A rapid method for determining rate constants by molecular dynamics[a)]

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A simple method is presented for determining rate constants in activated barrier crossing in a computer simulation. Instead of calculating the reactive flux, this method focuses on dynamics in the system with an absorbing barrier placed at the transition state. This method leads to a large reduction in CPU time for the low and high friction regimes.

INTRODUCTION

In activated barrier crossing, one is interested in calculating the rate of transition between stable species separated by an energy barrier. In systems with large energies of activation, barrier crossing is an infrequent event. Straightforward molecular dynamics simulations would then be impractical. Since the crossings are infrequent, most of the computation time required is spent following trajectories in their wells as they await energy activation.

To simulate this process, and to thereby determine rate constants, we have found it useful (and necessary) to determine the reactive flux[1(a)-(e)]

$$\hat{k}(t) = \frac{k_B(t)}{k_{\mathrm{TST}}} = \frac{\int d\Gamma\, \rho_{\mathrm{eq}}(\Gamma)\dot{x}\delta(x)\theta_B[x(t)]}{\int d\Gamma\, \rho_{\mathrm{eq}}(\Gamma)\dot{x}\theta_B(\dot{x})\delta(x)}, \tag{1}$$

where x is the reaction coordinate, $x = 0$ is the position of the barrier maximum (or transition state), $\dot{x} = dx/dt$, $\theta_B[x(t)]$ is the step function which is unity if the particle is to the right of the maximum at time t and zero otherwise, $d\Gamma$ is an element of volume in phase space, $\rho_{\mathrm{eq}}(\Gamma) = Q^{-1}\exp -\beta H(\Gamma)$, and k_{TST} is the transition state theory (TST) value of the kinetic rate constant $(k_f + k_b)$, where k_f and k_b are the forward and backward rate constants. In simulations using Eq. (1), one samples initial states with the particle placed on the transition state. This permits one to calculate only initially "activated" trajectories and thus to avoid calculating trajectories which take a long time before being activated.

If the energy barrier $E^{\neq}/kT \gg 1$, the reactive flux will decay on two widely different time scales. There will be a fast initial decay followed by a very slow decay,

$$\hat{k}(t) \to \lambda_{\mathrm{PLAT}} e^{-(k_f + k_b)t}, \tag{2}$$

where λ_{PLAT} is the "plateau value" of the reactive flux

$$\lambda_{\mathrm{PLAT}} = \frac{(k_f + k_b)}{k_{\mathrm{TST}}} = \frac{(k_f + k_b)}{(k_f + k_b)_{\mathrm{TST}}}. \tag{3}$$

Thus to determine the kinetic rate constant $(k_f + k_b)$, two simulations are required. In the first simulation, λ_{PLAT} is determined by sampling all trajectories that start at $x = 0$, and calculating $\hat{k}(t)$. This function will decay rapidly to the plateau λ_{PLAT}.[2-4] Of course, one must convince oneself that this is the true plateau by continuing to a longer time. A second simulation must then be done to determine $k_{\mathrm{TST}} = \langle \dot{x}\theta(\dot{x})\rangle S(x=0)/x_A x_B$, where $S(x)$ is the equilibrium configuration distribution function for the particle. k_{TST} can be determined by Monte Carlo techniques.[5-7]

An alternative to this is to determine $\hat{k}(t)$ for long times so that $\exp -(k_f + k_b)t$ can be observed. $(k_f + k_b)$ can then be determined from this decay.

In this paper we present an alternative method for determining the transition state theory normalized rate constant λ_{PLAT}, which requires much less computation time.

A RAPID COMPUTATIONAL METHOD

Equation (1) can also be expressed as

$$\hat{k}(t) = \int d\Gamma [P^{(+)}(\Gamma) - P^{(-)}(\Gamma)]\theta_B[x(t)] \tag{4}$$

or

$$\hat{k}(t) = \langle \theta_B[x(t)]\rangle_+ - \langle \theta_B[x(t)]\rangle_-, \tag{5}$$

where $\langle \theta_B[x(t)]\rangle_{\pm}$ are the fractions of trajectories which are in the product well at time t given that at time $t = 0$, $x = 0$, the velocity is either $\dot{x} > 0$ or $\dot{x} < 0$, respectively, and where

$$P^{(\pm)}(\Gamma) = \frac{\dot{x}\theta_B(\pm\dot{x})\delta(x)e^{-\beta H(\Gamma)}}{\int d\Gamma\, \dot{x}\theta_B(\pm\dot{x})\delta(x)e^{-\beta H(\Gamma)}} \tag{6}$$

are well defined probabilities that can be sampled by Monte Carlo techniques.

