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Diffusion-Influenced Reactions

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We summarize three of our recent results on diffusion-influenced reactions in solutions. All deal with the concentration dependence of the reaction rate when the reactants must first diffuse together before reaction can occur. When one species (the sink species) is not dilute, the rate cannot be obtained by solution of a pair diffusion equation; the correlations among the sinks for the diffusing species must be accounted for. First, we consider fluorescence quenching when the quenchers are not dilute. For charged quenchers and fluorophores we discuss how the solution dielectric constant and ionic strength can strongly influence the deviations from the linear Stern–Volmer behavior (the dilute sink result) which arise due to the sink correlations. Second, we consider heterogeneous catalysis where a reactive species is adsorbed onto a surface and must surface diffuse to reactive sites (the sinks). We find that surface diffusion can be an important factor contributing to the rate of reaction; especially when surface diffusion is rapid relative to the adsorption/desorption rate. Third, we discuss diffusion influenced reactions with sinks which are long ellipsoids. Dilute long ellipsoids provide a large rate enhancement relative to a spherical sink; we show that this rate enhancement survives when nondilute ellipsoids are considered.

KEY WORDS: Diffusion-influenced reactions; chemical reactions; surface diffusion; fluorescence quenching.

1. INTRODUCTION

The rate of a bimolecular reaction in solution can be limited by the diffusion of the reactant species to their encounter distance. For example, Smoluchowski(1,2) obtained the diffusion control rate constant $k_D^{(0)} = 4\pi Da$, where D is the sum of the reactant diffusion coefficients and a is their encounter separation where the reaction can occur. When one of the species is not dilute, the rate coefficient depends on its concentration. We

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will call the nondilute species *sinks*, and let $k_D(c)$ designate the diffusion control reaction rate constant as a function of sink number density c. The modification of the reactive density field of the dilute species arising from the nondilute sinks is responsible for the concentration dependence of k_D.

If the reaction were activation controlled, that is, if the rate of diffusion were slow with respect to the intrinsic rate of reaction (the rate when the reactants are at their encounter separation), then homogeneous kinetics would prevail. In homogeneous kinetics, diffusion is so fast relative to the rate of reaction at the encounter separation that the bulk reactive density is maintained throughout the solution. Therefore, the bimolecular rate constant would be independent of sink concentration.

We will designate the intrinsic bimolecular rate constant (at encounter separation a) by k_0 and the overall bimolecular rate constant by k_f. Thus, for example, k_f is the rate constant for the process

$$A + B \xrightarrow{k_f} C \tag{1.1}$$

where A and B must first diffuse together to separation a and then they may react, with rate constant k_0. For dilute reactants

$$k_f^{(0)} = k_0 k_D^{(0)}/(k_0 + k_D^{(0)}) \tag{1.2}$$

For nondilute sinks, k_f will be little changed from $k_f^{(0)}$ for $\nu = k_0/k_D^{(0)}$ very small (activation control) but substantially changed for $\nu \to \infty$ (diffusion control).

In this paper we summarize our efforts in three areas where these concentration effects are important.

First, we consider the dependence on quencher concentration of fluorescence quenching. With reference to Eq. (1.1), A would be an excited fluorophere A* and B a quencher Q. When the quenchers are not dilute deviations from the Stern–Volmer(4) (SV) linear dependence of fluoresence inverse lifetime on quencher concentration are expected. Quenching of charged reactants leads to deviations from linear SV behavior that depend on the solution ionic strength and dielectric constant. Our theoretical development identifies a length $\tilde{a}$ that controls the deviations from SV behavior through an effective volume fraction $\phi = 4\pi\tilde{a}^3c/3$, with c the quencher concentration. This length $\tilde{a}$ depends on the solution's dielectric constant and ionic strength and can be much greater than a, the encounter separation. Therefore deviations from the linear SV result can occur at much lower quencher concentration then would be predicted on the basis of the quencher material volume fraction $\phi = 4\pi a^3c/3$.

