Dynamics of reactions involving diffusive barrier crossing

Klaus Schulten[a] and Zan Schulten[a]

Max-Planck-Institut für Biophysikalische Chemie, Am Fassberg, D-3400 Göttingen, Federal Republic of Germany

Attila Szabo[b]

Department of Chemistry, Indiana University, Bloomington, Indiana 47405

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We develop a first passage time description for the kinetics of reactions involving diffusive barrier crossing in a bistable (and also in a more general) potential, a situation realized, for example, in some photoisomerization processes. In case the reactant is in thermal equilibrium, the first passage times account well for the reaction dynamics as shown by comparison with exact numerical calculations. A simple integral expression for the rate constants is presented. For a case involving a reactant initially far off equilibrium, a two relaxation time description for the particle number $N(t)$ is derived and compared with the results of an "exact" calculation. This description results from a knowledge of $N(t=0)$, $\dot{N}(t=0)$, $\int_0^\infty dt\, N(t)$, i.e., the first passage time, and $\int_0^\infty dt\, t\, N(t)$.

I. INTRODUCTION

Recently, the problem of reactions involving diffusive barrier crossing between two stable states A and B (see Fig. 1), e.g., *cis–trans* isomerization, has attracted renewed attention. As discussed in the classic paper by Kramers,[1] when the system is strongly coupled to the surroundings, the motion along the reaction path is diffusive in nature.

Systems crossing the reaction barrier by diffusion have no memory of their velocity and therefore are likely to repeatedly reverse their motion near the barrier top. Examples where such a diffusion description is valid include reactions involving the motion of large molecular units, broad barriers, and dense viscous solvents,[2] e.g., many photoisomerization processes. Many activated isomerization processes and related biochemical processes in proteins and lipids are also expected to show diffusive behavior.[3]

Several recent studies have considered the dynamics of barrier crossing using the Fokker–Planck[4] and other[5] models to couple the system to the environment. In this article, however, we will consider only reactions for which a diffusion description applies (i.e., we use the Smoluchowski model). We also restrict this treatment to reactions along a one-dimensional reaction coordinate x. The time evolution of the diffusion distribution accounting for all reaction paths along x is described by the Smoluchowski equation (SE)

$$\frac{\partial}{\partial t} p(x,t\,|\,x_0) = \mathbf{L}(x) p(x,t\,|\,x_0)\ , \tag{1.1}$$

where $\mathbf{L}(x)$ represents the forward diffusion operator

$$\mathbf{L}(x) = \frac{\partial}{\partial x} D(x) \left(\frac{\partial}{\partial x} + \beta \frac{\partial U}{\partial x} \right)\ , \tag{1.2}$$

and where $\beta^{-1} = k_B T$. $U(x)$ is the potential governing the reaction (see Fig. 1) and $D(x)$ is a configuration-dependent diffusion coefficient. The solution of Eq. (1.1) is also subject to the initial condition

$$p(x, t=0\,|\,x_0) = \delta(x - x_0)\ , \tag{1.3}$$

i.e., it is assumed that the system is initially in the configuration described by $x = x_0$.

On the basis of the SE, Kramers[1] derived the well-known expression for the effective first-order rate constant for a system to cross from A to B (see Fig. 1):

$$k_f(\text{Kramers}) = (\omega_A \omega_C\, \mu D / 2\pi k T) \exp[-\beta(U_C - U_A)]\ , \tag{1.4}$$

where $U(x)$ has been approximated locally around x_A and x_C by a quadratic potential

$$U(x) \approx U_Z \pm \tfrac{1}{2}\mu\omega_Z^2 (x - x_Z)^2, \quad Z = \text{A, C}\ , \tag{1.5}$$

and the motion along the reaction coordinate is assumed to involve the mass μ. Kramers's result, however, holds only in the limit of large barriers. Several recent studies have addressed the interesting problem of generalizing the Kramers's formula to arbitrary barriers or else of deriving it from exact solutions of the SE. Edholm and Leimar,[6] by means of an eigenfunction expansion of a particular bistable potential, developed an

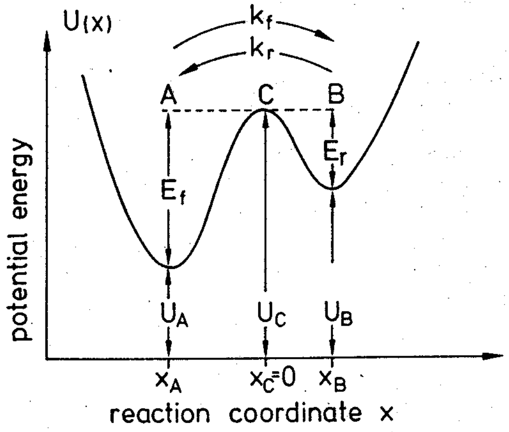

FIG. 1. Schematic representation of a bistable potential governing diffusive barrier crossing.

