Effect of Anisotropic Reactivity on the Rate of Diffusion-Controlled Reactions: Comparative Analysis of the Models of Patches and Hemispheres

A. V. Barzykin* and A. I. Shushin[†]

*National Institute of Materials and Chemical Research, Tsukuba, Ibaraki 305-8565, Japan and [†]Institute of Chemical Physics, Russian Academy of Sciences, GSP-1, Kosygin str. 4, Moscow 117977, Russia

ABSTRACT　A comparative analysis of two models of anisotropic reactivity in bimolecular diffusion-controlled reaction kinetics is presented. One is the conventional model of reactive patches (MRP), where the surface of a molecule is assumed to be reactive over a certain region (circular patch) with the rest of the surface being inert. Another one is the model of reactive hemispheres (MRH), assuming that a molecule is reactive within a certain distance from a point on its surface. The accuracy of the known and newly derived simple analytical expressions for the reaction rate is tested by comparison with the simulation results obtained by the original Brownian dynamics method. These formulas prove to be quite accurate in the practically important limit of strong anisotropy corresponding to small size of the reactive patches or hemispheres. Numerical calculations confirm earlier predictions that the MRP rates are much smaller than the MRH rates for the same radii of the reactive regions, especially in the case where both reacting molecules are anisotropic.

INTRODUCTION

Anisotropic reactivity is a typical feature of the molecules of large size, especially biomolecules. Ligand binding to proteins, enzyme catalysis, self-aggregation of colloids, and polymerization are examples of diffusion-mediated processes involving anisotropically reactive species. Anisotropic reactivity is generally associated with a considerable slowing down of the reaction rate with respect to that for isotropic molecules of the same size (McCammon, 1984). To what extent the rate will be reduced is a nontrivial question that cannot be accounted for on the basis of simple geometrical arguments.

Different models of anisotropic reactivity have been suggested. The most popular one is the model of reactive patches (MRP) (Solc and Stockmayer, 1971, 1973; Schmitz and Schurr, 1972; Schurr and Schmitz, 1976; Hill, 1975; Berg and Purcell, 1977; Shoup et al., 1981; Northrup et al., 1984; Temkin and Yakobson, 1984; Pritchin and Salikhov, 1985; Berg, 1985; Lee and Karplus, 1987; Zwanzig and Szabo, 1991; Traytak, 1994, 1995). It assumes that a portion of the surface of a molecule is reactive while the rest of the surface is inert. The reaction occurs upon diffusive encounter of two molecules with favorable orientations. Usually, to make the problem tractable, the molecules are assumed to be spherical and the reactive patches are assumed to be circular. Although this formulation seems too idealistic from the practical point of view, it still poses quite a complicated mathematical task, even in the case where only one molecule is anisotropic while the other is uniformly

reactive. Exact expression for the reaction rate in this case has been obtained in the limit of small angular size of the patch (Hill, 1975; Berg and Purcell, 1977; Shushin, 1986). In particular, it was found that the rate constant is proportional to the radius of the patch instead of its square, as one would expect from a naive geometrical consideration. To be able to analyze analytically the whole range of angular sizes and to consider even more complicated problems, such as the case of two anisotropic molecules, approximations have been introduced. The most actively used are the closure approximation (Wilemski and Fixman, 1973; Doi, 1975) and the constant flux approximation (Shoup et al., 1981), which are, in fact, proved to be equivalent. The expressions for the rate constant derived in these approximations are still fairly cumbersome and demand certain numerical efforts. Considerable simplification without essential loss of accuracy can be obtained by using further the so-called quasi-chemical approximation, proposed by Solc and Stockmayer (1973) and elaborated upon by Berg (1985).

The MRP offers a clear view on many important features of the manifestation of anisotropic reactivity in the kinetics of diffusion-controlled reactions. However, the assumption of the patch-like reactive regions is not always realistic. The reactivity typically depends on distance between certain reactive centers (atoms or molecular fragments) on surfaces of molecules. Therefore, the reactivity regions are actually expected to be convex rather than of patch-like shape. Importance of the effect of "thickness" of the reaction zone on the diffusion-controlled reaction rate is often overlooked. A particular realization of such a situation is found in the model of reactive hemispheres (MRH) (Shushin, 1986, 1988a). It assumes that a molecule is reactive within a certain distance from a point reactive center on its surface. In other words, the reactive region is hemispherical. The reaction occurs whenever the reactive hemispheres of two different molecules overlap.

A powerful method of local analysis has been developed allowing for rigorous analytical treatment of quite realistic models of anisotropic reactivity and interaction, including both the MRP and the MRH, in the practically most interesting limit of strong anisotropy, where the size of the reactive region is much smaller than the size of the molecule (Shushin, 1986, 1988a, 1988b, 1999). The method is based on a simple observation that, in this limit, the reactive flux is determined by the specific features of relative motion of the molecules in the vicinity of reactive orientations. It was found that the MRH predicts much higher reaction rates than the MRP for reactive regions of similar size. The difference was shown to be especially large in the case of two anisotropic molecules (as much as orders of magnitude for typical values of parameters) (Shushin, 1988a, 1988b, 1999, 2000).

Simultaneously with intensive analytical analysis of different models of anisotropic reactivity, much effort has been devoted to the development of efficient numerical methods aimed to test the existing theories and to explore realistic systems, where analytical solution is not feasible. Among a variety of simulation techniques, the Brownian dynamics (BD) approach is found to be particularly suitable for studying the kinetics of diffusion-influenced reactions. Northrup et al. suggested a BD method to extract the stationary rate constant using the capture probability of one reactant molecule started on a spherical surface enclosing the other reactant molecule (Northrup et al., 1984; McCammon et al., 1986; Luty et al., 1992). Lee and Karplus proposed an alternative BD method based on calculating the time-dependent probability that a pair of reactant molecules, having started in the reaction zone, will be found again in this zone in the absence of reaction (Lee and Karplus, 1987; Yang et al., 1999). Zhou developed an efficient algorithm to calculate the time-dependent rate coefficient via the survival probability of the pair of reactants started in the reaction zone (Zhou, 1990, 1993). He also suggested a method based on the mean residence time in the reaction zone (Zhou, 1998). A weighted-ensemble BD algorithm has been recently proposed by Huber and Kim (1996), which enables one to more efficiently sample the reactive trajectories. Another algorithm is based on averaging the reaction functional over nonreactive BD trajectories in the path-integral sense (Lamm and Schulten, 1983; Zhou and Szabo, 1996a, 1996b). All these methods have recently been compared in practical applications, and their merits are now well understood (Zhou and Szabo, 1996b; Zhou, 1998; Yang et al., 1999).

This paper is concerned with a comparative analysis of the MRP and the MRH. In particular, the accuracy of the known and newly derived simple analytical expressions for the stationary diffusion-controlled reaction rate constant K of neutral spherical molecules is tested by comparison with numerical results obtained using the original BD method. The simulation scheme is based on the exact asymptotic

formula for the long-time behavior of the pair survival probability $S(t)$ (Shushin, 1988b, 1999). We found this method to be most convenient for the purpose of calculating K.

Comparison with the simulation results for the MRP demonstrates that the quasi-chemical approximation provides sufficient accuracy, and there is no practical need to resort to more elaborate approaches. It is also shown that simple formulas derived for the MRH, using the method of local analysis, are quite accurate in the limit of strong anisotropy corresponding to small size of the reactive regions. To reproduce the numerically calculated MRH rates in a wide range of model parameters, simple interpolation formulas in the spirit of the quasi-chemical approximation are proposed. Numerical calculations confirm earlier predictions that the MRP rates are much smaller than the MRH rates for the same radii of the reactive regions, especially in the case where both reacting molecules are anisotropic.

