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Diffusion Mediated Localization on Membrane Surfaces

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INTRODUCTION

Proteins and other membrane components are not static entities but rather carry on a considerable dynamics on the membrane surface, particularly by translational and rotational diffusion (1). Knowledge about the speed of movement of proteins as they diffuse laterally in the membrane is crucial for understanding many of their cellular functions (2), and it is becoming increasingly clear, that knowledge about the localization and aggregation of membrane components, either due to contact with another cell (3-5) or due to the effect of extracellular ligands (6-9), is important as well. To understand the localization phenomena, Chao, Young and Poo (10) have described a model of localization in which the motion of the membrane components is assumed to be diffusive, with the diffusing species being "trapped" in a certain region of the membrane surface when their diffusive motion brings them into contact with the "trap" boundary. A similar model has been proposed by Edwards and Frisch (11) for the localization of acetylcholine receptors at the muscle endplate (see Poo (12) for further evidence regarding this hypothesis). In related studies, Adam and Delbruck (13) have considered the possibility that some biologically interesting diffusional processes occur by first lowering the dimensionality of the diffusion space via a trapping mechanism, and they have made numerical estimates in support of their hypothesis. Also, Berg and Purcell (14) have studied diffusive transport to a cell with specific receptors to measure the concentration of a chemical species and influence chemotactic behavior. In Ref. (10), the numerical results of Hall (15) were used to approximately compute the surface density of trappable membrane proteins and the average time required for a trappable particle

to reach the trap boundary by diffusion, using the simplest boundary condition that any particle which reaches the trap boundary is trapped and no longer diffuses in the membrane.

There are a number of points at which the above mentioned model of diffusion mediated localization on membrane surfaces (diffusion driven trapping, referred to below as the DDT model) may be generalized to make a more realistic approach to localization phenomena, particularly with regard to the behavior of the protein at the trap boundary, and with regard to the possibility that only a fraction of the potentially trappable components actually become localized. In Ref. (10) it was indicated that at least 26% of the SBA receptors in the membrane are electrophoretically mobile, and that only a small fraction of the mobile receptors actually become trapped. It was, however, assumed in Ref. (10) that all the potentially trappable receptors were trapped. In addition, by carrying out an approximate analytical treatment of the DDT model, some insight into the relative importance of various cell and membrane protein parameters on the localization may be obtained.

In order to estimate the trapping rates of various membrane components, one may calculate under various assumptions about intrinsic trapping probability, initial distribution of diffusing membrane components and number of trapping sites, the mean time for a particular species to be trapped. It is also possible, in fact, that not all of a particular membrane component is, indeed, trapped. That is, there may be an equilibrium established on the membrane surface in which only a fraction of a given trappable component eventually resides within the trap site. Various possibilities are considered in the next section where, to the extent possible, exact results are derived for the mean trapping times implied by

the different situations enumerated above. This section is followed by a discussion of the results and their connection with experimentally observed membrane component localization.

THEORY

A. Introduction

The model of a cell membrane to be used here is that of a spherical surface of radius R in which membrane components may diffuse with diffusion coefficient D (assumed to be constant in most of the discussion below).

The general diffusion equation for such a system is

$$\frac{\partial \rho}{\partial t} = D\nabla^2\rho \qquad (1)$$

where ρ is the concentration of membrane components at time t. If diffusion is limited to the surface of the spherical cell then the radial coordinate in Eq. (1) is fixed at a value of R, the cell radius, and the concentration depends only on the polar angle θ and azimuthal angle ϕ of spherical polar coordinates, as shown in Fig. 1. Thus, Eq. (1) becomes

$$\frac{\partial \rho}{\partial t} = \frac{D}{R^2 \sin\theta}\left\{\frac{\partial}{\partial\theta}\left(\sin\theta\,\frac{\partial \rho}{\partial \theta}\right) + \frac{1}{\sin\theta}\,\frac{\partial^2 \rho}{\partial \phi^2}\right\}. \qquad (2)$$

Suppose that the cell coordinates are oriented so that a trap is near $\theta=\pi$ and that there is no dependence on azimuthal angle. Then, Eq. (2) is independent of ϕ and may be rewritten, letting $w = \cos\theta$, as

$$\frac{\partial \rho}{\partial t} = \frac{D}{R^2}\frac{\partial}{\partial w}\left\{(1-w^2)\frac{\partial \rho}{\partial w}\right\}. \qquad (3)$$