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[a] New address: Department of Physics, Technical University of Munich, 8046 Garching, Federal Republic of Germany.

[b] Alfred P. Sloan Fellow.

estimate of the accuracy of Kramers's expression and some generalization of it. Eigenfunction expansions had also been employed by van Kampen[7] and by Larson and Kostin[8] to derive Kramers's formula from exact solutions. In an interesting paper, Northrup and Hynes[2] have developed an analytic theory for diffusive barrier crossing valid for the situation when the barrier is comparable to kT. They construct a rather elaborate framework based on dividing the potential into three regions: reactant, barrier, and product. They then express the full reaction rate constants in terms of a barrier rate constant and internal rate constants which describe the relaxation to equilibrium near the reactant and product configurations. Finally, they show that if the partitions are chosen so as to minimize the calculated relaxation rate, the resulting rate is in excellent agreement with that calculated by direct numerical integration of the time-dependent SE even for low barriers where the classical result of Kramers errs significantly. A purpose of this paper is to point out that the NH theory is unnecessarily sophisticated. We divide the potential into reactant and product regions at the top of the barrier and, using the theory of first passage times, we derive a single integral expression for the rate constant. In the case of high barriers, we recover Kramers's formula (1.4) while in the case of low barriers, this expression gives results that are virtually identical to the "exact" results obtained by NH by numerical integration of the time-dependent SE. In addition, we make contact with a generalization of Kramers's result given by Edholm and Leimar.[6]

In Sec. II of this paper, we will derive the first passage time expression for reaction rate constants for diffusive barrier crossing. In Sec. III, we compare for symmetric wells the resulting predictions with the exact results of NH. In Sec. IV, we generalize the description to nonsymmetric wells and in Sec. V to multiwell situations.

Most descriptions of the reaction A → B assume first-order kinetics,[8,11] i.e., use a single relaxation (reaction) time. However, approximations can also be formulated which involve several relaxation times in a description of the reaction dynamics. In Sec. VI, we will generalize the theory to allow for two relaxation times to describe a reaction step A → B within the diffusive description of the dynamics.

II. FIRST PASSAGE TIME THEORY APPLIED TO DIFFUSIVE BARRIER CROSSING

We consider a system of two stable states A and B separated by a barrier as shown in Fig. 1. As the system is conservative (no particles added or deleted), the SE for the conditional probability $p(x,t|x_0)$ for the system to start its motion at $x=x_0$ and to be found at x at time t has to be complemented by the boundary conditions

$$\lim_{x\to\pm\infty} D(x)\left[\frac{\partial}{\partial x}+\beta\left(\frac{\partial U}{\partial x}\right)\right] p(x,t|x_0)=0 \, . \tag{2.1}$$

However, in order to determine the reaction time, we like to set up a situation that a particle starting out at x_0 is being "collected" as soon as it reaches a certain domain $x \geq x_1 > x_0$. As any particle reaching x_1 is taken out of the system, this situation is obviously described by the new boundary condition

$$p(x_1,t|x_0)=0 \, . \tag{2.2}$$

There is, of course, a certain distribution of times for arrival at x_1. For many applications it is sufficient, however, to describe the diffusive motion by the average time of arrival $\tau_1(x_0,x_1)$, the so-called first passage time (FPT). This approximate description corresponds to casting the reaction process into first-order kinetics[9,11] and will be generalized in Sec. VI. The FPT is

$$\tau_1(x_0,x_1)=\int_0^\infty dt \int_{-\infty}^{x_1} dx\, p(x,t|x_0) \, . \tag{2.3}$$

In Ref. 9 it was shown that $\tau_1(x_0,x_1)$ obeys the equations

$$-1=\mathbf{L}^+(x_0)\,\tau_1(x_0,x_1) \, , \tag{2.4}$$

$$\lim_{x_0\to-\infty} \frac{\partial}{\partial x_0}\tau_1(x_0,x_1)=0 \, , \tag{2.5}$$

$$\tau_1(x_1,x_1)=0 \, , \tag{2.6}$$

where $\mathbf{L}^+(x_0)$ represents the backward diffusion operator

$$\mathbf{L}^+(x_0)=\exp[\beta(x_0)]\frac{\partial}{\partial x_0} D(x_0)\exp[-\beta U(x_0)]\frac{\partial}{\partial x_0} \, . \tag{2.7}$$

