrinello Lagrangian [11], the second term is the (fictitious) kinetic energy of the s_α's, the third term is a sum of harmonic potentials that restrain the value of $S_\alpha(R_I)$ close to the corresponding dynamic collective variable s_α, and $V(t, \mathbf{s})$ is a history-dependent potential whose functional form is defined below. We assume that the $S_\alpha(R_I)$'s are dimensionless and rescaled so that, in a finite temperature MD run performed with $V(t, \mathbf{s})$ set to zero, the amplitude of their fluctuations, $\max(|S_\alpha - \langle S_\alpha \rangle|)$, is equal to 1 for all α's. The mass M_α and the coupling constant k_α determine how fast s_α evolves in time with respect to the ionic degrees of freedom. If the masses M_α are large, the collective variables s_α are slow, so that the dynamics in the collective variables is adiabatically separated from the ionic and electronic ones [11,15]. The dynamics of the s_α is driven by these forces $\phi_\alpha = k_\alpha [S_\alpha(R_I) - s_\alpha]$ plus the forces coming from the history-dependent term, and the instantaneous values of the collective variables $S_\alpha(R_I)$ fluctuate around the corresponding s_α. One basic ingredient of the method is that, in conditions of adiabatic separation, the ϕ_α's provide an estimate of the derivative of the free energy with respect to the collective variables. Namely, in the limit of very large M_α, s_α is approximately fixed and ϕ_α is dynamically averaged over the electronic and ionic degrees of freedom. Hence, s_α efficaciously evolves with the force $\langle \phi_\alpha \rangle$ that is the derivative of the free energy with respect to s_α as in standard umbrella sampling and constrained dynamics [16,17].

$V(t, \mathbf{s})$ is constructed to fill the free energy wells and drive the system towards the lowest saddle points. If $V(t, \mathbf{s})$ is properly chosen and the adiabatic conditions are satisfied, the history-dependent term compensates the underlying FES well, so that we can assume $\lim_{t\to\infty} V(t, \mathbf{s}) = F(\mathbf{s}) + \text{const}$. This property can be verified by the application of the method to known energy surfaces, as discussed in Ref. [14]. Contrary to Ref. [14], where the dynamics followed by the collective variables is discontinuous, here we want to deal with continuous trajectories in order to retain the advantages of Car-Parrinello MD [11]. Hence we choose the potential $V(t, \mathbf{s})$ of the form

$$V(t, \mathbf{s}) = \int_0^t dt' |\dot{\mathbf{s}}(t')| W(t') \exp\left\{-\frac{[\mathbf{s} - \mathbf{s}(t')]^2}{2(\Delta s^\perp)^2}\right\} \delta\left(\frac{\dot{\mathbf{s}}(t')}{|\dot{\mathbf{s}}(t')|} \cdot [\mathbf{s} - \mathbf{s}(t')]\right) \tag{2}$$

that describes a N_s-dimensional Gaussian tube, with axis along the trajectory. $V(t, \mathbf{s})$ results from the accumulation of tube slices of infinitesimal thickness $dt'|\dot{\mathbf{s}}(t')|$ in the direction of the trajectory, whereas, in the orthogonal direction, their size is given by $\Delta s^\perp$. For an optimally efficient filling, $\Delta s^\perp$ is taken to be comparable to the estimated well size [14]. The prefactor $W(t)$ has the dimensions of an energy, and it is chosen so as to adapt the time-dependent potential to the the free energy landscape, as we show in the following.

