Multisite reversible geminate reaction

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We provide an analytic solution for diffusion-influenced geminate reaction with multiple (N) reversible binding sites (of which one may be irreversible). The solution obtained in the Laplace domain, for two different initial conditions, is valid for the case when the sites are overlapping spheres with no long-range interactions with the diffusing particle. The possibility to invert into the time domain is determined by a characteristic polynomial. When all its roots are distinct, it is possible to apply the Lagrange interpolation formula and obtain a partial-fraction expansion that can be termwise inverted. At long times the occupancy of all sites, and for all initial conditions, decays as $r^{-3/2}$. The behavior at short times depends on the initial condition: when starting from contact, the binding probability rises as $t^{1/2}$, but if the particle is initially bound to one of the sites, the occupancy of the others rises as $t^{3/2}$. In between these two power laws we observe an intermediate-time kinetics consisting of N decaying exponentials. Those which are slower than a characteristic diffusion time are in the reaction-control regime and fit a discrete-state kinetic approximation with no adjustable parameters, whereas the faster kinetic steps are diffusion controlled. The model solved herein may depict a wide range of physical situations, from multisite proton transfer kinetics to hydrogen-bond dynamics of liquid water. © 2009 American Institute of Physics. [DOI: 10.1063/1.3074305]

I. INTRODUCTION

Geminate recombination is a fundamental problem of diffusion-influenced reactions in solution.1 The pair of particles may be initially separated to a specified distance or initially bound, and their binding reaction may be irreversible or reversible. The simplest geminate recombination models are spherically symmetric so that only translational diffusion comes into play. Their good agreement with experimental binding probabilities (below) may partly result from lack of sensitivity to additional microscopic detail. The case of initially separated pairs that recombine irreversibly occurs in radical recombination in radiation chemistry1–3 or laser photolysis experiments,4–6 and for the recombination of solvated electrons with their parent cation or radical.7–17

When the pair forms only a weak bond, both recombination and dissociation steps can be ultrafast, resulting in a reversible diffusion-influenced reaction. Weak covalent bonds occur in excited electronic states, leading to phenomena such as excited-state proton transfer (ESPT).18 Its study has led to the development of the theory of reversible geminate recombination,19–25 comparing favorably with solution-phase experiments.26–35

Mathematically, the irreversible problem is isomorphic to heat conduction outside a sphere and was first solved in this context.36 The reversible geminate problem has no analogies in heat conduction, so it was first solved much more recently.19 The case of potential interactions, which cannot be treated analytically,37 can nevertheless be solved numerically (for example, via the SSDP software).38

There is also a noticeable physical difference between the two problems in three dimensions. In the irreversible case, part of the population rebinds and the remainder escapes. The survival probability of an unbound pair approaches its ultimate value with a $t^{-1/2}$ time course. In the reversible case, even the fraction that rebinds eventually dissociates and separates to infinity. Thus the binding probability decays to zero, albeit with a different, $r^{-3/2}$, power law. This behavior is clearly seen in time-resolved experiments of ESPT to solvent.18

The power-law behaviors are characteristics of diffusion, arising from transport via a random-walk mechanism. Consequently, they depend on the dimensionality, $d$. Single-site reversible geminate reaction shows an asymptotic decay of $t^{-d/2}$ for the binding probability at long times.21,27 Unlike the long-time behavior, the short-time asymptotics depends on the initial condition. When the reaction commences from the bound state, its probability decays initially exponentially due to dissociation. However, when the pair is initially unbound but at contact, the binding probability rises with a $t^{1/2}$ power law ($d=1$ or 3).39

Thus far, multistate geminate problems were solved for additional states in series with the bound state. Such are the cases of an excited geminate reaction with two different lifetimes for the bound and unbound states,23–25 or the case of Michaelis–Menten kinetics at low substrate concentrations,39,40 which mathematically is a special case thereof. Here we treat the case that the various binding states occur in parallel rather than in series. There are several examples where such scenarios arise.

Low temperature ESPT kinetics within the green fluorescence protein lead to long-time fluorescence tails which decay as $t^{-1/2}$, and this was attributed to one-dimensional migration along an internal “proton wire.”41 At higher
temperatures, an exit pathway to solution supposedly opens,\textsuperscript{42} and then the asymptotic behavior switches to \( r^{-3/2} \). This power law is not a result of a change in dimensionality but rather due to the addition of an irreversible binding site in parallel to the reversible one. Thus multisite geminate reaction in one dimension exhibits interesting effects. Here we focus on the behavior of such schemes in three dimensions.

Reversible diffusion-influenced reactions are not limited to the excited state but rather to weak-binding scenarios. An example of weak binding in the ground state is the ultrafast, diffusion-influenced regime.\textsuperscript{43} An example of weak binding in the ground state is provided by the excited state but rather to weak-binding scenarios. An example of weak binding in the ground state is provided by the excited state but rather to weak-binding scenarios. An example of weak binding in the ground state is provided by the excited state but rather to weak-binding scenarios.

We are considering here an extension to the reversible geminate recombination problem for single-pair kinetics,\textsuperscript{19–25} which maintains spherical symmetry (so that the interparticle distance \( r \) is the sole spatial coordinate). While a model consisting of overlapping sites with spherical symmetry might not be fully realistic, it captures the basic physical behavior while still being amenable to mathematical analysis. We are interested in the time \( t \) dependent probabilities, \( c_j(t) \), for observing these complexes, and the probability density, \( p(r,t) \), for an unbound pair to be separated to distance \( r \). Clearly, by matter conservation

\[
\sum_{j=1}^{N} c_j(t) + \int_{a}^{\infty} dr 4\pi r^2 p(r,t) = 1.
\]

It is important to clarify the conditions on the rate constants under which analytic solution is possible. The basic demand is that the characteristic polynomial (below) has distinct roots. Unfortunately, the general condition on the rate constants which ensures this is not easy to obtain. As a minimal requirement, we assume herein that \( k_{d_j} > 0 \). The case that one of the dissociation rate constants vanishes (i.e., binding to one of the sites is irreversible) is treated in Appendix A. If two or more \( k_{d_j} = 0 \), then their corresponding sites can be unified into a single site.