FORMULATION OF THE PROBLEM

General equations

We consider a bimolecular reaction between two spherical molecules A and B of radii R_A and R_B undergoing translational diffusion with a relative diffusion coefficient $D = D_A + D_B$ and rotational diffusion with the coefficients D_{r_A} and D_{r_B}, respectively. Configuration of the reacting pair can be fully described by the relative position $\mathbf{r}$ and individual orientations $\boldsymbol{\Omega}_A$ and $\boldsymbol{\Omega}_B$, combined into a general configuration vector $\mathbf{Q} = (\mathbf{r}, \boldsymbol{\Omega}_A, \boldsymbol{\Omega}_B)$. The steady-state kinetics and, in particular, the rate of the considered bimolecular reaction is determined by the pair distribution function $\rho(\mathbf{Q})$, which satisfies the Smoluchowski equation

$$(\nabla \cdot \mathbf{J}) = 0 \quad \text{with} \quad \mathbf{J} = -\hat{D}(\nabla \rho + \rho \nabla u). \quad (1)$$

Here the operator ∇ represents multidimensional gradient in the curvilinear coordinates $\mathbf{Q}$, $\hat{D}$ is the diffusion matrix expressed in terms of the diffusion coefficients D, D_{r_A} and D_{r_B} (see below), and $u(\mathbf{Q}) = U(\mathbf{Q})/k_B T$ is the intermolecular mean force potential. In this work, we consider reactions without interaction, i.e., with $u(\mathbf{Q}) = 0$.

The function $\rho(\mathbf{Q})$ is defined outside the surface of closest approach $S(\mathbf{Q})$, whose small part $S_r(\mathbf{Q})$ corresponds to reactive orientations. For spherical molecules, $S(\mathbf{Q})$ is determined by $r = |\mathbf{r}| = R = R_A + R_B$. Eq. 1 should be solved with the following boundary conditions:

$$\lim_{r \to \infty} \rho(\mathbf{Q}) = 1, \quad (2)$$

$$(\mathbf{n} \cdot \mathbf{J})|_{\mathbf{Q} \in S_n} = 0, \quad -(\mathbf{n} \cdot \mathbf{J})|_{\mathbf{Q} \in S_r} = \kappa(\mathbf{Q})\rho(\mathbf{Q}), \quad (3)$$

where $S_n = S - S_r$ denotes the nonreactive part of S and $\mathbf{n}$ is the outward vector normal to S. Hereafter, the reactivity at contact $\kappa(\mathbf{Q})$ is assumed to be strong, corresponding to the diffusion-controlled limit.

The reaction rate constant K is expressed in terms of the steady-state reaction flux $\mathbf{J}$,

$$K = 4\pi RD f = -\int_{S_r} dS(\mathbf{n} \cdot \mathbf{J}), \qquad (4)$$

where $K_s = 4\pi RD$ is the Smoluchowski rate constant for uniformly reacting molecules, and f is the so-called steric factor. It is important to note that only the rate constant itself is a real physically sensible kinetic parameter, whereas the steric factor is generally not. The latter can be uniquely defined only in some particular (MRP-like) models of reactivity and for spherical shape of the molecules (see below). The ambiguity of f results from that of K_s, which, for nonspherical molecules, depends not only on translational but also on rotational diffusion coefficients. Nevertheless, the steric factor defined in Eq. 4 appears to be very helpful in the analysis of the problem at hand, especially in constructing interpolation formulas.

Models of reactivity

The shape of the reactive surface S_r, which determines the value of the reaction rate, depends on the model of reactivity. Here we consider two models: the model of reactive patches (MRP) and the model of reactive hemispheres (MRH), as illustrated in Fig. 1.

The model of reactive patches

The conventional MRP (Solc and Stockmayer, 1971, 1973) has been very popular for many years. It is mathematically the simplest model of anisotropic reactivity, which assumes that a circular patch of angular size θ_v and the corresponding radius $r_v = 2R_v \sin(\theta_v/2)$ on the surface of a spherical molecule, $v = A, B$, is reactive while the rest of the surface
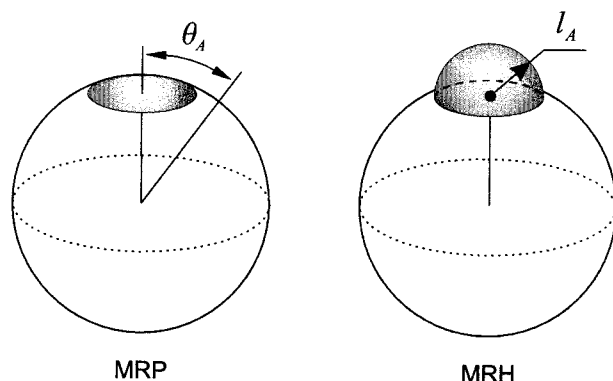

MRP   MRH

FIGURE 1 Schematic picture of two models of anisotropic reactivity, the MRP and the MRH. In the MRP, the surface of a molecule is reactive over a circular patch with the rest of the surface being inert. In the MRH, a molecule is reactive within a certain distance from a point reaction center on its surface.

is inert. The reaction occurs upon diffusive encounter of two molecules with favorable orientations.

The MRP has its range of applicability as a qualitative model but with a certain reservation because it neglects any realistic features of the shape of an active site and does not explicitly account for any physical mechanism of reactivity. Moreover, in this model, the shape of the reactive surface S_r was shown to be nonsmooth (Shushin, 1988a, 1999), i.e., not quite realistic. Noteworthy also is that the physical meaning of the patch radius is not always entirely clear (see below).

The model of reactive hemispheres

The MRH is an alternative model of anisotropic reactivity, recently discussed in detail by one of us (Shushin, 1986, 1988a, 1988b, 1999, 2000). It assumes that a molecule, $v = A, B$, is reactive within a certain distance l_v from a point-reactive center on its surface. The reaction occurs whenever the reactive hemispheres of two different molecules overlap or, equivalently, when the distance l between the reactive centers becomes smaller than $l_r = l_A + l_B$.

The MRH can be regarded as being more realistic than the MRP in a sense that it includes a certain mechanism of reactivity. It can be looked upon as a limiting case of the distance-dependent reaction model (such as electron or excitation transfer) where the reactivity $\kappa(l)$ is a sharply decreasing function of distance between the reactive centers on the surfaces of molecules, e.g., $\kappa(l) = \kappa_0 \exp(-\alpha l)$ with $\alpha \gg 1/R$ (Shushin, 1999). The parameter l_r can be easily estimated using the well-known formulas (Rice, 1985). The model where the reaction is described by the capture of molecules into the potential well $U(l)$ sharply depending on l also reduces to the MRH (Shushin, 1988a, 1999) with l_r being equal to the Onsager radius of $U(l)$.

SIMULATION ALGORITHM

Here we propose a simulation scheme that we found to be most convenient for calculating the stationary diffusion-controlled reaction rate constant K. The method is based on the exact asymptotic formula for the long-time behavior of the pair survival probability $S(t)$ (Shushin, 1988b, 1999),

$$S(t) = S(\infty)\left[1 + \frac{K}{4\pi D}(\pi D t)^{-1/2}\right], \qquad (5)$$

that is valid for $t \gg R^2/D$ for any model of anisotropic reactivity, any shape of molecules, and any model of relative diffusion (except for the case of frozen rotation of both molecules). The parameter $S(\infty)$ defines the total escape probability and depends on the initial condition. It should be emphasized that $S(t)$ is independent of R. This fact can be considered as an additional evidence that Eq. 5 is valid for molecules of any shape. The above universal asymptotic

behavior of the survival probability entails the same universal behavior of the time-dependent rate coefficient (Shushin, 1988b, 1999; Zhou and Szabo, 1996b).

Numerically, it is more efficient to initiate the trajectories near the reaction region and to take larger time steps as the separation between the reactants is increased. The molecules were moved using standard BD algorithms. The trajectories were terminated either when the reaction criteria were satisfied or when a sufficiently large cutoff time was exceeded. For each set of parameters, at least $2 \cdot 10^4$ trajectories were run and the asymptotic decay kinetics of the resulting average survival probability was fit to Eq. 5, as illustrated in Fig. 2. Technical details can be found in Appendix A.