Second, we discuss reactions that can occur on surfaces. In heterogeneous catalysis reaction occurs at specific surface features such as steps and kinks.(5)

The diffusing species must first be adsorbed onto the surface and then it surface diffuses to the sites where reaction occurs. This problem has a strong two-dimensional flavor, even though the third dimension is present via an adsorption/desorption step, and displays some of the behavior perculiar to two-dimensional systems.

Third, we investigate the problem of nondilute sinks where the sinks are long ellipsoids. In DNA–repressor interactions it has been suggested(6,7) that a diffusing species locates a target site on the DNA molecule by a two-step process: first, diffusing and binding nonspecifically to the DNA and second, sliding along the DNA surface to the target site. This leads to a model of a long thin sink (a long ellipsoid), the DNA, acting as a reactive sink for the diffusing repressor species. We show that because such a sink acts as if it were a reactive sphere of radius corresponding to the *long* ellipsoid axis, the sinks can appear to be nondilute even when they are dilute materially. Therefore, the sink concentration dependence of the rate constant must be accounted for even for materially dilute DNA solutions.

The problem of nondilute sinks was addressed by several authors(8–15) in the context of the following model; a set of stationary, spherical, randomly distributed sinks in a solution with a diffusing species which reacts irreversibly and instantaneously on encounter with a sink.

We introduced two basic techniques for addressing this problem. First, a perturbative expansion with its origin in the multiple scattering expansion method used in diverse many-body problems.(10,13) Here, the rate coefficient is expressed as a sum over all possible "scatterings" of the diffusive propagator G_0 (the inverse of the diffusion operator $D_0\nabla^2$, where D_0 is the diffusion coefficient in the absence of the sinks) among the sinks. When this is done divergent integrals arise due to the long range of $G_0 \sim 1/r$. Summation of infinite sequences of scattering events before the spatial integrals are carried out leads to finite results but k_f is found to be a nonanalytic function of sink concentration c. An analogous effect arises in the Debye–Hückel theory of electrolytes(16); the long-range Coulomb interaction leads to divergences and, when these are removed, properties such as the conductance depend on the square root of the ionic strength $\sim\sqrt{c}$. Diagrammatic methods are useful when such infinite summations are required.

In order to provide a rigorous, systematic method of assigning an order to the various diagrams that appear in the multiple scattering expansion, we used a scaling expansion method.(13) This method was developed by Mori(17) and permits one to derive macroscopic transport equations by a space-time coarse graining of the microscopic process. The method ensures that the expansion in space gradients and time scales required to obtain a macroscopic (averaged over the distribution function of sinks) transport equation is carried out consistently with the expansion in sink concentration. All diagrams can be assigned an order in terms of one parameter and the various classes of diagrams can be summed order by order. For example, we find that k_D is given by the expression(13)

$$k_D = k_D^{(0)}\{1 + (3\phi)^{1/2} + (\phi/2)(5 + 3\ln 3) + [3\phi(\gamma_E + \ln 2 + (3/2)\ln 3 + (1/2)\ln\phi)]\} + \cdots \tag{1.3}$$

where $\phi = 4\pi a^3 c/3$ is the sink volume fraction. Note the appearance of $c \ln c$ terms; this is typical of the nonanalytic dependence beyond the lowest $(\sqrt{c})$ behavior that arises with $1/r$ divergence difficulties.

Naturally, this perturbative point of view is not useful when ϕ is not small, so approximate techniques must be used. The second technique we used is an effective medium procedure. To introduce it, consider the microscopic equation for the reactive diffusing density $n(\mathbf{r}, t)$:

$$\frac{\partial n(\mathbf{r}, t)}{\partial t} = D_0 \nabla^2 n(\mathbf{r}, t) - \sum_{\alpha=1}^{N} \int d\Omega_\alpha\, \delta(\mathbf{r} - \mathbf{R}_\alpha)\, \sigma_\alpha(\Omega_\alpha, t) \tag{1.4}$$