We describe the reaction by a spherically symmetric diffusion equation with \( N \) spatially overlapping “sink terms,”

\[
\frac{\partial}{\partial t} p(r,t) = \mathcal{L} p(r,t) + \sum_{j=1}^{N} k_{d_j} c_j(t) - k_{a_j} p(r,t) \delta(r-a),
\]

where we have defined, for brevity,

\[
\delta(r-a) = \delta(r-a)/(4\pi a^2),
\]

with \( \delta(r) \) as the Dirac delta function. The spherically symmetric diffusion operator in three dimensions (in the absence of \( A-B \) interactions) is given by

\[
\mathcal{L} = r^{-2} \frac{\partial}{\partial r} D(r) r^2 \frac{\partial}{\partial r}.
\]

Moreover, we assume that the mutual diffusion coefficient, \( D = D_A + D_B \), is independent of the interparticle separation \( r \) and thus can be taken out of the differentiation operator. Because all reactions are described by sink terms, a reflective boundary condition is imposed at contact,

\[
\frac{\partial p(r,t)}{\partial r} \bigg|_{r=a} = 0.
\]

This partial differential equation is now coupled to \( N \) ordinary differential equations which depict the kinetics of the \( N \) bound states,

\[
\text{A} + \text{B} \rightleftharpoons \text{C}_j.
\]
\[
\frac{dc_j(t)}{dt} = k_{ij}p(a,t) - k_{ji}c_j(t), \quad j = 1, \ldots, N. \tag{2.6}
\]

The goal of the present work is to provide an analytic solution to this system of \(N+1\) coupled differential equations and analyze its behavior.

### B. Laplace transformed equations

Let us first solve this system of equations in Laplace space, subject to an initial condition for

\[
\{p(r,0), c_j(0)|j = 1, \ldots, N\}.
\]

The LT of a function \(f(t)\), denoted \(\hat{f}(s)\), is defined by

\[
\hat{f}(s) = \int_0^{\infty} f(t)e^{-st}dt. \tag{2.7}
\]

The LT of Eqs. (2.2) and (2.6) then gives

\[
(s - \mathcal{L})\hat{p}(r,s) - p(r,0) = \sum_{j=1}^{N} [k_{ij}\hat{c}_j(s) - k_{ji}\hat{p}(r,s)]\hat{\delta}(r|a), \tag{2.8a}
\]

\[
(s + k_{ij})\hat{c}_j(s) - c_j(0) = k_{ij}\hat{p}(r,s). \tag{2.8b}
\]

We proceed by introducing specific initial conditions for \(p(r,0)\) and \(c_j(0)\). If the \(A-B\) pair is initially unbound and separated to a distance \(r_0\), we denote its probability density by \(p(r,t|r_0)\) and its binding probabilities by \(c_j(t|r_0)\). The initial conditions are then

\[
p(r,0|r_0) = \delta(r|r_0), \quad c_j(0|r_0) = 0. \tag{2.9}
\]

Substitution into Eqs. (2.8) results in an ordinary differential equation for the Green’s function, \(\hat{p}(r,s|r_0)\),

\[
(s - \mathcal{L})\hat{p}(r,s|r_0) = \delta(r|r_0) - K(s)\hat{p}(a,s|r_0)\hat{\delta}(r|a), \tag{2.10}
\]

where we have defined the “rate kernel” \(K(s)\) by

\[
K(s) = \sum_{j=1}^{N} \frac{s k_{ij}}{s + k_{ij}}. \tag{2.11}
\]

We also consider an initially bound state (denoted by an asterisk), when its Green’s function is initially

\[
p(r,0|* ) = 0, \quad c_1(0|*) = 1, \quad c_j(0|*) = 0 \quad (j = 2, 3, \ldots, N). \tag{2.12}
\]

We do not need to consider explicitly the case when \(c_j(0|*)=1\) because it can be obtained from the above by interchanging the indices 1 and \(j\). Substitution into Eqs. (2.8) gives

\[
(s - \mathcal{L})\hat{p}(r,s|*) = \frac{k_{d1}}{s + k_{d1}}\delta(r|a) - K(s)\hat{p}(a,s|*)\hat{\delta}(r|a). \tag{2.13}
\]

Upon comparison with the case \(r=a\) in Eq. (2.10), it is seen that this solution is just proportional to that of an unbound pair which starts at contact

\[
\hat{p}(r,s|*) = \frac{k_{d1}}{s + k_{d1}}\hat{p}(r,s|a). \tag{2.14}
\]

It thus suffices to obtain the Green’s function solution, \(\hat{p}(r,s|r_0)\), for the unbound pair.

### C. Connection with nonreactive diffusion

We can rewrite the LT of the solution in terms of the LT of the Green’s function for non-reactive diffusion, \(g(r,s|r_0)\), which obeys

\[
(s - \mathcal{L})g(r,s|r_0) = \delta(r|r_0). \tag{2.15}
\]

Here, too, a reflective boundary condition, \(\partial g(r,s|r_0)/\partial r = 0\), is imposed at \(r=a\), while all the rate constants vanish. Assuming that the operator \(s - \mathcal{L}\) is invertible, we can write this equation as \(g(r,s|r_0) = (s - \mathcal{L})^{-1}\delta(r|r_0)\). Operating on both sides of Eq. (2.10) with \((s - \mathcal{L})^{-1}\) and substituting, one obtains

\[
\hat{p}(r,s|r_0) = g(r,s|r_0) - K(s)\hat{p}(a,s|r_0)g(r,s|a), \tag{2.16}
\]

The substitution is valid because both functions obey the same boundary condition. In particular, by setting \(r=a\), one obtains

\[
\hat{p}(a,s|r_0) = [1 + K(s)g(a,s|a)]^{-1}g(a,s|r_0). \tag{2.17}
\]

By insertion into the previous equation, one expresses the Green’s function solution with reaction in terms of the same solution without reaction,

\[
\hat{p}(r,s|r_0) = g(r,s|r_0) - \frac{g(r,s|a)K(s)g(a,s|r_0)}{1 + K(s)g(a,s|a)}. \tag{2.18}
\]

This extends similar results for irreversible and reversible reactions. The physical interpretation of such a relation is that the pair either proceeds from \(r_0\) to \(r\) without hitting the boundary (first term), or else A and B first reach \(r=a\), where reaction is manifested by the term \(K(s)/[1 + K(s)g(a,s|a)]\), and then proceed to separate to distance \(r\).

