Time dependent rate of diffusion-influenced ligand binding to receptors on cell surfaces

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ABSTRACT The theory of the kinetics of binding of ligands to a sphere partially covered by receptors is extended to provide the full time dependence of the reactive flux. The ligands diffuse to the receptors; the receptors are either fully or partially absorbing. The total flux into the sphere with many receptors is expressed analytically in terms of the flux into a single isolated receptor on the sphere. At steady state, the Berg-Purcell formula is generalized to the case where the binding to a single receptor is only partially diffusion controlled. At short times, the receptors behave independently and the total flux is the sum of the fluxes to the isolated receptors.

INTRODUCTION

The kinetics of binding of ligands to a sphere partially covered by receptors has received considerable theoretical attention. Previous treatments (1–3) relied on a steady-state calculation of the diffusive flux of ligands into the receptors. We present a fully time-dependent treatment of the same problem. In addition, we relax the previous assumption that the rate of binding to a receptor is completely diffusion controlled. After some introductory remarks, the results are described in some detail. A separate section is devoted to the mathematical details of the derivation.

The problem is formulated as follows. The concentration of ligands at spatial position r and time t is $C(r, t)$. This satisfies the diffusion equation

$$\frac{\partial}{\partial t} C(r,t) = D\nabla^2 C(r,t), \tag{1}$$

where D is the diffusion coefficient. Initially the ligand concentration is uniform outside the sphere,

$$C(r,0) = C_0 = 1 \quad [\text{all } r > R], \tag{2}$$

where R is the radius of the sphere. All results are proportional to the initial concentration C_0, so this is set equal to 1. The solution of the diffusion equation also involves boundary conditions. The sphere itself is reflecting; the receptors placed on it are partially absorbing. Then the boundary conditions are

$$D\frac{\partial}{\partial n} C = \kappa C \quad [\text{on the receptors}] \quad \text{and} \tag{3a}$$

$$D\frac{\partial}{\partial n} C = 0 \quad [\text{off the receptors}]. \tag{3b}$$

If κ is infinite, the receptors are perfectly absorbing and the concentration vanishes on the receptors. For finite κ, the receptors are partially absorbing. In these equations, $\partial/\partial n$ is the radial derivative at $r = R$. The goal is to find the total flux $k(t)$ into the receptors. This is given by the surface integral

$$k(t) = \oint dS D \frac{\partial}{\partial n} C(r,t). \tag{4}$$

Because the flux vanishes on that part of the sphere that is not covered by receptors, only the receptors contribute to the surface integral.

The specific aspect of the problem to be discussed here is how to handle the diffusive interference between individual receptors. We assume that the time dependent flux to a *single* receptor on the surface of a reflecting sphere is given. The question is how to use information about a single receptor to make a theory for N randomly distributed receptors. The main difficulty in doing this is that the flux of ligands into any single receptor disturbs the distribution of ligands near other receptors. This "diffusive interference" makes it difficult to satisfy boundary conditions uniformly on all receptors.

An approximate steady-state theory for ligand binding to receptors on a sphere was presented by Berg and Purcell (1). Their results may be summarized briefly as follows. The total flux of ligands into a single receptor, treated as a disk of radius a is

$$k_{\text{disk}} = 4Da. \tag{5}$$

(This is actually the flux into a disk of radius a on a flat plate, and not a disk on the surface of a sphere. If the radius of the sphere is much greater than the radius of the disk, we expect this to be a reliable estimate for k_{disk}.)

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The total diffusive flux of ligands into a fully absorbing sphere of radius R is given by the well known Smoluchowski formula

$$k_{\text{sphere}} = 4\pi DR. \tag{6}$$

Then, according to Berg and Purcell, the total flux into a reflecting sphere covered by N absorbing disks is approximately

$$k = \frac{k_{\text{sphere}} \cdot Nk_{\text{disk}}}{k_{\text{sphere}} + Nk_{\text{disk}}}. \tag{7}$$

At low coverage, the flux is controlled by individual disks, so that k is approximately Nk_{disk}. The actual flux is always smaller than Nk_{disk}. At high coverage, the flux approaches the Smoluchowski value k_{sphere}. One does not need to cover much of the sphere's area by disks in order to reach the Smoluchowski limit.

Recently an effective medium treatment (3) was used to rederive the Berg-Purcell (BP) result, and to obtain at the same time a small correction,

$$k = \frac{k_{\text{sphere}} \cdot Nk_{\text{disk}}}{(1-p)k_{\text{sphere}} + Nk_{\text{disk}}}, \tag{8}$$

in which p is the fraction of surface covered by receptors, $p = N\pi a^2/4\pi R^2$. (Appendix A contains some information about the agreement of Eq. 8 with the results of computer simulations [4]). The main result of the present paper is a generalization of this formula to the time-dependent case.

