A probabilistic model of diffusion through a semi-permeable barrier

Paul C. Bressloff
Department of Mathematics, University of Utah 155 South
1400 East, Salt Lake City, UT 84112, USA

Diffusion through semi-permeable structures arises in a wide range of processes in the physical and life sciences. Examples at the microscopic level range from artificial membranes for reverse osmosis to lipid bilayers regulating molecular transport in biological cells to chemical and electrical gap junctions. There are also macroscopic analogues such as animal migration in heterogeneous landscapes. It has recently been shown that one-dimensional diffusion through a barrier with constant permeability $\kappa_0$ is equivalent to snapping out Brownian motion (BM). The latter sews together successive rounds of partially reflecting BMs that are restricted to either the left or the right of the barrier. Each round is killed when its Brownian local time exceeds an exponential random variable parameterized by $\kappa_0$. A new round is then immediately started in either direction with equal probability. In this article, we use a combination of renewal theory, Laplace transforms and Green’s function methods to show how an extended version of snapping out BM provides a general probabilistic framework for modelling diffusion through a semi-permeable barrier. This includes modifications of the diffusion process away from the barrier (e.g. stochastic resetting) and non-Markovian models of membrane absorption that kill each round of partially reflected BM. The latter leads to time-dependent permeabilities.

1. Introduction

Diffusion through semi-permeable barriers or membranes arises in a wide range of processes in the physical and life sciences. At the microscopic level, a semi-permeable membrane is a biological or artificial membrane that only allows certain molecules to pass
through it. This can be quantified more precisely in terms of the membrane permeability, which is the passive diffusion rate of molecules across the membrane. The permeability of any specific molecule depends on properties such as its size and ionic charge. Artificial semi-permeable membranes include a variety of materials that are specifically designed for filtration. A well-known example is water filtration via reverse osmosis. There are many examples of permeable structures in biological cells, which regulate the flow of proteins and ions between different subcellular compartments and the exchange of molecules with the extracellular environment [1–3].分子的运输通常由蛋白基孔嵌入脂质双层的细胞膜和膜内细胞器调节。在生物膜内，半渗透屏障尤其重要，例如在多细胞水平上的间隙连接。间隙连接是两个相邻细胞之间的小的非选择性通道，提供了直接的扩散路径。它们由来自两个耦合细胞的头部对头部连接的两个半通道或半级联组成 [5–7]。间隙连接在大多数动物器官和组织中普遍存在，提供了一种电学和化学通信的机制。最后，半渗透屏障在生态学水平上存在，例如动物的扩散受道路和围栏在异质景观中的影响 [8–10]。在宏观模型中，半渗透膜的边界条件表征为通过膜的通量连续，并与两侧浓度差成正比。具体来说，考虑一维扩散与一个半渗透边界在 \( x = 0 \)。令 \( u(x,t) \) 为位置 \( x \in \mathbb{R} \) 上的时间 \( t \) 的浓度。边界值问题 (BVP) 采取形式

\[
\frac{\partial u(x,t)}{\partial t} = D \frac{\partial^2 u(x,t)}{\partial x^2}, \quad x \neq 0 \tag{1.1a}
\]

以及

\[
J(0^\pm, t) = \kappa_0 [u(0^-, t) - u(0^+, t)], \tag{1.1b}
\]

其中 \( J(x, t) = -D \frac{\partial u(x,t)}{\partial x} \)，\( D \) 是扩散系数且 \( \kappa_0 \) 是（常数）渗透率。半渗透或皮革边界条件（1.1b）是热力学推导的Kedem–Katchalsky方程 [16,17] 的一个特定版本。宏观模型的一个局限性是它没有基于单一粒子扩散的基本微观理论。这激发了许多研究随机走的 lattice 中半渗透屏障的代表性工作 [18,19]。此外，Fokker–Planck 描述的单粒子扩散通过半渗透膜的最近导引是通过取适当的连续极限导出随机走模型 [20]。一个替代的建模单一粒子扩散的方法是使用随机微分方程 (SDEs)。已知长期的必要性是修改标准的 Wiener 过程来形成 Brownian 过程 (BM)。例如，可以实施完全和部分反射边界通过引入 Brownian 功能性已知为边界局部时间 [21–26]。后者决定了时间中 Brownian 粒子在边界近邻的停留时间。 (按Fokker–Planck 描述，一个完全 (部分) 反射边界对应于 Neumann (Robin) 边界条件。) 通过诱人的单粒子扩散，将半渗透膜包括在内是最新的发展，并基于所谓的断开 BM [27]。断开 BM 涉及缝合两个部分反射 BM，一个限制在 \( x < 0 \) 而另一个限制在 \( x > 0 \)。假设粒子从区域 \( x > 0 \) 开始。它在界面前时间超过一个指数随机变量，参数 \( \kappa_0 \)。它立即重新开始或负反射 BM 与相等概率，等等。注意断开的 BM 相对于更熟悉的 skew BM 第一次由 Ito 和 McKean [28] 提出。Skew BM 作为标准 BM，粒子在初始化时的位置决定了下一次的路径选择为正。
a fixed probability $p$. It has a wide range of applications, particularly in mathematical finance [29–32].

In this article, we show how the snapping out BM introduced in [27] can be used to develop more general probabilistic models of one-dimensional diffusion through semi-permeable membranes. We begin, in §2, by describing how to formulate totally and partially reflecting BM in terms of Brownian local times. We then derive a last renewal equation that relates the probability density of snapping out BM with the corresponding probability density for partially reflected BM. The renewal equation is solved using Laplace transforms and Green’s function methods, resulting in an explicit expression for the probability density of snapping out BM. We thus establish that the probability density satisfies equation (1.1). Note that our renewal method is equivalent to the resolvent operator formulation of [27], since they both rely on the strong Markov property. However, expressing the dynamics in terms of a renewal process facilitates the various extensions considered in the remainder of the article.

In §3, we extend the snapping out BM by incorporating the effects of stochastic resetting, whereby the position of the particle is randomly reset according to a Poisson process with resetting rate $r$. Stochastic resetting has become an important paradigm for understanding non-equilibrium stochastic processes, with a variety of applications in optimal search problems and biophysics (see the review [33] and references therein.) Examples in cell biology include Michaelis–Menten reaction schemes [34,35], DNA elongation and backtracking [36], cytoneme-based morphogenesis [37] and the binding of focal adhesions during cell motility [38]. One of the particularly useful features of stochastic resetting is that it can be applied to virtually any stochastic process. In addition, if resetting erases all previous history of particle position then renewal theory can be used to obtain explicit analytical solutions. As far as we are aware, the problem of diffusion through a semi-permeable membrane with resetting has not been considered before. One non-trivial feature of this example is that there are two distinct renewal processes, one associated with position resetting and the other with each round of absorption and restart at the membrane interface. We show how to modify the renewal equation of snapping out BM and use this to calculate the non-equilibrium stationary state (NESS) in the presence of resetting. We show that the NESS is independent of $\kappa_0$, but that relaxation to the NESS is $\kappa_0$-dependent.

In §4, we combine snapping out BM with the so-called encounter-based model of partial absorption [39–42]. The basic idea is to kill a given round of partially reflecting BM when the local time exceeds a non-exponential rather than an exponential random variable. This is motivated by experimental observations that various surface-based reactions are better modelled in terms of a reactivity that depends on the amount of time a particle is in contact with the surface (as determined by the local time) [43,44]. For example, the surface may need to be progressively activated by repeated encounters with a diffusing particle, or an initially highly reactive surface may become less active due to multiple interactions with the particle, a process known as passivation. To determine the probability density in the case of generalized surface reactions, we construct a first rather than a last renewal equation. We show that the corresponding boundary condition at the interface involves a time-dependent permeability with memory. Finally, in §5, we indicate how to extend the theory to higher spatial dimensions.

2. The snapping out Brownian motion

To develop a general probabilistic model of a semi-permeable membrane, we first need to consider the probabilistic version of the one-dimensional model (1.1) based on the snapping out BM introduced by Lejay [27]. One of the key ingredients is formulating partially reflecting BM on $[0, \infty)$ in terms of the local time $L_t$ at $x = 0$.

(a) Partially reflected Brownian motion

Let $W$ be a Wiener process on $\mathbb{R}$ and define totally reflected BM according to the function $X_t = F(W_t) \equiv \sqrt{2D}|W_t|$. To determine the stochastic differential equation (SDE) for $X_t$, we use the
standard Ito formula \[21,22,25\]

\[
dX_t = f'(W_t) \, dW_t + \frac{1}{2} f''(W_t) \, dt.
\]

These derivatives are understood in the distributional sense. That is, \( f' (x) = \sqrt{2D} \, \text{sgn}(x) \) and \( f'' (x) = 2\sqrt{2D} \delta(x) \),

where \( \text{sgn}(x) = -1 \) for \( x \leq 0 \) and \( +1 \) for \( x > 0 \). Hence,

\[
dX_t = \sqrt{2D} \, \text{sgn}(W_t) \, dW_t + D \delta(X_t) \, dt,
\]

with \( \delta(X_t) \) defined on the half-line. Integrating with respect to time implies that

\[
X_t = \int_0^t \text{sgn}(W_s) \, dW_s + L_t,
\]

where

\[
L_t = D \int_0^t \delta(X_s) \, ds,
\]

and \( dL_t = D \delta(X_t) \, dt. \) This is the distribution-based version of the local time of \( X \) at \( t = 0 \), which is defined as follows:

\[
L_t = \lim_{\epsilon \to 0^+} \frac{D}{\epsilon} \int_0^t I(0 \leq X_s \leq \epsilon) \, ds,
\]

where \( I \) is the indicator function. It can be shown that \( L_t \) exists and is a non-decreasing, continuous function of \( t \). Moreover, the corresponding probability density \( p(x, t | x_0) \), \( p(x, t | x_0) \, dx = \mathbb{P}[x \leq X_t < x + dx | X_0 = x_0] \) satisfies the diffusion equation on \( [0, \infty) \) with the totally reflecting boundary condition \( J(0, t) = 0 \). Here, \( J(x, t) = -D \delta_x \rho(x, t) \) is the probability flux.

