Search for a small hole in a cavity wall by intermittent bulk and surface diffusion

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We study the search of a small round hole in the wall of a spherical cavity by a diffusing particle, which can reversibly bind to the cavity wall and diffuse on the surface being in the bound state. There are two channels for the particle first passage to the hole, through the bulk, and through the surface. We propose a coarse-grained model of the search process and use it to derive simple approximate formulas for the mean time required for the particle to reach the hole for the first time and for the probability of the first passage to the hole through the bulk channel. This is done for two distributions of the particle starting point: (1) Uniform distribution over the cavity volume and (2) uniform distribution over the cavity wall. We check the accuracy of the approximate formulas by comparing their predictions with the corresponding quantities found by solving the mixed bulk-surface diffusion problem numerically by the finite difference method. The comparison shows excellent agreement between the analytical and numerical results. © 2012 American Institute of Physics. [doi:10.1063/1.3682243]

I. INTRODUCTION

The problem of a diffusing particle searching for a round exiting hole in the cavity wall (Fig. 1) arises in a variety of situations ranging from signal compartmentalization in dendritic spines of neurons^{1–5} to endosomal sorting⁶ and controlled drug delivery,⁷ to mention just a few. One of the key quantities characterizing the search process is the particle mean first passage time to the hole, τ . When the hole is small enough, the search time is much larger than the relaxation time of the particle distribution in the isolated cavity. In such a case, τ is given by

$$\tau = \frac{V}{4D_b a}, \quad (1.1)$$

where V is the cavity volume, a is the hole radius, and D_b is the particle diffusion constant in the bulk (b) of the cavity. This formula shows that τ is independent of both the shape of the cavity and the particle initial position. The latter is true only when the particle starting point is located not too close to the hole. Rigorous derivations of the result in Eq. (1.1) are given in Refs. 8 and 9. One can find a back-of-the-envelope derivation of Eq. (1.1) in Ref. 10, which also contains its numerical test for spherical and cubic cavities.

The result in Eq. (1.1) was obtained assuming that the cavity wall is a perfectly reflecting surface. An interesting generalization of the initial, so-called narrow escape problem was recently proposed in Refs. 11–13, which consider the problem assuming that the particle can reversibly bind to the cavity wall and diffuse on the surface, being in the bound state, so that the particle motion is intermittent bulk and surface diffusion. In such a case, there are two channels for the

particle first passage to the hole, through the bulk and through the surface.

The present paper also focuses on the narrow escape problem assuming intermittent bulk and surface diffusion of the particle. We describe binding of the particle diffusing in the bulk to the cavity wall by imposing radiation boundary condition on the wall, and characterize the binding efficiency by the association rate constant α . We assume that the particle survival probability in the bound state on the surface (s) decays as a single exponential, $S_s(t) = e^{-\beta t}$, where β is the dissociation rate constant of the bound state. The rate constants α and β together with the bulk and surface diffusion constants, D_b and D_s , respectively, control the contributions of the bulk and surface channels into the particle first passage to the hole.

To characterize these contributions, we introduce the probabilities of the particle first passage to the hole through the bulk, W_b , and through the surface, W_s , $W_b + W_s = 1$. Assuming that the cavity is a sphere, we propose a coarse-grained model of the search process and use it to derive simple approximate formulas for τ and W_b for two initial distributions of the particle starting position: uniform distribution in the bulk and uniform distribution over the cavity surface. These formulas show how τ and W_b depend on the rate constants α and β , the diffusion constants D_b and D_s , and the geometric parameters, radius R of the cavity and radius a of the hole. To check the accuracy of our approximate formulas, we found τ and W_b for the two initial distributions of the particle starting position by solving the problem of mixed bulk-surface diffusion numerically by the finite difference method. Comparison of the predictions of the coarse-grained model and numerical results shown in Figs. 2 and 3 demonstrates excellent agreement between the two. The relative error is below 3% over the entire range of the parameters.

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FIG. 1. Schematic representation of a spherical cavity of radius R containing a perfectly absorbing disk of radius a on the cavity wall.

The outline of the paper is as follows. In Sec. II, we develop a coarse-grained model of the search process under consideration. Our main results, simple formulas for τ and W_b , Eqs. (3.1)–(3.4), and their numerical test (Figs. 2 and 3), are presented in Sec. III.