The BP result, and the modification containing the extra factor $1-p$, apply to the steady state only, and it is evident that the time-dependent theory must be different. For example, the flux into a single disk can only approach the steady-state value k_{disk} after some time has passed. The flux starts out proportional to the area of the disk rather than its radius. It takes a while for an initially uniform ligand distribution to relax to what one finds in the steady state, and for the flux to relax to $4Da$. In the same way, the total flux into N disks is initially proportional to the total area of the disks, and is not the same as the steady-state flux.

RESULTS

The main results of the treatment to be discussed here can be stated in a way that closely resembles the steady-state result. To account for time dependence, we use Laplace transforms in time, with the general definition

$$\hat{f}(z) = \int_0^\infty dt\, e^{-zt} f(t). \tag{9}$$

The Laplace transform of the time-dependent total flux into a reflecting sphere covered with N receptors is $\hat{k}$; this is what we want. The transform of the flux into a single absorbing disk on an otherwise reflecting sphere is $\hat{k}_{\text{disk}}$; this is what we are given. The transform of the total flux into an absorbing sphere is $\hat{k}_{\text{sphere}}$; this comes from the time-dependent version of the Smoluchowski theory. Then, these fluxes are related by

$$\hat{k} = \frac{\hat{k}_{\text{sphere}} \cdot N\hat{k}_{\text{disk}}}{(1-p)\hat{k}_{\text{sphere}} + N\hat{k}_{\text{disk}}}. \tag{10}$$

This expression is valid even when the disks are partially absorbing, i.e., when boundary condition (Eq. 3*a*) is used. Then $\hat{k}_{\text{sphere}}(z)$ must be replaced by the flux into a uniformly partially absorbing sphere obtained using the same boundary condition.

The preceding formula reduces properly to the earlier modified BP formula in the steady state. This is a simple consequence of the observation that if any time-dependent function $f(t)$ approaches a steady state value $f(\infty)$ at long times, its Laplace transform $\hat{f}(z)$ approaches $f(\infty)/z$ in the limit $z \to 0$. Then all $\hat{k}$'s can be replaced by their steady state values. In the following, we use f without the ˆ for the steady-state value $f(\infty)$.

To use this, we must know the time-dependent fluxes $k_{\text{sphere}}(t)$ and $k_{\text{disk}}(t)$, or more conveniently, their Laplace transforms $\hat{k}_{\text{sphere}}$ and $\hat{k}_{\text{disk}}$. The first of these is well known,

$$\hat{k}_{\text{sphere}}(z) = \frac{4\pi RD}{z}\left(1 + R\sqrt{\frac{z}{D}}\right). \tag{11}$$

This is the time-dependent version of the Smoluchowski formula. The generalization of this to a uniformly partially absorbing sphere (denoted by a prime on k) is[5]

$$\hat{k}'_{\text{sphere}}(z) = \frac{4\pi R^2\kappa\hat{k}_{\text{sphere}}(z)}{4\pi R^2\kappa + z\hat{k}_{\text{sphere}}(z)} \tag{12}$$

where $\hat{k}_{\text{sphere}}(z)$ is given by Eq. 11. At steady state this becomes

$$k'_{\text{sphere}} = \frac{4\pi R^2\kappa 4\pi DR}{4\pi R^2\kappa + 4\pi DR} = \frac{4\pi\kappa DR^2}{R\kappa + D} \tag{13}$$

The corresponding quantities for a disk have not been evaluated in closed form. For a fully absorbing disk, several terms in the short-time[6] ($z \to \infty$) and long-time[7] ($z \to 0$) expansions have been obtained. The following expression reproduces the first two terms in both of these expansions,

$$\hat{k}_{\text{disk}}(z) \cong \frac{4aD}{z}\left[1 + \frac{\pi a}{4}\sqrt{\frac{z}{D}} + \left(\frac{\pi}{4} - 1\right)a\sqrt{\frac{z}{D}}\frac{1}{\alpha + a\sqrt{\frac{z}{D}}}\right], \tag{14}$$

in which $\alpha = \pi(4 - \pi)/(\pi^2 - 8)$. The corresponding expression in the time domain is exact at short and long times; at intermediate times it is within one percent of the results of numerical solutions of the diffusion equation.[7] For a partially absorbing disk (denoted by a prime) a useful estimate for the steady-state rate constant can be obtained by mimicking the structure of the result for the sphere in Eq. 13,

$$k'_{\text{disk}} \cong \frac{\pi a^2 \kappa 4Da}{\pi a^2 \kappa + 4Da} = \frac{4Da}{1 + 4D/\pi a \kappa}. \tag{15}$$

