Research Article

Unbiased Diffusion through a Linear Porous Media with Periodic Entropy Barriers: A Tube Formed by Contacting Ellipses

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This work is devoted to the study of unbiased diffusion of point-like Brownian particles through channels with radial symmetry of varying cross-section and elliptic shape. The effective one-dimensional reduction is used with distinct forms of a position-dependent diffusion coefficient, $D(x)$, found in literature, to obtain expressions for (I) narrow escape times from a single open-ended tube, (II) its correspondent effective diffusion coefficient, both as functions of the eccentricity of the tube, ε , where $\varepsilon = 0$ returns the system to a spherical vesicle with two open opposite sides, and (III) finally, Lifson-Jackson formula that is used to compute expressions to assess the mean effective diffusion coefficient for a periodic elliptic channel formed by contacting ellipses, also as a function of the eccentricity. Mathematical expressions are presented and contrasted against computational simulations to validate them.

1. Introduction

Among many systems, well spread in nature and technological applications, the unbiased diffusion of point-like particles confined within quasi-one-dimensional systems, such as pores and channels, is ubiquitous and has been subjected to increasing attention in recent years [1–6]. Diffusive transport in confined environments arises from different contexts of practical and theoretical interest. It is relevant to study in fields as nanotechnology, chemistry, and biology, having direct applications to channels such as pores in zeolites [7], carbon nanotubes [8], synthetic nanopores [9–11], artificial pores produced in solid thin films [12], channels in biological systems [13], 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 [14, 15]. 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 becomes intuitively appealing to introduce an effective one-dimensional description. In a three-dimensional tube of varying radius, $r(x)$, the x -axis directed along the centerline of the tube, the one-dimensional concentration of point-like particles $c(x, t)$ is related to their three-dimensional concentration $C(x, y, z, t)$ by the expression

$$c(x, t) = \int_{A(x)} C(x, y, z, t) dy dx, \quad (1)$$

which averages the spatial concentration over the channel's position-dependent cross-section, $A(x)$. Given the condition of uniform concentration in any cross-section, $c(x, t)$ satisfies the Fick-Jacobs equation

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

where D_0 is the particle's bulk diffusion coefficient. Later, this result was generalized by Zwanzig [16], showing that the

diffusion entering in (2) becomes position-dependent, $D(x)$, by means of introducing fluctuations in the concentration of particles in any cross-section, provided $r(x)$ is a slowly varying function of x ; that is, $|dr(x)/dx| \ll 1$. Thus the generalized Fick-Jacobs equation takes the form

$$\frac{\partial c(x, t)}{\partial x} = \frac{\partial}{\partial x} \left\{ D(x) A(x) \frac{\partial}{\partial x} \left[\frac{c(x, t)}{A(x)} \right] \right\}. \quad (3)$$

Zwanzig also proposed an explicit form to $D(x)$:

$$D(x) = \frac{D_0}{1 + (1/2) r'(x)^2}, \quad (4)$$

which has been extensively used throughout literature but in many cases poorly adjusted to simulated data. Later, Reguera and Rubí generalized Zwanzig's result, and based on heuristic arguments they suggested that $D(x)$ entering into (3) is given by [17]

$$D(x) = \frac{D_0}{\sqrt{1 + r'(x)^2}}. \quad (5)$$

That has proved to be more reliable given several geometrical conditions [18–22], when used along with (3). Surprisingly, in the same literature, this approach has also shown to be valid, even for a less restrictive condition upon the radius' rate of change: $|dr(x)/dx| \leq 1$, thus giving the generalized Fick-Jacobs equation a considerably extended range of applicability. In the same spirit Kalinay and Percus [23, 24] developed a more general theory of reduction to the effective one-dimensional description for radially symmetrical two-(2D) and three-dimensional (3D) tubes, and Dagdug and Pineda [25] later extended these results to nonsymmetrical 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 [26]. Indeed, chemical and biochemical reactions [27, 28], animals searching for food [29], and trafficking receptors on biological membranes [30] are often controlled by first-encounter events [31]. Among first-passage events, 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 a quantity of particular importance. Its applications range from cellular biology to biochemical reactions in cellular microdomains, such as dendritic spines, synapses, and micro vesicles, among others [30, 32]. 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 [31].

