Letter

Diffusion through permeable interfaces: Fundamental equations and their application to first-passage and local time statistics

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The diffusion equation is the primary tool to study the movement dynamics of a free Brownian particle, but when spatial heterogeneities in the form of permeable interfaces are present, no fundamental equation has been derived. Here we obtain such an equation from a microscopic description using a lattice random walk model. The sought after Fokker-Planck description and the corresponding backward Kolmogorov equation are employed to investigate first-passage and local time statistics and gain new insights. Among them a surprising phenomenon, in the case of a semibounded domain, is the appearance of a regime of dependence and independence on the location of the permeable barrier in the mean first-passage time. The new formalism is completely general: it allows to study the dynamics in the presence of multiple permeable barriers as well as reactive heterogeneities in bounded or unbounded domains and under the influence of external forces.

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Random movement is ubiquitous, appearing in many physical, biological, and social systems, and is traditionally modeled by diffusion in a homogeneous environment. But, in realistic systems the homogeneity of the environment is often interspersed by spatial heterogeneities that interfere significantly with diffusive transport. In many instances these heterogeneities are due to the presence of permeable interfaces, often referred to as semi- or partially permeable barriers. They appear at microscopic scales in different porous media, such as biological tissue [1–6], but also at larger scales when whole organisms interact with chemical or physical cues [7–9].

Cell biology is replete with examples of permeable structures whose function is to regulate the flux of biochemical substances between different spatial regions [10]. In magnetic imaging techniques the diffusion of water molecules through different cellular compartments is exploited to understand physiological and anatomical properties of the human body [11,12]. The lateral movement of molecules within the bilayer plasma membrane of eukaryotic cells is inhibited by the formation of submicron compartments due to anchored-transmembrane proteins and other macromolecules bound to the underlying actin-based cytoskeleton network [13]. Permeability is also of relevance to ecology where animal dispersal is affected by the heterogeneity of the landscape, e.g., the type of habitat [14,15] or the presence of roads and fences [16].

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Various theoretical approaches to study diffusion through permeable interfaces have been proposed in the past: Green's functions in discrete [17–19] and continuous space [20–23], spectral decompositions [22,24] and scattering techniques [25]. These techniques, while valuable, have been limited in their scope as they either demand spatial symmetries, e.g., analytical Green's functions or employ a coarse-grained representation of the heterogeneities, e.g., effective medium approximations. In addition, these various approaches have failed to construct a unified framework capable of representing the diffusive dynamics with both permeable and reactive heterogeneities and to derive important quantities, such as first-passage and local time (or other Brownian functionals) statistics (i.e., through a backward Fokker-Planck representation). Given the wide-spread occurrence of permeable membranes, the above limitations call for the development of a fundamental theory of diffusion through permeable interfaces.

In this Letter we aim to provide such theory through a fully analytic treatment of the problem. First we show how the permeable boundary condition arises from microscopic considerations in a simple unbiased lattice random walk model. Such a model allows us to derive an inhomogeneous diffusion equation (DE) where the inhomogeneity accounts for the presence of a porous barrier. Extensions to the general case of finite domains and when an external force is present are also provided. As applications of our formalism we study explicitly first-passage and local time statistics of diffusion with a permeable barrier.

Theoretical derivation. We consider a nearest-neighbor unbiased random walker on an infinite one-dimensional lattice. The jump rate of the random walk between neighboring sites equals F except between the lattice points r and $r+1$ where the rate is f with $F > f$. The master equation that represents the dynamics of the occupation probability $\mathcal{P}_m(t)$ of the random walker at the mth lattice point can be constructed as follows [18]:

$$\frac{d\mathcal{P}_m(t)}{dt} = F[\mathcal{P}_{m+1}(t) + \mathcal{P}_{m-1}(t) - 2\mathcal{P}_m(t)] \\ -\Delta[\mathcal{P}_{r+1}(t) - \mathcal{P}_r(t)](\delta_{m,r} - \delta_{m,r+1}), \quad (1)$$

where $\Delta = F - f$ accounts for a partially reflecting defect between the sites r and $r+1$ and $\delta_{m,r}$ is the Kronecker δ. With the help of the so-called defect technique [26] Eq. (1) is solved [27].