Since only diffusing particles that are essentially confined to the surface of the cell are under consideration here, the volume concentration ρ may be replaced by a surface concentration $\sigma(\theta,t)$. That is, $\rho = 0$ except at radius R, so Eq. (3) may be integrated over the radial coordinate, the result being

$$\frac{\partial \sigma}{\partial t} = \frac{D}{R^2} \frac{\partial}{\partial w} \{ (1-w^2) \frac{\partial \sigma}{\partial w} \} \qquad (4)$$

Integrating σ over the surface of the sphere gives the number of particles in the system at a particular time N(t).

To proceed further in the analysis of membrane surface diffusion, initial and boundary conditions must be specified. A variety of physical situations are outlined below and their trapping rates derived and analyzed.

B. Perfect Trap

The simplest possibility is that every diffusing particle that approaches within a certain distance of $w = -1$ ($\theta = \pi$) is trapped ("perfect" trap model). Then, as discussed by Chao, Young and Poo (10) the boundary condition at the trap is $\sigma = 0$. To be specific, let the trap region be defined by a cap centered at $w = -1$ and extending to $w_a = \cos\theta_a$. That is,

$$\sigma(w_a, t) = 0, \qquad (5)$$

The surface concentration is zero at θ_a because every particle that reaches θ_a from the region $\theta < \theta_a$ is immediately captured permanently by the trap, and any particle with $\theta \geq \theta_a$ remains always with $\theta \geq \theta_a$ in this, the simplest example of trapping.

To determine the trapping rate under these conditions, it is sufficient to calculate the number n(t) of particles in the cap region as a function of time, which is related to the number of particles N(t) remaining untrapped at the same time by

$$n(t) = N_o - N(t) \qquad (6)$$

where $N_o = N(o)$ the number of diffusing particles initially outside of the cap. One finds that

$$N(t) = 2\pi R^2 \int_{w_a}^{1} dw\sigma(w,t). \tag{7}$$

When the diffusion space is finite as in this case of diffusion on the surface of a sphere of fixed radius, the particle number N(t) is expressed as an infinite series of terms each decaying exponentially with time. However, except at very short times, the infinite series may to good approximation (16) be replaced by a single exponential decaying with time, the time constant being the mean trapping time τ_p as introduced by Weiss (17). Methods for calculating τ_p exactly have been developed by Weaver (18,19), Szabo et al. (20), and Deutch (21) using the definition

$$\tau_p = \int_0^{\infty} dt\, N(t)/N_o. \tag{8}$$

Application of these methods (see the Appendix) yields the result

$$\tau_p = \frac{R^2}{D} \left\{ \frac{2}{1-w_a} \ln \left(\frac{2}{1+w_a} \right) - 1 \right\}. \tag{9}$$

Eq. 9 is an exact analytical calculation to be compared with the numerical treatment of Ref. 10 in which the lowest eigenvalue approximation to τ_p was used. As shown in Refs. 16 and 20, the approximation

$$N(t) \simeq N_o\, e^{-t/\tau_p} \tag{10}$$

is in very good agreement with accurate numerical calculations of N(t) over a wide range of parameter sizes. Comparison of Eq. 9 with the numerical approximation of Ref. 10 shows better than one percent agreement for small traps ($1 + W_a < .01$) and lesser agreement (but still quite good) as the trap gets larger. As seen from Eq. 9, the dependence of τ_p on the cap surface area given by $S_c = 2\pi R^2(1+w_a)$ is not very pronounced

when S_c is small compared to the total surface area $A = 4\pi R^2$. This may be seen by rewriting the expression for τ_p as

$$\tau_p = \frac{R^2}{D} \left\{\frac{A/S_c}{A/S_c - 1} \ln A/S_c - 1\right\}$$

$$\sim \frac{R^2}{D} \{\ln A/S_c - 1\}, A/S_c >> 1. \qquad (11)$$

Thus, the dependence of τ_p on S_c occurs mainly in the logarithmic term and, therefore, is considerably suppressed. For example,

$$\frac{\tau_p(\frac{A}{S_c} = 100)}{\tau_p(\frac{A}{S_c} = 10)} = 2.34. \qquad (12)$$

However, as the cap area becomes a significant fraction of the total surface area, the dependence on S_c becomes much stronger. For example, as $S_c \to A$,

$$\tau_p \to \frac{R^2}{2D} (\frac{A}{S_c} - 1) \qquad (13)$$

Thus, when A/S_c changes from 1.1 to 1.01, τ_p decreases by a factor of 10.

