On Determining Reaction Kinetics by Molecular Dynamics Using Absorbing Barriers

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The absorbing barrier method for using molecular dynamics to determine rate constants for activated barrier crossing is generalized to allow determination of the full reactive flux. This method requires much less CPU time than the straightforward simulation of the reactive flux in the low- and high-friction regimes. When applied to the Langevin equation the absorbing barrier method gives excellent agreement with the results of Kramers' theory.

Introduction

There are many instances in chemistry and physics where it is important to simulate reactions

$$A \underset{k_b}{\overset{k_f}{\rightleftarrows}} B$$
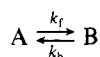
involving a transition between stable species separated by an energy barrier. If the activation energy, $E^{\ddagger}$, is large compared to kT, barrier crossing is infrequent and a straightforward computer simulation will result in too few barrier crossings to allow determination of the rate constants. To avoid this problem one determines the reactive flux[1a-e]

$$\hat{k}(t) = \frac{\langle \dot{x}\delta(x)\theta(x(t)) \rangle}{\langle \dot{x}\delta(x)\theta(\dot{x}) \rangle} \tag{1}$$

where $\langle ... \rangle$ indicates a canonical or microcanonical average, x is the reaction coordinate, $x = 0$ is the position of the barrier (i.e., the transition state), and $\dot{x} = dx/dt$; $\theta(x)$ is the unit step function; $\theta(x(t))$ is unity only if the system at time t is to the right of the transition state (that is, in well B).

If $E^{\ddagger} \gg kT$, $\hat{k}(t)$ will decay on two widely different time scales.[1d] There will be a fast transient decay from the initial value, followed by a very slow decay

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

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

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

$k = k_f + k_b$ is the exact kinetic rate constant, and $k_{TST} = (k_f + k_b)_{TST}$ is the transition-state theory (TST) approximation to k, given by $k_{TST} = \langle \dot{x}\delta(x)\theta(\dot{x}) \rangle / X_A X_B$ where X_A and X_B are the equilibrium mole fractions for wells A and B, respectively.

It is possible to express the reactive flux as[1e]

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

$$= \langle \theta(x(t)) \rangle_+ - \langle \theta(x(t)) \rangle_-$$

where

$$P^{(\pm)}(\Gamma) = \frac{\dot{x}\theta(\pm\dot{x})\delta(x)e^{-\beta H(\Gamma)}}{\int d\Gamma \ \dot{x}\theta(\pm\dot{x})\theta(x)e^{-\beta H(\Gamma)}} \tag{5}$$

are normalized phase space distribution functions. To calculate $\hat{k}(t)$ one samples points in phase space from these distribution functions, and runs molecular dynamics trajectories for each of the sampled points.[2-4] Given the δ function and step functions

we see that in all sampled states the reaction coordinate starts at the barrier maximum; that is, at the transition state. In the $P^{(+)}(\Gamma)$ distribution the velocity $\dot{x}$ is positive and the system starts out moving toward well B whereas in $P^{(-)}(\Gamma)$, $\dot{x}$ is negative and the system moves toward well A. $\langle \theta(x(t)) \rangle_+$ and $\langle \theta(x(t)) \rangle_-$ are the fractions of sampled trajectories which are in well B at time t given that at time $t = 0$, $x = 0$ and the initial velocity is either $\dot{x} > 0$ or $\dot{x} < 0$, respectively.

Thus to simulate a reacting system[5-7] one can use Monte Carlo techniques to sample initial states from $P^{(\pm)}(\Gamma)$ and molecular dynamics to calculate $\hat{k}(t)$ using eq 4. This procedure requires following a large number of trajectories for a sufficiently long time to determine λ_{PLAT}. To determine $k = k_f + k_b$ from λ_{PLAT} a separate Monte Carlo simulation is required to determine

$$k_{TST} = \frac{1}{X_A X_B}\langle \dot{x}\delta(x)\theta(\dot{x}) \rangle = \frac{1}{2X_A X_B}\langle |\dot{x}| \rangle S(0) \tag{6}$$

where $S(0)$ is the probability distribution of finding the reaction coordinate at the transition state $x = 0$. Alternatively, one could follow the trajectories for a very long time and thereby determine the exponential decay of $\hat{k}(t)$ but this requires an enormous amount of computer time. Since all trajectories needed to determined λ_{PLAT} originate at the top of the barrier, this reactive flux method avoids the need for trajectories to be activated.