ONE ANISOTROPIC MOLECULE

For definiteness, we assume that molecule A is anisotropic, whereas molecule B is uniformly reactive.

The model of a reactive patch

The reactive patch on the surface of A is assumed to be circular with the angular radius $\theta_A = \theta_0$. For simplicity of notation we also denote $D_{r_A} \equiv D_r$. The resulting mixed boundary-value problem can be reduced to a linear matrix equation of infinite order (see Appendix B), which can be solved numerically to any degree of accuracy by iteration or truncation (Traytak, 1994, 1995). We used this method as an exact reference. A relatively simple and quite accurate expression for the rate was derived within the closure (constant flux) approximation (Shoup et al., 1981). An even simpler but still sufficiently accurate formula suitable for practical applications is provided by the quasi-chemical

approximation (Solc and Stockmayer, 1973; Berg, 1985). We are not going to analyze this approximation in detail but restrict ourselves to outlining its idea and presenting the final result.

The idea of the quasi-chemical approximation is based on the assumption that the reaction kinetics is exponential and that reactive and non-reactive orientations can be treated as two different states of the system. Diffusive reorientation is described as transitions between these two states with the rates proportional to the statistical weights of the corresponding types of orientations. The expression for the combination of the transition rates in the final formula for the overall reaction rate is obtained by comparison with that derived in the closure (constant flux) approximation. An especially simple and accurate formula is obtained with the use of the interpolation expression proposed for this combination by Berg (1985). In so doing, one arrives at the following result for the steric factor:

$$f = \frac{\xi/\sqrt{2} + \sin(\theta_0/2)\cos(\theta_0/2)}{\xi/\sqrt{2} + \cot(\theta_0/2)}, \tag{6}$$

where $\xi = \sqrt{1 + D_r R^2/D}$. In what follows, we will use this formula for comparison with the MRH predictions and simulations.

In the limit of small reactive patch, $\theta_0 \ll 1$, Eq. 6 reduces to

$$f = \xi\theta_0/(2\sqrt{2}), \tag{7}$$

which agrees quite well with the exact formula (Berg and Purcell, 1977; Shushin, 1986),

$$f = \xi\theta_0/\pi. \tag{8}$$

In the opposite limit of isotropic reactivity, $\theta_0 = \pi$, we obtain from Eq. 6 $f = 1$, as expected.

The model of a reactive hemisphere

The case of one anisotropic molecule in the MRH has not been analyzed so far. Therefore, we present some details of this analysis here. The general problem is mathematically very complicated. Fortunately, in the most interesting limit of strongly anisotropic reactivity ($l_A \ll R_A$) it can be markedly simplified by using the method of local analysis (Shushin, 1986, 1988a). This method allows one to reduce the general Eq. 1 in curvilinear coordinates to that in the local Cartesian coordinates in the vicinity of reactive orientations. In the case of one anisotropic molecule, the local Cartesian coordinates are the distance between the surfaces of the molecules, $x = (r - R)/R$, and two angular deviations θ_1 and θ_2 of the center of the reactive hemisphere (on the surface of molecule A) from the intermolecular axis **r** (see Fig. 3) (Shushin, 1999). Here we define the reaction radius
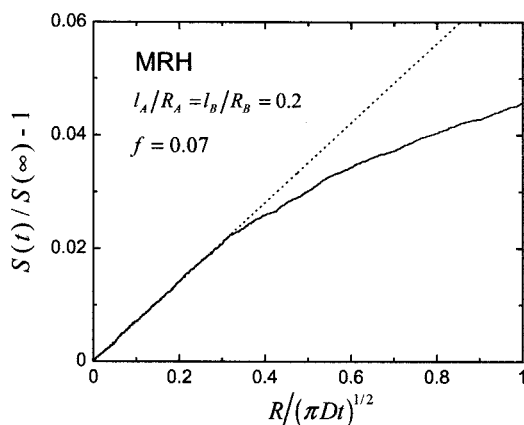
FIGURE 2 Normalized time-dependent survival probability $S(t)/S(\infty) - 1$ as a function of $R/(\pi Dt)^{1/2}$ obtained by averaging $2 \cdot 10^4$ BD trajectories for the MRH with $R_A = R_B$, $D_{r_A}R_A^2/D = D_{r_B}R_B^2/D = 0.75$, and $l_A/R_A = l_B/R_B = 0.2$ (*solid curve*). Dotted line is the result of an asymptotic least-squares fit to Eq. 5.
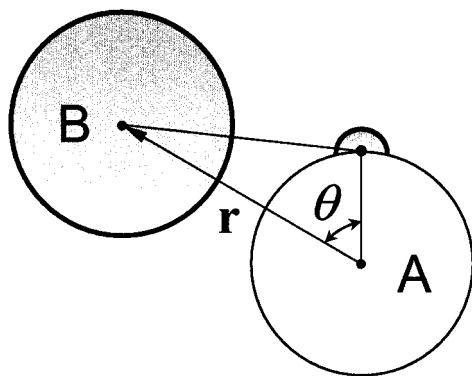
FIGURE 3 The coordinates describing relative orientation of molecules in the case of one anisotropic molecule (*A*).

as $l_r = l_A$ to have a unified notation with the case of two anisotropic molecules.

First, we need to obtain the shape of the reaction surface S_r. The formula for S_r is represented as a dependence of x on $\theta = \sqrt{\theta_1^2 + \theta_2^2}$ (the surface S_r is axially symmetric, i.e., x depends only on the absolute value θ of the angular deviation vector). An equation for $x(\theta)$ can be easily written when taken into account that the surfaces of B and the reactive hemisphere on A are in contact if the distance l between the center of B and the reactive center on A is given by $l = R_B + l_r$ (see Fig. 3), i.e.,

$$\mu_A^2 + (1 + x)^2 - 2\mu_A(1 + x)\cos\theta = (\mu_B + \lambda_r)^2, \quad (9)$$

where

$$\lambda_r = l_r/R \quad \text{and} \quad \mu_v = R_v/R \quad (v = A, B). \quad (10)$$

For relatively large $l_r \lesssim R_A$ the shape of S_r is quite peculiar, but it can be characterized by two length parameters, the height Λ_n (corresponding to $\theta = 0$) and the radius Λ_t of the circular base (corresponding to $x = 0$),

$$\Lambda_n = \lambda_r, \quad (11)$$

$$\Lambda_t = \arccos\{[1 + \mu_A^2 - (\mu_B + \lambda_r)^2]/(2\mu_A)\}. \quad (12)$$

In the limit of strongly anisotropic reactivity, $l_r \ll R_A$ (but for arbitrary R_B), the shape reduces to ellipsoidal,

$$(\mu_B + x)^2 + \mu_A\theta^2 = (\mu_B + \lambda_r)^2. \quad (13)$$

S_r is a segment of this ellipsoid ($x > 0$) with the height λ_n and the radius λ_t of the circular base given by

$$\lambda_n = \lambda_r \quad \text{and} \quad \lambda_t = \sqrt{\lambda_r(2\mu_B + \lambda_r)/\mu_A}. \quad (14)$$

Eq. 14 shows that, for molecules B of small radius $R_B < l_r \ll R_A$, the surface S_r is a hemisphere with $\lambda_t \approx \lambda_n = l_r/R$. However, in the opposite limit of large molecule B, $R_B \gtrsim R_A$, the surface S_r is of a patch-like shape with the base radius much larger than the height, $\lambda_t \approx [(2R_B/R_A)(l_r/R)]^{1/2} \gg$

$\lambda_n = l_r/R$. As the radius R_B is increased, the height λ_n decreases, tending to 0 while λ_t monotonically grows approaching the asymptotic value of $\lambda_t^\infty = \sqrt{2l_r/R_A}$. These estimations show that the characteristic size of the reaction region S_r increases from l_r/R to $\sqrt{2l_r/R_A} \gg l_r/R$ as R_B/R_A is increased from $R_B/R_A \ll 1$ to $R_B/R_A \gg 1$.