To determine which form of $D(x)$ to enter in (3) for a given set of geometries and boundary conditions, we took advantage of the fact that the Mean First-Passage Time (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—, τ , is

a quantity often obtained by means of computer simulations. The MFPT is found to satisfy a backward equation:

$$e^{\beta U(x_0)} \frac{\partial}{\partial x_0} \left\{ e^{-\beta U(x_0)} D(x_0) \frac{\partial \tau}{\partial x_0} \right\} = -1, \quad (6)$$

where $\beta = 1/(k_B T)$, k_B is the Boltzmann constant, and T is the absolute temperature, and x_0 is the initial position where any particle begins its random walk. The potential $U(x_0)$ is defined as follows:

$$U(x_0) = -\frac{1}{\beta} \ln \frac{A(x_0)}{A(x_R)}. \quad (7)$$

Equation (7), called *entropic-like* potential, 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, placed somewhere in the system). Then (6) is solved for the appropriate boundary conditions, to obtain an algebraic expression that relates τ with $D(x)$ and the system's geometrical parameters.

Complex geometries, such as those found in nature [13] and manmade structures at the small scale [33, 34], hardly resemble the simple shapes used so far to model them. Nonetheless, particle transport through these very complex geometries still can be tackled as a problem of diffusion in quasi-one-dimensional structures [5]. Again, Zwanzig had worked, back in 1983, a solution to the study of diffusion of Brownian particles in two-dimensional channels made of periodic boundaries [35], using a sophisticated mathematical result, known as the Lifson-Jackson theorem [36]. More recently, the correspondent Lifson-Jackson formula

$$D_{\text{eff}} = \frac{1}{\langle e^{-\beta U(x)} \rangle \langle e^{\beta U(x)} / D(x) \rangle} \quad (8)$$

has been successfully used in several works on 2D and 3D systems [19, 20, 22, 37, 38], to obtain a mathematical expression for the effective one-dimensional diffusion coefficient averaged for periodic channels, which represents a good assessment of the effective diffusion coefficient behavior in real long, narrow channels (i.e., their length is significantly greater than their radii), with internal structure (also known as *corrugated* channels).

The present work is divided in three main parts:

- (I) Following the methodology developed in previous studies [20, 22], we treat the system shown in Figure 1, a single tube of uniform cross-section and elliptic shape (which we call *elliptic tube* hereafter) of length $2L$, where L is given by $L = R\sqrt{(1 - (a/R)^2)/(1 - \epsilon^2)}$, R is the semilength of the minimum diameter (minor axis), γ is the semi length of the maximum diameter (major axis) given by the expression $\gamma = R/\sqrt{1 - \epsilon^2}$, and ϵ is the eccentricity. The openings placed at opposite sides of the tube are of radius a . In this system we solve (6) entering (7) and several expressions for the position dependent diffusion coefficient $D(x)$: $D(x) = D^{\text{FJ}}(x) = D_0$ (the *Fick-Jacobs approximation*), $D(x) = D^{\text{RR}}(x)$, and

FIGURE 1: Elliptic tube. (a) A tube of circular cross-section where the position-dependent radius is given by $r(x) = (1 - \varepsilon^2) \sqrt{\gamma^2 - x^2}$, an ellipse in the longitudinal plane, as shown in (b), where $\gamma^2 = R^2/(1 - \varepsilon^2)$ is the square of its major radius. R is the size of the minor radius of the elliptic shape; the tube's length is $2L$, where $L = R \sqrt{(1 - (a/R)^2)/(1 - \varepsilon^2)}$. The radius of the openings, at opposing sides of the tube, is a , else $a^2 = \xi^2(\gamma^2 - L^2)$, where $\xi^2 = 1 - \varepsilon^2$. Panel (c) shows a representation of the entropic-like potential associated with the change of shape in this tube.

$D(x) = D^{\text{Zw}}(x)$, given by (4) and (5), respectively, and subject to the appropriate boundary conditions (see Figure 3), thus obtaining algebraic expressions of τ as a function of geometrical parameters of the system (ε , a , R). The resulting theoretical curves will be compared with data obtained by computer simulations.

- (II) We assess the effective diffusion coefficient for this tube, using the exact solution of (6) for a cylindrical tube (given $U(x_0) = 0$, and $a = R$) to establish the relation $D_{\text{eff}} = L^2/(3\tau)$, where we have assumed that D_{eff} has the same structure than the bulk diffusion D_0 . Then we compare the theoretical curves of D_{eff} with values obtained by computer simulations.
- (III) Finally, we use the Lifson-Jackson formula (8), along with different forms of $D(x)$ —the same set of expressions as before—to obtain mathematical expressions of the mean effective diffusion coefficient, $\langle D_{\text{eff}} \rangle$, as a function of geometrical parameters of the system. This last system is a periodic channel, made of juxtaposed elliptic tubes, as seen in Figure 2 (from now on called *periodic elliptic tube*). The various analytical expressions of τ , D_{eff} , elliptic tube, and $\langle D_{\text{eff}} \rangle$, periodic elliptic tube, obtained along with the

graphical comparisons between theory and computer simulated data, constitute the main results of this paper.

