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DIFFUSION-CONTROLLED MEAN REACTION TIMES IN BIOLOGICAL SYSTEMS WITH ELLIPTICAL SYMMETRY *

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The mean reaction (encounter or absorption) time is calculated in terms of the system size and reaction probability parameters for three-dimensional systems with diffusion-controlled dynamics and in which there is spherical, prolate spheroidal or oblate spheroidal geometry. Analytical and numerical comparisons are made among the three geometries. For completeness, similar results are derived for a two-dimensional elliptically symmetrical system, and the probability of non-absorption (or reaction) is found for a semi-infinite three-dimensional space with prolate or oblate spheroidal symmetry.

Among the outstanding problems in molecular biology is the question of the dynamics of biological processes. That is, by what physical mechanisms do biologically important molecules carry out the movements necessary to their functions in living systems. As emphasized by Eigen [1], one expects diffusional encounters between two molecular species to play an important role in biochemical reactions and thus in their dynamics. Diffusional encounters between subunits of the same protein molecule are also expected to be important in protein folding dynamics [2]. In addition, diffusional encounters between bacterial receptors and various molecules are important in bacterial chemotaxis [3,4]. A quantity of physical interest for finite systems of the above kind is the mean encounter or absorption time for the two species to diffuse together and interact strongly (coalesce). This characteristic time has been estimated for various physical situations involving systems with real or assumed spherical geometry. As emphasized, however, by Richter and Eigen [1,5], the assumption of spherical symmetry applies well to small molecular species but may be quite far from reality for biological macromolecules such as nucleic acids and bacterial surfaces, in which prolate or oblate spheroidal geometry may be more appropriate. Therefore, the main purpose of this note is to extend the known spherically symmetrical derivation and results for the mean encounter time, τ, to elliptically symmetrical geometry in two and particularly in three-dimensions (prolate and oblate spheroids) by deriving the exact mean absorption time for a quasi one-dimensional diffusion-encounter problem in which the single variable is one of the spheroidal coordinates (the one corresponding to the radius for spherical symmetry), in which the diffusion space is finite and bounded by an inner and an outer elliptically symmetrical surface, in which there is complete reflection at the outer surface and in which there is partial or complete absorption at the inner surface (target) with each encounter.

In the systems to be considered, the dynamics is that of an object subject to random, dissipative forces, as well as, perhaps, conservative forces derivable from a potential energy function. Such a classical, dynamical system is governed by the Langevin equation, which, in the overdamped regime of small diffusion coefficients of interest here, is equivalent to the Smoluchowski equation [6] with the form

$$\partial\rho/\partial t = \nabla\cdot\{D(\nabla\rho + \rho\nabla V)\}, \tag{1}$$

where $\rho(x, x_0, t)$ is the probability density for finding

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the particle at position x at time t, if it had been at x_0 at $t = 0$. D is the (possibly position dependent) diffusion coefficient and $V(x)$ is the potential energy of interaction (in units of $k_B T$ where k_B is Boltzmann's constant and T the absolute temperature) between the diffusing particle and the target. At $t = 0$ the probability density is considered to be a δ-function center at x_0. The boundary conditions on the solution to eq. (1) are written in terms of ρ itself and the probability current density $J(x)$ which is proportional to $\nabla\rho + \rho\nabla V$. At $x = x_b$, the outer surface, the boundary condition of Adam and Delbrück [8] is for complete reflection, that is $J_n(x_b)$, the normal component of J, is zero. At $x = x_a$, the inner, absorbing surface, the target, the condition for complete absorption is $\rho = 0$. If the probability of absorption at each encounter with the target is less than one, a mixed boundary condition connecting the probability density and probability current density at $x = x_a$ is to be used.