The summed term represents the boundary conditions on each sink's surface. That is, it accounts for the reaction between the diffusing species and the N sinks. The $\{\sigma_\alpha\}$ are Lagrange multipliers which are eliminated with the use of the boundary conditions. The expected macroscopic transport equation in this reaction–diffusion system is

$$\frac{\partial N(\mathbf{r}, t)}{\partial t} = D_0 \nabla^2 N(\mathbf{r}, t) - \int_0^t dt' \int d\mathbf{r}'\, \Sigma(\mathbf{r} - \mathbf{r}', t - t')\, N(\mathbf{r}', t) \tag{1.5}$$

In Eq. (1.5) $N(\mathbf{r}, t) = \langle n \rangle(\mathbf{r}, t)$ is the sink configuration average of the microscopic reactive density field $n(\mathbf{r}, t)$, and $\Sigma(\mathbf{r}, t)$ is a "memory function" (self-energy) which accounts for the averaged modification of the diffusing density field arising from the reactive sinks. Expanding Σ in space and time gradients leads to the expected transport equation

$$\frac{\partial N(\mathbf{r}, t)}{\partial t} = D \nabla^2 N(\mathbf{r}, t) - c k_D N(\mathbf{r}, t) \tag{1.6}$$

where k_D is the lowest order (in space-time gradients) term, $k_D = \int_0^\infty dt \int d\mathbf{r}\, \Sigma(\mathbf{r}, t)$, and $\delta D = D - D_0$ is the second-order term.(10) In the effective medium approach(11,14) we add to both sides of Eq. (1.4) an unknown memory function $W(\mathbf{r}, t)$ and use it with the bare propagator $D_0\nabla^2$ as the propagator in the effective medium. A relation of the form $\Sigma - W = f(W)$ is then generated. Setting $W = \Sigma$ yields the identity $f(\Sigma) = 0$, which is then truncated at some (low) order in scattering in the effective medium. Then a self-consistent solution for Σ, or for its moments k_f and D, is calculated. The effective medium technique is known to give reasonable approximations over a wide range of concentration.

In the following three sections we apply the ideas discussed here to investigate the three problems listed above: fluorescence quenching, surface diffusion, and ellipsoidal sinks.

2. FLUORESCENCE QUENCHING AND ELECTRON SCAVENGING

A typical fluorescence quenching scheme is

$$\mathrm{A} \xrightarrow{h\nu} \mathrm{A}^*, \qquad \mathrm{A}^* \xrightarrow{1/\tau_0} \mathrm{A}, \qquad \mathrm{A}^* + \mathrm{Q} \xrightarrow{k_f} \mathrm{A} + \mathrm{Q} \tag{I}$$

A dilute species A is excited to A* which then deexcites by fluorescing at a rate $1/\tau_0$ or by quenching with rate constant k_f. The lifetime of A* in the presence of quenchers is shortened to $1/\tau$ according to

$$1/\tau = 1/\tau_0 + k_f \tag{2.1}$$

For quenching by dilute quenchers $k_f = k_f^{(0)}c$ is given by Eq. (1.2). This result with Eq. (2.1) leads to the Stern–Volmer intensity law,(2) $I_0/I = 1 + ck_f^{(0)}\tau_0$, which is linear in quencher concentration.

As the quencher concentration increases the fluorophor spatial distribution about a given quencher is modified by the presence of the other quenchers; the sink (here quencher) correlations must be accounted for. Then k_f develops a concentration dependence of the form discussed in the Introduction. Because k_f increases faster than linear, I_0/I (or τ_0/τ) shows upward curvature when plotted versus c; this is observed in some quenching experiments.(19) Several theoretical approaches to this quenching problem have appeared.(20–23) Of particular interest is quenching of charged fluorophores by charged quenchers. Many inorganic electron transfer reactions involve charged species, for example.(24) Also, if charged reactants are considered the important problem of electron scavenging by charged scavengers can be addressed. In this case there is no $1/\tau_0$ process, so it just involves the calculation of k_f.