2. Theory and Computational Details

2.1. Elliptic Tube: Obtaining Analytical Expressions for the MFPT. Solving (6), given the entropic-like potential (7), requires an explicit form for $A(x_0)$ and second-order boundary conditions. As can be seen in Figure 1, the elliptic tube has cross-sections of uniform circular shape, and position dependent radius, $r(x)$, given by

$$r(x) = \sqrt{1 - \varepsilon^2} \sqrt{\frac{R^2}{1 - \varepsilon^2} - x^2} \quad (9)$$

which, plotted against the transversal plane along the x -axis, resembles the characteristic shape of an ellipse, whose center—for convenience—we chose to place at the origin of coordinates. In this way we will have the open ends of the tube at the planes $x_0 = \pm L$ and then model them as absorbing discs. Thus the cross-section, $A(x) = \pi r(x)^2$, takes the form

$$A(x_0) = \pi (1 - \varepsilon^2) \left(\frac{R^2}{1 - \varepsilon^2} - x_0^2 \right). \quad (10)$$

FIGURE 2: Periodic elliptic tube. (a) A tube made of juxtaposed elliptic sections (each an elliptic tube as depicted in Figure 1) is called a periodic elliptic tube. Its shape is schematically shown in (b).

FIGURE 3: Region used to set the limits for integration in this work. The boundary conditions required to solve (6) are explained in text.

Taking this expression to (7), we have the explicit form of the entropic-like potential $U(x_0)$, which we need to enter in (6)

$$U(x_0) = -\frac{1}{\beta} \ln \frac{R^2/(1-\varepsilon^2) - x_0^2}{R^2/(1-\varepsilon^2)}, \quad (11)$$

where we have already chosen $x_0 = 0$, as the reference position. Regarding the form of (11), it is advisable to introduce the notation $\xi = \sqrt{1-\varepsilon^2}$, and $\gamma^2 = R^2/(1-\varepsilon^2) = R^2/\xi^2$, which in turn gives $r(x) = \xi\sqrt{\gamma^2 - x^2}$, in order to simplify the forthcoming algebra. Notice that γ is the major radius of the ellipse in Figure 1. In this fashion, we may rewrite (11) to read

$$U(x_0) = -\frac{1}{\beta} \ln \frac{\gamma^2 - x_0^2}{\gamma^2}. \quad (12)$$

Thus, using this result in (6), we obtain

$$\frac{\partial}{\partial x_0} \left\{ \frac{\gamma^2 - x_0^2}{\gamma^2} D(x_0) \frac{\partial \tau}{\partial x_0} \right\} = -\frac{\gamma^2 - x_0^2}{\gamma^2} \quad (13)$$

which, upon integration, yields

$$\frac{\gamma^2 - x_0^2}{\gamma^2} D(x_0) \frac{\partial \tau}{\partial x_0} = -x_0 + \frac{x_0^3}{3\gamma^2} + k_1. \quad (14)$$

Then, in order to fix the value of k_1 , a boundary condition is needed.

Taking advantage of the symmetry of the system, we can cope with the elliptic semitube, shown in Figure 3, instead of the whole, to carry on the integration process. Thus we place a reflective surface at the middle plane in $x_0 = 0$:

$$\left. \frac{\partial \tau}{\partial x_0} \right|_{x_0=0} = 0 \quad (15)$$

while the tube's opening at $x_0 = L$ can be treated as an absorbing surface, where

$$\tau|_{x_0=L} = 0. \quad (16)$$

Given these boundary conditions, we can use (15) with (14) to find $k_1 = 0$. Therefore, we can write

$$\frac{\partial \tau}{\partial x_0} = -\frac{\gamma^2}{D(x_0)} \frac{x_0}{\gamma^2 - x_0^2} + \frac{1}{3D(x_0)} \frac{x_0^3}{\gamma^2 - x_0^2}. \quad (17)$$

Further treatment of (17) requires us to supply an adequate form of $D(x_0)$. In this work we will use three expressions.

