Phys550. Lecture Notes III - Module 2: Smoluchowski Equation for Potentials

In this section we will consider the general properties of the solution $p(\vec{r}, t)$ of the Smoluchowski equation in the case that the force field is derived from a potential, i.e., $\vec{F}(\vec{r}) = -\nabla U(\vec{r})$ and that the potential is finite everywhere in the diffusion doamain Ω. We will demonstrate first that the solutions, in case of reaction-free boundary conditions, obey an extremum principle, namely, that during the time evolution of $p(\vec{r}, t)$ the total free energy decreases until it reaches a minimum value corresponding to the Boltzmann distribution.
We will then characterize the time-evolution through a so-called spectral expansion, i.e., an expansion in terms of eigenfunctions of the Smoluchowski operator $\mathcal{L}(\vec{r})$. Since this operator is not self-adjoint, expressed through the fact that, except for free diffusion, the adjoint operator $\mathcal{L}^\dagger(\vec{r})$ which is not equal to $\mathcal{L}(\vec{r})$, the existence of appropriate eigenvalues and eigenfunctions is not evident. However, in the present case $[\vec{F}(\vec{r}) = -\nabla U(\vec{r})]$ the operators $\mathcal{L}(\vec{r})$ and $\mathcal{L}^\dagger(\vec{r})$ are similar to a self-adjoint operator for which a complete set of orthonormal eigenfunctions exist. These functions and their associated eigenvalues can be transferred to $\mathcal{L}(\vec{r})$ and $\mathcal{L}^\dagger(\vec{r})$ and a spectral expansion can be constructed. The expansion will be formulated in terms of projection operators and the so-called propagator, which corresponds to the solutions $p(\vec{r}, t|\vec{r}_0, t0)$, will be stated in a general form.
A pointed out, we consider in this chapter specifically solutions of the Smoluchowski equation

$$\partial_t p(\vec{r}, t) \;=\; \mathcal{L}(\vec{r})\, p(\vec{r}, t) \tag{1}$$

in case of diffusion in a potential $U(\vec{r})$, i.e., for a Smoluchowski operator of the form

$$\mathcal{L}(\vec{r}) \;=\; \nabla \cdot D(\vec{r})\, e^{-\beta U(\vec{r})}\, \nabla\, e^{\beta U(\vec{r})} \,. \tag{2}$$

We assume the general initial condition

$$p(\vec{r}, t_o) \;=\; f(\vec{r}) \tag{3}$$

and appropriate boundary conditions

$$\text{(i)} \quad \hat{a}(\vec{r})\; D \left(\vec{\nabla} \;-\; \beta\, \vec{F}(\vec{r}) \right) h(\vec{r}) \;=\; 0 \,, \qquad \vec{r} \in \partial\Omega \tag{4}$$

$$\text{(ii)} \quad h(\vec{r}) \;=\; 0 \,, \qquad \vec{r} \in \partial\Omega \tag{5}$$

$$\text{(iii)} \quad \hat{a}(\vec{r})\; D \left(\vec{\nabla} \;-\; \beta\, \vec{F}(\vec{r}) \right) h(\vec{r}) \;=\; w(\vec{r})\; h(\vec{r}) \,, \quad \vec{r} \in \partial\Omega \tag{6}$$

It is understood that the initial distribution is properly normalized

$$\int_\Omega d\vec{r}\; f(\vec{r}) \;=\; 1 \,. \tag{7}$$

The results of the present section are fundamental for many direct applications as well as for a formal approach to the evaluation of observables, e.g., correlation functions, which serves to formulate useful approximations. We have employed already, in Chapter , spectral expansions for free diffusion, a casew in which the Smoluchowski operator $\mathcal{L}(\vec{r}) = D\nabla^2$ is self-adjoint ($\mathcal{L}(\vec{r}) = \mathcal{L}^\dagger(\vec{r})$). In the present chapter we consider spectral expansion for diffusion in arbitrary potentials $U(x)$ and demonstrate the expansion for a harmonic potential.

1 Minimum Principle for the Smoluchowski Equation

In case of diffusion in a domain Ω with a 'non-reactive' boundary $\partial\Omega$ the total free energy of the system develops toward a minimum value characterized through the Boltzmann distribution. This property will be demonstrated now. The stated boundary condition is according to

$$\hat{n}(\vec{r}) \cdot \vec{\jmath}(\vec{r}, t) \; = \; 0 \tag{8}$$

where the flux $\vec{\jmath}(\vec{r}, t)$ is

$$\vec{\jmath}(\vec{r}, t) \; = \; D(\vec{r}) \, e^{-\beta U(\vec{r})} \, \nabla \, e^{\beta U(\vec{r})} \, p(\vec{r}, t) \; . \tag{9}$$

The total free energy for a given distribution $p(\vec{r}, t)$, i.e., the quantity which develops towards a minimum during the diffusion process, is a functional defined through

$$G[p(\vec{r}, t)] \; = \; \int_\Omega d\vec{r} \, g(\vec{r}, t) \tag{10}$$

where $g(\vec{r}, t)$ is the free energy density connected with $p(\vec{r}, t)$

$$g(\vec{r}, t) \; = \; U(\vec{r}) \, p(\vec{r}, t) \; + \; k_B T \, p(\vec{r}, t) \ln \frac{p(\vec{r}, t)}{\rho_o} \; . \tag{11}$$

Here ρ_o is a constant which serves to make the argument of $\ln(\cdots)$ unitless. ρ_o adds effectively only a constant to $G[p(\vec{r}, t)]$ since, for the present boundary condition (8) [use (1, 2)],

$$\begin{aligned} \partial_t \int_\Omega d\vec{r} \, p(\vec{r}, t) \; &= \; \int_\Omega d\vec{r} \, \partial_t p(\vec{r}, t) \; = \; \int_\Omega d\vec{r} \, \nabla \cdot D(\vec{r}) \, e^{-\beta U(\vec{r})} \nabla \, e^{\beta U(\vec{r})} \, p(\vec{r}, t) \\ &= \; \int_{\partial\Omega} d\vec{a} \cdot D(\vec{r}) \, e^{-\beta U(\vec{r})} \nabla \, e^{\beta U(\vec{r})} \, p(\vec{r}, t) \; = \; 0 \; . \end{aligned} \tag{12}$$

From this follows that $\int_\Omega d\vec{r} \, p(\vec{r}, t)$ is constant and, hence, the contribution stemming from ρ_o, i.e., $-k_B T \, p(\vec{r}, t) \ln \rho_o$ contributes only a constant to $G[p(\vec{r}, t)]$ in (10). The first term on the r.h.s. of (10) describes the local energy density

$$u(\vec{r}, t) \; = \; U(\vec{r}) \, p(\vec{r}, t) \tag{13}$$

and the second term, written as $-T \, s(\vec{r}, t)$, the local entropy density[1]

$$s(\vec{r}, t) \; = \; -k \, p(\vec{r}, t) \ln \frac{p(\vec{r}, t)}{\rho_o} \; . \tag{14}$$

We want to assume for some t

$$p(\vec{r}, t) \; > \; 0 \qquad \forall \vec{r}, \; \vec{r} \in \Omega \; . \tag{15}$$

This assumption can be made for the initial condition, i.e., at $t = t_o$, since a negative initial distribution could not be reconciled with the interpretation of $p(\vec{r}, t)$ as a probability. We will see below that if, at any moment, (15) does apply, $p(\vec{r}, t)$ cannot vanish anywhere in Ω at later times. For the time derivative of $G[p(\vec{r}, t)]$ can be stated

$$\partial_t G[p(\vec{r}, t)] \; = \; \int_\Omega d\vec{r} \, \partial_t g(\vec{r}, t) \tag{16}$$

[1] For a definition and explanation of the entropy term, often referred to as mixing entropy, see a textbook on Statistical Mechanics, e.g., "Course in Theoretical Physics, Vol. 5, Statistical Physics, Part 1, 3rd Edition", L.D. Landau and E.M. Lifshitz, Pergamon Press, Oxford)

where, according to the definition (11),

$$\partial_t g(\vec{r},t) \;=\; \left[U(\vec{r}) \;+\; k_B T \ln \frac{p(\vec{r},t)}{\rho_o} \;+\; k_B T \right] \partial_t p(\vec{r},t) \; . \tag{17}$$

