21.1 Smoluchowski reaction rate

An important example of a first passage time process arises in Smoluchowski rate theory for diffusion–controlled reactions. The simplest version of the theory concerns the bimolecular reaction $A + B \rightarrow AB$ for which the concentrations evolve according to the following law of mass action:

$$\frac{d[AB]}{dt} = k[A][B].$$

Assume that an $A$ molecule and a $B$ molecule react immediately to form the complex $AB$ when they encounter each other within a reaction radius $a$, so that the speed of reaction $k$ is limited by their encounter rate via diffusion.

**Note 7.** $k$ has units of volume $s^{-1}$. Concentrations are typically measured in molar $M$ with 1 molar $= 1000$ moles/m$^3$ and 1 mole $\approx 6 \times 10^{23}$ molecules (Avagadro’s number).)

Formulate the problem as an idealized first passage process, in which one $A$ molecule, say, is fixed and treated as the center of a spherical target domain of reaction radius $a$, whilst the $B$ molecules diffuse and are absorbed if they hit the boundary of the target domain, see Fig. 74a. It is assumed that the density of the particles is sufficiently small, so that reactions with other $A$ molecules have a negligible effect on the concentration of $B$ molecules in a neighborhood of the target molecule.

The steady–state flux to the target (if it exists) is then identified as the mean reaction rate $k$ across many targets. Let $\Omega$ denote the target domain and $\partial \Omega$ its absorbing boundary. We then need to
solve the diffusion equation for the concentration $c(x, t)$ of background molecules exterior to the domain $\Omega$:

$$\frac{\partial c(x, t)}{\partial t} = D \nabla^2 c(x, t), \quad c(x \in \partial \Omega, t) = 0, \quad c(x, 0) = c_0,$$

subject to the far-field boundary condition $c(x, t) = c_0$ for $x \rightarrow \infty$. The flux through the target boundary is

$$J = D \int_{\partial \Omega} \nabla c \cdot dS.$$

Note the sign, which is due to the fact that the flux is from the exterior to the interior of the target.

Let $d$ denote the spatial dimension of the target. For $d > 2$, a diffusing particle is transient, which means that there is a non-zero probability of never reaching the target. Hence, the loss of reactants by target absorption is balanced by their resupply from infinity. It follows that there exists a steady state in which the reaction rate is finite. On the other hand, for $d \leq 2$, reactants are sure to hit the target (recurrent diffusion) and a depletion zone continuously develops around the target so that the flux and reaction rate decay monotonically to zero with respect to time. Although a reaction rate does not strictly exist, it is still useful to consider the time-dependent flux as a time-dependent reaction rate. The two-dimensional case is particularly important when considering interactions of molecules embedded in the plasma membrane of a cell or the lipid bilayer surrounding an intracellular compartment.

### 21.2 Spherical target

Consider the case of a spherical target of radius $a$ ($d = 3$). Exploiting the radial symmetry of the problem, it is possible to set $u(r, t) = rc(r, t)$ such that the 3D diffusion equation for $c$ reduces to a 1D diffusion equation for $u$:

$$\frac{\partial u(r, t)}{\partial t} = D \frac{\partial^2 u(r, t)}{\partial r^2}$$

with $u(r, 0) = rc_0$, $u(a, t) = 0$ and $u(r, t) = rc_0$ as $r \rightarrow \infty$. Laplace transforming this equation gives $s\tilde{u}(r, s) - rc_0 = D\tilde{u}''(r, s)$, which has the solution

$$\tilde{u}(r, s) = \frac{c_0}{s} \left[ r - ae^{-r/a}\sqrt{s/D} \right].$$

Since the inverse Laplace transform of $s^{-1}[1 - e^{-r/\sqrt{s/D}}]$ is the error function $\text{erf}(r/\sqrt{4Dt})$, see Table 2.1, where

$$\text{erf}(z) = \frac{2}{\sqrt{\pi}} \int_0^z e^{-r^2} dr,$$

one finds that

$$c(r, t) = c_0 \left( 1 - \frac{a}{r} \right) + \frac{ac_0}{r} \text{erf} \left( \frac{r - a}{\sqrt{4Dt}} \right).$$

It follows that the time-dependent flux is

$$J(t) = 4\pi a^2 D \left. \frac{\partial c}{\partial r} \right|_{r=a}$$

$$= 4\pi a D c_0 \left( 1 + \frac{a}{\sqrt{\pi Dt}} \right) \xrightarrow{t \to \infty} 4\pi a D c_0.$$
Hence, we obtain the Smoluchowski reaction rate $k = 4\pi aD$.