C. Imperfect Trap

There are two ways in which the trap of part B can be imperfect. First, if every time a particle reaches θ_a, it is not captured with a probability β of one but rather with $\beta < 1$ so that more than one (perhaps many) diffusion to the $\theta = \theta_a$ boundary is necessary before capture occurs. Second, if every particle that is captured does not remain permanently in the cap region but may recross the boundary and continue to diffuse on the sphere, perhaps to be recaptured again, and so on. In this case an equilibrium state will be

reached eventually with some portion of the diffusing species remaining uncaptured. The two possibilities are considered below.

1. Imperfect Capture Probability

This is the case when the probability that a particle which diffuses to the boundary at θ_a is captured (which was taken to be one in section B above) is less than one. Then, the mean trapping time τ will be larger than the value found in section B. To incorporate the capture probability into the above analysis, the boundary condition at $\theta = \theta_a$, Eq. (5) must be modified so that $\sigma(w_a,t)$ is no longer zero. To the extent that the boundary condition must remain linear in σ and its derivatives, the usual way to incorporate partial capture is to note that the net particle flux at θ_a is the difference between the particles reaching the boundary and those not captured at that time. The flux is proportional to the first derivative of σ with respect to w (or θ) so the boundary condition at θ_a is modified to be

$$\frac{\partial\sigma}{\partial w} = \frac{\alpha}{\sqrt{1-w^2}}\sigma, \quad w = w_a \ . \tag{14}$$

The parameter α ranges from zero (no trapping with all particles being reflected at the θ_a boundary) to infinity ($\sigma(w_a,t) = 0$ case). The interpretation of α in terms of molecular parameters is discussed below.

With the boundary condition above, the mean trapping time is (see Appendix for details)

$$\tau = \frac{R^2}{\alpha D} \tan \frac{\theta_a}{2} + \tau_p = \tau_I + \tau_p \tag{15}$$

where τ_p is defined by Eq. (9), that is, τ as $\alpha \to \infty$, and a uniform initial distribution has again been assumed. The factor $\tan(\theta_a/2)$ in Eq. (15) has a simple geometrical interpretation as follows. The surface area ΔA in which diffusion takes place is

$$\Delta A = A - S_c = 2\pi R^2(1-w_a) \tag{16}$$

and the circumference C of the trap is

$$C = 2\pi R \sin\theta_a. \tag{17}$$

Then

$$\frac{\Delta A}{C} = R \frac{(1-\cos\theta_a)}{\sin\theta_a} \tag{18}$$

$$= R \tan\theta_a/2.$$

Thus, τ_I is inversely proportional to the "size" of the "target" available to the diffusing particles, and directly proportional to the space available for diffusion, as well as varying inversely with the trapping probability.

The ratio of the two capture times is

$$\frac{\tau_p}{\tau_I} = \alpha \frac{\sin\theta_a}{1-\cos\theta_a} \left\{ \frac{2}{1-\cos\theta_a} \ln \left(\frac{2}{1+\cos\theta_a} - 1 \right) \right\} = \alpha f(\theta_a) \tag{19}$$

the product of the trapping probability factor α and a geometry factor $f(\theta_a)$. The geometry factor goes to zero both as $\theta_a \to 0$ and as $\theta_a \to 180°$ and has a broad maximum around 140° of about 1/2 as shown in Fig. 1. Thus, for a trapping probability factor $\alpha << 1$, the imperfect capture time dominates, and, conversely, for $\alpha >> 1$. the perfect capture time will be dominant.