Since the diffusion equation in spheroidal coordinates would be extremely difficult to solve directly in order to obtain the mean encounter (absorption) time, and because a complete solution to the diffusion problem is, in fact, not needed to calculate τ, one may proceed from eq. (1) in the following way. Let $N(x_0, t)$ be the probability of finding the diffusion particle somewhere in the space (x_a, x_b) at time t, starting from x_0. That is,

$$N(x_0,t) = \int_{x_a}^{x_b} \mathrm{d}^3x\, \rho(x,x_0,t). \qquad (2)$$

As one may readily verify, $N(x_0, t)$ satisfies the differential equation in x_0 adjoint to eq. (1):

$$\partial N/\partial t = \nabla_0 \cdot (D\nabla_0 N) - D(\nabla_0 V)\cdot(\nabla_0 N). \qquad (3)$$

With $N(x_0, 0)$ normalized to one, $1 - N(x_0, t)$ is the probability of absorption before time t and $\partial(1-N)/\partial t$ is the fraction of particles leaving the diffusion space due to absorption at x_a between t and $t + \mathrm{d}t$. Hence the mean absorption (encounter) time $\tau(x_0)$ is given by

$$\tau(x_0) = -\int_0^\infty \mathrm{d}t\, t\, \partial N/\partial t = \int_0^\infty \mathrm{d}t\, N(x_0,t). \qquad (4)$$

Application of eq. (3) to eq. (4) gives one an ordinary differential equation [7] for $\tau(x_0)$ which may be solved exactly in some cases of physical interest as outlined below.

The three geometries for which the most complete results will be given in this note are radial diffusion in the space between two concentric spherical shells of inner radius r_a, the target, and outer radius r_b for which some results have already been presented in the literature [2,5,8,9] and with which comparisons may be made; diffusion in the variable ξ (of prolate spheroidal shells of inner "size" ξ_a and outer "size" ξ_b; and diffusion in the variable σ (of oblate spheroidal coordinates [10]) in the space between an inner oblate shell of "size" σ_a and a confocal outer shell of "size" σ_b. The three coordinates systems are tabulated in table 1 along with the connections between the spheroidal size variables and the semimajor and semiminor axes of the coresponding ellipses from which the spheroids are generated. Two important geometrical quantities for diffusion–collision processes are the volume of the diffusion space itself and the surface area of the target (the inner surface defined by r_a, ξ_a or σ_a). Listed in table 2 are the surface area and volume for each of the three figures of revolution considered here.

As indicated above, the mean absorption or encounter time τ may be shown to satisfy a differential equation in the initial position x_0. For the one variable problems considered in this note, for a constant diffusion coefficient and for a potential energy depending only on the single variable, the differential equations may be readily derived and are given in table 3. These differential equations may be solved in a number of situations of physical interest to obtain τ, when the potential energy function and the boundary conditions are given. The most general solution is obtained when V is unspecified and the boundary conditions are $\mathrm{d}\tau/\mathrm{d}x_0 = 0, x_0 = x_b$ (for complete reflection of the diffusing particle) and $\gamma\mathrm{d}\tau/\mathrm{d}x_0 = (\beta/l)\tau$ at $x_0 = x_a$. This boundary condition applies when the diffusing particle has a probability of absorption β and a probability of reflection γ at the target surface. The parameter l has units of length. Its interpretation depends on the physical situation causing partial absorption. Different possibilities are discussed in refs. [4] and [9]. For complete absorption at the target surface $\beta = 1, \gamma = 0$ and l does not enter the calculation of τ. Table 4 lists the general solutions for the three geo-

Table 1
Coordinates

Figure	Coordinates			Major and minor axes a)
Sphere	$r \geqslant 0,$	$0 \leqslant \theta \leqslant \pi,$	$0 \leqslant \varphi \leqslant 2\pi$	$r_{maj} = r_{min} = r$
Prolate spheroid	$\xi \geqslant 1,$	$-1 \leqslant \eta \leqslant 1,$	$0 \leqslant \varphi \leqslant 2\pi$	$r_{maj} = f\xi$ $r_{min} = f\sqrt{\xi^2 - 1}$
Oblate spheroid	$\sigma \geqslant 0,$	$-1 \leqslant \tau \leqslant 1,$	$0 \leqslant \varphi \leqslant 2\pi$	$r_{maj} = f\sqrt{\sigma^2 + 1}$ $r_{min} = f\sigma$

a) The foci for the spheroids are at $x = 0, y = 0, z = \pm f$ and the z-axis is the axis of revolution for the three figures.