Equations (2.4)–(2.7) can be readily solved to yield[9,12]

$$\tau_1(x_0,x_1)=\int_{x_0}^{x_1} dx[D(x)p_{\mathrm{eq}}(x)]^{-1}\int_{-\infty}^{x} dy\, p_{\mathrm{eq}}(y) \, , \tag{2.8}$$

where

$$p_{\mathrm{eq}}(x)=Z^{-1}\exp[-\beta U(x)] \, , \tag{2.9}$$

$$Z=\int_{-\infty}^{x_1} dx\exp[-\beta U(x)] \, , \tag{2.10}$$

Z representing a partition function. The FPT's obey the addition theorem $(x_0\leq x_1\leq x_2)$

$$\tau_1(x_0,x_2)=\tau_1(x_0,x_1)+\tau_1(x_1,x_2) \, . \tag{2.11}$$

If the particle starts initially in a distribution $d(x)$ assumed to be normalized, i.e.,

$$\int_{-\infty}^{x_1} dx\, d(x)=1 \, , \tag{2.12}$$

the FPT is

$$\tau_1[d(x),x_1]=\int_{-\infty}^{x_1} dx_0\, d(x_0)\tau_1(x_0,x_1) \, . \tag{2.13}$$

III. APPLICATION TO BARRIER CROSSING IN A SYMMETRIC DOUBLE WELL

In order to describe the barrier crossing reaction A → B corresponding to the potential situation in Fig. 1, we define the system to be in state A (B) as long as $x<0$ $(x>0)$. The corresponding concentrations for a system starting at $x=x_0$ are

$$N_{\mathrm{A}}(t|x_0)=\int_{-\infty}^{0} dx\, p(x,t|x_0) \, , \tag{3.1}$$

$$N_{\mathrm{B}}(t|x_0)=\int_{0}^{\infty} dx\, p(x,t|x_0) \, . \tag{3.2}$$

As argued by NH the relaxation to equilibrium can be approximated by first-order kinetics (however, see Sec. VI)

$$\dot{N}_A(t|x_0) = -k_f(x_0)N_A(t|x_0) + k_r(x_0)N_B(t|x_0) \ , \qquad (3.3)$$

$$\dot{N}_B(t|x_0) = -k_r(x_0)N_B(t|x_0) + k_f(x_0)N_A(t|x_0) \ , \qquad (3.4)$$

which is to say that the rate constants $k_f(x_0)$ and $k_r(x_0)$ can be determined as first passage times. In this section we will only consider the situation of symmetric wells for which $k_f(x_0) = k_r(x_0)$.

Obviously, $N_A + N_B = \text{const}$. The relaxation of the system initially prepared in the configuration x_0 is then completely accounted for by the exponential decay of the quantity

$$\Delta(t|x_0) = N_A(t|x_0) - N_B(t|x_0) \ , \qquad (3.5)$$

which according to Eqs. (3.3) and (3.4) is

$$\Delta(t|x_0) = \exp[-2k_f(x_0)t] \ . \qquad (3.6)$$

Because of symmetry $N_A(t|x_0) = N_B(t|-x_0)$ and therefore $\Delta(t|0) = 0$. This requires the condition

$$[2k_f(x_0 = 0)]^{-1} = 0 \ . \qquad (3.7)$$

Hence, $[2k_f(x_0)]^{-1}$ represents the first passage time for the system to start at x_0 and to reach the point $x = 0$ on the barrier top, i.e.,

$$[2k_f(x_0)]^{-1} = \tau_1(x_0, 0) \ . \qquad (3.8)$$

NH assumed that the system is initially in thermal equilibrium in well A described by the equilibrium distribution

$$p_{eq}^A(x) = Z_A^{-1} \exp[-\beta U(x)], \quad x \leqq 0 \ , \qquad (3.9)$$

$$Z_A = \int_{-\infty}^{0} dx \exp[-\beta U(x)] \ . \qquad (3.10)$$

The corresponding relaxation time k_{ch}^{-1} is

$$k_{ch}^{-1} = \tau_1[p_{eq}^A(x_0), 0] \ . \qquad (3.11)$$

According to Ref. 9,

$$k_{ch}^{-1} = \int_{-\infty}^{0} dx [D(x) p_{eq}^A(x)]^{-1} \left[\int_{-\infty}^{x} dy\, p_{eq}^A(y) \right]^2 \ . \qquad (3.12)$$

Equation (3.11) can be also derived using a simple physical argument. Once the system has reached the top of the barrier, the probability of going over is 1/2. Since the average time to reach the barrier starting from an equilibrium distribution is $\tau_1[p_{eq}^A(x_0), 0]$, k_f is well approximated by $\{2\tau_1[p_{eq}^A(x_0), 0]\}^{-1}$. Since $k_{ch} = k_f + k_r$ and $k_r = k_f$ for a symmetric well, Eq. (3.11) follows immediately. Conceptually, this result is clearly stated by NH [in their notation our k_{ch} is $k_{ch}(\delta = 0)$]. However, using an entirely different mathematical analysis, the expression they in fact derive for the relaxation rate, when cast into our notation, is

$$k_{ch}^{-1}(\delta = 0) = \tau_1(-\infty, 0) \ . \qquad (3.13)$$

From the addition theorem (2.11) it is clear that

$$\tau_1(-\infty, 0) > \tau_1[p_{eq}^A(x_0), 0] \qquad (3.14)$$

and hence it is not surprising that their $k_{ch}(\delta = 0)$ is a poor approximation (except for high barriers) to the exact relaxation rate constant obtained by numerically integrating the time-dependent SE starting with an equilibrium distribution in well A. Thus, it would appear that as a result of their misevaluation of $k_{ch}(\delta = 0)$, they had to introduce a high energy (barrier) region, and devise a criterion (i.e., their minimum principle) for selecting the optimum partitioning of the potential, in order to reproduce their exact results. As we shall show below, all this is unnecessary and Eqs. (3.11) and (3.12) predict results in excellent agreement with the exact ones.

