DIFFUSION-CONTROLLED BIMOLECULAR REACTION RATES

THE EFFECT OF ROTATIONAL DIFFUSION AND ORIENTATION CONSTRAINTS

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ABSTRACT A new approach to the calculation of bimolecular association constants for partially diffusion-limited reactions between asymmetric species (e.g. the ligand binding site of a macromolecule covers only a portion of its surface) is presented. The usual formulation, which is almost always analytically intractable, is based on the solution of a steady-state rotational-translational diffusion equation subject to the mixed boundary conditions that (A) the ligand concentration vanishes over the reactive part of the macromolecular surface and (B) the flux vanishes over the remainder. We show that if A is replaced by the requirement that the flux is a constant over the reactive part of the macromolecular surface and this constant is evaluated by requiring the concentration to vanish on the average over the sink region, a whole class of problems can be solved analytically. We consider both the translational and rotational diffusion of the reactants and treat partially diffusion- controlled reactions using the so-called radiation boundary condition. To establish the validity of our approach, we study a simple model using the usual mixed as well as our boundary conditions. As illustrations of our method, we analytically solve and analyze the properties of two models that have been previously studied using numerical methods.

INTRODUCTION

The binding of oxygen to myoglobin, the formation of enzyme-substrate complexes and the binding of hormones to receptors on cell surfaces are examples of bimolecular reactions between asymmetric species. To describe the diffusion-controlled association rate of such reactions, the classic Smoluchowski theory must be extended to handle molecules that are not uniformly reactive over their surfaces. Solc and Stockmayer (1) formally solved the problem for two spherical molecules that have axially symmetric reactive patches covering a portion of their surfaces. They considered rotational diffusion and treated partially diffusion-controlled reactions via the "radiation" boundary condition of Collins and Kimball (2). In a subsequent paper (3), Solc and Stockmayer numerically studied the special case where one of the molecules was uniformly reactive. This model (referred to as the model of Solc and Stockmayer) describes the binding of a small, essentially uniformly reactive, ligand to a macromolecule that has a localized reactive site on its otherwise inert surface. Samson and Deutch (4) reconsidered this model and also presented an approximate solution for the case where the reactive site of the macromolecule is buried. Schmitz and Schurr (5, 6) numerically investigated the reaction between mobile orientable spheres, bearing single reactive sites, with localized hemispherical sites on a plane. This model (referred to as the model of Schmitz and Schurr) is appropriate for the reaction of large asymmetric ligands or proteins with sites localized on a membrane. Hill (7) considered a problem similar to that of Schmitz and Schurr (5) using an approximate transition-state theory approach.

Mathematically, the problems described above are usually formulated as mixed boundary value problems. For example, for the model of Solc and Stockmayer (3) in the completely diffusion-controlled limit, one must solve the steady-state translational-rotational diffusion equation subject to the boundary conditions that the ligand concentration vanishes over the reactive part of the macromolecular surface (A) and the flux vanishes over the remainder (B). Such mixed boundary value problems are almost never analytically tractable and numerical schemes sometimes converge slowly.

In this paper we present a new approach for calculating diffusion-controlled rate constants for bimolecular reactions between asymmetric molecules. A large class of problems can be analytically solved using our method. We take into account both the translational and rotational diffusion of the reactants and treat partially diffusion-controlled reactions via the radiation boundary condition. The basic idea of our approach is to replace the usual boundary conditions, which describe a reactive encounter, by new boundary conditions. Specifically, for the model of Solc and Stockmayer (3), we replace boundary condition A by the requirement that the flux is a constant over the reactive part of the macromolecular surface. After solving the relevant equations, the constant is determined by requiring that the ligand concentration vanishes on the average over the angular range in which the reaction can take place. For partially diffusion-controlled reactions, we require the radiation boundary condition to be satisfied on the average over the reactive part of the macromolecular surface. The rate constants we obtain analytically using our formulation agree very well with the results obtained (numerically in most cases) with the usual boundary conditions. For example, one of the few problems that can be solved analytically using mixed boundary conditions is the reaction of a ligand with a circular site located on an infinite plane. In Appendix A, we solve this problem using our method and show that the difference between the two results is ~7%.

The outline of this paper is as follows: first, we introduce our method and analytically solve a class of problems in which the rotational-translational diffusion equation depends on a radial and an angular coordinate. Next, as special cases of the above development, we present analytic solutions to the models of Solc and Stockmayer (3) and of Schmitz and Schurr (5). We analyze in detail the effect of rotational diffusion and orientational constraints on the rate constants for each of these models. The accuracy of our method is established by a comparison with numerical results. Finally we compare the two models, placing special emphasis on the different orientational constraints imposed on the reactants. One of the interesting results of our analysis is that the model of Solc and Stockmayer (3) (which describes the reaction of a small uniformly reactive ligand with a macromolecule with a localized reactive patch) predicts that the diffusion-controlled rate constant is significantly larger than would be naively expected from surface area considerations (i.e., by multiplying the rate for a uniformly reactive molecule by the fraction of its surface that is reactive).

THEORY

We consider those diffusion-controlled reactions between asymmetric molecules for which the steady-state rotational-translational diffusion equation and the boundary conditions specifying the orientation constraints can be expressed in terms of a radial (r) and an angular coordinate (θ). We will see that the models of Solc and Stockmayer (3) and of Schmitz and Schurr (5) belong to this class. The mathematical formulation to be presented is somewhat abstract and the physical significance of the various parameters and equations will only become apparent later. However, this developmental clearly highlights the mathematics behind our approach and it will allow us to simply solve the two previously mentioned models in a unified manner.