Partially reflected BM, also known as elastic BM, combines reflected BM \( X_t \) with a stopping condition that halts the stochastic process when the local time \( L_t(X) \) exceeds a random exponentially distributed threshold \( \ell \) \[26\]. That is, the particle is absorbed at \( x = 0 \) at the stopping time

\[
T = \inf\{t > 0 : L_t \geq \ell\}, \quad \mathbb{P}[\ell > \ell] = \Psi(\ell) = e^{-\kappa_0 \ell / D}.
\]

It can then be shown that the marginal density for particle position (before absorption),

\[
p(x, t | x_0) \, dx = \mathbb{P}[x \leq X_t < x + dx, \ t < T | X_0 = x_0],
\]

satisfies the diffusion equation with a Robin boundary condition at \( x = 0 \) \[26\]:

\[
\frac{\partial p(x, t | x_0)}{\partial t} = D \frac{\partial^2 p(x, t | x_0)}{\partial x^2}, \quad x > 0
\]

and

\[
D \partial_x p(0, t | x_0) = \kappa_0 p(0, t | x_0), \quad p(x, 0 | x_0) = \delta(x - x_0).
\]

The constant \( \kappa_0 \) is known as the reactivity or rate of absorption.

(b) Brownian motion in the presence of a semi-permeable membrane

We now turn to the snapping out BM introduced by Lejay \[27\] and show how it is equivalent to single-particle diffusion through a semi-permeable barrier. We proceed by constructing a last renewal equation that relates the probability density of snapping out BM with the corresponding probability density of partially reflected BM. Our analysis is equivalent to the resolvent operator formalism presented in \[27\], but it is more amenable to generalizations developed in subsequent sections.

The behaviour of the stochastic process is described as follows. Without loss of generality, assume that the particle starts at \( X_0 = x_0 \geq 0 \). It realizes positively reflected BM until its local time \( L_t \) at \( x = 0^+ \) is greater than an independent exponential random variable \( \ell \) of parameter \( \kappa_0 \). Let \( T_0 \) denote the corresponding stopping time. The process immediately restarts as a new reflected BM.
with probability 1/2 in either \([0^+, \infty)\) or \((-\infty, 0^-)\) and a new local time \(\ell_t\) at \(x = 0^\pm\) for \(t_1 = t - T_0\). Again the reflected BM is stopped when \(\ell_t\) exceeds a new exponential random variable at the stopping time \(T_2\), etc. It can be proven that the snapping out BM is a strong Markov process\(^1\) on the disjoint space \(\mathbb{G} = (-\infty, 0^-) \cup [0^+, \infty)\). The strong Markov property means that we can use renewal theory to analyze the evolution of the associated probability density and show that it satisfies the classical semi-permeable boundary condition (1.1b).

Let \(\rho(x, t|x_0)\) denote the probability density of the snapping out BM with the initial condition \(X_0 = x_0\) and set
\[
\rho(x, t) = \int_{-\infty}^{\infty} \rho(x, t|x_0) g(x_0) \, dx_0, \tag{2.6}
\]
for any continuous function \(g\) on \(\mathbb{G}\) with \(\int_{-\infty}^{\infty} g(x_0) \, dx_0 = 1\). Similarly, set
\[
p(x, t) = H(x) \int_{0}^{\infty} p(x, t|x_0) g(x_0) \, dx_0 + H(-x) \int_{-\infty}^{0} p(-x, t|x_0) g(x_0) \, dx_0, \tag{2.7}
\]
where \(H(x)\) is the Heaviside function and \(p(x, t|x_0)\) for \(x, x_0 \geq 0\) is the solution to the Robin BVP (2.5). It follows that \(\rho(x, 0) = p(x, 0) = g(x)\). In the special case that \(g(x)\) is an even function of \(x\), then \(\rho(x, t) = \rho(-x, t)\) for all \(x \geq 0\), and there is no net flux through the membrane although individual particles cross the membrane. On the other hand, if \(g(x_0) = 0\) for \(x_0 < 0\) and \(\kappa_0 > 0\), then \(\rho(x, t)\) will have positive definite measure on \((-\infty, 0]\) even though \(p(x, t) = 0\) for \(x < 0\) and all \(t \geq 0\). (An analogous result holds if \(g(x_0)\) vanishes on \([0, \infty)\).)

Given these definitions and the strong Markov property, there exists a last renewal equation of the form
\[
\rho(x, t) = p(x, t) + \frac{\kappa_0}{2} \int_{0}^{t} p(|x|, \tau|0)[\rho(0^+, t - \tau) + \rho(0^-, t - \tau)] \, d\tau, \quad x \in \mathbb{G}, \kappa_0 > 0. \tag{2.8}
\]
The first term on the right-hand side represents all sample trajectories that have never been absorbed by the barrier at \(x = 0^\pm\) up to time \(t\). The corresponding integrand represents all trajectories that were last absorbed (stopped) at time \(t - \tau\) in either the positively or negatively reflected BM state and then switched to the appropriate sign to reach \(x\) with probability 1/2. Since the particle is not absorbed over the interval \((t - \tau, t]\), the probability of reaching \(x \in \mathbb{G}\) starting at \(x = 0^\pm\) is \(p(|x|, \tau|0)\). The probability that the last stopping event occurred in the interval \((t - \tau, t - \tau + d\tau)\) irrespective of previous events is \(\kappa_0 d\tau\). It is convenient to Laplace transform the renewal equation (2.8) with respect to time \(t\) by setting \(\tilde{\rho}(x, s) = \int_{0}^{\infty} e^{-st} \rho(x, t) \, dt\), etc. This gives
\[
\tilde{\rho}(x, s) = \tilde{p}(x, s) + \frac{\kappa_0}{2} \tilde{p}(|x|, s|0)[\tilde{\rho}(0^+, s) + \tilde{\rho}(0^-, s)], \quad x \in \mathbb{G}. \tag{2.9}
\]
(Note that equation (2.9) is equivalent to the resolvent operator equation (8) of [27].) Setting \(x = 0^\pm\) in equation (2.9), summing the results and rearranging shows that
\[
\tilde{\rho}(0^+, s) + \tilde{\rho}(0^-, s) = \frac{\Gamma(s)}{1 - \kappa_0 \tilde{\rho}(0, s|0)},
\]
with \(\Gamma(s) \equiv \tilde{p}(0^+, s) + \tilde{p}(0^-, s)\). Substituting back into equations (2.9) yields the explicit solution:
\[
\tilde{p}(x, s) = \tilde{p}(x, s) + \frac{\kappa_0 \Gamma(s)}{1 - \kappa_0 \tilde{p}(0, s|0)} \tilde{p}(|x|, s|0), \quad x \in \mathbb{G}. \tag{2.10}
\]
The next step is to evaluate \(\tilde{p}(|x|, s|x_0)\). Laplace transforming equations (2.5) shows that \(\tilde{p}(x, t|x_0), x > 0\) satisfies the BVP
\[
D \frac{\partial^2 \tilde{p}(x, s|x_0)}{\partial x^2} - s\tilde{p}(x, s|x_0) = -\delta(x - x_0), \quad x > 0 \tag{2.11a}
\]
\(^1\)Recall that a continuous stochastic process \(|X_t, t \geq 0\) is said to have the Markov property if the conditional probability distribution of future states of the process (conditional on both past and present states) depends only on the present state not on the sequence of events that preceded it. That is, for all \(t' > t\), we have \(\mathbb{P}[X_{t'} \leq x|X_t \leq x, s \leq t] = \mathbb{P}[X_{t'} \leq x|X_t \leq x]\). The strong Markov property is similar to the Markov property, except that the ‘present’ is defined in terms of a stopping time.
and
\[
D \frac{\partial \tilde{p}(0,s|x_0)}{\partial x} = \kappa_0 \tilde{p}(0,s|x_0).
\]  
(2.11b)

That is, we can identify \( \tilde{p}(x,s|x_0) \) with the Robin Green’s function for the modified Helmholtz equation on \([0, \infty)\). Writing the general solution for \( x < x_0 \) as
\[
\tilde{p}(x,s|x_0) = A e^{-\sqrt{s/D}x} + B e^{\sqrt{s/D}x}
\]
and substituting into the Robin boundary condition shows that
\[
\tilde{p}(x,s|x_0) = B \left( e^{\sqrt{s/D}x} + \frac{\sqrt{sD} - \kappa_0}{\sqrt{sD} + \kappa_0} e^{-\sqrt{s/D}x} \right).
\]  
(2.13)

By using the fact that the bounded solution for \( x > x_0 \) is proportional to \( e^{-\sqrt{s/D}x} \), imposing continuity of \( \tilde{p}(x,s|x_0) \) across \( x_0 \) and matching the discontinuity in the first derivative yields the solution
\[
\tilde{p}(x,s|x_0) = \frac{1}{2 \sqrt{sD}} \left( e^{-\sqrt{s/D}x} - e^{-\sqrt{s/D}(x-x_0)} \right) + \frac{\kappa_0 e^{-\sqrt{s/D}|x|}}{2 \sqrt{sD}} \Gamma(s), \quad x \in \mathbb{R}.
\]  
(2.14)

It immediately follows that
\[
\tilde{p}(x,s|0) = \frac{1}{\sqrt{sD} + \kappa_0} e^{-\sqrt{s/D}|x|},
\]  
(2.15)

and, hence, equation (2.10) becomes
\[
\tilde{p}(x,s) = \tilde{p}(x,s) + \frac{\kappa_0 e^{-\sqrt{s/D}|x|}}{2 \sqrt{sD}} \Gamma(s), \quad x \in \mathbb{R}.
\]  
(2.16)

Note that in the limit \( \kappa_0 \to 0 \), we have \( \tilde{p}(x,s) \to \tilde{p}(x,s) \). The fact that the particle may be found on either side of the barrier, even though it is now impenetrable, is simply an artefact of the initial distribution \( g(x_0) \).

