Searching for partially reactive sites: Analytical results for spherical targets

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How do single or multiple (sub)diffusing particles search for a target with a partially reactive boundary? A finite reaction rate which is typical for many chemical or biochemical reactions is introduced as the possibility for a particle to find a target but not to "recognize" it. The search is not finished until the target is found and recognized. For a single searching particle, the short- and long-time regimes are investigated, with a special focus on comparison between perfectly and partially reactive boundaries. For multiple searching particles, explicit formulas for the probability density of the search time are given for subdiffusion in one and three dimensions. The dependence of the mean search time on the density of particles and the reaction rate is analyzed. Unexpectedly, in the high density limit, the particles undergoing slower subdiffusive motion find a target faster.
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I. INTRODUCTION

Searching for a reactive site is a common process in physics, chemistry, and biology. Typical examples are diffusing molecules searching for catalytic grains in a chemical reactor[1–5] or proteins searching for specific DNA target sites in a living cell.[6–8] In both cases, crowding and caging, geometrical traps and energetic barriers, and other mechanisms often lead to anomalous diffusion with a sublinear growth of the mean-square displacement: $\langle [x(t)-x(0)]^2\rangle \propto t^{\alpha}$, with an exponent α between 0 and 1.[9–17] The distribution of search times in such reactive media characterizes their overall functioning.

Many theoretical, numerical, and experimental studies are concerned with search times for normal diffusion.[18–25] Recently, several groups investigated this question for subdiffusion. Lua and Grosberg[26] studied the first-passage times for a particle, executing one-dimensional diffusive and subdiffusive motions in an asymmetric sawtooth potential, to exit one of the boundaries. Yuste and Lindenberg[27] computed the asymptotic survival probability of a spherical target in the presence of a single subdiffusive trap or surrounded by a sea of subdiffusive traps. Condamin and co-workers[28,29] derived a relationship between the moments of the first-passage time for normal diffusion and the first-passage time density for subdiffusive processes. All these studies are concerned with the first-passage time when a subdiffusive process is stopped (i.e., a target is found) after the first encounter with the target.

When a target is found, the particle *may or may not* interact with the target via chemical transformation, relaxation, adsorption on or transfer through its boundary, etc.[3–5,30–39] For biological applications, the interaction can also mean a "recognition" of the target. If no interaction occurs (the target is not recognized), the particle is released to continue its motion in the bulk until finding a target again. The subdiffusive process is stopped (i.e., the search is over) when the target is found and recognized. The probability of interaction (or recognition) at each encounter with the target is related to permeability, reactivity, or relaxivity W of its boundary. Among various examples, we mention macromolecules diffusing in the extracellular space and searching for cells to permeate through the cellular membrane (as well as viruses searching for a nucleus inside a living cell and permeating through the boundary of the nucleus);[40–42] species diffusing in a chemical reactor and reacting on catalytic grains with a finite reaction rate,[1–5,30,43,44] spin-bearing molecules moving in a medium filled with relaxing sites.[45]

We aim at answering the following two questions: "how does the surface reactivity influence the distribution of search times?" and "what is the role of the exponent α characterizing the subdiffusive process?" The former question was studied in depth for normal diffusion ($\alpha=1$) by Barzykin and Tachiya,[5] while the latter question was addressed by Yuste and Lindenberg[27] for perfectly reactive boundary ($W=\infty$). We present an extension of these works by considering a general situation of subdiffusive searching ($\alpha\leq 1$) for partially reactive sites ($W\leq\infty$).

In Sec. II, we calculate the Laplace transform of the survival probability of a single particle subdiffusing in a space outside a spherical target. We also consider searching by many particles and derive formulas for the corresponding survival probability. For subdiffusion in one and three dimensions, the latter survival probability will be written in an exact explicit form. We analyze its short-time and long-time asymptotic behaviors, with a special emphasis on comparison between perfectly and partially reactive targets. In Sec. III, we compute the mean multiple-particles search time (MPST) and study its dependence on surface relaxivity, density of particles, and exponent α.