With the lattice spacing $\alpha \to 0$, we let m, r, f, and F become infinitely large such that $m\alpha \to x$, $r\alpha \to x_b$, $f\alpha \to \kappa$, $F\alpha^2 \to D$, and $\mathcal{P}_m(t)/\alpha \to P(x,t)$. That is $P(x,t)$ is the probability density for a diffusing particle (with a diffusion coefficient D) to be at the spatial position x at time t with a barrier located at x_b whose permeability is κ with units of velocity. One can show [27] that $P(x,t)$ in this case satisfies the DE, $\partial_t P(x,t) = \partial_x^2 P(x,t)$ with the so-called leather or permeable boundary condition (PBC) [20,28,29],

$$J(x_b^{\pm}, t) = \kappa[P(x_b^-, t) - P(x_b^+, t)]. \quad (2)$$

Here, the $\pm$ superscript denotes the respective side of the barrier and $J(x,t) = -D\,\partial_x P(x,t)$ is defined as the probability current. In other words we have proved that the continuum limit of $\mathcal{P}_m(t)$ becomes the solution of the DE with the PBC, Eq. (2).

We now proceed to derive a more practical equation to study Brownian dynamics through permeable structures, by taking the continuum limit of Eq. (1). We utilize the relationship between the continuous limit of a finite difference and a derivative. In that limit, the left-hand side and the first term on the right-hand side (RHS) of Eq. (1) corresponds to the DE. For the last term in Eq. (1) we consider the spatially discrete form of the probability current $\mathcal{J}_m(t) = F[\mathcal{P}_m(t) - \mathcal{P}_{m+1}(t)]$ with F replaced by f when $m = r$ [30] and we rewrite $\Delta[\mathcal{P}_{r+1}(t) - \mathcal{P}_r(t)](\delta_{m,r} - \delta_{m,r+1})$ as $(\Delta/f)\mathcal{J}_r(t)(\delta_{r+1,m} - \delta_{r,m})$. With the Kronecker δ becoming the Dirac-δ function, we obtain the following inhomogeneous DE:

$$\frac{\partial P(x,t)}{\partial t} = D\frac{\partial^2 P(x,t)}{\partial x^2} + \frac{D}{\kappa}\delta'(x - x_b)J(x_b,t), \quad (3)$$

where $J(x,t)$ is the probability current as defined previously and $\delta'(x)$ represents the derivative of the Dirac-δ function.

Let us introduce the free propagator of the DE $G_0(x,t|x_0) = \exp\{-(x-x_0)^2/4Dt\}/\sqrt{4\pi Dt}$. The solution of Eq. (3) with the localized initial condition $P(x,0) = \delta(x - x_0)$ is given in the Laplace domain [for any function $f(t)$, $\widetilde{f}(\epsilon) = \int_0^\infty f(t)e^{-\epsilon t}dt$] by [27]

$$\widetilde{P}(x,\epsilon|x_0) = \widetilde{G}_0(x,\epsilon|x_0) \\ -\partial_{x_0}\widetilde{G}_0(x,\epsilon|x_b)\frac{\widetilde{J}_0(x_b,\epsilon|x_0)}{\frac{\kappa}{D} + \partial_{x_0}\widetilde{J}_0(x_b,\epsilon|x_b)}. \quad (4)$$

In Eq. (4) we have used the notation $P(x,t|x_0)$ to indicate the localized initial condition and $J_0(x,t|x_0) = -D\,\partial_x G_0(x,t|x_0)$ is defined as the free probability current $[\partial_x h(y) = \frac{\partial}{\partial x}h(x)|_{x=y}$ for a generic function $h(x)]$ [31]. By inserting the correct propagator and its current into Eq. (4), one recovers the solution of the DE with the PBC (2).