It follows from equation (2.16) that the density \( \rho(x,s) \) satisfies the Laplace transform of the semi-permeable membrane BVP (1.1) under the initial condition \( \rho(x,0) = g(x) \) and \( \kappa_0 \to \kappa_0/2 \). First, taking the second derivative of equations (2.16) for \( x \neq 0^\pm \) and using equation (2.11a) shows that
\[
D \frac{\partial^2 \tilde{p}(x,s)}{\partial x^2} = -s \tilde{p}(x,s) = -g(x), \quad x \in \mathbb{R}.
\]  
(2.17)

Second, equation (2.16) implies that
\[
\tilde{p}(x,s) + \tilde{p}(-x,s) = \tilde{p}(x,s) + \tilde{p}(-x,s) + \frac{\kappa_0 e^{-\sqrt{s/D}|x|}}{\sqrt{sD}} \Gamma(s)
\]  
(2.18a)

and
\[
\tilde{p}(x,s) - \tilde{p}(-x,s) = \tilde{p}(x,s) - \tilde{p}(-x,s)
\]  
(2.18b)

for \( x > 0 \). Differentiating equation (2.18a) with respect to \( x \) and taking \( x = 0^+ \) we have
\[
\partial_x \tilde{p}(0^+,s) - \partial_x \tilde{p}(0^-,s) = \partial_x \tilde{p}(0^+,s) - \partial_x \tilde{p}(0^-,s) - \frac{\kappa_0}{D} \Gamma(s).
\]  
(2.19)

The Robin boundary condition (2.11b) implies that
\[
\partial_x \tilde{p}(0^+,s) - \partial_x \tilde{p}(0^-,s) = \frac{\kappa_0}{D} [\tilde{p}(0^+,s) + \tilde{p}(0^-,s)] = \frac{\kappa_0}{D} \Gamma(s).
\]  
(2.20)

Hence,
\[
D \partial_x \tilde{p}(0^+,s) = D \partial_x \tilde{p}(0^-,s).
\]  
(2.20)

Similarly, differentiating equation (2.18b) with respect to \( x \) and taking \( x = 0^+ \) gives
\[
\partial_x \tilde{p}(0^+,s) + \partial_x \tilde{p}(0^-,s) = \partial_x \tilde{p}(0^+,s) + \partial_x \tilde{p}(0^-,s)
\]  
(2.21a)

\[
= \kappa_0 [p(0^+,s) - p(0^-,s)] = \kappa_0 [\tilde{p}(0^+,s) - \tilde{p}(0^-,s)].
\]  
(2.21b)
Finally, combining equations (2.20) and (2.21) yields the permeable boundary condition
\[ D \partial_x \tilde{\rho}(x^+, s) = \frac{k_0}{2} [\tilde{\rho}(0^+, s) - \tilde{\rho}(0^-, s)]. \tag{2.22} \]
This establishes that the snapping out BM \( X_t \) is the single-particle realization of the stochastic process whose probability density evolves according to the diffusion equation with a semi-permeable membrane at \( x = 0 \). It also follows that if \( g(x_0) \) is an even function of \( x_0 \), then \( \tilde{\rho}(x, s) \) is an even function of \( x \) so that the flux through the membrane is zero. In other words, it effectively acts as a totally reflecting barrier even though \( \kappa_0 > 0 \). It can also be checked that the solution of equation (2.16) reduces to
\[ \tilde{\rho}(x, s) = \frac{1}{4\sqrt{\pi D}} \left( e^{-\sqrt{s/D}|x-x_0|} + e^{-\sqrt{s/D}(x+x_0)} \right), \quad x > 0. \tag{2.23} \]

There are a number of reasons why it is advantageous to formulate diffusion through a semi-permeable barrier in terms of snapping out BM. Firstly, it provides a method for simulating Brownian motion in the presence of such a barrier [27]. Second, rather than solving a Fokker–Planck of the form (1.1), we can express the (weak) solution for \( \rho \) in terms of the solution \( p \) of partially reflected BM. However, the major advantage within the context of the current article is that it provides a powerful framework for developing more general probabilistic models of diffusion through semi-permeable membranes, as we illustrate in §§3 and 4.

(c) Thin-layer approximation

It is instructive to relate the above probabilistic model of single-particle diffusion through a semi-permeable barrier to a recent study based on a Fokker–Planck description [20]. The latter was derived by taking a continuum limit of a continuous-time random walk model with a defect. Here, we briefly show how the Fokker–Planck description is equivalent to using a thin-layer approximation of a semi-permeable barrier. In [27], it is proven that the solution of the thin-layer BVP converges in distribution to the solution of the snapping out BM.

To derive the thin-layer approximation, we first consider BM in \( \mathbb{G} \) with a jump discontinuity in the diffusivity at \( x = 0 \). That is, \( D(x) = [D_+ - D_-]H(x) + D_- \). Introduce the stochastic process
\[ X_t = F(X_t) \equiv \sqrt{2D_+H(W_t)}W_t + \sqrt{2D_-H(-W_t)}W_t. \]
Applying Ito’s formula (2.1) with
\[ f'(x) = \sqrt{2D_+H(x)} + \sqrt{2D_-H(-x)}, \quad f''(x) = \sqrt{2D_+\delta(x)} - \sqrt{2D_-\delta(-x)} \]
yields the SDE
\[ dX_t = [\sqrt{2D_+H(W_t)} + \sqrt{2D_-H(-W_t)}] dW_t + \frac{1}{2} [\sqrt{2D_+\delta(W_t)} - \sqrt{2D_-\delta(-W_t)}] dt. \]
Using \( \text{sgn}(X_t) = \text{sgn}(W_t) \) and \( \delta(\pm W_t) = \sqrt{2D_\pm \delta(X_t)} \) gives the skew BM [27,29,31]:
\[ dX_t = [\sqrt{2D_+H(X_t)} + \sqrt{2D_-H(-X_t)}] dW_t + [D_+ - D_-] \delta(X_t) dt \]
\[ = \sqrt{2D(X_t)} dW_t + \frac{D_+ - D_-}{D_+ + D_-} dL_t^0(X), \tag{2.24} \]
where \( L_t^0(X) \) is the local time
\[ L_t^0(X) = \frac{D_+ + D_-}{2} \int_0^t \delta(X_s) \, ds. \tag{2.25} \]
The corresponding Ito Fokker-Planck equation (FPE) is then
\[ \frac{\partial p}{\partial t} = \frac{\partial}{\partial x} \left( D(x) p(x, t) \right) - \frac{\partial [D_+ - D_-] \delta(x) p(x, t)}{\partial x} = \frac{\partial}{\partial x} \left[ D(x) \frac{\partial p(x, t)}{\partial x} \right]. \tag{2.26} \]
Now consider the thin-layer problem shown in figure 1. Outside the layer \([-a, a]\), the diffusivity is \( D \), whereas within the layer, it is \( D_0 \). Following from the previous calculation, we
Figure 1. Thin-layer problem. In the small $a$ limit, we have $J(-a^-) \approx J(a^+) \approx (\kappa_0/2)[p(a^+) − p(a^-)]$. (Online version in colour.)

have the Ito SDE:

$$\text{d}X_t = \sqrt{D(X_t)} \text{d}W_t + \frac{D - D_0}{D + D_0} \text{d}L^D_t(X) + \frac{D_0 - D}{D + D_0} \text{d}L^{-\delta}(X),$$

(2.27)

where $D(x) = D$ for $|x| > a$ and $D(x) = D_0$ for $|x| < a$, and the corresponding FPE

$$\frac{\partial p}{\partial t} = \frac{\partial}{\partial x} \left[ D(x) \frac{\partial p(x, t)}{\partial x} \right].$$

(2.28)

Integrating the FPE across $x = -a$ and $x = +a$, respectively, yields the flux continuity conditions

$$D \partial_x p(-a^-, t) = D_0 \partial_x p(-a^+, t), \quad D_0 \partial_x p(a^-, t) = D \partial_x p(a^+, t).$$

(2.29)

Suppose that $D_0 = \kappa_0 a$ and consider the limit $a \to 0$. In the small-$a$ regime, we have

$$p(a, t) − p(-a, t) \approx 2a \partial_x p(-a^+, t) \approx 2a \partial_x p(a^-, t).$$

(2.30)

Combining the various results gives, to leading order,

$$D \partial_x p(-a, t) \approx D \partial_x p(a, t) \approx \frac{D_0}{2a} [p(a, t) − p(-a, t)].$$

Finally, taking the limit $a \to 0^+$ recovers the permeable barrier boundary condition. Moreover, equation (2.28) is equivalent to the FPE description derived in [20].

3. Diffusion through a semi-permeable membrane with stochastic resetting

Let us return to the case of partially reflected BM in $[0, \infty)$, which is now supplemented by the resetting condition $X_t \to \xi \in [0, \infty)$ at a random sequence of times generated by a Poisson process with constant rate $r$. This particular problem has previously been studied in [45,46]. The probability density $p_r(x, t|x_0)$ evolves according to the modified Robin BVP

$$\frac{\partial p_r}{\partial t} = D \frac{\partial^2 p_r}{\partial x^2} − rp_r + rQ_r(x_0, t)\delta(x - \xi), \quad x > 0$$

(3.1a)

and

$$D \frac{\partial p_r}{\partial x} = \kappa_0 p_r, \quad x = 0, \quad p_r(x, 0|x_0) = \delta(x - x_0).$$

(3.1b)

We have introduced the marginal distribution

$$Q_r(x_0, t) = \int_0^\infty p_r(x, t|x_0) \text{d}x,$$

(3.2)
which is the survival probability that the particle has not been absorbed at $x = 0$ in the time
interval $[0, t]$, having started at $x_0$. The $r$ subscript indicates the solution is in the presence of
resetting. Note that in the limit $\kappa_0 \to 0$, the boundary at $x = 0$ becomes totally reflecting so
that $Q_r = 1$, and we recover the standard forward equation for one-dimensional diffusion with
resetting $[47,48]$. On the other hand, if $\kappa_0 \to \infty$, then the boundary is totally absorbing.