II. SURVIVAL PROBABILITY

Anomalous diffusions may result from various physical mechanisms: trapping with a long-tailed distribution of waiting times [continuous-time random walks (CTRWs)]; strong

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corrections between microscopic displacements (e.g., fractional Brownian motion); and diffusion on fractal sets.[17] Although all these mechanisms lead to a sublinear growth of the mean-square displacement, the underlying physics and mathematics are very different. In this paper, we focus on the CTRW which can be equivalently described by fractional Fokker–Planck equations.[17] In the CTRW framework, a subdiffusive process is a sequence of random independent microscopic displacements in space with random waiting times between each two displacements. The probability density of the waiting times decays at long times as $t^{-1-\alpha}$ (with $0<\alpha<1$) so that the mean waiting time is infinite, while the mean-square displacement is sublinear. Since the spatial displacements of a CTRW are governed by the same probability laws as those for normal diffusion, this subdiffusive process and normal diffusion differ only by "time clocks." As a consequence, many results for subdiffusion follow straightforwardly from those for normal diffusion by an appropriate change of "time clocks," which is known as subordination.[46–48] In particular, a number of formulas established by Barzykin and Tachiya[5] will be directly extended for subdiffusion.

A. Fractional diffusion equation

We consider particles which (sub)diffuse in the space Ω outside a target. The central quantity of our analysis is the survival probability $Q_\alpha(\mathbf{r},t)$ that is a particle started at $\mathbf{r}\in\Omega$ at time 0 does not find (and recognize) the target up to a later time t. The time derivative of $Q_\alpha(\mathbf{r},t)$ gives the probability density for the single-particle search time (SPST)

$$q_\alpha(\mathbf{r},t) = -\frac{\partial}{\partial t}Q_\alpha(\mathbf{r},t). \tag{1}$$

The combined survival probability $S_N(t)$ for N independent subdiffusing particles is simply the probability that none of the N particles found and recognized the target up to time t. If the particles are uniformly distributed in a volume V, then

$$S_N(t) = \left[\frac{1}{V}\int_\Omega d\mathbf{r}Q_\alpha(\mathbf{r},t)\right]^N.$$

In the thermodynamic limit with $N\to\infty$ and $V\to\infty$ holding the density $\rho=N/V$, the survival probability becomes[4]

$$S_\infty(t) = \exp[-\rho R^d f(t)], \tag{2}$$

where

$$f_d(t) = \frac{1}{R^d}\int_\Omega d\mathbf{r}[1-Q_\alpha(\mathbf{r},t)]. \tag{3}$$

Note that the derivative of $f_d(t)$ can be interpreted as the bulk reaction rate.[4,5]

The classical diffusion equation for the survival probability[3] is replaced by a fractional Fokker–Planck equation for subdiffusion

$$\left[\frac{\partial}{\partial t} - D_\alpha\, {}_0D_t^{1-\alpha}\Delta\right]Q_\alpha(\mathbf{r},t) = 0 \quad (\mathbf{r}\in\Omega), \tag{4}$$

$$\Lambda\frac{\partial}{\partial n}Q_\alpha(\mathbf{r},t) + Q_\alpha(\mathbf{r},t) = 0 \quad (\mathbf{r}\in\partial\Omega), \tag{5}$$

$$\lim_{|\mathbf{r}|\to\infty} Q_\alpha(\mathbf{r},t) = 1, \tag{6}$$

$$Q_\alpha(\mathbf{r},t=0) = 1, \tag{7}$$

where $\Delta\equiv\partial^2/\partial_1^2+\ldots+\partial^2/\partial_d^2$ is the d-dimensional Laplace operator, $\partial/\partial n$ is the normal derivative at the target boundary $\partial\Omega$ pointing toward the exterior of the domain Ω, Λ is a positive parameter homogeneous to a length, and D_α is a generalized diffusion coefficient (in units $\mathrm{m}^2/\mathrm{s}^\alpha$). Memory effects of a subdiffusive process are introduced through the Riemann-Liouville fractional differential operator ${}_0D_t^{1-\alpha}$,

$${}_0D_t^{1-\alpha}g(t) = \frac{1}{\Gamma(\alpha)}\frac{\partial}{\partial t}\int_0^t dt'\frac{g(t')}{(t-t')^{1-\alpha}}, \tag{8}$$

which is defined for any sufficiently well-behaved function $g(t)$, and $\Gamma(z)$ is the Gamma function.[49,50]