The probabilities for the bound states are then obtained by inserting Eq. (2.17) into Eq. (2.8b),

\[
\hat{c}_j(s|r_0) = \frac{k_{d1}g(a,s|r_0)}{(s + k_{d1})[1 + K(s)g(a,s|a)]}. \tag{2.19}
\]

This completes the solution for an initially unbound pair, where \(c_j(0|r_0)=0\).

For an initially bound state, \(c_1(0)=1\), the solution for the probability density follows immediately from Eqs. (2.14) and (2.18),

\[
\hat{p}(r,s|*) = \frac{k_{d1}g(r,s|a)}{(s + k_{d1})[1 + K(s)g(a,s|a)]}, \tag{2.20}
\]

in agreement with the detailed-balance condition: \(k_{d1}\hat{c}_1(s|r)=k_{a1}\hat{p}(r,s|*)\). The binding probabilities are obtained from inserting the above equation into Eq. (2.8b) as
\[ \hat{c}_j(s) = \frac{1}{s + k_{d_j}} \left( \delta_{j,1} + \frac{k_{d_j} g(a_s|a)}{(s + k_{d_j})(1 + K(s) g(a_s|a))} \right), \]

where \( \delta_{m,n} = 1 \) for \( n = m \) and 0 otherwise. Note that for \( j \neq 1 \), \( (s + k_{d_j}) \hat{c}_j(s) = k_{d_j} \hat{c}_j(s|a) \). This completes the derivation of the LT of the solutions for the two initial conditions.

D. The characteristic polynomial for noninteracting pairs

In the absence of an interaction potential, the nonreactive Green’s function in Laplace space, \( g(r,s|r_0) \), can be obtained analytically,\(^36\)

\[ g(r,s|r_0) = \hat{f}(r,s|r_0) - \frac{e^{-\sigma_{r_0} - \rho r^2}}{k_D \rho_0 \sigma \sigma + 1}. \]

(2.22)

Here \( \tau = a^2/D, k_D = 4 \pi a D \), and we have introduced the dimensionless variables \( \rho = r/a, \rho_0 = r_0/a \), and \( \sigma = \sqrt{\pi} \tau \). The function \( \hat{f}(r,s|r_0) \) obeys a one-dimensional diffusion equation with similar initial and boundary conditions,\(^36\)

\[ f(r,t|r_0) = \frac{1}{4\pi r_0^2} \left[ e^{-\frac{(r - r_0)^2}{4t}} + e^{-\frac{(r + r_0 - 2a)^2}{4t}} \right]. \]

(2.23a)

Its LT is

\[ \hat{f}(r,s|r_0) = \frac{1}{2k_D \rho_0 \sigma} [e^{-\sigma_{r_0} - \rho} + e^{-\sigma_{r_0} + \rho - 2}]. \]

(2.23b)

For convenience, we also summarize the limiting cases of \( g(r,s|r_0) \) when one or both spatial coordinates is set to contact,

\[ g(r,s|a) = g(a,s|r) = \frac{e^{-\sigma_{r_0} - 1}}{k_D \rho_0 (\sigma + 1)}, \]

(2.24a)

\[ g(a,s|a) = \frac{1}{k_D (\sigma + 1)}. \]

(2.24b)

We can now substitute the above equations into Eq. (2.18), obtaining

\[ \hat{p}(r,s|r_0) = \hat{f}(r,s|r_0) - \frac{k_D + K(s)}{(\sigma + 1) k_D + K(s)} \frac{e^{-\sigma_{r_0} + \rho - 2}}{k_D \rho_0 \sigma}. \]

(2.25)

In terms of the dimensionless rate coefficients \( \alpha_j = k_{d_j}/k_D \) and \( \beta_j = k_{d_j} \tau \), the rate-kernel \( K(s) \) has been written here as

\[ K(s) = \frac{\sigma^2}{k_D} \sum_{j=1}^{N} \frac{\alpha_j}{\sigma^2 + \beta_j}. \]

(2.26)

We proceed to rewrite the coefficient of the exponential in Eq. (2.25) as a ratio of polynomials. To achieve this, let us define the “dissociation polynomial” and its derivative as

\[ A(\sigma) = \prod_{j=1}^{N} (\sigma^2 + \beta_j), \]

(2.27a)

\[ A_j(\sigma) = \frac{\partial A(\sigma)}{\partial \beta_j} = \prod_{k=1}^{N} (\sigma^2 + \beta_k) = \frac{A(\sigma)}{\alpha^2 + \beta_j}. \]

(2.27b)

Note that if \( \beta_j = 0 \), the polynomial \( A(\sigma) \) has a root \( \sigma = 0 \) with multiplicity of 2. This situation is considered in Appendix A. In the remainder of this section we thus assume that \( \beta_j \neq 0 \).