We have recently considered these problems using the perturbative and effective medium techniques discussed in the Introduction.(22,23) When the reactants are charged a new length $\tilde{a}$ becomes important. For charged reactants Debye$^{(25)}$ found that $k_D^{(0)} = 4\pi D\tilde{a}$, where

$$\tilde{a} = \left[\int_a^\infty \frac{e^{\beta V(x)}}{x^2}\, dx \right]^{-1} \tag{2.2}$$

Here $V(x)$ is the potential acting between the reactants. For a Coulomb potential between oppositely charged ions $\tilde{a} \to r_c = \beta e^2/4\pi\varepsilon_0\varepsilon_r$ with e the electron's charge and ε_r the dielectric constant. Typical values of $\tilde{a}/a$ range from 1 to about 40, so $\tilde{a}$ can be much larger than the encounter length a.

The perturbative calculation presented in Ref. 22 leads to

$$k_D = k_D^{(0)}[1 + (3\tilde{\phi})^{1/2}] \tag{2.3}$$

where $\tilde{\phi} = 4\pi\tilde{a}^3c/3$ is an *effective* volume fraction. Since $\tilde{a}/a$ can be large $\tilde{\phi}$ can be much larger than ϕ. Thus, quencher concentration effects can enter at a much lower concentration than for neutral reactants. A corresponding effective medium calculation$^{(22)}$ leads to a result, which for high $\tilde{\phi}$, is $ck_D = ck_D^{(0)}(6\tilde{\phi})$, a quadratic dependence on quencher concentration. Naturally, we must view results in the regime $\tilde{\phi} \gg 1$ with caution.

When we incorporate the effect of partial reaction control, that is, $v = k_0/k_D^{(0)}$ is finite, where recall that k_0 is the activation control rate constant (the contact rate constant), the calculations become very complex. We have carried out$^{(23)}$ a simplified effective medium calculation based on the following assumed form for the fluorophore density $n(r)$ around a given quencher in the presence of a finite concentration of quenchers:

$$n(r) = \left[1 - \frac{v}{v + (1 + \lambda a)} \frac{a}{r} e^{-\lambda(r-a)} \right] n_0 \tag{2.4}$$

where $\lambda = (k_f/D)^{1/2}$ and n_0 is the bulk fluorescence concentration. This form introduces the idea that there is a finite chance of quenching before a specific fluorophore–quencher pair can diffuse together, as becomes more likely for increasing quencher concentration. It is obtained by solution of a screened diffusion equation with the radiation boundary condition$^{(40)}$ to account for finite v. Note that $1/\lambda$ is a length that characterizes the quenching power of the medium, relative to the rate of diffusion, that intervenes between the specific fluorophore–quencher pair.$^{(20)}$ Equation (2.4) is written for neutral reactants but an analogous result can be developed for charged reactants. When the rate constant k_f is obtained from Eq. (2.4), by calculating the fluorophore flux into a given quencher an implicit equation of the form $\lambda = \lambda(\tilde{\phi}, v)$ results. (We use $\tilde{\phi}$ because, for charged reactants, the result based on Eq. (2.4) which produces $\lambda = (\phi, \nu)$ becomes the same function of $\tilde{\phi}$ as in the neutral case).

When this implicit equation is solved for k_f three regimes are found: First, when ν is small, deviations from linear SV behavior are found to be small for all $\tilde{\phi}$. As noted in the Introduction, ν small is the limit where homogeneous kinetics is dominant, so concentration effects should not arise.

Second, when $\nu \to \infty$ (diffusion control) we obtain (basically) the same results as our perturbative and effective medium calculations.(22) In particular, the first correction to the dilute behavior displayed in Eq. (2.3) is regained. Furthermore, k_D also goes to the quadratic dependence found previously, though the coefficient is different. The approximation of the formal effective medium theory is not equivalent to the simple assumed form of the fluorophore density in Eq. (2.4).