The reactive flux approach requires much less computer time than other methods. It has already been used to simulate reactions in the liquid state.[2-4] Nevertheless, for very small or very large friction, the trajectories recross the transition state many times before becoming trapped and even the reactive flux becomes very costly in CPU time.

Recently we proposed an approximate method in which the initial states are sampled according to $P^{(\pm)}(\Gamma)$ after which each trajectory is computed only until it is absorbed by an "*absorbing barrier*" at the transition state.[8] This method allows determination of λ_{PLAT} and requires much less CPU time than does the full reactive flux calculation outlined above when applied to very low and very high friction regimes (i.e., when there are large deviations from the transition-state rate constant). However, this method still requires an additional simulation to determine k_{TST} and thereby $k = k_f + k_b$.

In this paper we present a generalization of the absorbing barrier method for determining both λ_{PLAT} and the time dependence of the reactive flux, and use it to determine both $k_f + k_b$ and $(k_f + k_b)_{TST}$ in one simulation. It is very efficient and leads to considerable savings in CPU time over previously used methods. Its accuracy is demonstrated by applying it to a simulation of one-

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

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dimensional Langevin dynamics in a symmetric double well. The resulting rate constant as a function of the friction constant agrees with Kramers' theoretical predictions over a very wide density regime. We also compare the full time dependence of the reactive flux in a two-dimensional system with that determined by the absorbing barrier method. The agreement is very good and the method agrees with both the transition-state rate and the real rate constants.

Absorbing Barrier Method

For simplicity consider a symmetric double-well potential with wells A and B. Let $P(t - t')$ be the fraction of trajectories which at time t' are at the transition state (TS) ($x = 0$) moving toward well B ($\dot{x} > 0$) and by time t have not yet recrossed $x = 0$. The flux crossing $x = 0$ for the first time is then $j(t - t') = -\partial P(t - t')/\partial t$. If it is assumed that when recrossing the barrier the distribution of particles at the transition state is given by $P^{(\pm)}(\Gamma)$ then the population of particles that recross the TS at time t' which have not recrossed a second time by time t is just $P(t - t')$. If we assume that on *every* recrossing the distribution of particles at the TS is $P^{(\pm)}(\Gamma)$, then $\langle \theta(t) \rangle_+$ can be expressed in terms of $P(t)$ and $j(t)$ as

$$\langle \theta(t) \rangle_+ = P(t) + \int_0^t dt_2 \int_0^{t_2} dt_1\, P(t - t_2)j(t_2 - t_1)j(t_1) +$$
$$\int_0^t dt_4 \int_0^{t_4} dt_3 \int_0^{t_3} dt_2 \int_0^{t_2} dt_1\, P(t - t_4)j(t_4 - t_3) \times$$
$$j(t_3 - t_2)j(t_2 - t_1)j(t_1) + \dots \quad (7)$$

The first term on the right represents the fraction of trajectories still in B at time t. The second term represents the fraction of trajectories that have crossed once from B to A, then crossed back to B and got trapped. The quantity $j(t_1)\, dt_1$ is the fraction of trajectories crossing for the first time from B to A between t_1 and $t_1 + dt_1$, the quantity $j(t_2 - t_1)\, dt_2$ is the fraction of trajectories that having arrived in well A at time t_1 cross for the first time back into B between t_2 and $t_2 + dt_2$, and the quantity $P(t - t_2)$ is the fraction of trajectories that have never left B by time t given that they first entered B at time t_2. It follows that $\int_0^t dt_2 \int_0^{t_2} dt_1\, P(t - t_2)j(t_2 - t_1)j(t_1)$ is simply the fraction of trajectories that have undergone the sequence of transitions B $\rightarrow$ A $\rightarrow$ B in time t. The third term in eq 7 represents trajectories making the sequence of crossings B $\rightarrow$ A $\rightarrow$ B $\rightarrow$ A $\rightarrow$ B in the time t. In this way it is easy to write the term corresponding to the sequence B $\rightarrow$ (A $\rightarrow$ B)^n. Equation 7 represents the summation of all such terms for $n = 1$ to ∞. Laplace transformation of eq 7 gives