Laplace transforming equations (3.1a) and (3.1b) gives

$$D \frac{d^2 \tilde{p}_r(x, s|x_0)}{dx^2} - (s + r) \tilde{p}_r(x, s|x_0) = -[\delta(x - x_0) + rQ_r(x_0, s)\delta(x - \xi)], \quad x > 0 \tag{3.3a}$$

and

$$D \frac{d \tilde{p}_r(x, s|x_0)}{dx} = \kappa_0 \tilde{p}_r(x, s|x_0), \quad x = 0. \tag{3.3b}$$

Using the fact that $\tilde{p}(x, s|x_0)$ is the Green’s function for partially reflecting BM without resetting,
see equation (2.14), it follows that

$$\tilde{p}_r(x, s|x_0) = \tilde{p}(x, r + s|x_0) + rQ_r(x_0, s)\tilde{p}(x, r + s|\xi), \quad 0 < x < \infty. \tag{3.4}$$

Finally, Laplace transforming equation (3.2) and using (3.4) shows that

$$Q_r(x_0, s) = \int_0^\infty \tilde{p}_r(x, s|x_0) \, dx = \int_0^\infty \tilde{p}(x, r + s|x_0) \, dx + r\tilde{Q}_r(x_0, s) \int_0^\infty \tilde{p}(x, r + s|\xi) \, dx$$

$$= \tilde{Q}(x_0, r + s) + r\tilde{Q}_r(x_0, s)\tilde{Q}(\xi, r + s), \tag{3.5}$$

where $\tilde{Q}$ is the Laplace transform of the survival probability without resetting:

$$\tilde{Q}(x_0, s) = \frac{1 - e^{-\sqrt{s/D}x_0}}{s} + \frac{e^{-\sqrt{s/D}x_0}}{s + \kappa_0 \sqrt{s/D}}. \tag{3.6}$$

Rearranging equation (3.5) thus determines the survival probability with resetting in terms of the
corresponding probability without resetting:

$$Q_r(x_0, s) = \frac{\tilde{Q}(x_0, r + s)}{1 - r\tilde{Q}(\xi, r + s)}. \tag{3.7}$$

For $\kappa_0 > 0$, the steady-state survival probability vanishes with or without resetting, since one-
dimensional diffusion is recurrent so that absorption eventually occurs. Indeed,

$$Q^*_r(x_0) = \lim_{s \to 0} s\tilde{Q}_r(x_0, s) = \lim_{s \to 0} \frac{s\tilde{Q}(x_0, r)}{1 - r\tilde{Q}(\xi, r)} = 0. \tag{3.8}$$

(Note that $\tilde{Q}(\xi, r) \neq 1/r$ when $\kappa_0 > 0$.) On the other hand, if $\kappa_0 = 0$ (totally reflecting boundary at
$x = 0$), then $Q_r(x_0, s) = 1/s$ for all $x_0 < \infty$, and thus, $Q^*_r(x_0) = 1$. In this special case, there exists a
non-equilibrium stationary state (NESS) given by

$$p^*_r(x) = \lim_{s \to 0} s\tilde{p}_r(x, s|x_0) = \lim_{s \to 0} s[\tilde{p}(x, r + s|x_0) + r\tilde{Q}_r(x_0, s)\tilde{p}(x, r + s|\xi)]$$

$$= r\tilde{p}(x, r|\xi) = \frac{r}{2\sqrt{rD}} \left[ e^{-\sqrt{r/D}|x-\xi|} + e^{-\sqrt{r/D}|x+\xi|} \right], \quad x > 0, \tag{3.9}$$

which recovers the well-known result of $[47,48]$.

We now observe that partially reflecting BM with resetting is also a strong Markov process,
since there is no memory of previous histories following resetting to $\xi$. This means that a modified
version of the renewal equation (2.10) for snapping out BM holds when resetting is included. For
simplicity, suppose that we sew together positively and negatively reflecting BMs such that the
former resets to $\xi$ and the latter to $-\xi$ with $\xi \geq 0^+$, see figure 2. This symmetric resetting protocol
means that $\tilde{p}_r(x,s) = \tilde{p}_r(-x,s)$. It follows that the renewal equation (2.10) becomes

$$
\tilde{p}_r(x,s) = \tilde{p}_r(x,s) + \frac{k_0 \Gamma_r(s)/2}{1 - k_0 \tilde{p}_r(0,s|0)} \tilde{p}_r(|x|,s|0), \ x \in \mathbb{G}, \ k_0 > 0
$$

(3.10)

with $\Gamma_r(s) = \tilde{p}_r(0^+,s) + \tilde{p}_r(0^-,s)$. Note that our resetting protocol is space dependent due to the fact that we exclude resetting events that involve a particle crossing the semi-permeable membrane to the other side. Hence, spatial position $X_t \geq 0^+$ ($X_t \leq 0^-$) can only reset to $x = \xi$ ($x = -\xi$). (Most models of stochastic resetting take resetting to be independent of the current location $X_t$ [33]. Examples of space-dependent resetting protocols can be found in [48–50].) This means that we have to work with the modified renewal equation (3.10) that keeps track of which side of the membrane a particle is located, rather than using a renewal equation that directly relates $\rho_r(x,t)$ to $\rho(x,t)$. In other words, we cannot simply introduce the resetting protocol into the Fokker–Planck equation for $\rho(x,t)$.

(a) Non-equilibrium stationary state

One of the common characteristic features of non-absorbing diffusion processes with stochastic resetting is that there exists a non-equilibrium stationary state (NESS), which is maintained by non-zero probability fluxes [33]. In the case of snapping out BM with resetting, the points $x = \pm \xi$ act as probability sources, whereas all positions $x \neq \pm \xi$ are potential probability sinks. Although each partially reflected BM is killed by absorption at the semi-permeable barrier, the stochastic process is immediately restarted so that snapping out BM is not killed. We will derive the NESS using the renewal equation (3.10). Multiplying both sides by $s$ and taking the limit $s \to 0$ gives

$$
\rho_r^*(x) = \lim_{t \to \infty} \rho_r(x,t) = \lim_{s \to 0} s \tilde{p}_r(x,s) = \frac{k_0}{2} \lim_{s \to 0} \frac{s \Gamma_r(s)}{1 - k_0 \tilde{p}_r(0,s|0)} \tilde{p}_r(|x|,s|0).
$$

(3.11)

We have used the fact that partially reflected BM with resetting does not have a non-trivial NESS, that is, $\lim_{t \to \infty} p_r(x,t) = 0$. The existence of the NESS for snapping out BM can be established by showing that $1 - k_0 \tilde{p}_r(0,s|0) = O(s)$. Setting $x = x_0 = 0$ in equation (3.4) and using equation (2.14)

---

2 We could consider a more general resetting protocol in which $X_t \to \xi_+ > 0$ when $X_t \geq 0^+$ and $X_t \to \xi_- < 0$ when $X_t \leq 0^-$ with $|\xi_+| \neq |\xi_-|$ by an appropriate modification of the renewal equation.
Hence, the NESS takes the form

\[ \bar{\rho}_r(0, s|0) = \bar{\rho}(0, r + s|0) + r \bar{Q}_r(0, s) \bar{\rho}(0, r + s|\xi) \]

\[ = \frac{1}{\sqrt{(r+s)D} + \kappa_0} \left[ 1 + r e^{-\sqrt{(r+s)/D} \xi} \tilde{Q}_r(0, s) \right]. \]  

(3.12)

Equations (3.6) and (3.7) give

\[ \tilde{Q}_r(0, s) = \frac{1/[r + s + \kappa_0 \sqrt{(r+s)/D}]}{1 - (r/(r+s)) \left( 1 - e^{-\sqrt{(r+s)/D} \xi} \right) - (r/(r+s + \kappa_0 [r+s]/D)) e^{-\sqrt{(r+s)/D} \xi}}. \]

(3.13)

By substituting into equation (3.12) and rearranging, we find that

\[ \tilde{\rho}_r(0, s|0) = \frac{1}{\sqrt{(r+s)D} + \kappa_0} \left[ 1 + \frac{1}{\kappa_0} \left( 1 + \frac{s}{\kappa_0} r \sqrt{(r+s)/D} \right) \right] \]

\[ = \frac{1}{\sqrt{(r+s)D} + \kappa_0} \left[ 1 + \sqrt{(r+s)/D} \left( 1 - \frac{s}{\kappa_0} r \sqrt{(r+s)/D} e^{\sqrt{r/s}D \xi} + O(s^2) \right) \right] \]

\[ = \frac{1}{\kappa_0} \left( 1 - \frac{s}{\kappa_0} \sqrt{r/D} e^{\sqrt{r/s}D \xi} \right) + O(s^2). \]

(3.14)

It immediately follows that \( 1 - \kappa_0 \tilde{\rho}_r(0, s|0) = O(s) \), and thus,

\[ \rho_r^*(x) = \frac{\kappa_0^2}{2} \frac{r}{D} e^{-\sqrt{r/s}D \xi} \Gamma_r(0) \tilde{\rho}_r(|x|, 0|0). \]

(3.15)

The factor \( \Gamma_r(0) \) is

\[ \Gamma_r(0) = \tilde{\rho}_r(0^+, 0) + \tilde{\rho}_r(0^-, 0) = \int_{-\infty}^{\infty} g(x_0) \left[ \bar{\rho}(0, r|x_0) + r \bar{Q}_r(|x_0|, 0) \bar{\rho}(0, r|\xi) \right] dx_0 \]

\[ = \frac{1}{\sqrt{r/D} + \kappa_0} \int_{-\infty}^{\infty} g(x_0) \left[ e^{-\sqrt{r/D} |x_0|} + \frac{r \bar{Q}(0, r) e^{-\sqrt{r/D} \xi}}{1 - r \bar{Q}(\xi, r)} \right] dx_0 \]

\[ = \frac{1}{\kappa_0} \int_{-\infty}^{\infty} g(x_0) dx_0 = \frac{1}{\kappa_0}. \]

(3.16)

Hence, the NESS takes the form

\[ \rho_r^*(x) = \frac{\kappa_0}{2} \frac{r}{D} e^{-\sqrt{r/s}D \xi} \tilde{\rho}_r(|x|, 0|0). \]

(3.17)

As expected, \( \rho_r^*(x) \) is independent of the initial distribution \( g(x_0) \) and is an even function of \( x \in \mathbb{G} \). Finally, combining equations (3.4), (3.6) and (3.7) shows that

\[ \tilde{\rho}_r(x, 0|0) = p(x, r|0) + \frac{\sqrt{r/D}}{\kappa_0} e^{\sqrt{r/D} \xi} \tilde{\rho}(x, r|\xi) \]

\[ = \frac{1}{\sqrt{r/D} + \kappa_0} \left( e^{-\sqrt{r/D} |x| - \xi} + \frac{\sqrt{r/D} - \kappa_0}{\sqrt{r/D} + \kappa_0} e^{-\sqrt{r/D} (x + \xi)} \right) \]

\[ = \frac{1}{2\kappa_0} \left( e^{-\sqrt{r/D} |x|} + e^{\sqrt{r/D} \xi} e^{-\sqrt{r/D} |x - \xi|} \right) \]

(3.18)

and

\[ \rho_r^*(x) = \frac{r}{2} \frac{1}{\sqrt{r/D}} \left( e^{-\sqrt{r/D} (x + \xi)} + e^{-\sqrt{r/D} |x - \xi|} \right) = \frac{\rho_r^*(|x|)}{2}, \]

(3.19)

where we have used equation (3.9). Note that the NESS is independent of \( \kappa_0 \) for \( \kappa_0 > 0 \) and has the following interpretation. In the long time limit, the particle spends an equal amount of time.
on either side of the barrier where it undergoes repeated rounds of partially reflecting BM with resetting. Thus, each side forms the NESS $p^r_\ast(x)$ but is weighted by a factor of $1/2$. The limit $\kappa_0 \to 0$ is singular, since the relative weight of the density on either side of the barrier will depend on the initial density $g(x_0)$. In figure 3, we show that there is good agreement between the exact analytical solution (3.19) and Monte-Carlo simulations of snapping out BM with resetting.