We consider a steady-state rotational-transitional diffusion equation of the form

$$L(r,\theta)c(r,\theta) = 0 \tag{1}$$

where the operator $L(r,\theta)$ has the property that

$$L(r,\theta)P_l(\cos\theta) = L_l(r,\theta)P_l(\cos\theta) \tag{2}$$

where $P_l(x)$ is the lth order Legendre polynomial. The diffusion-limited rate constant is

$$k_{\mathrm{DC}} = \frac{2\pi R^2 D}{c_0}\int_0^{\pi} \left.\frac{\partial c}{\partial r}\right|_{r=R} \sin\theta \mathrm{d}\theta \tag{3}$$

where D is a translational diffusion constant and c_0 is the bulk concentration,

$$c_0 = \lim_{r\to\infty} c(r,\theta). \tag{4}$$

The usual mixed boundary conditions are

$$\left.\frac{\partial c}{\partial r}\right|_{r=R} = \frac{\kappa}{D}c(R,\theta) \qquad 0 \le \theta \le \theta_0 \tag{5}$$

where κ is a measure of the extent of diffusion control ($\kappa \to \infty$ corresponds to the completely diffusion-controlled limit) and

$$\left.\frac{\partial c}{\partial r}\right|_{r=R} = 0 \qquad \theta_0 < \theta \le \pi. \tag{6}$$

Our approach is based on replacing boundary condition Eq. 5 by

$$\left.\frac{\partial c}{\partial r}\right|_{r=R} = Q \qquad 0 \le \theta \le \theta_0 \tag{7}$$

where the constant Q is determined by requiring Eq. 5 to be satisfied on the average in the region $0 \le \theta \le \theta_0$, i.e.,

$$\int_0^{\theta_0} \left.\frac{\partial c}{\partial r}\right|_{r=R} \sin\theta \mathrm{d}\theta = \frac{\kappa}{D}\int_0^{\theta_0} c(R,\theta)\sin\theta \mathrm{d}\theta. \tag{8}$$

The solution to Eq. 1 can be written as

$$c(r,\theta) = \alpha + \sum_{l=0}^{\infty} \mathrm{a}_l f_l(r) P_l(\cos\theta) \tag{9}$$

where $f_l(r)$ are solutions of

$$L_l(r) f_l(r) = 0 \tag{10}$$

which vanish for large r. The boundary condition of Eq. 4 is satisfied when

$$\alpha = c_0. \tag{11}$$

Using the expansion Eq. 9 in boundary conditions Eqs. 6 and 7 we have

$$\begin{aligned} \sum_{l=0}^{\infty} f_l(R)\, a_l P_l(\cos\theta) &= Q \qquad 0 \le \theta \le \theta_0 \\ &= 0 \qquad \theta_0 < 0 \le \pi \end{aligned} \tag{12}$$

Multiplying both sides of this equation by $P_l(\cos\theta)\sin\theta$, integrating from 0 to π and using the orthonormality relation for Legendre polynomials (8)

$$\int_{-1}^{1} P_m(x) P_n(x)\, dx = (m + 1/2)^{-1} \delta_{mn} \tag{13}$$

where $x = \cos\theta$, we find the expansion coefficients a_l to be

$$a_l = Q(l + 1/2)\, [f_l'(R)]^{-1} \int_{\cos\theta_0}^{1} P_l(x)\, dx \tag{14}$$

Q is determined by substituting Eq. 9 (with α given by Eq. 11 and a_l given by Eq. 14) into Eq. 8, evaluating the integrals using (9)

$$P'_{l+1}(x) - P'_{l-1}(x) = (2l + 1) P_l(x) \tag{15}$$

and finally solving for Q. In this way we find

$$Q = \frac{4\kappa(1 - \cos\theta_0) c_0}{4D(1 - \cos\theta_0) - \kappa \sum_{l=0}^{\infty} \frac{f_l(R)[P_{l-1}(\cos\theta_0) - P_{l+1}(\cos\theta_0)]^2}{f_l'(R)(l + 1/2)}} \tag{16}$$

where $P_{-1}(\cos\theta_0) = 1$.

Using boundary conditions Eqs. 6 and 7 in Eq. 3 for k_{DC}, we have

$$k_{DC} = \frac{2\pi D R^2 (1 - \cos\theta_0) Q}{c_0}. \tag{17}$$

Finally, using Eq. 16 for Q, we have

$$k_{DC} = \frac{8\pi R^2 D\kappa (1 - \cos\theta_0)^2}{4D(1 - \cos\theta_0) - \kappa \sum_{l=0}^{\infty} \frac{f_l(R)[P_{l-1}(\cos\theta_0) - P_{l+1}(\cos\theta_0)]^2}{f_l'(R)(l + 1/2)}}. \tag{18}$$

The specific form of $f_l(R)$ depends of course on the nature of the operator L. We are now in a position to apply the above formalism to some specific models.

THE MODEL OF SOLC AND STOCKMAYER

The model of Solc and Stockmayer is shown in Fig. 1. A spherical molecule (A) (e.g. a protein) of radius r_A is centered at the origin of a spherical polar coordinate system. The

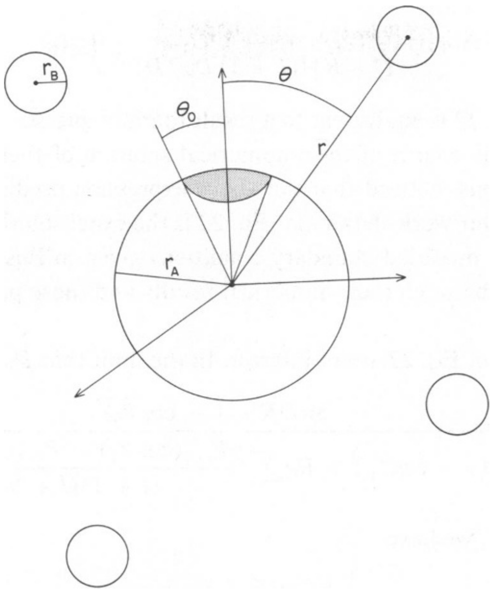

FIGURE 1 The model of Solc and Stockmayer.

surface of this molecule is reactive only over the axially symmetric region $0 < \theta < \theta_0$ with the remainder of the surface being inert. The spherical molecules B (e.g. ligands) of radius r_B are uniformly reactive over their entire surfaces. A reactive encounter may occur only if the center of the B molecule is located at the reaction radius $R = r_A + r_B$ and is in the region $0 < \theta \leq \theta_0$. Not all reactive encounters are successful (i.e. $\kappa \neq \infty$).