(I) *Fick-Jacobs Approximation*. Taking $D(x_0) = D_0$ to expression (17) yields

$$\tau = \frac{\gamma^2 - x_0^2}{6D_0} + \frac{\gamma^2}{3D_0} \ln(\gamma^2 - x_0^2) + k_2 \quad (18)$$

which, along with the boundary condition given in (16), yields k_2 :

$$k_2 = -\frac{\gamma^2 - L^2}{6D_0} - \frac{\gamma^2}{3D_0} \ln(\gamma^2 - L^2). \quad (19)$$

Then, introducing (19) in (18), we obtain

$$\tau = \frac{(\gamma^2 - x_0^2) - (\gamma^2 - L^2)}{6D_0} + \frac{\gamma^2}{3D_0} \ln \frac{\gamma^2 - x_0^2}{\gamma^2 - L^2}. \quad (20)$$

Now, we will use the relation (which can be verified from the definition of L ; see Figure 1)

$$a^2 = \xi^2 (\gamma^2 - L^2) \quad (21)$$

to rewrite (20) as

$$\tau = \frac{1}{6\xi^2 D_0} \left\{ \xi^2 (\gamma^2 - x_0^2) - a + 2\xi^2 \gamma^2 \ln \frac{\xi^2 (\gamma^2 - x_0^2)}{a^2} \right\} \quad (22)$$

or in a more useful form:

$$\tau = \frac{1}{6\xi^2 D_0} \left\{ (R^2 - \xi^2 x_0^2) - a + 2R^2 \ln \frac{(R^2 - \xi^2 x_0^2)}{a^2} \right\}, \quad (23)$$

where we have used the definition $\gamma = R/\xi$. Setting $R = 1$ and the initial position of all random walks in $x_0 = 0$, we will have an expression for τ which is parametrically dependent *solely on the eccentricity* ε , and the opening-size at the ends of the elliptic tube is as follows:

$$\tau = \frac{1}{6(1 - \varepsilon^2) D_0} \{1 - a - 4 \ln a\}. \quad (24)$$

As soon as we have this result, it is noticeable that (24) reduces to the exact result for a spherical vesicle with two opposite openings, as $\varepsilon \rightarrow 0$, in perfect agreement with the previous work by Vazquez and Dagdug [21].

(II) *Zwanzig Approximation*. Taking the expression of $D(x_0)$ given by (4) into (17) to carry on the second integration leads us first to write (4) in an explicit form. Here we use $r(x) = \xi \sqrt{\gamma^2 - x^2}$ to find

$$r'(x) = \frac{-\xi x}{\sqrt{\gamma^2 - x^2}}. \quad (25)$$

So far, we have (4) written down as follows:

$$D_{Zw}(x) = \frac{2(\gamma^2 - x^2) D_0}{2\gamma^2 - \alpha^2 x^2}. \quad (26)$$

In (26) we have defined $\alpha = 2 - \xi^2 = 1 + \varepsilon^2$. Now, with this result in (17), we may write

$$\begin{aligned} \frac{\partial \tau}{\partial x_0} = & -\frac{\gamma^2}{2D_0} \frac{(2\gamma^2 - \alpha^2 x_0^2) x_0}{(\gamma^2 - x_0^2)^2} \\ & + \frac{1}{6D_0} \frac{(2\gamma^2 - \alpha^2 x_0^2) x_0^3}{(\gamma^2 - x_0^2)^2} \end{aligned} \quad (27)$$

or, in a simplified form,

$$\begin{aligned} \frac{\partial \tau}{\partial x_0} = & -\frac{\gamma^4}{D_0} \frac{x_0}{(\gamma^2 - x_0^2)^2} \\ & + \frac{\gamma^2}{D_0} \left(\frac{\alpha^2}{2} + \frac{1}{3} \right) \frac{x_0^3}{(\gamma^2 - x_0^2)^2} \\ & - \frac{\alpha^2}{6D_0} \frac{x_0^5}{(\gamma^2 - x_0^2)^2}, \end{aligned} \quad (28)$$

where, upon integration, we obtain

$$\begin{aligned} \tau = & \frac{\gamma^4 (\alpha^2 - 2)}{6D_0 (\gamma^2 - x_0^2)} + \frac{\alpha^2 (\gamma^2 - x_0^2)}{12D_0} \\ & + \frac{\gamma^2}{6D_0} \left(1 + \frac{\alpha^2}{2} \right) \ln(\gamma^2 - x_0^2) + k'_2. \end{aligned} \quad (29)$$

Then, to fix the value of k'_2 , we use (16):

$$\begin{aligned} k'_2 = & -\frac{\gamma^4 (\alpha^2 - 2)}{6D_0 (\gamma^2 - L^2)} - \frac{\alpha^2 (\gamma^2 - L^2)}{12D_0} \\ & - \frac{\gamma^2}{6D_0} \left(1 + \frac{\alpha^2}{2} \right) \ln(\gamma^2 - L^2) \end{aligned} \quad (30)$$

which, after some algebra, leads to

$$\begin{aligned} \tau = & \frac{\gamma^4 (\alpha^2 - 2)}{6D_0} \left\{ \frac{1}{\gamma^2 - x_0^2} - \frac{1}{\gamma^2 - L^2} \right\} \\ & + \frac{\alpha^2}{12D_0} \{L^2 - x_0^2\} \\ & + \frac{\gamma^2}{6D_0} \left(1 + \frac{\alpha^2}{2} \right) \ln \frac{\gamma^2 - x_0^2}{\gamma^2 - L^2}. \end{aligned} \quad (31)$$