Using the definition of the local flux density one can write (17)

$$\partial_t g(\vec{r},t) \;=\; \left[U(\vec{r}) \;+\; k_B T \ln \frac{p(\vec{r},t)}{\rho_o} \;+\; kT \right] \nabla \cdot \vec{\jmath}(\vec{r},t) \tag{18}$$

or, employing $\nabla \cdot w(\vec{r}) \vec{v}(\vec{r}) \;=\; w(\vec{r}) \nabla \cdot \vec{v}(\vec{r}) \;+\; \vec{v}(\vec{r}) \cdot \nabla w(\vec{r})$,

$$\begin{aligned} \partial_t g(\vec{r},t) \;&=\; \nabla \cdot \left\{ \left[U(\vec{r}) \;+\; k_B T \ln \frac{p(\vec{r},t)}{\rho_o} \;+\; k_B T \right] \vec{\jmath}(\vec{r},t) \right\} \\ &\quad - \vec{\jmath}(\vec{r},t) \cdot \nabla \left[U(\vec{r}) \;+\; k_B T \ln \frac{p(\vec{r},t)}{\rho_o} \;+\; k_B T \right] . \end{aligned} \tag{19}$$

Using

$$\begin{aligned} \nabla \left[U(\vec{r}) \;+\; k_B T \ln \frac{p(\vec{r},t)}{\rho_o} \;+\; k_B T \right] \;&=\; - \vec{F}(\vec{r}) \;+\; \frac{k_B T}{\vec{p}(\vec{r},t)} \nabla p(\vec{r},t) \\ &=\; + \frac{k_B T}{\vec{p}(\vec{r},t)} \left[\nabla p(\vec{r},t) \;-\; \beta \vec{F}(\vec{r}) \, p(\vec{r},t) \right] \\ &=\; \frac{k_B T}{\vec{p}(\vec{r},t)} \vec{\jmath}(\vec{r},t) \end{aligned} \tag{20}$$

one can write (19)

$$\partial_t g(\vec{r},t) \;= - \frac{k_B T}{\vec{p}(\vec{r},t)} \vec{\jmath}^{\,2}(\vec{r},t) \;+\; \nabla \cdot \left\{ \left[U(\vec{r}) \;+\; k_B T \ln \frac{p(\vec{r},t)}{\rho_o} \;+\; k_B T \right] \vec{\jmath}(\vec{r},t) \right\} \; . \tag{21}$$

For the total free energy holds then, according to (16),

$$\begin{aligned} \partial_t G[p(\vec{r},t)] \;&=\; - \int_\Omega d\vec{r} \, \frac{k_B T}{p(\vec{r},t)} \vec{\jmath}^{\,2}(\vec{r},t) \\ &\quad + \int_{\partial\Omega} d\vec{a} \cdot \left\{ \left[U(\vec{r}) \;+\; k_B T \ln \frac{p(\vec{r},t)}{\rho_o} \;+\; k_B T \right] \vec{\jmath}(\vec{r},t) \right\} \; . \end{aligned} \tag{22}$$

Due to the boundary condition (8) the second term on the r.h.s. vanishes and one can conclude

$$\partial_t G[p(\vec{r},t)] \;=\; - \int_\Omega d\vec{r} \, \frac{k_B T}{p(\vec{r},t)} \vec{\jmath}^{\,2}(\vec{r},t) \;\leq\; 0 \; . \tag{23}$$

According to (23) the free energy, during the time course of Smoluchowski dynamics, develops towards a state $p_o(\vec{r})$ which minimizes the total free energy G. This state is characterized through the condition $\partial_t G \;=\; 0$, i.e., through

$$\vec{\jmath}_o(\vec{r}) \;=\; D(\vec{r}) \, e^{-\beta U(\vec{r})} \, \nabla \, e^{\beta U(\vec{r})} \, p_o(\vec{r}) \;=\; 0 \; . \tag{24}$$

The Boltzmann distribution

$$p_o(\vec{r}) \;=\; N \, e^{-\beta U(\vec{r})} \; , \qquad N^{-1} \;=\; \int_\Omega d\vec{r} \, p_o(\vec{r}) \tag{25}$$

obeys this condition which we, in fact, enforced onto the Smoluchowski equation. Hence, the solution of (1–3, 8) will develop asymptotically , i.e., for $t \to \infty$, towards the Boltzmann distribution. We want to determine now the difference between the free energy density $g(\vec{r}, t)$ and the equilibrium free energy density. For this purpose we note

$$U(\vec{r})\, p(\vec{r}, t) \;=\; -k_B T\, p(\vec{r}, t) \ln\left[e^{-\beta U(\vec{r})}\right] \tag{26}$$

and, hence, according to (11)

$$g(\vec{r}, t) \;=\; k_B T\, p(\vec{r}, t) \ln \frac{p(\vec{r}, t)}{\rho_o e^{-\beta U(\vec{r})}} \;. \tag{27}$$

Choosing $\rho_o^{-1} \;=\; \int_\Omega d\vec{r}\, \exp[-\beta U(\vec{r})]$ one obtains, from (25)

$$g(\vec{r}, t) \;=\; k_B T\, p(\vec{r}, t) \ln \frac{p(\vec{r}, t)}{p_o(\vec{r})} \;. \tag{28}$$

For $p(\vec{r}, t) \;\to\; p_o(\vec{r})$ this expression vanishes, i.e., $g(\vec{r}, t)$ is the difference between the free energy density $g(\vec{r}, t)$ and the equilibrium free energy density.
We can demonstrate now that the solution $p(\vec{r}, t)$ of (1–3, 8) remains positive, as long as the initial distribution (3) is positive. This follows from the observation that for positive distributions the expression (28) is properly defined. In case that $p(\vec{r}, t)$ would then become very small in some region of Ω, the free energy would become $-\infty$, except if balanced by a large positive potential energy $U(\vec{r})$. However, since we assumed that $U(\vec{r})$ is finite everywhere in Ω, the distribution cannot vanish anywhere, lest the total free energy would fall below the zero equilibrium value of (28). We conclude that $p(\vec{r}, t)$ cannot vanish anywhere, hence, once positive everywhere the distribution $p(\vec{r}, t)$ can nowhere vanish or, as a result, become negative.

2 Similarity to Self-Adjoint Operator

In case of diffusion in a potential $U(\vec{r})$ the respective Smoluchowski operator (2) is related, through a similarity transformation, to a self-adjoint or Hermitean operator $\mathcal{L}_h$. This has important ramifications for its eigenvalues and its eigenfunctions as we will demonstrate now.
The Smoluchowski operator $\mathcal{L}$ acts in a function space with elements $f, g, \ldots$. We consider the following transformation in this space

$$f(\vec{r}),\; g(\vec{r}) \quad \to \quad \tilde{f}(\vec{r}) \;=\; e^{\frac{1}{2}\beta U(\vec{r})}\, f(\vec{r}),\; \tilde{g}(\vec{r}) \;=\; e^{\frac{1}{2}\beta U(\vec{r})}\, g(\vec{r}) \;.$$

Note that such transformation is accompanied by a change of boundary conditions.
A relationship

$$g \;=\; \mathcal{L}(\vec{r})\, f(\vec{r}) \tag{29}$$

implies

$$\tilde{g} \;=\; \mathcal{L}_h(\vec{r})\, \tilde{f}(\vec{r}) \tag{30}$$

where $\mathcal{L}_h$,

$$\mathcal{L}_h(\vec{r}) \;=\; e^{\frac{1}{2}\beta U(\vec{r})}\, \mathcal{L}(\vec{r})\, e^{-\frac{1}{2}\beta U(\vec{r})} \tag{31}$$

is connected with $\mathcal{L}$ through a similarity transformation. Using (2) one can write

$$\mathcal{L}_h(\vec{r}) \;=\; e^{\frac{1}{2}\beta U(\vec{r})}\, \nabla \cdot D(\vec{r})\, e^{-\beta U(\vec{r})}\, \nabla\, e^{\frac{1}{2}\beta U(\vec{r})} \;. \tag{32}$$

We want to prove now that $\mathcal{L}_h(\vec{r})$, as given by (32), is a self-adjoint operator for suitable boundary conditions restricting the elements of the function space considered. Using, for some scalar test function f, the property $\nabla \exp[\frac{1}{2}\beta U(\vec{r})]\, f \;=\; \exp[\frac{1}{2}\beta U(\vec{r})]\nabla f \;-\; \frac{1}{2}\beta \vec{F}\, f$ yields

$$\mathcal{L}_h(\vec{r}) \;=\; e^{\frac{1}{2}\beta U(\vec{r})}\, \nabla \cdot D(\vec{r})\, e^{-\frac{1}{2}\beta U(\vec{r})} \left[\nabla \;-\; \frac{1}{2}\vec{F} \right] \;. \tag{33}$$

Employing the property $\nabla \cdot \exp[-\frac{1}{2}\beta U(\vec{r})]\, \vec{v} \;=\; \exp[-\frac{1}{2}\beta U(\vec{r})]\, (\nabla \cdot \vec{v} \;+\; \frac{1}{2}\beta \vec{F} \cdot \vec{v})$, which holds for some vector-valued function $\vec{v}$, leads to

$$\mathcal{L}_h(\vec{r}) \;=\; \nabla \cdot D\, \nabla \;-\; \frac{1}{2}\beta \nabla \cdot D\, \vec{F} \;+\; \frac{1}{2}\beta \vec{F} \cdot (\, D \nabla \;-\; \frac{1}{2}\beta \vec{F}\,) \;. \tag{34}$$

