Chapter 10

Rates of Diffusion-Controlled Reactions

Contents

The metabolism of the biological cell, the control of its development and its communication with other cells in the organism or with its environment involves a complex web of biochemical reactions. The efficient functioning of this web relies on the availability of suitable reaction rates. Biological functions are often controlled through inhibition of these reaction rates, so the base rates must be as fast as possible to allow for a wide range of control. The maximal rates have been increased throughout the long evolution of life, often surpassing by a wide margin rates of comparable test tube reactions. In this respect it is important to realize that the rates of biochemical reactions involving two molecular partners, e.g., an enzyme and its substrate, at their optimal values are actually determined by the diffusive process which leads to the necessary encounter of the reactants. Since many biochemical reactions are proceeding close to their optimal speed, i.e., each encounter of the two reactants leads to a chemical transformation, it is essential for an understanding of biochemical reactions to characterize the diffusive encounters of biomolecules.

In this section we want to describe first the relative motion of two diffusing biomolecules subject to an interaction between the partners. We then determine the rates of reactions as determined by the diffusion process. We finally discuss examples of reactions for various interactions.

10.1 Relative Diffusion of two Free Particles

We consider first the relative motion in the case that two particles are diffusing freely. One can assume that the motion of one particle is independent of that of the other particle. In this case the diffusion is described by a distribution function $p(\boldsymbol{r}_1, \boldsymbol{r}_2, t | \boldsymbol{r}_{10}, \boldsymbol{r}_{20}, t_0)$ which is governed by the diffusion equation

$$\partial_t\, p(\boldsymbol{r}_1, \boldsymbol{r}_2, t | \boldsymbol{r}_{10}, \boldsymbol{r}_{20}, t_0) \;=\; \left(D_1 \nabla_1^2 \;+\; D_2 \nabla_2^2 \right)\, p(\boldsymbol{r}_1, \boldsymbol{r}_2, t | \boldsymbol{r}_{10}, \boldsymbol{r}_{20}, t_0) \qquad (10.1)$$

where $\nabla_j = \partial/\partial \boldsymbol{r}_j$, $j = 1, 2$. The additive diffusion operators $D_j \nabla_j^2$ in (10.1) are a signature of the statistical independence of the Brownian motions of each of the particles.

Our goal is to obtain from (10.1) an equation which governs the distribution $p(\boldsymbol{r}, t | r_0, t_0)$ for the relative position

$$\boldsymbol{r} = \boldsymbol{r}_2 - \boldsymbol{r}_1 \tag{10.2}$$

of the particles. For this purpose we express (10.1) in terms of the coordinates $\boldsymbol{r}$ and

$$\boldsymbol{R} = a\,\boldsymbol{r}_1 + b\,\boldsymbol{r}_2 \tag{10.3}$$

which, for suitable constants a, b, are linearly independent. One can express

$$\nabla_1 = a\nabla_{\boldsymbol{R}} - \nabla\,, \quad \nabla_2 = b\nabla_{\boldsymbol{R}} + \nabla \tag{10.4}$$

where $\nabla = \partial/\partial\boldsymbol{r}$. One obtains, furthermore,

$$\nabla_1^2 = a^2\nabla_{\boldsymbol{R}}^2 + \nabla^2 - 2a\,\nabla_{\boldsymbol{R}}\nabla \tag{10.5}$$

$$\nabla_2^2 = b^2\nabla_{\boldsymbol{R}}^2 + \nabla^2 + 2b\,\nabla_{\boldsymbol{R}}\nabla \tag{10.6}$$

The diffusion operator

$$\widehat{\mathcal{D}} = D_1\nabla_1^2 + D_2\nabla_2^2 \tag{10.7}$$

can then be written

$$\widehat{\mathcal{D}} = (D_1 a^2 + D_2 b^2)\,\nabla_{\boldsymbol{R}}^2 + (D_1 + D_2)\,\nabla^2 + 2\,(D_2 b - D_1 a)\,\nabla_{\boldsymbol{R}}\nabla \tag{10.8}$$

If one defines

$$a = \sqrt{D_2/D_1}\,, \quad b = \sqrt{D_1/D_2} \tag{10.9}$$

one obtains

$$\widehat{\mathcal{D}} = (D_1 + D_2)\,\nabla_{\boldsymbol{R}}^2 + (D_1 + D_2)\,\nabla^2\,. \tag{10.10}$$