For a quantitative evaluation of the rate constants derived, we follow NH and consider the symmetric potential

$$\beta U(x) = U_0[z^2 + 3\exp(-2z^2)] \ , \qquad (3.15)$$

where $z = x/\sigma$. We also assume a *constant diffusion coefficient*. The barrier height is (see Fig. 1)

$$\beta E_f = \beta E_r = \beta U(0) - \beta U(x_A) \ , \qquad (3.16)$$

where x_A is the position of the minimum of well A. For the potential (3.15), NH obtained "experimental" results for k_{ch} by numerical integration of the corresponding SE (1.1) assuming initial equilibration in well A. Unfortunately, NH characterized their potential by the βE_f value rather than by U_0. We had to determine, therefore, U_0 as the solution of a transcendental equation attributed with a certain numerical error. The authors also did not specify exactly in which space interval they integrated the SE and evaluated the integral expressions for their approximate rate constants. This missing information hampers somewhat a comparison of our predictions with the results of NH.

In Table I we compare the predictions of our Eq. (3.12) and the results of NH for diffusive crossing over reaction barriers of different height. The simple first passage time prediction by Eq. (3.12) compares well with the exact rate constants and the more elaborate approximation $k_{ch}(\delta_{min})$ (see Ref. 2 for the definition of this expression) of NH. The relationship (3.14) is also demonstrated. For large barriers, e.g., $\beta E_f = 10$, all rate constants show a close comparison. This is also the regime where Kramers's formula (1.4) holds. As a further illustration of the passage time concept, we present without further comment in Table II various FPT's corresponding to a barrier $\beta E_f = 5.0$.

In order to show the convergence of Eq. (3.12) towards Kramers's formula in the limit of high barriers, we note that in this limit

$$h(x) = \int_{-\infty}^{x} dy\, p_{eq}^A(y) \qquad (3.17)$$

becomes independent of x and equal to unity in the region near the barrier where $[p_{eq}^A(x)]^{-1}$ becomes large. Therefore,

$$k_{ch}^{-1} \approx D^{-1} \int_{-\infty}^{0} dx [p_{eq}^A(x)]^{-1}. \qquad (3.18)$$

The expansions (1.5) yield immediately $[2k_f\,(\text{Kramers})]^{-1}$ as given by Eq. (1.4). One can readily see that also $k_{ch}(\delta = 0)$ as given by Eq. (3.13) converges towards the

TABLE I. Comparison of rate constants (in units of $D\sigma^{-2}$).[a]

Barrier height βE_f[a]	1.6	3.0	5.0	10.0
$k_{\mathrm{ch}}^{\mathrm{ob}}$ (NH)[b]	0.469 ± 0.004	0.211 ± 0.003	$(0.505 \pm 0.002) \times 10^{-1}$	0.707×10^{-3}[g]
k_{ch} (this work)[c]	0.471	0.215	0.506×10^{-1}	0.723×10^{-3}
$k_{\mathrm{ch}}(\delta_{\min})$[d]	0.465	0.215	0.506×10^{-1}	0.707×10^{-3}
$2k_f$ (Kramers)[e]	0.545	0.252	0.570×10^{-1}	0.768×10^{-3}
$k_{\mathrm{ch}}(\delta = 0)$[f]	0.31	0.19	0.497×10^{-1}	0.723×10^{-3}

[a] For the symmetric potential of Eq. (3.15), the four barrier heights chosen in our calculation correspond to U_0 values of 0.99743, 1.8702, 3.1170, and 6.2339, respectively. The range of integration in Eqs. (3.12), (3.13), and (2.8) were chosen to achieve convergence to within three significant figures.

[b] Calculated by NH by numerical integration of the SE (1.1).

[c] Calculated according to Eq. (3.12).

[d] Calculated by NH, for the definition consult Ref. 2.

[e] Calculated by NH according to Eq. (1.4).

[f] Calculated according to Eqs. (3.13) and (2.8); the corresponding values of NH show small discrepancies which are probably due to slightly different choices of U_0 in Eq. (3.15).

[g] This value was estimated to be identical to $k_{\mathrm{ch}}(\delta_{\min})$ and $k_{\mathrm{ch}}(\delta = 0)$ as calculated by NH.

Kramers's formula in the case of a steep potential and a high barrier.

