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Unbiased Diffusion to Escape through Small Windows: Assessing the Applicability of the Reduction to Effective One-Dimension Description in a Spherical Cavity

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Abstract

This study is devoted to unbiased motion of a point Brownian particle that escapes from a spherical cavity through a round hole. Effective one-dimensional description in terms of the generalized Fick-Jacobs equation is used to derive a formula which gives the mean first-passage time as a function of the geometric parameters for any value of a, where a is the hole's radius. This is our main result and is given in Equation (19). This result is a generalization of the Hill's formula, which is restricted to small values of a.

Keywords: Diffusion, Brownian Particle, Fick-Jacobs Equation, Narrow-Escape Time

1. Introduction

The first-passage time, namely, the probability that a diffusing particle or a random-walk first reaches a specified site (or set of sites) at a specified time, is known to underlie a wide range of stochastic processes of practical interest [1]. Indeed, chemical and bio-chemical reactions [2,3], animals searching for food [4], the spread of sexually transmitted diseases in a human social network or of viruses through the world wide web [5], and trafficking receptors on biological membranes [6], are often controlled by first encounter events [7]. Studying the narrow scape time (NET), the mean time which a Brownian particle spends before to be trapped in an opening window to exit a cavity for the first time, has particular importance. The applications goes from cellular biology to biochemical reactions in cellular micro-domains as dendritic spines, synapses and micro-vesicles, among others [6,8]. For those cases where the particles first must exit the domain in order to live up to their biological function, the narrow scape time is the limiting quantity and the first step in the modeling of such processes [7].

Experimentally, high-resolution crystallography of bacterial porins and other large channels demonstrates that their pores can be envisaged as tunnels whose cross sections change significantly along the channel axis. For some of them, variation in cross-section area exceeds an order of magnitude [9,10]. This leads to the so-called entropic walls and barriers in theoretical description of transport through such structures. In addition to biological systems, diffusion in confined geometries are also important for understanding transport in synthetic nanopores [11-13], transport in zeolites [14], controlled drugs release [15], and nanostructures of complex geometries [16], among others.

Theoretically, the transport in systems of varying geometry has been deeply studied in recent years since these systems are ubiquitous in nature and technology [18-23]. Diffusion in two and three dimension, has been formulated as a one dimension problem in terms of the effective one-dimensional concentration of diffusing molecules. If one assumes that the distribution of the solute in any cross section of the tube is uniform as it is at equilibrium, directing the x-axis along the center line of a tube, one can write an approximate one-dimensional effective diffusion equation as

$$\frac{\partial c(x,t)}{\partial t}=\frac{\partial}{\partial x}\left\{D(x)A(x)\frac{\partial}{\partial x}\left[\frac{c(x,t)}{A(x,t)}\right]\right\}, \tag{1}$$

where $D(x)$ is a position-dependent diffusion coefficient, $A(x)=\pi\left[r(x)\right]^2$ is the cross section area of the tube of radius $r(x)$, and $c(x,t)$ is the effective one-dimensional concentration of the diffusing particles at a given x. This equation was derived by Jacobs in 1967 [17]. $c(x,t)$ is related to the three-dimensional concentration $C(x,y,z,t)$ by

$$c(x,t)=\int_{A(x)}C(x,y,z,t)\,\mathrm{d}y\mathrm{d}z. \tag{2}$$

As Zwanzig pointed out [18], (1) can be considered as the Smoluchowski equation for diffusion in the entropy potential $U(x)$ defined as,

$$U(x)=-k_BT\ln\frac{A(x)}{A(x_C)}, \tag{3}$$

where k_B is the Boltzmann constant and T the absolute temperature, and $U(x)$ at $x=x_C$ is taken to be zero, $U(x_C)=0$.

Equation (1) with position-independent diffusion coefficient, $D(x)=D$, is known as the Fick-Jacobs (FJ) equation [17]. To improve FJ's reduction, Zwanzig (Zw) derived one-dimension diffusion equation assuming that the tube radius $r(x)$ is a slowly varying function, $|r'(x)|\ll 1$ [18]. He showed that $c(x,t)$ satisfies the probability conservation equation

$$\frac{\partial c(x,t)}{\partial t}=-\frac{\partial j(x,t)}{\partial x} \tag{4}$$

where the flux, $j(x,t)$, is given by,

$$j(x,t)=-A(x)D(x)\frac{\partial}{\partial x}\left[\frac{c(x)}{A(x)}\right] \tag{5}$$

The expression for $D(x)$ derived by Zwanzing is as follows [18],

$$D_{Zw}(x)=\frac{D}{1+r'(x)^2/2}. \tag{6}$$

Later, in the same spirit of amending the FJ's reduction, Reguera and Rub (RR) proposed the following expression for $D(x)$ [19],

$$D_{RR}(x)=D\left[1-\frac{1}{2}r'(x)^2\right]\approx\frac{D}{\sqrt{1+r'(x)^2}}. \tag{7}$$

In order to determine what the explicit form of $D(x)$ should be used in a given geometry (and its associated boundary conditions), we can exploit 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 a random walker spends to reach a specified place for the first time, averaged over all the trajectories or realizations of a random walk, is found to satisfy a backwards equation [20],

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

where $\beta=1/(k_BT)$ (k_B and T retain their usual meaning), and the potential $U(x_0)$, defined in (3), is due to the change in the cross-sectional area along the axial length of the tubes. Then (8) is solved for the appropriate boundary conditions to obtain an algebraic expression that relates τ with $D(x)$ and geometrical parameters of the system.