It is straightforward to generalize the steady–state result to other three–dimensional targets by making a connection with electrostatics. That is, setting $\phi(x) = 1 - c(x)/c_0$ in steady–state, it follows that $\phi$ satisfies Laplace’s equation with $\phi = 1$ on the target boundary and $\phi = 0$ at infinity, so that $\phi$ is equivalent to the electrostatic potential generated by a perfectly conducting object $\Omega$ held at unit potential. Moreover, the steady–state reaction rate $k = 4\pi DQ$ where $Q$ is the total charge on the surface of the conductor, which for a unit potential is equal to the capacitance, $Q = C$. Thus, determining the reaction rate for a general 3D target is equivalent to finding the capacitance of a perfect conductor with the same shape.

### 21.3 2D target

Although it is possible to calculate the exact time–dependent flux for $d \leq 2$, a much simpler method is to use a quasi–static approximation. Consider, for example a target disk of radius $r = a$. The region exterior to the disk is divided into a near zone that extends a distance $\sqrt{Dt}$ from the surface and a complementary far zone, see Fig. 74b. In the near zone, it is assumed that diffusing particles have sufficient time to explore the domain before being absorbed by the target so that the concentration in the near zone can be treated as almost steady or quasi–static. Conversely, it is assumed that the probability of a particle being absorbed by the target is negligible in the far zone, since a particle is unlikely to diffuse more than a distance $\sqrt{Dt}$ over a time interval of length $t$. Thus, $c(r) \approx c_0$ for $r > \sqrt{Dt} + a$. The near zone concentration is taken to be a radially symmetric solution of Laplace’s equation, which for $d = 2$ is $c(r) = A + B \log r$. Matching the solution to the boundary conditions $c(a) = 0$ and $c(a + \sqrt{Dt}) = c_0$ then gives (for $\sqrt{Dt} \gg a$)

$$c(r, t) \approx \frac{c_0 \log(r/a)}{\log(\sqrt{Dt}/a)}.$$

The corresponding time–dependent flux is

$$J(t) \approx \frac{2\pi D c_0}{\log(\sqrt{Dt}/a)}.$$

### 21.4 Radiation boundary condition

Collins and Kimball generalized the Smoluchowski theory to the case of a radiation or partially absorbing boundary condition

$$-4\pi r^2 J(r, t) = 4\pi r^2 D \frac{dc(r, t)}{dr} = k_{\text{on}} c(r, t), \quad (21.2)$$

where $k_{\text{on}}$ is an intrinsic biomolecular reaction rate constant. If $k_{\text{on}} \to \infty$ then we recover the fully diffusion–limited regime. At steady–state, we can integrate the radiation condition to give

$$c(r) - c(a) = \int_a^r k_{\text{on}} c(a) \frac{4\pi D r^2}{4\pi Dr^2} dr = \frac{k_{\text{on}} c(a)}{4\pi D} \left( \frac{1}{a} - \frac{1}{r} \right).$$
Finally, using the far-field condition \( c(\infty) = c_0 \), the concentration at the surface is

\[
c(a) = \frac{c_0}{1 + Nk_{on}/(4\pi Da)}.
\]

We thus have the following result: the steady-state reaction rate is

\[
k = \frac{4\pi Da k_{on}}{4\pi Da + k_{on}} \quad (21.3)
\]

In the limit \( k_{on} \to \infty \) one obtains the result for a perfect absorber with \( k \to 4\pi Da \). On the other hand, if \( k_{on} \ll Da \) then the depletion rate is so slow that \( c(a) \approx c_0 \), the background concentration, and \( k \to k_{on} \).

### 21.5 Chemoreception

One application of diffusion-limited reactions is to chemoreception. In the case of a bacterium such as \( E. coli \), the cell surface is covered in receptors that detect signaling molecules in the surrounding environment, see Fig. 75. Treating the cell as a perfect absorber assumes that there is a sufficient number of receptors distributed on the cell surface and that binding of a signaling molecule is instantaneous when it hits the surface. There are two major simplifications of such a model - (i) the rate of receptor/ligand binding \( k_{on} \) is finite, and (ii) receptors tend to be non-uniformly distributed on the cell surface. The role of receptor clustering in signal amplification will be addressed in Chap. 10, where we discuss the biochemical networks involved in bacterial chemosensing. In the case of a uniform distribution of \( N \) receptors, we can simply use equation (21.3) under the scaling \( k_{on} \to Nk_{on} \).

**Diffusion-limited reaction rate.** Consider a spherical cell with \( N \) receptors distributed uniformly across its surface. The net absorption rate of ligands by a spherical cell with \( N \) receptors distributed uniformly across its surface is

\[
k = \frac{4\pi Da Nk_+}{4\pi Da + Nk_+} \quad (21.4)
\]

where \( k_+ \) is the binding rate at contact. In the limit \( Nk_+ \to \infty \) one obtains the result for a perfect absorber with \( k \to 4\pi Da \). On the other hand, if \( Nk_+ \ll Da \) then the depletion rate is so slow that \( c(a) \approx c_0 \), the background concentration, and \( k \to k_+ \).