The operator (10.10) can be considered as describing two independent diffusion processes, one in the coordinate $\boldsymbol{R}$ and one in the coordinate $\boldsymbol{r}$. Thus, the distribution function may be written $p(\boldsymbol{R}, t | \boldsymbol{R}_0, t_0)p(\boldsymbol{r}, t | \boldsymbol{r}_0, t_0)$. If one disregards the diffusion along the coordinate $\boldsymbol{R}$ the relevant remaining relative motion is governed by

$$\partial_t p(\boldsymbol{r}, t | \boldsymbol{r}_0, t_0) = (D_1 + D_2)\,\nabla^2 p(\boldsymbol{r}, t | \boldsymbol{r}_0, t_0)\,. \tag{10.11}$$

This equation implies that the relative motion of the two particles is also governed by a diffusion equation, albeit for a diffusion coefficient

$$D = D_1 + D_2\,. \tag{10.12}$$

Relative Motion of two Diffusing Particles with Interaction

We seek to describe now the relative motion of two molecules which diffuse while interacting according to a potential $U(\boldsymbol{r})$ where $\boldsymbol{r} = \boldsymbol{r}_2 - \boldsymbol{r}_1$. The force acting on particle 2 is $-\nabla_2 U(\boldsymbol{r}) = \boldsymbol{F}$; the force acting on particle 1 is $-\boldsymbol{F}$. The distribution function $p(\boldsymbol{r}_1, \boldsymbol{r}_2, t | \boldsymbol{r}_{10}, \boldsymbol{r}_{20}, t_0)$ obeys the Smoluchowski equation

$$
\begin{aligned}
\partial_t p &= \big[\,(\,D_1 \nabla_1^2 \,+\, D_2 \nabla_2^2\,) \\
&\quad -\, D_2 \beta \,\nabla_2 \cdot \boldsymbol{F}(\boldsymbol{r}) \,+\, D_1 \beta \,\nabla_1 \cdot \boldsymbol{F}\,\big]\, p\,.
\end{aligned}
\tag{10.13}
$$

The first two terms on the r.h.s. can be expressed in terms of the coordinates $\boldsymbol{R}$ and $\boldsymbol{r}$ according to (10.10). For the remaining terms holds, using (10.4, 10.9),

$$
D_2 \nabla_2 \,-\, D_1 \nabla_1 \,=\, (\,D_1 \,+\, D_2)\,\nabla
\tag{10.14}
$$

Hence, one can write the Smoluchowski equation (10.13)

$$
\partial_t p \,=\, \big[\,(\,D_1 \,+\, D_2)\,\nabla_{\boldsymbol{R}}^2 \,+\, (D_1 + D_2)\,\nabla \cdot (\nabla \,-\, \beta\,\boldsymbol{F})\,\big]\, p\,.
\tag{10.15}
$$

This equation describes two independent random processes, free diffusion in the $\boldsymbol{R}$ coordinate and a diffusion with drift in the $\boldsymbol{r}$ coordinate. Since we are only interested in the relative motion of the two molecules, i.e., the motion which governs their reactive encounters, we describe the relative motion by the Smoluchowski equation

$$
\partial_t p(\boldsymbol{r}, t | \boldsymbol{r}_0, t_0) \,=\, D\nabla \cdot (\nabla \,-\, \beta\,\boldsymbol{F})\, p(\boldsymbol{r}, t | \boldsymbol{r}_0, t_0)\,.
\tag{10.16}
$$

10.2 Diffusion-Controlled Reactions under Stationary Conditions

We want to consider now a reaction vessel which contains a solvent with two types of particles , particle 1 and particle 2, which engage in a reaction

$$
\text{particle 1} \,+\, \text{particle 2} \,\rightarrow\, \text{products}\,.
\tag{10.17}
$$

We assume that particle 1 and particle 2 are maintained at concentrations c_1 and c_2, respectively, i.e., the particles are replenished as soon as they are consumed by reaction (10.17). We also consider that the reaction products are removed from the system as soon as they are formed.

One can view the reaction vessel as containing pairs of particles 1 and 2 at various stages of the relative diffusion and reaction. This view maintains that the concentration of particles is so small that only rarely triple encounters, e.g., of two particles 1 and one particle 2, occur, so that these occurences can be neglected. The system considered contains then many particle 1 and particle 2 pairs described by the Smoluchowski equation (10.16). Since the concentration of the particles is maintained at a steady level one can expect that the system adopts a stationary distribution of inter-pair distances $p(\boldsymbol{r})$ which obeys (10.16), i.e.,

$$
\nabla D(\boldsymbol{r}) \cdot (\nabla \,-\, \beta\,\boldsymbol{F})\, p(\boldsymbol{r}) \,=\, 0\,,
\tag{10.18}
$$

subject to the condition

$$
p(\boldsymbol{r}) \,\asymp\, |\boldsymbol{r}| \rightarrow \infty\, c_1\, c_2\,.
\tag{10.19}
$$

Reaction (10.17) is described by the boundary condition

$$\hat{n} \cdot D(\boldsymbol{r}) \, (\nabla \, - \, \beta \boldsymbol{F}) \, p(\boldsymbol{r}) \; = \; w \, p(\boldsymbol{r}) \qquad \text{at } |\boldsymbol{r}| \; = \; R_o. \tag{10.20}$$

for some constant w.