Now we may use (21), and our prior definitions of γ and α , to put (31) in a more useful form:

$$\begin{aligned} \tau = & -\frac{R^4}{6D_0} \left\{ \frac{1}{R^2 - (1 - \varepsilon^2) x_0^2} - \frac{1}{a^2} \right\} \\ & + \frac{1}{12D_0} \frac{1 + \varepsilon^2}{1 - \varepsilon^2} (R^2 - a^2 - (1 - \varepsilon^2) x_0^2) \\ & + \frac{R^2}{12D_0} \frac{3 + \varepsilon^2}{1 - \varepsilon^2} \ln \frac{R^2 - (1 - \varepsilon^2) x_0^2}{a^2}. \end{aligned} \quad (32)$$

Again, by choosing $R = 1$ and $x_0 = 0$, we obtain, after simplification, an expression of τ , as a function of geometrical parameters:

$$\tau = \frac{1}{6D_0} \left(\frac{a^2(1+\varepsilon^2) + 2(1-\varepsilon^2)}{2a^2(1-\varepsilon^2)} (1-a^2) - \left(\frac{3+\varepsilon^2}{1-\varepsilon^2} \right) \ln a \right). \quad (33)$$

(III) *Reguera-Rubí Approximation*. Following the procedure, previously outlined, we took (5), now written, according to (25), in the form

$$D_{RR}(x) = \frac{\sqrt{\gamma^2 - x_0^2}}{\sqrt{\gamma^2 - \varepsilon^2 x_0^2}} D_0 \quad (34)$$

and then we use this expression in (17),

$$\frac{\partial \tau}{\partial x_0} = -\frac{\gamma^2}{D_0} \frac{x_0 \sqrt{\gamma^2 - \varepsilon^2 x_0^2}}{(\gamma^2 - x_0^2)^{3/2}} + \frac{1}{3D_0} \frac{x_0^3 \sqrt{\gamma^2 - \varepsilon^2 x_0^2}}{(\gamma^2 - x_0^2)^{3/2}} \quad (35)$$

to carry on the second integration, thus yielding

$$\begin{aligned} \tau = & \frac{\sqrt{\gamma^2 - \varepsilon^2 x_0^2}}{D_0} \left(-\frac{2\gamma^2}{3} \frac{1}{\sqrt{\gamma^2 - x_0^2}} + \frac{1}{6} \sqrt{\gamma^2 - x_0^2} \right) \\ & - \frac{\gamma^2(1+3\varepsilon^2)}{12\varepsilon D_0} \\ & \cdot \ln \frac{2\varepsilon^2 x_0^2 - (1+\varepsilon^2)\gamma^2 + 2\varepsilon\sqrt{\gamma^2 - \varepsilon^2 x_0^2}\sqrt{\gamma^2 - x_0^2}}{\gamma^2(1-\varepsilon^2)} \\ & + k_2''. \end{aligned} \quad (36)$$

Using (16), to fix k_2'' , we have

$$\begin{aligned} k_2'' = & -\frac{\sqrt{\gamma^2 - \varepsilon^2 L^2}}{D_0} \left(-\frac{2\gamma^2}{3} \frac{1}{\sqrt{\gamma^2 - L^2}} \right. \\ & \left. + \frac{1}{6} \sqrt{\gamma^2 - L^2} \right) + \frac{\gamma^2(1+3\varepsilon^2)}{12\varepsilon D_0} \\ & \cdot \ln \frac{2\varepsilon^2 L^2 - (1+\varepsilon^2)\gamma^2 + 2\varepsilon\sqrt{\gamma^2 - \varepsilon^2 L^2}\sqrt{\gamma^2 - L^2}}{\gamma^2(1-\varepsilon^2)}. \end{aligned} \quad (37)$$

