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Unbiased Diffusion to Escape Complex Geometries: Is Reduction to Effective One-Dimensional Description Adequate to Assess Narrow Escape Times?

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Abstract

This study is devoted to unbiased diffusion of point Brownian particles inside a tube of varying cross-section (see **Figure 1**). An expression for the mean survival time, τ, of the particles inside the tube is obtained in terms of the bulk diffusion constant, D_0 and the system's geometrical parameters, namely, the tube's axial semi-length, L, the minor radius, a, and the slope of the tube's wall, λ. Our expression for τ correctly retrieves the limit behavior of the system under several conditions. We ran Monte Carlo numerical simulations to compute the mean survival time by averaging the survival time of 5×10^4 trajectories, with time step $\Delta t = 10^{-6}$, $D_0 = 1$, and $L = 1$. The simulations show good agreement with our model. When the geometrical parameters of this system are varied while keeping constant the tube's enclosed volume, it resembles the problems of Narrow Escape Time (*J. Chem. Phys.* **116(22)**, 9574 (2007)). A previous study on the use of the reduction to effective one-dimension technique (*J. Mod. Phys.* **2**, 284 (2011)) in complex geometries has shown excellent agreement between the theoretical model and numerical simulations. However, in this particular system, the general assumptions of the Hill problem are seemingly inapplicable. The expression obtained shows good agreement with our simulations when $0 \leq \lambda \leq 1$, but fails when λ grows larger. On the other hand, some errors are found when $a \rightarrow 0$, but the expression holds reasonably well for a broad range of values of a. These comparisons between simulations and theoretical predictions, and the expressions obtained for τ, are the main results of this work.

Keywords

Component, Formatting, Style, Styling, Insert

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1. Introduction

The unbiased motion of point particles confined within quasi-one-dimensional systems, such as pores and channels, has drawn great interest in recent years, due to the ubiquity of these systems in nature and technology [1]-[3]. The problem of spatially-constrained diffusion arises from different contexts of practical and theoretical interest, and is relevant to nanotechnology, chemistry, and biology, having direct applications to channels such as pores in zeolites [4], carbon nanotubes [5], synthetic nanopores [6]-[8], artificial pores produced in solid thin films [9], channels in biological systems [10], and single-nanopore sensors, designed to detect, quantify, and characterize many different types of molecules, for example, single- and double-stranded DNA chains.

Experimental techniques, such as high-resolution crystallography of bacterial porins and other large channels, have demonstrated that these can be envisaged as tubes with significantly varying cross-sections along their principal axis. In some of these channels, variations in cross-section areas exceed one order of magnitude [11] [12]. This leads to the so-called entropic-like walls and barriers in the theoretical description of transport through such structures.

When diffusion occurs in quasi-one-dimensional structures, it is intuitively appealing to introduce an effective one-dimensional description. In a three-dimensional tube of varying radius $r(x)$ with the x-axis directed along the centerline of the tube, the one-dimensional concentration of point particles $c(x,t)$ is related to their three-dimensional concentration $C(x, y, z, t)$ by the relationship

$$c(x,t) = \int_{A(x)} C(x, y, z, t) \mathrm{d}y \mathrm{d}z \tag{1}$$

Here, $A(x)$ is the position-dependent cross-section area of the tube, where integration is carried out. Given the condition of uniform distribution of particles in any cross-section, $c(x,t)$, obeys the Fick-Jacobs equation, then

$$\frac{\partial c(x,t)}{\partial t} = D_0 \frac{\partial}{\partial x} \left\{ A(x) \frac{\partial}{\partial x} \left[\frac{c(x,t)}{A(x)} \right] \right\} \tag{2}$$

where D_0 is the particle's diffusion coefficient in free space. Robert Zwanzig [13] generalized this result, showing that the diffusion coefficient entering into (2) becomes position-dependent, $D(x)$, provided the radius is a slowly varying function of x, *i.e.*,

$$\left| \mathrm{d}r(x) / \mathrm{d}x \right| \ll 1 \tag{3}$$

Therefore, the generalized Fick-Jacobs equation takes the form,

$$\frac{\partial c(x,t)}{\partial t} = \frac{\partial}{\partial x} \left\{ D(x) A(x) \frac{\partial}{\partial x} \left[\frac{c(x,t)}{A(x)} \right] \right\}. \tag{4}$$