Eq. 1 for this model is (1)

$$Lc = D\left(\frac{\partial^2 c}{\partial r^2} + \frac{2}{r}\frac{\partial c}{\partial r}\right) + \left(D_R + \frac{D}{r^2}\right)\frac{1}{\sin\theta}\frac{\partial}{\partial\theta}\left(\sin\theta\frac{\partial c}{\partial\theta}\right) = 0 \tag{19}$$

where D_R is the rotational diffusion constant of the A molecule centered at the origin, D is the sum of the translational diffusion constants of molecules A and B, and $c(r, \theta)$ is the concentration of B molecules at the point (r, θ). The radial functions $f_l(r)$ (see Eq. 10) corresponding to the above operator are modified spherical Bessel functions of the third kind.

$$f_l(r) = (\pi / 2\xi_l r)^{1/2} K_{l+1/2}(\xi_l r) \tag{20}$$

where

$$\xi_l = [l(l+1)D_R/D]^{1/2} \tag{21}$$

Using this in Eq. 18 for k_{DC}, we find

$$k_{DC} = \frac{8\pi D R^2 \kappa (1 - \cos\theta_0)^2}{4D(1 - \cos\theta_0) - \kappa R \sum_{l=0}^{\infty} \frac{[P_{l-1}(\cos\theta_0) - P_{l+1}(\cos\theta_0]^2 K_{l+1/2}(\xi_l^*)}{(l + 1/2)[l K_{l+1/2}(\xi_l^*) - \xi_l^* K_{l+3/2}(\xi_l^*)]}} \tag{22}$$

where

$$\xi_l^* = R[l(l+1)D_R/D]^{1/2}. \tag{23}$$

It is remarkable that Eq. 22 is equivalent to a result literally guessed by Solc and Stockmayer (3). These authors, in the course of their numerical solution of their model using the usual mixed boundary conditions, noticed that the above expression predicted results very close to their numerical values. Our work shows that Eq. 22 is the exact solution for the problem when it is formulated with the modified boundary conditions given in Eqs. 7 and 8. Table I shows the excellent agreement between their numerical results and those predicted by Eq. 22 in the limit that $\kappa \longrightarrow \infty$.

Several limiting cases of Eq. 22 are of interest. In the limit that $D_R \longrightarrow 0$, we have

$$k_{DC} = \frac{8\pi DR^2\kappa(1-\cos\theta_0)^2}{4D(1-\cos\theta_0) + R\kappa\sum_{l=0}^{\infty}\frac{[P_{l-1}(\cos\theta_0) - P_{l+1}(\cos\theta_0)]^2}{(l+1)(l+\frac{1}{2})}}. \tag{24}$$

In the limit that $D_R \longrightarrow \infty$, we have

$$k_{DC} = \frac{4\pi DR^2\kappa(1-\cos\theta_0)}{2D + \kappa R(1-\cos\theta_0)}. \tag{25}$$

If in Eq. 25 we let $\kappa \longrightarrow \infty$, we find

$$k_{DC} = 4\pi DR. \tag{26}$$

TABLE I

COMPARISON OF NUMERICAL RESULTS OBTAINED USING MIXED BOUNDARY CONDITIONS WITH OUR ANALYTICAL RESULTS FOR THE MODEL SHOWN IN FIG. 1

θ_0	k_{eff}‡	k_{eff}§
	$M^{-1}s^{-1}$	$M^{-1}s^{-1}$
20°	1.63×10^9	1.59×10^9
45°	3.73×10^9	3.66×10^9
60°	4.86×10^9	4.78×10^9
90°	6.63×10^9	6.56×10^9
120°	7.73×10^9	7.68×10^9
150°	8.22×10^9	8.21×10^9

($k_{eff} = k_{DC}N/1{,}000$ where N is Avogadro's number).

Results for both cases were calculated using the Stokes-Einstein expressions for D_R and D at $T = 300°K$ and $\eta = 0.008P$ using the value $r_B/r_A = 1.0$.

‡Numerical results of Solc and Stockmayer (3).

§Results calculated from Eq. 22 when $\kappa \longrightarrow \infty$.

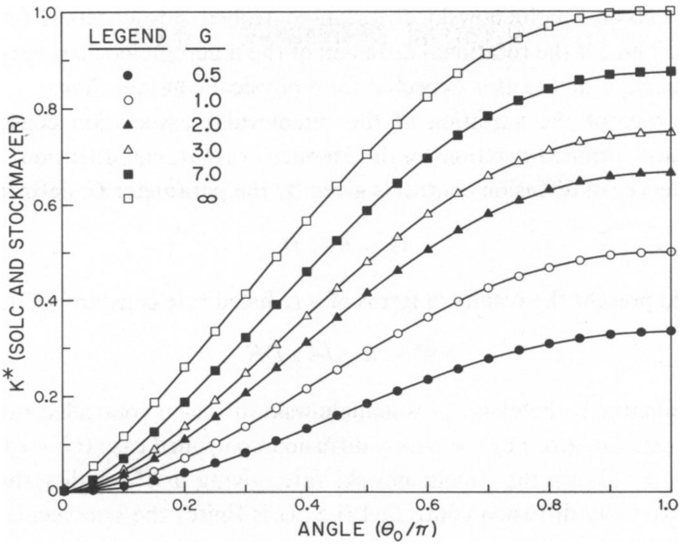

FIGURE 2 The bimolecular association constant for the model in Fig. 1. for partially diffusion-controlled reactions in the absence of rational diffusion. ($G = \kappa R/D$).