In the present paper we derive a formula which gives the mean first-passage time as function of the geometrical parameters using the effective one-dimension description for a sphere with absorbing spots. This formula will be proved to reproduce the data obtained by Monte-carlo simulations for any value of the hole radius, a, when (7) is used.

2. Results and Discussion

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 [24]. Two main results were reported: 1) an algebraic proof that for small holes the decay is exponential, based on the spectral representation of the survival probability, and 2) 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,

$$k=\frac{4Da}{V}=\frac{1}{\tau} \tag{9}$$

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 founded that when the spot radius is small enough ($a/R<0.1$ for a spherical cavity, R is the radius of the sphere), the decay is exponential and the rate constants found in simulations are in a good agreement with those predicted by (9). For the means first-passage time predicted by Hill's formula for a sphere with two absorbent holes, the following volume has to be introduced in (9), see **Figure 1**,

$$V_{\mathrm{sph}}=\frac{4\pi R^3}{3}-\frac{2\pi}{3}\left(R-\sqrt{R^2-a^2}\right)^2\left(2R-\sqrt{R^2-a^2}\right) \tag{10}$$

obtaining,

$$\tau_{\mathrm{sph}}^{\mathrm{Hill}}=\frac{\pi}{12Da}\left(2R^3-\left(R-\sqrt{R^2-a^2}\right)^2\left(2R-\sqrt{R^2-a^2}\right)\right) \tag{11}$$

Equation (11) is just applicable when $a/R>0.1$. In the following lines we will obtain an expression for any value of a.

To solve (8) for a sphere with two absorbing windows (see **Figure 1**), we have to take the potential $U(x_0)$

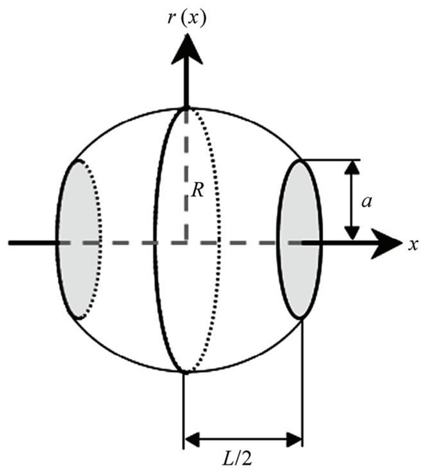

Figure 1. Sphere of radius R with two absorbing windows of radii a (shaded inthe picture, while the remaining surface is reflective). Its height is given by $r(x)=\sqrt{R^2-x^2}$. The enclosed volume is changed as one varies a because of $L/2=\sqrt{R^2-a^2}$.

defined as,

$$\mathrm{e}^{-\frac{1}{\beta}U(x)}=\frac{A(x)}{A(0)}=\frac{\pi r(x)^2}{\pi r(0)^2}=\frac{R^2-x^2}{R^2} \quad (12)$$

where $A(x_0)$ is the cross-sectional area, and $r(x_0)=\sqrt{R^2-x_0^2}$ is the height of the sphere. In these calculations x_0 denotes the initial position of each trajectory of a Brownian particle. Then, using $D_{\mathrm{RR}}(x_0)$ as given by

$$D(x_0)=D_{\mathrm{RR}}(x_0)=\frac{D}{\sqrt{1+r'(x_0)^2}}=\frac{\sqrt{R^2-x_0{}^2}}{R}D \quad (13)$$

we replace $D(x_0)$ and $e^{-\beta U(x_0)}$ in (8) to yield,

$$\frac{\mathrm{d}}{\mathrm{d}x_0}\left(\frac{R^2-x_0{}^2}{R^2}\frac{\sqrt{R^2-x_0{}^2}}{R}D\frac{\mathrm{d}\tau}{\mathrm{d}x_0}\right)=-\frac{R^2-x_0{}^2}{R^2} \quad (14)$$

which happens to be a separable ordinary differential equation. Integrating twice we obtain,

$$\tau(x_0)=-\frac{R^3}{D}\frac{1}{\sqrt{R^2-x_0^2}}+\frac{R}{3D}\left\{\sqrt{R^2-x_0^2}+\frac{R^2}{\sqrt{R^2-x_0^2}}\right\}+\frac{R^3}{D}\frac{x_0}{R^2\sqrt{R^2-x_0^2}}C_1+C_2 \quad (15)$$