Third, for $\nu \geqslant 1$ (finite ν) and high effective quencher concentration $\tilde{\phi} \gg 1$, k_f approaches the *dilute, activation* control result $k_f = k_0 c$. In this case τ_0/τ appears to obey a linear SV law with slope given by the activation control rate constant k_0. This allows the possibility of measuring reaction rates which would ordinarily be dominated by diffusion. Since the chemical information is contained in k_0, this last regime may be of great use to, for example, studies of electron transfer reactions. Many k_0's are so large that they are usually not measurable due to the diffusive step.

So far we have only considered irreversible reactions. In electron transfer reactions a more typical scheme than scheme I would have as the quenching reaction(26)

$$A^* + Q \underset{k_{-D}}{\overset{k_D}{\rightleftharpoons}} A^*Q \xrightarrow{k_0} AQ \tag{II}$$

where the "quenching" step corresponds to the electron transfer step, and A*Q is the quencher–fluorophore complex which can dissociate and diffuse apart. The dilute quencher rate constant is $k_f^{(0)} = k_0 k_D^{(0)}/(k_{-D}^{(0)} + k_0)$. For $\nu_- = k_0/k_{-D}^{(0)}$ small (large) $k_f^{(0)} \to k_0 (k_f^{(0)} \to k_D)$. At finite quencher concentration both k_D and k_{-D} are concentration dependent. These concentration dependences must be related since $K_A = k_D/k_{-D}$ is the association equilibrium constant.

In the Fuoss(27) point of view the association constant K_A is calculated on the basis of equilibrium considerations and yields $K_A = v_s e^{-\beta V(a)}$, where $v_s = 4\pi a^3/3$ is the volume of one encounter pair and $V(a)$ is the value of the potential at the encounter distance. From a dynamical point of view, adopted by Eigen,(28) the rate constant $k_{-D}^{(0)}$ is calculated (for dilute quenchers), by solving the following diffusion problem. One quencher–fluorophore pair, with $n(r = a) = v_s$, diffusing apart to infinity such that $n(r \to \infty) = 0$.

This yields $k_{-D} = 4\pi D\tilde{a}e^{\beta V(a)}v_s$. The ratio k_D/k_{-D} is then K_A as given by Fuoss, and of course the dynamical quantity D cancels in the ratio.

We have calculated k_{-D} at finite quencher concentration on the basis of a similar assumed form for $n(r)$ used in Eq. (2.4) to obtain k_D.(29) This yields a second implicit equation; when one is substituted in the other to obtain k_D/k_{-D} the correct equilibrium form results. We may then use our simple effective medium theory for the reversible reaction case with some confidence.

The three cases of the irreversible reaction have their analogies here. For v small k_f is essentially $k_f^{(0)}$, for $v \to \infty$ diffusion control is obtained and for $v \simeq 1$, $\tilde{\phi}$ large, $k_f \to k_0 K_A c$ which corresponds to the dilute result with the reversible diffusion step preequilibrated before the electron transfer step.

The ionic reactant problems present two difficulties in going beyond the lowest-order corrections to dilute behavior, such as given by Eq. (2.3). First, the diffusion flux now includes the long range force term $-\nabla V$. Thus, the diffusive propagator is not representable in a simple fashion. We have used a transformation of variables adopted by Flannery(30) whereby, in the new variables, an ordinary diffusion equation is obtained but with a space-dependent diffusion "constant." Ignoring this spatial dependence does lead to the Smoluchowski–Debye dilute result for $k_D^{(0)}$. We use this scheme for all quencher concentration. This issue requires more careful treatment. Second, the effective medium approximation is not controlled: this is relevant to the neutral reactant calculations too. Fixman(31) has carried out simulations on the neutral sink problem which show that effective medium calculations are adequate up to rather high sink concentrations [$\phi \sim 0(1)$]. But in the ionic reactant case the effective volume fraction $\tilde{\phi}$ can be much greater than 1 and there is no guidance as to the quality of the effective medium theory in this regime. Simulation of the ionic reactant problem would be very useful.