It is already clear from the above analysis that, for molecules of comparable size ($R_A \sim R_B$), the MRH rate will be much larger than the MRP rate corresponding to the reactive patch of angular size of the reactive hemisphere ($\sim l_r/R_A$). This interesting and important effect is similar to that predicted for the case of two anisotropic molecules (Shushin, 1988a, 1988b) (see below). Although the assumption of uniform reactivity for a large molecule is, perhaps, not quite realistic, discussion of this case is very instructive and useful for further analysis because the origin of the rate enhancement effect is especially clear.

Relative diffusion of molecules A and B is described as diffusion of a point particle in the local coordinates (θ_1, θ_2, x). The corresponding diffusion matrix $\hat{D}$ is diagonal in these coordinates with

$$D_{11} = D_{22} = D_r + D/R^2 \quad \text{and} \quad D_{xx} = D/R^2. \quad (15)$$

To obtain a fairly accurate estimation for the rate, valid for any relation between λ_n and λ_t, we can approximate S_r by an oblate ellipsoid with semiaxes λ_n and λ_t. In so doing, we get, for the steric factor,

$$f = \tfrac{1}{2}\xi^2\lambda_n(\sigma/\arctan\sigma), \quad (16)$$

where

$$\sigma = \sqrt{\lambda_t^2/(\xi^2\lambda_n^2) - 1}, \quad (17)$$

and $\xi = \sqrt{1 + D_rR^2/D}$, as before. In the limit of $\xi\lambda_n \ll \lambda_t$, corresponding to the patch, one can put $\sigma \to \infty$ and obtain $f = \lambda_t\xi/\pi$ (Shushin, 1986, 1999).

For not very strong anisotropy of reactivity ($l_r \lesssim R_A, R_B$) the size Λ_t of the base of the reaction region appears to be fairly large: $\Lambda_t \sim 1$. In this case, one can estimate the rate by using the quasi-chemical approximation for an effective patch of radius $r_{\text{eff}} = \Lambda_tR$. It is expected to slightly underestimate the rate because it does not take into account the thickness of the reaction region. However, the effect of thickness turns out to be not so strong for realistic values of $D_rR^2/D \sim 1$ (as long as R_B is large).

Another simple way to extend the theory beyond the strict limit of strong anisotropy for arbitrary R_B is by drawing a correspondence between the MRP and the MRH. Thus, the effective patch should be chosen to give the same steric factor as predicted by the method of local analysis (MLA) for the MRH, i.e.,

$$\theta_{\text{eff}} = f_{\text{MLA}}(2\sqrt{2}/\xi), \quad (18)$$

where f_{MLA} is given by Eq. 16. θ_{eff} is then used in Eq. 6 instead of θ_0.

By definition of the steric factor, the rate K is referred to $K_s = 4\pi RD$, which is the reaction rate for uniformly reacting molecules. This formula for K_s is evidently valid in the MRP but it is generally not in the MRH. Clearly, as soon as $l_r > R$, the rate constant $K_s \approx 4\pi Dl_r$. The simplest expression that combines the two limits is $K_s = 4\pi D(R + l_r)$. It should be noted, however, that, in principle, the rate K_s also depends on the ratio D_rR^2/D. We are not going to discuss this problem in more detail because, first, this dependence does not seem to be very strong, and, second, in the most realistic case of $D_rR^2/D \lesssim 1$ and $l_r \lesssim 0.5R$ considered here, the deviation of K_s from $4\pi RD$ is fairly small and can be neglected. The simplest approximation which takes this effect into account yields,

$$f_{MRH} \simeq f_{QC}(\theta_{eff})(1 + l_r/R), \tag{19}$$

where f_{QC} is given by the quasi-chemical Eq. 6.

Comparison with numerical results

The first thing we have to do is to make sure that our BD algorithm actually works. Exact solution for the MRP can serve as a reference. Figure 4 shows that numerical simulations indeed reproduce quite well the dependence of the steric factor on the angular size of the patch for different values of D_rR^2/D. The parameter D_rR^2/D describes the influence of the rotational motions of A. Assuming that friction is of Stokes type (with stick boundary conditions) we have

$$D_rR^2/D = \tfrac{3}{4}(R_B/R_A)(1 + R_B/R_A), \tag{20}$$

i.e., this is just a geometric factor. Thus, for molecules of comparable size, $D_rR^2/D \sim 1$, whereas, for $R_B \ll R_A$, such

as in the case of ligand binding to proteins, $D_rR^2/D \to 0$. Our choice of parameters will be based on these arguments.

The main problem in the comparison of the MRP and the MRH is to relate their size parameters. Although the reaction radius l_r in the MRH can be readily estimated for certain models of distance-dependent reactivity (see the preceding section), the angular size θ_0 of the patch in the MRP is not directly related to the reaction mechanism. In what follows, we assume a reasonable relation,

$$r_A = 2R_A\sin(\theta_0/2) = l_r, \tag{21}$$

i.e., the reaction radius l_r in the MRH is assumed to be equal to the radius r_A of the patch in the MRP.

Figure 5 compares the steric factors $f = K/(4\pi RD)$ calculated for the MRP and the MRH against the numerical results for $R_A = R_B$ and $R_A = 10^3 R_B$ ($D_rR^2/D = 1.5$ and

FIGURE 5 A plot of the BD simulation results for the effective steric factor as a function of the reaction radius in the case of one anisotropic molecule, comparing the MRP (*triangles*) versus the MRH (*circles*) for $R_A = R_B$, $D_rR^2/D = 1.5$ (*top*) and $R_A = 10^3 R_B$, $D_rR^2/D = 0$ (*bottom*). Dashed lines correspond to Eqs. 7 and 16 obtained in the limit of strong anisotropy for the MRP and the MRH, respectively. The correspondence between the MRH- and MRP-size parameters of S_r is established by Eq. 21. Solid lines represent the quasi-chemical approximation, Eqs. 6 and 19. In the case of the MRH, the effective patch size is used as explained in the text.
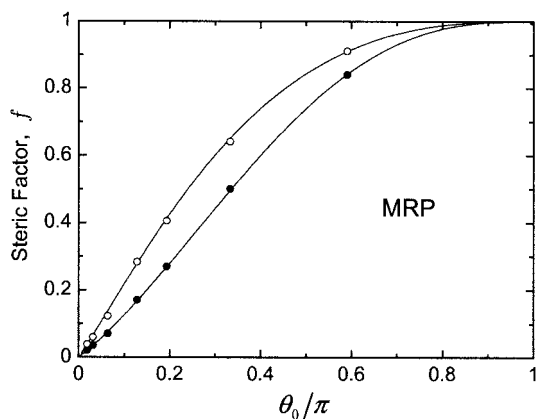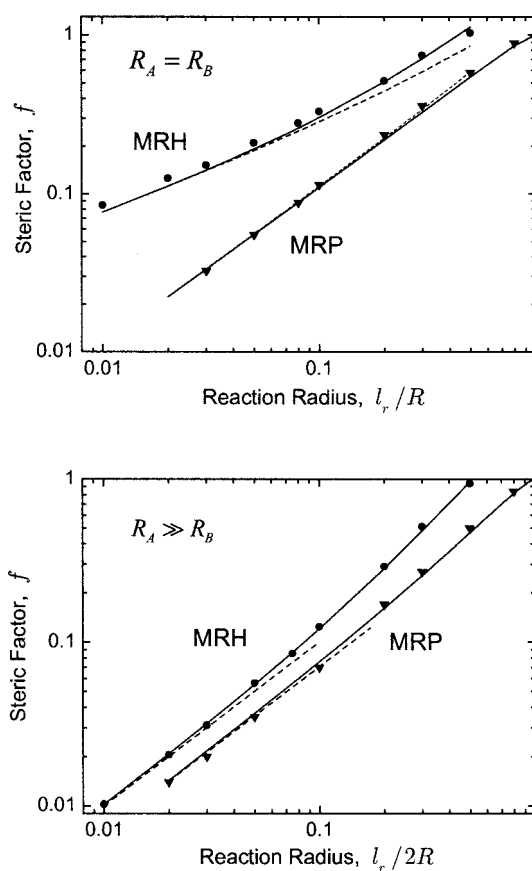

FIGURE 4 BD simulation results (*circles*) versus the exact solution (*lines*) for the effective steric factor in the case of one anisotropic molecule bearing an MRP site as a function of angular size of the patch for $D_rR^2/D = 3$ (*upper curve*) and 0 (*lower curve*).