$$\langle \tilde{\theta}(s) \rangle_+ = \tilde{P}(s) \sum_{n=0}^{\infty} [\tilde{j}(s)^2]^n \quad (8)$$

where $\tilde{P}(s)$ and $\tilde{j}(s)$ are the Laplace transforms of $P(t)$ and $j(t)$, respectively. Since $j(t) = -\partial_t P(t)$, $\tilde{P}(s) = (1 - \tilde{j}(s))/s$ and summation gives

$$\langle \tilde{\theta}(s) \rangle_+ = \frac{1}{s} \frac{(1 - \tilde{j}(s))}{1 - \tilde{j}(s)^2} = \frac{1}{s} \frac{1}{1 + \tilde{j}(s)} \quad (9)$$

To calculate $\langle \theta(t) \rangle_-$ we must recognize that the trajectories start out moving toward well A. Thus we must consider the fractions of trajectories corresponding to (A $\rightarrow$ B)^n for $n = 1$ to ∞. This gives

$$\langle \tilde{\theta}(s) \rangle_- = \tilde{P}(s)\tilde{j}(s) \sum_{n=0}^{\infty} [\tilde{j}(s)^2]^n$$
$$= \frac{\tilde{j}(s)(1 - \tilde{j}(s))}{s(1 - \tilde{j}(s)^2)} = \frac{\tilde{j}(s)}{s(1 + \tilde{j}(s))} \quad (10)$$

From eq 4 it follows that the Laplace transform of the reactive flux is given by

$$\tilde{k}(s) = \langle \tilde{\theta}(s) \rangle_+ - \langle \tilde{\theta}(s) \rangle_- = \frac{1}{s} \frac{(1 - \tilde{j}(s))}{(1 + \tilde{j}(s))} \quad (11)$$

or

$$\tilde{k}(s) = \frac{\tilde{P}(s)}{2 - s\tilde{P}(s)} \quad (12)$$

The following model provides some insight. Assume that the fraction of particles entering the well at $t = 0$ which have not recrossed the transition state by time t is

$$P(t) = (1 - T_0)\theta(-t) + T_0 e^{-k_2 t} \quad (13)$$

where $(1 - T_0)$ is the fraction of trajectories which quickly leave well B and $T_0 e^{-kt}$ represents the trajectories which get trapped and subsequently leave with rate constant k_2 (or equivalent mean first passage time k_2^{-1}). The Laplace transform of $P(t)$ is

$$\tilde{P}(s) = \frac{1}{s}\left[T_0 - \frac{k_2 T_0}{s + k_2} \right] \quad (14)$$

Inserting eq 14 in eq 12 and Laplace inverting gives

$$\hat{k}(t) = \frac{T_0}{2 - T_0}\exp\{-[2k_2 t/(2 - T_0)]\} \quad (15)$$

The prefactor is the plateau value for the rate constant found in our previous analysis (cf. eq 2 and ref 8):

$$\lambda_{\text{PLAT}} = \frac{k_f + k_b}{k_{\text{TST}}} = \frac{T_0}{2 - T_0} \quad (16)$$

From eq 2 we recognize the argument of the exponential to be

$$k_f + k_b = 2k_2/(2 - T_0) \quad (17)$$

Combining eq 16 and 17 we find

$$k_{\text{TST}} = 2k_2/T_0 \quad (18)$$

where the transition-state rate constant is given simply in terms of the fraction of trajectories trapped quickly, T_0, and the rate for once trapped trajectories to pass out of the well to the transition state, k_2.

T_0 and k_2 can be found by taking a single well with an absorbing barrier at the transition state. The trajectories are sampled as in the calculation of $\hat{k}(t)$ (cf. eq 4); 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 of trapped trajectories will decay as $T_0 e^{-k_2 t}$ so that k_2 may be found from this long time exponential decay.