Defining the additional polynomials

\[ I(\sigma) = A(\sigma) + \sum_{j=1}^{N} \alpha_j \sigma^2 A_j(\sigma), \]

(2.28a)

\[ \Delta(\sigma) = \sigma A(\sigma) + I(\sigma), \]

(2.28b)

and substituting into Eq. (2.25), one can rewrite \( \hat{p}(r,s|r_0) \), analogous to \( g(r,s|r_0) \), as

\[ \hat{p}(r,s|r_0) = \hat{f}(r,s|r_0) - \frac{I(\sigma) e^{-\sigma_{r_0} + \rho - 2}}{\Delta(\sigma) k_D \rho_0 \sigma}. \]

(2.29)

Indeed when there are no binding sites \( (N=0) \), \( A(\sigma) = 1 \) and the above result reduces to Eq. (2.22). This analytic expression for the LT of the multisite Green’s function depends on the monic polynomial \( \Delta(\sigma) \), which is termed therefore the “characteristic polynomial” of the geminate problem. It has degree \( 2N + 1 \), with its odd and even terms originating from \( A(\sigma) \) and \( I(\sigma) \), respectively. Let us denote its roots by \( \sigma_k \) \( (k=1, \ldots, 2N+1) \), so that it factorizes as

\[ \Delta(\sigma) = \prod_{k=1}^{2N+1} (\sigma - \sigma_k). \]

(2.30)

Analytic inversion of the LT in Eq. (2.29) is possible when the \( \sigma_k \) are all different \( [i.e., \Delta(\sigma) \text{ has simple roots}] \). In particular, this requires that \( \beta_j > 0 \) for all \( j \).

E. Partial-fraction Laplace inversion

To proceed, we assume that the characteristic polynomial has distinct roots. In this case, the “Lagrange interpolation formula” applies to any polynomial, \( Q(\sigma) \), of degree \( 2N \) or less,

\[ Q(\sigma) = \sum_{k=1}^{2N+1} Q(\sigma_k) \frac{\Delta_k(\sigma)}{\Delta_k(\sigma_k)}. \]

(3.31)

Here \( \Delta_k(\sigma)/\Delta_k(\sigma_k) \) is the Lagrange polynomial, where

\[ \Delta_k(\sigma) = \prod_{j=1}^{2N+1} (\sigma - \sigma_j) \]

(3.32)

This allows one to express \( I(\sigma)/\Delta(\sigma) \) as a sum of its partial fractions

\[ \frac{I(\sigma)}{\Delta(\sigma)} = - \sum_{k=1}^{2N+1} \frac{A(\sigma_k)}{\Delta_k(\sigma_k) \sigma - \sigma_k}, \]

(3.33)

where we have substituted \( I(\sigma_k) = -\sigma_k A(\sigma_k) \). When inserted into Eq. (2.29), one obtains terms of the form \( \exp(-\sigma r_0)/[\sigma(\sigma - \sigma_k)] \), which can be inverted.\(^36\) Hence the Green’s function, \( p(r,t|r_0) \), is obtained analytically as
\[ p(r,t|r_0) = f(r,t|r_0) + \sum_{k=1}^{2N+1} \frac{A(\sigma_k) \sigma_k}{\Delta_k(\sigma_k)} \frac{\sigma_k}{4\pi r_0 d} \times W \left( r + r_0 - 2a \sqrt{4Dt}, -\sigma_k \sqrt{\frac{t}{\tau}} \right), \]  

where \( W(x, y) = \exp(-x^2)\Omega(x+y) \) and \( \Omega(z) = \exp(z^2)\text{erfc}(z) \). Because the roots may be complex, the complementary error function, \( \text{erfc}(z) = 1 - \text{erf}(z) \), may be a complex function of a complex argument \( z \).

The LT of the binding probabilities from Eq. (2.19) can be written as

\[ \hat{c}_j(s)|r_0 = \frac{\tau \alpha_j A_j(\sigma_j)}{\rho_0 \Delta(\sigma)} e^{-\alpha (\rho_0 - 1)}, \]

where \( A_j(\sigma) \) is defined in Eq. (2.27b). To obtain a sum of LTs each having the same form as before, we multiply and divide this equation by \( \sigma \). Then \( \alpha A_j(\sigma) \), which is a polynomial of the order of \( 2N-1 \), can be substituted into Eq. (2.31). Thus, in analogy to Eqs. (2.33) and (2.34), we obtain the partial-fraction expansion,

\[ \frac{\sigma A_j(\sigma)}{\Delta(\sigma)} = \sum_{k=1}^{2N+1} \frac{A_j(\sigma_k)}{\Delta_k(\sigma_k)} \frac{\sigma_k}{\sigma - \sigma_k}, \]

and subsequently the inverse LT of \( c_j(t|r_0) \),

\[ c_j(t|r_0) = \sum_{k=1}^{2N+1} \frac{A_j(\sigma_k) \sigma_k}{\rho_0 \Delta_k(\sigma_k)} W \left( r_0 - a \sqrt{4Dt}, -\sigma_k \sqrt{\frac{t}{\tau}} \right). \]

It is interesting to consider the total binding probability, \( \sum_{j=1}^N c_j(t) \), which is connected to the survival probability, \( S(t) \), of an unbound pair by the conservation relation

\[ \sum_{j=1}^N c_j(t) + S(t) = 1. \]

From Eqs. (2.28) with \( \Delta(\sigma)=0 \), we obtain the identity

\[ \sum_{j=1}^N \alpha_j A_j(\sigma_k) = -(\sigma_k + 1)\sigma_k^2 A(\sigma_k). \]

Applying it to Eq. (2.37), we obtain

\[ \sum_{j=1}^N c_j(t|r_0) = -\frac{2N+1}{\sum_{k=1}^{2N+1} A(\sigma_k) \sigma_k + 1} \sum_{k=1}^{2N+1} \frac{A(\sigma_k) \sigma_k}{\Delta_k(\sigma_k)} \rho_0 \frac{W \left( r_0 - a \sqrt{4Dt}, -\sigma_k \sqrt{\frac{t}{\tau}} \right)}{\sigma_k}. \]