Table 2
Surface area and volume

Figure	Surface area	Volume
Sphere	$4\pi r^2$	$\frac{4}{3}\pi r^3$
Prolate spheroid	$2\pi f^2(\xi^2 - 1)\left[1 + \frac{\xi^2}{\sqrt{\xi^2 - 1}} \sin^{-1}(1/\xi)\right]$	$\frac{4}{3}\pi f^3 \xi(\xi^2 - 1)$
Oblate spheroid	$2\pi f^2(\sigma^2 + 1)\left[1 + \frac{\sigma^2}{2\sqrt{\sigma^2 + 1}} \ln \frac{\sqrt{1 + \sigma^2} + 1}{\sqrt{1 + \sigma^2} - 1}\right]$	$\frac{4}{3}\pi f^3 \sigma(\sigma^2 + 1)$

Table 3
Differential equation for τ

Figure	Differential equation
Sphere	$\frac{d}{dr_0}\{r_0^2 \exp(-V(r_0)) d\tau_s/dr_0\} = -\frac{r_0^2}{D}\exp(-V(r_0))$
Prolate spheroid	$\frac{d}{d\xi_0}\{(\xi_0^2 - 1)\exp(-V(\xi_0)) d\tau_p/d\xi_0\} = -\frac{f^2}{D}(\xi_0^2 - 1/3)\exp(-V(\xi_0))$
Oblate spheroid	$\frac{d}{d\sigma_0}\{(\sigma_0^2 + 1)\exp(-V(\sigma_0)) d\tau_0/d\sigma_0\} = -\frac{f^2}{D}(\sigma_0^2 + 1/3)\exp(-V(\sigma_0))$

metries as a function of the starting position of the particle. Some particular solutions are discussed below.

Adam and Delbrück [8], approximately, and Berg and Purcell [4], exactly, have calculated τ_s for the physical situation in which $V = 0$ and in which each encounter with the target results in absorption ($\beta = 1$, $\gamma = 0$). Similar results for the prolate and oblate spheroidal geometries have been calculated using table 4 and the three exact expressions for the mean absorption time are tabulated in table 5. That the three formulas are consistent may be noted in the limit that the focal distance $f \to 0$. Then

$$\frac{1}{2f}\ln\frac{\xi + 1}{\xi - 1} \to \frac{1}{r} \quad \text{and} \quad \frac{1}{f}\tan^{-1}\sigma \to \frac{\pi}{2f} - \frac{1}{r}$$

so that τ_p and $\tau_o \to \tau_s$. In order to make detailed comparisons among the three cases, one must first average r_0, ξ_0 and σ_0 over the possible starting positions between the inner and outer boundaries. The result, denoted by $\bar{\tau}$, is thus

Table 4
τ for general boundary conditions

Figure	τ
Sphere	$\tau_s(r_0) = \frac{l\gamma}{D\beta}\frac{\exp(V(r_a))}{r_a^2}\int_{r_a}^{r_b} dx x^2 \exp(-V(x)) + \frac{1}{D}\int_{r_a}^{r_0} dy \frac{\exp(V(y))}{y^2}\int_{y}^{r_b} dx x^2 \exp(-V(x))$
Prolate spheroid	$\tau_p(\xi_0) = \frac{l\gamma f}{D\beta}\frac{\exp(V(\xi_a))}{(\xi_a^2-1)}\int_{\xi_a}^{\xi_b} dx (x^2-\frac{1}{3})\exp(-V(x)) + \frac{f^2}{D}\int_{\xi_a}^{\xi_0} dy \frac{\exp(V(y))}{y^2-1}\int_{y}^{\xi_b} dx (x^2-\frac{1}{3})\exp(-V(x))$
Oblate spheroid	$\tau_o(\sigma_0) = \frac{l\gamma f}{D\beta}\frac{\exp(V(\sigma_a))}{(\sigma_a^2+1)}\int_{\sigma_a}^{\sigma_b} dx (x^2+\frac{1}{3})\exp(-V(x)) + \frac{f^2}{D}\int_{\sigma_a}^{\sigma_0} dy \frac{\exp(V(y))}{y^2+1}\int_{y}^{\sigma_b} dx (x^2+\frac{1}{3})\exp(-V(x))$