A probabilistic interpretation of Eqs. (4)–(7) is straightforward. The fractional diffusion Eq. (4) states that the time evolution of the survival probability is caused by local migration of subdiffusing particles (described by the Laplace operator). The Robin boundary condition [Eq. (5)] includes a possibility of reflection on the target boundary $\partial\Omega$ (the normal derivative) when the target is not recognized. The two other relations state that the survival probability is 1 at the beginning of the experiment [Eq. (7)] and for a particle which was initially located infinitely far from the target [Eq. (6)].

The Robin boundary condition (also known as radiation, Fourier, third, etc.) is a linear combination of Dirichlet and Neumann boundary conditions.[30–33] This is a form of a mass conservation law when the diffusive flux toward the boundary is equal to the flux across the boundary. Collins and Kimball introduced the Robin boundary condition in order to describe partially diffusion-controlled reactions,[30] while Seki *et al.*[51] and later Eaves and Reichman[52] justified this condition for subdiffusion-controlled reactions. They showed that a positive parameter Λ which is homogeneous to a length, is the ratio between the bulk and surface transport coefficients: $\Lambda=D_\alpha/W_\alpha$, W_α being the (generalized) surface permeability, relaxivity or reactivity (although Λ may depend on α, we keep writing Λ instead of Λ_α). The parameter Λ characterizes the recognition phase, i.e., interactions at the encounter with the target. In the limiting case $\Lambda=0$ (infinite reactivity), one retrieves the description by Yuste and Lindenberg[27] for a perfectly reactive target, without recognition phase (the

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search is over when a target is reached for the first time). The opposite case of $\Lambda=\infty$ (zero reactivity) corresponds to Neumann boundary condition for a "blind particle" which never recognizes the target. Although more sophisticated boundary conditions may sometimes be required in order to describe surface exchange processes,[42,53,54] our focus is on the Robin boundary condition [Eq. (5)].

The set of time-dependent Eqs. (4)–(7) can be equivalently represented in Laplace domain. We consider a set of equations for the Laplace transform $\mathcal{L}$ of the probability density $q_\alpha(\mathbf{r},t)$

$$\tilde{q}_\alpha(\mathbf{r},s) \equiv \mathcal{L}[q_\alpha(\mathbf{r},t)](s) \equiv \int_0^\infty dt e^{-ts} q_\alpha(\mathbf{r},t)$$

(Laplace transformed quantities are denoted by tilde throughout the text). Since the fractional derivative in Eq. (8) has a form of a convolution, its Laplace transform is simply the product of two Laplace transforms, namely, $\mathcal{L}[{}_0D_t^{1-\alpha}g(t)](s)=s^{1-\alpha}\mathcal{L}[g(t)](s)$. The fractional diffusion Eq. (4) for $Q_\alpha(\mathbf{r},t)$ is therefore reduced to a Helmholtz equation for $\tilde{Q}_\alpha(\mathbf{r},s)$ or $\tilde{q}_\alpha(\mathbf{r},s)$ which are related as $\tilde{q}_\alpha(\mathbf{r},s)=1-s\tilde{Q}_\alpha(\mathbf{r},s)$ according to Eq. (1). One gets

$$s^\alpha \tilde{q}_\alpha(\mathbf{r},s) - D_\alpha \Delta \tilde{q}_\alpha(\mathbf{r},s) = 0 \quad (\mathbf{r} \in \Omega), \tag{9}$$