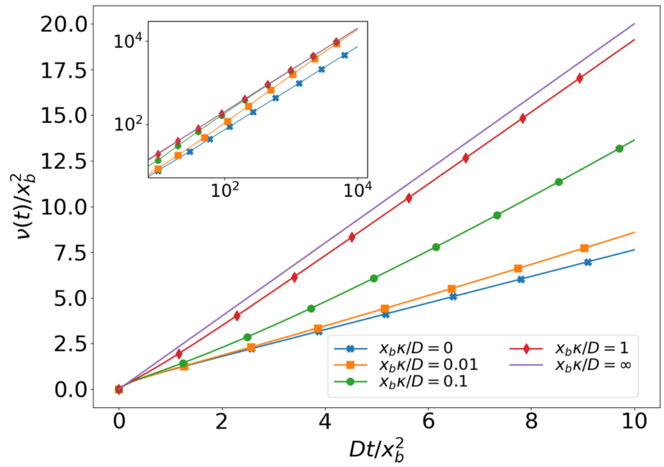

FIG. 1. The MSD $\nu(t)$ as a function of time for a Brownian particle initially placed at the origin, in the presence of a permeable barrier with permeability κ, placed at x_b for different values of the scaled permeability parameter $x_b\kappa/D$. An infinite permeability indicates the absence of a barrier and a zero permeability indicates a fully reflecting barrier. The inset: corresponding long-time behavior of the MSD plotted against time on a logarithmic scale, showing how it has the asymptotic form $2Dt$ except for $\kappa = 0$ which has $2(1 - 2/\pi)Dt$.

It is instructive to look at the moments of $P(x,t|x_0)$, i.e., $\langle x^n(t)\rangle = \int_{-\infty}^{\infty} x^n P(x,t|x_0)dx$. Using Eq. (3) we find the following equations for the first and second moments $\frac{d}{dt}\langle x(t)\rangle = -DJ(x_b,t)/\kappa$ and $\frac{d}{dt}\langle x^2(t)\rangle = 2D - 2x_b DJ(x_b,t)/\kappa$, respectively. As $J(x_b,t)$ is readily obtained from Eq. (4), these equations are solved by

$$\langle x(t)\rangle = x_0 - \mathrm{sgn}(x_b - x_0)\frac{D}{2\kappa}\beta(t), \quad (5)$$

and

$$\langle x^2(t)\rangle = 2Dt + x_0^2 - \mathrm{sgn}(x_b - x_0)\frac{Dx_b}{\kappa}\beta(t), \quad (6)$$

where $\mathrm{sgn}(z)$ is the sign function and

$$\beta(t) = \mathrm{erfc}\left\{\frac{|x_0 - x_b|}{2\sqrt{Dt}}\right\} \\ - \exp\left\{\frac{2\kappa}{D}(|x_0 - x_b| + 2\kappa t)\right\}\mathrm{erfc}\left\{\frac{|x_0 - x_b| + 4\kappa t}{2\sqrt{Dt}}\right\}. \quad (7)$$

Here $\mathrm{erfc}(z) = 1 - \mathrm{erf}(z)$ with $\mathrm{erf}(z)$ the error function. In the limit of $\kappa \to \infty$ and $\kappa \to 0$ Eqs. (6) and (7) tend to their counterparts for free diffusion and diffusion with a perfectly reflecting boundary, respectively. As $\lim_{t\to\infty}\beta(t) = 1$, the mean reaches a stationary value, $\lim_{t\to\infty}\langle x(t)\rangle = x_0 - \mathrm{sgn}(x_b - x_0)D/(2\kappa)$. In Fig. 1 we use Eqs. (6) and (7) to plot the mean-square displacement (MSD) $\nu(t) = \langle[x(t) - \langle x(t)\rangle]^2\rangle$. The curves clearly show that the presence of the permeable barrier reduces the magnitude of the MSD for short times, yet at long times the $2Dt$ term is dominant, and we have the standard diffusive linear increase.

We now rewrite Eq. (3) in the following form, $\partial_t P(x,t) = L_x P(x,t)$, where L_x is a linear differential operator with respect to x. To proceed, we exploit the property $\delta'(x -$

$x_b)J(x_b,t) = \delta(x-x_b)\partial_x J(x,t) + \delta'(x-x_b)J(x,t)$, and the definition of $J(x,t)$ to write $L_x = (D^2/\kappa)\partial_x\delta'(x-x_b) + \partial_x^2[D-(D^2/\kappa)\delta(x-x_b)]$. The operator L corresponds to the one in the following Fokker-Planck equation (FPE) [32],

$$\frac{\partial}{\partial t}P(x,t) = -\frac{\partial}{\partial x}[A(x)P(x,t)] + \frac{\partial^2}{\partial x^2}[B(x)P(x,t)], \tag{8}$$

with $A(x) = -(D^2/\kappa)\delta'(x-x_b)$ and $B(x) = D - (D^2/\kappa)\delta(x-x_b)$. Through this description we see that the presence of a permeable barrier can be described by an infinitely large positive potential $(D^2/\kappa)\delta(x-x_b)$ that pushes away the Brownian particle from x_b and by a diffusion coefficient that is modified at the interface, becoming infinitely negative thereby trapping the particle instead of dispersing it.