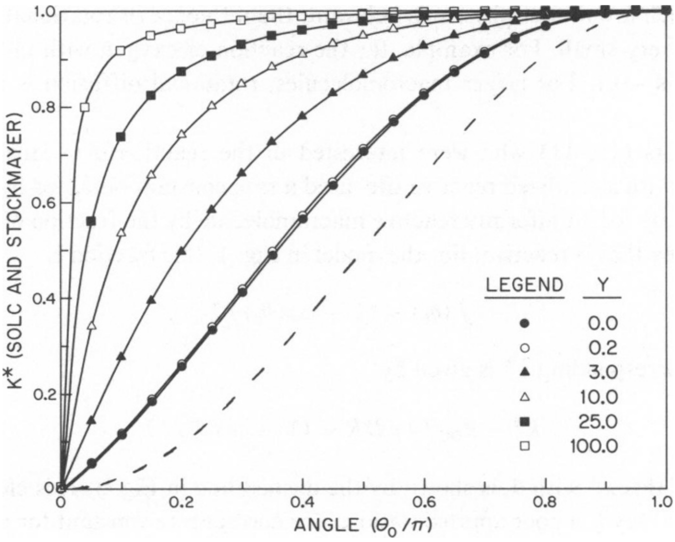

FIGURE 3 The effect of rotational diffusion on the diffusion-limited rate constant ($\kappa \rightarrow \infty$) for the model in Fig. 1. $Y = R(D_R/D)^{1/2}$. The dashed line corresponds to the rate constant obtained by multiplying the Smoluchowski result ($4\pi DR$) for a uniformly reactive sphere by the fraction of the surface area that is reactive [$(1\text{-}\cos\theta_0)/2$] in the absence of rotational diffusion.

This is just the classic Smoluchowski diffusion-controlled rate constant for two uniformly reacting spheres. Thus, if the rotational diffusion of the macromolecule is very fast, it behaves as a uniformly reactive sphere as is expected from physical considerations.

In Fig. 2 we present the variation of the bimolecular association constant with θ_0 for partially diffusion-controlled reactions in the absence of rotational diffusion. A dimensionless measure of the degree of diffusion control is given by the parameter G, defined as

$$G = R\kappa / D. \tag{27}$$

It is convenient to present the results in terms of a reduced rate constant k^* defined as

$$k^* = k_{\text{DC}} / 4\pi DR \tag{28}$$

where the denominator is the classical Smoluchowski diffusion controlled rate for uniformly reactive spheres (see Eq. 26). For the purely diffusion-controlled case ($G = \infty$), the orientation constraint ($\theta_0 \neq \pi$) lowers the Smoluchowski rate, giving a k^* smaller than unity. If the reaction is only partially diffusion controlled (i.e., G is finite) the bimolecular rate is further reduced.

In Fig. 3 we show the influence of rotational diffusion on the variation of k^* with θ_0 for completely diffusion-controlled reactions ($G = \infty$). A dimensionless measure of the importance of rotational diffusion is given by the parameter Y, defined as

$$Y = R(D_{\text{R}} / D)^{1/2} \tag{29}$$

We note that for a reactive site of a given size, rotational diffusion increases the reaction rate. Thus, rotational diffusion of the macromolecule compensates for the partial reactivity of its surface and for large Y, k^* approaches unity even for small values of θ_0. However, for small values of Y, which are in fact physically relevant, the influence of rotational diffusion on the reaction rate is very small. For example, for the reaction of oxygen with myoglobin at room temperature Y is ~0.1. For larger macromolecules, rotational diffusion is clearly even less important.

Several authors (10, 11) who were interested in the reaction of a small ligand with a macromolecule with a localized reactive site, used a rate constant obtained by multiplying the Smoluchowski rate for a uniformly reactive macromolecule by the fraction of the macromolecular surface area that is reactive. For the model in Fig. 1, this fraction is

$$f(\theta_0) = (1 - \cos\theta_0)/2 \tag{30}$$

and hence the corresponding k^* is given by

$$k^* = k_{\text{DC}} / 4\pi DR = (1 - \cos\theta_0)/2. \tag{31}$$

The variation of this k^* with θ_0 is shown by the dashed line in Fig. 3. It is clear that the rate calculated in this way is a poor approximation. The correct rate constant for the model shown in Fig. 1 is significantly larger than the result expected from naive considerations based on the surface area.

To explore this point further, we consider the limit of k_{DC} given by Eq. 22 when $\theta_0 \rightarrow 0$ in the case that $\kappa = \infty$ and $D_{\text{R}} = 0$. We can verify numerically that for very small θ_0, k_{DC} behaves

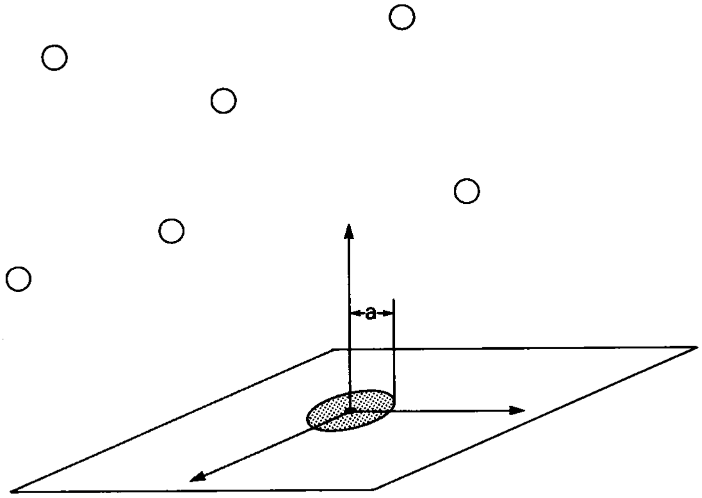

FIGURE 4 A circular reactive site of radius a on an infinite plane. The model of Solc and Stockmayer (Fig. 1) becomes this model in the limit that $\theta_0 \rightarrow 0$, $r_A \gg r_B$ and $a = r_A\theta_0$.