Zwanzig also derived the following expression for $D(x)$:

$$D_{\mathrm{Zw}}(x) = \frac{D_0}{1 + \frac{1}{2} r'(x)^2} \tag{5}$$

Later, Reguera and Rubí [14] generalized this result and suggested,

$$D_{\mathrm{RR}}(x) = \frac{D_0}{\sqrt{1 + r'(x)^2}} \tag{6}$$

In an earlier numerical study [15], the generalized Fick-Jacobs Equation (4), with $D(x)$ given by (6), was

shown to be valid for

$$\left| \mathrm{d}r(x)/\mathrm{d}x \right| \leq 1, \tag{7}$$

which compared with the requirement expressed by (3), is less restrictive, thus giving the generalized Fick-Jacobs equation a considerably extended range of applicability. Kalinay and Percus [16] [17] developed a more general theory of reduction to the effective one-dimensional description for radially symmetrical 2D tubes, and Dagdug and Pineda [18] extended these results to non-symmetrical 2D systems.

A wide range of stochastic processes of practical interest underlies first-passage events, such as the first-passage time, namely, the probability that a diffusing particle or a random walk will first reach a specified site (or set of sites) at a specified time [19]. Indeed, chemical and biochemical reactions [20] [21], animals searching for food [22], and trafficking receptors on biological membranes [23], are often controlled by first-encounter events [24]. The narrow escape time (NET)—the mean time a Brownian particle spends before being trapped by an opening window in exiting the cavity for the first time—is of particular importance. Its applications range from cellular biology to biochemical reactions in cellular micro-domains, such as dendritic spines, synapses, and micro-vesicles, among others [23] [25]. The NET is the limiting quantity and the first step in the mathematical modeling of such processes where particles must first exit their domains in order to live up to their biological function [24].

To determine which form of $D(x)$ to use in (4) for a given set of geometries and boundary conditions, we took advantage of the fact that the Mean First-Passage Time (MFPT), τ, is a quantity often obtained by means of computer simulations. Then, the MFPT—defined as the time it takes a random walker to reach a specified place for the first time, averaged over all the trajectories or realizations of the random walk—is found to satisfy a backward equation,

$$\mathrm{e}^{\beta U(x_0)} \frac{\partial}{\partial x_0} \left\{ \mathrm{e}^{-\beta U(x_0)} D(x_0) \frac{\partial \tau}{\partial x_0} \right\} = -1, \tag{8}$$

where $\beta = 1/(k_B T)$ (k_B is the Boltzmann constant and T the absolute temperature), and the potential $U(x_0)$, is defined as follows,

$$U(x) = -\frac{1}{\beta} \ln \frac{A(x)}{A(x_r)} \tag{9}$$

Equation (9) accounts for the change in cross-section area along the axial length of the tube, taken to be zero at $x = x_r$ (a reference position). Then (8) is solved for the appropriate boundary conditions, to obtain an algebraic expression that relates τ with $D(x)$ and the system's geometrical parameters.

Following a previous study of narrow escape times in a spherical cavity with two holes [26], this paper proposes a system made by juxtaposing two identical semi-cones of length *L*, by their larger radii, as shown in **Figure 1**, and solves the generalized backward Equation (8) for τ with different expressions of $D(x)$. Computer simulations were carried out for comparison with theoretical predictions across a wide range of geometrical parameter values for the proposed system. The potential use of the equations obtained to assess narrow escape times is then discussed.