II. COARSE-GRAINED MODEL

Consider a particle diffusing in a closed spherical cavity of radius R . The particle can reversibly bind to the cavity surface and diffuse on the surface. In the limiting case of low binding rate, one can describe reversible binding of the particle to the wall by the kinetic scheme

$$P_b(t) \xrightleftharpoons[\beta]{\alpha} P_s(t), \quad (2.1)$$

where $P_b(t)$ and $P_s(t)$ are the probabilities of finding the particle in the bulk and on the surface at time t , respectively, while α and β are the association and dissociation rate constants. This scheme implies that the probabilities $P_b(t)$ and $P_s(t)$ satisfy the rate equations

$$\frac{dP_b(t)}{dt} = -\frac{dP_s(t)}{dt} = -\alpha P_b(t) + \beta P_s(t). \quad (2.2)$$

As $t \rightarrow \infty$, $P_b(t)$ and $P_s(t)$ approach their equilibrium values,

$$P_b^{(eq)} = \frac{\beta}{\alpha + \beta}, \quad P_s^{(eq)} = \frac{\alpha}{\alpha + \beta}. \quad (2.3)$$

FIG. 2. Comparison of the theoretical predictions and numerical results (solid curves and symbols, respectively) at uniform distribution of the particle starting point over the cavity volume. Two upper panels show six sections of the surface $\tau^{(b)}(\alpha, \beta|k_b, k_s)$, while two lower panels show six sections of the surface $W_b^{(b)}(\alpha, \beta|k_b, k_s)$.

FIG. 3. Comparison of the theoretical predictions and numerical results (solid curves and symbols, respectively) at uniform distribution of the particle starting point over the non-absorbing part of the cavity wall. Two upper panels show six sections of the surface $\tau^{(s)}(\alpha, \beta|k_b, k_s)$, while two lower panels show six sections of the surface $W_b^{(s)}(\alpha, \beta|k_b, k_s)$.

The association rate constant can be expressed in terms of the trapping rate κ entering into the radiation boundary condition on the cavity wall (see Eq. (A.2) in the exact formulation of the problem in Appendix),

$$\alpha = \frac{A_R}{V_R} \kappa = \frac{3}{R} \kappa, \quad (2.4)$$

where $A_R = 4\pi R^2$ and $V_R = 4\pi R^3/3$ are the surface area and volume of the sphere of radius R . One can formally introduce α defined in Eq. (2.4) for an arbitrary value of κ . Although the rate equations in Eq. (2.2) are applicable only when κ is small enough, nevertheless, they lead to the correct equilibrium probabilities, Eq. (2.3), at arbitrary κ .

Our goal is to study the first passage of the particle to a small circular hole of radius a in the cavity wall. To do this, we consider different realizations of the particle trajectory, assuming that the trajectory is terminated as soon as it reaches the hole for the first time. This means that we consider the hole as a perfectly absorbing boundary and study

particle trapping by a perfectly absorbing disk of radius a on the cavity wall (Fig. 1).

In the absence of binding to the wall ($\alpha = 0$), the particle, starting in the bulk reaches the disk due to bulk diffusion. When a is small enough, the particle survival probability for time t at uniform distribution of the particle starting point over the cavity volume, $S_b(t)$, decays as a single exponential

$$S_b(t) = e^{-k_b t}, \quad k_b = \frac{1}{t_b} = \frac{3D_b a}{\pi R^3}, \quad (2.5)$$

where $t_b = V_R/(4D_b a)$ is the mean lifetime of the particle; the expression for t_b is a special case of the general formula for mean lifetime given in Eq. (1), which corresponds to the spherical cavity of radius R .

When the particle diffuses on the cavity wall ($\beta = 0$), the trapping kinetics is also single-exponential at sufficiently small a . For uniform distribution of the particle starting point over the surface, the particle survival probability for time t ,

$S_s(t)$, is

$$S_s(t) = e^{-k_s t}, \quad k_s = \frac{1}{t_s}, \quad (2.6)$$

where t_s is the mean lifetime of the particle. At arbitrary angle θ_a (see Fig. 1) time t_s is given by¹⁴

$$t_s = \frac{R^2}{D_s} \left\{ \frac{2}{[\cos(\theta_a/2)]^2} \ln \left[\frac{1}{\sin(\theta_a/2)} \right] - 1 \right\}. \quad (2.7)$$

At $a \ll R$, $\theta_a \approx a/R$ is much smaller than unity, and the expression for t_s takes the form

$$t_s \approx \frac{R^2}{D_s} \left[2 \ln \left(\frac{2R}{a} \right) - 1 \right], \quad a \ll R. \quad (2.8)$$

This leads to

$$k_s \approx \frac{D_s}{R^2 [2 \ln(2R/a) - 1]}, \quad a \ll R. \quad (2.9)$$

Trapping of particles diffusing on the surface of a sphere by several small non-overlapping circular patches is considered in Ref. 15.