We have concentrated on steady state results in this discussion. The initial value problem is also of interest to fluorescence quenching. Our calculations(22) show that the initial value problem has the following subtle feature. The time-dependent rate "constant" obtained from the Smoluchowski–Debye equation for dilute sinks is not consistent. Terms of higher order in concentration also contribute to the time-dependent rate; when these are included the time dependence of $k_f^{(0)}(t)$ from the dilute result is exactly canceled and therefore the rate constant to this order is the same as the steady state rate. This point has been made before.(12,13)

Finally, we note that an assumption of our calculations is that the sinks are stationary. For electron scavenging this is not a problem; however, for quenching there is no reason to expect that the quencher mobility is smaller than the fluorophor mobility. When the quenchers are dilute, relative coordinates are appropriate, but for nondilute quenchers relative coordinates do not lead to a simplification of the problem. This remains as an outstanding problem.

3. SURFACE REACTION RATES

Reactions on surfaces are often catalyzed at specific surface sites such as edges and steps.(5) Typically, the steps that influence the overall reaction rate are(32): (1) diffusion of the reactants to the surface, (2) adsorption onto the surface, (3) surface diffusion to active sites, (4) reaction at the site, (5) desorption, and (6) diffusion away from the surface.

The role of surface diffusion to the active sites is not well understood in the above overall process. We have introduced a model that attempts to explore this feature of heterogeneous catalysis. We assume that the surface reactive sites are distributed randomly and idealize them as small absorbing circles. We then have a two-dimensional version of the reaction–diffusion problem.

The steady-state two-dimensional reaction–diffusion system does not have a solution for *dilute* sinks; a collective (finite c) approach must be used from the outset. This can be done, but for the problem at hand it makes more sense to explicitly include the diffusion to and from the surface, which must occur. Thus a Langmuir adsorption–desorption mechanism with rate coefficients k_+ and k_- is incorporated in the surface diffusion equation. Once this is done, a "two-dimensional" steady state exists even for dilute sinks. We have carried out this calculation(33) using the effective medium techniques developed for the three-dimensional reaction–diffusion system.

For *dilute* sinks we find

$$k_D^{(0)} = 2\pi D_0/|\ln \lambda|, \qquad Rc = k_D^{(0)} u_e = 2\phi k_+ N/(\lambda^2 \ln \lambda) \tag{3.1a}$$

$$D/D_0 = 1 + \phi[2 + 1/(\gamma_E + \ln \lambda/2)] \qquad (\lambda \ll 1) \tag{3.1b}$$

and

$$k_D^{(0)} = 4\pi D_0 \lambda, \qquad Rc = 4\phi k_+ N/\lambda \tag{3.2a}$$

$$D/D_0 = 1 + \phi/\lambda \qquad (\lambda \gg 1) \tag{3.2b}$$

In the above equations we have defined the surface fraction of reactive sites of radius "a" as $\phi = \pi a^2 c$, the dimensionless parameter $\lambda^2 = (k_- + k_+ N)/(D_0/a^2)$, with N the bulk concentration of diffusing reactant and $u_e = k_+ N/(k_- + k_+ N)$. Note that λ^2 is the ratio of adsorption/desorption rate to surface diffusion rate. In Eqs. (3.1) and (3.2) we introduce Rc, the loss rate of the reactant. When λ is small, surface diffusion is rapid relative to the adsorption/desorption rate, and Rc increases. The modification of D for small λ is linear in ϕ, while for large λ D is little changed from the zero reactive site result.

The $|\ln \lambda|$ behavior is characteristic of a two-dimensional problem; as λ becomes smaller the effect of two dimensions is more pronounced. This result contrasts with the three-dimensional diffusion control result $ck_D^{(0)} = 4\pi D_0 ac$. The interplay between surface saturation, favored by high bulk reactant concentration, and the relative rates of adsorption/desorption and surface diffusion measured by λ^2 produces this complex behavior. We note that the small λ logarithmic behavior of $k_D^{(0)}$ was also found by Prager and Frisch(34) for a lattice model analog of the continuum problem we have treated.