For simplicity consider a symmetric double well potential with wells A and B and transition state TS. Consider all trajectories originating at TS. These can be divided into a set with $\dot{x} > 0$ and $\dot{x} < 0$. Consider first the set with $\dot{x} > 0$. Let us assume a certain fraction of trajectories T_0 will not quickly leave B, whereas $(1 - T_0)$ will quickly recross the barrier. Then if we follow the motion of these $\dot{x} > 0$ trajectories, a fraction T_0 will immediately get trapped in B, a fraction $(1 - T_0)^2 T_0$ will get trapped after first visiting A, a fraction $(1 - T_0)^4 T_0$ will get trapped after twice visiting A, and so on. Thus,

$$\langle \theta_B[x(t)]\rangle_+ = \sum_{n,\mathrm{even}} (1 - T_0)^n T_0, \tag{7}$$

where we have assumed that the fraction of trajectories quickly trapped in well A is also T_0 because the wells are symmetric. Now consider the set of trajectories $\dot{x} < 0$. These move initially towards well A so that the fraction trapped in B on first visit is $(1 - T_0)T_0$, the fraction trapped on second visit is $(1 - T_0)^3 T_0$, etc. Thus,

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$$\langle \theta_B[x(t)] \rangle_- = \sum_{n,\text{odd}} (1-T_0)^n T_0. \quad (8)$$

From Eqs. (2), (3), (5), (7), and (8) we then find that for $t \ll (k_f + k_b)^{-1}$, $\langle \theta_B(t) \rangle_+ - \langle \theta_B(t) \rangle_- = \lambda_{\text{PLAT}}$ is given by

$$\lambda_{\text{PLAT}} \cong \sum_{n=0}^{\infty} (-1)^n (1-T_0)^n T_0 = \frac{T_0}{2-T_0}. \quad (9)$$

T_0 can be found by taking a single well with an absorbing barrier at the transition state. The trajectories are sampled as if in the calculation of $\hat{k}(t)$ [cf. Eq. (2)]; however when a trajectory recrosses the transition state we remove it. After a short time all the trajectories that "leave quickly" will have been absorbed and the fraction that remains is T_0. Thus the number of trajectories required for the determination of T_0 is smaller than for the determination of $\hat{k}(t)$ in Eq. (2). This leads to a large saving of computer time.

This procedure can be extended to asymmetric wells, where the trapping fractions will differ for each well. If T_A and T_B designate the trapping fractions in wells A and B, respectively, then

$$\lambda_{\text{PLAT}} = \frac{T_A T_B}{T_A + T_B - T_A T_B}. \quad (10)$$

Two simulations are then required to determine T_A and T_B.

NUMERICAL RESULTS

The reactive flux [cf. Eq. (1)] has proven very useful in simulations of reactions in condensed matter. These studies involve the solution of the equations of motion of a large number of molecules and require considerable CPU time. Even when the solvent is represented as a stochastic bath the simulations require long times especially when the friction coefficient is very large or very small. The above method leads to a considerable saving of computer time in these simulations. We illustrate this by applying the method to a simple stochastic simulation. We are currently applying this method to determine rate constants in liquids using full molecular dynamic simulations.

The dynamical system consists of a reaction coordinate x, moving in a quartic symmetric double well potential with energy barrier Q, and a nonreaction coordinate y moving stochastically with friction ζ, in a harmonic potential with frequency ω. The coupling between x and y is ϵxy. The potential is therefore

$$V(x,y) = x^4 - \left(2 - \frac{\epsilon^2}{2\omega^2}\right)x^2 + \frac{\omega^2}{2}y^2 + \epsilon xy + 1. \quad (11)$$

The Langevin equations for the system are

$$\ddot{x} = -\frac{\partial V(x,y)}{\partial x}, \quad \ddot{y} = -\zeta\dot{y} - \frac{\partial V(x,y)}{\partial y} + f_y(t), \quad (12)$$

where $f_y(t)$ is a Gaussian random force with covariance $\langle f_y(0) f_y(t) \rangle = 2kT\zeta\theta(t-\tau_c)/\tau_c$, where τ_c is the correlation time of the force. These Langevin equations were integrated using a fourth-order Adams Moulton predictor–corrector algorithm for $Q/kT = 10$, $\zeta = 2$, $\tau_c = 10^{-4}$, and the two values of $\epsilon = 0.3, 1.2$. The coupling of x to y gives rise to an effective friction on x which increases as ϵ^2. Thus $\epsilon = 0.3$ and $\epsilon = 1.2$ correspond, respectively, to the "low" and "high" effective friction regimes.