In Appendix B, this expression is derived as the first member of a series of successively more accurate approximations. Eq. 15 turns out to be reasonably accurate for all values of κ, with a maximum deviation of less than four percent. For the time dependent flux to a partially absorbing disk, we expect that the analog of Eq. 12,

$$\hat{k}'_{\text{disk}}(z) \cong \frac{\pi a^2 \kappa \hat{k}_{\text{disk}}(z)}{\pi a^2 \kappa + z\hat{k}_{\text{disk}}(z)}, \tag{16}$$

where $\hat{k}_{\text{disk}}(z)$ is given by Eq. 14, should be a useful approximation, although we have not investigated this in detail. Eq. 16 reduces to Eq. 15 at long times, while at short times it correctly predicts that $k'_{\text{disk}} = \pi a^2 \kappa$.

We have already mentioned that at long times Eq. 10 correctly reduces to the modified BP formula for completely absorbing disks. We can generalize this to the partially absorbing case by using Eqs. 13 and 15. The final result is written most simply in reciprocal form,

$$\frac{1}{k} = \frac{1}{4\pi DR} + \frac{(1-p)}{N4Da} + \frac{1}{N\pi a^2 \kappa}, \tag{17}$$

When the binding to a single receptor is reaction limited ($\pi a^2 \kappa \ll 4Da$), then Eq. 17 simplifies to

$$k = \frac{4\pi DRN\pi a^2 \kappa}{4\pi DR + N\pi a^2 \kappa}. \tag{18}$$

To investigate the short time behavior of the time-dependent flux, we note that, irrespective of the boundary conditions, both $\hat{k}_{\text{sphere}}(z)$ and $\hat{k}_{\text{disk}}(z)$ are proportional to the area as $z \to \infty$. In particular, $\hat{k}_{\text{sphere}} \to 4\pi R^2 f(z)$ and $\hat{k}_{\text{disk}} \to \pi a^2 f(z)$, where in both cases, $f(z) \to \kappa/z$ when κ is finite, and $f(z) \to (D/z)^{1/2}$ when κ is infinite. On using these results in Eq. 10, we find

$$\hat{k}(z) \to N\hat{k}_{\text{disk}}(z) \quad \text{as} \quad z \to \infty. \tag{19}$$

Thus, at short times, the N receptors behave independently of each other.

To find the actual time dependence of $k(t)$, one must invert Laplace transforms. In the perfectly absorbing case, this can be done analytically (in terms of error functions) if the approximation given in Eq. 14 is used for $\hat{k}_{\text{disk}}(z)$. Otherwise, one may have to do the inversion numerically.

Finally, we emphasize that in calculating the flux, we assumed that the receptors provide an infinitely capacious sink for ligands. In the context of the Smoluchowski approach to diffusion influenced reactions, this suffices to obtain the time-dependent concentration of cells to which *no* ligands are bound. In particular, if the ligand concentration $[L]$ is much greater than the receptor concentration, the relative concentration of cells with all N receptors unoccupied is $\exp(-[L]\int_0^t k(\tau)d\tau)$. In the opposite limit, when the concentration of cells $[C]$ is much greater than the ligand concentration, the probability that no ligand is bound before time t has the same form, except that $[L]$ is replaced by $[C]$. This might be useful in describing the infection of a cell culture by a virus. If each cell has N receptors for the virus, the probability that infection (i.e., binding of the virus) has occured before time t is $1 - \exp(-[C]\int_0^t k(\tau)d\tau)$. The calculation of the time dependence of the average number of bound ligands requires further investigation; an interesting approach has been made by Geurts and Wiegel (8).

Our results may be more immediately applicable in electrochemistry; electrodes do act as infinitely capacious sinks, and the electric current into them is proportional to the flux. Recently, random arrays of microdisk electrodes imbedded in an electrochemically inert plane have been prepared (9). We have considered elsewhere (10), the application of the results derived in this paper to the problem of calculating the time-dependent current at such arrays.

Prager and Frisch (11) studied the apparently related problem of calculating the steady-state permeability of a planar membrane containing randomly distributed circular perforations. Using a different effective medium treatment, they found a logarithmic dependence on the number density n of holes when n is small. In the main result of our paper, we find that $\hat{k}$ is a rational function of n. The relation between their work and ours is not clear to us.