Table 5
τ for complete absorption at target

Figure	Boundary conditions	τ
Sphere	$\tau_s(r_a) = 0$ $d\tau_s/dr_0\|_{r_b} = 0$	$\tau_s = \frac{(r_a^2 - r_0^2)}{6D} + \frac{r_b^3}{3D}\left(\frac{1}{r_a} - \frac{1}{r_0}\right)$
Prolate spheroid	$\tau_p(\xi_a) = 0$ $d\tau_p/d\xi_0\|_{\xi_b} = 0$	$\tau_p = \frac{f^2(\xi_a^2 - \xi_0^2)}{6D} + \frac{f^2\xi_b(\xi_b^2-1)}{3D}\,\frac{1}{2}\left[\ln\frac{\xi_a+1}{\xi_a-1} - \ln\frac{\xi_0+1}{\xi_0-1}\right]$
Oblate spherolid	$\tau_o(\sigma_a) = 0$ $d\tau_o/d\sigma_0\|_{\sigma_b} = 0$	$\tau_o = \frac{f^2}{6D}(\sigma_a^2 - \sigma_0^2) + \frac{f^2\sigma_b(\sigma_b^2+1)}{3D}[\tan^{-1}\sigma_0 - \tan^{-1}\sigma_a]$

$$\bar{\tau} = \int_{x_a}^{x_b} d^3x_0\, \tau(x_0) \Big/ \int_{x_a}^{x_b} d^3x_0 \qquad (5)$$

and the three cases are given in table 6. Again, a check of the $f \to 0$ limit verifies the correctness of the spheroidal expressions for $\bar{\tau}$. One limit of interest that has been discussed by Adam and Delbrück [8] in the spherical cases is when the size of the outer boundary is much greater than the target. In that limit

$$\bar{\tau}_s \approx \frac{r_b^2}{3D}\frac{r_b}{r_a}, \qquad r_b/r_a \gg 1. \qquad (6)$$

For a prolate spheroidal geometry, the corresponding limit is

$$\bar{\tau}_p \approx \frac{f^2\xi_b^2}{3D}\frac{\xi_b}{2}\ln\frac{\xi_a+1}{\xi_a-1}, \qquad \xi_b/\xi_a \gg 1 \qquad (7)$$

and for oblate spheroidal geometry, one obtains

$$\bar{\tau}_o \approx \frac{f^2}{3D}\{\sigma_b(\sigma_b^2+1)[\tan^{-1}\sigma_b - \tan^{-1}\sigma_a] - \tfrac{4}{5}\sigma_b^2\},$$
$$\sigma_b/\sigma_a \gg 1 \qquad (8)$$

In eqs. (7) and (8), if, in addition to the size restriction already imposed, one has $\xi_a \gg 1$ and $\sigma_a \gg 1$, the equations become the exact analogues of eq. (7). That is, in such a limit $\bar{\tau}_p \approx (f^2\xi_b^2/3D)\xi_b/\xi_a$ and $\bar{\tau}_o \approx (f^2\sigma_b^2/3D)\sigma_b/\sigma_a$. Some other limiting cases of eq. (8) are the following

$$\sigma_a \ll 1, \quad \sigma_b \gg 1, \quad \bar{\tau}_o \approx \frac{f^2\sigma_b^3}{3D}(\pi/2), \qquad (9)$$

$$\sigma_a \ll 1, \quad \sigma_b \ll 1, \quad \sigma_b/\sigma_a \gg 1, \quad \bar{\tau}_o \approx \frac{f^2\sigma_b^2}{3D}$$

that is, $\bar{\tau}_o$ becomes independent of the target "size" when σ_a is very small. Comparing eqs. (6) through (9)