$$\Lambda \frac{\partial}{\partial n} \tilde{q}_\alpha(\mathbf{r},s) + \tilde{q}_\alpha(\mathbf{r},s) = 1 \quad (\mathbf{r} \in \partial\Omega), \tag{10}$$

$$\lim_{|\mathbf{r}|\to\infty} \tilde{q}_\alpha(\mathbf{r},s) = 0. \tag{11}$$

Note that the factor s^α appears as a fixed parameter in the Helmholtz equation. As a consequence, its solution for subdiffusion $(0<\alpha<1)$ can be directly derived from the solution for normal diffusion $(\alpha=1)$ by substituting s/D_1 by s^α/D_α. This is an example of "subordination" meaning that diffusion and subdiffusion differ by time clocks, the difference being expressed through s^α/D_α in Laplace space.[46–48] The analysis of the search time for a subdiffusive process is therefore reduced to "rescaling" of the same characteristics for normal diffusion. On one hand, one can readily use numerous analytical results for normal diffusion.[55] On the other hand, fast random walk algorithms which were implemented for computing passage times for normal diffusion in complex geometries[21,56–60] can be adapted for subdiffusion.

B. Spherical target

For a spherical target of radius R, one has $\Omega=\{\mathbf{r}\in\mathbb{R}^d:|\mathbf{r}|>R\}$, and Eq. (9) is reduced to a modified Bessel equation

$$g''(z) + \frac{d-1}{z} g'(z) - g(z) = 0,$$

where $g(z)\equiv\tilde{q}_\alpha(\mathbf{r},s)$ and $z\equiv|\mathbf{r}|\sqrt{s^\alpha/D_\alpha}$. A regular solution of this equation satisfying the Robin boundary condition [Eq. (10)] is

$$\tilde{q}_\alpha(\mathbf{r},s) = \left(\frac{|\mathbf{r}|}{R}\right)^{1-d/2} \frac{K_{d/2-1}\left(|\mathbf{r}|\sqrt{s^\alpha/D_\alpha}\right)}{W_d(s)}, \tag{12}$$

with

$$W_d(s) = K_{d/2-1}\left(R\sqrt{s^\alpha/D_\alpha}\right) + \Lambda\sqrt{s^\alpha/D_\alpha} K_{d/2}\left(R\sqrt{s^\alpha/D_\alpha}\right), \tag{13}$$

where $K_\nu(z)$ is the modified Bessel function of the second kind (note that a similar equation was given by Barzykin and Tachiya[5] for normal diffusion with $\alpha=1$).

In order to calculate the survival probability $S_\infty(t)$, we find the Laplace transform of the function $f_d(t)$ from Eq. (3)

$$\tilde{f}_d(s) = \frac{1}{R^d}\int_{|\mathbf{r}|>R} d\mathbf{r} \frac{\tilde{q}_\alpha(\mathbf{r},s)}{s} = S_d \frac{K_{d/2}\left(R\sqrt{s^\alpha/D_\alpha}\right)}{sW_d(s)R\sqrt{s^\alpha/D_\alpha}}, \tag{14}$$

where $S_d=2\pi^{d/2}/\Gamma(d/2)$ is the surface area of the d-dimensional unit sphere, and we used the identity

$$\int_1^\infty dx\, x^{d/2} K_{d/2-1}(xa) = \frac{K_{d/2}(a)}{a}.$$

C. Short-time behavior

The short-time behavior of time-dependent quantities corresponds to the limit $s\to\infty$ for their Laplace transforms. In this limit, we get

$$\tilde{q}_\alpha(\mathbf{r},s) \simeq \left(\frac{R}{|\mathbf{r}|}\right)^{(d-1)/2} \frac{e^{(R-|\mathbf{r}|)\sqrt{s^\alpha/D_\alpha}}}{1+\Lambda\sqrt{s^\alpha/D_\alpha}}. \tag{15}$$