The rate constant for barrier crossing is calculated using 1000 sampled trajectories by the two methods outlined above, i.e., (a) by directly computing $\hat{k}(t)$ [cf. Eq. (4)] and from this determining λ_{PLAT} [cf. Eq. (2)] and (b) by determining λ_{PLAT} using Eq. (9), i.e., by following nonabsorbed trajectories, and computing T_0. The results are summarized in Table I.

TABLE I. Comparison of rate constants determined by the reactive flux and the absorbing barrier methods.

ϵ	ζ	T_0	$T_0/(2-T_0)$	λ_{PLAT}	τ(a.b.)/τ(r.f.)
1.20	2.0	0.73 ± 0.04	0.58 ± 0.05	0.60 ± 0.08	0.74
0.30	2.0	0.20 ± 0.03	0.11 ± 0.02	0.13 ± 0.04	0.25

Let τ(r.f.) and τ(a.b.) denote the integration time required to determine λ_{PLAT} using the reactive flux (r.f.) method and the absorbing barrier (a.b.) method, respectively. To determine τ(r.f.), N trajectories are followed for a time τ_λ necessary to determine λ_{PLAT}. Then $\tau(\text{r.f.}) = N\tau_\lambda$. To determine τ(a.b.) each of the N trajectories are followed until absorbed. Since $(1-T_0)N$ trajectories are absorbed rapidly and NT_0 are followed for τ_λ, $\tau(\text{a.b.}) \simeq NT_0\tau_\lambda$. Thus, $\tau(\text{a.b.})/\tau(\text{r.f.}) \simeq T_0$. This shows that when $T_0 \ll 1$; that is when only a very small fraction of trajectories get trapped rapidly, $\tau(\text{a.b.}) \ll \tau(\text{r.f.})$; that is the reactive flux method takes much more computer time than the absorbing barrier method. Thus in both the very low friction and very high friction regimes, where the reactive flux method takes very long times, the absorbing barrier method should be used. The last column in Table I confirms $\tau(\text{a.b.})/\tau(\text{r.f.}) \simeq T_0$.

We have shown how the rate constants $k_f + k_b$ and k_{TST} may be found using the parameters for trapping and escape from a single well with an absorbing barrier at the transition state. The main assumption in our model is that the dynamics of trajectories before and after crossing the transition state are uncorrelated, i.e., upon recrossing the transition state the trajectory may be placed with another trajectory randomly chosen from the distributions $P^{(\pm)}$ of Eq. (6). [The randomness is mathematically expressed by the simple product in Eqs. (7)–(9).] This is a probabilistic argument which should be accurate in the limit when there is a high degree of chaos in the dynamical system. It is worth noting that this method gives accurate results for one-dimensional barrier crossing in both the high and low friction regimes (in agreement with Kramer's theory).

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[1](a)T. Yamamoto, J. Chem. Phys. **33**, 281 (1960); (b) J. C. Keck, Discuss. Faraday Soc. **33**, 173 (1962); (c) Adv. Chem. Phys. **13**, 85 (1967); (d) D. Chandler, J. Chem. Phys. **68**, 2959 (1978); (e) See, for example, the chapter by B. J. Berne, in *Multiple Time Scales*, edited by J. U. Brackbill and B. I. Cohen (Academic, New York, 1985), and references cited therein.

[2]J. A. Montgomery, D. Chandler, and B. J. Berne, J. Chem. Phys. **70**, 4056 (1979).

[3]R. O. Rosenberg, B. J. Berne, and D. Chandler, Chem Phys. Lett. **75**, 162 (1980).

[4]J. E. Adams and J. D. Doll (preprint).

[5]J. P. Valleau and S. G. Whittington, in *Statistical Mechanics*, edited by B. J. Berne (Plenum, New York, 1977), Part A, p. 137.

[6]D. Rebertus, B. J. Berne, and D. Chandler, J. Chem. Phys. **70**, 3395 (1979).

[7]R. Rosenberg, M. Rao, and B. J. Berne, J. Am. Chem. Soc. **104**, 7647 (1982).