The dimensionless trapping probability factor α may be decomposed into

several multiplicative parameters according to the following definition

$$\alpha = \frac{R}{\ell} \quad \beta/1-\beta. \tag{20}$$

The parameter R, the radius of the cell, appears naturally in Eq. (14) because the dependent position variable is the angle θ (22). The parameter β is the probability that a collision with the trap circumference causes capture, so that $0 \leq \beta \leq 1$, and ℓ is a length parameter which is, in general expected to be smaller than the characteristic dimension of the trap. If the probability β is small, then most of the collisions with the trap perimeter do not result in capture. As β approaches one, however, the interpretation of Eq. (14) is to divide by α so that $1/\alpha$ appears on the left-hand side. Since $\alpha \to \infty$ as $\beta \to 1$, Eq. (13) approaches the boundary condition of Eq. (5) for trapping at each collision with the trap. If the lack of trapping at each collision is due to a potential energy barrier at the trap edge, then ℓ may be interpreted as the width of this barrier which the particle must cross to get from "outside" to "inside" the trap area. Alternatively, a kinetic theory interpretation of the boundary condition leads to an estimate of ℓ of $2D/\bar{v}$ for small β where $\bar{v}$ is the average particle speed at the given temperature (23, 24). In either case, when $\beta << 1$, one expects that α is considerably less than one as well and, thus, cause τ_I to dominate the expression for the trapping time τ, with the consequence of a considerably lengthened mean trapping time compared to the perfect trap case. Interpretation of these results in the context of experiemental observations will be discussed below.

2. Equilibrium Established

This is the case when some of the trapped particles "escape" from the trap and commence diffusion again, perhaps to be trapped again at a later time. Then, one no longer speaks of a mean trapping time τ (whether the trapping probability is one or smaller than one), but, instead, one must consider the time to reach the equilibrium state for this system in which some fraction of the particles remain trapped and the rest continue to diffuse freely in the membrane with the members of these two categories changing places repeatedly. Discussion of the approach to equilbirium requires introduction of a new parameter, the equilibrium constant K defined as

$$K = \lim_{t\to\infty} \frac{n(t)}{N(t)} \tag{21}$$

In order to introduce the equilibrium constant into the diffusion problem, the boundary conditions must be modified by the subtraction of the term $\sigma_o n(t)/N_o K$ from $\sigma(\theta_a,t)$ in Eqs. (5) and (14). As a result of this change, the mean time to reach equilibrium τ_{eq} is calculated (25) to be simply related to τ of Eqs. (9) or (15), the result being

$$\tau_{eq} = \left(\frac{K}{1+K}\right)\tau \tag{22}$$

where K/(1+K) is the fraction of particles trapped at equilibrium, that is

$$n_{eq}/N_o = K/(1+K). \tag{23}$$

Note that as $K \to \infty$, the situation becomes one in which no trapped particle escapes, and $\tau_{eq} \to \tau$. Conversely, if most trapped particles subsequently

escape, so that $K << 1$, then $\tau_{eq} << \tau$ and equilibrium is (relatively) rapidly reached with only a small fraction of the diffusing particles being trapped.

The above analysis represents the simplest case in which an equilibrium is established between the trap region and the rest of the cell surface. In this case, as inidcated above, it is meaningful to discuss the approach to equilibrium in terms of a single time constant, τ_{eq}, and to have an exponential increase in the number of particles trapped as a function of time. If, however, some particles are initially trapped by the mechanism of trap formation itself (see, for example, Ref. 10), then it is possible that the single exponential approximation does not apply. Consider, for example, the experimental situation in which the initial concentration of diffusing species in the trap region and the rest of the cell surface is the same, say σ_o. Then the ratio of numbers of diffusing particles in and out of the trap is

$$\frac{n(o)}{N(o)} = \frac{\sigma_o S_c}{\sigma_o (A-S_c)} = \frac{S_c/A}{1-S_c/A} \tag{24}$$

If $n(1)/N(o)$ is large compared to K, then the single exponential approximation will not be valid. If, however, K is large compared to $n(o)/N(o)$, the considerations discussed above which assume $n(o) = 0$ will approximately apply.

DISCUSSION

The DDT model of Chao, Young and Poo (10) has been analyzed with regard to the possibility of capture of mobile proteins at a trap site on the surface of a spherical cell. A single relaxation time approximation has been outlined, and the time parameter τ (or τ_{eq}) shown to depend on the cell surface area and trap circumference as on the probability of trapping and the trapped/untrapped equilibrium constant.