DERIVATION

Mathematical details concerning the derivation of our principal result, Eq. 10, are presented in this section of the paper. To repeat the formulation of the problem, we want to solve the diffusion equation for the ligand concentration outside the sphere, with specified boundary conditions on the surface of the sphere. The sphere is covered by N receptors or disks. Off the disks, the sphere is perfectly reflecting. On the disks, the boundary conditions are either absorbing or partially absorbing. In the initial state, the ligand concentration is spatially uniform. We want the time dependent flux into the disks.

The derivation of our main result is based on the same effective medium approximation that was used earlier to derive the steady state result. The idea is a simple one. To a distant observer who cannot see fine details, the reflecting sphere with N receptors looks like a sphere that is partially absorbing everywhere on its surface. This is called the "effective" sphere, and is labeled by E. The total flux into the effective sphere is denoted by $\hat{k}_E$; this is what we want. Now return to the original system, a reflecting sphere covered by N receptors. Select a point at random. The probability that this point is in an absorbing receptor is the fraction $p = N\pi a^2/4\pi R^2$ of the surface that is covered by receptors, and the probability that it is in the inert part of the sphere is $1-p$. Construct a disk-shaped region around this point. We consistently refer to this region as "in," and the remainder of the sphere as "out." In case A, this region is assigned single disk boundary conditions, as in Eq. 3a. The total flux is denoted by $\hat{k}_A$. In case R, it is assigned reflecting boundary conditions, as in Eq. 3b. The total flux is denoted by $\hat{k}_R$. Case A has probability p; case B has probability $1-p$. The surface area outside this special region appears uniform to a distant observer and is assigned the same "effective" boundary conditions in both cases. The total flux, averaged over the two cases A and R, should look like the total flux in case E; this is the effective medium condition

$$\hat{k}_E = p\hat{k}_A + (1-p)\hat{k}_R. \tag{20}$$

Because cases A and R both involve the same boundary condition in the outer region as case E, this equation determines self consistently the boundary conditions that apply on the effective sphere.

A fourth case, labeled S for single disk, is also needed. This is the case of one receptor on a reflecting sphere; the total flux is denoted by $\hat{k}_S$. It is what we earlier called $\hat{k}_{disk}$. As stated in the introduction, we assume that this quantity is known. All results depend on its value.

To apply the effective medium condition, we first have to work out the various fluxes. These are determined in principle by solving the time dependent diffusion equation with appropriate boundary conditions. Fortunately, we only need to solve cases E and S; E is easy because the sphere is uniform, and we already assumed that S is known. The rest is some rather disagreeable algebraic manipulation.

The Laplace transform of the diffusion equation is

$$z\hat{C}(r,z) - 1 = D\nabla^2\hat{C}(r,z) \quad (r > R). \tag{21}$$

The solution of this equation is fully determined by the boundary conditions satisfied by $\hat{C}$ on the surface $r = R$. These boundary conditions vary in different parts of the surface, depending on which of the cases E, A, R, and S is chosen. The boundary conditions involve the value $\hat{C}$ and the normal flux, denoted by

$$\hat{j} = D\frac{\partial}{\partial n}\hat{C}, \tag{22}$$

at all locations on the surface. For a fully absorbing boundary condition, we require that $\hat{C} = 0$; for a reflecting boundary condition we require that $\hat{j} = 0$; and for a partially absorbing boundary condition, we require

$$\hat{j} = \kappa\hat{C}, \tag{23}$$

where κ measures the degree to which the specified part of the surface is absorbing.

The total flux into the sphere is determined by the surface integral of the local flux,

$$\hat{k} = \oint dS\hat{j}. \tag{24}$$

In case S, a single receptor on a reflecting sphere, the boundary conditions are: in the reflecting region

$$\hat{j}_S = 0 \quad [\text{out}] \tag{25}$$

and on the receptor or disk

$$\hat{j}_S = \kappa\hat{C}_S \quad [\text{in}]. \tag{26}$$

Note that the single disk is treated as partially absorbing; for a fully absorbing disk, κ is infinite and $\hat{C}_S = 0$ on the disk. These stated boundary conditions, and the initial condition, fully determine the complete solution for this case, and in particular the total flux is

$$\hat{k}_S = \oint_{in} dS\hat{j}_S. \tag{27}$$

This is the same quantity as the earlier $\hat{k}_{disk}$.