The occurence of reaction (10.17) implies that a stationary current develops which describes the continuous diffusive approach and reaction of the particles. We consider in the following the case that the particles are governed by an interaction potential which depends solely on the distance $|\boldsymbol{r}|$ of the particles and that the diffusion coefficient D also depends solely on $|\boldsymbol{r}|$. The stationary Smoluchowski equation (10.18) reads then

$$(\, \partial_r D(r) \,)(\, (\, \partial_r \, - \, \beta \, F(r) \,) \, p(\boldsymbol{r}) \,) \; = \; 0 \tag{10.21}$$

to which is associated the radial current

$$J_{\text{tot}}(r) \; = \; 4\pi r^2 D(r)(\partial_r \, - \, \beta \, F(r) \,) \, p(\boldsymbol{r})) \tag{10.22}$$

where we have summed over all angles θ, ϕ obtaining the total current at radius r. For $F(r) \; = \; - \partial_r U(r)$ one can express this

$$J_{\text{tot}}(r) \; = \; 4\pi r^2 D(r) \, \exp[-\beta U(r)] \, (\, \partial_r \, \exp[\beta U(r)] \, p \,) \, . \tag{10.23}$$

However, $J_{\text{tot}}(r)$ must be the same at all r since otherwise $p(r)$ would change in time, in contrast to the assumption that the distribution is stationary. It must hold, in particular,

$$J_{\text{tot}}(R_o) \; = \; J_{\text{tot}}(r) \, . \tag{10.24}$$

The boundary condition (10.20), together with (10.23), yields

$$4\pi R_o^2 \, w \, p(R_o) \; = \; 4\pi r^2 \, D(r) \, \exp[-\beta U(r)] \, (\, \partial_r \, \exp[\beta U(r)] \, p(r) \,) \, . \tag{10.25}$$

This relationship, a first order differential equation, allows one to determine $p(r)$.

For the evaluation of $p(r)$ we write (10.25)

$$\partial_r \left(e^{\beta U(r)} \, p(r) \right) \; = \; \frac{R_o^2 w}{r^2 D(r)} \, p(R_o) \, e^{\beta U(r)} \, . \tag{10.26}$$

Integration $\int_r^\infty dr \, \cdots$ yields

$$p(\infty) \, e^{\beta U(\infty)} \, - \, p(r) \, e^{\beta U(r)} \; = \; R_o^2 w \, p(R_o) \int_r^\infty dr' \frac{e^{\beta U(r')}}{r'^2 \, D(r')} \tag{10.27}$$

or, using (10.19) and $U(\infty) = 0$

$$p(r) \, e^{\beta U(r)} \; = \; c_1 c_2 \, - \, R_o^2 w \, p(R_o) \int_r^\infty dr' \frac{e^{\beta U(r')}}{r'^2 \, D(r')} \tag{10.28}$$

Evaluating this at $r = R_o$ and solving for $p(R_o)$ yields

$$p(R_o) \; = \; \frac{c_1 c_2 \, e^{-\beta U(R_o)}}{1 \, + \, R_o^2 w \, e^{-\beta U(R_o)} \int_{R_o}^\infty dr \, e^{\beta U(r)}/r^2 D(r)} \, . \tag{10.29}$$

Using this in (10.28) leads to an expression of $p(r)$.

We are presently interested in the rate at which reaction (10.17) proceeds. This rate is given by $J_{\text{tot}}(R_o) = 4\pi R_o^2 w\, p(R_o)$. Hence, we can state

$$\text{Rate} \;=\; \frac{4\pi R_o^2 w\, c_1 c_2\, e^{-\beta U(R_o)}}{1 \;+\; R_o^2 w\, e^{-\beta U(R_o)} \int_{R_o}^{\infty} dr\, e^{\beta U(r)}/r^2 D(r)} \;. \tag{10.30}$$

This expression is proportional to $c_1 c_2$, a dependence expected for a bimolecular reaction of the type (10.17). Conventionally, one defines a bimolecular rate constant k as follows

$$\text{Rate} \;=\; k\, c_1 c_2 \;. \tag{10.31}$$

This constant is then, in the present case,

$$k \;=\; \frac{4\pi}{e^{\beta U(R_o)}/R_o^2 w \;+\; \int_{R_o}^{\infty} dr\, \mathcal{R}(r)} \;. \tag{10.32}$$

Here, we defined

$$\mathcal{R}(r) \;=\; e^{\beta U(r)}/r^2 D(r) \tag{10.33}$$

a property which is called the resistance of the diffusing particle, a name suggested by the fact that $\mathcal{R}(r)$ describes the Ohmic resistance of the system as shown further below.