2. Theory and Simulations

To solve (8), we refer to **Figure 2**, and the boundary conditions described thereunder. Given the tube's radius as a function of the axial coordinate, x, $r(x) = a + \lambda x$, the cross-section area is given by

$$A(x) = \pi r(x)^2 = \pi (a + \lambda x)^2.$$

Then, by choosing the reference position $x_r = 0$ we found, from (9),

$$U(x_0) = -\frac{1}{\beta} \ln \frac{(a + \lambda x_0)^2}{a^2}.$$
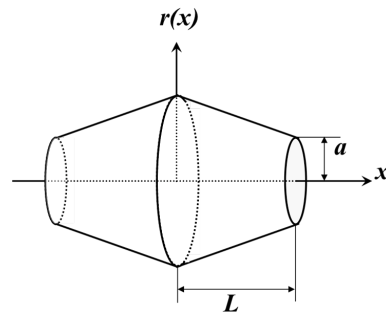
And from here, we rewrote (8) as follows,

Figure 1. The tube of varying cross-section studied in this work. The slope of the tube's wall, with length 2L, has the absolute value λ, and the major radius b is given by $a + \lambda L$. This system can be taken as a narrow escape time problem, as stated by Grigoriev *et al.* [27].
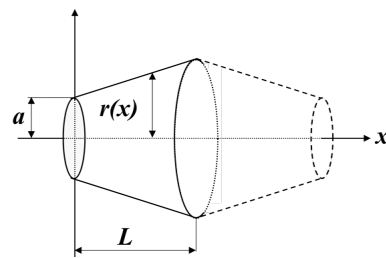

Figure 2. Conveniently chosen to help simplify the algebra, for this system $r(x) = a + \lambda x$ for $0 \le x \le L$, and the boundary conditions are: (I) $d\tau/dx_0 = 0$ at $x_0 = L$ (reflecting wall, center plane where the tube has its major radius), and (II) $\tau = 0$ at $x_0 = 0$ (absorbent wall, shaded).

$$\frac{\partial}{\partial x_0}\left\{\frac{(a+\lambda x_0)^2}{a^2}D(x_0)\frac{\partial \tau}{\partial x_0}\right\} = -\frac{(a+\lambda x_0)^2}{a^2} \tag{10}$$

which is a separable ordinary differential equation. At this point, we did not need to choose an explicit for $D(x_0)$, as this was done in due time using (5) and (6). Now, the first integration of (10) yields,

$$\frac{(a+\lambda x_0)^2}{a^2}D(x_0)\frac{d\tau}{dx_0} = -\frac{1}{3a^2\lambda}(a+\lambda x_0)^3 + C_1, \tag{11}$$

Here, we used the boundary condition of zero flux in the reflecting wall at $x_0 = L$, to find the value of the integration constant to be

$$C_1 = \frac{(a+\lambda L)^3}{3a^2\lambda}.$$

Applying this result to (11), after some algebra it became,

$$\frac{d\tau}{dx_0} = -\frac{a+\lambda x_0}{3\lambda D_\lambda} + \frac{(a+\lambda L)^3}{3\lambda D_\lambda}\frac{1}{(a+\lambda x_0)^2}, \tag{12}$$

where we used the fact that $D(x_0)$, either from (5) or (6), is a function only of the first derivative of $r(x_0)$, a linear function of x_0, and therefore, a constant, denoted here as D_λ. Thus, we can integrate (12) a second time to yield,

$$\tau = -\frac{1}{3\lambda D_\lambda}\left(ax_0 + \frac{\lambda}{2}x_0^2\right) - \frac{(a+\lambda L)^3}{3\lambda^2 D_\lambda}\frac{1}{a+\lambda x_0} + C_2 . \tag{13}$$

Then, by using the second boundary condition, a perfectly absorbent wall at $x_0 = 0$, we found C_2,

$$C_2 = \frac{a^2}{6\lambda^2 D_\lambda} + \frac{(a+\lambda L)^3}{3\lambda^2 D_\lambda a} .$$

With this result in (13), we manipulated the resulting expressions to yield,

$$\tau = -\frac{1}{6\lambda^2 D_\lambda}\left\{a^2 - (a+\lambda x_0)^2\right\} + \frac{b^3}{3\lambda D_\lambda a}\left\{\frac{x_0}{a+\lambda x_0}\right\}, \tag{14}$$

which is one of the main results of this work. Here, we used $b = a + \lambda L$. Furthermore, evaluating (14) at the reflecting wall's position, $x_0 = L$, and setting $a = 1$, one finds

$$\tau(L) = \frac{L^2}{6D_\lambda}(3+2\lambda L),$$

which is a known result previously reported by Berezhkovskii *et al.* [15].