$\simeq 0$, respectively). It is seen that the MRH rate becomes significantly larger than the MRP rate as the ratio of R_B/R_A is increased. This effect can be attributed solely to the difference in the area of the reactive sites only in the limit of $R_B/R_A \ll 1$.

The accuracy of our simple limiting expression, Eq. 16, for the MRH proves to be quite reasonable in the limit of strongly anisotropic reactivity, $l_r \ll R$. Further improvement of the theory is achieved by using the quasi-chemical interpolation formula, Eq. 19. Good accuracy of the quasi-chemical approximation in the MRP is, in principle, well established (Berg, 1985; Zhou, 1993). Here we just emphasize once again its practical power as applied to the MRH. The effective angular radius θ_{eff} (see Eq. 18), which determines the MRP representation of the MRH steric factor f_{MRH} in Eq. 19, can significantly exceed $\theta_0 = 2 \arcsin(l_r/2R)$ for molecules of comparable size. Note that the steric factor for the MRH can be larger than 1. This is because the effective contact radius becomes larger than R as soon as l_r and R become comparable, as discussed in the preceding subsection.

TWO ANISOTROPIC MOLECULES

The model of reactive patches

No exact analytical expressions are available for the rate constant in the case of two anisotropic molecules. Nevertheless, quite accurate formulas are derived in the closure (constant flux) approximation (Temkin and Yakobson, 1984; Lee and Karplus, 1987). Unfortunately, these formulas are fairly cumbersome and thus not very much convenient for applications. Considerable simplification without essential loss of accuracy is obtained by using the quasi-chemical approximation (Solc and Stockmayer, 1973; Berg, 1985). The basic idea underlying this approximation was briefly discussed in the preceding section. It allows one to express the rate through the parameters obtained for the case of one reactive patch (Berg, 1985):

$$f = F_0/(G_A G_B + \psi), \qquad (22)$$

where $F_0 = F_A F_B$, $F_v = \sin^2(\theta_v/2)$ $(v = A, B)$ are the geometric steric factors,

$$\frac{G_v}{F_v} = \frac{(\xi_v/\sqrt{2}) + \cot(\theta_v/2)}{(\xi_v/\sqrt{2}) + \sin(\theta_v/2)\cos(\theta_v/2)}, \qquad (23)$$

where $\xi_v = \sqrt{1 + D_{rv}R^2/D}$, and

$$\psi = (1 - G_A)(1 - G_B)$$
$$\times \left[1 + \frac{1 - G_A}{G_A - F_A} + \frac{1 - G_B}{G_B - F_B} \right]^{-1}. \qquad (24)$$

In the limit of strongly anisotropic reactivity, $\theta_{A,B} \ll 1$, Eq. 22 reduces to a simple formula:

$$f = (1/8\sqrt{2})\theta_A \theta_B (\xi_B \theta_A + \xi_A \theta_B). \qquad (25)$$

In the opposite limit of isotropic reactivity, $\theta_A = \theta_B = \pi$, Eq. 22 gives $f = 1$, as it should.

In the limit when one of the molecules is much larger than the other ($R_B \gg R_A$, i.e., the surface of B approaches a plane), f is not an appropriate kinetic parameter because $K_s = 4\pi DR$ becomes infinite, though the rate constant K naturally retains its physical meaning. In this case, the reduced rate constant is conveniently defined in terms of a new dimensionless steric factor f_A,

$$K = 4\pi DR_A f_A. \qquad (26)$$

By taking the limit $R_B \to \infty$, one obtains, in the quasi-chemical approximation,

$$f_A = \frac{\rho_B}{2\sqrt{2}} \frac{(\gamma_A \rho_B/2) + \sin(\theta_A/2)\cos(\theta_A/2)}{(\gamma_A \rho_B/2) + \cot(\theta_A/2)}, \qquad (27)$$

where $\rho_B = r_B/R_A$ is the dimensionless parameter, determined by the radius $r_B = R_B \theta_B$ of the reactive patch on the (plane-like) surface of the molecule B, and $\gamma_A = (D_{r_A}R_A^2/D_A)^{1/2}$. For strongly anisotropic molecule A, i.e., for $\theta_A \ll 1$, Eq. 27 simplifies into

$$f_A = (1/8\sqrt{2})\theta_A \rho_B (\theta_A + \gamma_A \rho_B). \qquad (28)$$

The model of reactive hemispheres

Approximate formulas for the reaction rate in the MRH have been derived so far only in the limit of strongly anisotropic reactivity ($l_r \ll R_A, R_B$) using the method of local analysis (Shushin, 1986, 1988a). The details of the derivation have been thoroughly considered in a number of articles (Shushin, 1988a, 1999, 2000). Therefore, here we restrict ourselves to a brief discussion of the principal ideas of the method and present only the final analytical expression, which is to be compared with the simulation results.

In the MLA, one considers relative diffusive motion of the molecules in close vicinity of the reactive orientations, where the system configuration can be represented as a point in five-dimensional space $\mathfrak{M}_5$ of Cartesian coordinates. These coordinates are the normalized distance between the surfaces of the molecules, $x_N = (r - R)/R$, and the angular deviations of the reactive centers from the intermolecular axis $\mathbf{r}$, i.e., the normalized projection vectors $\mathbf{x}_v = \mathbf{z}_v/R_v$ $(v = A, B)$ of the reactive centers onto the plane perpendicular to $\mathbf{r}$, as shown in Fig. 6.

The shape of the reaction region S_r is determined by the condition that the distance l between the reactive centers is equal to the reaction radius, $l = l_r \equiv l_A + l_B$, leading to

$$(\mu_A \mathbf{x}_A - \mu_B \mathbf{x}_B)^2 + (x_N + \tfrac{1}{2}\mu_A x_A^2 + \tfrac{1}{2}\mu_B x_B^2)^2 = \lambda_r^2, \qquad (29)$$

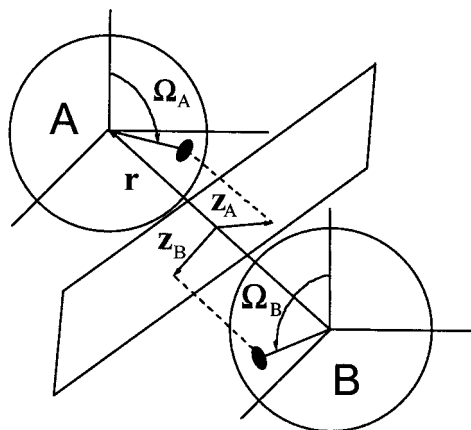where λ_r and μ_v are defined in Eq. 10.

FIGURE 6 The coordinates describing relative orientation in the case of two anisotropic molecules.

FIGURE 7 Schematic picture of the reaction regions in the MRP (*small rectangle*) and the MRH (*ellipsoid*). Big square represents the projection of the boundary in the subspace $\{\mathbf{x}_A, \mathbf{x}_B\}$.