In case E, referring to the effective sphere, the boundary condition is the same everywhere, and may be written as

$$\hat{j}_E = \hat{\kappa}_E\hat{C}_E \quad [\text{entire sphere}]. \tag{28}$$

The effective sphere is partially absorbing; the coefficient $\hat{\kappa}_E$ is generally a function of z. Actually we don't need to specify it at all. What is significant is just the normal flux $\hat{j}_E$. The total flux $\hat{k}_E = 4\pi R^2\hat{j}_E$ is what comes out of the derivation.

In case A, the boundary condition outside the disk-shaped special region is chosen to be exactly the same as for the effective sphere,

$$\hat{j}_A = \hat{j}_E \quad [\text{out}]. \tag{29}$$

On the disk-shaped region, the boundary condition is chosen to be exactly the same as for the single disk,

$$\hat{j}_A = \kappa \hat{C}_A \quad [\text{in}]. \tag{30}$$

These boundary conditions determine the solution completely. The resulting total flux comes from the normal derivatives on the surface, and has two parts,

$$\hat{k}_A = (4\pi R^2 - \pi a^2)\hat{j}_E + \oint_{\text{in}} dS \hat{j}_A. \tag{31}$$

In case R, the boundary condition off the special region is exactly the same as for the effective sphere,

$$\hat{j}_R = \hat{j}_E \quad [\text{out}], \tag{32}$$

and because the special region is reflecting,

$$\hat{j}_R = 0 \quad [\text{in}]. \tag{33}$$

The total flux is simply

$$\hat{k}_R = (4\pi R^2 - \pi a^2)\hat{j}_E. \tag{34}$$

When the various fluxes are combined in the effective medium condition, we find

$$\hat{k}_E = p\left[(4\pi R^2 - \pi a^2)\hat{j}_E + \oint_{\text{in}} dS \hat{j}_A\right] + (1-p)(4\pi R^2 - \pi a^2)\hat{j}_E$$

$$= \hat{k}_E - \pi a^2 \hat{j}_E + p\oint_{\text{in}} dS \hat{j}_A, \tag{35}$$

or

$$\pi a^2 \hat{j}_E = p\oint_{\text{in}} dS \hat{j}_A. \tag{36}$$

To continue, we must find $\hat{j}_A$.

At this point, we are dealing with four different solutions of the diffusion equation, labeled by E, S, A, and R. They differ only in the boundary conditions that they satisfy. However, there are similarities in the four sets of boundary conditions, and the solutions are linearly dependent on the boundary conditions. So it is reasonable to expect similarities in the solutions. This suggests that we try a relation between cases A, S, and E,

$$\hat{C}_A(r) \stackrel{?}{=} \mu_S \hat{C}_S(r) + \mu_E \hat{C}_E(r) + \mu_C, \tag{37}$$

where μ_s, μ_E, and μ_C are constants to be determined. The individual functions $\hat{C}_S$, $\hat{C}_E$, and $\hat{C}_A$ satisfy Laplace's equation, and this imposes one constraint on the constants (all concentrations being evaluated on the surface),

$$z[\mu_S \hat{C}_S + \mu_E \hat{C}_E + \mu_C] - 1 = D\nabla^2[\mu_S \hat{C}_S + \mu_E \hat{C}_E + \mu_C]$$
$$= \mu_S[z\hat{C}_S - 1] + \mu_E[z\hat{C}_E - 1]. \tag{38a}$$

This leads to the constraint

$$z\mu_C - 1 = -\mu_S - \mu_E. \tag{38b}$$

Next we check to see if the conjectured $\hat{C}_A$ satisfies the right boundary conditions. Off the disk, we want $\hat{j}_A = \hat{j}_E$; the conjecture gives $\hat{j}_A = \mu_S \hat{j}_S + \mu_E \hat{j}_E$. But $\hat{j}_S = 0$ off the disk. Then we must impose the constraint

$$\mu_E = 1. \tag{39}$$

On the disk, we want

$$\hat{j}_A = \kappa \hat{C}_A = \kappa\{\mu_S \hat{C}_S + \mu_E \hat{C}_E + \mu_C\}; \tag{40a}$$

the conjecture gives

$$\hat{j}_A = \mu_S \hat{j}_S + \mu_E \hat{j}_E = \mu_S \kappa \hat{C}_S + \mu_E \hat{j}_E. \tag{40b}$$

On comparing these, we find the constraint

$$\kappa[\mu_E \hat{C}_E + \mu_C] = \mu_E \hat{j}_E. \tag{40c}$$

All constants are now determined, and the final result for $\hat{C}_A(r)$, which involves both the general r and the specific R, is

$$\hat{C}_A(r) = \hat{C}_E(r) + \left[\hat{C}_E(R) - \frac{1}{\kappa}\hat{j}_E\right][z\hat{C}_S(r) - 1]. \tag{41}$$