The second result is obtained by averaging $\tau(x_0)$ over the entire range of variation of x_0, namely $0 \le x_0 \le L$, thus defining this average as follows,

$$\langle\tau\rangle = \frac{1}{L}\int_0^L \tau(x_0)\mathrm{d}x_0 . \tag{15}$$

Then, after some algebra, we can write the general result:

$$\langle\tau\rangle = \frac{1}{6\lambda^2 D_\lambda L}\left\{\frac{a^3-b^3}{3\lambda} + \frac{L}{a}(a^3+2b^3) - \frac{2b^3}{\lambda}\ln\frac{b}{a}\right\}. \tag{16}$$

Along with (14) and (16), we can use any expression of D_λ, namely,

$$D_\lambda^{Zw} = \frac{D_0}{1+\frac{1}{2}\lambda^2} , \tag{17}$$

or from (5) or (6),

$$D_\lambda^{RR} = \frac{D_0}{\sqrt{1+\lambda^2}} . \tag{18}$$

For subsequent comparisons, we will use (18) only, as it has been shown to yield better results in previous works.

In simulations, we found the mean first-passage time, τ (MFPT), defined above. The particle's initial position, x_0, is distributed uniformly within the cavity's volume. The MFPT is denoted as $\tau(x_0)$. When running simulations, we took $L=1$, $D_0=1$ and the time step $\Delta t = 10^{-6}$, so that $\sqrt{2D_0\Delta t} = \sqrt{2}\times 10^{-3} \ll 1$. The actual particle's position, r_n, is given by $r_n = r_0 + r_{ran}$, where r_0 is the previous position, and r_{ran} is a vector of pseudo-random numbers generated with a Gaussian distribution ($\mu = 0$, $\sigma = \sqrt{2D_0\Delta t}$). Each MFPT was obtained by averaging the first-passage times of 5×10^4 trajectories.

3. Results and Discussion

Figure 3 and Figure 4 show the main comparisons made in this work between MFPT obtained by computer simulations and theoretical predictions from Equation (16) using Reguera-Rubí's effective diffusion coefficient (18). Both figures show good agreement virtually across the entire range of parameter values. Each point in Figure 3 is related to a system of fixed volume (arbitrarily chosen to be the unit sphere), so the main difference would be the size of the absorbent windows. For such purpose, while keeping L constant and varying a parametrically, λ should be a function of these parameters, as follows,
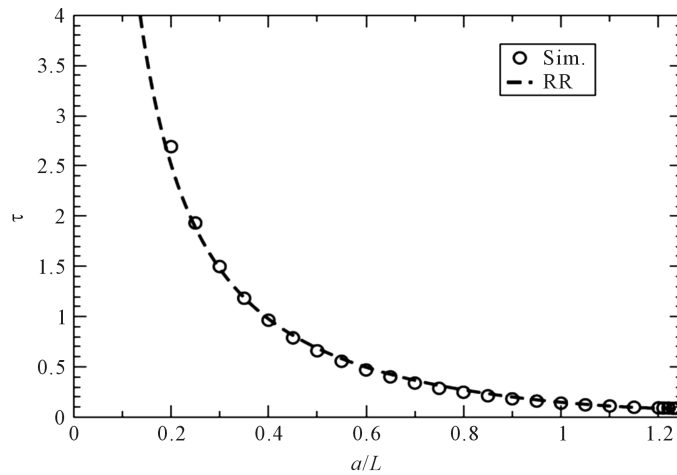
Figure 3. Mean first-passage time as a function of the parameter *a/L*, absorbent window's size over the tube's semi-length. Each point corresponds to a different value of λ, chosen to fix the system's volume at a constant value (arbitrarily set as the volume of a sphere of unit radius). The theoretical curve (solid line) corresponds to Equation (16), with D_λ given in (18), and $\lambda(a, L, R)$ from (19).
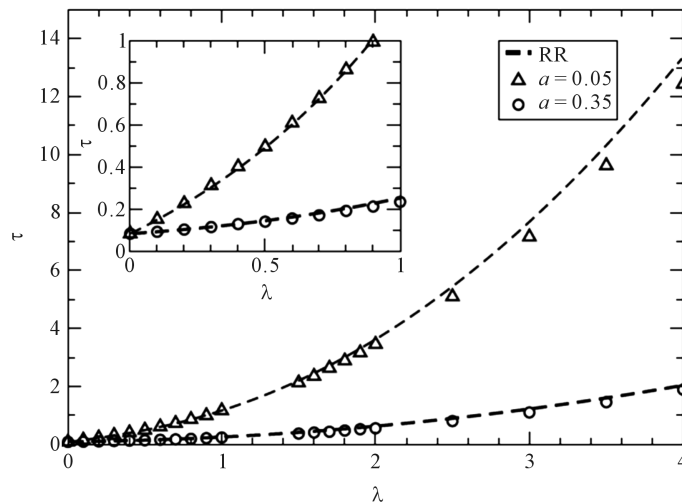