Equation 12 may easily be extended to the case of the asymmetric double-well potential. We find

$$\tilde{k}(s) = \frac{\tilde{P}_A(s)\tilde{P}_B(s)}{\tilde{P}_A(s) + \tilde{P}_B(s) - s\tilde{P}_A(s)\tilde{P}_B(s)} \quad (19)$$

where $\tilde{P}_A(s)$ and $\tilde{P}_B(s)$ are the Laplace-transformed well population values for particles not having recrossed the transition state from wells A and B, respectively. If we calculate the reactive flux for the asymmetric double-well potential using eq 19 along with

$$\tilde{P}_A(s) = \frac{1}{s}\left[T_A - \frac{k_A T_A}{s + k_A} \right] \quad (20a)$$

$$\tilde{P}_B(s) = \frac{1}{s}\left[T_B - \frac{k_B T_B}{s + k_B} \right] \quad (20b)$$

we find that

$$\hat{k}(t) = \frac{T_A T_B}{(T_A + T_B - T_A T_B)} \exp\left[-\frac{(T_A k_B + T_B k_A)}{(T_A + T_B - T_A T_B)}t \right] \quad (21)$$

Again, the prefactor agrees with the plateau value found in our previous analysis. If we combine eq 2,3, and 21 the transition-state theory rate constant is found to be

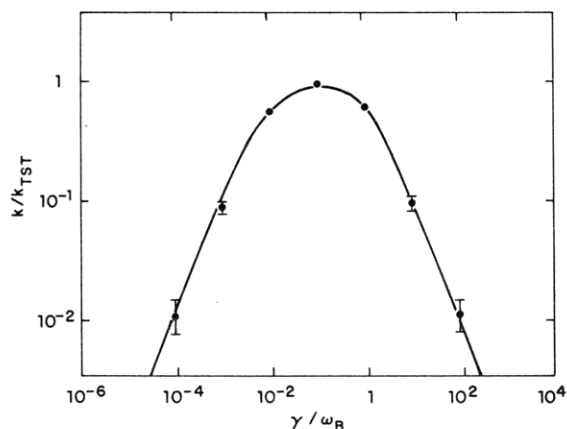$$k_{\text{TST}} = \frac{k_A}{T_A} + \frac{k_B}{T_B} \quad (22)$$

Figure 1. Barrier crossing rate constants vs. the friction constant, γ, for one-dimensional Langevin dynamics (eq 23). The prediction of the Kramers theory for the overall rate constant k/k_{TST} is compared with the simulation results by the absorbing barrier method (eq 16). Error bars give the 95% confidence interval.

Numerical Results

The reactive flux (cf. eq 1) has proved 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 much more time especially when the friction coefficient is very large or very small. The absorbing barrier method leads to a considerable saving of computer time in these simulations. We illustrate this by applying the method to a simple stochastic simulation of two model systems. We are currently applying this method to determine rate constants in liquids using full molecular dynamic simulations.

To test the accuracy of the absorbing barrier method in determining the transition-state normalized rate constant, λ_{PLAT}, we have simulated a one-dimensional system using Langevin dynamics. The potential is piecewise parabolic with barrier height $E^{\ddagger}$, reactive well frequency ω_0, and barrier frequency, ω_B. The Langevin equation for this system is

$$\ddot{x} = -\gamma\dot{x} - \frac{\partial V(x)}{\partial x} + f(t) \quad (23)$$

where $f(t)$ is a Gaussian random force with covariance $\langle f(0)f(t)\rangle = 2kT\gamma\theta(t - \tau_c)/\tau_c$ and τ_c is the correlation time of the force. This Langevin equation was integrated by using a fourth-order Adams–Moulton Preditor–Corrector algorithm for $E^{\ddagger}/kT = 10$, $\omega_0/\omega_B = 2$, and 1000 trajectories for varying γ and τ_c. τ_c was adjusted to ensure that the system dynamics were Markovian.

The results for several different γ are shown in Figure 1 along with the theoretical predictions from the theory of Kramers. We find excellent agreement between theory and simulation in both the low and high γ limits (Figure 1). This agreement lends support to the validty of the assumptions underlying this method.