Table 6
Mean absorption time averaged over starting positions

Figure	Boundary conditions	$\bar{\tau}$
Sphere	$\tau_s(r_a) = 0$ $d\tau_s/dr_0\vert_{r_b} = 0$	$\bar{\tau}_s = \frac{r_b^6}{3Dr_a(r_b^3 - r_a^3)}\left\{1 - \frac{9}{5}\frac{r_a}{r_b} + \frac{r_a^3}{r_b^3} - \frac{1}{5}\frac{r_a^6}{r_b^6}\right\}$
Prolate spheroid	$\tau_p(\xi_a) = 0$ $d\tau_p/d\xi_0\vert_{\xi_b} = 0$	$\bar{\tau}_p = \frac{f^2}{6D}\left\{\xi_a^2 + \xi_b(\xi_b^2 - 1)\ln\frac{\xi_a + 1}{\xi_a - 1} - \frac{[\frac{3}{5}(\xi_b^5 - \xi_a^5) - \frac{1}{3}(\xi_b^3 - \xi_a^3)]}{\xi_b(\xi_b^2 - 1) - \xi_a(\xi_a^2 - 1)} - \xi_b(\xi_b^2 - 1)\frac{[\xi_b(\xi_b^2 - 1)\ln(\xi_b + 1)/(\xi_b - 1) - \xi_a(\xi_a^2 - 1)\ln(\xi_a + 1)/(\xi_a - 1) + \xi_b^2 - \xi_a^2]}{\xi_b(\xi_b^2 - 1) - \xi_a(\xi_a^2 - 1)}\right\}$
Oblate spheroid	$\tau_o(\sigma_a) = 0$ $d\tau_o/d\sigma_0\vert_{\sigma_b} = 0$	$\bar{\tau}_o = \frac{f^2}{6D}\left\{\sigma_a^2 - 2\sigma_b(\sigma_b^2 + 1)\tan^{-1}\sigma_a - \frac{[\frac{3}{5}(\sigma_b^5 - \sigma_a^5) - \frac{1}{3}(\sigma_b^3 - \sigma_a^3)]}{\sigma_b(\sigma_b^2 + 1) - \sigma_a(\sigma_a^2 + 1)} + \sigma_b(\sigma_b^2 + 1)\frac{[2\sigma_b(\sigma_b^2 + 1)\tan^{-1}\sigma_b - 2\sigma_a(\sigma_a^2 + 1)\tan^{-1}\sigma_a - \sigma_b^2 + \sigma_a^2]}{\sigma_b(\sigma_b^2 + 1) - \sigma_a(\sigma_a^2 + 1)}\right\}$

Table 7
τ for weak partial absorption at the target

Figure	Boundary conditions	τ
Sphere	$d\tau_s/dr_0 = (\beta/l)\tau_s, \quad r_0 = r_a$ $d\tau_s/dr_0\vert_{r_b} = 0$	$\tau_s = \frac{l}{D\beta}\frac{(r_b^3 - r_a^3)}{3r_a^2} = \frac{l}{D\beta}\frac{\Delta V}{A_a}$
Prolate spheroid	$d\tau_p/d\xi_0 = (\beta f/l)\tau_p, \quad \xi_0 = \xi_a$ $d\tau_p/d\xi_0\vert_{\xi_b} = 0$	$\tau_p = \frac{lf}{D\beta}\frac{[\xi_b(\xi_b^2 - 1) - \xi_a(\xi_a^2 - 1)]}{(\xi_a^2 - 1)} = \frac{l}{D\beta}\frac{\Delta V}{A_a}g_p$
Oblate spheroid	$d\tau_o/d\sigma_0 = (\beta f/l)\tau_o, \quad \sigma_0 = \sigma_a$ $d\tau_o/d\sigma_0\vert_{\sigma_b} = 0$	$\tau_o = \frac{lf}{D\beta}\frac{[\sigma_b(\sigma_b^2 + 1) - \sigma_a(\sigma_a^2 + 1)]}{3(\sigma_a^2 + 1)} = \frac{l}{D\beta}\frac{\Delta V}{A_a}g_o$

one notices that the dependence of $\bar{\tau}$ on the shell sizes can be quite different in each of the three geometries considered and may, therefore, have quite different sizes for situations in which the diffusion volume and the target surface area are the same.

Referring again to table 4, one may look at a physical situation in which $V = 0, \beta \ll 1$ and $\gamma \approx 1$, that is, the probability of absorption at the target surface for a given encounter is very small. This situation may arise, for example, in the folding of globular proteins from the set of random conformations to the native structure [2,9]. In this limit, only the first term in the expressions for τ in table 4 are significant. They are collected for the three geometries in table 7. As shown in table 7, the expressions for τ take a particularly simple form in this case being simply:

$$\tau = \frac{l}{D\beta}\frac{\text{(diffusion volume)}}{\text{(target surface area)}}\text{(shape factor)}, \qquad (10)$$

In the one-dimensional and two-dimensional circularly symmetrical analogues of the three-dimensional situation considered here, Karplus and Weaver [9] have shown that a formula equivalent to eq. (10) (with a shape factor of 1 as in the spherically symmetrical case) represents the mean absorption time. Some numerical values for the shape factors are listed in table 8. Limiting cases for the shape factors are:

Table 8
Shape factors

r_{maj}/r_{min}	ξ (prolate)	σ (oblate)	g_p	g_o
2	1.155	0.577	1.71	0.690
5	1.021	0.204	3.99	0.547
10	1.005	0.1005	7.89	0.515
20	1.001	0.0501	15.7	0.505
50	1.0002	0.0200	39.3	0.501
100	1.00005	0.0100	78.5	0.500

$$\begin{aligned} &r_{maj}/r_{min} \to \infty, && g_p \to (\pi/4) r_{maj}/r_{min}, && g_o \to \tfrac{1}{2} \\ &r_{maj}/r_{min} \to 1, && g_p \to 1 && g_o \to 1 \end{aligned} \tag{11}$$

Again the behavior may be quite different for the different geometries.

As a final example of a special case of the general expressions for τ in table 4 consider the situation in which there is complete absorption at each encounter with the target but that there is a "square" potential barrier to be surmounted extending out from the target to x_1. Furthermore, let the diffusing particle begin its motion outside the barrier region. The results for such conditions are given in table 9 for the three cases. They correspond to solving the "escape over a barrier" problem discussed and solved approximately by Kramers [11].

The results in tables 3 through 9 are the main content of this note. Application of the formulas to some particular biophysical systems will be deferred to a subsequent publication.

For completeness on the subject of elliptically symmetrical diffusion, the results for two other cases will be briefly outlined:

1. Confocal elliptic geometry (two-dimensions) [10].

Consider a particle diffusing in the two-dimensional space between two confocal ellipses defined by ξ_a (inner ellipse) and ξ_b (outer ellipse). In this case the equation for τ_E becomes

$$(d/d\xi_0)\{\sqrt{\xi_0^2 - 1}\, \exp(-V(\xi_0) d\tau_E/d\xi_0\} = -\frac{f^2}{D} \frac{(\xi_0^2 - \frac{1}{3})}{\sqrt{\xi_0^2 - 1}} \exp(-V(\xi_0)) \tag{12}$$

Table 9
τ for "square" barrier

Figure	Boundary conditions	Potential barrier	τ
Sphere	$\tau_S(r_a) = 0$ $d\tau_S/dr_0\|_{r_b} = 0$	$V = 0,\ r_0 > r_1$ $V = V_0,\ r_0 \leqslant r_1$	$\tau_S = \frac{\exp(V_0)(r_b^3 - r_1^3)}{3D}\left[\frac{1}{r_a} - \frac{1}{r_1}\right] - \frac{(r_0^2 - r_a^2)}{6D}$ $+ \frac{r_b^3}{3D}\left[\frac{1}{r_1} - \frac{1}{r_0}\right] + \frac{r_1^3}{3D}\left[\frac{1}{r_a} - \frac{1}{r_1}\right]$
Prolate spheroid	$\tau_p(\xi_a) = 0$ $d\tau_p/d\xi_0\|_{\xi_b} = 0$	$V = 0,\ \xi_0 > \xi_1$ $V = V_0,\ \xi_0 \leqslant \xi_1$	$\tau_p = \frac{\exp(V_0) f^2}{3D}\,[\xi_b(\xi_b^2 - 1) - \xi_a(\xi_a^2 - 1)]\left[\frac{1}{2}\ln\frac{\xi_a + 1}{\xi_a - 1} - \frac{1}{2}\ln\frac{\xi_1 + 1}{\xi_1 - 1}\right]$ $- \frac{f^2}{6D}(\xi_0^2 - \xi_a^2) + \frac{f^2 \xi_b(\xi_b^2 - 1)}{3D}\left[\frac{1}{2}\ln\frac{\xi_1 + 1}{\xi_1 - 1} - \frac{1}{2}\ln\frac{\xi_0 + 1}{\xi_0 - 1}\right]$ $+ \frac{f^2 \xi_1(\xi_1^2 - 1)}{3D}\left[\frac{1}{2}\ln\frac{\xi_a + 1}{\xi_a - 1} - \frac{1}{2}\ln\frac{\xi_1 + 1}{\xi_1 - 1}\right]$
Oblate spheroid	$\tau_o(\sigma_a) = 0$ $d\tau_o/d\sigma_0\|_{\sigma_b} = 0$	$V = 0,\ \sigma_0 > \sigma_1$ $V = V_0,\ \sigma_0 \leqslant \sigma_1$	$\tau_o = \frac{\exp(V_0) f^2}{3D}\,[\sigma_b(\sigma_b^2 + 1) - \sigma_a(\sigma_a^2 + 1)]\,[\tan^{-1}\sigma_1 - \tan^{-1}\sigma_a]$ $- \frac{f^2}{6D}(\sigma_0^2 - \sigma_a^2) + \frac{f^2 \sigma_b(\sigma_b^2 + 1)}{3D}\,[\tan^{-1}\sigma_0 - \tan^{-1}\sigma_1]$ $+ \frac{f^2 \sigma_1(\sigma_1^2 + 1)}{3D}\,[\tan^{-1}\sigma_1 - \tan^{-1}\sigma_a]$