It may be noted finally that the generalization of Kramers's formula presented by Edholm and Leimar[6] corresponds to our $\tau_1(x_{\mathrm{A}}, x_{\mathrm{B}})$ if one replaces in Eq. (2.8) the integration limit x by $x = 0$.

IV. BARRIER CROSSING IN ASYMMETRIC DOUBLE WELL POTENTIALS

We will now generalize our treatment to the case of an asymmetric double well potential. We denote by C the state at the top of the barrier (see Fig. 1) and consider the barrier crossing as a two step reaction

$$\mathrm{A} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{C} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathrm{B}\,. \tag{4.1}$$

Following NH, we assume a steady state concentration for C, eliminate C, and describe the reaction by means of the first-order kinetic equations (3.3) and (3.4) with rate constants

$$k_f^{-1} = k_1^{-1} + k_{-2}^{-1} Z_{\mathrm{A}}/Z_{\mathrm{B}}\,, \tag{4.2}$$

$$k_r^{-1} = k_{-2}^{-1} + k_1^{-1} Z_{\mathrm{B}}/Z_{\mathrm{A}}\,, \tag{4.3}$$

where Z_{A} is defined by Eq. (3.10):

$$Z_{\mathrm{B}} = \int_0^{\infty} dx \exp[-\beta U(x)]\,, \tag{4.4}$$

and where we used $Z_{\mathrm{B}}/Z_{\mathrm{A}} = k_f/k_r$.

Equations (4.2) and (4.3) express the forward and backward rate constants k_f and k_r, respectively, in terms of the first passage times k_1^{-1} and k_{-2}^{-1} to reach the barrier top starting from the equilibrium distribution in well A and well B, respectively.

Obviously,

$$k_1^{-1} = k_{\mathrm{ch}}^{-1} \text{ [as given by Eq. (3.12)]}\,, \tag{4.5}$$

$$k_{-2}^{-1} = \int_0^{\infty} dx [D(x) p_{\mathrm{eq}}^{\mathrm{B}}(x)]^{-1} \left[\int_x^{\infty} dy\, p_{\mathrm{eq}}^{\mathrm{B}}(y)\right]^2\,, \tag{4.6}$$

where

$$p_{\mathrm{eq}}^{\mathrm{B}}(x) = Z_{\mathrm{B}}^{-1} \exp[-\beta U(x)]\,, \quad x \geqq 0\,. \tag{4.7}$$

From Eqs. (3.3) and (3.4) one can derive the relaxation behavior for a system initially in state A as

$$N_{\mathrm{A}}(t) = [Z_{\mathrm{A}}/(Z_{\mathrm{A}} + Z_{\mathrm{B}})] + [1 - Z_{\mathrm{A}}/(Z_{\mathrm{A}} + Z_{\mathrm{B}})] \exp[-(k_f + k_r)t]\,, \tag{4.8}$$

i.e., the relaxation time is $(k_f + k_r)^{-1}$. By virtue of Eqs. (4.2) and (4.3),

$$(k_f + k_r)^{-1} = (k_{-2}^{-1} Z_{\mathrm{A}} + k_1^{-1} Z_{\mathrm{B}})/(Z_{\mathrm{A}} + Z_{\mathrm{B}})\,. \tag{4.9}$$

To illustrate the accuracy of this description, we compare again with results by NH who considered the potential ($z = x/\sigma$)

$$\beta U(z) = 1.3716\{(z + 0.34848)^2 + 3 \exp[-2(z + 0.05848)^2]\}\,. \tag{4.10}$$

For this potential NH obtained the exact rate constant $k_{\mathrm{ch}}^{\mathrm{ob}} = (0.438 \pm 0.002) D\sigma^{-2}$ and the approximate rate constant $0.440 D\sigma^{-2}$. On the basis of Eqs. (4.9), (4.6), and (4.5) we obtain the value $0.435 D\sigma^{-2}$. Noting that the potential (4.10) exhibits rather low reaction barriers, i.e., $\beta E_f = 3.0$ and $\beta E_r = 1.5$, the good agreement of our simple expressions for k_1^{-1} and k_{-2}^{-1} is very satisfying.

TABLE II. First passage times for the symmetric well [Eq. (3.15)] with $\beta E_f = 5.0$.

$\tau_1(-\infty, x_{\mathrm{A}})$	0.221
$\tau_1(-\infty, 0)$	20.097
$\tau_1[p_{\mathrm{eq}}(x_0), 0]$	19.782
$\tau_1[x_{\mathrm{A}}, 0]$	19.876
$\tau_1[x_{\mathrm{A}}, x_{\mathrm{B}}]$	40.014
$\tau_1[0, x_{\mathrm{B}}]$	20.138

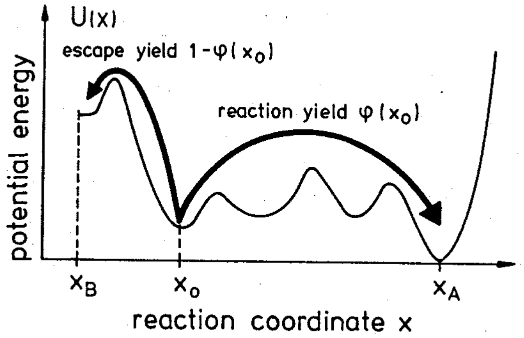

FIG. 2. Reaction in a multiple well potential: The system starts at the configuration x_0 to either reach the well at x_A or to escape to x_B.