For the initially bound state, we always consider the case that \( c_j(0)=1 \). Now the probability density, \( p(r,t|*) \), can be obtained from the detailed-balance relation,

\[ k_{dl} p(r,t|*) = k_{dl} c_j(t|r), \]

which follows from Eqs. (2.19) and (2.20). It thus remains to calculate the binding probabilities. Their LT, Eq. (2.21), can be rewritten as

\[ \hat{c}_j(s)|* = \frac{\tau \delta_{j,1}}{\sigma^2 + \beta_1} + \frac{\tau \alpha_j A_j(\sigma)}{(\sigma^2 + \beta_1)\Delta(\sigma)} \]

provided that \( \beta_j \neq \beta_m \) (\( j \neq m \)), \( \sigma = \pm i \sqrt{\beta_j} \) are simple roots of the polynomial \( (\sigma^2 + \beta_1)\Delta(\sigma) \). This follows because, from the definitions of \( A(\sigma) \), \( A_j(\sigma) \), \( \theta(\sigma) \), and \( \Delta(\sigma) \), we have

\[ \Delta(\pm i \sqrt{\beta_j}) = -\alpha_j \beta_j A_j(\pm i \sqrt{\beta_j}), \]

which does not vanish. We can then apply the Lagrange interpolation formula for \( \alpha A_j(\sigma) \) with respect to the characteristic polynomial \( (\sigma^2 + \beta_1)\Delta(\sigma) \). Because its degree is \( 2N-3 \), we get two additional terms in the expansion, whose sum gives the last term in the following equation:

\[ \frac{\alpha A_j(\sigma)}{(\sigma^2 + \beta_1)\Delta(\sigma)} = \sum_{k=1}^{2N+1} \frac{A_j(\sigma_k)}{(\sigma^2 + \beta_1)\Delta_k(\sigma_k)} \frac{\sigma_k}{\sigma - \sigma_k} \]

\[ -\frac{\delta_{j,1}}{\alpha_j \beta_j \sigma + \beta_1}. \]

Upon insertion into Eq. (2.42), the \( \delta_{j,1} \) terms cancel so that the inverse LT of \( \hat{c}_j(s|*) \) into the time domain is obtained as

\[ c_j(t|*) = \alpha \sum_{j=1}^{2N+1} \frac{\beta_j A_j(\sigma_j) \sigma_j}{(\sigma^2 + \beta_1)\Delta_k(\sigma_k)} \Omega(-\sigma_k \sqrt{t/\tau}). \]

The total binding probability is obtained, by applying Eq. (2.39) and the definition of \( A_j(\sigma) \), as

\[ \sum_{j=1}^N c_j(t|*) = -\beta \sum_{j=1}^{2N+1} A_j(\sigma_j) \sigma_j + \frac{1}{\Delta_k(\sigma_k)} \Omega(-\sigma_k \sqrt{t/\tau}). \]

The above results hold also when one of the binding steps, say \( j=N \), is irreversible (\( k_{dl}=0 \)). However, in this case two of the roots vanish so that one should be careful in taking the limit \( k_{dl} \to 0 \) correctly. This is detailed in Appendix A.

**F. Asymptotic behavior**

We have also obtained the asymptotic short- and long-time behavior of all the above functions. While the detailed derivation will be given elsewhere, it can be summarized as follows: at long times \( c_j(t) \) and \( p(a,t) \) decay with the ubiquitous \( r^{-3/2} \) power law, a characteristic of three-dimensional reversible diffusion-influenced reactions, irrespective of the initial condition. In contrast, the short-time behavior is a power law that depends on the initial condition: \( r^{1/2} \) for \( p(a,t|a) \), \( t^{1/2} \) for \( c_j(t|a) \) or \( p(a,t|*) \), and \( t^{3/2} \) for \( c_j(t|*) \) for \( j \neq 1 \), whereas \( c_1(t|*) \) decays initially as \( \exp(-k_{dl}t) \).

Because the short-time power laws are rarely mentioned [but see Eq. (54) in Ref. 39], we provide here a qualitative derivation. Consider first the case where the population is initially concentrated at \( r=a \). At very short times, before the reaction has had its effect,

\[ p(a,t|a) \sim f(a,t|a) = 1/(4\pi a^3 \sqrt{\pi t/\tau}), \]

[see Eq. (2.23a)]. The binding rate in Eq. (2.6) at short times (when the bound fraction is still negligible) is \( dc_j(t|a)/dt \sim k_{dl} p(a,t|a) \), and therefore \( c_j(t|a) \) increases near \( t=0 \) as \( t^{1/2} \). For the initially bound state, we note from Eq. (2.41)
that \( p(a,t|\ast) \) is proportional to \( c_1(t|a) \) and therefore rises like \( t^{1/2} \). Therefore \( c_j(t|\ast) \) (for \( j > 1 \)), which at \( t \rightarrow 0 \) is proportional to the time integral of \( p(a,t|\ast) \), increases initially as \( t^{3/2} \).

At long times, one can neglect the reflective sphere in comparison to the width of the distribution \( p(a,t|a) \). This function is proportional to \( t^{-3/2} \) (the normalization of the Gaussian solution for free diffusion in three dimensions without any boundary condition at \( t=a \)). The binding populations, \( c_j(t) \), are in quasiequilibrium with the contact density, and hence, they also decay as \( t^{-3/2} \) asymptotically long times.

### III. NUMERICAL CALCULATIONS

We now exemplify the time-dependent solutions for the binding probabilities, \( c_j(t) \), the survival probability, \( S(t) \), and the contact probability density, \( p(a,t) \), for the two initial conditions: either starting at contact or in the bound state number 1. In order to demonstrate the effect of adding binding sites, we compare the results for \( N=1, 2, \) and 3. The \( N=1 \) and 2 cases can also be calculated numerically using SSDP, version 2.66.\(^{38} \) We have found agreement of four significant digits between this calculation and our analytical results up to the long-time asymptotic limit.

Figures 1(a) and 1(b) depict the solutions for the two initial conditions when all the dissociation rate constants are similar in magnitude. The association rate constants are chosen so that the reactions are in the diffusion-controlled regime. For both initial conditions, the initial and ultimate asymptotic behaviors are independent of the number of binding sites, \( N \). The ultimate \( t^{-3/2} \) decay is independent also of the initial condition. The \( t \rightarrow 0 \) behavior seen in the figures demonstrates the various power-law behaviors discussed in Sec. II F.