The identity $\nabla D \vec{F} f \;=\; D\vec{F} \cdot \nabla f \;+\; f\, \nabla \cdot D\vec{F}$ allows one to express finally

$$\mathcal{L}_h(\vec{r}) \;=\; \nabla \cdot D\, \nabla \;+\; \frac{1}{2}\beta ((\nabla \cdot \vec{F})) \;-\; \frac{1}{4}\beta^2 \vec{F}^{\,2} \tag{35}$$

where $((\cdots))$ indicates a multiplicative operator, i.e., indicates that the operator inside the double brackets acts solely on functions within the bracket. One can write the operator (35) also in the form

$$\begin{aligned} \mathcal{L}_h(\vec{r}) \;&=\; \mathcal{L}_{oh}(\vec{r}) \;+\; U(\vec{r}) && (36) \\ \mathcal{L}_{oh}(\vec{r}) \;&=\; \nabla \cdot D\, \nabla && (37) \\ U(\vec{r}) \;&=\; \frac{1}{2}\beta ((\nabla \cdot \vec{F})) \;-\; \frac{1}{4}\beta^2 \vec{F}^{\,2} && (38) \end{aligned}$$

where it should be noted that $U(\vec{r})$ is a multiplicative operator.
One can show now, using (40–43), that Eqs. (36–38) define a self-adjoint operator. For this purpose we note that the term (38) of $\mathcal{L}_h$ is self-adjoint for any pair of functions $\tilde{f}, \tilde{g}$, i.e.,

$$\int_\Omega d\vec{r}\, \tilde{g}(\vec{r})\, U(\vec{r})\, \tilde{f}(\vec{r}) \;=\; \int_\Omega d\vec{r}\, \tilde{f}(\vec{r})\, U(\vec{r})\, \tilde{g}(\vec{r}) \;. \tag{39}$$

Applying

$$\begin{aligned} \int_\Omega d\vec{r}\; g(\vec{r})\; \mathcal{L}(\vec{r})\; h(\vec{r}) \;&=\; \int_\Omega d\vec{r}\; h(\vec{r})\; \mathcal{L}^\dagger(\vec{r})\; g(\vec{r}) \;+\; \int_{\partial\Omega} d\vec{a}\; \vec{P}(g,h) && (40) \\ \mathcal{L}(\vec{r}) \;&=\; \vec{\nabla}\; D\, \vec{\nabla} \;-\; \beta\, \vec{\nabla}\; D\, \vec{F}(\vec{r}) && (41) \\ \mathcal{L}^\dagger(\vec{r}) \;&=\; \vec{\nabla}\; D\, \vec{\nabla} \;+\; \beta\, D\, \vec{F}(\vec{r})\; \vec{\nabla} && (42) \\ \vec{P}(g,h) \;&=\; g(\vec{r})\; D\, \vec{\nabla}\, h(\vec{r}) \;-\; h(\vec{r})\; D\, \vec{\nabla}\, g(\vec{r}) \\ &\qquad -\; \beta\, D\, \vec{F}(\vec{r})\; g(\vec{r})\; h(\vec{r}) \;. && (43) \end{aligned}$$

for the operator $\mathcal{L}_{oh}(\vec{r})$, i.e., in the case $\vec{F} \;\equiv\; 0$, implies

$$\begin{aligned} \int_\Omega d\vec{r}\, \tilde{g}(\vec{r})\, \mathcal{L}_{oh}(\vec{r})\, \tilde{f}(\vec{r}) \;&=\; \int_\Omega d\vec{r}\, \tilde{f}(\vec{r})\, \mathcal{L}^\dagger_{oh}(\vec{r})\, \tilde{g}(\vec{r}) \;+\; \int_{\partial\Omega} d\vec{a} \cdot \vec{P}(\tilde{g}, \tilde{f}) && (44) \\ \mathcal{L}^\dagger_{oh}(\vec{r}) \;&=\; \nabla \cdot D(\vec{r})\, \nabla && (45) \\ \vec{P}(\tilde{g}, \tilde{f}) \;&=\; \tilde{g}(\vec{r}) D(\vec{r}) \nabla \tilde{f}(\vec{r}) \;-\; \tilde{f}(\vec{r}) D(\vec{r}) \nabla \tilde{g}(\vec{r}) \;. && (46) \end{aligned}$$

In the present case holds $\mathcal{L}_{oh}(\vec{r}) = \mathcal{L}^{\dagger}_{oh}(\vec{r})$, i.e., in the space of functions which obey

$$\hat{n}(\vec{r}) \cdot \vec{P}(\tilde{g}, \tilde{f}) = 0 \qquad \text{for } \vec{r} \in \partial\Omega \tag{47}$$

the operator $\mathcal{L}_{oh}$ is self-adjoint. The boundary condition (47) implies

$$
\begin{array}{lrcll}
(\tilde{\imath}) & \hat{n}(\vec{r}) \cdot D(\vec{r}) \nabla \tilde{f}(\vec{r}) & = & 0, & \vec{r} \in \partial\Omega \quad (48) \\
(\widetilde{\imath\imath}) & \tilde{f}(\vec{r}) & = & 0, & \vec{r} \in \partial\Omega \quad (49) \\
(\widetilde{\imath\imath\imath}) & \hat{n}(\vec{r}) \cdot D(\vec{r}) \nabla \tilde{f}(\vec{r}) & = & w(\vec{r})\, \tilde{f}(\vec{r}), & \vec{r} \in \partial\Omega \quad (50)
\end{array}
$$

and the same for $\tilde{g}(\vec{r})$, i.e., $(\tilde{\imath})$ must hold for both $\tilde{f}$ and $\tilde{g}$, or $(\widetilde{\imath\imath})$ must hold for both $\tilde{f}$ and $\tilde{g}$, or $(\widetilde{\imath\imath\imath})$ must hold for both $\tilde{f}$ and $\tilde{g}$.
In the function space characterized through the boundary conditions (48–50) the operator $\mathcal{L}_h$ is then also self-adjoint. This property implies that eigenfunctions $\tilde{u}_n(\vec{r})$ with real eigenvalues exists, i.e.,

$$\mathcal{L}_h(\vec{r})\, \tilde{u}_n(\vec{r}) = \lambda_n \tilde{u}_n(\vec{r})\,, n = 0, 1, 2, \ldots, \qquad \lambda_n \in \tag{51}$$

a property, which is discussed at length in textbooks of quantum mechanics regrading the eigenfunctions and eigenvalues of the Hamiltonian operator[2]. The eigenfunctions and eigenvalues in (51) can form a discrete set, as indicated here, but may also form a continuous set or a mixture of both; continuous eigenvalues arise for diffusion in a space Ω, an infinite subspace of which is accessible. We want to assume in the following a discrete set of eigenfunctions.
The volume integral defines a scalar product in the function space

$$\langle f | g \rangle_\Omega = \int_\Omega d\vec{r}\, f(\vec{r})\, g(\vec{r})\,. \tag{52}$$

With respect to this scalar product the eigenfunctions for different eigenvalues are orthogonal, i.e.,

$$\langle \tilde{u}_n | \tilde{u}_m \rangle_\Omega = 0 \qquad \text{for } \lambda_n \neq \lambda_m. \tag{53}$$

This property follows from the identity

$$\langle \tilde{u}_n | \mathcal{L}_h\, \tilde{u}_m \rangle_\Omega = \langle \mathcal{L}_h\, \tilde{u}_n | \tilde{u}_m \rangle_\Omega \tag{54}$$

which can be written, using (51),

$$(\lambda_n - \lambda_m)\, \langle \tilde{u}_n | \tilde{u}_m \rangle_\Omega = 0\,. \tag{55}$$

For $\lambda_n \neq \lambda_m$ follows $\langle \tilde{u}_n | \tilde{u}_m \rangle_\Omega = 0$. A normalization condition $\langle \tilde{u}_n | \tilde{u}_n \rangle_\Omega = 1$ can be satisfied for the present case of a finite diffusion domain Ω or a confining potential in which case discrete spectra arise. The eigenfunctions for identical eigenvalues can also be chosen orthogonal, possibly requiring a linear transformation[3], and the functions can be normalized such that the following orthonormality property holds

$$\langle \tilde{u}_n | \tilde{u}_m \rangle_\Omega = \delta_{nm}\,. \tag{56}$$

[2]See also textbooks on Linear Alegebra, e.g., "Introduction to Linear Algebra", G. Strang (Wellesley-Cambridge Press, Wellesley, MA, 1993)

[3]A method to obtain orthogonal eigenfunctions is the Schmitt orthogonalization.