(b) Relaxation time

Although $\rho^r_\ast(x)$ is independent of the permeability $\kappa_0$, the time-dependent relaxation to the NESS will be $\kappa_0$ dependent. In the case of homogeneous diffusion in $\mathbb{R}^d$, one can use large deviation theory to show that the approach to the stationary state exhibits a dynamical phase transition, which can be interpreted as a traveling front separating spatial regions for which the probability density has relaxed to the NESS from those where transients persist [51]. Recently, we introduced an alternative method for characterizing the relaxation process, which is based on the notion of an accumulation time [52]. We proceeded by decomposing the probability density into decreasing and accumulating components and showed how the latter evolved in an analogous fashion to the formation of a concentration gradient in diffusion-based morphogenesis. The accumulation time for the latter is the analogue of the mean first passage time of a search process, in which the survival probability density is replaced by an accumulation fraction density [53–55].

Following [52], consider the function

$$Z_r(x, t) = 1 - \frac{\rho_r(x, t)}{\rho^r_\ast(x)}, \quad (3.20)$$

and define

$$T_r(x) = \int_0^\infty Z_r(x, t) \, dt = \lim_{s \to 0} \tilde{Z}_r(x, s). \quad (3.21)$$

Laplace transforming equation (3.20) gives

$$\tilde{Z}_r(x, s) = \frac{1}{s} \left[ 1 - \frac{s \tilde{\rho}_r(x, s)}{\rho^r_\ast(x)} \right],$$
that if we had considered Tr probability density or generalized propagator for the pair (Xt, Lt), see equation (2.4), by a non-exponential distribution. The basic idea is to introduce the joint phenomenon, whereby T with κ0 = 1 and r = 1. (Since, Tr(x) is an even function of x, we only show plots for x > 0.) (Online version in colour.)

and, hence,

\[ T_r(x) = \lim_{s \to 0} \frac{1}{s} \left[ 1 - \frac{s \tilde{\rho}_r(x, s)}{\rho_r^* (x)} \right] = -\frac{1}{\rho_r^* (x)} \frac{d}{ds} [s \tilde{\rho}_r(x, s)] \bigg|_{s=0} . \] (3.22)

We have used the identity \( \rho_r^* (x) = \lim_{s \to 0} s \tilde{\rho}_r(x, s) \). In applications to morphogenesis where particle number is not conserved, it is typically assumed that \( Z_r(x, t) \) is a non-negative function of x for all t > 0 (no overshooting), so that \( T_r(x) \) can be interpreted as the mean accumulation time to the stationary state. However, positivity of \( Z_r(x, t) \) for all x does not hold in the case of stochastic processes due to probability conservation. Nevertheless, as shown in [3], one can decompose \( T_r(x) \) into negative and positive parts and interpret the latter as an accumulation time. Since the first term in equation (3.10) does not contribute to the NESS and generates a negative contribution to \( T_r(x) \), we define the accumulation time as follows:

\[ T_r^*(x) = -\frac{1}{\rho_r^* (x)} \frac{d}{ds} [s (\tilde{\rho}_r(x, s) - \tilde{\rho}_r(x, s))] \bigg|_{s=0} . \] (3.23)

In figure 4, we plot \( T_r^*(x) \) as a function of x, x > 0, for various choices of model parameters and the initial condition \( g(x_0) = \delta(x - x_0) \). A number of observations can be made. Firstly, \( T_r^*(x) \) for fixed x is a decreasing function of \( \kappa_0 \) and an increasing function of \( \xi \), which reflects the fact that each round of partially reflected BM takes longer on average. Secondly, there is a cross-over phenomenon, whereby \( T_r^*(x) \) is a non-monotonic function of the resetting rate r for fixed x. This is further illustrated in figure 5, which indicates that \( T_r^*(x) \) for fixed x is a unimodal function of r with a minimum at an x-dependent rate \( r^*(x) \). Thirdly, \( T_r^*(x) \) asymptotically approaches a linear function of x, which is consistent with previous findings in other systems [51,52]. Finally, note that if we had considered \( T_r(x) \) rather than \( T_r^*(x) \), then \( T_r(x) \) would be negative for locations close to the membrane.

4. Encounter-based version of snapping out Brownian motion

Another possible extension of snapping out BM is to modify the rule for killing each round of partially reflected BM. This is equivalent to changing the absorption process on either side of the semi-permeable barrier. We proceed by using the so-called encounter-based model of absorption [39–42], which replaces the exponential distribution for the stopping local time threshold \( \hat{\ell} \), see equation (2.4), by a non-exponential distribution. The basic idea is to introduce the joint probability density or generalized propagator for the pair \( (X_t, L_t) \), where \( X_t \in [0, \infty) \) is partially
Figure 5. Accumulation time for the snapping out BM with resetting. \(T^x_r(x)\) is plotted as a function of \(r\) for various spatial locations \(x\). We also set \(D = 1, \xi = 1, \kappa_0 = 1\) and \(g(x_0) = \delta(x - x_0)\) with \(x_0 = 1\). (Online version in colour.)

reflected BM and \(L_t\) is the local time at \(x = 0\):

\[
P(x, \ell, t|x_0)\,dx\,d\ell := \mathbb{P}[x \leq X_t < x, x + dx, \ell \leq L_t < \ell + d\ell|X_0 = x_0, \ell_0 = 0].
\]

Since the local time only changes at the membrane boundary \(x = 0\), the evolution equation within the bulk of the domain is simply

\[
\frac{\partial P}{\partial t} = D \frac{\partial^2 P}{\partial x^2}, \quad x > 0, \quad \ell \geq 0, \quad t > 0.
\]

The non-trivial step is determining the boundary condition at \(x = 0\). Here, we give a heuristic derivation that considers a thin layer in a neighbourhood of the boundary given by the interval \([0, h]\) with

\[
L_h^t = \frac{D}{h} \int_0^t \left[ \int_0^h \delta(X_{t'} - x)\,dx \right] \,d\ell'.
\]

By definition, \(hL_h^t/D\) is the residence or occupation time of the process \(X_t\) in the boundary layer \([0, h]\) up to time \(t\). Although the width \(h\) and the residence time in the boundary layer vanish in the limit \(h \to 0\), the rescaling by \(1/h\) ensures the non-trivial limit \(L_t = \lim_{h \to 0} L_h^t\). Moreover, from conservation of probability, the flux into the boundary layer over the residence time \(h\delta\ell/D\) generates a corresponding shift in the probability \(P\) within the boundary layer from \(\ell \to \ell + \delta\ell\). That is, for \(\ell > 0\),

\[
-J(h, \ell, t|x_0)h\delta\ell = [P(0, \ell + \delta\ell, t|x_0) - P(0, \ell, t|x_0)]h,
\]

where \(j(x, \ell, t|x_0) = -D\delta_x P(x, \ell, t|x_0)\). Dividing through by \(h\delta\ell\) and taking the limits \(h \to 0\) and \(\delta\ell \to 0\) yields \(-J(0, \ell, t|x_0) = \delta\ell P(0, \ell, t|x_0), \quad \ell > 0\). Moreover, when \(\ell = 0\), the probability flux \(J(0, 0, t|x_0)\delta\ell\) is identical to that of a Brownian particle with a totally absorbing boundary at \(x = 0\), which we denote by \(J\infty(0, t|x_0)\). Combining all of these results yields the boundary condition

\[
-J(0, \ell, t|x_0) = -J\infty(0, t|x_0)\delta(\ell) + \frac{\partial P(0, \ell, t|x_0)}{\partial\ell}.
\]

It can also be shown that \(P(0, 0, t|x_0) = -J\infty(0, t|x_0)\). For a more detailed derivation of the boundary condition (4.3), see [39,41]. Finally, Laplace transforming equations (4.1) and (4.3) with respect to
\[ \tilde{P}(x, z, t|x_0) = \int_0^\infty e^{-\ell t} P(x, \ell, t|x_0) \, d\ell, \quad (4.4) \]

we find that the \( \tilde{P}(x, z, t|x_0) \) is the solution to the Robin BVP (2.5) with \( \kappa_0 = Dz \) and \( z \) the Laplace variable.

The aforementioned is consistent with the observation that partially reflected BM is obtained by supplementing reflected BM with a stopping condition that halts the stochastic process when the local time \( L_t(X) \) exceeds a random exponentially distributed threshold \( \ell \). This can be established as follows. Given that \( L_t \) is a non-decreasing process, the condition \( t < T \) is equivalent to the condition \( L_t < \ell \). This implies that

\[
\begin{align*}
p(x, t|x_0) \, dx &= P[x \leq X_t < x + dx, \ L_t < \ell | X_0 = x_0] \\
&= \int_0^\infty d\ell \, \psi(\ell) P[x \leq X_t < x + dx, \ L_t < \ell | X_0 = x_0] \\
&= \int_0^\infty d\ell \, \psi(\ell) \int_0^\ell d\ell' [P(x, \ell', t|x_0) \, dx],
\end{align*}
\]

where \( \psi(\ell) = -\Psi'(\ell) = (\kappa_0/D)e^{-\kappa_0\ell/D} \). By using the identity

\[
\int_0^\infty d\ell \, u(\ell) \int_0^\ell d\ell' \, v(\ell') = \int_0^\infty d\ell' \, v(\ell') \int_0^{\ell'} d\ell \, u(\ell)
\]

doing arbitrary integrable functions \( u, v \), it follows that

\[
p(x, t|x_0) = \int_0^\infty P(x, \ell', t|x_0) \left[ \int_0^\infty \psi(\ell) \, d\ell \right] \, d\ell' = \int_0^\infty \Psi(\ell) P(x, \ell, t|x_0) \, d\ell. \quad (4.5)
\]

Hence, the probability density of partially reflected BM is equivalent to the Laplace transform of the local time propagator with \( z = \kappa_0/D \) acting as the Laplace variable. Assuming that the Laplace transform can be inverted, we can then incorporate a non-exponential probability distribution \( \Psi(\ell) \) such that the corresponding marginal density is

\[
p(x, t|x_0) = \int_0^\infty \Psi(\ell) P(x, \ell, t|x_0) \, d\ell = \int_0^\infty \Psi(\ell) \Delta^{-1}_t \tilde{P}(x, z, t|x_0) \, d\ell. \quad (4.6)
\]

One major difference from the exponential law \( \Psi(\ell) = e^{-\kappa_0\ell/D} \) is that the stochastic process \( X_t \) is no longer Markovian. One way to see this is to note that a non-exponential distribution can be generated by an \( \ell \)-dependent absorption rate, \( \kappa = \kappa(\ell) \). That is,

\[
\Psi(\ell) = \exp(-D^{-1} \int_0^\ell \kappa(\ell') \, d\ell'). \quad (4.7)
\]

Given that the probability of absorption now depends on how much time the particle spends in a neighbourhood of the boundary, as specified by the local time, it follows that the stochastic process has memory.