At higher reactive site concentration c, the correlation among the sites is accounted for with the effective medium theory.(33) The principal conclusions of this analysis are as follows.

For λ^2 large ($\lambda^2 \geqslant 1$) the rate constant at concentration c relative to its dilute c value (k_D/k_D^0), is essentially unchanged. So is D/D_0. For large values of λ^2 the role of surface diffusion is suppressed. Thus each reaction site acts quite independently since the adsorption/desorption process provides reactive material close to the reaction sites without need of surface diffusion. This leads to k_D and D being little changed from their dilute values $k_D^{(0)}$ and D_0.

In contrast, for $\lambda^2 \ll 1$ $k_D/k_D^{(0)}$ shows a substantial enhancement as ϕ increases (to about 30 for $\lambda^2 = 10^{-4}$ at $\phi = 0.6$). The ratio D/D_0 also increases but much more gently (to about 1.5 for $\lambda^2 = 10^{-4}$ at $\phi = 0.6$). When surface diffusion is an important mechanism for transporting reactive material to the catalytic sites, the correlations among the active sites cause a severe distortion in the reactive material density about a given site. This leads to the substantial rate constant increase we find. Note that the rate constant pertains to the entire sample; it yields, when multiplied by the bulk density, the rate of formation of the product. We therefore have found that a much better product yield *per active site* can be obtained by using sufficiently high values of ϕ such that reactive site correlations are significant.

As noted above, the adsorption/desorption terms play a crucial role in the calculation; without them a steady state does not exist for the reactive flux into *one* site. This problem is readily resolved by the observation that low site concentration does not correspond to one site in an infinite medium; the other sites contribute at any concentration and provide a large distance cutoff proportional to intersink spacing. Various authors(35) have solved the two-dimensional "single-site" problem by introducing a reflecting boundary condition at some distance $b \sim 1/\sqrt{c}$ large compared with the sink radius a. They obtain k_D as given by Eq. (3.1a) for small λ^2 with λ^2 now proportional to $(a/b)^2$. (Note that $(a/b)^2 \sim \phi$ since $b \sim 1/\sqrt{c}$). This result can be correctly obtained, and extended to larger ϕ values, from the effective medium results discussed in this section.(36) By letting $\lambda^2 \to 0$ pure surface diffusion is obtained; but in the effective medium formalism the true (but as yet unknown) rate constant appears in the diffusive propagator.(33) This provides the required reactive screening, absent in a perturbative calculation, to lead to a steady state. To the extent that effective medium calculations are accurate, we then obtain the pure two-dimensional rate constant as a function of surface coverage ϕ.

4. ELLIPSOIDS

About 10 years ago Richter and Eigen(6) suggested a mechanism for how a repressor molecule R locates a target site 0 on a DNA molecule. As a first step R diffuses through the solution (a cell interior) and binds nonspecifically to the DNA molecule. R then slides along the surface until it finds the target site 0 and reacts. (Reference 7 summarizes the biochemical implications of this problem.) As long as the dissociation rate of R from the DNA surface is slow compared with the rate of surface sliding, the model is equivalent to the *whole* DNA molecule acting as a sink for the diffusing species R. The crucial experimental observation is that the rate constant $k_D^{(0)}$ can exceed $10^{10}\,\mathrm{l\,mol^{-1}\,s^{-1}}$. If $k_D^{(0)}$ is calculated on the basis of a one step mechanism, where R diffuses directly to the target site 0 and reacts, then using $k_D^{(0)} = 4\pi Da$, where a is an appropriate encounter length for R and 0 leads to $k_D^0 \sim 10^7\text{–}10^8\,\mathrm{l\,mol^{-1}\,s^{-1}}$.(7)