as

$$k_{DC} = \frac{3\pi^2}{8} DR\theta_0 = 3.7\, DR\theta_0. \tag{32}$$

On the other hand, k_{DC} obtained using the fractional surface area argument (see Eq. 31) behaves as

$$k_{DC} = \pi DR\theta_0^2. \tag{33}$$

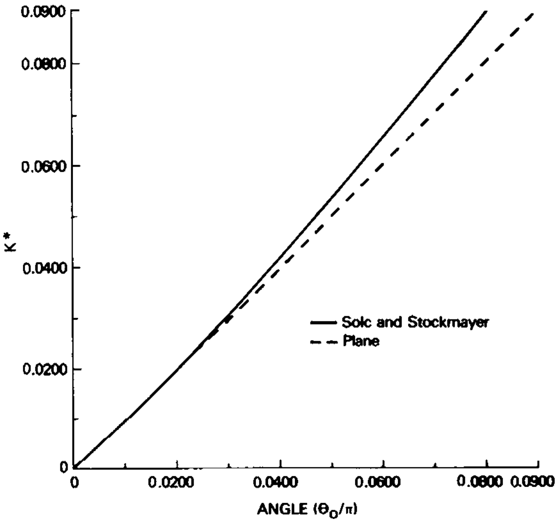

FIGURE 5 Comparison of the small angle behavior of Eq. 24 ($\kappa \rightarrow \infty$) with the plane result of Eq. 35.

We shall now show why the linear dependence of k_{DC} on θ_0 shown in Eq. 32 is to be expected from physical considerations. In the limit r_A becomes large and θ_0 becomes small such that $r_A \theta_0 = a$, we expect the model of Fig. 1 to become identical to the model shown in Fig. 4. In Appendix A, we show the k_{DC} for this model using our modified boundary conditions is

$$k_{DC} = \frac{3\pi^2}{8} D_B a \tag{34}$$

Since $r_A \gg r_B$, $R \rightarrow r_A$ and $D \rightarrow D_B$ in Eq. 32, Eqs. 32 and 34 are indeed identical since $r_A \theta_0 = a$.

The expression for k_{DC}, corresponding to the model in Fig. 4, obtained using the usual mixed boundary conditions is (7)

$$k_{DC} = 4D_B a = 4D_B r_A \theta_0 \tag{35}$$

It turns out, fortuitously, that Eq. 35 describes the small angle behavior of k_{DC} given in Eq. 22 ($\kappa \rightarrow \infty$, $D_R = 0$) over a larger angular range than Eq. 34 (see Fig. 5). We note that Eq. 35 is accurate to within 14% for angles up to 16°.

Up to this point, the development assumed that a reactive encounter may occur only if the center of molecule B is in the angular range $0 < \theta < \theta_0$ (see Fig. 1). If we think of the reactive patch on the macromolecule A as a "hole," it is more reasonable to assume that for a reactive encounter to take place, the entire (not just its center) molecule B must be in the angular range $0 < \theta < \theta_0$. We can adapt all the equations of this section to satisfy this revised boundary condition simply by replacing θ_0 by

$$\theta_0' = \left\{ \left| \theta_0 - \arcsin\left(\frac{r_B}{r_A + r_B}\right) \right| + \left[\theta_0 - \arcsin\left(\frac{r_B}{r_A + r_B}\right) \right] \right\} \Big/ 2 \tag{36}$$

where $|x|$ is the absolute value of x. In particular, Eq. 35 becomes

$$k_{DC} = 2D_B[|a - r_B| + (a - r_B)]. \tag{37}$$

We note that if $r_B > a$, $k_{DC} = 0$ (i.e., the ligand is too large to fit into the hole). On the other hand, if $r_B < a$ then

$$k_{DC} = 4D_B(a - r_B). \tag{38}$$

Thus, the effective radius of the hole is $(a - r_B)$.

THE MODEL OF SCHMITZ AND SCHURR

The model of Schmitz and Schurr is shown in Fig. 6. Orientable spheres of radius R_H suspended in an infinite half-space interact with a site located on the surface of a plane. The translational and rotational diffusion constants of the orientable sphere are D and D_R, respectively. For reaction to occur, the center of the sphere must lie on a hemisphere of radius R_T centered at a distance R_H above the reactive site and the sphere must have the correct orientation ($0 < \theta < \theta_0$). Note that θ is the angle between the symmetry axis of the reactive patch and the normal to the plane.

According to Schmitz and Schurr (5) the appropriate steady-state rotation-translational

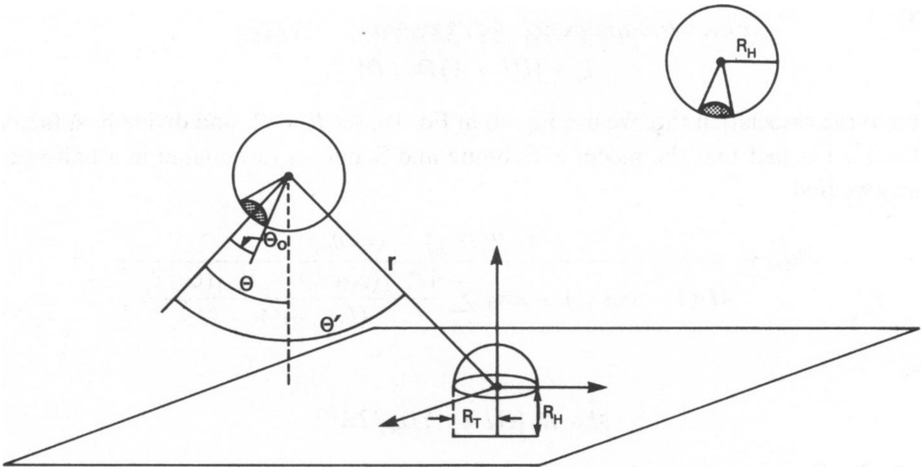

FIGURE 6 The model of Schmitz and Schurr.

diffusion equation corresponding to Eq. 1 is

$$Lc = D\left(\frac{\partial^2 c}{\partial r^2} + \frac{2}{r}\frac{\partial c}{\partial r}\right) + \frac{D_R}{\sin\theta}\frac{\partial}{\partial\theta}\left(\sin\theta\frac{\partial c}{\partial\theta}\right) = 0. \tag{39}$$