We now define a generalized snapping out BM as follows. Again we assume that the particle starts at \( X_0 = x_0 \geq 0 \). It realizes positively reflected BM until its local time \( L_t \) at \( x = 0^+ \) is greater than an independent random variable \( \ell \) with a non-exponential distribution \( \Psi(\ell) = P[\ell > \ell] \). It then randomly determines its sign with probability 1/2 and restarts as a new reflected BM in either \([0^+, \infty)\) or \((\infty, 0^-)\), and so on. Although each round of partially reflected Brownian motion is non-Markovian, all history is lost following absorption and restart so that we can construct a renewal equation. However, it is now more convenient to use a first rather than a last renewal equation.
Let $p_\psi(x, t)$ denote the extended probability density on $x \in \mathbb{G}$ with

$$p_\psi(x, t) = H(x) \int_0^\infty p_\psi(x, t|x_0)g(x_0)\,dx_0 + H(-x) \int_{-\infty}^0 p_\psi(-x, t|-x_0)g(x_0)\,dx_0,$$  \hfill (4.8)

where $p_\psi(x, t|x_0)$ for $x, x_0 \geq 0$ is the generalized partially reflecting BM. Let $Q_\psi(t)$ denote the corresponding survival probability

$$Q_\psi(t) = \int_{-\infty}^\infty p_\psi(x, t)\,dx. \hfill (4.9)$$

It follows that the first passage time density for absorption is $f_\psi(t) = -dQ_\psi(t)/dt$. The first renewal equation then takes the form

$$\rho_\psi(x, t) = p_\psi(x, t) + \frac{1}{2} \int_0^t [\rho_\psi(x, t-\tau|0^+) + \rho_\psi(x, t-\tau|0^-)]f_\psi(\tau)\,d\tau, \quad x \in \mathbb{G}. \hfill (4.10)$$

The first term on the right-hand side represents all sample trajectories that have never been absorbed by the barrier at $x = 0^\pm$ up to time $t$. The corresponding integrand represents all trajectories that were first absorbed (stopped) at time $\tau$ and then switched to either positively or negatively reflected BM state with probability $1/2$, after which an arbitrary number of switches can occur before reaching $x$ at time $t$. The probability that the first stopping event occurred in the interval $(\tau, \tau + d\tau)$ is $f_\psi(\tau)d\tau$. Laplace transforming the renewal equation (4.10) with respect to time $t$ by setting $\tilde{\rho}_\psi(x, s) = \int_0^\infty e^{-st} \rho_\psi(x, t)\,dt$ etc. gives

$$\tilde{\rho}_\psi(x, s) = \tilde{p}_\psi(x, s) + \frac{1}{2}[\tilde{\rho}_\psi(x, s|0^+) + \tilde{\rho}_\psi(x, s|0^-)]\tilde{f}_\psi(s), \quad x \in \mathbb{G}. \hfill (4.11)$$

Moreover, $\tilde{f}_\psi(s) = 1 - s\tilde{Q}_\psi(s)$. To determine the factor $\tilde{\rho}_\psi(x, s|0^+) + \tilde{\rho}_\psi(x, s|0^-)$, we set $g(x_0) = [\delta(x_0 - 0^+) + \delta(x - 0^-)]/2$ in equation (4.11). This gives

$$\tilde{\rho}_\psi(x, s|0^+) + \tilde{\rho}_\psi(x, s|0^-) = \tilde{p}_\psi(|x|, s|0) + [\tilde{\rho}_\psi(x, s|0^+) + \tilde{\rho}_\psi(x, s|0^-)]\tilde{f}_\psi(0, s),$$

which can be arranged to obtain the result

$$\tilde{\rho}_\psi(x, s|0^+) + \tilde{\rho}_\psi(x, s|0^-) = \frac{\tilde{p}_\psi(|x|, s|0)}{s\tilde{Q}_\psi(0, s)}.$$

Substituting back into equations (4.11) yields the explicit solution

$$\tilde{\rho}_\psi(x, s) = \tilde{p}_\psi(x, s) + \frac{1 - s\tilde{Q}_\psi(s)}{2s\tilde{Q}_\psi(0, s)}\tilde{p}_\psi(|x|, s|0), \quad x \in \mathbb{G}. \hfill (4.12)$$

It can be checked that equations (2.10) and (4.12) agree when $\Psi(t) = e^{-\kappa_0 t/D}$ so that $\tilde{\rho}_\psi(x, s|x_0) \rightarrow \tilde{p}(x, s|x_0)$ and $\tilde{Q}_\psi(x_0, s) \rightarrow \tilde{Q}(x_0, s)$ with $\tilde{p}$ and $\tilde{Q}$ given by equations (2.14) and (3.6), respectively. Indeed, since

$$\tilde{p}(0, s|x_0) = \frac{1}{\sqrt{sD} + \kappa_0} e^{-\sqrt{sD}x_0},$$

we see that $1 - s\tilde{Q}(x_0, s) = \kappa_0\tilde{p}(0, s|x_0)$ and, hence,

$$1 - s\tilde{Q}(s) = \kappa_0 \Gamma(s) \quad \text{and} \quad s\tilde{Q}(0, s) = 1 - \kappa_0\tilde{p}(0, s|0).$$

It remains to calculate $\tilde{p}_\psi$. From equation (2.14), we have

$$\mathcal{P}(x, z, s|x_0) \equiv \int_0^\infty e^{-st} \left[ \int_0^\infty e^{-\sqrt{sD}|x-x_0|}|x_0| e^{-\sqrt{sD}z} \right] dt \hfill (4.13)$$

$$= \frac{1}{2\sqrt{sD}} \left( e^{-\sqrt{sD}|x-x_0|} + \frac{\sqrt{sD} - Dz}{\sqrt{sD} + Dz} e^{-\sqrt{sD}(x+x_0)} \right).$$
Inverting the Laplace transform in $z$ gives

$$\tilde{P}(x, t, s|x_0) = \frac{1}{2\sqrt{sD}} \left( e^{-\sqrt{s/D}|x-x_0|} - e^{-\sqrt{s/D}(x+x_0)} \right) \delta(t) + \frac{1}{D} e^{-\sqrt{s/D}(x+x_0)} e^{-\sqrt{s/D}t}. \quad (4.14)$$

By substituting into equation (4.6) after Laplace transforming the latter with respect to $t$, we obtain the result

$$\tilde{p}_\Psi(x, s|x_0) = \frac{1}{2\sqrt{sD}} \left( e^{-\sqrt{s/D}|x-x_0|} - e^{-\sqrt{s/D}(x+x_0)} \right) + \frac{1}{D} e^{-\sqrt{s/D}(x+x_0)} \Psi(\sqrt{s/D}). \quad (4.15)$$

It immediately follows that

$$\tilde{p}_\Psi(x, s|0) = \tilde{p}_\Psi(0, s|x) = \frac{1}{D} e^{-\sqrt{s/D}x} \Psi(\sqrt{s/D}) \quad (4.16)$$

and

$$\tilde{Q}_\Psi(x_0, s) = \frac{1 - e^{-\sqrt{s/D}x_0}}{s} + e^{-\sqrt{s/D}x_0} \Psi(\sqrt{s/D}). \quad (4.17)$$

Hence, equation (4.12) reduces to the form

$$\tilde{\psi}(x, s) = \tilde{\psi}(x, s) + \frac{e^{-\sqrt{s/D}|x|}}{2\sqrt{sD}} \Gamma_\Psi(s), \quad x \in \mathbb{G}, \quad (4.18)$$

where

$$\Gamma_\Psi(s) = \left[ 1 - \sqrt{\frac{s}{D}} \Psi(\sqrt{s/D}) \right] \int_{-\infty}^{\infty} e^{-\sqrt{s/D}|x_0|} f(x_0) \, dx_0. \quad (4.19)$$

Since the propagator satisfies the diffusion equation in the bulk of the domain, the density $\rho_\Psi(x, t)$ does too. The remaining issue concerns the boundary condition at the interface. By using similar arguments to §2, equations (2.18)–(2.21), we find

$$\tilde{\rho}_\Psi(x, s) = \tilde{\rho}_\Psi(x, s) + \frac{e^{-\sqrt{s/D}|x|}}{\sqrt{sD}} \Gamma_\Psi(s), \quad (4.20a)$$

$$\tilde{\rho}_\Psi(x, s) - \tilde{\rho}_\Psi(-x, s) = \tilde{\rho}_\Psi(x, s) - \tilde{\rho}_\Psi(-x, s), \quad (4.20b)$$

$$D\partial_x \tilde{\rho}_\Psi(0^+, s) - D\partial_x \tilde{\rho}_\Psi(0^-, s) = D\partial_x \tilde{\rho}_\Psi(0^+, s) - D\partial_x \tilde{\rho}_\Psi(0^-, s) - \Gamma_\Psi(s), \quad (4.21a)$$

and

$$D\partial_x \tilde{\rho}_\Psi(0^+, s) + D\partial_x \tilde{\rho}_\Psi(0^-, s) = D\partial_x \tilde{\rho}_\Psi(0^+, s) + D\partial_x \tilde{\rho}_\Psi(0^-, s). \quad (4.21b)$$

Differentiating equation (4.15) for $x < x_0$ implies that

$$D\partial_x \tilde{\psi}(x, s|x_0) = \frac{1}{2} \left( e^{\sqrt{s/D}(x+x_0)} + e^{-\sqrt{s/D}(x+x_0)} \right) - \sqrt{\frac{s}{D}} e^{-\sqrt{s/D}(x+x_0)} \tilde{\psi}(\sqrt{s/D}), \quad (4.22)$$

and, hence,

$$D\partial_x \tilde{\psi}(0, s|x_0) = \left[ 1 - \sqrt{\frac{s}{D}} \tilde{\psi}(\sqrt{s/D}) \right] e^{-\sqrt{s/D}x_0}. \quad (4.23)$$

This shows that

$$D\partial_x \tilde{\psi}(0^+, s) - D\partial_x \tilde{\psi}(0^-, s) = \Gamma_\Psi(s). \quad (4.24)$$