Although standard techniques allow to relate the underlying Langevin equation corresponding to Eq. (8), the appearance of the Dirac-δ function and its derivative would render such an exercise of little practical use. Instead, we use the FPE to find the corresponding backward (Kolmogorov) FPE. In terms of L, the backward FPE is $-\partial_{t_0}P(x_0,t_0) = L^\dagger_{x_0}P(x_0,t_0)$, where $L^\dagger$ is the formal adjoint of L, i.e., $L^\dagger_{x_0} = A(x_0)\partial_{x_0} + B(x_0)\partial^2_{x_0}$. Note that this equation is now in terms of x_0 and t_0, where $t_0 < t$. The adjoint is then, $L^\dagger_{x_0} = -(D^2/\kappa)\delta'(x_0-x_b)\partial_{x_0} + [D-(D^2/\kappa)\delta(x_0-x_b)]\partial^2_{x_0}$, meaning L is self-adjoint.

First-passage processes. Using the backward FPE we study the process in the presence of a perfectly absorbing point at x_c to the left or right of both x_0 and x_b. Note, if this absorbing boundary is placed at the same point as the permeable barrier $x_c = x_b$, a radiation boundary [33–36] is recovered [27]. Defining the survival probability as $S(t|x_0) = \int_{-\infty}^{x_c} P(x,t|x_0)dx$ or $S(t|x_0) = \int_{x_c}^{\infty} P(x,t|x_0)dx$, respectively, for $x_0 < x_b < x_c$ or $x_c < x_b < x_0$. Taking $t_0 = 0$, exploiting the time homogeneity of the process and utilizing the self-adjoint nature of L, we find that for $S(t|x_0)$,

$$\frac{\partial S(t|x_0)}{\partial t} = D\frac{\partial^2 S(t|x_0)}{\partial x_0^2} - \frac{D^2}{\kappa}\delta'(x_0-x_b)\frac{\partial S(t|x_0)}{\partial x_0}\bigg|_{x_0=x_b}. \tag{9}$$

Equation (9) is supplemented by the initial condition $S(0|x_0) = 1$ and the Dirichlet BCs, $S(t|x_c) = 0$ and $\lim_{x_0\to\pm\infty} S(t|x_0) = 1$. Using the free propagator, we satisfy the Dirichlet BC via $G(x,t|x_0) = G_0(x,t|x_0) - G_0(x,t|2x_c - x_0)$ [36] and write the solution to Eq. (9) as

$$\widetilde{S}(\epsilon|x_0) = \widetilde{S}_0(\epsilon|x_0) + \partial_{x_0}\widetilde{S}_0(\epsilon|x_b)\frac{\partial_x \widetilde{G}(x_b,\epsilon|x_0)}{\frac{\kappa}{D^2} - \partial^2_{x,x_0}\widetilde{G}(x_b,\epsilon|x_b)}, \tag{10}$$

where the free survival probability (i.e., for $\kappa = \infty$) is $S_0(t|x_0) = \mathrm{erf}\{|x_c - x_0|/\sqrt{4Dt}\}$ [36]. From $\widetilde{\mathcal{F}}(x_c,\epsilon|x_0) = 1 - \epsilon\widetilde{S}(\epsilon|x_0)$, we obtain the Laplace transform of the first-passage probability (FPP) distribution (see Ref. [27] for the expression for when x_0 is between x_b and x_c),

$$\widetilde{\mathcal{F}}(x_c,\epsilon|x_0) = \frac{2\kappa e^{-|x_c-x_0|\sqrt{\frac{\epsilon}{D}}}}{\sqrt{D\epsilon}[1 + e^{-2|x_c-x_b|\sqrt{(\epsilon/D)}}] + 2\kappa}. \tag{11}$$