leading to the resulting general expression for τ_E

$$\tau_E = \frac{\gamma l f}{\beta D} \frac{\exp(V(\xi_a))}{\sqrt{\xi_a^2 - 1}} \int_{\xi_a}^{\xi_b} dx \frac{(x^2 - \frac{1}{3})}{\sqrt{x^2 - 1}} \exp(-V(x))$$

$$+ \frac{f^2}{D} \int_{\xi_a}^{\xi_0} dy \frac{\exp(V(y))}{\sqrt{y^2 - 1}} \int_{y}^{\xi_b} dx \frac{(x^2 - \frac{1}{3})}{\sqrt{x^2 - 1}}$$

$$\times \exp(-V(x)) \tag{13}$$

This expression may be evaluated in various special cases as done for the other geometries.

2. Semi-infinite diffusion space

Suppose that the outer reflecting barrier is removed. Then the diffusion space extends from a target spheroid to infinity. In this situation the mean absorption time is infinite. It is, then, useful to calculate the probability that a particle which starts from a given position and diffuses in the space will not be absorbed after a long time. Letting $x_b \to \infty$ in eq. (2), $N(x_0, \infty)$ is the desired probability. It satisfies eq. (3) with $\partial N/\partial t = 0$. The boundary conditions for the prolate (oblate) geometry is $N \to 0$ as $\xi_0 \to \xi_a (\sigma_0 \to \sigma_a)$ and $N \to 1$ as $\xi_0 \to \infty (\sigma_0 \to \infty)$. The solutions are ($V = 0$)

$$N(\xi_0, \infty) = 1 - \ln \frac{\xi_0 + 1}{\xi_0 - 1} \Big/ \ln \frac{\xi_a + 1}{\xi_a - 1}, \tag{14}$$

$$N(\sigma_0, \infty) = 1 - \frac{(\pi/2 - \tan^{-1} \sigma_0)}{(\pi/2 - \tan^{-1} \sigma_a)}. \tag{15}$$

In the limit of spherical symmetry, eqs. (14) and (15) reduce to $N(r_0, \infty) = 1 - r_a/r_0$, a result well-known for spherical diffusing units [12]. If the semi-infinite system has a constant probability density at infinity, then the relevant quantity to calculate for these systems is the flux into the target at $\xi_a(\sigma_a)$ as discussed in detail by Richter and Eigen [5].

In summary, the mean reaction time τ has been calculated exactly for three-dimensional systems with diffusion-controlled dynamics and with prolate or oblate spheroidial geometry. Knowledge of τ allows one to have a good approximation for the reaction dynamics of the system because one may write

$$N(x_0, t) \approx \exp(-t/\tau) \tag{16}$$

which has the same time-normalization as the exact solution, that is

$$\int_0^\infty dt N(x_0, t) = \tau \tag{17}$$

by definition of the mean reaction time. Thus, except for the earliest times, knowledge of τ which may be found exactly in many cases of interest, gives one the time-dependence of the reaction.

It is important to realize that the mean reaction time and the associated reaction dynamics is obtained in this paper for systems with *finite* geometry and a *finite* number of reactive species. This is in contrast with the work of Richter and Eigen [5] who dealt with an *infinite* system with spheroidal geometry and with an *infinite* number of reactive species whose steady-state flux at the target determined the rate constants. Thus the results presented in this paper and the results obtained in ref. [5] are complementary and *together* cover the range of physical systems for which spheroidal diffusion-controlled reactions may be important.

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