The effect of adding binding sites is manifested only at intermediate times. Because the rate constants for the different sites are similar in this time, the course for the initially unoccupied sites in case (a) is similar, and they attain their maxima at similar times. Adding sites in this case increases the overall binding probability at intermediate times, thus delaying the rise of the survival probability \( S(t|a) \) to its ultimate value of unity.

In case (b), the probability of the initially bound state \( c_1(t|\ast) \) decreases monotonically, while \( p(a,t|\ast) \) rises to a maximum. In comparison to \( p(a,t|\ast) \), we note that \( c_2(t|\ast) \) and \( c_3(t|\ast) \) reach their maxima with a delay. Interestingly, \( c_1(t|\ast) \) is rather insensitive to \( N \) over the whole time regime.\(^{44} \) Hence experiments that only monitor \( c_1(t|\ast) \) are not likely to reveal the participation of additional binding sites in the kinetics.

Figures 2(a) and 2(b) depict a situation when \( k_{dj} \) and \( k_{dj} \) decrease significantly with every added binding site. As can be expected from ordinary chemical kinetics, the particle first occupies site 1 (which has the fastest binding/unbinding rate constants), then site 2, etc., until it finally escapes. In between the initial and final power-law behaviors we observe a “bumpy” time course, each bump corresponding to an exponential depicting the population decay of one reversible site.

![Fig. 1. (Color) Time dependence of the binding probabilities, contact probability density, and the survival probability when the \( k_{dj} \)’s and \( k_{jd} \)’s have similar values.](image)

It is interesting to see the multiexponential behavior predicted by ordinary chemical kinetics sandwiched between the power-law regimes of diffusion-influenced kinetics.

#### A. Kinetic approximation

The multiexponential behavior at intermediate times in Fig. 2 is characteristic of a set of coupled rate equations. Therefore, we consider here a simplified chemical-kinetic scheme, that for three sites is

\[
\begin{align*}
C_1 & \xrightarrow{k'_{d1}} C_1P_{k_{d1}} \\
C_2 & \xrightarrow{k'_{d2}} C_2P_{k_{d2}} \\
C_3 & \xrightarrow{k'_{d3}} C_3P_{k_{d3}}
\end{align*}
\]

(3.1)

Here pair separation is depicted by just two states (instead of a continuous distance variable): a “contact state” \( P \) which leads irreversibly to a “separated state” (cf. Appendix A in Ref. 49). The assumption of irreversible separation is not a limitation because reversibility produces the \( t^{-3/2} \) asymptotic
behavior which is beyond the applicability limit of the kinetic model. The array of binding sites is linked reversibly to the contact state with effective unimolecular rate parameters. This means that the bimolecular rate parameters \( k_a \) and \( k_p \) are divided by a reaction volume to give the primed unimolecular rate parameters. Thus there are no adjustable parameters in this kinetic model, all are determined from those of the diffusive problem. The ensuing rate equations and their solution are given in Appendix B.

Figure 3 compares the solution of the geminate diffusion model for three binding sites (Fig. 2) with the solution of the corresponding kinetic model. As expected, the kinetic approximation misses the short- and long-time asymptotic behavior, where it predicts much faster (exponential) kinetics than the (power law) diffusive kinetics. Nevertheless, it reproduces some of the intermediate-time multiexponential behavior. It appears that of the \( N \) exponents, only those occurring at \( t > \tau \) are well reproduced (until the onset of the \( t^{-3/2} \) decay). To check this, we present in Fig. 4 a similar plot for much smaller values of the rate parameters. Now all of the binding steps occur at \( t > \tau \) and the kinetic model is in very good agreement with all three exponents, using no adjustable parameters.

IV. CONCLUSION

The conventional problem of geminate recombination involves a pair of diffusing particles capable of mutually binding (irreversibly or reversibly) or, stated differently, a single particle interacting with a single binding site. The present work extended this problem to the case when the pair can form several different recombination products, or when a particle binds to a receptor possessing multiple binding sites.

The motivation for this study was the small inconsistency between \( c_j(t|\ast) \) and \( p(a,t|\ast) \) in molecular dynamics results for hydrogen-bonded water molecule pairs: both agreed with the model for \( N=1 \), but with different parameters. Adding a binding site \( (N=2) \) rectified this, demonstrating that diffusion models may be quite useful in analyzing molecular simulation data for liquid water. The good agreement with simulations indicates that approximations (such as spherical-symmetry or neglecting short-range interactions) do not affect drastically the functional form of the solution. However, the parameters obtained from the fits should be considered as effective parameters, whose values reflect the approximations invoked.

In biological systems, multisite receptors are quite common. For example, postsynaptic \( N \)-methyl-D-aspartate (NMDA) receptors in the synaptic gap of central nervous system neurons are probably double-site receptors, and this affects their binding kinetics.

The present work focused on the multisite geminate problem for free diffusion (no potential interactions). It was shown that when the characteristic polynomial [Eq. (2.28b)] has distinct roots, the Lagrange interpolation formula can be utilized to factorize the LT into partial fractions which can be
individually inverted. This extension of the Agmon–Weiss solution for single-site geminate kinetics provides analytic expressions for all the components of the Green’s function: binding and survival probabilities as well as the probability density in space, for both initial conditions of an initially bound or unbound pair.

The analytic solution allowed us to investigate the behavior as a function of the rate parameters and the number \( N \) of parallel binding sites. We found that the additional binding sites delay the diffusion of the particle away from the multisite trap. The particle may interact with all the binding sites before leaving the reaction zone. The solution then becomes a mixture of kinetics and diffusion. After an initial power-law behavior, there is multi-(\( N \))-exponential kinetics due to multistate reversible unimolecular kinetics of the \( N \) sites. Eventually, as the particle escapes from the reaction zone by diffusion, all binding probabilities switch to the ubiquitous \( t^{-3/2} \) decay, a reflection of diffusive transport in three-dimensional space. Thus interestingly, a chemical-kinetic behavior appears in between two diffusive power-law regimes. To our knowledge, such an effect has not been described before.