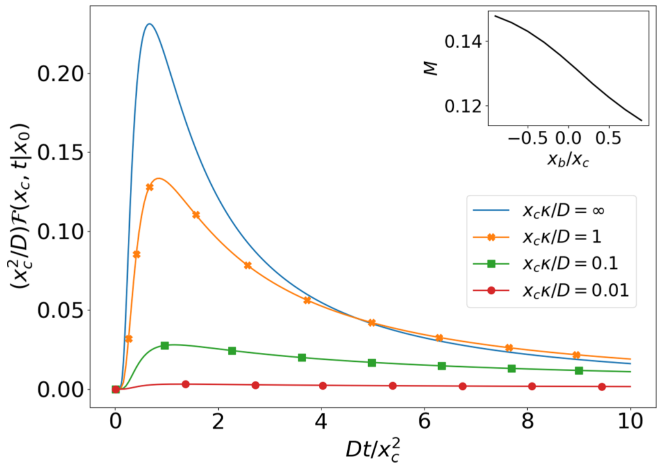

FIG. 2. The FPP distribution of a Brownian particle $\mathcal{F}(x_c,t|x_0)$ is computed via numerical inversion [38] of Eq. (11) for different values of the scaled permeability parameter $x_c\kappa/D$. The particles starting location is x_0 with $x_0/x_c = -1$, and a permeable barrier is placed in between x_0 and x_c at the origin. The inset: magnitude of the modal peak of the FPP distribution M plotted against different scaled barrier positions x_b/x_c with $x_0\kappa/D = -1$.

Through Tauberian theorems [37] we find the long-time dependence of the FPP distribution as

$$\mathcal{F}(x_c,t|x_0) \approx \frac{|x_c - x_0| + D/\kappa}{\sqrt{4\pi Dt^3}}. \tag{12}$$

Equation (12) shows that the FPP distribution possesses the same $t^{-3/2}$ asymptotic dependence as free diffusion, but the coefficient includes the additional term D/κ. In Fig. 2 we draw Eq. (11) to show the full time dependence, whereas the inset shows the nonlinear dependence of the magnitude of the mode of the distribution M as a function of the barrier position relative to x_c.

To gain further understanding of the impact a permeable barrier has on the dynamics of a Brownian particle, we study the mean first-passage time (MFPT) to x_c, $\tau(x_0) = \int_0^\infty t\mathcal{F}(x_c,t|x_0)dt$. Since, the MFPT of a Brownian particle is infinite in a semi-infinite domain, we add a perfectly reflecting boundary at x_r such that the permeable barrier lies between x_r and x_c. As $\tau(x_0) = \int_0^\infty S(t|x_0)dt$, from Eq. (9) we have

$$-1 = D\tau''(x_0) - \frac{D^2}{\kappa}\delta'(x_0-x_b)\tau'(x_b), \tag{13}$$

where $\tau'(x_0) = \frac{d}{dx_0}\tau(x_0)$. Equation (13) is then supplemented by the Dirichlet and Neumann BC $\tau(x_c) = 0$ and $\tau'(x_r) = 0$, respectively. Equation (13) is solved to give [27]

$$\tau(x_0) = \begin{cases} \frac{x_c^2 - x_0^2 + 2x_r(x_0-x_c)}{2D} + \frac{|x_b - x_r|}{\kappa}, & x_0 \in [x_r, x_b), \\ \frac{x_c^2 - x_0^2 + 2x_r(x_0-x_c)}{2D}, & x_0 \in (x_b, x_c]. \end{cases} \tag{14}$$

Equation (14) shows the interesting feature that when the barrier is not placed between x_0 and x_c, the MFPT is identical to the barrier free case. Yet when the barrier is placed between x_0 and x_c the impact to the MFPT is merely the addition of a term dependent on the position of the barrier that is scaled by the strength of its permeability. To clarify this aspect we may split the contributions to $\tau(x_0)$ between those trajectories that travel to x_c without returning to x_0 and those that do return. The permeable interface clearly has no effect on the former trajectories as x_b does not lie between x_0 and x_c. For the latter trajectories, the particle may return to x_0 multiple times before directly traveling to x_c from x_0. Since the mean return time for an unbiased Brownian particle to any point is only dependent on the overall domain size [39], the presence of a permeable interface will have no impact on these trajectories either.