V. MULTIPLE BARRIER CROSSING REACTIONS

The expression for the passage time derived in Sec. II can also be applied to potentials which have multiple minima and maxima along the reaction coordinate. A typical situation which is of particular relevance to biochemical processes is illustrated in Fig. 2. A particle is initially at $x=x_0$ and one wants to describe its binding at the potential minimum at $x=x_A$ assumed to lie considerably below the potential at $x=x_0$, i.e., $U(x_0) - U(x_A) \gg kT$. Typically, the particle may also have a chance to escape the binding at x_A by passing over a barrier to some external space at x_B. The situation described is, for example, reminiscent of the binding of O_2 at the heme group of hemoglobin after its diffusive penetration through the protein. (However, see also the description in the next section for this case.) If the possibility of escape is excluded, the description given here may account for internal motions of protein side groups, e.g., group rotation, or photochemical isomerization processes.

In this section we would like to cast the reaction process corresponding to Fig. 2 again in a first-order kinetic description. In this approximation, the fraction of particles bound at x_A is described by

$$\tilde{C}_A(t) = \phi(x_0)\{1-\exp[-t/\tau_1(x_0)]\} , \tag{5.1}$$

where $\phi(x_0)$ represents the reaction yield and $\tau_1(x_0)$ the FPT for the situation that the particle starts out at $x=x_0$. $\tau_1(x_0)$ obeys again the inhomogeneous equation (2.4); however, the boundary conditions are now

$$\tau_1(x_0=x_A)=0 , \tag{5.2}$$

$$\tau_1(x_0=x_B)=0 . \tag{5.3}$$

It is for this change of boundary condition that we have altered the notation of the FPT. The solution of Eq. (2.4) subject to these boundary conditions is $\{p_{eq}(x) = \exp[-\beta U(x)]\}$

$$\begin{aligned}\tau_1(x_0) = &\int_{x_0}^{x_A} dx[D(x)p_{eq}(x)]^{-1}\int_{x_B}^{x} dy\, p_{eq}(x) \\ &- \int_{x_B}^{x_A} dx[D(x)p_{eq}(x)]^{-1}\int_{x_B}^{x} dy\, p_{eq}(y) \\ &\times \int_{x_0}^{x_A} dx[D(x)p_{eq}(x)]^{-1} \Big/ \int_{x_B}^{x_A} dx[D(x)p_{eq}(x)]^{-1} .\end{aligned} \tag{5.4}$$

The reaction yield has been shown by Tachiya[13] to obey the equation

$$\frac{\partial}{\partial x} D(x)p_{eq}(x)\frac{\partial}{\partial x}\phi(x) = 0 \tag{5.5}$$

subject to the boundary conditions

$$\phi(x_B) = 0 , \tag{5.6}$$

$$\phi(x_A) = 1 . \tag{5.7}$$

These equations are solved by

$$\phi(x_0) = \int_{x_B}^{x_0} dx[D(x)p_{eq}(x)]^{-1} \Big/ \int_{x_B}^{x_A} dx[D(x)p_{eq}(x)]^{-1} . \tag{5.8}$$

By virtue of Eq. (5.8) we obtain

$$\begin{aligned}\tau_1(x_0) = \phi(x_0) &\int_{x_B}^{x_A} dx[D(x)p_{eq}(x)]^{-1}\int_{x_B}^{x} dy\, p_{eq}(y) \\ &- \int_{x_B}^{x_0} dx[D(x)p_{eq}(x)]^{-1}\int_{x_B}^{x} dy\, p_{eq}(y) .\end{aligned} \tag{5.9}$$

The expressions (5.8) and (5.9) serve to determine the time evolution of the binding reaction. In the case of steep potentials, the approximation of locally quadratic potential minima and maxima can be applied as in the derivation of Kramers's formula in Sec. III.

If the system starts in an initial distribution $d(x_0)$, the expressions for $\phi(x_0)$ and $\tau_1(x_0)$ have to be averaged according to Eq. (2.13). In fact, one would expect the FPT description presented here to hold the better the closer the system initially approaches the Boltzmann distribution. However, the FPT theory can also be generalized to account for systems which are initially far off equilibrium as shown in the following section.