The corresponding radial functions $f_l(r)$ (see Eq. 10) are (5)

$$f_l(r) = \frac{e^{-\xi r}}{r} \tag{40}$$

TABLE II

COMPARISON OF NUMERICAL RESULTS OBTAINED USING MIXED BOUNDARY CONDITIONS WITH OUR ANALYTICAL RESULTS FOR THE MODEL SHOWN IN FIG. 6

θ_0	R_H/R_T	k_{eff}‡	k_{eff}§
radians		$M^{-1}\,s^{-1}$	$M^{-1}\,s^{-1}$
1.04	1	4.3×10^8	4.18×10^8
0.30	3.53	1.39×10^7	1.56×10^7
0.20	5.0	4.13×10^6	4.79×10^6
0.149	6.72	1.74×10^6	2.01×10^6
0.143	7.0	1.53×10^6	1.78×10^6
0.098	10.0	5.19×10^5	6.01×10^5
0.048	20.0	6.18×10^4	7.47×10^4

$\kappa = 10R_HD/R_T^2$. ($k_{eff} = k_{DC}N/1{,}000$ where N is Avogadro's number).

Results for both cases were calculated using the Stokes-Einstein expressions for D_R and D at T = 300° and η = 0.0080.

‡Numerical results of Schmitz and Schurr (5).

§Results calculated from Eq. 42.

where

$$\xi_l = [l(l+1)D_R/D]^{1/2}. \tag{41}$$

To obtain the association rate we use Eq. 40 in Eq. 18, set $R = R_T$ and divide by a factor of 2 to allow for the fact that the model of Schmitz and Schurr is formulated in a half-space. In this way we find

$$k_{DC} = \frac{4\pi R_T^2 D\kappa(1 - \cos\theta_0)^2}{4D(1 - \cos\theta_0) + \kappa R_T \sum_{l=0}^{\infty} \frac{[P_{l-1}(\cos\theta_0) - P_{l+1}(\cos\theta_0)]^2}{(l + \frac{1}{2})(1 + \xi_l^*)}} \tag{42}$$

where

$$\xi_l^* = R_T[l(l+1)D_R/D]^{1/2}. \tag{43}$$

In Table II we compare the prediction of Eq. 42 with numerical results obtained by Schmitz and Schurr (5). The agreement is seen to be satisfactory.

Several limiting cases of Eq. 42 are of interest. In the limit that $D_R \rightarrow \infty$ we have

$$k_{DC} = \frac{2\pi D R_T^2 \kappa(1 - \cos\theta_0)}{2D + \kappa R_T(1 - \cos\theta_0)}. \tag{44}$$

If we further let $\kappa \rightarrow \infty$, we find

$$k_{DC} = 2\pi D R_T \tag{45}$$

This is just the classic Smoluchowski diffusion-controlled rate between a uniformly reacting sphere and a hemisphere on an infinite plane.

In the limit that $D_R \rightarrow 0$ Eq. 42 simplifies to

$$k_{DC} = \frac{\pi D R_T^2 \kappa(1 - \cos\theta_0)}{D + R_T\kappa}. \tag{46}$$

If we further let $\kappa \rightarrow \infty$ we find

$$k_{DC} = 2\pi D R_T(1 - \cos\theta_0)/2. \tag{47}$$

This relation has a simple interpretation. It is the Smoluckowski half-space result (see Eq. 45) multiplied by the fraction of orientable spheres which have the proper orientation to react. This fraction is the same as the fraction of reactive surface area. Note that Eq. 47 has a quadratic dependence on θ_0 for small θ_0. This is in contrast to the linear dependence of the rate constant on θ_0 that was obtained for the model of Solc and Stockmayer (3). Recall that for the model of Solc and Stockmayer (in the limit $D_R \rightarrow 0$, $\kappa \rightarrow \infty$) it is not correct simply to multiply the classical Smoluchowski rate by the fraction of active surface area. The reason for this difference is explored in detail in Appendix B.

We now examine the variation of the bimolecular association constant with θ_0 for partially diffusion-controlled reactions in the absence of rotational diffusion (Fig. 7) and the influence of rotational diffusion on the complete diffusion controlled rate (Fig. 8). In analogy to Eq. 28

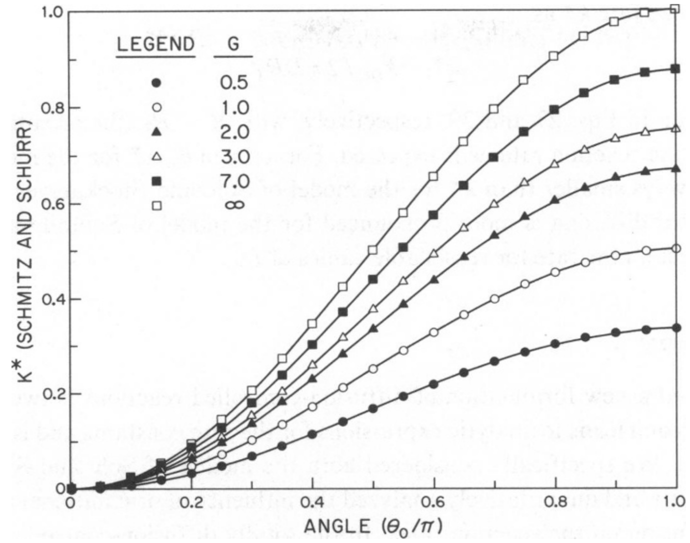

FIGURE 7 The bimolecular association constant for the model in Fig. 6 for partially diffusion-controlled reactions in the absence of rotational diffusion. ($G = \kappa R_T/D$).