And taking the last result to (36), after some algebra,

$$\begin{aligned} \tau = & \frac{2\gamma^2}{3D_0} \left(\frac{\sqrt{\gamma^2 - \varepsilon^2 L^2}}{\sqrt{\gamma^2 - L^2}} - \frac{\sqrt{\gamma^2 - \varepsilon^2 x_0^2}}{\sqrt{\gamma^2 - x_0^2}} \right) \\ & - \frac{1}{6D_0} \left(-\sqrt{\gamma^2 - x_0^2} \sqrt{\gamma^2 - \varepsilon^2 x_0^2} \right. \\ & \left. + \sqrt{\gamma^2 - L^2} \sqrt{\gamma^2 - \varepsilon^2 L^2} \right) + \frac{\gamma^2(1+3\varepsilon^2)}{12\varepsilon D_0} \\ & \cdot \ln \frac{2\varepsilon^2 L^2 - (1+\varepsilon^2)\gamma^2 + 2\varepsilon\sqrt{\gamma^2 - \varepsilon^2 L^2}\sqrt{\gamma^2 - L^2}}{2\varepsilon^2 x_0^2 - (1+\varepsilon^2)\gamma^2 + 2\varepsilon\sqrt{\gamma^2 - \varepsilon^2 x_0^2}\sqrt{\gamma^2 - x_0^2}}. \end{aligned} \quad (38)$$

Substituting some previous definitions, $a = \xi\sqrt{\gamma^2 - L^2}$, $\gamma^2 = R^2/(1-\varepsilon^2)$, $\varepsilon^2 L^2 = R^2 - a^2$, we may rewrite (38) in a more useful form:

$$\begin{aligned} \tau = & \frac{2\gamma^2}{3D_0} \left(\frac{\sqrt{R^2/(1-\varepsilon^2) - R^2 + a^2}}{a/\sqrt{1-\varepsilon^2}} - \frac{\sqrt{R^2/(1-\varepsilon^2) - \varepsilon^2 x_0^2}}{\sqrt{R^2/(1-\varepsilon^2) - x_0^2}} \right) \\ & - \frac{1}{6D_0} \left(-\sqrt{\frac{R^2}{1-\varepsilon^2} - x_0^2} \sqrt{\frac{R^2}{1-\varepsilon^2} - \varepsilon^2 x_0^2} + \frac{a}{\sqrt{1-\varepsilon^2}} \sqrt{\frac{R^2}{1-\varepsilon^2} - R^2 + a^2} \right) \\ & + \frac{R^2(1+3\varepsilon^2)}{12\varepsilon(1-\varepsilon^2)D_0} \ln \frac{2(R^2 - a^2) - ((1+\varepsilon^2)/(1-\varepsilon^2))R^2 + 2\varepsilon\sqrt{R^2/(1-\varepsilon^2) - R^2 + a^2}(a/\sqrt{1-\varepsilon^2})}{2\varepsilon^2 x_0^2 - ((1+\varepsilon^2)/(1-\varepsilon^2))R^2 + 2\varepsilon\sqrt{R^2/(1-\varepsilon^2) - \varepsilon^2 x_0^2}\sqrt{R^2/(1-\varepsilon^2) - x_0^2}}. \end{aligned} \quad (39)$$

Then, by setting $x_0 = 0$ and $R = 1$ in (39), we obtain a simpler relation for the MFPT in terms of geometrical parameters:

$$\tau = \frac{1}{2(1-\varepsilon^2)D_0} \left\{ -1 + \frac{4-a^2}{3a} \sqrt{1-\varepsilon^2 + \varepsilon^2 a^2} + \frac{1+3\varepsilon^2}{6\varepsilon} \right\}$$

$$\cdot \ln \left(\frac{2\varepsilon^2(1-a^2) - (1+\varepsilon^2) + 2\varepsilon a \sqrt{1-\varepsilon^2 + \varepsilon^2 a^2}}{2\varepsilon - (1+\varepsilon^2)} \right) \}. \quad (40)$$

2.2. Elliptic Tube: Computing Effective Diffusion Coefficients for the Elliptic Tube. Let us assume that the effective diffusion coefficient for the elliptic tube (of length $2L$ and open ends) has the same structure than the bulk diffusion; then

$$D_{\text{eff}} = \frac{L^2}{3\tau}. \quad (41)$$

Thus, using in (41) the various expressions already obtained for the MFPT, (24), (33), and (40), we can write expressions for the D_{eff} in terms of geometrical parameters of the elliptic tube, given $L = \sqrt{(1-a^2)/(1-\varepsilon^2)}$.