Of course, single-exponential decay of the survival probabilities in Eqs. (2.5) and (2.6) is an approximation. However, when a is small enough, this approximation is quite accurate since the equilibration both in the bulk and on the cavity wall takes much less time than searching for the disk.

Using the rate constants k_b and k_s , we modify the kinetic scheme in Eq. (2.1) to incorporate particle trapping by the disk,

Corresponding rate equations, which generalize the rate equations in Eq. (2.2), are

$$\frac{dP_b(t)}{dt} = -(\alpha + k_b)P_b(t) + \beta P_s(t), \quad (2.11)$$

$$\frac{dP_s(t)}{dt} = \alpha P_b(t) - (\beta + k_s)P_s(t). \quad (2.12)$$

In what follows, we use these equations to find the mean lifetime of the particle, τ , and the trapping probability W_b . The kinetic scheme in Eq. (2.10) and the equivalent rate equations, Eqs. (2.11) and (2.12), provide a coarse-grained description of the particle trapping by the absorbing disk on the cavity wall. One can find the exact formulation of the problem in Appendix.

At first glance, it would seem that the coarse-grained model, Eqs. (2.11) and (2.12), is applicable only if the binding and dissociation rates, α and β , are low, since when these rates are high, there are space correlations between the points of successive binding and dissociation events. However, as we will see in the Sec. III, predictions of the coarse-grained model are in excellent agreement with the numerical results not only at small α and β , but over the entire range of their values. The reason why the coarse-grained model, which completely ignores the correlations, is nevertheless successful in predicting the properties of the particle first passage to the disk, is the hierarchy of the time scales: Since the disk is small, the characteristic time scale of the first passage significantly exceeds all other characteristic time scales of the

problem, including the bulk and surface equilibration times, on which the particle loses its memory about the correlations.

The particle survival probability for time t , $S(t)$, is the sum of the probabilities of finding the particle in the bulk and on the cavity wall at time t , $P_b(t)$ and $P_s(t)$, respectively, (formal definitions of $P_b(t)$ and $P_s(t)$ in the framework of the exact formulation of the problem are given in Eqs. (A.5) and (A.6) of Appendix)

$$S(t) = P_b(t) + P_s(t). \quad (2.13)$$

The probability density of the particle lifetime $\varphi(t)$ is given by $\varphi(t) = -dS(t)/dt$. The mean lifetime of the particle, which is its mean first passage time to the hole, correspondingly, is

$$\tau = \int_0^\infty t \varphi(t) dt = \int_0^\infty S(t) dt. \quad (2.14)$$

Using Eq. (2.13), we obtain

$$\tau = \int_0^\infty P_b(t) dt + \int_0^\infty P_s(t) dt. \quad (2.15)$$

The product $k_b P_b(t)$ is the probability flux entering the disk from the bulk at time t . The probability W_b is the integral of this flux over the time from zero to infinity (a formal definition of W_b in the framework of the exact formulation of the problem is given in Eq. (A.8) of Appendix),

$$W_b = k_b \int_0^\infty P_b(t) dt. \quad (2.16)$$

Introducing the notations

$$\hat{P}_{b,s} = \int_0^\infty P_{b,s}(t) dt, \quad (2.17)$$

we can write τ and W_b given in Eqs. (2.15) and (2.16) as

$$\tau = \hat{P}_b + \hat{P}_s, \quad (2.18)$$

$$W_b = k_b \hat{P}_b. \quad (2.19)$$

Integrating Eqs. (2.11) and (2.12) over time from zero to infinity, one can find that $\hat{P}_b$ and $\hat{P}_s$ satisfy

$$(\alpha + k_b)\hat{P}_b - \beta\hat{P}_s = P_b(0), \quad (2.20)$$

$$-\alpha\hat{P}_b + (\beta + k_s)\hat{P}_s = P_s(0), \quad (2.21)$$

where $P_b(0)$ and $P_s(0)$ are the probabilities of finding the particle in the bulk and bound to the wall at $t = 0$. Solving these simple linear equations one can find $\hat{P}_b$ and $\hat{P}_s$, and then τ and W_b by Eqs. (2.18) and (2.19).