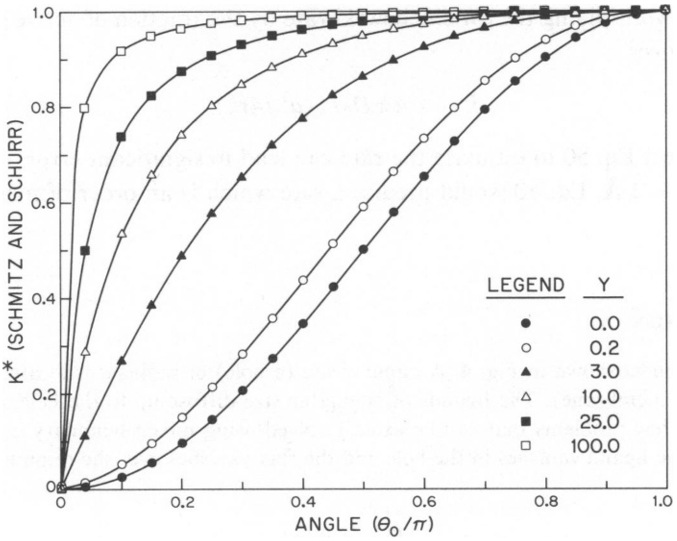

FIGURE 8 The effect of rotational diffusion on the diffusion-limited rate constant ($\kappa \rightarrow \infty$) for the model in Fig. 6. $Y = R_T(D_R/D)^{1/2}$.

we define a reduced rate k^* as

$$k^* = k_{\mathrm{DC}}/2\pi D R_{\mathrm{T}}. \tag{48}$$

G and Y are given in Eqs. 27 and 29, respectively, with $R = R_{\mathrm{T}}$. the orientation constraint ($\theta_0 \neq \pi$) lowers the reaction rate as is expected. For a given θ_0, k^* for the model of Schmitz and Schurr is always smaller than k^* for the model of Solc and Stockmayer. Moreover, the effect of rotational diffusion is more pronounced for the model of Schmitz and Schurr and may have an effect on the rate for reasonable values of D_{R}.

SUMMARY

We have presented a new formulation of diffusion-controlled reactions between asymmetric species. Our approach leads to analytic expressions for the rate constants and is applicable to a variety of models. We specifically considered both the models of Solc and Stockmayer and Schmitz and Schurr and quantitatively analyzed the influence of orientational constraints and of rotational diffusion on the reaction rates. In the totally diffusion-controlled limit with no rotational diffusion, the rate constants of these models can be expressed as the classic Smoluchowski rate for uniformly reactive species multiplied by a reduction factor. The form of this correction factor is model dependent. It is important to note that only for the model of Schmitz and Schurr is this factor the fraction of active surface area of the asymmetric molecule. For the model of Solc and Stockmayer, which describes the binding of small ligands to globular macromolecules, in the limit of small θ_0, $r_{\mathrm{A}} \gg r_{\mathrm{B}}$ and $\kappa \longrightarrow \infty$, the rate constant can be written as (see Eq. 35)

$$k_{\mathrm{DC}} = 4\pi D_{\mathrm{B}} r_{\mathrm{A}}(a/\pi r_{\mathrm{A}}) \tag{49}$$

where $a = r_{\mathrm{A}}\theta_0$. Multiplying the Smoluchowski rate by the fraction of active surface area, on the other hand, gives

$$k'_{\mathrm{DC}} = 4\pi D_{\mathrm{B}} r_{\mathrm{A}}(a^2/4r_{\mathrm{A}}^2). \tag{50}$$

Using the incorrect Eq. 50 to estimate the rate can lead to significant errors. For example, if $r = 20$ Å and $a = 2$ Å, Eq. 50 would predict a rate which is an order of magnitude smaller than it should be.

APPENDIX A

We consider the model shown in Fig. 4. A circular site (a hole) of radius a is located on an otherwise inert plane (e.g. a membrane). The ligands of negligible size diffuse up to the hole and are absorbed. This is one of the few problems that can be exactly solved using mixed boundary conditions (i.e., the concentration of the ligand vanishes in the hole and the flux vanishes over the remainder of the plane). The result is (7)

$$k_{\mathrm{DC}} = 4Da \tag{A1}$$

where D is the diffusion constant of the ligand.

To demonstrate the validity of our approach, we shall now solve this problem using our modified boundary conditions. We use cylindrical coordinates. Mathematically, the problem to be solved is

$$\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial c}{\partial r}\right)+\frac{\partial^2 c}{\partial z^2}=0 \tag{A2}$$

subject to

$$\lim_{\substack{r\to\infty\\ z\to\infty}} c(r,z)=c_0. \tag{A3}$$

$$\left.\frac{\partial c}{\partial z}\right|_{z=0}=Q \qquad r\leq a \tag{A4}$$

$$\left(\frac{\partial c}{\partial z}\right)_{z=0}=0 \qquad r>a \tag{A5}$$

with the constant Q determined from

$$\int_0^a c(r,0)r\,\mathrm{d}r=0. \tag{A6}$$

The diffusion-controlled rate constant is

$$k_{\mathrm{DC}}=\frac{2\pi D}{c_0}\int_0^a\left(\frac{\partial c}{\partial z}\right)_{z=0} r\mathrm{d}r. \tag{A7}$$

The general solution of Eq. A2 is of the form ($z>0$)

$$c=\alpha+\int_0^\infty \mathrm{d}kf(k)l^{-kz}J_0(kr) \tag{A8}$$

where $J_0(x)$ is the zeroth-order Bessel function. Boundary condition Eq. A3 gives

$$\alpha=c_0. \tag{A9}$$

Substituting Eq. A8 into Eqs. A4 and Eq. A5, multiplying by $rJ_0(kr)$, integrating over r and making use of (12)

$$\int_0^\infty J_0(kr)J_0(k'r)r\mathrm{d}r=\frac{1}{k}\delta(k-k') \tag{A10}$$

we find

$$f(k)=-Q\int_0^a J_0(kr)r\mathrm{d}r. \tag{A11}$$

Using Eq. A8 (with α given by Eq. A9 and $f(k)$ given by Eq. A11) in Eq. A6 and evaluating the integrals using (13)

$$\int_0^a J_0(kr)r\mathrm{d}r=\frac{a}{k}J_1(ka) \tag{A12}$$

and (14)

$$\int_0^\infty \frac{J_1^2(ka)dk}{k^2}=4a/3\pi \tag{A13}$$

we find for Q

$$Q = 3\pi c_0/8a. \tag{A14}$$

Using Eq. A4 in A7, we have

$$k_{DC} = \pi a^2 DQ/c_0. \tag{A15}$$

Finally, substituting for Q, we obtain

$$\begin{aligned} k_{DC} &= 3\pi^2 Da/8 \\ &\simeq 3.70\, Da \end{aligned} \tag{A16}$$

which is to be compared with the result in Eq. A1 (i.e. 7.5% difference).