Finally, the eigenfunctions form a complete basis, i.e., any function f in the respective function space, observing boundary conditions (48–50), can be expanded in terms of the eigenfunctions

$$\tilde{f}(\vec{r}) = \sum_{n=0}^{\infty} \alpha_n \tilde{u}_n(\vec{r}) \tag{57}$$

$$\alpha_n = \langle \tilde{u}_n | \tilde{f} \rangle_\Omega . \tag{58}$$

The mathematical theory of such eigenfunctions is not trivial and has been carried out in connection with quantum mechanics for which the operator of the type $\mathcal{L}_h$, in case of constant D, plays the role of the extensively studied Hamiltonian operator. We will assume, without further comments, that the operator $\mathcal{L}_h$ gives rise to a set of eigenfunctions with properties (51, 56–58)[4].

3 Eigenfunctions and Eigenvalues of the Smoluchowski Operator

The eigenfunctions $\tilde{u}_n(\vec{r})$ allow one to obtain the eigenfunctions $v_n(\vec{r})$ of the Smoluchowski operator $\mathcal{L}$. It holds, inverting the transformation (29),

$$v_n(\vec{r}) = e^{-\beta U/2} \, \tilde{u}_n(\vec{r}) \tag{59}$$

For this function follows from (2, 31, 51)

$$\begin{aligned} \mathcal{L}\, v_n &= e^{-\beta U/2} \, e^{\beta U/2} \nabla \cdot D(\vec{r}) \, e^{-\beta U(\vec{r})} \, \nabla \, e^{\beta U(\vec{r})/2} \, \tilde{u}_n \\ &= e^{-\beta U/2} \, \mathcal{L}_h \tilde{u}_n = e^{-\beta U/2} \, \lambda_n \, \tilde{u}_n , \end{aligned} \tag{60}$$

i.e.,

$$\mathcal{L}(\vec{r}) \, v_n(\vec{r}) = \lambda_n v_n(\vec{r}) . \tag{61}$$

The eigenfunctions w_n of the adjoint Smoluchowski operator $\mathcal{L}^\dagger$ (64) are given by

$$w_n(\vec{r}) = e^{\beta U(\vec{r})/2} \, \tilde{u}_n(\vec{r}) \tag{62}$$

and can be expressed equivalently, comparing (62) and (59),

$$w_n(\vec{r}) = e^{\beta U(\vec{r})} \, v_n(\vec{r}) . \tag{63}$$

In fact, using

$$\mathcal{L}^\dagger(\vec{r}) = e^{\beta\, U(\vec{r})} \, \vec{\nabla} \; D \; e^{-\beta\, U(\vec{r})} \, \vec{\nabla} . \tag{64}$$

and(2, 61), one obtains

$$\mathcal{L}^\dagger w_n = e^{\beta U} \nabla \cdot D \, e^{-\beta U} \, \nabla \, e^{\beta U} \, v_n = e^{\beta U} \, \mathcal{L}\, v_n = e^{\beta U} \, \lambda_n \, v_n \tag{65}$$

or

$$\mathcal{L}^\dagger(\vec{r}) \, w_n(\vec{r}) = \lambda_n \, w_n(\vec{r}) \tag{66}$$

which proves the eigenfunction property.

[4] see also "Advanced Calculus for Applications, 2nd Ed." F.B.. Hildebrand, Prentice Hall 1976, ISBN 0-13-011189-9, which contains e.g., the proof of the orthogonality of eigenfunctions of the Smoluchowski operator.

The orthonormality conditions (56) can be written

$$\begin{aligned}\delta_{nm} &= \langle \tilde{u}_n | \tilde{u}_m \rangle_\Omega = \int_\Omega d\vec{r}\, \tilde{u}_n(\vec{r})\, \tilde{u}_m(\vec{r}) \\ &= \int_\Omega d\vec{r}\, e^{-\beta U(\vec{r})/2}\, \tilde{u}_n(\vec{r})\, e^{\beta U(\vec{r})/2}\, \tilde{u}_m(\vec{r}) \,. \end{aligned} \tag{67}$$

or, using (59, 62),

$$\langle w_n | v_m \rangle_\Omega = \delta_{nm} \,. \tag{68}$$

Accordingly, the set of eigenfunctions $\{w_n, n = 0, 1, \ldots\}$ and $\{v_n, n = 0, 1, \ldots\}$, defined in (62) and (59), form a so-called *bi-orthonormal system*, i.e., the elements of the sets $\{w_n, n = 0, 1, \ldots\}$ and $\{v_n, n = 0, 1, \ldots\}$ are mutually orthonormal.

We want to investigate now the boundary conditions obeyed by the functions $e^{\beta U/2}\, \tilde{f}$ and $e^{-\beta U/2}\, \tilde{g}$ when $\tilde{f}, \tilde{g}$ obey conditions (48–50). According to (29) holds, in case of $e^{\beta U/2}\, \tilde{f}$,

$$e^{\beta U/2}\, \tilde{f} = e^{\beta U} f \,. \tag{69}$$

According to (48–50), the function f obeys then

$$\text{(i)} \qquad \hat{n}(\vec{r}) \cdot D(\vec{r}) \nabla\, e^{\beta U} f(\vec{r}) = 0, \qquad \vec{r} \in \partial\Omega \tag{70}$$

$$\text{(ii)} \qquad e^{\beta U} f(\vec{r}) = 0, \qquad \vec{r} \in \partial\Omega \tag{71}$$

$$\text{(iii)} \qquad \hat{n}(\vec{r}) \cdot D(\vec{r}) \nabla\, e^{\beta U} f(\vec{r}) = w(\vec{r})\, e^{\beta U} f(\vec{r}), \; \vec{r} \in \partial\Omega \tag{72}$$

which is equivalent to the conditions for the solutions of the Smoluchowski equation. We have established, therefore, that the boundary conditions assumed for the function space connected with the self-adjoint Smoluchowski operator $\mathcal{L}_h$ are consistent with the boundary conditions assumed previously for the Smoluchowski equation.

Projection Operators

We consider now the following operators defined through the pairs of eigenfunctions v_n, w_n of the Smoluchowski operators $\mathcal{L}, \mathcal{L}^\dagger$

$$\hat{J}_n\, f = v_n\, \langle w_n | f \rangle_\Omega \tag{73}$$

where f is some test function. For these operators holds

$$\hat{J}_n \hat{J}_m\, f = \hat{J}_n v_m\, \langle w_m | f \rangle_\Omega = v_n\, \langle w_n | v_m \rangle_\Omega\, \langle w_m | f \rangle_\Omega \,. \tag{74}$$

Using (68) one can write this

$$\hat{J}_n \hat{J}_m\, f = v_n\, \delta_{nm} \langle w_m | f \rangle_\Omega \tag{75}$$

and, hence, using the definition (73)

$$\hat{J}_n \hat{J}_m = \delta_{nm} \hat{J}_m \,. \tag{76}$$

This property identifies the operators $\hat{J}_n$, $n = 0, 1, 2, \ldots$ as mutually complementary projection operators, i.e., each $\hat{J}_n$ is a projection operator ($\hat{J}_n^2 = \hat{J}_n$) and two different $\hat{J}_n$ and $\hat{J}_m$ project onto orthogonal subspaces of the function space.

The completeness property (57, 58) of the set of eigenfunctions $\tilde{u}_n$ can be expressed in terms of the operators $\hat{J}_n$. For this purpose we consider

$$\alpha_n = \langle \tilde{u}_n | \tilde{f} \rangle_\Omega = \int_\Omega d\vec{r}\, \tilde{u}_n\, \tilde{f} \tag{77}$$

Using $\tilde{u}_n = \exp(\beta U/2)\, v_n$ and $\tilde{f} = \exp(\beta U/2)\, f$ [see (59, 29)] as well as (63) one can express this

$$\alpha_n \;=\; \int_\Omega d\vec{r}\, \exp(\beta U/2)\, v_n\, \exp(\beta U/2)\, f \;=\; \int_\Omega d\vec{r}\, \exp(\beta U)\, v_n\, f \;=\; \langle w_n | f \rangle_\Omega$$

Equations (57, 58) read then for $\tilde{f} = \exp(\beta U/2)\, f$

$$f \;=\; \sum_{n=0}^{\infty} e^{\beta U/2}\, u_n\, \langle w_n | f \rangle_\Omega \tag{78}$$

and, using again (59) and (73)

$$f \;=\; \sum_{n=0}^{\infty} \hat{J}_n\, f \tag{79}$$

Since this holds for any f in the function space with proper boundary conditions we can conclude that within the function space considered holds

$$\sum_{n=0}^{\infty} \hat{J}_n \;=\; \quad . \tag{80}$$

The projection operators $\hat{J}_n$ obey, furthermore, the property

$$\mathcal{L}(\vec{r})\, \hat{J}_n \;=\; \lambda_m\, \hat{J}_n\ . \tag{81}$$

This follows from the definition (73) together with (61).