When $|\mathbf{r}|>R$, the short-time asymptotic behavior of the right-hand side of Eq. (15) was shown to be[61]

$$q_\alpha(\mathbf{r},t) \simeq \left(\frac{|\mathbf{r}|}{R}\right)^{(1-d)/2} \frac{t^{-1}}{\sqrt{\pi(2-\alpha)}} \exp\left[-(2-\alpha)\left(\frac{(R-|\mathbf{r}|)^2\alpha^\alpha}{4D_\alpha t^\alpha}\right)^{1/(2-\alpha)}\right] \times \begin{cases} \alpha^{1/2}\left(\dfrac{(R-|\mathbf{r}|)^2\alpha^\alpha}{4D_\alpha t^\alpha}\right)^{1/[2(2-\alpha)]} & (\Lambda=0), \\ \alpha^{(1-\alpha)/2}\left(\dfrac{(R-|\mathbf{r}|)^2\alpha^\alpha}{4D_\alpha t^\alpha}\right)^{(1-\alpha)/[2(2-\alpha)]} \dfrac{\sqrt{D_\alpha t^\alpha}}{\Lambda} & (\Lambda>0). \end{cases}$$

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The asymptotic behavior is dominated by the exponential factor that leads to a rapid decrease of the probability density when t goes to 0. In the short-time regime, a particle started far from the target does not have enough time to find it.

We also find the asymptotic behavior of the function $\tilde{f}_d(s)$ which determines the survival probability $S_\infty(t)$

$$\tilde{f}_d(s) \simeq \frac{S_d}{sR\sqrt{s^\alpha/D_\alpha}(1+\Lambda\sqrt{s^\alpha/D_\alpha})} \quad (s\to\infty),$$

from which

$$f_d(t) \simeq \begin{cases} \dfrac{S_d}{\Gamma\left(1+\frac{\alpha}{2}\right)}\dfrac{\sqrt{D_\alpha t^\alpha}}{R} & (\Lambda=0), \\ \dfrac{S_d}{\Gamma(1+\alpha)}\dfrac{D_\alpha t^\alpha}{\Lambda R} & (\Lambda>0). \end{cases} \tag{16}$$

Since the particles which started near the boundary of a target reach it fast, there is no dominating exponential factor in Eq. (16), and the distinction between two cases $\Lambda=0$ and $\Lambda>0$ is now more explicit. According to Eq. (2), the survival probability $S_\infty(t)$ decreases slower with time for $\Lambda>0$ because longer time is needed to find and recognize a partially reactive target. The short-time behavior of the survival probability allows one to determine the length Λ and to characterize the surface reactivity.

D. Long-time behavior

The analysis of the long-time behavior ($t\to\infty$) relies on series expansions of functions $\tilde{q}_\alpha(\mathbf{r},s)$ and $\tilde{f}_d(s)$ as s going to 0. The asymptotic properties of the modified Bessel functions suggest to consider the cases $d<2$, $d=2$, and $d>2$ separately. Although the computation can be done for any real dimensionality[5,27] d, we focus on three practically important values: $d=1,2,3$. In what follows, we derive exact explicit formulas for the function $f_d(t)$ in one and three dimensions. The long-time behavior is also discussed.

1. One dimension

Given that

$$K_{-1/2}(z) = K_{1/2}(z) = \sqrt{\frac{\pi}{2}}\frac{e^{-z}}{\sqrt{z}},$$

we get the following exact results:

$$W_1(s) = \sqrt{\frac{\pi}{2}}\frac{e^{-R\sqrt{s^\alpha/D_\alpha}}}{(R\sqrt{s^\alpha/D_\alpha})^{1/2}}(1+\Lambda\sqrt{s^\alpha/D_\alpha}),$$

$$\tilde{q}_\alpha(\mathbf{r},s) = \frac{e^{(R-|\mathbf{r}|)\sqrt{s^\alpha/D_\alpha}}}{1+\Lambda\sqrt{s^\alpha/D_\alpha}},$$

$$\tilde{f}_1(s) = \frac{2\sqrt{D_\alpha}/R}{s^{1+\alpha/2}} - \frac{2\Lambda/R}{s(1+\Lambda\sqrt{s^\alpha/D_\alpha})}.$$