The equation above have two integration constants, namely, C_1 and C_2, which can be fixed by using appropriate boundary conditions. Since we have absorbing windows in the positions $x_0=+L/2$, and $x_0=L/2$, we can state this type of boundary conditions as follows,

$$\tau(-L/2)=\tau(L/2)=0 \quad (16)$$

with these conditions in (15), we found, $C_1=0$ and $C_2=\frac{2R^3}{3Da}-\frac{aR}{3D}$. Thus we have an expression of τ as a function of the initial position x_0,

$$\tau(x_0)=-\frac{2R^3}{3D}\frac{1}{\sqrt{R^2-x_0^2}}+\frac{R}{3D}\sqrt{R^2-x_0^2}+\frac{2R^3}{3Da}-\frac{aR}{3D} \quad (17)$$

If we also want the solution when the initial positions of the particles are distributed uniformly in the cavity, we have to consider the average over all the accessible initial positions in the interval $-L/2\le x_0\le L/2$ given by

$$\langle\tau\rangle=\frac{1}{L}\int_{-L/2}^{L/2}\tau(x_0)\,\mathrm{d}x_0. \quad (18)$$

Substituting $\tau(x_0)$ from (17), in the above definition allows one to obtain an expression for τ,

$$\tau_{sph}^{\mathrm{RR}}(a)=\frac{R^3}{6Da}\left\{4-\left(\frac{a}{R}\right)^2-\frac{3a}{\sqrt{R^2-a^2}}\arcsin\frac{\sqrt{R^2-a^2}}{R}\right\}. \quad (19)$$

Equation (19) along with (17) are the main results of this work. Equation (19) depends only on the geometrical parameters *R* and *a*, and the bulk diffusion constant *D*. The comparison of this expression with the data obtained by Montecarlo simulations shows and excellent agreement for any value of *a*, see **Figure 2**. Additionally, in the limit $a\to 0$, the ratio τ_{RR}/τ_{Hill} goes to the constant value $4/\pi$.

The results obtained here can be extended to any number of spots—provided these spots are far enough to not interact with each other, dividing Equation (19) by two, times the number of holes. The procedure outlined in this work can be used to obtain the mean first-passage time for any geometry when $D_{\mathrm{RR}}(x)$ is applicable.

3. Computational Details

The problem is to find the survival time of a Brownian particle escaping from a domain of size *V*, whose boundary is reflective, except for a small absorbing window of circular shape and radius *a*. In simulations we obtain the mean time to absorption τ, a mean first-passage time.

When running simulations we take $D_0=1$ and the

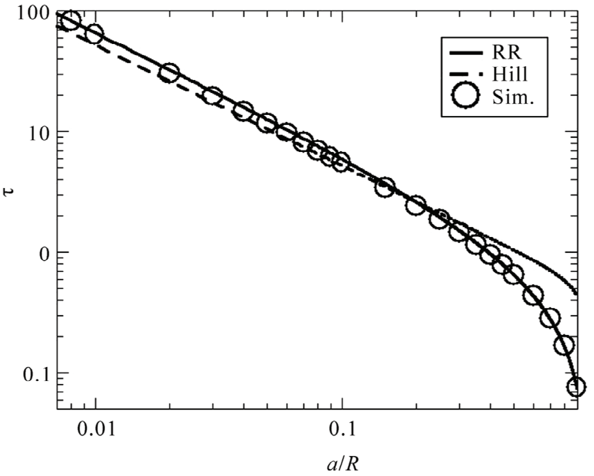

Figure 2. Narrow escape time for the sphere with two holes (in Figure 1), in a Log-Log scale to emphasize the differences between theoretical curves and simulated data. Hill's formula (11) (dashed line) shows a poor agreement with simulated data (circles) in the range *a* > 0.1, while (19) (solid line) fits better the data for all *a* in 0.008 ≤ a ≤ 0.9.

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, $\boldsymbol{r}_n$, is given by $\boldsymbol{r}_n = \boldsymbol{r}_0 + \boldsymbol{r}_{\text{ran}}$, where $\boldsymbol{r}_0$ is the former position, and $\boldsymbol{r}_{\text{ran}}$ is a vector of pseudo random numbers generated with a Gaussian distribution ($\mu = 0$, $\sigma = \sqrt{2D_0 \Delta t}$). Each MFPT is obtained by averaging the first-passage times of 2.5×10^4 trajectories whose starting positions are uniformly distributed inside the cavity.

The system under study is shown in **Figure 1**, a sphere of radius *R* with two round holes of the same size. The length *L* between the two absorbing holes is related to the sizes of the sphere, *R*, and the hole, *a*, by the relation,

$$L/2 = \sqrt{R^2 - a^2} \tag{20}$$

Equation (20) implies that the volume of the domain is a function of the length $L/2$, so the former shrinks as *a* increases (and $L/2$ decreases). The height of the sphere as a function of the axial coordinate *x* is $r(x) = \sqrt{R^2 - x^2}$. The present methodology can be applied, nonetheless to any geometry, provided it is radially symmetric.

Figure 2 shows the comparison between Narrow Escape Times computed from Brownian dynamics simulations (circles) and those predicted by Hill's formula (dashed line), Equation (11), and our result (solid line), Equation (19). The simulated data ranges from $a = 0.007$ to $a = 0.900$. Equation (11) falls far from the computed narrow escape times in the range $a > 0.1$ while (19) fits for all *a* in a broader range.

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