In the above analysis we determined Q from the requirement that the ligand concentration vanishes on the average over the hole (see Eq. A6). Another way of determining Q is to require the ligand concentration to vanish at the center of the hole, that is, replace Eq. A6 by

$$c(0, 0) = 0 \tag{A17}$$

It can be shown that this condition leads to

$$k_{DC} = \pi Da \tag{A18}$$

which differs from the result in Eq. A1 by 21%. Therefore, it is preferable to use boundary condition Eq. A6. It is interesting to note that if, for the model of Solc and Stockmayer in the absence of rotational diffusion, we had determined Q (given in Eq. 7) by using

$$c(R,0) = 0 \tag{A19}$$

instead of Eq. 8, we would obtain an expression for k_{DC} identical to that found by Samson and Deutch (4) using an approach based on the completeness relation for Legendre polynomials.

APPENDIX B

The purpose of this appendix is to discuss in detail the differences between the models of Solc and Stockmayer (3) and Schmitz and Schurr (5). In particular, we will compare the orientation constraints and the effects of rotational diffusion for these two models. To make the comparison easier, we introduce a modified version of the model of Solc and Stockmayer (3), referred to hereafter as model I, in which the asymmetry has been transferred from the macromolecule at the origin to the surrounding ligands and in which chemical reactions only take place in the half-space defined by a plane containing the origin. Model I is geometrically identical to the model of Schmitz and Schurr (hereafter referred to as model II), except that the orientation of the asymmetric molecule is described using the angle θ' relative to the radius vector rather than θ relative to the normal to the plane (see Fig. 6). Solc and Stockmayer (1) showed that the asymmetry can be translated from A molecules to B molecules without altering the form of the diffusion equation. Therefore the diffusion process for model I is still described by Eq. 19. The factor $(D_R + D/r^2)$ multiplying the angular part of Eq. 19 is due to the fact that a change in θ' (see Fig. 6) can come about even by pure translational motion. In model II, however, θ is unaltered by mere translations and in the diffusion process (Eq. 39) the coupling of translational and rotational diffusion is absent. The boundary conditions for models I and II are formally identical; however, since θ and θ' are defined relative to different axes, the effect of the orientation constraints on the rate constant is very different in the two models. Fig. B1 shows an enlarged cross section of the target hemisphere with molecules attached at the reaction radius that are reactive only on a small region of their surfaces, as indicated by the arrow. Fig. B1 is useful for describing the orientation constraints that the molecules must satisfy in order to react for both models I and II. θ' is the orientation angle of model I and θ is the

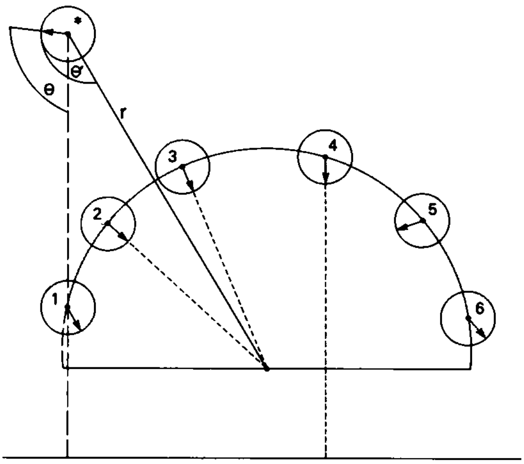

FIGURE B1 A comparison of the orientation constraints for the two models.

orientation angle of model II. Notice that they are defined differently. When a molecule (indicated by *) moves by rotational diffusion alone, both θ and θ' change. If the arrow remains fixed in direction (no rotational diffusion) and ligand * moves by translational diffusion alone, only θ' changes and θ remains unchanged.

The molecules attached to the hemisphere may or may not react in different models because the orientation constraints for both models are different. For model I, in order for a reaction to occur, the asymmetric species must have its center located on the surface of the hemisphere and have its orientation vector coincident with its radius vector (i.e. $\theta' = 0$). In Fig. B1 molecules 2 and 3 are both favorably positioned and oriented for a reaction to occur in model I. For model II, in addition to satisfying the position constraint, a molecule must have its orientation vector normal to the boundary plane for this halfspace (i.e. $\theta = 0$). In Fig. B1 molecule 4 is both positioned and oriented properly for a reaction to occur in model II.

Consider the case where there is no rotational diffusion. Only molecule 4 would react in model II. Since the other molecules cannot change θ by rotational diffusion, no other molecule can satisfy the orientation constraint and then react. For model I, on the other hand, we see that molecules 2 and 3 will react. However, since θ' can change by translational diffusion in this model, all molecules have a chance to react even when there is no rotational diffusion. To see this, consider molecule 6 which is unfavorably oriented for it to react. If it translationally diffuses over to where molecule 2 is (without changing the direction of its orientation vector) it will be favorably oriented and can react. We see that, in the case where there is no rotational diffusion, the orientation constraint of model II is more restrictive than that of model I. As a consequence of this, only the fraction of molecules with the proper orientation can react in model II whereas all the molecules in model I have a chance to react. So we see that model I will have a larger reaction rate than model II for the case $D_R \rightarrow 0$, $\kappa \rightarrow \infty$.

The above considerations also explain why turning on rotational diffusion has a much greater effect on the rate constants of model II (compare $Y = 0.0$ with $Y = 0.2$ in Figs. 3 and 8). In Fig. B1, in the absence of rotational diffusion, only molecule 4 can react in model II whereas all molecules can potentially react in model I. However, if rotational diffusion is turned on all the molecules become potentially reactive in model II also. Thus, rotational diffusion is expected to have a more dramatic effect on the rate constants of model II.

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