The Propagator

The solution of (1–3) can be written formally

$$p(\vec{r},t) \;=\; \left[e^{\mathcal{L}(\vec{r})(t-t_o)} \right]_{\rm bc} f(\vec{r})\ . \tag{82}$$

The brackets $[\cdots]_{\rm bc}$ indicate that the operator is defined in the space of functons which obey the chosen spatial boundary conditions. The exponential operator $\exp[\mathcal{L}(\vec{r})(t-t_o)]$ in (82) is defined through the Taylor expansion

$$\left[e^{A} \right]_{\rm bc} \;=\; \sum_{\nu=0}^{\infty} \frac{1}{\nu!}\, [A]^{\nu}_{\rm bc}\ . \tag{83}$$

The operator $[\exp[\mathcal{L}(\vec{r})(t-t_o)]\,]_{\rm bc}$ plays a central role for the Smoluchowski equation; it is referred to as the *propagator*. One can write, dropping the argument $\vec{r}$,

$$\left[e^{\mathcal{L}(t-t_o)} \right]_{\rm bc} \;=\; e^{\mathcal{L}(t-t_o)} \sum_{n=0}^{\infty} \hat{J}_n \tag{84}$$

since the projection operators project out the functions with proper boundary conditions. For any function $Q(z)$, which has a convergent Taylor series for all $z = \lambda_n$, $n = 0, 1, \ldots$, holds

$$Q(\mathcal{L})\, v_n \;=\; Q(\lambda_n)\, v_n \tag{85}$$

and, hence, according to (81)

$$Q(\mathcal{L})\, \hat{J}_n \;=\; Q(\lambda_n)\, \hat{J}_n \tag{86}$$

This property, which can be proven by Taylor expansion of $Q(\mathcal{L})$, states that if a function of $\mathcal{L}$ "sees" an eigenfunction v_n, the operator $\mathcal{L}$ turns itself into the scalar λ_n. Since the Taylor expansion of the exponential operator converges everywhere on the real axis, it holds

$$e^{\mathcal{L}(t-t_o)}\, v_n \;=\; e^{\lambda_n(t-t_o)}\, v_n \;. \tag{87}$$

The expansion can then be written

$$\left[e^{\mathcal{L}(t-t_o)} \right]_{\rm bc} \;=\; \sum_{n=0}^{\infty} e^{\lambda_n(t-t_o)}\, \hat{J}_n \;. \tag{88}$$

We assume here and in the following the ordering of eigenvalues

$$\lambda_0 \;\geq\; \lambda_1 \;\geq\; \lambda_2 \;\cdots \tag{89}$$

which can be achieved by choosing the labels n, $n = 0, 1, \ldots$ in the appropriate manner.

4 Brownian Oscillator

We want to demonstrate the spectral expansion method, introduced in this chapter, to the case of a Brownian oscillator governed by the Smoluchowski equation for a harmonic potential

$$U(x) \;=\; \frac{1}{2}\, f\, x^2 \;, \tag{90}$$

$$namely, by \partial_t p(x,t|x_0,t_0) = D(\partial_x^2 + \beta f\;\partial_x x)\, p(x,t|x_0,t_0) \tag{91}$$

with the boundary condition

$$\lim_{x\to\pm\infty} x^n\, p(x,t|x_0,t_0) = 0, \quad \forall n \in I\!N \tag{92}$$

and the initial condition

$$p(x,t_0|x_0,t_0) = \delta(x - x_0)\,. \tag{93}$$

In order to simplify the analysis we introduce dimensionless variables

$$\xi \;=\; x/\sqrt{2}\delta\;, \qquad \tau \;=\; t/\tilde{\tau}\;, \tag{94}$$

where

$$\delta = \sqrt{k_B T/f}\;, \qquad \tilde{\tau} \;=\; 2\delta^2/D\;. \tag{95}$$

The Smoluchowski equation for the normalized distribution in ξ, given by

$$q(\xi,\tau|\xi_0,\tau_0) \;=\; \sqrt{2}\,\delta\; p(x,t|x_0,t_0)\;, \tag{96}$$

is then

$$\partial_\tau q(\xi,\tau|\xi_0,\tau_0) = (\partial_\xi^2 + 2\,\partial_\xi\;\xi)\, q(\xi,\tau|\xi_0,\tau_0) \tag{97}$$

with the initial condition

$$q(\xi,\tau_0|\xi_0,\tau_0) \;=\; \delta(\xi - \xi_0) \tag{98}$$

and the boundary condition

$$\lim_{\xi\to\pm\infty} \xi^n\, q(\xi,\tau|\xi_0,\tau_0) = 0, \quad \forall n \in I\!N\;. \tag{99}$$

This equation describes diffusion in thepotential $\tilde{U}(\xi) = \xi^2$. Using (94, 94, 90) one can show $\tilde{U}(\xi) = \beta U(x)$.
We seek to expand $q(\xi, \tau_0|\xi_0, \tau_0)$ in terms of the eigenfunctions of the operator

$$\mathcal{L}(\xi) = \partial_\xi^2 + 2\partial_\xi \xi \,, \tag{100}$$

restricting the functions to the space

$$\{h(\xi) \,|\, \lim_{\xi \to \pm\infty} \xi^n \, h(\xi) = 0\} \,. \tag{101}$$

The eigenfunctions $f_n(\xi)$ of $\mathcal{L}(\xi)$ are defined through

$$\mathcal{L}(\xi) f_n(\xi) = \lambda_n f_n(\xi) \tag{102}$$

Corresponding functions, which also obey (99), are

$$f_n(\xi) = c_n \, e^{-\xi^2} \, H_n(\xi) \,. \tag{103}$$

where $H_n(x)$ is the n-th Hermite polynomials and where c_n is a normalization constant chosen below. The eigenvalues are

$$\lambda_n = -2n, \tag{104}$$

As demonstrated above, the eigenfunctions of the Smoluchowski operator do not form an orthonormal basis with the scalar product and neither do the functions $f_n(\xi)$ in (103). Instead, they obey the orthogonality property

$$\int_{-\infty}^{+\infty} d\xi \, e^{-\xi^2} H_n(\xi) H_m(\xi) = 2^n n! \sqrt{\pi} \delta_{nm} \,. \tag{105}$$

which allows one to identify a bi-orthonormal system of functions. For this purpose we choose for $f_n(\xi)$ the normalization

$$f_n(\xi) = \frac{1}{2^n n! \sqrt{\pi}} \, e^{-\xi^2} \, H_n(\xi) \tag{106}$$

and define

$$g_n(\xi) = H_n(\xi) \,. \tag{107}$$

One can readily recognize then from (105) the biorthonormality property

$$\langle g_n | f_n \rangle = \delta_{nm} \,. \tag{108}$$

The functions $g_n(\xi)$ can be identified with the eigenfunctions of the adjoint operator

$$\mathcal{L}^+(\xi) = \partial_\xi^2 - 2\xi \partial_\xi \,, \tag{109}$$

obeying

$$\mathcal{L}^+(\xi) g_n(\xi) = \lambda_n g_n(\xi) \,. \tag{110}$$

Comparing (103) and (107) one can, in fact, discern

$$g_n(\xi) \sim e^{\xi^2} \, g_n(\xi). \tag{111}$$

and, since $\xi^2 = f x^2 / 2 k_B T$ [c.f. (94, 96)], the functions $g_n(\xi)$, according to (63), are the eigenfunctions of $\mathcal{L}^+(\xi)$.