Richter and Eigen(6) pointed out that a long thin sink [modeled as a long prolate ellipsoid of major (minor) semiaxis $A(B)$] has a diffusion-controlled rate constant

$$k_D^{(0)} = 4\pi D_0 A/\ln(2A/B) \qquad (A/B \gg 1) \tag{4.1}$$

Except for the (small) logarithmic correction, a long ellipsoid acts as if it were a *sphere* of radius A. The origin of this effect is the space-filling nature of diffusion; once close to the ellipsoid, a diffuser will sample the neighboring space extensively. The result of Eq. (4.1) then provides a mechanism for defeating diffusional limitation. For $(A/B) \sim 10^3$ a large rate enhancement relative to a spherical sink of the same total volume is predicted, and rates $k_D^{(0)} \sim 10^{10}\,\mathrm{l\,mol^{-1}\,s^{-1}}$ can be achieved.

From the results of Section 2 we can surmise that when the ellipsoid concentration effect must be accounted for, it will enter via an *equivalent* *sphere volume fraction* $\phi = (4\pi/3)\, A^3 c$ rather than the ellipsoid volume fraction $\phi_e = (4\pi/3)\, AB^2 c$. Since $\phi = \phi_e (A/B)^2$, materially dilute ellipsoids $\phi_e \ll 1$ may correspond to effective concentrated spheres $\phi \gtrsim 1$.

Both the rate coefficient k_D and the diffusion coefficient D depend on ϕ_e. Once again an effective medium theory(37) is used to obtain a formal expression for $\Sigma(r)$, the memory function. This is expanded in space gradients to give k_D and D and these equations are solved in a self-consistent fashion. An advantage of the multiple scattering formalism that we use is that the specific sink geometry does not have to be decided until late in the calculation. As long as a surface inverse can be evaluated the problem can be solved. For a prolate ellipsoid the Green's function of the modified Helmholtz equation can be written down in ellipsoidal coordinates,(38) and we have succeeded in inverting it. A solution of the resulting coupled implicit equations for arbitrary (A/B) ratio is possible but requires extensive numerical work. Fortunately, the interesting regime is $(A/B) \gg 1$ and for this limit the analysis can be carried out analytically.

We find that

$$k_D = \left[1 - \frac{\phi}{3} \frac{1}{\ln[(2A/B)^2]} \right]^{-1} k_D^{(0)} \tag{4.2}$$

The inverse factor is D/D_0 and it can produce a divergence in k_D for $\phi_e \ll 1$ for $(A/B) \gg 1$.

Effective medium theories do predict divergences in transport properties.(39) Obviously, the rate k_D cannot become infinite; such a divergence is an indication either that a new physical regime is reached, or the effective medium approximation is failing. More to the point here, we note that $\nu = k_0/k_D^{(0)}$ is finite [k_0 is once again the intrinsic (contact) rate constant of reaction]. As (A/B) gets large so does $k_D^{(0)} \sim A$ and ν is no longer large. So the diffusion control boundary condition fails.

Reanalysis of the problem with finite ν by use again of the radiation boundary condition(40) to account for finite ν in fact leads to the conclusion that D/D_0 does *not* diverge with ϕ. Instead, $k_f \sim k_f^{(0)}$ with a small correction arising from D/D_0. It turns out that D/D_0 depends on the product $(\nu - 1)(B/A)^2$. To obtain the diffusion control regime the condition is $(\nu - 1)(B/A)^2 \gg 1$, *not* $\nu \gg 1$. Consideration of typical values for k_0, A, and B then shows that the physically realistic case is $\nu (B/A)^2 \ll 1$ and we find $[(D - D_0)/D_0] \sim \phi_e$ (not ϕ). Thus the modification to the diffusion coefficient is quite small.

We conclude that for nondilute ellipsoids the rate is actually close to the dilute value, when the ellipsoids are very long $(A/B) \gg 1$. This puts the Richter–Eigen observation on a sound basis since it is just for large (A/B) that we can no longer trust the dilute ellipsoid result.

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