It is important to consider the effect of a trapping probability $\beta < 1$. This would affect the determination of the diffusion coefficient using trapping experiments. Figure 2 shows the dependence of $\alpha D\tau/R^2$ on trap size for several values of the probability parameter α. The log-log plot is essentially a straight line in the range of θ_a and α shown, since from Eq. 15, $\log_{10}(\alpha D\tau/R^2)$ is directly proportional to $\log_{10}(1+\cos\theta_a)$. Further numerical estimates of $D\tau/R^2$ are given in Table I as a function of θ_a for particular values of α. These studies show that when the trapping probability parameter α is small, the estimated diffusion coefficient from trapping time data is strongly influenced. A more specific example is shown in Table II in which the experimental parameters of Ref. 10 (namely, $R = 1.5(10)^{-3}$ cm, $\theta_a = 151.35°$ and $\tau = 200$ sec) are used to calculate D. The strong dependence of D on a small trapping probability is apparent.

The mean trapping time approximation cannot be used, at present, to make a direct comparison with the experiments of Chao, Young and Poo (10), because, as discussed above, the cell components may come to equilibrium with the trap region rather than approach the situation in which $\sigma(t \to \infty) \to 0$ as would be the case for $K \to \infty$. If K is finite, then the eigenvalues obtained in a solution of Eq. 4 will have zero as the lowest eigenvalue (corresponding to equilibrium) and the rest of the eigenvalues are not necessarily small in absolute value. Thus, extensive numerical estimates

must be made to compare with the explicit experimental parameter determined in Ref. 10 (their A.I.) and consequently a number of terms in the series solution for τ may be needed. It would be helpful in understanding the motions of cell components if a more direct measurement of n(t) could be performed, preferably with the trap region empty initially.

In order to clarify the theoretical situation further, numerical calculations are in progress to predict the behavior of τ and n under various assumptions about the equilibrium state, trapping probability, initial concentration distribution and number of trap sites.

APPENDIX: CALCULATION OF MEAN TRAPPING TIME

To compute the mean trapping time one may integrate Eq. 4 using the appropriate boundary conditions and a uniform initial distribution outside the trap. One gets

$$\int_w^1 dw' \frac{\partial \sigma}{\partial t} = \frac{D}{R^2} \int_w^1 dw' \frac{\partial}{\partial w'} \{ (1-w'^2) \frac{\partial \sigma}{\partial w'} \} \tag{A-1}$$

$$= - \frac{D}{R^2} (1-w^2) \frac{\partial \sigma}{\partial w}$$

Suppose that $K = \infty$ so the boundary condition is (Eq. 14)

$$\frac{\partial \sigma}{\partial w} = \frac{\alpha}{\sqrt{1-w^2}} \sigma, \; w = w_a \tag{A-2}$$

Then, since

$$\frac{\partial \sigma}{\partial w}\Big|_{w_a} = - \frac{R^2}{D(1-w_a^2)} \int_{w_a}^1 dw' \frac{\partial \sigma}{\partial t} \tag{A-3}$$

one finds that

$$\sigma(w_a,t) = - \frac{R^2}{\alpha D \sqrt{1-w_a^2}} \int_{w_a}^1 dw' \frac{\partial \sigma}{\partial t} \tag{A-4}$$

Further integration of Eq. A-1 leads to

$$\sigma(w,t) = \sigma(w_a,t) - \frac{R^2}{D} \int_{w_a}^{w} \frac{dy}{1-y2} \int_y^1 dz \frac{\partial \sigma}{\partial t} (z,t) \tag{A-5}$$

$$= - \frac{R^2}{D\alpha \sqrt{1-w_a^2}} \int_{w_a}^1 dw' \frac{\partial \sigma}{\partial t} - \frac{R^2}{D} \int_{w_a}^{w} \frac{d\gamma}{1-y^2} \int_y^1 dz \frac{\partial \sigma}{\partial t}$$

The mean trapping time is defined by Eq. 8 to give the approximation for N(t) of Eq. 10. The result for N(t) that one obtains from Eq. A-5 is

$$N(t) = 2\pi R^2 \int_{w_a}^{1} dx\,\sigma(x,t) \tag{A-6}$$

$$= -2\pi R^2 \left\{ -\frac{R^2}{D\alpha}\sqrt{\frac{1-w_a}{1+w_a}} \int_{w_a}^{1} dx\,\frac{\partial\sigma}{\partial t} - \frac{R^2}{D}\int_{w_a}^{1} dw \int_{w_a}^{w} \frac{d\gamma}{1-y^2} \int_{y}^{1} dz\,\frac{\partial\sigma}{\partial t} \right\}$$