Although the probability density $q_\alpha(\mathbf{r},t)$ is formally given through the inverse Laplace transform of $\tilde{q}_\alpha(\mathbf{r},s)$, there is no explicit form, except for $\alpha=1$.[5] In turn, the inverse Laplace transform of $\tilde{f}_1(s)$ is

$$f_1(t) = \frac{\sqrt{4D_\alpha t^\alpha}/R}{\Gamma\left(1+\frac{\alpha}{2}\right)} - 2\frac{\Lambda}{R}\left[1-E_{\alpha/2}\left(-\sqrt{D_\alpha t^\alpha}/\Lambda\right)\right], \tag{17}$$

where $E_\alpha(z)$ is the Mittag–Leffler function,

$$E_\alpha(z) = \sum_{n=0}^{\infty}\frac{z^n}{\Gamma(\alpha n+1)}.$$

Equation (17) is an exact result which is applicable for any time t. In the limit $\Lambda\to 0$, the second term in Eq. (17) vanishes, and one retrieves the result by Yuste and Lindenberg.[27]

In the long-time limit, the Mittag–Leffler function decays as a power law, so that the second term is small, and

$$f_1(t) \simeq \frac{\sqrt{4D_\alpha t^\alpha}/R}{\Gamma\left(1+\frac{\alpha}{2}\right)}. \tag{18}$$

Reactivity properties of the target (the value of Λ) become irrelevant in this limit.

2. Two dimensions

In two dimensions ($d=2$), the long-time asymptotic behavior of $f_2(t)$ can be deduced by considering its Laplace transform $\tilde{f}_2(s)$ in the limit of s going to 0. Since

$$K_0(z) \simeq -\ln(z/2) - \gamma + O(z^2) \quad (z\to 0),$$

where $\gamma\simeq 0.577\,216$ is the Euler–Mascheroni constant, one has

$$W_2(s) \simeq -\ln(R\sqrt{s^\alpha/D_\alpha}/2) - \gamma + \Lambda/R,$$

from which

$$\tilde{f}_2(s) \simeq \frac{4\pi D_\alpha/R^2}{s^{1+\alpha}\alpha\ln(s_0/s)},$$

where

$$s_0 = 4^{1/\alpha}\exp\left[-\frac{2}{\alpha}(\gamma-\Lambda/R)\right]\left(\frac{D_\alpha}{R^2}\right)^{1/\alpha}.$$

Using the Tauberian theorem,

$$\mathcal{L}\left[\frac{t^{\beta-1}}{\ln(ts_0)}\right](s) \simeq \frac{\Gamma(\beta)}{s^\beta\ln(s_0/s)},$$

we get the following approximate result:

$$f_2(t) \simeq \frac{4\pi D_\alpha t^\alpha/R^2}{\Gamma(1+\alpha)[\ln(4D_\alpha t^\alpha/R^2) - 2\gamma + 2\Lambda/R]}. \tag{19}$$

Interestingly, the time derivative of this function, which is equal to the bulk reaction rate,[5] decays much slower (logarithmically) for normal diffusion ($\alpha=1$) than for subdiffusion ($\alpha<1$).