The eigenfunctions $f_n(\xi)$ form a complete basis for all functions with the property (99). Hence, we can expand $q(\xi, \tau|\xi_0, \tau_0)$

$$q(\xi, \tau|\xi_0, \tau_0) = \sum_{n=0}^{\infty} \alpha_n(t) f_n(\xi) \; . \tag{112}$$

Inserting this into the Smoluchowski equation (97, 100) results in

$$\sum_{n=0}^{\infty} \dot{\alpha}_n(\tau) f_n(\xi) \;=\; \sum_{n=0}^{\infty} \lambda_n \; \alpha_n(\tau) \; f_n(\xi) \, . \tag{113}$$

Exploiting the bi-orthogonality property (108) one derives

$$\dot{\alpha}_m(\tau) \;=\; \lambda_m \; \alpha_m(\tau) \, . \tag{114}$$

The general solution of of this differential equation is

$$\alpha_m(\tau) = \beta_m \; e^{\lambda_m \tau} \; . \tag{115}$$

Upon substitution into (112), the initial condition (98) reads

$$\sum_{n=0}^{\infty} \beta_n \, e^{\lambda_n \tau_0} \, f_n(\xi) \;=\; \delta(\xi - \xi_0) \; . \tag{116}$$

Taking again the scalar product with $g_m(\xi)$ and using (108) results in

$$\beta_m \; e^{\lambda_m \tau_0} = g_m(\xi_0) \, , \tag{117}$$

or

$$\beta_m = e^{-\lambda_m \tau_0} \; g_m(\xi_0) \; . \tag{118}$$

Hence, we obtain finally

$$q(\xi, \tau|\xi_0, \tau_0) \;=\; \sum_{n=0}^{\infty} e^{\lambda_n (\tau - \tau_0)} \, g_n(\xi_0) \, f_n(\xi) \, , \tag{119}$$

or, explicitly,

$$q(\xi, \tau|\xi_0, \tau_0) \;=\; \sum_{n=0}^{\infty} \frac{1}{2^n n! \sqrt{\pi}} \, e^{-2n(\tau - \tau_0)} \, H_n(\xi_0) \, e^{-\xi^2} \, H_n(\xi) \; . \tag{120}$$

Expression (120) can be simplified using the generating function of a product of two Hermit polynomials

$$\frac{1}{\sqrt{\pi(1-s^2)}} \, \exp\left[-\tfrac{1}{2}(y^2 + y_0^2) \, \tfrac{1+s^2}{1-s^2} \; + \; 2 y y_0 \, \tfrac{s}{1-s^2} \right]$$

$$= \sum_{n=0}^{\infty} \frac{s^n}{2^n n! \sqrt{\pi}} \, H_n(y) \, e^{-y^2/2} \, H_n(y_0) \, e^{-y_0^2/2} \; . \tag{121}$$

Using

$$s = e^{-2(\tau - \tau_0)} \, , \tag{122}$$

one can show

$q(\xi, \tau|\xi_0, \tau_0)$

$$= \frac{1}{\sqrt{\pi(1-s^2)}} \exp\left[-\frac{1}{2}(\xi^2 + \xi_0^2)\,\frac{1+s^2}{1-s^2} \,+\, 2\xi\xi_0\,\frac{s}{1-s^2} \,-\, \frac{1}{2}\xi^2 \,+\, \frac{1}{2}\xi_0^2 \right] . \tag{123}$$

We denote the exponent on the r.h.s. by E and evaluate

$$\begin{aligned} E &= -\xi^2 \frac{1}{1-s^2} \,-\, \xi_0^2 \frac{s^2}{1-s^2} \,+\, 2\xi\xi_0 \frac{1}{1-s^2} \\ &= -\frac{1}{1-s^2}(\xi^2 \,-\, 2\xi\xi_0 s \,+\, \xi_0^2 s^2) \\ &= -\frac{(\xi - \xi_0 s)^2}{1-s^2} \end{aligned} \tag{124}$$

We obtain then

$$q(\xi,\tau|\xi_0,\tau_0) \;=\; \frac{1}{\sqrt{\pi(1-s^2)}} \exp\left[-\frac{(\xi-\xi_0 s)^2}{1-s^2} \right] , \tag{125}$$

where s is given by (122).
Let us now consider the solution for an initial distribution $f(\xi_0)$. The corresponding distribution $\tilde{q}(\xi,\tau)$ is ($\tau_0 = 0$)

$$\tilde{q}(\xi,\tau) \;=\; \int d\xi_0 \,\frac{1}{\sqrt{\pi(1-e^{-4\tau})}} \exp\left[-\frac{(\xi - \xi_0 e^{-2\tau})^2}{1-e^{-4\tau}} \right] f(\xi_0) \,. \tag{126}$$

It is interesting to consider the asymptotic behaviour of this solution. For $\tau \to \infty$ the distribution $\tilde{q}(\xi,\tau)$ relaxes to

$$\tilde{q}(\xi) \;=\; \frac{1}{\sqrt{\pi}}\, e^{-\xi^2} \int d\xi_0\, f(\xi_0) \,. \tag{127}$$

If one carries out a corresponding analysis using (119) one obtains

$$\tilde{q}(\xi,\tau) \;=\; \sum_{n=0}^{\infty} e^{\lambda_n \tau}\, f_n(\xi) \int d\xi_0\, g_n(\xi_0)\, f(\xi_0) \tag{128}$$

$$\sim\; f_0(\xi) \int d\xi_0\, g_n(\xi_0)\, f(\xi_0) \quad \text{as } \tau \to \infty \,. \tag{129}$$

Using (106) and (107), this becomes

$$\tilde{q}(\xi,\tau) \;\sim\; \frac{1}{\sqrt{\pi}}\, e^{-\xi^2} \underbrace{H_0(\xi)}_{=1} \int d\xi_0 \underbrace{H_0(\xi_0)}_{=1} f(\xi_0) \tag{130}$$

in agreement with (127). One can recognize from this result that the expansion (128), despite its appearance, conserves total probability $\int d\xi_0\, f(\xi_0)$. One can also recoginze that, in general, the relaxation of an initial distribution $f(\xi_0)$ to the Boltzmann distribution involves numerous relaxation times $\tau_n = -1/\lambda_n$, even though the original Smoluchowski equation contains only a single rate constant, the friction coefficient γ.

5 Rates of Diffusion-Controlled Reactions

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 apply the methods for solving the Smoluchowski Equation in order 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.

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 $p(\vec{r}_1, \vec{r}_2, t|\vec{r}_{10}, \vec{r}_{20}, t_0)$ which is governed by the diffusion equation

$$\partial_t \, p(\vec{r}_1, \vec{r}_2, t|\vec{r}_{10}, \vec{r}_{20}, t_0) \; = \; \left(D_1 \nabla_1^2 \; + \; D_2 \nabla_2^2 \right) \, p(\vec{r}_1, \vec{r}_2, t|\vec{r}_{10}, \vec{r}_{20}, t_0) \tag{131}$$

where $\nabla_j \; = \; \partial / \partial \vec{r}_j$, $j = 1, 2$. The additive diffusion operators $D_j \nabla_j^2$ in (131) are a signature of the statistical independence of the Brownian motions of each of the particles.
Our goal is to obtain from the aforementioned diffusion equation an equation which governs the distribution $p(\vec{r}, t|r_0, t_0)$ for the relative position

$$\vec{r} \; = \; \vec{r}_2 \; - \; \vec{r}_1 \tag{132}$$

of the particles. For this purpose we express the diffusion equation in terms of the coordinates $\vec{r}$ and

$$\vec{R} \; = \; a \, \vec{r}_1 \; + \; b \, \vec{r}_2 \tag{133}$$

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

$$\nabla_1 \; = \; a \nabla_{\vec{R}} \; - \; \nabla \, , \quad \nabla_2 \; = \; b \, \nabla_{\vec{R}} \; + \; \nabla \tag{134}$$

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

$$\nabla_1^2 \;\; = \;\; a^2 \nabla_{\vec{R}}^2 \; + \; \nabla^2 \; - \; 2a \, \nabla_{\vec{R}} \nabla \tag{135}$$

$$\nabla_2^2 \;\; = \;\; b^2 \nabla_{\vec{R}}^2 \; + \; \nabla^2 \; + \; 2b \, \nabla_{\vec{R}} \nabla \tag{136}$$

The diffusion operator

$$\widehat{\mathcal{D}} \; = \; D_1 \nabla_1^2 \; + \; D_2 \nabla_2^2 \tag{137}$$

can then be written

$$\widehat{\mathcal{D}} \; = \; (D_1 a^2 \; + \; D_2 b^2) \, \nabla_{\vec{R}}^2 \; + \; (D_1 \; + \; D_2) \, \nabla^2 \; + \; 2 \, (D_2 b \; - \; D_1 a) \, \nabla_{\vec{R}} \nabla \tag{138}$$

If one defines

$$a \; = \; \sqrt{D_2 / D_1} \, , \quad b \; = \; \sqrt{D_1 / D_2} \tag{139}$$

one obtains

$$\widehat{\mathcal{D}} \;=\; (D_1 \;+\; D_2)\,\nabla^2_{\vec{R}} \;+\; (D_1 \;+\; D_2)\,\nabla^2 \;. \tag{140}$$

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

$$\partial_t p(\vec{r},t|\vec{r}_0,t_0) \;=\; (D_1 \;+\; D_2)\,\nabla^2 p(\vec{r},t|\vec{r}_0,t_0)\;. \tag{141}$$

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

$$D \;=\; D_1 \;+\; D_2\;. \tag{142}$$

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 $U(\vec{r})$ where $\vec{r} = \vec{r}_2 - \vec{r}_1$. The force acting on particle 2 is $-\nabla_2 U(\vec{r}) = \vec{F}$; the force acting on particle 1 is $-\vec{F}$. The distribution function $p(\vec{r}_1,\vec{r}_2,t|\vec{r}_{10},\vec{r}_{20},t_0)$ obeys the Smoluchowski equation

$$\begin{aligned} \partial_t\, p \;&=\; \Big[\,\big(\,D_1\nabla_1^2 \;+\; D_2\nabla_2^2\,\big) \\ &-\; D_2\beta\,\nabla_2\cdot\vec{F}(\vec{r}) \;+\; D_1\beta\,\nabla_1\cdot\vec{F}\,\Big]\;p\;. \end{aligned} \tag{143}$$