The radial derivative is needed to get the flux. On the disk, this becomes

$$\hat{j}_A = \hat{j}_E + \left[\hat{C}_E - \frac{1}{\kappa}\hat{j}_E\right] z\hat{j}_S. \tag{42}$$

This is substituted in the effective medium condition, Eq. 36,

$$\pi a^2 \hat{j}_E = p\oint_{\text{in}} dS \left\{\hat{j}_E + \left[\hat{C}_E - \frac{1}{\kappa}\hat{j}_E\right] z\hat{j}_S\right\}. \tag{43}$$

But $\hat{C}_E$ and $\hat{j}_E$ are independent of position on the surface, and the surface integral of $\hat{j}_S$ is $\hat{k}_S$, the total flux into a single receptor, as in Eq. 27. This leads to

$$(1-p)\pi a^2 \hat{j}_E = p\left[\hat{C}_E - \frac{1}{\kappa}\hat{j}_E\right] z\hat{k}_S. \tag{44}$$

On solving Laplace's equation for case E, which is easy because all points on the surface are equivalent, we find

$$\hat{C}_E(r) = \frac{1}{z} - \frac{\hat{j}_E R^2/D}{1 + R\sqrt{\frac{z}{D}}} \frac{1}{r} \exp\left[\sqrt{\frac{z}{D}}(r - R)\right]. \tag{45}$$

This has the right initial value and the specified normal derivative at R. Then we have a direct relation between

$\hat{C}_E(R)$ and $\hat{j}_E$. When this is substituted in Eq. 44, we have an expression for $\hat{j}_E$ (and therefore $\hat{k}_E$) in terms of $\hat{k}_S$. The rest of the derivation of Eq. 10, which we omit, involves recognizing terms that reduce to $\hat{k}'_{\text{sphere}}$ as in Eq. 12, and using the definition $p = N\pi a^2/4\pi R_2$ (which is how the factor N appears). To correspond to earlier notation, $\hat{k}_S$ is replaced by $\hat{k}_{\text{disk}}$. The result is Eq. 10.

APPENDIX A

Eq. 8 provides a more accurate prediction of binding rates than the original Berg-Purcell formula. Scott H. Northrup (4) performed computer simulations of the binding process and reported his results in graphical form. He has very kindly given us his actual numerical results, which are presented in this appendix. In the Table 1, N is the number of receptors on the surface, SIM denotes the simulation results, BP is the prediction of the BP formula, Eq. 7, and Z is the prediction of the modified Eq. 8. The parameter p is given by $(0.0628)^2 N/4$.

APPENDIX B

A partially absorbing circular disk is placed on a reflecting plane. We want to find the steady-state diffusive flux k into the disk when the concentration $C(r)$ of the diffusing material is maintained at a constant value $C_0 = 1$ far from the disk.

The problem is formulated mathematically as follows. In cartesian coordinates, the disk is a circular region in the plane $z = 0$, centered on the origin, with radius a. The steady-state concentration at r is the solution of Laplace's equation in the upper half space $z > 0$,

$$D\nabla^2 C(r) = 0 \tag{B1}$$

which satisfies the boundary conditions

$$C(r) \rightarrow C_0 = 1 \quad \text{as} \quad r \rightarrow \infty, \tag{B2}$$

$$\frac{\partial C}{\partial z} = 0 \quad \text{on} \quad \{x^2 + y^2 > a^2, \quad z = 0^+\}, \tag{B3}$$

and the partially absorbing or radiation boundary condition on the disk,

$$D\frac{\partial}{\partial z}C = \kappa C \quad \text{on} \quad \{x^2 + y^2 < a^2, \quad z = 0^+\}. \tag{B4}$$

TABLE 1 Comparison of theory with simulations

N	$k(SIM)$	$k(BP)$	$k(Z)$
1	0.019 ± 0.002	0.0196	0.0196
2	0.038 ± 0.002	0.0385	0.0385
4	0.073 ± 0.003	0.0741	0.0743
6	0.106 ± 0.004	0.1072	0.1076
8	0.137 ± 0.004	0.1380	0.1388
12	0.194 ± 0.005	0.1937	0.1953
16	0.244 ± 0.007	0.2426	0.2452
32	0.402 ± 0.006	0.3904	0.3977
50	0.525 ± 0.007	0.5002	0.5125
64	0.583 ± 0.007	0.5616	0.5772
128	0.749 ± 0.006	0.7193	0.7454
256	0.877 ± 0.008	0.8367	0.8725