Local time. Returning to the backward FPE, we can study the probability distribution of various functionals of Brownian motion. One of interest is the so-called local time of Brownian motion, defined as $\ell_t = \int_0^t \delta[x(t') - a]dt'$, which characterizes the amount of time a Brownian particle spends at a given point a [40]. We seek the probability density describing the random variable ℓ_t, namely, the local time distribution (LTD) $\rho(\ell, t|x_0)$ of a Brownian particle in the presence of a permeable barrier. To do so we take the Laplace transform of the LTD with respect to ℓ, i.e., $\varrho(p, t|x_0) = \int_0^\infty \rho(\ell, t|x_0)e^{-p\ell}d\ell$. Such a quantity may be written in terms of a conditional expectation [41] $\varrho(p, t|x_0) = \langle \exp\{-p \int_0^t \delta[x(t') - a]dt'\}|x(0) = x_0\rangle$ where the expectation is over all trajectories of the particle starting at $x(0) = x_0$ up to time t. Through the Feynman-Kac formula [42,43], $\varrho(p, t|x_0)$ satisfies the following;

$$\frac{\partial \varrho}{\partial t} = A(x_0)\frac{\partial \varrho}{\partial x_0} + B(x_0)\frac{\partial^2 \varrho}{\partial x_0^2} - p\delta(x_0 - a)\varrho, \tag{15}$$

where A and B are defined after Eq. (8). Equation (15) is supplemented by the initial condition $\varrho(p, 0|x_0) = 1$ and the BC $\varrho(p, t|x_0 \to \pm\infty) = 1$ [44]. By treating the last term on the RHS of Eq. (15) as an inhomogeneity, it is straightforward to construct the general solution via the solution of the homogeneous equation (i.e., for $p = 0$). For a localized initial condition, the solution of the homogeneous part is equivalent to the solution of Eq. (8) through Eq. (4). The Laplace transform of the solution of Eq. (15) is, thus,

$$\widetilde{\varrho}(p, \epsilon|x_0) = \frac{1}{\epsilon}\left[1 - \frac{\widetilde{P}(a, \epsilon|x_0)}{\frac{1}{p} + \widetilde{P}(a, \epsilon|a)}\right]. \tag{16}$$

Considering that we have a permeable barrier in an unbounded domain, we exploit the translational invariance of the problem and set $x_b = 0$ and calculate the LTD at the barrier, that is, $a = x_b$. Recalling the PBC (2), we need to distinguish whether we are looking at x_b^+ or x_b^-. Furthermore, let us consider the case $x_b = 0^+$ and $x_0 = 0^+$; using Eq. (16) and after inverse Laplace transforming with respect to p, we find the barrier LTD to be

$$\widetilde{\rho}(\ell, \epsilon|0^+) = \frac{(2\kappa\sqrt{D\epsilon} + D\epsilon)}{\epsilon(\sqrt{D\epsilon} + \kappa)} \exp\left\{-\frac{(2\kappa\sqrt{D\epsilon} + D\epsilon)}{\sqrt{D\epsilon} + \kappa}\ell\right\}. \tag{17}$$

The limit $\lim_{\epsilon\to 0} \epsilon\widetilde{\rho}(\ell, \epsilon|0^+) = 0$ shows that Eq. (17) has no steady-state distribution at long times, indicative of the unbounded nature of the dynamics. In the limit $\kappa \to \infty$ we recover the barrier free distribution $\rho(\ell, t|0) = 2\sqrt{D/\pi t}e^{-D\ell^2/t}$ and for $\kappa \to 0$ we obtain the perfectly reflecting distribution $\rho(\ell, t|0) = \sqrt{D/\pi t}e^{-D\ell^2/4t}$ [45]. From Eq. (17) we can also find the mean,