We now consider a nontrivial dynamical system consisting of a particle of mass m and reaction coordinate x, moving in a quartic symmetric double-well potential with energy barrier $E^{\ddagger}$, and a nonreaction coordinate y moving stochastically with friction ζ, in a harmonic potential with frequency ω. The coupling between x and y is $\epsilon x y$. The potential, with units such that $E_{\ddagger}$, m, and the well minimum along the reaction coordinate equal 1, is therefore

$$V(x,y) = x^4 - \left(2 - \frac{\epsilon^2}{2\omega^2}\right)x^2 + \frac{\omega^2}{2}y^2 + \epsilon x y + 1 \quad (24)$$

The Langevin equations for the system are

$$\ddot{x} = -\frac{\partial V(x,y)}{\partial x}; \quad \ddot{y} = -\zeta\dot{y} - \frac{\partial V(x,y)}{\partial y} + f_y(t) \quad (25)$$

where $f_y(t)$ is a Gaussian random force with covariance $\langle f_y(0)f_y(t)\rangle = 2kT\zeta\theta(t - \tau_c)/\tau_c$, and τ_c is the correlation time of the force.
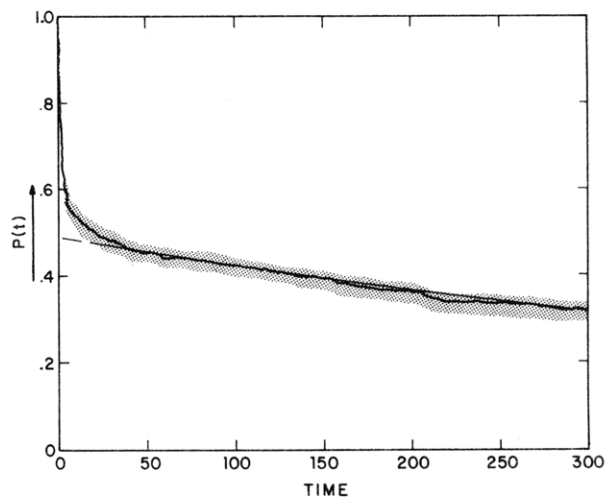

Figure 2. Normalized well population, $P(t)$, as a function of time shown with single-exponential (eq 13) fit (parameters given in Table I). Error bars are indicated by the shaded region shown to 1 standard deviation, for the calculated $P(t)$.

TABLE I: Comparison of Rate Constants from Different Methods

	T_0	$10^3\, k_2$	λ_{PLAT}	$10^3\, k_{TST}$
single exponential[a]	0.50	1.4	0.33	5.6
full reactive flux simulation[b]			0.35	
exact k_{TST} (6)[c]				5.77

[a] As given by eq 16. [b] As given by eq 3. [c] As given by eq 26.

These Langevin equations were integrated by using a fourth-order Adams–Moulton Predictor–Corrector algorithm for $E^{\ddagger}/kT = 5$, $\zeta = 2$, $\tau_c = 10^{-4}$, and $\epsilon = 1.2$.

A computer simulation of the single well with absorbing barrier gives the well population $P(t)$ which allows the calculation of the trapping coefficients and the decay rate constants. Figure 2 compares the simulated $P(t)$ for 500 trajectories to the single-exponential model of eq 15. Table I lists the parameter values used. We compare the full reactive flux calculation for the double well to the results predicted on the basis of eq 12 and 14 for the single-exponential model. The agreement in plateau value is within the experimental error of the calculation.

The transition-state rate constant was calculated both analytically by using

$$k_{TST} = \frac{1}{QX_A X_B}\int d\Gamma\, \rho_{eq}(\Gamma)\dot{x}\theta(\dot{x})\delta(x) \quad (26)$$

where Q is the canonical partition function, $Q = \int d\Gamma\, \exp(-\beta H(\Gamma))$, and X_A and X_B are the equilibrium mole fractions for wells A and B, respectively, and by the method outlined above employing eq 18 for the single-exponential flux model. The results of this calculation are displayed in Table I along with the flux parameters. The simulation result for k_{TST} agrees within the experimental error of the calculations.