In practical implementations, a discretized version of $V(t, \mathbf{s})$ is used and the potential is updated at intervals Δt that are 1 or 2 orders of magnitude larger than the MD integration step. Indeed, Δt must be small enough to allow a sufficient sampling of every oscillation in the collective variables, but large enough to filter out the inessential ionic and electronic fluctuations. If we use the Gaussian approximation of the delta function $\delta(x) \simeq (1/\beta\sqrt{2\pi}) \exp\{-\frac{x^2}{2\beta^2}\}$, with $\beta = \Delta t |\dot{\mathbf{s}}(t)|$, we get

$$V(t, \mathbf{s}) = \sum_{t_i < t} \left[W_i \exp\left\{-\frac{(\mathbf{s} - \mathbf{s}^i)^2}{2(\Delta s^\perp)^2}\right\} \exp\left\{-\frac{[(\mathbf{s}^{i+1} - \mathbf{s}^i) \cdot (\mathbf{s} - \mathbf{s}^i)]^2}{2(\Delta s_i^{\parallel})^4}\right\}\right], \tag{3}$$

where $\mathbf{s}^i = \{s_\alpha(t_i)\}$ and $\Delta s_i^{\parallel} = |(\mathbf{s}^{i+1} - \mathbf{s}^i)|$. The adaptive prefactor W_i is given by $W_i = \lambda \sum_\alpha (s_\alpha^{i+1} - s_\alpha^i) \langle k_\alpha [S_\alpha(R_I) - s_\alpha] \rangle$, where $\lambda < 1$ and the average is taken over the time interval Δt. This form amounts to estimating $W_i \simeq \int_{t_i}^{t_i+\Delta t} dt' \dot{\mathbf{s}}(t') \frac{\partial F}{\partial \mathbf{s}}$, in order to balance the force coming from the underlying FES. All the parameters described above are system dependent and they strongly affect the efficiency in escaping from the local minima, as well as the resolution in reconstructing the underlying FES. Although the trajectories generated by the algorithm discussed describe the most probable mechanisms of the process, we remark that they are not true dynamical trajectories, not even in the neighborhood of the transition state [7], nor can the relation between metadynamics and real dynamics be easily expressed.

We apply this method to two examples. The first one is the well-known and much studied electrocyclic reaction in the C_4H_6 system [18]. This molecule has three stable configurations, the cyclobutene (cycle), the *s-cis*-buta-1,3-diene (*cis*), and the most stable *s-trans*-buta-1,3-diene (*trans*) [18]. Starting from the cycle, the reaction involves the breaking of the C1-C4 bond (see Fig. 1) and the rotation of the two groups CH_2 in order to form the planar *cis* or *trans* geometries, with a barrier of $\sim$30 kcal/mol [19]. The two events can be simultaneous or slightly separated in time, but according to orbital symmetry considerations, the electrocyclic reaction occurs in a concerted corotatory fashion on the electronic ground state surface [19]. As reaction coordinates we choose the carbon-carbon distances C1-C2, C3-C4, and C1-C4. Obviously this choice is not unique, but we checked that different sets of variables, such us, e.g., dihedral angles,

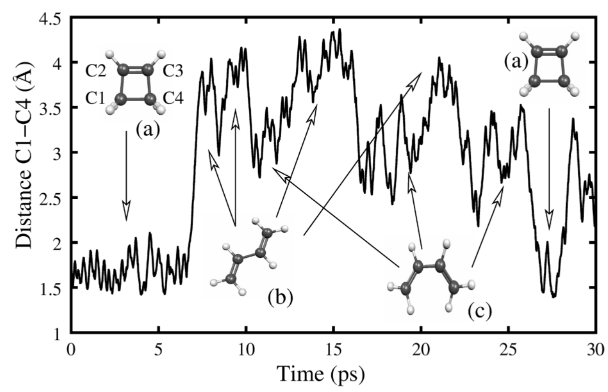

FIG. 1. C1-C4 distance during the MD run. The masses are set to 50 amu and the k_α's to 0.3. $V(t, \mathbf{s})$ is updated every 0.012 ps, $\Delta s^\perp$ is 0.15, $\Delta s^\parallel$ fluctuates in the interval [0.07:0.1], and W between 1.0 and 8.0 kcal/mol. The arrows indicate which configuration the system is in: (a) is the cycle, (b) the *trans*, and (c) the *cis* configuration. With larger Gaussians [$\Delta s^\perp = 0.2$, and consequently larger $\Delta s^\parallel$ and W ($\simeq$ 6.5 kcal/mol)] and smaller M_α (1 amu), the transition is observed within 1 ps, at a cost of a more coarse evaluation of the energy profile.