(I) *Fick-Jacobs*

$$D_{\text{eff}} = \frac{2(1-a^2)D_0}{1-a-4\ln a}. \quad (42)$$

(II) *Zwanzig*

$$D_{\text{eff}} = \frac{4(1-a^2)a^2D_0}{a^2(1+\varepsilon^2)(1-a^2) + 2(1-\varepsilon^2)(1-a^2) - 2a^2(3+\varepsilon^2)\ln a}. \quad (43)$$

(III) *Reguera-Rubí*

$$D_{\text{eff}} = \frac{2(1-a^2)D_0}{3 \left[-1 + \frac{4-a^2}{3a} \sqrt{1-\varepsilon^2 + \varepsilon^2 a^2} + f \right]}, \quad (44)$$

where f is given by

$$f = \frac{1+3\varepsilon^2}{6\varepsilon} \cdot \ln \left(\frac{2\varepsilon^2(1-a^2) - (1+\varepsilon^2) + 2\varepsilon a \sqrt{1-\varepsilon^2 + \varepsilon^2 a^2}}{2\varepsilon - (1+\varepsilon^2)} \right). \quad (45)$$

2.3. Periodic Elliptic Channel: Computing Averaged Diffusion Coefficients. The effective diffusion coefficient averaged for a tube made of identical sections (the elliptic tube of previous section) is given by (8), the Lifson-Jackson formula, where the expected value of a function $F(x)$ over an interval of values accessible to x (see Figure 3) is defined as

$$\langle F(x) \rangle = \frac{1}{L} \int_0^L F(x) dx. \quad (46)$$

Given the definition of $U(x)$ in (7), we have

$$e^{-\beta U(x_0)} = \frac{A(x_0)}{A(0)} = \frac{\gamma^2 - x_0^2}{\gamma^2}. \quad (47)$$

Then, we can write the integrals in (8) to read as

$$\begin{aligned} & \langle e^{-\beta U(x_0)} \rangle \left\langle \frac{1}{D(x_0) e^{-\beta U(x_0)}} \right\rangle \\ &= \langle \gamma^2 - x_0^2 \rangle \left\langle \frac{1}{D(x_0) (\gamma^2 - x_0^2)} \right\rangle. \end{aligned} \quad (48)$$

Now we can use appropriate expressions of $D(x_0)$ to carry out the integration process.

(I) *Fick-Jacobs*. Taking the Fick-Jacobs approximation, $D(x_0) = D_0$ in (48), we can rewrite (8) to read

$$\frac{D_0}{D_{\text{eff}}} = \langle \gamma^2 - x_0^2 \rangle \left\langle \frac{1}{\gamma^2 - x_0^2} \right\rangle, \quad (49)$$

and carrying out the integrals, we obtain

$$\langle \gamma^2 - x_0^2 \rangle = \gamma^2 - \frac{L^2}{3}, \quad (50)$$

$$\begin{aligned} & \left\langle \frac{1}{\gamma^2 - x_0^2} \right\rangle \\ &= \frac{1}{2\gamma^2 \sqrt{1-a^2/R^2}} \ln \left(\frac{1 + \sqrt{1-a^2/R^2}}{1 - \sqrt{1-a^2/R^2}} \right). \end{aligned} \quad (51)$$

Finally, combining these two results, we have

$$\frac{D_0}{D_{\text{eff}}} = \frac{2+a^2/R^2}{6\sqrt{1-a^2/R^2}} \ln \left(\frac{1 + \sqrt{1-a^2/R^2}}{1 - \sqrt{1-a^2/R^2}} \right). \quad (52)$$

(II) *Zwanzig*. Now, taking (26) in (48) allows us to rewrite (8) in the form

$$\begin{aligned} & \langle e^{-\beta U(x_0)} \rangle \left\langle \frac{1}{D(x_0) e^{-\beta U(x_0)}} \right\rangle \\ &= \langle \gamma^2 - x_0^2 \rangle \left\langle \frac{2\gamma^2 - \alpha^2 x^2}{2(\gamma^2 - x^2)^2 D_0} \right\rangle \end{aligned} \quad (53)$$

which, in turn, leads to

$$\frac{D_0}{D_{\text{eff}}} = \frac{2+a^2/R^2}{12(a^2/R^2)} f_1, \quad (54)$$

where f_1 is given by

$$\begin{aligned} f_1 &= 1 - \varepsilon^2 \\ &+ \frac{(3+\varepsilon^2)(a^2/R^2)}{2\sqrt{1-a^2/R^2}} \ln \left(\frac{1 + \sqrt{1-a^2/R^2}}{1 - \sqrt{1-a^2/R^2}} \right). \end{aligned} \quad (55)$$

(III) *Reguera-Rubí*. Finally, taking $D(x_0)$ from (34) to (48), we may rewrite (8) in the form

$$\frac{D_0}{D_{\text{eff}}} = \langle \gamma^2 - x_0^2 \rangle \left\langle \frac{\sqrt{\gamma^2 - \varepsilon^2 x_0^2}}{(\gamma^2 - x^2)^{3/2}} \right\rangle \quad (56)$$

which leads to the result

$$\frac{D_0}{D_{\text{eff}}} = \left(\frac{1}{\sqrt{1 - a^2/R^2}} - \frac{1}{3} \sqrt{1 - \frac{a^2}{R^2}} \right) \int_0^{\sqrt{1 - a^2/R^2}} \frac{\sqrt{1 - \varepsilon^2 \phi^2}}{(1 - \phi^2)^{3/2}} d\phi. \quad (57)$$