As a further test of how well the absorbing barrier method reproduces the full reactive flux we have substituted the numerical Laplace transform of the well population $P(t)$ into eq 12. This gives an approximation to $\tilde{k}(s)$. Inverse Laplace transformation of $\tilde{k}(s)$ gives $\hat{k}(t)$. In Figure 3 the resulting approximate time-dependent flux is plotted against the full reactive flux determined by simulation. The agreement is very good. The absorbing barrier method even shows the wiggle in the transient decay regime.

The tests indicate that the absorbing barrier method is accurate and useful for determining reaction rates and fluxes.

Discussion

We have shown how the rate constants $k_f + k_b$ and k_{TST} and even the time dependence of the decay of $\hat{k}(t)$ may be found by using the parameters for trapping and escape from a single well with an absorbing barrier at the transition state. The main as-
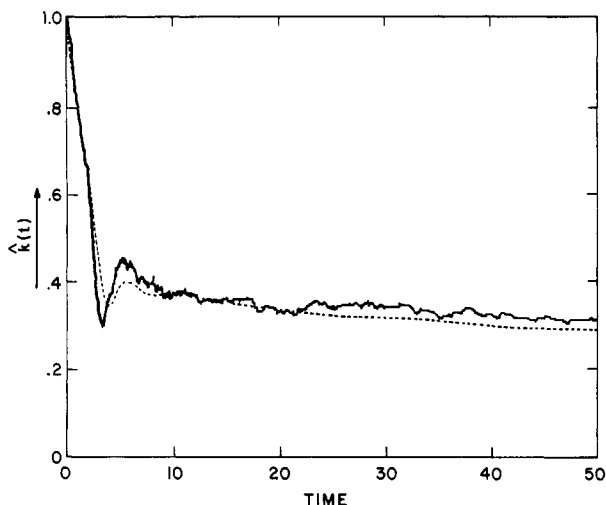
Figure 3. Normalized reactive flux, $\hat{k}(t)$, as a function of time (- - -) inverse Laplace transform of eq 12 (···) by using the simulation results for the well population $P(t)$ (Figure 2).

sumption in our model is that the distribution of particles on recrossing the TS is given by the distribution $P^{(\pm)}(\Gamma)$. This assumption is mathematically expressed by the simple product of fluxes in eq 7. It is useful to test this assumption before applying the absorbing boundary method. We thus analyze the trajectories corresponding to eq 23 as they are absorbed for the first time. In Figure 4 are displayed velocity distributions for particles recrossing the TS as they are being absorbed. In the high-friction regime, $\gamma = 10$, the velocity distribution agrees with $P^{(\pm)}(\Gamma)$ implying that the absorbing barrier method should be an excellent approximation for this case. In the low-friction regime, $\gamma = 0.01$, however, the agreement is less satisfactory. This can be understood as follows. At low γ the momentum relaxation time will be long compared to the time spent in the well for those particles recrossing quickly. If the trapping probability decreases with initial energy, the low energy trajectories will be trapped more frequently than others. Since the relaxation time is long, the particles recrossing will not relax quickly enough to conform to $P^{(\pm)}(\Gamma)$ and so we find deviations. Although these deviations give some indication of the accuracy of the absorbing barrier method, even for low friction, $\gamma = 0.01$, the method appears to give λ_{PLAT} values in agreement with the Kramers result.

It is useful to make an estimate of the time saved in the absorbing barrier method. Let $\tau(\text{rf})$ and $\tau(\text{ab})$ denote the integration time required to determine λ_{PLAT} and $k_f + k_b$ by using the reactive flux (rf) method and the absorbing barrier (ab) method, respectively. To determine $\tau(\text{rf})$, N trajectories are followed for a time τ_λ necessary to determine $\lambda_{PLAT}e^{-(k_f+k_b)t}$. Then $\tau(\text{rf}) = N\tau_\lambda$. To determine $\tau(\text{ab})$ each of the N trajectories is followed until absorbed. Since $P(t) \simeq T_0e^{-kt}$ is the probability that a trajectory has not yet left well B in time t the average time that a trajectory is followed is

$$\langle \tau \rangle = \int_0^{\tau_\lambda} dt\ e^{-k_2 t} = \frac{1}{k_2}(1 - e^{-k_2\tau_\lambda}) \qquad (27)$$