Under certain conditions this intermediate-time kinetics can be quantitatively approximated by the multiexponential solution of a chemical-kinetic scheme with \( N \) binding sites. Depending on their decay times, some of these exponentials may be in the diffusion-controlled regime and others in the reaction-controlled regime. The solution of the kinetic scheme reproduces the latter very accurately. In the case of a single binding site, there is only one time constant to the corresponding kinetic scheme, and the effect does not arise. The multisite scenario thus provides a unique example of a reaction which is simultaneously in the diffusion- and reaction-controlled regimes.

Unfortunately, experimental work such as for ESPT to solvent typically monitors only the binding or survival probabilities and is thus not very sensitive to the existence of additional binding sites. Consequently, it always appears to agree with the single-site geminate model. For example, the photoacid 8-hydroxypyrene 1,3,6-trisulfonate (HPTS) has three negatively charged sulfonate groups which may weakly bind the dissociated proton and delay its escape from the fluorophore (Fig. 5). To detect this, one might need to monitor directly the protonation state of the sulfonate groups. More detailed experimentation may thus reveal a richer behavior than what has been reported thus far.

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In this appendix we consider the case when one of the binding sites (but not that which is initially occupied) is irreversible. It is sufficient to consider only one irreversible site because several irreversible sites can always be lumped together. Without loss of generality, let site N be the irreversible one. When $\beta_N=0$, the definitions in Eqs. (2.27) imply that

$$A(\sigma) = A_N(\sigma)\sigma^2.$$  

(A1)

Inserting into Eqs. (2.28) and rearranging in increasing powers of $\sigma$, we rewrite the characteristic polynomial as

$$\frac{\Delta(\sigma)}{A_N(\sigma)} = (1 + \alpha_N)\sigma^2 + \sum_{j=1}^{N-1} \frac{\alpha_j}{\sigma^2 + \beta_j} \sigma^4.$$  

(A2)

This polynomial is proportional to $\sigma^2$ so that two of its roots are zero. Let us denote these vanishing roots by $\sigma_{2N}$ and $\sigma_{2N+1}$.

In order to reduce the general solution to the $\beta_N=0$ case, we treat the $k=2N$ and $2N+1$ terms in the summation separately by inserting the appropriate values for $\sigma_k/\Delta_k(\sigma_k)$. Noting that

$$\Delta_k(\sigma_k) = \frac{d}{d\sigma} \Delta(\sigma) \bigg|_{\sigma=\sigma_k},$$  

(A3)

and retaining only the lowest order term in Eq. (A2), we find in the limit that $\sigma_k \to 0$ that

$$\frac{\Delta_k(\sigma_k)}{\sigma_k} \to 2(1 + \alpha_N)A_N(0).$$  

(A4)

The reduction is now straightforward. For the Green’s function in Eq. (2.34), the terms with $k=2N$ and $2N+1$ vanish by Eq. (A1). Denoting $x = (r-a)/\sqrt{4Dt}$, and similarly defining $x_0$, we obtain

$$p(r,t|r_0) = f(r,t|r_0)$$  

$$+ \sum_{k=1}^{2N-1} \frac{A(\sigma_k)}{\Delta_k(\sigma_k)4\pi r\sigma_d} W(x + x_0 - \sigma_k\sqrt{t/\tau}),$$  

(A5)

For the binding probabilities of the initially unbound state, we use also $W(x,0) = \text{erfc}(x)$ and $A_j(0) = 0$ for $j < N$ in Eq. (2.37) to obtain

$$c_j(t|r_0) = \frac{\alpha_N}{1 + \alpha_N} \text{erfc}(x_0) \delta_{j,N}$$  

$$+ \alpha_j \sum_{k=1}^{2N-1} \frac{A_j(\sigma_k)}{\Delta_k(\sigma_k)} \sigma_k W(x_0 - \sigma_k\sqrt{t/\tau}).$$  

(A6)

Finally, for the initially bound state, we use $\Omega(0)=1$ and

$$\frac{\beta_1 A_1(\sigma_k)}{\sigma_k^2 + \beta_1} = \frac{\beta_1 A_j(\sigma_k)}{\sigma_k^2 + \beta_j} \to A_j(0)$$  

(A7)

as $\sigma_k \to 0$, to obtain

$$c_j(t) = \frac{\alpha_N}{1 + \alpha_N} \delta_{j,N}$$  

$$+ \alpha_j \sum_{k=1}^{2N-1} \frac{\beta_1 A_1(\sigma_k)}{\sigma_k^2 + \beta_1} \sigma_k \Omega(- \sigma_k\sqrt{t/\tau}).$$  

(A8)

Note that the same results can be obtained by the inverse LT of Eqs. (2.29), (2.35), and (2.42) by setting $k_{dN}=0$, which validates our procedure.

**APPENDIX B: KINETIC SCHEME FOR MULTISITE RECOMBINATION**

In this appendix, we present and solve the ensuing rate equations for the kinetic scheme in Eq. (3.1) with an arbitrary number of sites, N. In order that all the kinetic steps be unimolecular, the connection with the diffusional problem in the text is as follows: $P(t) = 4\pi a^3 p(a,t)$ represents the contact state P, where the particle is in the vicinity of the multisite trap. $P_S(t) = S(t) - P(t)$ represents the separated state with the pair away from contact. Together with the binding probabilities, $c_j(t)$, these satisfy the normalization condition,

$$\sum_{j=1}^{N} c_j(t) + P(t) + P_S(t) = 1.$$  

(B1)

The dissociation rate parameters are identical to those in the geminate diffusion model in the text, whereas the bimolecular rate parameters, $k_{ij}$ and $k_{ij}'$, are divided by an appropriate volume factor, $4\pi a^3$. A detailed derivation of these kinetic equations as an approximation to the diffusion problem is deferred to future work. In the dimensionless units introduced in the text, we have $k_{ij} = \beta_j/\tau$, $k_{ij}' = k_{ij}/(4\pi a^3) = \alpha_j/\tau$, and $k_{ij}' = k_{ij}/(4\pi a^3) = 1/\tau$.