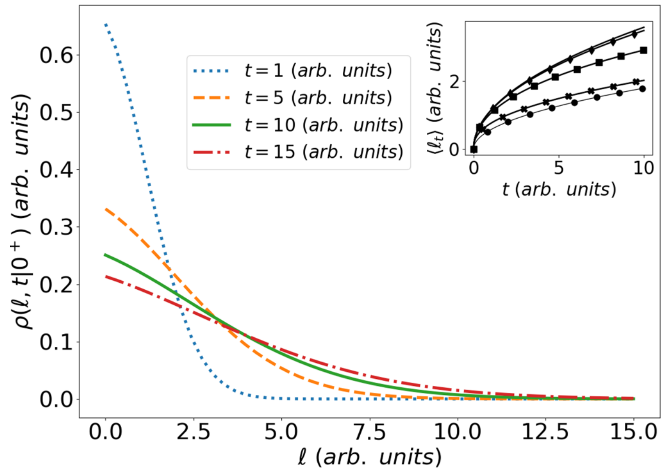

FIG. 3. The barrier local time distribution for $\kappa = 0.1$ and $D = 1$ (in arbitrary units), computed via a numerical inverse Laplace transform [38] of Eq. (17) and plotted against ℓ at different times $t = 1, 5, 10, 15$, respectively. The inset: the mean barrier local time Eq. (18) plotted over a time window for varying permeability values $\kappa = \infty, 1, 0.1, 0.01, 0$ (in arbitrary units) represented by the markers: circular, cross, square, diamond, and no marker, respectively. For $\kappa \to \infty$, we have the barrier free mean local time $\sqrt{t/\pi D}$ and for $\kappa \to 0$, we have the perfectly reflecting barrier mean local time $2\sqrt{t/\pi D}$.

$$\langle \ell_t \rangle = \frac{1}{4\kappa}\left[1 - e^{(4\kappa^2 t/D)}\text{erfc}\left\{2\kappa\sqrt{\tfrac{t}{D}}\right\}\right] + \sqrt{\tfrac{t}{\pi D}}. \tag{18}$$

At long times the mean local time at the barrier is dominated by the final term on the RHS of Eq. (18), i.e., $\langle \ell_t \rangle \sim t^{1/2}$ as in the barrier-free case. A comparison of the temporal dependence of the mean local time $\langle \ell_t \rangle$ for different values of permeability is displayed in the inset of Fig. 3. The unbounded nature of its long-time dependence can also be evinced from the main plot of Fig. 3, which shows the flattening of the LTD as time increases.

External forces. We have shown so far the applications of our formalism to situations where no external forces are present. However, the formalism is completely general and may include the dynamics in the presence of a potential $U(x)$ in some domain $x \in \Omega$. In this case the homogeneous system is described by the Smoluchowski equation (SE) [46] $\partial_t P(x, t) = \partial_x[U'(x)P(x, t)] + D\,\partial_x^2 P(x, t)$. If we have a permeable barrier at $x_b \in \Omega$, the SE gets modified to

$$\frac{\partial P(x, t)}{\partial t} = \frac{\partial}{\partial x}[U'(x)P(x, t)] + D\frac{\partial^2 P(x, t)}{\partial x^2} + \frac{D}{\kappa}\delta'(x - x_b)J(x_b, t), \tag{19}$$

where the probability current is now $J(x, t) = -U'(x)P(x, t) - D\,\partial_x P(x, t)$. Let us call the propagator of the SE $G_0(x, t|x_0)$, which exists over Ω with $J_0(x, t|x_0)$ the barrier-free counterpart of $J(x, t)$. The solution of Eq. (19), with localized initial conditions, may be written as in Eq. (4). We are again able to transform Eq. (19) into the FPE (8) with $A(x) = -U'(x)[1 - (D/\kappa)\delta(x - x_b)] - (D^2/\kappa)\delta'(x - x_b)$ and $B(x) = D - (D^2/\kappa)\delta(x - x_b)$, and then construct the analogous of Eqs. (9), (13), and (15) in the presence of a potential.

To summarize, we have derived an inhomogeneous form of the DE and SE to account for the presence of a permeable barrier. We have used the former to investigate first-passage and local time statistics of a Brownian particle through the construction of a backward FPE. Explicit analytic dependence of the LTD and FPP distribution and their respective means have also been presented. Due to the linearity of the problem, our methods readily extend to the case of multiple permeable interfaces by appending the inhomogeneity for each interface position to Eq. (19). Reactive heterogeneities can be accounted for in Eq. (19) via the standard defect technique [26]. Future directions include the extension of these methodologies to higher dimensions and the application of our formalism to anomalous diffusion [47].

This study did not involve any underlying data.

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