One finally obtains for τ the result

$$\tau = \int_0^{\infty} dt\,\frac{N(t)}{N_o}$$

$$= \frac{R^2}{\alpha D}\tan\frac{\Theta_a}{2} + \frac{R^2}{D}\left\{\frac{2}{1-w_a}\ln\left(\frac{2}{1+w_a}\right) - 1\right\} \tag{A-7}$$

as discussed above (see Eq. 15 and the following discussion) using the limiting cases $\sigma(w,\infty) = o$ and $\sigma(w,o) = \sigma_o$ a constant with the value $N_o/(A-S_c)$.

Although somewhat more complicated algebraically, τ_{eq} may be derived by a similar method with the result being Eq. 22.

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TABLE I

The dimensionless ratio $D\tau/R^2$ calculated from Eq. 15 for several values of $1 + W_a$ (where $W_a = \cos \theta_a$) at fixed α(the trapping probability parameter defined by Eq. 20).

	$D\tau/R^2$							
$1 + W_a$	$\alpha=10^{-3}$	10^{-2}	10^{-1}	10^{0}	10^{1}	10^{2}	10^{3}	10^{4}
1. E-004	1.41E+005	1.42E+004	1.42E+003	1.50E+002	2.30E+001	1.03E+001	9.05E+000	8.92E+000
2. E-004	1.00E+005	1.00E+004	1.01E+003	1.08E+002	1.82E+001	9.21E+000	8.31E+000	8.22E+000
4. E-004	7.07E+004	7.08E+003	7.15E+002	7.82E+001	1.46E+001	8.23E+000	7.59E+000	7.53E+000
6. E-004	5.77E+004	5.78E+003	5.84E+002	6.48E+001	1.29E+001	7.69E+000	7.17E+000	7.12E+000
8. E-004	5.00E+004	5.01E+003	5.07E+002	5.68E+001	1.18E+001	7.33E+000	6.88E+000	6.83E+000
1. E-003	4.47E+004	4.48E+003	4.54E+002	5.13E+001	1.11E+001	7.05E+000	6.65E+000	6.61E+000
2. E-003	3.16E+004	3.17E+003	3.22E+002	3.75E+001	9.08E+000	6.23E+000	5.95E+000	5.92E+000
4. E-003	2.23E+004	2.24E+003	2.29E+002	2.76E+001	7.46E+000	5.45E+000	5.25E+000	5.23E+000
6. E-003	1.82E+004	1.83E+003	1.87E+002	2.31E+001	6.65E+000	5.01E+000	4.84E+000	4.83E+000
8. E-003	1.58E+004	1.53E+003	1.62E+002	2.03E+001	6.12E+000	4.70E+000	4.56E+000	4.55E+000
1. E-002	1.41E+004	1.41E+003	1.45E+002	1.84E+001	5.74E+000	4.47E+000	4.34E+000	4.33E+000
2. E-002	9.95E+003	9.99E+002	1.03E+002	1.36E+001	4.65E+000	3.75E+000	3.66E+000	3.65E+000
4. E-002	7.00E+003	7.03E+002	7.30E+001	9.99E+000	3.69E+000	3.06E+000	3.00E+000	2.99E+000
6. E-002	5.69E+003	5.71E+002	5.95E+001	8.30E+000	3.18E+000	2.67E+000	2.62E+000	2.62E+000
8. E-002	4.90E+003	4.92E+002	5.13E+001	7.25E+000	2.84E+000	2.40E+000	2.36E+000	2.35E+000
1. E-001	4.36E+003	4.38E+002	4.57E+001	6.51E+000	2.59E+000	2.20E+000	2.16E+000	2.15E+000
2. E-001	3.00E+003	3.02E+002	3.16E+001	4.56E+000	1.86E+000	1.59E+000	1.56E+000	1.56E+000
4. E-001	2.00E+003	2.01E+002	2.10E+001	3.01E+000	1.21E+000	1.03E+000	1.01E+000	1.01E+000
6. E-001	1.53E+003	1.53E+002	1.60E+001	2.25E+000	8.73E-001	7.35E-001	7.21E-001	7.20E-001
8. E-001	1.23E+003	1.23E+002	1.28E+001	1.75E+000	6.50E-001	5.39E-001	5.28E-001	5.27E-001
1. E+000	1.00E+003	1.00E+002	1.04E+001	1.39E+000	4.86E-001	3.96E-001	3.97E-001	3.86E-001

TABLE II

Diffusion coefficient calculated from Eq. 15 for $\theta_a = 151.35°$ and $t = 200$ sec.