The kinetic equations for the probabilities of the various states is consequently

$$\tau \frac{d}{dt} P(t) = \sum_{j=1}^{N} [\beta_j c_j(t) - \alpha_j P(t)] - P(t),$$  

(B2a)
\[ \tau \frac{d}{dt} P_S(t) = P(t), \quad \text{(B2b)} \]
\[ \tau \frac{d}{dt} c_j(t) = \alpha_j P(t) - \beta_j c_j(t). \quad \text{(B2c)} \]

Paralleling the solution of the diffusion equation, these equations can also be solved in Laplace space for the two initial conditions considered. This solution can be obtained from the exact solution in the text by setting \( g(a, s|a) = (s + k_{ij}^a)^{-1} \), which implies that for vanishing \( k_{ij}^a \) s and \( k_{ij}^b \) s the contact state decays exponentially, \( P(t) = \exp(-k_{ij}^b t) \). This solution indeed corresponds to the reduced scheme \( P \rightarrow P_s \) that allows no binding to any of the sites.

When the particle is initially in the contact state \( P \),
\[ \{ P(0) = 1, \; P_S(0) = c_j(0) = 0 \mid j = 1, 2, \ldots, N \}, \]
the solution is obtained as
\[ \hat{P}(s) = z \hat{P}_S(s|a) = \frac{\tau B(z)}{\Gamma(z)}, \quad \text{(B3a)} \]
\[ \hat{c}_j(s|a) = \frac{\tau k_{ij}^b B(z)}{z + \beta_j}. \quad \text{(B3b)} \]

For the other initial condition (the bound state 1),
\[ \{ \bar{P}(0) = P_S(0) = 0, \; c_1(0) = 1, \; c_{j > 1}(0) = 0 \}, \]
we similarly obtain
\[ \hat{P}(s) = \hat{P}_S(s|a) = \frac{\tau B_1(z)}{\Gamma(z)}, \quad \text{(B4a)} \]
\[ \hat{c}_j(s|a) = \frac{\tau \delta_{j1} B(z)}{z + \beta_j} + \frac{\tau \alpha_j B_1(z)}{(z + \beta_j)\Gamma(z)}. \quad \text{(B4b)} \]

Here, we have introduced the dimensionless Laplace variable \( z = \omega^2 = k \). The dissociation polynomial \( B(z) \) is now of the order of \( N \) (rather than \( 2N \), as in the diffusion case). \( B(z) \) and \( B_j(z) \) are defined as
\[ B(z) = \prod_{j=1}^{N} (z + \beta_j), \quad \text{(B5)} \]
\[ B_j(z) = \prod_{k=1 \neq j}^{N} (z + \beta_k) = \frac{B(z)}{z + \beta_j}, \quad \text{(B6)} \]

whereas the characteristic polynomial \( \Gamma(z) \) of the order of \( N+1 \) is defined as
\[ \Gamma(z) = (z + 1)B(z) + \sum_{j=1}^{N} \alpha_j z B_j(z). \quad \text{(B7)} \]

Its roots should be negative real numbers. \( z = 0 \) becomes a root of \( \Gamma(z) \) only when \( \beta_j = 0 \).

When \( \Gamma(z) \) has distinct roots, we can obtain the analytic solution in the time domain by applying the Lagrange interpolation formula with respect to \( \Gamma(z) \) to Eqs. (B3) and (B4), where the Lagrange polynomial, \( \Gamma_k(z)/\Gamma_k(z_k) \), is obtained from
\[ \Gamma_k(z) = \prod_{l=1 \neq k}^{N} (z - z_l) = \frac{\Gamma(z)}{z - z_k}. \quad \text{(B8)} \]

The analytic expressions of the inverse LT of Eqs. (B3) and (B4) are obtained, for the initial state \( P(0) = 1 \), as
\[ P(t|a) = \sum_{k=1}^{N+1} \frac{B(z_k)}{\Gamma_k(z_k)} e^{\zeta_k t}, \quad \text{(B9a)} \]
\[ c_j(t|a) = \sum_{k=1}^{N+1} \frac{\alpha_k B_1(z_k)}{z_k \Gamma_k(z_k)} e^{\zeta_k t}, \quad \text{(B9b)} \]
\[ P_S(t|a) = 1 + \sum_{k=1}^{N+1} \frac{B(z_k)}{z_k \Gamma_k(z_k)} e^{\zeta_k t}, \quad \text{(B9c)} \]
and, for the initial state \( c_1(0) = 1 \), as
\[ P(t|a) = \sum_{k=1}^{N+1} \frac{\beta_k B_1(z_k)}{\Gamma_k(z_k)} e^{\zeta_k t}, \quad \text{(B10a)} \]
\[ c_j(t|a) = \sum_{k=1}^{N+1} \frac{\alpha_k \beta_j B_1(z_k)}{(z_k + \beta_j) \Gamma_k(z_k)} e^{\zeta_k t}, \quad \text{(B10b)} \]
\[ P_S(t|a) = 1 + \sum_{k=1}^{N+1} \frac{\beta_k B_1(z_k)}{z_k \Gamma_k(z_k)} e^{\zeta_k t}. \quad \text{(B10c)} \]

The normalization condition [Eq. (B7)] can be easily verified by using the identity
\[ \Gamma(z_k) = (z_k + 1)B(z_k) + \sum_{j=1}^{N} \alpha_j z B_j(z_k) = 0. \quad \text{(B11)} \]

The above kinetic approximation reproduces the intermediate-time multiexponential behavior of the exact solution excellently between \( t \sim \tau \) and the onset of the \( t^{-3/2} \) tail, as shown in Figs. 3 and 4.