VI. DESCRIPTION INVOLVING TWO RELAXATION TIMES

The FPT approximation corresponds to the assumption of first-order kinetics. This assumption is justified in case the reaction starts in a near equilibrium configuration, and if the equilibrium is approximately maintained during the reaction. A deviation of this situation occurs if the reaction starts from a single configuration $x=x_0$ rather than the equilibrium distribution. The reaction rate derived from Eq. (5.1), i.e.,

$$\tau_1(x_0)^{-1}\phi(x_0)\exp[-t/\tau_1(x_0)] ,$$

has its maximum at $t=0$. However, in the situation assumed, the reaction rate $\dot{C}_A(t)$ should vanish initially, reach some maximum value at later times, and decay again to zero. To describe such behavior, one needs at least two relaxation times, one for the rise and one for the decay of $\dot{C}_A(t)$. The FPT approximation presented above allows only a *single relaxation time* to describe $\dot{C}_A(t)$. In this section we will generalize this treatment to a description which involves *two relaxation times*. A more general description involving *further relaxation times* will be the subject of a future publication.

We will assume in the following that there exists no route of escape as in Sec. V, i.e., $\phi(x_0)=1$. In order that $\dot{C}_A(t)$ exhibits the proper behavior, namely,

(1) the total number of particles reacted is unity, $$\quad (6.1)$$

(2) $\dot{C}_A(t)=0$ at $t=0$, $$\quad (6.2)$$

the concentration $C_A(t)$ in a two-relaxation-time description must assume the functional form

$$C_A(t)=1-[t_1\exp(-t/t_1)-t_2\exp(-t/t_2)]/(t_1-t_2)\ . \qquad (6.3)$$

Our aim is to determine the time constants t_1 and t_2 on the basis of the SE (1.1). For this purpose we impose the following conditions on $C_A(t)$:

$$(3)\quad \int_0^\infty dt[1-C_A(t)]=\tau_1(x_0, x_A)\ , \qquad (6.4)$$

$$(4)\quad \int_0^\infty dt\, t[1-C_A(t)]=\tau_2(x_0, x_A)\ . \qquad (6.5)$$

Since $1-C_A(t)$ represents the number of particles unreacted at time t, i.e.,

$$1-C_A(t)=\int_{x_1}^\infty dx\, p(x,t\,|\,x_0)=N(t\,|\,x_0) \qquad (6.6)$$

condition (6.4) states that the time integral over 1-$C_A(t)$ should assume its *exact* value $\tau_1(x_0,x_A)$. Similarly, we impose by Eq. (6.5) the condition that the first moment

$$\int_0^\infty dt\, tN(t\,|\,x_0) \qquad (6.7)$$

will coincide with the *exact* value of this integral $\tau_2(x_0,x_A)$. $\tau_2(x_0,x_A)$ can be determined as readily as the FPT itself. To show this, one starts with the backward diffusion equation for $N(t\,|\,x_0)$ (see Ref. 9):

$$\frac{\partial}{\partial t}N(t\,|\,x_0)=\mathbf{L}^+(x_0)N(t\,|\,x_0)\ . \qquad (6.8)$$

The time integral in Eq. (6.7) yields the equation for $\tau_2(x_0, x_A)$ [note $N(t=0\,|\,x_0)=1$, $\lim_{t\to\infty}tN(t\,|\,x_0)=0$] (Ref. 10):

$$-\tau_1(x_0, x_A)=\mathbf{L}^+(x_0)\,\tau_2(x_0,x_A)\ . \qquad (6.9)$$

This equation is subject to the boundary conditions

$$\lim_{x_0\to-\infty}\frac{\partial}{\partial x_0}\tau_2(x_0, x_A)=0\ , \qquad (6.10)$$

$$\tau_2(x_A,x_A)=0\ . \qquad (6.11)$$

$\tau_1(x_0,x_A)$ is given by Eq. (2.8). For $\tau_2(x_0, x_A)$ one obtains

$$\tau_2(x_0,x_A)=\int_{x_0}^{x_A}dx[D(x)p_{\mathrm{eq}}(x)]^{-1}\times\int_{-\infty}^{x}dy\,p_{\mathrm{eq}}(y)\,\tau_1(y,x_A)\ . \qquad (6.12)$$

To determine t_1 and t_2 entering Eq. (6.3) we carry out the integrals on the lhs of Eqs. (6.4) and (6.5) to obtain

$$t_1+t_2=\tau_1(x_0,x_A)\ , \qquad (6.13)$$

$$t_1^2+t_1t_2+t_2^2=\tau_2(x_0,x_A)\ , \qquad (6.14)$$

i.e.,

$$t_{1,2}=\left[\tfrac{1}{2}\pm\sqrt{\tau_2(x_0,x_A)/\tau_1^2(x_0,x_A)-\tfrac{3}{4}}\right]\tau_1(x_0,x_A)\ . \qquad (6.15)$$