lead to quantitatively similar results. We run a Car-Parrinello MD [20] at $T = 300$ K driven by the Lagrangian in Eq. (1), with the additional history-dependent term in Eq. (3). The M_α's and the coupling constants k_α's are chosen so that the variables complete 3–5 fluctuations per picosecond, and the maximum value of $k_\alpha[S_\alpha(R_I) - s_\alpha]^2$ is not larger than a few kcal/mol, assuming that this allows a sufficient adiabatic separation. In the first 6 ps, the system remains in the initial configuration, as shown by the plot of the C1-C4 distance in Fig. 1. While the well is filled with more and more Gaussians, the total energy increases and the oscillations of the collective variables become wider. After about 6.5 ps a transition state is reached and the system moves fast toward the new minimum, transforming into the *trans* configuration. The transition is indicated by the large change in the C1-C4 distance (from 1.6 to 4 Å), while both the C1-C2 and the C3-C4 (not shown in the figure) are contracted, due to the formation of the double bonds. Analysis of the trajectory along the transition path shows that the corotatory movement of the CH_2 and the C1-C4 bond breaking take place simultaneously. After the first transition at 6.5 ps, the system crosses the energy barrier separating the *trans* from the *cis* configurations several times. After about 27 ps a recrossing of the first transition state occurs, and the system transforms back into the cycle configuration. Once the overall topology of the FES is known, we can adapt the resolution in order to determine more precisely the geometry and the energy of the stationary points, by tuning opportunely the size of the Gaussians and the separation time $t_{i+1} - t_i$. Since at 300 K the entropic contribution to the FES is negligible with respect to the barrier height, for large t $V(t, \mathbf{s})$ is a measure of the PES. It is reassuring that the differences in energy among the three minima and the height of the energy barrier, estimated through $V(t_{\mathrm{final}}, \mathbf{s})$, are in agreement, within 2 kcal/mol, with those calculated by the standard methods of geometry optimization and eigenvalue following [1,3,4]. Note that even if during the simulation the exact transition state geometry is not reached, the trajectory passes very close to it, providing a very good guess for the transition state geometry. From this guess any standard optimization method finds the exact geometry in very few iterations.

This simple example has been used to validate our approach in a case where the standard methods are capable of finding the transition state. The situation is different for more complex systems, where there are many and nontrivial transition states and minima. One such example is the dehydrogenation of clusters of the type Si_nH_x, the structure of which evolves as a function of n and x. Different methods have been applied to the study of this problem [21–24]. More recently Miyazaki *et al.* [25] have studied the $n = 6$ case and its hydrogenated derivatives. For each stoichiometry studied, possible equilibrium structures have been proposed, which usually

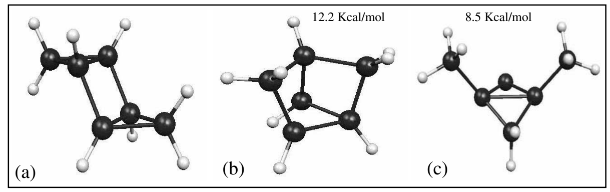

FIG. 2. Examples of minimum energy structures in the Si_6H_8 stoichiometry. (a) is the structure reported in Ref. [25], while (b) and (c) are encountered in the MD run performed with $\Delta s^\perp = 0.3$ and $M_\alpha = 1$ amu, where $V(t, \mathbf{s})$ is updated with a new Gaussian every 0.003 ps. (b) and (c) are, respectively, 12.2 and 8.5 kcal/mol lower in energy than (a).