2.4. Computational Details. Computational simulations were carried out to compute the mean first-passage time, τ (MFPT), defined above. The particle's initial position, x_0 , was distributed uniformly within the middle plane at $x_0 = 0$. The MFPT is denoted as τ . When running simulations, we took $R = 1$, $D_0 = 1$, 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, $\vec{r}$, is given by $\vec{r} = \vec{r}_0 + \vec{r}_{\text{ran}}$, where $\vec{r}_0$ is the previous position and $\vec{r}_{\text{ran}}$ 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.

In the elliptic tube, the effective diffusion coefficients were computed using the formula given by Berezhkovskii and Weiss [39]:

$$D_{\text{eff}} = \frac{L^2}{3\tau_1^2} \left(4W_-W_+(\tau_- + \tau_+) + \frac{\tau_-}{\tau_1} (W_+ - W_-)^2 - \tau_1 \right) \quad (58)$$

which requires the recording of several quantities from computer simulations: the global first and second moments of the MFPT, $\tau_1 = (1/N) \sum_{i=1}^N \tau_i$ and $\tau_2 = (1/N) \sum_{i=1}^N \tau_i^2$, the MFPT for particles exiting the system to the left and right openings, τ_- and τ_+ , respectively, and the correspondent fractions of exiting particles, W_- and W_+ (where $W_- + W_+ = 1$).

In the periodic elliptic tube, the effective diffusion coefficients were computed from the Einstein's relation:

$$\langle x^2 \rangle = 2D_{\text{eff}}t, \quad (59)$$

where the mean-square displacement, $\langle x^2 \rangle$, was recorded from computer simulations and tabulated for a total of 5×10^4 realizations of a random walk.

3. Results and Discussions

Comparisons between theoretical curves and data obtained from simulations (circles) are shown in Figures 4 to 6. In Figure 4, τ from (24) (black dash and dot line), (33) (blue dashed line), and (40) (orange continuous line) are plotted against the eccentricity ε of the elliptic tube ($R = 1$, $a = 0.05$); see Figure 1. The physical limit $\varepsilon \rightarrow 1$ corresponds to $L \rightarrow \infty$; thus, the three expressions show the right behavior $\tau \rightarrow \infty$, but only (40) shows a good agreement with simulations.

Figure 5 shows theoretical curves of D_{eff} from (42) (black dash and dot line), (43) (blue dashed line), and (44) (orange

FIGURE 4: Comparison of τ from (24), black dash and dot line, (33), blue dashed line, and (40), orange continuous line, with data from computer simulations (circles), are plotted against the eccentricity ε of the elliptic tube (given $R = 1$, $a = 0.05$).

FIGURE 5: D_{eff} from (42), black dash and dot line, (43), blue dashed line, and (44), orange continuous line, as a function of the eccentricity ε of the elliptic tube (given $R = 1$, $a = 0.05$), compared with Data from computer simulations (circles).

continuous line) as a function of the eccentricity ε of the elliptic tube. This time we have a quotient of two quantities that, individually, approach ∞ as $\varepsilon \rightarrow 1$; thus D_{eff} remains finite. As L^2 grows faster than τ , we observe a tendency to increase D_{eff} while approaching the limit $\varepsilon \rightarrow 1$. The best fit with simulation data comes for the Reguera-Rubí approximation, in (43).

Figure 6 shows theoretical curves of D_{eff} for the system in Figure 2, from (52) (black dash and dot line), (54) (blue dashed line), and (57) (orange continuous line), as a function of the eccentricity ε of each link in the periodic elliptic tube ($R = 1$, $a = 0.9$). The inset graphic shows the slight difference

FIGURE 6: D_{eff} for the system in Figure 2, from (52), black dash and dot line, (54), blue dashed line, and (57), orange continuous line, as a function of the eccentricity ε of each link in the periodic elliptic tube (given $R = 1$, $a = 0.9$), compared with Data from computer simulations (circles).

between (54) and (57), which is practically negligible. Despite the apparent difference shown in relation to simulation data, the mean error remains below 6%. Expression (54) has a clear advantage over (57); that is, the first is analytic, while the latter has an integral, which, in turn, has to be solved numerically. When choosing $a < 0.9$ error grows faster and above 10–30%, suggesting that the narrow-tube approximation is no longer applicable to this system.

Final expressions shown in Figures 4 to 6, discussed above, are the main result of this paper.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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