In Sec. III, we present the results obtained in this way for two initial distributions: uniform distribution of the starting point over the cavity volume, $P_b(0) = 1$ and $P_s(0) = 0$, and uniform distribution of the starting point over the non-absorbing part of the cavity wall, $P_b(0) = 0$ and $P_s(0) = 1$. We will see that the results are in excellent agreement with those obtained by solving the mixed bulk-surface diffusion problem numerically by the finite difference method.

III. RESULTS

We find the mean first passage time to the hole (the mean lifetime of the particle), τ , and the probability of the first passage to the hole from the bulk, W_b , by solving Eqs. (2.20) and (2.21), and then substituting the obtained solutions for $\hat{P}_b$ and $\hat{P}_s$ into Eqs. (2.18) and (2.19). For uniform distribution of the particle initial position over the cavity volume, $P_b(0) = 1$ and $P_s(0) = 0$, the results are

$$\tau^{(b)} = \frac{\alpha + \beta + k_s}{\alpha k_s + \beta k_b + k_b k_s}, \quad (3.1)$$

$$W_b^{(b)} = \frac{k_b(\beta + k_s)}{\alpha k_s + \beta k_b + k_b k_s}, \quad (3.2)$$

where the superscript (b) indicates that the initial distribution is uniform over the cavity volume. For uniform distribution of the particle initial position over the non-absorbing part of the cavity wall, $P_b(0) = 0$ and $P_s(0) = 1$, we obtain

$$\tau^{(s)} = \frac{\alpha + \beta + k_b}{\alpha k_s + \beta k_b + k_b k_s}, \quad (3.3)$$

$$W_b^{(s)} = \frac{k_b \beta}{\alpha k_s + \beta k_b + k_b k_s}, \quad (3.4)$$

where the superscript (s) indicates that the initial distribution is uniform over the cavity wall. Using Eqs. (3.2) and (3.4), one can find the probabilities of the first passage of the particle to the hole through the surface, $W_s^{(b,s)}$, by means of the relation $W_s^{(b,s)} = 1 - W_b^{(b,s)}$.

The expressions in Eqs. (3.1)–(3.4) are the main results of this paper. They show how the quantities of interest depend on the rate constants α , β , k_b , and k_s . The two latter rate constants are functions of the diffusion constants D_b and D_s , and the geometric parameters, radius R of the cavity and radius a of the hole. Thus, Eqs. (3.1)–(3.4) provide approximate solutions for $\tau^{(b,s)}$ and $W_b^{(b,s)}$ as functions of all the parameters of the problem. One can check that the predictions of these equations agree with the common sense expectations in the limiting cases: (1) When $\alpha \rightarrow 0$, $\tau^{(b)} \rightarrow k_b^{-1}$ and $W_b^{(b)} \rightarrow 1$; (2) when $\alpha \rightarrow \infty$, $\tau^{(b,s)} \rightarrow k_s^{-1}$ and $W_b^{(b,s)} \rightarrow 0$; (3) when $\beta \rightarrow 0$, $\tau^{(s)} \rightarrow k_s^{-1}$ and $W_b^{(s)} \rightarrow 0$; (4) when $\beta \rightarrow \infty$, $\tau^{(b,s)} \rightarrow k_b^{-1}$ and $W_b^{(b,s)} \rightarrow 1$; (5) when $\alpha, \beta \rightarrow \infty$, $\tau^{(b,s)} \rightarrow (P_b^{(eq)} k_b + P_s^{(eq)} k_s)^{-1}$, and $W_b^{(b,s)} \rightarrow k_b P_b^{(eq)} (P_b^{(eq)} k_b + P_s^{(eq)} k_s)^{-1}$, where $P_{b,s}^{(eq)}$ are the equilibrium probabilities given in Eq. (2.3).