In the limit of strong anisotropy of reactivity ($\lambda_r \ll 1$), a convenient approximate expression for S_r can be obtained in coordinates

$$\mathbf{X}_1 = (\mu_A \mathbf{x}_A - \mu_B \mathbf{x}_B)/\Delta, \tag{30}$$

$$\mathbf{X}_2 = (\mu_B \mathbf{x}_A + \mu_A \mathbf{x}_B)/\Delta, \tag{31}$$

$$X_N = x_N, \tag{32}$$

where $\Delta = \sqrt{\mu_A^2 + \mu_B^2}$. We have

$$\Delta^2 X_1^2 + [X_N + (\tfrac{1}{2}\mu_A \mu_B/\Delta^2)X_2^2]^2 \approx \lambda_r^2. \tag{33}$$

Analysis of this expression shows that the shape of S_r is close to ellipsoidal with semiaxes

$$\lambda_1 = \lambda_r/\Delta, \quad \lambda_2 = \Delta\sqrt{2\lambda_r/(\mu_A \mu_B)} \tag{34}$$

and

$$\lambda_N = \lambda_r.$$

The projection of S_r described by Eq. 33 is shown schematically in Fig. 7.

In **X**-coordinates the diffusion matrix is nondiagonal with the following diagonal elements:

$$D_{11} = (\mu_A^2 D_{r_A} + \mu_B^2 D_{r_B} + D_N)/\Delta^2, \tag{35}$$

$$D_{22} = D_{11} + [(\mu_A - \mu_B)^2 - 1]D_N/\Delta^2, \tag{36}$$

$$D_{NN} = D_N = D/R^2. \tag{37}$$

It can be rigorously shown that nondiagonal elements only weakly affect the absolute value of the reaction rate and thus can be neglected (Shushin, 2000). In fact, nondiagonal diffusion matrix elements are also neglected in the quasi-chemical approximation. The limit of strong anisotropy corresponds to $\lambda_r \ll 1$, and thus $\lambda_2 \gg \lambda_1, \lambda_N$. Therefore, one can use the so-called adiabatic approximation and ne-
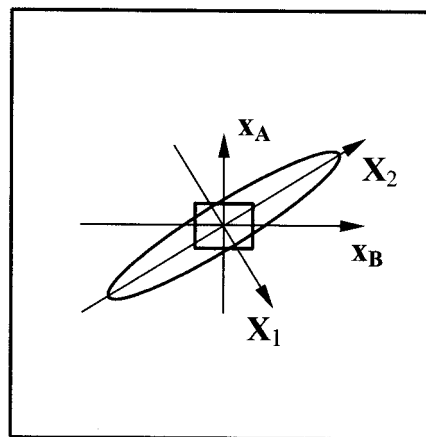
glect the effect of diffusion along the coordinates $\mathbf{X}_2$, i.e., put $D_{22} = 0$ (Shushin, 1988a, 1999). By further assuming, for simplicity, that the reaction region S_r is spherical in the subspace $\{\mathbf{X}_1, X_N\}$ with the radius $\lambda = \lambda_r \approx \lambda_1$ (this approximation leads to a minor underestimation of the rate) one finally obtains (Shushin, 1988a, 1999, 2000)

$$f = \frac{\pi}{16}\left(\frac{l_r^2}{R_A R_B}\right)\frac{\sqrt{\delta(1 + \delta)}}{\ln(\sqrt{1 + \delta} + \sqrt{\delta})}, \tag{38}$$

where

$$\delta = (D_{r_A} R_A^2 + D_{r_B} R_B^2)/D. \tag{39}$$

Eq. 38 predicts the principally different dependence of the reaction rate on the size of the reactive sites than the MRP. In the MRP we had $f \sim l_r^3$ for equal reactive sites, while $f \sim l_r^2$ in the MRH.

As in the case of one anisotropic molecule, we can extend the theory beyond the limit of strong anisotropy by using the quasi-chemical type of approximation. First of all, we notice the similarity of the reaction regions and the diffusion matrices in the MRH and the MRP. The reaction region S_r in the MRP is a patch (the height is $\lambda_N = 0$) of cylinder shape in $\mathfrak{M}_5$ space whose projections in the subspaces $\mathbf{x}_A$ and $\mathbf{x}_B$ are circles of radii $\lambda_\nu = \theta_\nu$ ($\nu = A, B$), whereas the projections onto the planes $\{x_A^{(i)}, x_B^{(k)}\}$ (the superscripts $i, k = 1, 2$ correspond to the coordinates in the two-dimensional subspaces $\mathbf{x}_A$ and $\mathbf{x}_B$) are rectangles, as pictured schematically in Fig. 7 (Shushin, 2000). The diffusion matrix used in the quasi-chemical approximation is diagonal in **x**-coordinates and the diagonal elements are given by

$$D_{\nu\nu} = D_{r_\nu} + D/R^2 \quad \text{and} \quad D_{NN} = D_N. \tag{40}$$

It is easily seen that, by changing S_r of Eq. 33 to the cylinder patch with the corresponding size parameters of Eq. 34 (but with $\lambda_N = 0$), the MRH formulation of the problem be-

comes identical to that in the MRP quasi-chemical approximation. The only difference is in the orthogonal transformation (rotation) of variables in Eqs. 30 and 31. This kind of modification of S_r is known to affect the absolute value of the rate only slightly (Shushin, 1999, 2000). Therefore, the MRH rate should be well approximated by the quasi-chemical expression of Eq. 22 after the corresponding transformation of the size parameters of S_r and the elements of the diffusion matrix,

$$\theta_v \rightarrow \lambda_j \quad \text{and} \quad \xi_v \rightarrow \sqrt{D_{jj}R^2/D}, \quad (41)$$

in which D_{jj} are defined in Eqs. 35–37. The rate is expected to be slightly underestimated in this way because the thickness of the reaction region was neglected.

Again, as in the case of one anisotropic molecule, the reaction rate constant for two uniformly reacting MRP molecules is given by $K_s = 4\pi RD$ only in the limit of strong anisotropy, $l_v \ll R_v$ ($v = A, B$), when the area of the reactive surface S_r in the four-dimensional angular space $\{\mathbf{x}_A, \mathbf{x}_B\}$ is much smaller than $(4\pi)^2$. The correction is expected to be $\sim l_r/R$. In the opposite limit of $l_v > 2R_v$, the molecules are uniformly reactive, though the centers of the reactive spheres are displaced from the centers of (spherical) molecules. This displacement affects the rate only for not very large $l_v \gtrsim 2R_v$. In the limit of $l_v \gg 2R_v$ this effect is negligible and $K_s \approx 4\pi l_r D$. These two estimations for K_s can be combined in a simple interpolation expression $K_s = 4\pi D(R + l_r)$, which is expected to be fairly accurate for relatively slow rotational diffusion, i.e., for $D_{r_{A,B}} \lesssim D/R^2$, typical of real systems.