Note that the boundary conditions on the plane are applied only on the positive z side of the plane. In the limit $\kappa \rightarrow \infty$, the disk is perfectly absorbing. In the limit $\kappa \rightarrow 0$, the disk is perfectly reflecting. The desired flux is the surface integral over the disk

$$k = \oint dSD\frac{\partial}{\partial z}C(r). \tag{B5}$$

It is convenient to change from cartesian to oblate spheroidal coordinates, $(x, y, z) \rightarrow (\xi, \eta, \varphi)$, according to

$$z = a\xi\eta \tag{B6}$$

$$x = a\,[(\xi^2 + 1)(1 - \eta^2)]^{1/2}\cos\varphi \tag{B7}$$

$$y = a\,[(\xi^2 + 1)(1 - \eta^2)]^{1/2}\sin\varphi. \tag{B8}$$

In oblate spheroidal coordinates, the disk is specified by $\xi = 0^+$. The xy plane outside the disk is specified by $\eta = 0^+$. The upper half space is $\eta > 0$.

Laplace's equation is separable in oblate spheroidal coordinates; its general solution involves products of Legendre functions and trigonometric functions. The solution having cylindrical symmetry and the correct limiting behavior far from the disk is

$$C(\xi, \eta) = 1 + \sum_n A_n P_n(\eta) Q_n(i\xi), \tag{B9}$$

where P_n and Q_n are Legendre functions of the first and second kind. Note that the argument of Q_n is imaginary. $P_n(z)$ is a polynomial in z; $Q_n(z)$ has logarithmic branch points. In particular, $Q_0(z)$ is

$$Q_0(z) = \frac{1}{2}\log\frac{z+1}{z-1}; \quad Q_0(i\xi) = -i\tan^{-1}\frac{1}{\xi}. \tag{B10}$$

Normal derivatives on the plane $z = 0$ are

$$\left.\frac{\partial C}{\partial z}\right)_{z=0\text{ outside}} = \frac{1}{a\xi}\left.\frac{\partial C}{\partial \eta}\right)_{\eta=0}, \tag{B11}$$

$$\left.\frac{\partial C}{\partial z}\right)_{z=0\text{ inside}} = \frac{1}{a\eta}\left.\frac{\partial C}{\partial \xi}\right)_{\xi=0}. \tag{B12}$$

The reflecting boundary condition outside the disk leads to the conclusion that only the even Legendre polynomials $P_{2n}(\eta)$ may appear in the general solution. Then the partially absorbing boundary condition on the disk takes the form

$$\frac{D}{a\eta}\sum_{n=0} A_{2n} i \left.\frac{\partial Q_{2n}(i\xi)}{\partial i\xi}\right]_{\xi=0^+} P_{2n}(\eta) = \kappa\,[1 + \sum_{n=0} A_{2n} Q_{2n}(i0^+) P_{2n}(\eta)]. \tag{B13}$$

This boundary condition must hold for all η between 0 and 1; negative η are not involved because only the upper half space is relevant. It determines the unknown coefficients A_{2n}.

On performing the surface integral of the normal derivative of C, one finds that the flux into the disk is given exactly by

$$k = 4Da\,(i\pi/2)\,A_0. \tag{B14}$$

To proceed, we must find the unknown coefficients. For convenience, we change the notation:

$$X_n = -A_{2n} Q_{2n}(i0^+),$$
$$c_n = -i\frac{\pi}{2}\left[\frac{1}{Q_{2n}(z)}\frac{\partial Q_{2n}(z)}{\partial z}\right]_{z=i0^+},$$
$$h = \frac{2}{\pi}\frac{D}{\kappa a}. \tag{B15}$$

Then the coefficients X_n are determined by

$$\sum_{n=0} [h\, c_n + \eta]\, P_{2n}(\eta)\, X_n = \eta,\ 0 < \eta < 1. \tag{B16}$$

The flux into the disk is given by

$$k = 4Da\, X_0. \tag{B17}$$

In solving for the coefficients, we need the c_n's. They involve the Legendre functions of the second kind, and their derivatives, at $z = i0^+$. To get $Q_{2n}(i0^+)$, use the recursion formula

$$2(n-1)\, zQ_{n-1}(z) = nQ_n(z) + (n-1)Q_{n-2}{}^{(z)}. \tag{B18}$$

On setting $z = i0^+$, we find

$$Q_n = -\frac{n-1}{n} Q_{n-2} \tag{B19}$$

and the initial value $Qo = -i\pi/2$ starts the recursion. The complete dependence on n is

$$Q_{2n}(i0^+) = (-1)^n \frac{(1/2)_n}{n!}\left(-i\frac{\pi}{2}\right) \tag{B20}$$