We deduce from equation (4.21a) that $D\partial_x \tilde{\rho}_\Psi(0^+, s) = D\partial_x \tilde{\rho}_\Psi(0^-, s)$. In other words, the flux through the membrane is continuous as it is in the standard permeable boundary condition.
Equation (4.21b) then implies that
\[
2D \partial_x \tilde{\rho}_\psi(0^\pm, s) = \frac{D \tilde{\psi}(\sqrt{s}/D)}{\tilde{\psi}(\sqrt{s}/D)} \left[ \tilde{\rho}_\psi(0^+, s) - \tilde{\rho}_\psi(0^-, s) \right] + \frac{D \tilde{\psi}(\sqrt{s}/D)}{\sqrt{s}} \int_{-\infty}^{\infty} e^{-\sqrt{s}/Dx_0} f(x_0) \, dx_0 - \int_{-\infty}^{0} e^{\sqrt{s}/Dx_0} f(x_0) \, dx_0
\]
and
\[
= \frac{D \tilde{\psi}(\sqrt{s}/D)}{\tilde{\psi}(\sqrt{s}/D)} [\tilde{\rho}_\psi(0^+, s) - \tilde{\rho}_\psi(0^-, s)]
\]
Equation (4.25)

In the exponential case, \( \psi(\ell) = (k_0/D) \psi(\ell) \), and we recover the permeable boundary condition (2.22). For non-exponential distributions, the boundary condition involves a time-dependent permeability. More specifically, setting
\[
\tilde{\kappa}(s) = \frac{D \tilde{\psi}(\sqrt{s}/D)}{\psi(\sqrt{s}/D)},
\]
and using the convolution theorem, the boundary condition in the time domain takes the form
\[
2D \partial_x \rho_\psi(0^\pm, t) = \int_{-\infty}^{\infty} \rho_\psi(0^+, t - \tau) - \rho_\psi(0^-, t - \tau) \, d\tau.
\]
Equation (4.27)

For the sake of illustration, suppose that \( \psi(\ell) \) is given by the gamma distribution:
\[
\psi(\ell) = \frac{\gamma(\gamma \ell)^{\mu-1} e^{-\gamma \ell}}{\Gamma(\mu)}, \quad \mu > 0,
\]
where \( \Gamma(\mu) \) is the gamma function. The corresponding Laplace transforms are expressed as follows:
\[
\tilde{\psi}(z) = \left( \frac{\gamma}{\gamma + z} \right)^{\mu} \quad \text{and} \quad \tilde{\psi}(z) = \frac{1 - \tilde{\psi}(z)}{z}.
\]
Equation (4.29)

Here, \( \gamma \) determines the effective absorption rate. If \( \mu = 1 \), then \( \psi \) reduces to the exponential distribution with constant reactivity \( \kappa_0 = D \gamma \). The parameter \( \mu \) thus characterizes the deviation of \( \psi(\ell) \) from the exponential case. If \( \mu < 1 \) (\( \mu > 1 \)), then \( \psi(\ell) \) decreases more rapidly (slowly) as a function of the local time \( \ell \). Substituting the gamma distribution into equation (4.26) yields
\[
\tilde{\kappa}(s) = \frac{\sqrt{s} D \gamma^{\mu}}{(\gamma + \sqrt{s}D)^\mu}.
\]
Equation (4.30)

If \( \mu = 1 \), then \( \tilde{\kappa}(s) = \gamma D = k_0 \) and \( \kappa(\tau) = k_0 \delta(\tau) \). An example of \( \mu \neq 1 \) that has a simple inverse Laplace transform is \( \mu = 2 \):
\[
\tilde{\kappa}(s) = \frac{D \sqrt{D} \gamma^2}{2 \sqrt{D} \gamma + \sqrt{s}} = \frac{k_0^2/\sqrt{D}}{2k_0/\sqrt{D} + \sqrt{s}}
\]
Equation (4.31)

and
\[
\kappa(\tau) = \frac{k_0^2}{\sqrt{D}} \left[ \frac{1}{\sqrt{\pi} \tau} - \frac{2k_0}{\sqrt{D}} e^{k_0^2/\tau(D)} \text{erfc}(2k_0\sqrt{\tau}/D) \right],
\]
Equation (4.32)

where \( \text{erfc}(x) = (2/\sqrt{\pi}) \int_{x}^{\infty} e^{-y^2} \, dy \) is the complementary error function. Example plots of \( \kappa(\tau) \) are shown in figure 6. It can be seen that \( \kappa \) is a monotonically decreasing function of time whose rate of decay depends on \( k_0 \) and \( D \). Asymptotically expanding \( \text{erfc}(x) \) in equation (4.32) using the formula
\[
\text{erfc}(x) \sim \frac{1}{\sqrt{\pi}} e^{-x^2} \sum_{k=0}^{\infty} (-1)^k \frac{(2k)!}{2^k k!^2} \frac{1}{x^{2k+1}}
\]
Equation (4.33)

shows that \( \kappa(\ell) \) is heavy-tailed with
\[
\kappa(\ell) \sim \sqrt{\frac{D}{\pi}} \frac{1}{8\ell^{3/2}}, \quad \ell \to \infty.
\]
Equation (4.34)
5. Conclusion

In this article, we have developed a general probabilistic framework for modelling one-dimensional diffusion through semi-permeable membranes. We took as our starting point the snapping out BM recently introduced by Lejay [27]. The latter sews together successive rounds of partially reflecting BM in either the positive or negative $x$ domains. The major advantage of this formulation is that the probability density of particle position satisfies a renewal equation that can be generalized by appropriate modifications of the underlying partially reflected BM. As our first example, we considered partially reflected BM with stochastic resetting, which resulted in a diffusion process through a semi-permeable membrane with a non-trivial NESS. Although the NESS was independent of the permeability $\kappa_0$, the associated relaxation process was $\kappa_0$ dependent. Our second example used an encounter-based method to modify the absorption process that kills a given round of partially reflected BM. This resulted in diffusion through a semi-permeable membrane with a time-dependent permeability.

Although we focused on one-dimensional diffusion processes, the basic renewal equation framework generalizes to higher spatial dimensions. However, the analysis is significantly more difficult. (Indeed most studies of skew BM and its generalizations are based on one-dimensional diffusions. A discussion of some mathematical papers on higher-dimensional skew BM can be found in [27].) For the sake of illustration, consider diffusion in $\mathbb{R}^d$ that contains a closed bounded subdomain $\mathcal{M}$. We treat the boundary $\partial \mathcal{M}$ separating the two open domains $\mathbb{R}^d \setminus \mathcal{M}$ and $\mathcal{M}$ as a semi-permeable membrane with $\partial \mathcal{M}^+ (\partial \mathcal{M}^-)$ denoting the side approached from outside (inside) $\mathcal{M}$. The higher-dimensional version of equation (1.1) is then

$$\frac{\partial u(x,t)}{\partial t} = D\nabla^2 u(x,t) \quad x \in \mathbb{G} \equiv (\mathbb{R}^d \setminus \mathcal{M}) \cup \mathcal{M}$$

and

$$f(x^\pm, t) = \kappa_0[u(x^-, t) - u(x^+, t)], \quad x^\pm \in \partial \Omega^\pm,$$

where $f(x, t) = -D\nabla u(x, t) \cdot \mathbf{n}$ and $\mathbf{n}$ is the unit normal directed out of $\mathcal{M}$, see figure 7.

The major difference from the one-dimensional case is that it is now necessary to keep track of where on the boundary each round of partially reflected BM is killed, and from where the next round is initiated. In particular, suppose that whenever partially reflected BM is killed at a point
Figure 7. Example configuration for diffusion through a higher-dimensional semi-permeable membrane. (Online version in colour.)

$y^+ \in \partial M^+$, a new round is immediately started from either $y^+$ or $y^-$ with equal probability, etc. The higher-dimensional version of the last renewal equation (2.8) is then

$$\rho(x, t) = p(x, t) + \frac{\kappa_0}{2} \int_0^t \left\{ \int_{\partial M} p(x, \tau | y^+)[\rho(y^+, t - \tau) + \rho(y^-, t - \tau)] \, dy \right\} \, d\tau, \ x \in \mathbb{R}^d \setminus \overline{\mathcal{M}}$$

(5.2a)

and

$$\rho(x, t) = q(x, t) + \frac{\kappa_0}{2} \int_0^t \left\{ \int_{\partial M} q(x, \tau | y^-)[\rho(y^+, t - \tau) + \rho(y^-, t - \tau)] \, dy \right\} \, d\tau, \ x \in \mathcal{M},$$

(5.2b)

where $p(x, t | y)$ and $q(x, t | y)$ are the probability densities for partially reflected BM in the domains $\mathbb{R}^d \setminus \overline{\mathcal{M}}$ and $\mathcal{M}$, respectively. In addition,

$$p(x, t) = \int_{\mathbb{R}^d \setminus \overline{\mathcal{M}}} p(x, t | x_0)g(x_0) \, dx_0, \quad q(x, t) = \int_{\mathcal{M}} q(x, t | x_0)g(x_0) \, dx_0,$$

(5.3)

where $g(x_0)$ is the initial probability density in $G$. Elsewhere we will show that the solution $\rho(x, t)$ of the integral equation (5.2) satisfies a BVP of the form (5.1). This will allow us to introduce stochastic resetting and encounter-based models of absorption in an analogous fashion to the one-dimensional case. However, finding an explicit solution for $\rho$ is more difficult than the one-dimensional case, even after Laplace transforming. One exception is taking $\partial M$ to be a $(d - 1)$-dimensional sphere and using spherical symmetry. This recovers a renewal equation similar in form to (2.8) with $x$ replaced by the radial coordinate. Another possibility is to Laplace transform the renewal equation and carry out a Neumann series expansion of the integral equation in $y$ for small $\kappa_0$.

Finally, as indicated by Lejay [27], since snapping out BM generates sample paths of single-particle diffusion through semipermeable interfaces, it could be used to develop numerical schemes for generating solutions to the corresponding BVP. Indeed, SDEs in the form of underdamped Langevin equations have recently been used to implement efficient computational schemes for finding solutions to the diffusion equation in the presence of one or more semipermeable interfaces [56,57].

Data accessibility. This article has no additional data.

Conflict of interest declaration. I declare I have no competing interests.

Funding. I received no funding for this study.