10.2.1   Examples

We consider first the case of very ineffective reactions described by small w values. In this case the time required for the diffusive encounter of the reaction partners can become significantly shorter than the time for the local reaction to proceed, if it proceeds at all. In this case it may hold

$$\frac{e^{\beta U(R_o)}}{R_o^2 w} \;>>\; \int_{R_o}^{\infty} dr\, \mathcal{R}(r) \tag{10.34}$$

and the reaction rate (10.32) becomes

$$k \;=\; 4\pi R_o^2\, w\, e^{-\beta U(R_o)} \;. \tag{10.35}$$

This expression conforms to the well-known Arrhenius law.
We want to apply (10.32, 10.33) to two cases, free diffusion ($U(r) \equiv 0$) and diffusion in a Coulomb potential ($U(r) = q_1 q_2/\epsilon r$, $\epsilon = $ dielectric constant). We assume in both cases a distance-independent diffusion constant. In case of free diffusion holds $\mathcal{R}(r) = D^{-1} r^{-2}$ and, hence,

$$\int_{R_o}^{\infty} dr\, \mathcal{R}(r) \;=\; 1/DR_o \;. \tag{10.36}$$

From this results

$$k \;=\; \frac{4\pi D R_o}{1 \;+\; D/R_o w} \;. \tag{10.37}$$

In case of very effective reactions, i.e., for very large w, this becomes

$$k \;=\; 4\pi D R_o \tag{10.38}$$

which is the well-known rate for diffusion-controlled reaction processes. No bi-molecular rate constant involving a diffusive encounter in a three-dimensional space without attracting forces between the reactants can exceed (10.38). For instance, in a diffusion-controlled reaction in a solvent with relative diffusion constant $D = 10^{-5}\,cm^2\,s^{-1}$ and with reactants such that $R_o = 1\,nm$, the maximum possible reaction rate is $7.56 \times 10^9\,L\,mol^{-1}\,s{-}1$.

In case of a Coulomb interaction between the reactants one obtains

$$
\begin{aligned}
\int_{R_o}^{\infty} dr\, \mathcal{R}(r) &= \frac{1}{D} \int_{R_o}^{\infty} dr\, \frac{1}{r^2}\, \exp\left[\frac{\beta q_1 q_2}{\epsilon r}\right] \\
&= \frac{1}{D} \int_{0}^{1/R_o} dy\, \exp\left[\frac{\beta q_1 q_2 y}{\epsilon}\right] \\
&= \frac{1}{R_L D}\left(e^{R_L/R_o} - 1\right)
\end{aligned}
\tag{10.39}
$$

where

$$
R_L = \beta q_1 q_2 / \epsilon
\tag{10.40}
$$

defines the so-called Onsager radius. Note that R_L can be positive or negative, depending on the sign of $q_1 q_2$, but that the integral over the resistance (10.39) is always positive. The rate constant (10.32) can then be written

$$
k = \frac{4\pi D R_L}{\frac{R_L D}{R_o^2 w} e^{R_L/R_o} + e^{R_L/R_o} - 1}\ .
\tag{10.41}
$$

For instance, suppose we wish to find the maximum reaction rate for a reaction between pyrene-N and N-dimethylaniline in acetoneitrile. The reaction consists of an electron exchange from pyrene to dimethylaniline, and the reactants have charges of $\pm e$. The relative diffusion constant of both reactants in acetonitrile at $25^\circ\,C$ is $4.53 \times 10^{-5}\,cm^2\,s^{-1}$, the dielectric constant of acetonitrile at that temperature is 37.5, and the effective reaction radius R_o of the reactants is $0.7\,nm$. Using these values, and assuming $w \to \infty$ in (10.41) we obtain an Onsager radius of $-10.8\,nm$, and a maximum reaction rate of $k = 6.44 \times 10^{11}\,L\,mol^{-1}\,s^{-1}$.

In a different solvent, C_3H_7OH, with relative diffusion constant $D = 0.77 \times 10^{-5}\,cm^2\,s^{-1}$ at $25^\circ\,C$ and a dielectric constant of 19.7, the Onsager radius is $-35.7\,nm$ and the maximum reaction rate is $k = 2.08 \times 10^{11}\,L\,mol^{-1}\,s^{-1}$.