The first two terms on the r.h.s. can be expressed in terms of the coordinates $\vec{R}$ and $\vec{r}$. For the remaining terms holds,

$$D_2\nabla_2 \;-\; D_1\nabla_1 \;=\; (\,D_1 \;+\; D_2)\,\nabla \tag{144}$$

Hence, one can write the Smoluchowski equation

$$\partial_t\, p \;=\; \Big[\,(\,D_1 \;+\; D_2)\;\nabla^2_{\vec{R}} \;+ (D_1 + D_2)\;\nabla\cdot(\nabla \;-\; \beta\,\vec{F})\,\Big]\;p\;. \tag{145}$$

This equation describes two independent random processes, free diffusion in the $\vec{R}$ coordinate and a diffusion with drift in the $\vec{r}$ 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

$$\partial_t\, p(\vec{r},t|\vec{r}_0,t_0) \;=\; D\nabla\cdot(\nabla \;-\; \beta\,\vec{F})\,p(\vec{r},t|\vec{r}_0,t_0)\;. \tag{146}$$

6 Mean First Passage Time

The mean first passage time (MFPT) can be interpreted as the characteristic time for particles at a given initial position to diffuse to a given final position. Let $\mathcal{L}$ denote the Smoluchowski operator:

$$\mathcal{L}(\mathbf{r}) = \nabla\cdot D(\mathbf{r})\nabla - \beta\nabla\cdot D(\mathbf{r})\mathbf{F}(\mathbf{r})\,. \tag{147}$$

In addition, we assume three possible boundary conditions on a solution $u(\mathbf{r})$ of the Smoluchowski equation:

$$(i)\;\hat{\mathbf{a}}(\mathbf{r})\cdot D(\mathbf{r})(\nabla - \beta\mathbf{F}(\mathbf{r}))u(\mathbf{r}) = 0\,,\;\mathbf{r}\in\partial\Omega \tag{148}$$

$$(ii)\;u(\mathbf{r}) = 0\,,\;\mathbf{r}\in\partial\Omega \tag{149}$$

$$(iii)\;\hat{\mathbf{a}}(\mathbf{r})\cdot D(\mathbf{r})(\nabla - \beta\mathbf{F}(\mathbf{r}))u(\mathbf{r}) = w(\mathbf{r})u(\mathbf{r})\,,\;\mathbf{r}\in\partial\Omega\,, \tag{150}$$

where $w(\mathbf{r})$ describes the rate of reaction as a function of space.

The first step to calculating the MFPT is to determine the adjoint Smoluchowski operator $\mathcal{L}^\dagger$. For this purpose, we prove the Lagrange identity for $\mathcal{L}$ (a good introduction to Lagrange identities can be found in Mathematics for Physics by Mike Stone and Paul Goldbart):

$$\int_\Omega d\mathbf{r}\, v(\mathbf{r})\mathcal{L}(\mathbf{r})u(\mathbf{r}) - \int_\Omega d\mathbf{r}\, u(\mathbf{r})\mathcal{L}^\dagger(\mathbf{r})v(\mathbf{r}) = \int_{\partial\Omega} d\mathbf{a}\cdot \mathbf{P}(u,v)\,, \tag{151}$$

where u and v are elements of the function space, defined on domain Ω, that $\mathcal{L}$ acts on, and

$$\mathcal{L}^\dagger(\mathbf{r}) = \nabla\cdot D(\mathbf{r})\nabla + \beta D(\mathbf{r})\mathbf{F}(\mathbf{r})\cdot\nabla \tag{152}$$

$$\mathbf{P}(u,v) = v(\mathbf{r})D(\mathbf{r})\nabla u(\mathbf{r}) - u(\mathbf{r})D(\mathbf{r})\nabla v(\mathbf{r}) - \beta D(\mathbf{r})\mathbf{F}(\mathbf{r})u(\mathbf{r})v(\mathbf{r})\,. \tag{153}$$

Using the product rule, we can write

$$\nabla\cdot(vD\nabla u - uD\nabla v) = (\nabla v)\cdot D\nabla u + v\nabla\cdot D\nabla u - (\nabla u)\cdot D\nabla v - u\nabla\cdot D\nabla v \tag{154}$$

$$= v\nabla\cdot D\nabla u - u\nabla\cdot D\nabla v\,. \tag{155}$$

We will also make use of the fact that

$$\nabla\cdot\beta D\mathbf{F}vu = v\nabla\cdot\beta D\mathbf{F}u + u\beta D\mathbf{F}\cdot\nabla v\,. \tag{156}$$

On the RHS of Eq. (151), Gauss' Law gives

$$\int_{\partial\Omega} d\mathbf{a}\cdot\mathbf{P}(u,v) = \int_\Omega d\mathbf{r}\,\nabla\cdot\mathbf{P}(u,v) \tag{157}$$

$$= \int_\Omega d\mathbf{r}\,\nabla\cdot(vD\nabla u - uD\nabla v) - \int_\Omega d\mathbf{r}\,\nabla\cdot\beta D\mathbf{F}vu\,. \tag{158}$$

Putting in Eq. (155, 156) gives then

$$\int_{\partial\Omega} d\mathbf{a}\cdot\mathbf{P}(u,v) = \int_\Omega d\mathbf{r}\,(v\nabla\cdot D\nabla u - u\nabla\cdot D\nabla v) - \int_\Omega d\mathbf{r}\,(v\nabla\cdot\beta D\mathbf{F}u + u\beta D\mathbf{F}\cdot\nabla v) \tag{159}$$

$$= \int_\Omega d\mathbf{r}\, v(\nabla\cdot D\nabla - \nabla\cdot\beta D\mathbf{F})u - \int_\Omega d\mathbf{r}\, u(\nabla\cdot D\nabla + \beta D\mathbf{F}\cdot\nabla)v \tag{160}$$

$$= \int_\Omega d\mathbf{r}\, v(\mathbf{r})\mathcal{L}(\mathbf{r})u(\mathbf{r}) - \int_\Omega d\mathbf{r}\, u(\mathbf{r})\mathcal{L}^\dagger(\mathbf{r})v(\mathbf{r})\,, \tag{161}$$

which proves Eq. (151). By definition of an adjoint operator, for Eq. (152) to give the correct adjoint Smoluchowski operator, we further impose the condition

$$\hat{\mathbf{a}}(\mathbf{r})\cdot\mathbf{P}(u,v) = 0\,\forall\,\mathbf{r}\in\partial\Omega\,, \tag{162}$$

or

$$u(\mathbf{r})\,\hat{\mathbf{a}}(\mathbf{r})\cdot D(\mathbf{r})\nabla v(\mathbf{r}) = v(\mathbf{r})\,\hat{\mathbf{a}}(\mathbf{r})\cdot[D(\mathbf{r})\nabla u(\mathbf{r}) - \beta D(\mathbf{r})\mathbf{F}(\mathbf{r})u(\mathbf{r})]\,. \tag{163}$$

Thus, the boundary conditions (i), (ii), (iii) of the forward equation respectively imply the following boundary conditions (i'), (ii'), (iii') for the backward equation:

$$(i')\,\hat{\mathbf{a}}(\mathbf{r})\cdot D(\mathbf{r})\nabla v(\mathbf{r}) = 0\,,\ \mathbf{r}\in\partial\Omega \tag{164}$$

$$(ii')\,v(\mathbf{r}) = 0\,,\ \mathbf{r}\in\partial\Omega \tag{165}$$

$$(iii')\,\hat{\mathbf{a}}(\mathbf{r})\cdot D(\mathbf{r})\nabla v(\mathbf{r}) - w(\mathbf{r})v(\mathbf{r}) = 0\,,\ \mathbf{r}\in\partial\Omega\,. \tag{166}$$