show high symmetry and an even distribution of the H atoms. Starting from the Si_6H_8 structure [see Fig. 2(a)] reported in Ref. [25], we apply our method to the dehydrogenation process. Natural variables of choice for such a process are the Si-Si, Si-H, and H-H coordination numbers. For the definition of the coordination numbers we use the expression

$$c_{AB} = \sum_{i=1}^{N_A} \frac{1}{N_A} \left[\sum_{j=1}^{N_B} \frac{1 - (\frac{r_{ij}}{d_{AB}})^6}{1 - (\frac{r_{ij}}{d_{AB}})^{12}} \right], \tag{4}$$

where N_A and N_B are the species' numbers of atoms, r_{ij} are the interatomic distances, and the scale parameters d_{AB} are $d_{\mathrm{SiSi}} = 2.6$ Å, $d_{\mathrm{SiH}} = 2.0$ Å, and $d_{\mathrm{HH}} = 1.1$ Å. The choice of these parameters and of the exponents in Eq. (4) are such as to ensure a smooth decay of the coordination number.

A rapid exploration of the FES is possible if one uses large Gaussians and small masses. In a few picoseconds the system explores several structures and is able to identify surprising new local minima, as, for example, the Si_6H_8 structures reported in Figs. 2(b) and 2(c), that are much lower in energy than 2(a), the one predicted in Ref. [25]. This shows that the method has the potential to outperform chemical intuition and to be more efficient than optimization methods such as simulated annealing. For a careful exploration of the FES, however, adiabatic s_α dynamics and smaller Gaussians are needed. In Fig. 3 we summarize the results of a run in which smaller Gaussians and larger masses are used. In this run we used only two collective variables, c_{SiH} and c_{HH} [26]. The system undergoes several dramatic changes while it climbs large energy barriers and visits several minima. From the initial structure (a), Si_6H_8 makes first a tautomeric transformation to the structure (b), which is lower in energy by 7 kcal/mol. From (b) it passes a large diffusive plateau, losing a first H_2 molecule in an endothermic reaction. Eventually it falls in the (c) Si_6H_6 structure, which is 10 kcal/mol lower in energy than the one assumed in Ref. [25] for the same stoichiometry. From (c) it loses a second H_2 molecule, also endothermically, and explores a variety of Si_6H_4 geometries, among

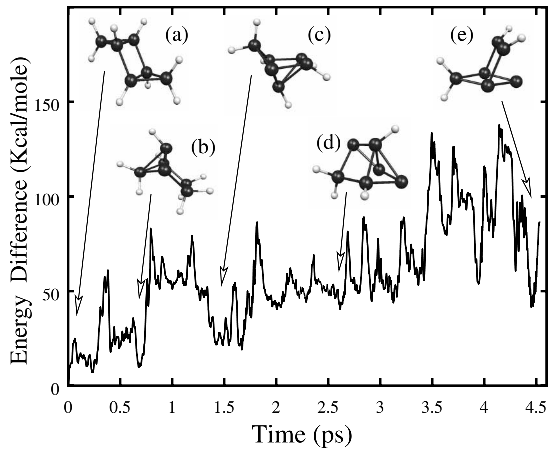

FIG. 3. Potential energy during the MD run at 300 K. The M_α are equal to 50 amu and $V(t, \mathbf{s})$ is incremented by a new Gaussian every 0.006 ps. $\Delta s^{\perp}$ is equal to 0.1, $\Delta s^{\parallel}$ fluctuates between 0.02 and 0.055, and W between 2 and 10 kcal/mol. Some minimum energy configurations, encountered along the trajectory, are reported. (a) and (b) are Si_6H_8, (c) is Si_6H_6, and (d) and (e) are Si_6H_4

which the lowest in energy are (d) and (e), although they are higher than the structures of Refs. [25,27].

In conclusion, the method presented here allows the PES of complex systems to be explored efficiently in a very short time and slow chemical reactions to be simulated with a minimum amount of chemical insight into the problem. We believe that this new method greatly expands the scope of *ab initio* molecular dynamics.

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