To get the derivatives of Q_{2n}, start with the integral representation

$$Q_{2n}(z) = P_{2n}(z)\int_z^\infty dt \frac{1}{t^2-1}\frac{1}{P_{2n}(t)^2}. \tag{B21}$$

Take the derivative with respect to z, and then set $z = i0^+$. The derivative of P_{2n} is odd in z and vanishes at $z = 0$. The remainder gives

$$\left.\frac{d}{dz} Q_{2n}(z)\right]_{i0^+} = \frac{1}{P_{2n}(0)} = (-1)^n \frac{n!}{(1/2)_n}. \tag{B22}$$

When these formulas are combined, we find an exact expression for the c_n's,

$$c_n = \left[\frac{n!}{(1/2)_n}\right]^2. \tag{B23}$$

We still have to solve for the coefficients. The boundary condition equation mixes terms that are even and odd in η, and does not appear to have a reasonable solution; however, the boundary condition is applied only for $\eta > 0$, and the parity of η is irrelevant. Convert the equation into an infinite set of simultaneous linear equations for the coefficients: multiply the equation by $P_{2m}(\eta)$ and integrate over η from 0 to 1. Define the resulting integrals:

$$U_m = \int_0^1 dx x P_{2m}(x),$$
$$V_{mn} = \int_0^1 dx x P_{2m}(x)\, P_{2n}(x). \tag{B24}$$

TABLE 2 The steady state rate coefficient, $k = 4DaX_0$, for a partially absorbing disk at various levels of truncation as a function of $h = 2D/\pi\kappa a$

h	$[X_0]_0$	$[X_0]_1$	$[X_0]_5$	$[X_0]_{10}$
0.1	0.83333	0.80908	0.803292	0.803227
0.2	0.71429	0.69001	0.686644	0.686616
0.3	0.625	0.60380	0.601609	0.601603
0.4	0.55556	0.53751	0.535981	0.535970
0.5	0.5	0.48466	0.483525	0.483517
1.0	0.33333	0.32574	0.325337	0.325334
2.0	0.2	0.19709	0.196966	0.196965
3.0	0.14286	0.14134	0.141279	0.141278
4.0	0.11111	0.11018	0.110146	0.110146
5.0	0.09091	0.09028	0.090259	0.090259

Then the boundary condition equation becomes

$$\frac{h}{4m+1} c_m X_m + \sum_{n=0}^{\infty} V_{mn} X_n = U_m.$$

We want to solve this for $X_0(h)$. It is an infinite set of linear equations; however, we can truncate it at various levels, by restricting m and n to integers $\le N$. On solving the truncated equations, we can investigate the convergence of numerical results as N increases.

A sequence of approximate solutions was found by using Wolfram's Mathematica. This software allows one to construct the Legendre polynomials, and to perform exact integration of the U_m and V_{mn} (which are integers). Finally it gives the exact solution of a truncated set of linear equations, expressing X_0 as the ratio of two polynomials in the variable h with integer coefficients. This was done with exact integer arithmetic for small N, and double precision numerical arithmetic for large N. The first two approximations ($N = 0, 1$ respectively) are

$$[X_0]_0 = \frac{1}{1+2h}, \tag{B25}$$

$$[X_0]_1 = \frac{15+128h}{15+168h+256h^2}. \tag{B26}$$

The first approximation ($N = 0$) is the one referred to in the main text as Eq. 15. This process was carried out to the thirtieth order, and the rational approximations were used to generate numerical values of $X_0(h)$ for $N = 0, 1, 2, 5, 10, 20$, and 30. The results, some of which are shown in Table 2, indicate quite good convergence; the tenth order approximation is probably a representation of the exact solution to four significant figures for $h > 0.01$. The first approximation ($N = 0$) misses the exact solution by less than four percent for small h. The second approximation ($N = 1$) is good to a few tenths of a percent for the entire range of h.

In a recent note, Phillips (12) concludes that at small h, $X_0(h)$ should go as $1 - (h/2) \ln h + 0(h)$. Our procedure cannot produce a logarithmic dependence on h; in effect, we are expanding in $1/h$. For $h = 0.001$, we needed to go to $N = 30$ to obtain X_0 to four significant figures ($X_0 = 0.9956$). Our numerical results are fully consistent with Phillips' logarithmic dependence.

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