Using Eqs. (3.1)–(3.4) one can find the asymptotic behavior of $\tau^{(b,s)}$ and $W_b^{(b,s)}$ as $a \rightarrow 0$. The formulas show that at finite α , β , D_b , and D_s , $W_b^{(b,s)}|_{a \rightarrow 0} \rightarrow 0$ and, hence, $W_s^{(b,s)}|_{a \rightarrow 0} \rightarrow 1$, i.e., the particle comes to the hole through the surface channel. According to Eqs. (3.1) and (3.3), the mean first passage times $\tau^{(b)}$ and $\tau^{(s)}$ are equal in this limiting case and given by

$$\tau^{(b)} = \tau^{(s)} = 1/(P_s^{(eq)} k_s) = t_s/P_s^{(eq)}, \quad (3.5)$$

as might be expected.

To check the accuracy of our approximate formulas, we found τ and W_b by solving the problem of mixed bulk-surface diffusion (see Appendix) numerically by the finite difference method, and compared our numerical results with

those predicted by the formulas in Eqs. (3.1)–(3.4). This was done for $D_b = D_s$, $a/R = 0.02$ (as tested numerically, Eqs. (2.5) and (2.6) are justified for $a/R < 0.1$), and time was measured in units of $R^2/D_{b,s}$. Fixing the diffusion constants and the geometrical parameters, we fix the rate constants k_b and k_s . As a result, the quantities of interest, τ and W_b , become functions of only two arguments, the association and dissociation rate constants, α and β , and can be considered as surfaces over the (α, β) -plane. The comparison of analytical and numerical results is made for six sections of these surfaces: $\beta = 0.1 k_s$, k_s , and $10 k_s$, and $\alpha = 0.1 k_b$, k_b , and $10 k_b$. For uniform distribution of the particle starting point over the cavity volume, the results are shown in Fig. 2. In Fig. 3 we show the results for the case of the uniform distribution of the particle starting point over the non-absorbing part of the cavity wall. Comparison of the analytical and numerical results shows excellent agreement between the two. The relative error does not exceed 3% over the entire range of the association and dissociation rate constants α and β .

Finally we discuss the relation between our study and those reported in Refs. 11–13. Our model describes particle binding to and dissociation from the cavity wall as local processes, so that the particle dynamics satisfies detailed balance. The models studied in Refs. 11–13 consider binding as a local process, assuming that the wall is perfectly absorbing (the particle binds the wall at the first contact). To make it possible for the particle to escape from the perfectly absorbing wall, they consider dissociation as a non-local (nl) process: after dissociation the particle is placed at distance l_{nl} from the wall. As a consequence, in the layer of thickness l_{nl} near the wall detailed balance is violated. When $l_{nl} \rightarrow 0$, the models considered in Refs. 11–13 become identical to our model in its exact formulation given in Appendix, in the limiting case of $\kappa = \alpha = \infty$. In Refs. 11–13 it is assumed that the particle starts from the surface. Therefore, as $l_{nl} \rightarrow 0$, the mean first passage times found in Refs. 11–13 reduce to $t_s = k_s^{-1}$ given in Eq. (2.8). This agrees with the limiting behavior of $\tau^{(s)}$ in Eq. (3.3) when $\alpha \rightarrow \infty$. While Eqs. (3.1) and (3.3) predict monotonic dependence of the mean first passage times on the association and dissociation rate constants, according to Refs. 12 and 13 the dependence of the mean first passage time on the dissociation rate constant is non-monotonic.

In summary, this paper is devoted to the diffusive search of a small round hole in the wall of a spherical cavity, assuming intermittent bulk and surface diffusion. The focus is on the mean first passage time to the hole and the probability of the first passage to the hole from the bulk. Our main results are the approximate formulas for these quantities in Eqs. (3.1)–(3.4) and their numerical test presented in Figs. 2 and 3. Formulas in Eqs. (3.1) and (3.2) give the results for the uniform distribution of the particle initial position over the cavity volume. The results for the uniform distribution of the particle starting point over the cavity wall outside the hole are given in Eqs. (3.3) and (3.4). The formulas show how the quantities of interest depend on the association and dissociation rate constants α and β , which characterize reversible binding of the particle to the cavity wall, and the rate constants k_b and k_s , which characterize the first passage through the bulk and surface, respectively, at $\alpha = \beta = 0$. The latter

rate constants are functions of the geometric parameters, radii of the sphere and hole, and the particle diffusion constants in the bulk of the cavity and on the wall. The comparison demonstrates excellent agreement between the predictions of the approximate formulas and the numerical results.