Since $N(1 - T_0)$ trajectories are rapidly absorbed and NT_0 trajectories are followed on the average for time $\langle \tau \rangle$, it follows that
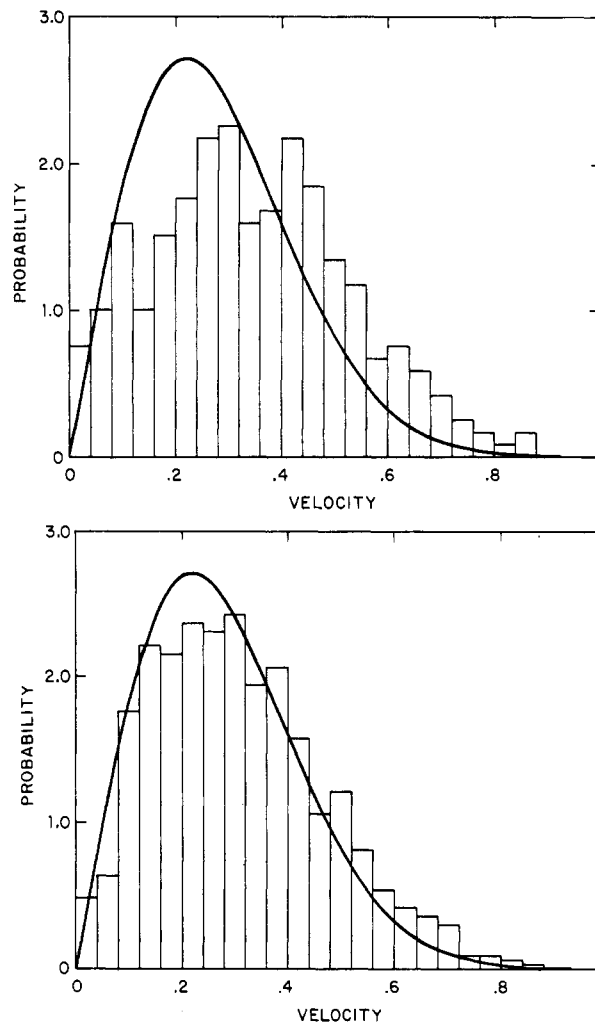

Figure 4. Velocity distributions for particles recrossing the TS as they are being absorbed. The continuous line shows the exact velocity distribution given by $P^{(\pm)}(\Gamma)$ (eq 5). The histogram displays normalized velocity distributions of those trajectories which recross quickly, numbering 1000 $(1 - T_0)$, for (a, top) $\gamma = 0.01$, $T_0 = 0.706$ (b, bottom) $\gamma = 10$, $T_0 = 0.176$.

$\tau(\text{ab}) = NT_0\langle \tau \rangle$ so that $\tau(\text{ab})/\tau(\text{rf}) = T_0(1 - e^{-k_2\tau_\lambda})/k_2\tau_\lambda$. Since $T_0 \ll 1$ in either the very high or very low friction regimes, it follows that then $\tau(\text{ab})/\tau(\text{rf}) \ll 1$ and the absorbing barrier method is greatly to be preferred over the reactive flux method. For $k_2\tau_\lambda > 1$ there is a further reduction in the time required for this method. It always pays to use this method. For the values of the parameters corresponding to Figure 3 we find that $\tau(\text{ab})/\tau(\text{rf}) = 0.50\ (1 - e^{-k_2\tau_\lambda})/k_2\tau_\lambda = 0.40$. In the comparison with Kramers' theory the points in the very low ($\gamma = 10^{-4}$) and very high ($\gamma = 10^{-2}$) friction limits correspond to values of $\tau(\text{ab})/\tau(\text{rf})$ equal to 0.021 and 0.0225, respectively. In such cases a full determination of the reactive flux takes prohibitively long times.