α	$D(cm^2/sec.)$
1000	2.227 E-009
100	2.266 E-009
10	2.663 E-009
1	6.628 E-009
0.1	4.628 E-008
0.01	4.428 E-007

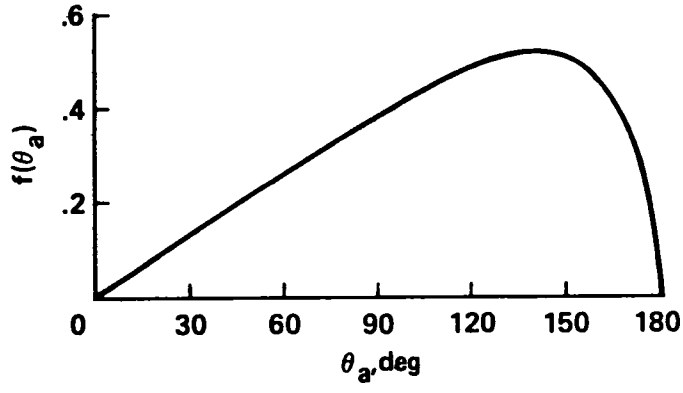

Figure 1. The ratio $f(\theta_a)$ as given by Eq. 19 is plotted versus the angle θ_a defining the trap region. The maximum is at $\theta_a = 140.07°$.

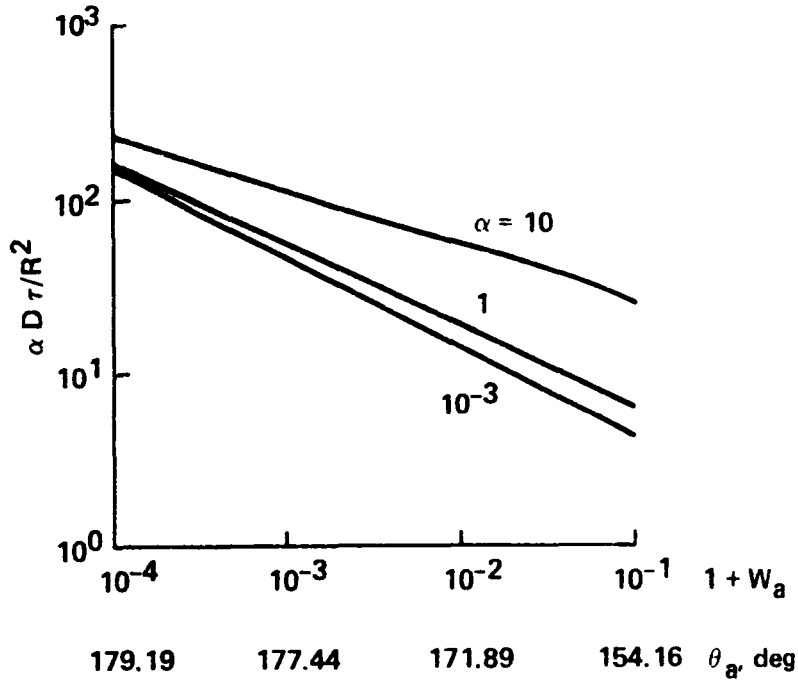

Figure 2. The normalized mean trapping time $\alpha D\tau/R^2$, as defined by Eq. 15, is plotted versus the angle θ_a defining the trap region ($W_a = \cos \theta_a$) for three values of α the trapping parameter defined by Eq. 14 and the discussion following Eq. 20.

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15 Supplementary Notes

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16 Abstract

Using the model of a cell membrane of a spherical surface in which membrane components may diffuse, the rate of localization due to trapping under diffusion control has been estimated by computing an analytical expression for the mean trapping time including the possibilities of a trapping probability less than one and/or the establishment of an equilibrium at the trap boundary.

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