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APPENDIX: FORMAL STATEMENT OF THE MIXED BULK-SURFACE DIFFUSION PROBLEM

Consider a point particle diffusing in a spherical cavity of radius R containing an absorbing disk of radius a on the cavity wall (Fig. 1). The particle can reversibly bind to the wall and diffuse on the surface. It is convenient to describe the particle motion in a spherical system of coordinates, r , θ , φ , whose origin is located in the center of the sphere, and angle θ is counted from the axis passing through the center of the disk. Let $p_b(r, \theta, \varphi, t)$ and $p_s(\theta, \varphi, t)$ be the probability densities of finding the particle in the bulk at point (r, θ, φ) and on the surface at point (θ, φ) at time t , respectively. When the initial distribution is independent of angle φ (azimuthal symmetry), the probability densities are independent of φ at all t and can be written as $p_b(r, \theta, \varphi, t) = p_b(r, \theta, t)/(2\pi)$ and $p_s(\theta, \varphi, t) = p_s(\theta, t)/(2\pi)$.

Function $p_b(r, \theta, t)$ satisfies

$$\frac{\partial p_b(r, \theta, t)}{\partial t} = \frac{D_b}{r^2} \left[\frac{\partial}{\partial r} \left(r^2 \frac{\partial p_b(r, \theta, t)}{\partial r} \right) + \frac{1}{\sin \theta} \frac{\partial}{\partial \theta} \left(\sin \theta \frac{\partial p_b(r, \theta, t)}{\partial \theta} \right) \right] \quad (\text{A.1})$$

with the absorbing boundary condition on the part of the cavity wall occupied by the disk, $p_b(R, \theta, t)|_{0 \leq \theta \leq \theta_a} = 0$, and the boundary condition

$$D_b \frac{\partial p_b(r, \theta, t)}{\partial r} \bigg|_{r=R} = -\kappa p_b(R, \theta, t) + \beta p_s(\theta, t) \quad (\text{A.2})$$

on the rest of the wall. Using the relation in Eq. (2.4), we can write the boundary condition in Eq. (A.2) in terms of the association rate constant α as

$$D_b \frac{\partial p_b(r, \theta, t)}{\partial r} \bigg|_{r=R} = -\frac{\alpha R}{3} p_b(R, \theta, t) + \beta p_s(\theta, t). \quad (\text{A.3})$$

Function $p_s(\theta, t)$ satisfies

$$\begin{aligned} \frac{\partial p_s(\theta, t)}{\partial t} &= \frac{D_s}{R^2 \sin \theta} \frac{\partial}{\partial \theta} \left(\sin \theta \frac{\partial p_s(\theta, t)}{\partial \theta} \right) \\ &\quad - \beta p_s(\theta, t) + \frac{\alpha R}{3} p_b(R, \theta, t) \end{aligned} \quad (\text{A.4})$$

with the absorbing boundary condition at the disk boundary, $p_s(\theta_a, t) = 0$.

The probabilities of finding the particle in the bulk of the cavity and on its surface at time t , $P_b(t)$ and $P_s(t)$, respectively, are given by

$$P_b(t) = \int_0^R r^2 dr \int_0^\pi \sin \theta p_b(r, \theta, t) d\theta, \quad (\text{A.5})$$

$$P_s(t) = R^2 \int_{\theta_a}^\pi \sin \theta p_s(\theta, t) d\theta. \quad (\text{A.6})$$

The sum of these probabilities is the particle survival probability for time t , $S(t)$, given in Eq. (2.13). The mean lifetime of the particle τ is the integral of $S(t)$ over time t from zero to infinity, Eq. (2.14).

The probability flux entering the absorbing disk at time t from the bulk, $w_b(t)$, is given by

$$w_b(t) = D_b R^2 \int_0^{\theta_a} \frac{\partial p_b(r, \theta, t)}{\partial r} \bigg|_{r=R} \sin \theta d\theta. \quad (\text{A.7})$$

The integral of this flux over time t from zero to infinity is the probability W_b ,

$$W_b = \int_0^\infty w_b(t) dt. \quad (\text{A.8})$$

An analog of this expression in the framework of the coarse-grained model is given in Eq. (2.16).

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