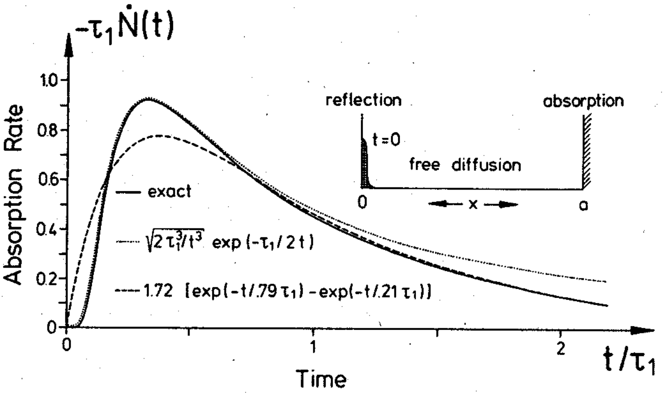

FIG. 3. Comparison of the absorption rates (6.25) (—), (6.19) (- - -), and (6.28) (•••) for a reaction system undergoing free diffusion; the reaction-diffusion system is illustrated by the insert of this figure [$\tau_1=\tau_1(0,a)$, $x_A=a$].

As a test of the description suggested, we consider the situation depicted in Fig. 3 with $U(x)=$const., $x_0=0$, and a reflective boundary at $x=0$ [the latter modification leads to a replacement of $-\infty$ by 0 in the integration limits in Eqs. (6.12) and (2.8)]. One determines

$$\tau_1(x_0,x_A)=(x_A^2-x_0^2)/2D \quad \text{(for variable } x_0\text{)}\ , \qquad (6.16)$$

$$\tau_2(0,x_A)=\tfrac{5}{6}\,\tau_1^2(0, x_A)\ , \qquad (6.17)$$

and hence

$$t_{1,2}=(\tfrac{1}{2}\pm\sqrt{1/12})\,\tau_1(0, x_A)\ . \qquad (6.18)$$

This yields the following for the rate $\dot{C}_A(t)$:

$$\dot{C}_A(t)\approx 1.72\tau_1(0,x_A)^{-1}\{\exp[-t/0.79\tau_1(0,x_A)] - \exp[-t/0.21\tau_1(0,x_A)]\} \qquad (6.19)$$

which reaches its maximum at $0.38\,\tau_1(0,x_A)$.

In order to test the validity of the rate expression (6.19), we will evaluate the exact rate. For this purpose we expand the diffusion distribution

$$p(x,t\,|\,0)=\sum_{n=0}^{\infty}A_nf_n(x)\exp(\lambda_nDt)\ , \qquad (6.20)$$

where $f_n(x)$ and λ_n are the eigenfunctions and eigenvalues, respectively, of the SE subject to the appropriate boundary conditions

$$f_n(x)=\cos[(2n+1)\pi x/2x_A]\ , \qquad (6.21)$$

$$\lambda_n=-[(2n+1)\pi/2x_A]\ . \qquad (6.22)$$

The expansion coefficients A_n are determined through the initial condition. One obtains

$$A_n=2/x_A\ . \qquad (6.23)$$

The reaction rate determined by virtue of

$$-D\,\frac{\partial}{\partial x}p(x,t\,|\,0),\quad \text{at } x=x_A \qquad (6.24)$$

is found to be

$$[\pi/2\tau_1(0,x_A)]\sum_{n=0}^{\infty}(2n+1)(-1)^ny^{(2n+1)^2}\ , \qquad (6.25)$$

$$y=\exp[-(\pi/2)^2t/2\tau_1(0,x_A)]\ . \qquad (6.26)$$

In Fig. 3 we compare this expression to the approximation (6.19). Within the limits of a two-relaxation-time description, the agreement appears to be very satisfactory.

We may note that for the reaction process considered, a simple short and medium $[t \approx \tau_1(0, x_A)]$ time approximation can be derived. In fact, if the reflective boundary at $x=0$ is removed, the resulting distribution $p_0(x, t|0)$ in the space $x>0$ will be close initially to $p(x, t|0)$ until, due to the reaction at the boundary $x=x_A$, the concentration of particles is depleted. The resulting decrease of the concentration gradient is sensed by the particles in $x<0$ which hence diffuse towards $x>0$ and at times longer than $2\tau_1(0, x_A)$ will react at $x=x_A$. $p_0(x, t|0)$ is well known to be

$$p_0(x, t|x_0) = \{\exp(-x^2/4Dt) - \exp[-(x-2x_A)^2/4Dt]\}/\sqrt{\pi Dt}\,. \quad (6.27)$$

The resulting reaction rate

$$\tau_1(0, x_A)^{-1}\sqrt{2\tau_1(0, x_A)^3/\pi t^3}\exp[-\tau_1(0, x_A)/2t] \quad (6.28)$$

compares very favorably with the exact rate as demonstrated in Fig. 3.

It may be pointed out that the two-relaxation-time reaction rate (6.3) is of direct relevance in the dynamics of the olfactory sensory process which involves a one-dimensional diffusion process.[14] It should also describe photoisomerization processes in condensed media when the motion on the excited state potential surface linking reactant and product states should resemble a diffusion process governed by the SE (1.1).

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