Figure 4. Mean first-passage times as a function of the parameter λ, keeping the value of the absorbent window's radius constant. Two sets of data, obtained from simulations, are shown: for $a = 0.05$ (triangles), and $a = 0.35$ (circles); both theoretical curves (dashed lines) correspond to Equation (16), with D_λ from (18).

$$\lambda = \frac{1}{2L^3}\left\{-3aL^2 + \left(a^2L^4 - 4a^3L^5 + 8L^3R^3\right)^{1/2}\right\}. \tag{19}$$

Then, the particles will have to explore a volume of the same size, but different radii of aperture to escape. As expected, survival times grow unbounded $(\tau \to \infty)$ as the aperture to escape from the domain tends to close $(a \to 0)$.

Back to the narrow escape problem, in 2002, I. V. Grigoriev *et al.*, studied the time-dependence of the survival probability of a Brownian particle that escapes from a cavity through a round hole [27]. Two main results were reported: Firstly, algebraic proof that decay is exponential for small holes, based on the spectral representation of the survival probability, and secondly, that the expression for the rate constant in terms of the problem

parameters (the diffusion constant D of the particles, the hole radius a, and the cavity volume V) is given by,

$$k = \frac{4Da}{V} = \frac{1}{\tau} . \tag{20}$$

In their work, they also ran Brownian dynamics simulations to calculate the survival probability in spherical and cubic cavities for different values of the absorbing-window's radius. They also found that when a is small enough, decay is exponential, and the rate constants found in simulations are in good agreement with those predicted by (20).

Previously, a work by Vázquez and Dagdug [26], theoretically and numerically studied a first-passage problem with this technique, which fits naturally in the NET category as one varies the positive constant a, *i.e.*, the aperture's radius. In that work, the expressions found fit the simulation data with great accuracy. Therefore, we now compared Equations (16) with D_λ from (18), against the MFPTs (survival times) from simulations. **Figure 4** shows, for two constant window sizes, $a = 0.35$ (circles), and $a = 0.05$ (triangles), the variation of survival times of Brownian particles as a function of the slope of the tube's wall, λ, as a geometrical parameter. In both cases, we found good agreement between theoretical and computer data across a wide range of values of λ, although slight deviations did occur at greater values of λ. Even though such deviations are expected to grow larger as λ increases, there is still a wide interval where agreement is good.

Finally, we obtained algebraic expressions (14) and (16) for the first-passage time of Brownian particles through the effective one-dimensional description of diffusion. These expressions, which are the main results of this work, are useful in assessing Narrow Escape Times in complex geometries, and fit well with simulated data for a wide range of values for this system's geometrical parameters.

Acknowledgements

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