We are now ready to write down the backward Smoluchowski equation. For that purpose, we state the definition of the Green's function:

$$p(\mathbf{r},t|\mathbf{r}_0,t_0) = e^{\mathcal{L}(\mathbf{r})t}\,\delta(\mathbf{r}-\mathbf{r}_0) \tag{167}$$

$$= \int_\Omega d\mathbf{r}'\,\delta(\mathbf{r}'-\mathbf{r})e^{\mathcal{L}(\mathbf{r}')t}\,\delta(\mathbf{r}'-\mathbf{r}_0)\,, \tag{168}$$

where $\mathbf{r}_0$ lies in the interior of Ω, $e^{\mathcal{L}(\mathbf{r})t}$ is the propagator and is evaluated by expanding in a Taylor expansion and applying $\mathcal{L}$ as many times as its powers in the resulting polynomial to the expression on the right. In practice, one expands the expression on the right in terms of eigenfunctions of $\mathcal{L}$ so that the $\mathcal{L}$ in the exponential can be replaced by the respective eigenvalues. Identifying now $\delta(\mathbf{r}'-\mathbf{r})$ and $\delta(\mathbf{r}'-\mathbf{r}_0)$ with $u(\mathbf{r}')$ and $v(\mathbf{r}')$ respectively in Eq. (151), we have $\int_{\partial\Omega} d\mathbf{a}\cdot\mathbf{P}(u,v)=0$, implying

$$\int_\Omega d\mathbf{r}'\,\delta(\mathbf{r}'-\mathbf{r})\mathcal{L}(\mathbf{r}')\delta(\mathbf{r}'-\mathbf{r}_0) = \int_\Omega d\mathbf{r}'\,\delta(\mathbf{r}'-\mathbf{r_0})\mathcal{L}^\dagger(\mathbf{r}')\delta(\mathbf{r}'-\mathbf{r})\,. \tag{169}$$

By linearity, it follows that

$$\int_\Omega d\mathbf{r}'\,\delta(\mathbf{r}'-\mathbf{r})e^{\mathcal{L}(\mathbf{r}')t}\,\delta(\mathbf{r}'-\mathbf{r}_0) = \int_\Omega d\mathbf{r}'\,\delta(\mathbf{r}'-\mathbf{r_0})e^{\mathcal{L}^\dagger(\mathbf{r}')t}\,\delta(\mathbf{r}'-\mathbf{r})\,. \tag{170}$$

Putting Eq. (170) into Eq. (168) gives us

$$p(\mathbf{r},t|\mathbf{r}_0,t_0) = \int_\Omega d\mathbf{r}'\,\delta(\mathbf{r}'-\mathbf{r_0})e^{\mathcal{L}^\dagger(\mathbf{r}')t}\,\delta(\mathbf{r}'-\mathbf{r}) \tag{171}$$

$$= e^{\mathcal{L}^\dagger(\mathbf{r}_0)t}\,\delta(\mathbf{r}_0-\mathbf{r})\,. \tag{172}$$

Differentiating with respect to t then gives us the backward Smoluchowski equation:

$$\dot{p}(\mathbf{r},t|\mathbf{r}_0,t_0) = \mathcal{L}^\dagger(\mathbf{r}_0)p(\mathbf{r},t|\mathbf{r}_0,t_0)\,. \tag{173}$$

The solutions $p(\mathbf{r},t|\mathbf{r}_0,t_0)$ must obey boundary conditions (i'), (ii') or (iii') in the $\mathbf{r}_0$ variable depending on which boundary conditions (i), (ii) or (iii) were applied to the forward equation. Before proceeding, we note that in case the deterministic force $\mathbf{F}(\mathbf{r})$ can be expressed in terms of a potential such that $\mathbf{F}(\mathbf{r}) = \nabla U(\mathbf{r})$, $\mathcal{L}(\mathbf{r})$ and $\mathcal{L}^\dagger(\mathbf{r}_0)$ can be written respectively as

$$\mathcal{L}(\mathbf{r}) = \nabla\cdot D(\mathbf{r})e^{-\beta U(\mathbf{r})}\nabla e^{\beta U(\mathbf{r})} \tag{174}$$

$$\mathcal{L}^\dagger(\mathbf{r}_0) = e^{\beta U(\mathbf{r}_0)}\nabla_{\mathbf{r}_0}D(\mathbf{r_0})e^{-\beta U(\mathbf{r}_0)}\nabla_{\mathbf{r}_0}\,, \tag{175}$$

where $\nabla_{\mathbf{r}_0}$ denotes the gradient taken with respect to coordinates in $\mathbf{r}_0$. From now on, we will use the above definitions of the operators.

With the adjoint Smoluchowski equation in hand, we now assume an absorptive or radiative sink in the system (particle number is hence not conserved) and calculate the characteristic time taken by a particle at a given initial position $\mathbf{r}_0$ to leave the system. We begin by integrating Eq. (173) over Ω, obtaining

$$\dot{\Sigma}(\mathbf{r}_0,t) = \mathcal{L}^\dagger(\mathbf{r}_0)\Sigma(\mathbf{r}_0,t)\,, \tag{176}$$

where $\Sigma(\mathbf{r}_0,t) = \int_\Omega d\mathbf{r}\,p(\mathbf{r},t|\mathbf{r}_0,t_0)$. Next, we approximate the time evolution of Σ as a decreasing exponential:

$$\Sigma(\mathbf{r}_0,t) \approx e^{-t/\tau(\mathbf{r}_0)}\,. \tag{177}$$

Under this approximation, we have

$$\tau(\mathbf{r}_0) = \int_0^\infty dt\, \Sigma(\mathbf{r}_0, t)\,. \tag{178}$$

Hence, we obtain an equation in $\tau(\mathbf{r}_0)$ by integrating Eq. (176) from $t = 0$ to $t \to \infty$:

$$-1 = \mathcal{L}^\dagger(\mathbf{r}_0)\tau(\mathbf{r}_0)\,, \tag{179}$$

with corresponding boundary conditions

$$(i'')\, \tau(\mathbf{r}_0) = 0\,,\ \mathbf{r}_0 \in \partial\Omega \tag{180}$$

$$(ii'')\, \nabla_{\mathbf{r}_0}\tau(\mathbf{r}_0) = 0\,,\ \mathbf{r}_0 \in \partial\Omega \tag{181}$$

$$(iii'')\, \nabla_{\mathbf{r}_0}\tau(\mathbf{r}_0) = w(\mathbf{r}_0)\tau(\mathbf{r}_0)\,,\ \mathbf{r}_0 \in \partial\Omega\,. \tag{182}$$

For the simple case in 1D of a radiative boundary at r_1 and a reflective boundary at r_2 and the particle initially at r_0, with $r_1 < r_0 < r_2$, we restate Eq. (179) explicitly as

$$e^{\beta U(r_0)}\partial_{r_0} D(r_0) e^{-\beta U(r_0)}\partial_{r_0}\tau(r_0) = -1\,. \tag{183}$$

Rearranging and integrating the equation from r to r_2 gives

$$D(r_2)e^{-\beta U(r_2)}\, \partial_{r_0}\tau(r_0)|_{r_2} - D(r)e^{-\beta U(r)}\, \partial_{r_0}\tau(r_0)|_r = -\int_r^{r_2} dr'\, e^{-\beta U(r')}\,. \tag{184}$$

The first term of the LHS vanishes after applying the reflective boundary condition at r_2. Then, another rearrangement and an integration from r_1 to r_0 with respect to r gives

$$\tau(r_0) - \tau(r_1) = \int_{r_1}^{r_0} dr\, D^{-1}(r) e^{\beta U(r)} \int_r^{r_2} dr'\, e^{-\beta U(r')}\,. \tag{185}$$

Now we have to find $\tau(r_1)$. To do so, we go back to Eq. (183) and integrate from r_1 to r_2 to get

$$D(r')e^{-\beta U(r')}\partial_{r'}\tau(r')|_{r_1}^{r_2} = -\int_{r_1}^{r_2} dr'\, e^{-\beta U(r')}\,. \tag{186}$$

Imposing again the boundary condition at r_2 and rearranging gives

$$\partial_{r'}\tau(r')|_{r_1} = \frac{1}{D(r_1)}\left[\frac{e^{-\beta U(r_1)}}{\int_{r_1}^{r_2} dr'\, e^{-\beta U(r')}}\right]^{-1} = \frac{1}{D(r_1)p_{eq}(r_1)}\,. \tag{187}$$

where we have introduced $p_{eq}(r_1)$ to denote the equilibrium probability of the particle to be found at r_1. Substituting then the above expression into the radiative boundary condition at r_1 gives

$$\tau(r_1) = \frac{1}{w}\partial_{r'}\tau(r')|_{r_1} = \frac{1}{D(r_1) w p_{eq}(r_1)}\,. \tag{188}$$

Finally, substituting the above result into Eq. (185) gives

$$\tau(r_0) = \int_{r_1}^{r_0} dr\, \frac{1}{D(r)} e^{\beta U(r)} \int_r^{r_2} dr'\, e^{-\beta U(r')} + \frac{1}{D(r_1) w p_{eq}(r_1)}\,. \tag{189}$$

In case of an absorptive boundary at r_1, $w \to \infty$, causing the second term on the RHS to vanish. The MFPT for a particle initially at r_0 to reach r_1 is then

$$\tau(r_0) = \int_{r_1}^{r_0} dr\, \frac{1}{D(r)} e^{\beta U(r)} \int_r^{r_2} dr'\, e^{-\beta U(r')}\,. \tag{190}$$