Comparison with numerical results

Figure 8 compares the steric factors $f = K/(4\pi DR)$ for $R_A = R_B$ and $f_A = K/(4\pi DR_A)$ for $R_B \gg R_A$ calculated in the MRP and the MRH against the numerical results for $l_A = l_B = l_r/2$ (recall that, in the MRH, the rate depends only on $l_r = l_A + l_B$ and the relation $l_A = l_B$ is taken only for definiteness). We assume, as before, that the reaction radius in the MRH is equal to the radius of the patch in the MRP,

$$r_v = 2R_v\sin(\theta_v) = l_v = l_r/2. \quad (42)$$

It is seen that the MRH rate is orders of magnitude larger than the MRP rate when $l_r \ll R$. Analytically predicted scaling behaviors, i.e., $f \sim l_r^2$ for the MRH and $f \sim l_r^3$ for the MRP are well confirmed numerically. In fact, the accuracy of the simple limiting expressions proves to be quite reasonable even beyond the strict limit of strong anisotropy. As we have already pointed out above, further improvement of the theory for large reaction radii in the MRP is achieved by using the quasi-chemical approximation. Surprisingly, however, there is no need for such improvement in the MRH. We must also say that, as far as biological systems are concerned, the size of the macromolecules involved is usu-
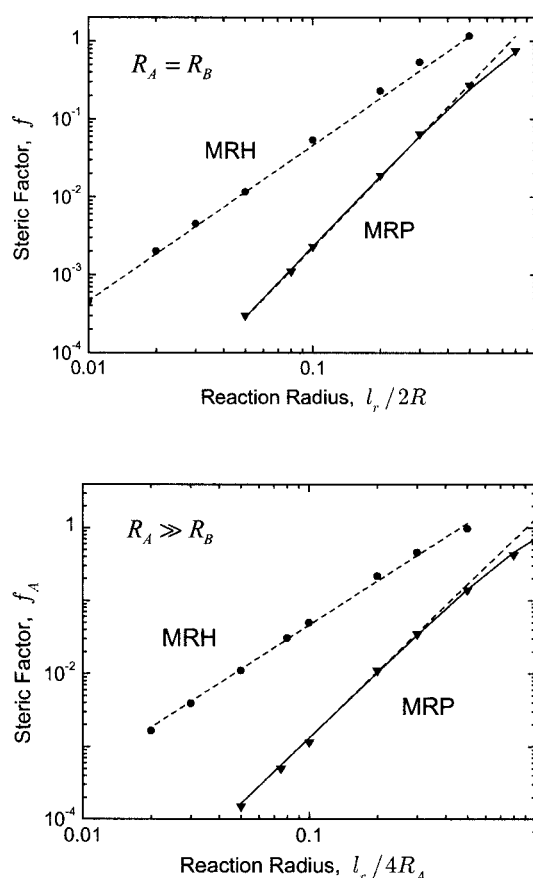

FIGURE 8 A plot of the BD simulation results for the effective steric factors $f = K/(4\pi DR)$ for $R_A = R_B$, $D_{r_A}R_A^2/D = D_{r_B}R_B^2/D = 0.375$ (*top*) and $f_A = K/(4\pi DR_A)$ for $R_B \gg R_A$, $D_{r_B} = D_B = 0$, $D_{r_A}R_A^2/D_A = 0.75$ (*bottom*) as a function of the reaction radius $l_r = l_A + l_B$ in the case of two anisotropic molecules, comparing the MRP (*triangles*) versus the MRH (*circles*) for $l_A = l_B$. The correspondence between the MRH- and MRP-size parameters of S_r is established by Eq. 42. Dashed lines correspond to the limit of strong anisotropy. Solid lines represent the quasi-chemical approximation, Eqs. 22 and 27.

ally much larger than the size of their active sites (and the length scale of the reactive interactions), and hence we expect that the accuracy of Eqs. 25 and 38 should, in any case, be sufficient for practical applications.

CONCLUDING REMARKS

We have considered two models of anisotropic reactivity, MRP and MRH, and tested the accuracy of the known and newly derived simple analytical expressions for the stationary diffusion-controlled reaction rate constant K by comparison with BD results. Our original simulation scheme is based on the exact asymptotic formula for the long-time behavior of the pair survival probability. The proposed method is found to be most convenient for the purpose of calculating K.

In this work, we have primarily focused on the practically important limit of strongly anisotropic reactivity corresponding to small size of the reactive regions. In this limit, theory becomes particularly simple. Important qualitative results of the theoretical analysis can be represented in terms of scaling dependencies of the steric factor on the reaction radius l_r,

$$f \sim l_r^\beta, \qquad (43)$$

for different cases, as summarized in Table 1. These dependencies result from a simple relation for the reaction rate K_n in the n-dimensional space: $K_n \sim D\bar{l}^{n-2}$, where $\bar{l}$ is the average size of the reaction region (Shushin, 1988a, 1999, 2000). This relation can be understood from simple scaling arguments, by taking into account that the product of K_n and the concentration $c_n \sim \bar{l}^{-n}$ of reactants in the n-dimensional space, i.e., $K_n c_n$, should have the dimensionality of inverse time. Correspondingly, the steric factor $f_n \sim \bar{l}^{n-2}$. This relation means that the above-mentioned scaling exponent β is determined by the dimensionality n of the space of relevant coordinates.

In the case of one anisotropic molecule, $n = 3$, and therefore $f \sim \bar{l}$. The difference in β for the MRP and the MRH results from the fact that, in the MRP $\bar{l} \sim l_r$, and thus $\beta_{MRP} = 1$, whereas in the MRH, $\bar{l}$ depends on the relationship between l_r and R, i.e., $\bar{l} \sim l_r$ for $R_B \ll l_r \ll R_A$ ($\beta_{MRH} = 1$) and $\bar{l} \sim \sqrt{R l_r}$ for $l_r \ll R_A$, R_B ($\beta_{MRH} = \frac{1}{2}$). In both of these models, the value of β is smaller than that corresponding to the geometric steric factor, $\beta = 2$.

In the case of two anisotropic molecules, $n = 5$, and thus $f \sim \bar{l}^3$. There is a large variety of possible shapes of the reaction region S_r in the five-dimensional space $\mathfrak{M}_5$, which are determined by the model of reactivity. In the MRP, S_r is of cylindrical shape with similar dimensions $\sim r_v \sim l_r$ along all coordinates (except the height, $r_N = 0$). Therefore, naturally, $\bar{l} \sim l_r$ and hence $f \sim l_r^3$, i.e., $\beta_{MRP} = 3$. It is worth noting that the model of Schmitz and Schurr (1972; Schurr and Schmitz, 1976), which considers the reaction between mobile orientable spheres bearing reactive sites of MRP-type with localized hemispherical sites on a plane, is analogous to the MRP in that the shape of S_r in this model is also a cylinder, and the characteristic dimensions along all co-

ordinates including the height are $\sim l_r$ (Shushin, 1999, 2000). Consequently, the model of Schmitz and Schurr predicts the same scaling dependence $f \sim l_r^3$.

In the MRH, S_r is of an ellipsoid-like shape with small dimensions $l_1 \sim l_r$ in the three-dimensional subspace $\{\mathbf{X}_1, X_N\}$ and large dimensions $l_2 \sim \sqrt{R l_r} \gg l_r$ in the two-dimensional subspace $\{\mathbf{X}_2\}$ (see Eq. 34). According to the predictions of the adiabatic approximation (Shushin, 1988a, 1999, 2000) applied in this limit, the total rate constant K is given by the rate in the three-dimensional subspace, $K_3 \sim l_1$ integrated over the area of S_r in the two-dimensional subspace, $\sim l_2^2$. Therefore, $K \sim l_1 l_2^2$ (i.e., $\bar{l} = \sqrt{l_1 l_2^2}$), and finally one obtains, $f \sim l_1 l_2^2 \sim l_r^2$, which means that $\beta_{MRH} = 2$. Noteworthy is that the reason why the size of S_r in the two-dimensional subspace is large and the reason why the size of the effective patch in the MRH for one anisotropic molecule with $l_r \ll R_A$, R_B is large are essentially of the same origin.

Similar to the case of one anisotropic molecule, both the MRP and the MRH predict the value of the scaling exponent β smaller than that corresponding to the geometric steric factor, $\beta = 4$.

Comparison with the simulation results has demonstrated very good accuracy of the simple limiting expressions, even beyond the strict limit of strong anisotropy. Further improvement of the theory for large reaction radii is achieved by using the quasi-chemical approximation. This simple approximation provides quite sufficient accuracy, and, thus, we believe that there is no practical need to resort to more elaborate approaches.