References

1. Alberts B, Johnson A, Lewis J, Morgan D, Raff M, Roberts K, Walter P. 2015 Molecular biology of the cell, 6th edn, ch. 11. New York, NY: Garland Science.
1. Phillips R, Kondev J, Theriot J, Garcia HG, Orme N. 2012 Physical biology of the cell. New York, NY: Garland.
2. Bressloff PC. 2021 Stochastic processes in cell biology. Switzerland: Springer.
3. Kusumi A, Nakada C, Ritchie K, Murase K, Suzuki K, Murakoshi H, Kasai RS, Kondo J, Fujiwara T. 2005 Paradigm shift of the plasma membrane concept from the two-dimensional continuum fluid to the partitioned fluid: high-speed single-molecule tracking of membrane molecules. Annu. Rev. Biophys. Biomol. Struct. 34, 351–378. (doi:10.1146/annurev.biophys.34.040204.144637)
4. Evans WJ, Martin PE. 2002 Gap junctions: structure and function. Mol. Membr. Biol. 19, 121–136. (doi:10.1080/09687680210139839)
5. Connors BW, Long MA. 2004 Electrical synapses in the mammalian brain. Annu. Re. Neurosci. 27, 393–418. (doi:10.1146/annurev.neuro.26.041002.131128)
6. Goodenough DA, Paul DL. 2009 Gap junctions. Cold Spring Harb. Perspect. Biol. 1, a002576. (doi:10.1101/cshperspect.a002576)
7. Assis JC, Giacomini HC, Ribeiro MC. 2019 Road permeability index: evaluating the heterogeneous permeability of roads for wildlife crossing. Ecol. Indic. 99, 365–374. (doi:10.1016/j.ecolind.2018.12.012)
8. Brink PR, Ramanan SV. 1985 A model for the diffusion of fluorescent probes in the septate giant axon of earthworm: axoplasmic diffusion and junctional membrane permeability. Biophys. J. 48, 299–309. (doi:10.1016/S0006-3495(85)83783-8)
9. Ramanan SV, Brink PR. 1990 Exact solution of a model of diffusion in an infinite chain or monolayer of cells coupled by gap junctions. Biophys. J. 58, 631–639. (doi:10.1016/S0006-3495(90)82406-1)
10. Kenkre VM, Giuggioli L. 2021 Theory of the spread of epidemics and movement ecology of animals: an interdisciplinary approach using methodologies of physics and mathematics. Cambridge, UK: Cambridge University Press.
11. Tanner JE. 1978 Transient diffusion in a system partitioned by permeable barriers. application to NMR measurements with a pulsed field gradient. J. Chem. Phys. 69, 1748–1754. (doi:10.1063/1.436751)
12. Brink PR, Ramanan SV. 1985 A model for the diffusion of fluorescent probes in the septate giant axon of earthworm: axoplasmic diffusion and junctional membrane permeability. Biophys. J. 48, 299–309. (doi:10.1016/S0006-3495(85)83783-8)
13. Moutal N, Grebenkov DS. 2019 Diffusion across semi-permeable barriers: spectral properties, efficient computation, and applications. J. Sci. Comput. 81, 1630–1654. (doi:10.1007/s10915-019-01055-5)
14. Katchalsky A, Kedem O. 1958 Thermodynamic analysis of the permeability of biological membrane to non-electrolytes. Biochim. Biophys. Acta 27, 229–246. (doi:10.1016/0006-3002(58)90330-5)
15. Moutal N, Grebenkov DS. 2019 Diffusion across semi-permeable barriers: spectral properties, efficient computation, and applications. J. Sci. Comput. 81, 1630–1654. (doi:10.1007/s10915-019-01055-5)
16. Papanicolaou VG. 1990 The probabilistic solution of the third boundary value problem for second order elliptic equations. Probab. Th. Rel. Fields 87, 27–77. (doi:10.1007/BF01217746)
17. Borodin AN, Salminen P. 1996 Handbook of Brownian motion: facts and formulae. Basel-Boston-Berlin: Birkhauser Verlag.
26. Grebenkov DS. 2006 Partially reflected Brownian motion: a stochastic approach to transport phenomena. In *Focus on Probability Theory* (ed. LR Velle), pp. 135–169. Hauppauge: Nova Science Publishers.

27. Lejay A. 2016 The snapping out Brownian motion. *Ann. Appl. Prob.* 26, 1727–1742. (doi:10.1214/15-AAP1131)

28. Ito K, McKean H. 1963 Brownian motions on a half line. *Illinois J.Math.* 7, 181–231. (doi:10.1215/ijm/1255644633)

29. Lejay A. 2016 On the constructions of the skew Brownian motion. *Probab. Surv.* 3, 413–466. (doi:10.1214/15-PS1131)

30. Decamps M, Goovaerts M, Schoutens W. 2006 Asymmetric skew Bessel processes and their applications to finance. *J. Comput. Appl. Math.* 186, 130–147. (doi:10.1016/j.cam.2005.03.067)

31. Appuhamillage T, Bokil V, Thomann E, Waymire E, Wood B. 2011 Occupation and local times for skew Brownian motion with applications to dispersion across an interface. *Ann. Appl. Probab.* 21, 183–214. (doi:10.1214/10-AAP691)

32. Gairat A, Shcherbakov V. 2017 Density of skew Brownian motion and its functionals with application in finance. *Math. Finance* 27, 1069–1088. (doi:10.1111/mafi.12120)

33. Evans M R, Majumdar S N, Schehr G. 2020 Stochastic resetting and applications. *J. Phys. A: Math. Theor.* 53, 193001. (doi:10.1088/1751-8121/ab7efe)

34. Reuveni S, Urbakh M, Klafter J. 2014 Role of substrate unbinding in Michaelis-Menten enzymatic reactions. *Proc. Natl Acad. Sci. USA* 111, 4391–4396. (doi:10.1073/pnas.1318122111)

35. Rothart T, Reuveni S, Urbakh M. 2015 Michaelis-Menten reaction scheme as a unified approach towards the optimal restart problem. *Phys. Rev. E* 92, 060101. (doi:10.1103/PhysRevE.92.060101)

36. Roldan E, Sanchez-Taltavull D, Grill SW. 2016 Stochastic resetting in backtrack recovery by RNA polymerases. *Phys. Rev. E* 93, 062411. (doi:10.1103/PhysRevE.93.062411)

37. Bressloff PC. 2020 Modeling active cellular transport as a directed search process with stochastic resetting and delays. *J. Phys. A* 53, 193001. (doi:10.1088/1751-8121/ab9f7b)

38. Bressloff PC. 2020 Stochastic resetting and the dynamics of focal adhesions. *Phys. Rev. E* 102, 022134. (doi:10.1103/PhysRevE.102.022134)

39. Grebenkov DS. 2020 Paradigm shift in diffusion-mediated surface phenomena. *Phys. Rev. Lett.* 125, 078102. (doi:10.1103/PhysRevLett.125.078102)

40. Grebenkov DS. 2022 An encounter-based approach for restricted diffusion with a gradient drift. *J. Phys. A* 55, 045203. (doi:10.1088/1751-8121/ac411a)

41. Bressloff PC. 2022 Diffusion-mediated absorption by partially reactive targets: Brownian functionals and generalized propagators. *J. Phys. A* 55, 205001. (doi:10.1088/1751-8121/ac5e75)

42. Bressloff PC. 2022 Spectral theory of diffusion in partially absorbing media. *Proc. R. Soc. A* 478, 20220319. (doi:10.1098/rspa.2022.0319)

43. Bartholomew CH. 2001 Mechanisms of catalyst deactivation. *Appl. Catal. A: Gen.* 212, 17–60. (doi:10.1016/S0926-860X(00)00843-7)

44. Filoche M, Grebenkov DS, Andrade Jr JS, Sapoval B. 2008 Passivation of irregular surfaces accessed by diffusion. *Proc. Natl Acad. Sci. USA* 105, 7636–7640. (doi:10.1073/pnas.0706915105)

45. Whitehouse J, Evans MR, Majumdar SN. 2013 Effect of partial absorption on diffusion with resetting. *Phys. Rev. E* 87, 022118. (doi:10.1103/PhysRevE.87.022118)

46. Bressloff PC. 2022 Diffusion-mediated surface reactions and stochastic resetting. *J. Phys. A* 55, 275002. (doi:10.1088/1751-8121/ac6138)

47. Evans MR, Majumdar SN. 2011 Diffusion with stochastic resetting. *Phys. Rev. Lett.* 106, 160601. (doi:10.1103/PhysRevLett.106.160601)

48. Evans MR, Majumdar SN. 2011 Diffusion with optimal resetting. *J. Phys. A Math. Theor.* 44, 435001. (doi:10.1088/1751-8113/44/43/435001)

49. Roldan E, Gupta S. 2017 Path-integral formalism for stochastic resetting: Exactly solved examples and shortcuts to confinement. *Phys. Rev. E* 96, 022130. (doi:10.1103/PhysRevE.96.022130)

50. Pinsky RG. 2020 Diffusive search with spatially dependent resetting. *Stoch Process their Appl* 130, 2954–2973. (doi:10.1016/j.spa.2019.08.008)

51. Majumdar S N, Sabhapandit S, Schehr G. 2015 Dynamical transition in the temporal relaxation of stochastic processes under resetting. *Phys. Rev. E* 91, 052131. (doi:10.1103/PhysRevE.91.052131)
52. Bressloff PC. 2021 Accumulation time of stochastic processes with resetting. *J. Phys. A* **54**, 354001. (doi:10.1088/1751-8121/ac16e5)

53. Berezhkovskii AM, Sample C, Shvartsman SY. 2010 How long does it take to establish a morphogen gradient? *Biophys. J.* **99**, L59–L61. (doi:10.1016/j.bpj.2010.07.045)

54. Berezhkovskii AM, Sample C, Shvartsman S. 2011 Formation of morphogen gradients: local accumulation time. *Phys. Rev. E* **83**, 051906. (doi:10.1103/PhysRevE.83.051906)

55. Gordon P, Sample C, Berezhkovskii AM, Muratov CB, Shvartsman S. 2011 Local kinetics of morphogen gradients. *Proc. Natl Acad. Sci. USA* **108**, 6157–6162. (doi:10.1073/pnas.1019245108)

56. Regev S, Farago O. 2018 Application of underdamped Langevin dynamics simulations for the study of diffusion from a drug-eluting stent. *Phys. A, Stat. Mech. Appl.* **507**, 231–239. (doi:10.1016/j.physa.2018.05.082)

57. Farago O. 2020 Algorithms for Brownian dynamics across discontinuities. *J. Comput. Phys.* **423**, 109802. (doi:10.1016/j.jcp.2020.109802)