We could see, and it is actually well established, that subtle interplay between orientational and translational diffusive motion of nonuniformly reactive molecules leads to a considerable enhancement of the reaction rate with respect to a purely geometrical estimate. The fact that the MRH rates significantly exceed the MRP rates offers a new insight into the problem of anisotropic reactivity, emphasizing the role of the third dimension of an active site normal to the surface of the molecule. In testing their BD simulation procedure, Yang et al. (1999) have recently witnessed an appreciable increase of the reaction rate with the thickness of the reaction zone. However, because their focus was on the MRP, they did not study this effect but extrapolated the observed dependence to zero thickness. As mentioned in the Introduction, the reactive regions are generally expected to be convex rather than of patch-like shape. This is a consequence of the distance-dependent nature of the reactive interactions. In our opinion, this effect is at least partially responsible for the experimentally observed large rate of certain biological association processes. It is known that, for many enzymes where the catalytic region constitutes only a small fraction of the surface, substrate association can still take place at very high rates as if a much larger fraction of the enzyme were the target (Chou and Zhou, 1982; Berg, 1985). Another example is protein–protein association

TABLE 1 Scaling exponent β in the dependence of the steric factor f on the reaction radius l_r, i.e., $f \sim l_r^\beta$, in the limit of strongly anisotropic reactivity ($l_r \ll R$) for different models

Model	Geometric	MRP	MRH
One anisotropic molecule, $R_B \ll l_r \ll R_A$	2	1	1
One anisotropic molecule, $l_r \ll R_A, R_B$	2	1	½
Two anisotropic molecules, $l_r \ll R_A, R_B$	4	3	2

The corresponding definition of patch sizes is given in Eqs. 21 and 42.

(Northrup and Ericksson, 1992; Zhou, 1993; Vijayakumar et al., 1998). The proposed mechanisms of these accelerated association phenomena were based on the MRP supplemented by a certain guiding attractive potential. The MRH reveals a different possible reason for the rate enhancement. Estimations show (Shushin, 1999) that the effect of potential and the distance-dependent reaction mechanism can be of the same order. Detailed comparison of the theory versus simulations for anisotropic reactions in the presence of the interaction potential will be reported elsewhere.

APPENDIX A:
SIMULATION DETAILS

Here we describe the details of our BD simulation scheme. We chose the initial separation between the centers of the reactant molecules to be

$$r_0 = R + \min(0.05R, l_A, l_B) + i_A l_A + i_B l_B, \quad (A1)$$

where i_v is the model index: 0 for the MRP, 1 for the MRH. The molecules were initially oriented to face each other's reactive sites: $\theta = 0$ for A and $\theta = \pi$ for B, and the relative angular position of the center of B with respect to A was sampled randomly within $\theta \leq \theta_A \equiv \arccos[1 - l_A^2/(2R_A^2)]$ (assuming that $l_A \leq l_B$ without loss of generality). The molecules were then moved using standard BD algorithms based on the discretized translational and rotational ordinary Langevin equations (Ermak and McCammon, 1978; Kim and Lee, 1990):

$$\mathbf{r}(t + \Delta t) = \mathbf{r}(t) + (2D\Delta t)^{1/2}\mathbf{G}, \quad (A2)$$

$$\mathbf{e}_v(t + \Delta t) = \mathbf{e}_v(t) + (2D_{r_v}\Delta t)^{1/2}\mathbf{G} \times \mathbf{e}_v(t), \quad (A3)$$

where $\mathbf{G}$ is the vector of Gaussian random numbers with mean zero and variance 1, and $\mathbf{e}_v$ denotes the body-fixed unit vector for molecule $v = A, B$. To improve the efficiency of the algorithm, larger time steps were taken as the separation between the reactants increased:

$$\Delta t = \Delta t_0 \quad \text{for } r \leq r_0, \quad (A4)$$

$$\Delta t = \Delta t_0 + 10^{-2}\frac{(r - r_0)^2}{2D} \quad \text{for } r > r_0, \quad (A5)$$

where

$$\Delta t_0 = 10^{-2}\frac{[\min(0.05R, l_A, l_B)]^2}{2\max(D, D_{r_A}R_A^2, D_{r_B}R_B^2)}. \quad (A6)$$

Trajectories were terminated either when the reaction criteria were satisfied or when a sufficiently large cutoff time of $10^4 D/R^2$ was exceeded. The reaction occurs in the MRP as soon as the conditions

$$r \leq R, \quad \mathbf{n} \cdot \mathbf{e}_A \geq \cos\theta_A, \quad -\mathbf{n} \cdot \mathbf{e}_B \geq \cos\theta_B, \quad (A7)$$

where $\mathbf{n} = \mathbf{r}/r$, are satisfied simultaneously. In the MRH, the reaction criterion is given by

$$|\mathbf{r} + R_B\mathbf{e}_B - R_A\mathbf{e}_A| \leq l_A + l_B. \quad (A8)$$

The reflecting boundary condition at encounter was treated by returning the particles back to their previous orientations and relative position if they penetrated each other ($r < R$) while no reaction took place. For each set of parameters, at least $2 \cdot 10^4$ trajectories were run and the asymptotic decay kinetics of the resulting average survival probability was fit to Eq. 5.

APPENDIX B:
EXACT SOLUTION OF THE MRP FOR ONE ANISOTROPIC MOLECULE

The problem of diffusion-controlled reaction kinetics between a spherical molecule A bearing a reactive circular patch and a uniformly reactive spherical molecule B is mathematically formulated as a mixed boundary-value problem in spherical coordinates. It can be solved, or at least brought to a simple form suitable for numerical analysis, by using the method of dual series relations (Sneddon, 1966). This approach has been used recently by Traytak (1994, 1995) to calculate the steric factor in the absence of rotational diffusion. The general problem with rotations can be treated in quite a similar fashion. Here we present an outline of this solution.

By substituting the general solution of the stationary diffusion equation into the mixed boundary condition, the problem can be reduced to the following dual series relations for the coefficients X_l:

$$\sum_{l=0}^{\infty}(2l + 1)X_l P_l(z) = 0 \quad \text{for } \theta > \theta_0, \quad (B1)$$

$$\sum_{l=0}^{\infty}(1 - q_l)X_l P_l(z) = \frac{1}{2} \quad \text{for } 0 \leq \theta \leq \theta_0, \quad (B2)$$

where

$$q_l = 1 - \frac{l + \frac{1}{2}}{\eta_l K_{l+3/2}(\eta_l)/K_{l+1/2}(\eta_l) - l}, \quad (B3)$$

$\eta_l = \sqrt{l(l + 1)D_r R^2/D}$, $z = \cos\theta$, $K_{l+1/2}(x)$ are modified spherical Bessel functions, and $P_l(z)$ are Legendre polynomials. The steric factor is given by

$$f = X_0. \quad (B4)$$

Using the known exact solution for the canonical form of the dual series relations, the original system can be brought to a simple linear matrix equation,

$$(\mathbf{I} - \mathbf{H} \cdot \mathbf{Q}) \cdot \mathbf{X} = \mathbf{X}^0, \quad (B5)$$

where $\mathbf{I}$ is the identity matrix, $Q_{nm} = \delta_{nm}q_n$,

$$\pi H_{nm} = \frac{\sin[(n + m + 1)\theta_0]}{n + m + 1}$$

$$+ \frac{\sin[(n - m)\theta_0]}{n - m}(1 - \delta_{nm}) + \theta_0\delta_{nm}, \quad (B6)$$

$X_n^0 = \frac{1}{2}H_{n0}$, and δ_{nm} denotes the Kronecker delta. In the limit of $D_r \rightarrow 0$, we have $q_l = [2(l + 1)]^{-1}$.

The solution $\mathbf{X}$ can be obtained numerically to any degree of accuracy by truncating the system in Eq. B5. The convergence of the obtained solution is known to be quite fast. In reality (for $D_r R^2/D \lesssim 1$), it is sufficient to take $N \simeq 20$.

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