3. Three dimensions

Using explicit formulas for $K_{1/2}(z)$ and $K_{3/2}(z)$, we find the following exact results:

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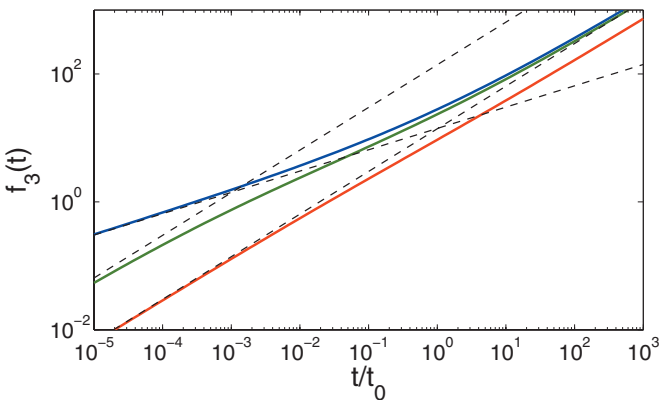

FIG. 1. The function $f_3(t)$ for $d=3$, $\alpha=2/3$, $D_\alpha=1$, $R=1$, and three values of Λ/R: 0 (top curve in blue), 0.1 (middle curve in green), and 1 (bottom curve in red). The time scale is $t_0=(R^2/D_\alpha)^{1/\alpha}$. Dashed lines show the short-time asymptotic behavior according to Eq. (16).

$$W_3(s) = \sqrt{\frac{\pi}{2}}\frac{e^{-R\sqrt{s^\alpha/D_\alpha}}}{(R\sqrt{s^\alpha/D_\alpha})^{1/2}}\left(1+\Lambda/R+\Lambda\sqrt{s^\alpha/D_\alpha}\right),$$

$$\tilde{q}_\alpha(\mathbf{r},s) = \frac{R}{|\mathbf{r}|}\frac{e^{(R-|\mathbf{r}|)\sqrt{s^\alpha/D_\alpha}}}{1+\Lambda/R+\Lambda\sqrt{s^\alpha/D_\alpha}},$$

$$\tilde{f}_3(s) = \frac{4\pi D_\alpha}{\Lambda R s^{1+\alpha}}\left(1-\frac{1}{1+\Lambda/R+\Lambda\sqrt{s^\alpha/D_\alpha}}\right).$$

As in one dimension, there is no explicit formula for the probability density $q_\alpha(\mathbf{r},t)$ except for $\alpha=1$.[5] In turn, the inverse Laplace transform of the last relation is

$$f_3(t) = 4\pi\left(\frac{D_\alpha t^\alpha/R^2}{(1+\Lambda/R)\Gamma(1+\alpha)}+\frac{\sqrt{D_\alpha t^\alpha}/R}{(1+\Lambda/R)^2\Gamma\left(1+\frac{\alpha}{2}\right)}\right.$$
$$\left.-\frac{\Lambda/R}{(1+\Lambda/R)^3}\left[1-E_{\alpha/2}\left(-\sqrt{D_\alpha t^\alpha}(1/\Lambda+1/R)\right)\right]\right). \tag{20}$$

This exact relation which is applicable for any time t, is one of our main results. Figure 1 shows the behavior of this function for three values of Λ/R and $\alpha=2/3$ as an arbitrary example. In the short-time limit, one can clearly notice different slopes for $\Lambda=0$ and $\Lambda>0$. In the long-time limit, all the curves follow a power law with the exponent α. The prefactor $(1+\Lambda/R)^{-1}$ in front of the first term of Eq. (20) is responsible for a shift of each curve along the vertical axis on the logarithmic scale.

4. Higher dimensions

Although explicit formulas are not always available for higher dimensions ($d>3$), the long-time asymptotic behavior is similar to that of the first term of Eq. (20)

$$f_d(t) \simeq \frac{(d-2)S_d}{1+(d-2)\Lambda/R}\frac{D_\alpha t^\alpha/R^2}{\Gamma(1+\alpha)}. \tag{21}$$

For $\Lambda=0$, one retrieves the result by Yuste and Lindenberg,[27] while the case $\alpha=1$ was considered by Barzykin and Tachiya.[5]

III. MULTIPLE-PARTICLES SEARCH TIME (MPST)

According to the explicit Eq. (12) for $\tilde{q}_\alpha(\mathbf{r},s)$, the mean search time $\langle\tau^s\rangle$ for a single (sub)diffusing particle is infinite

$$\langle\tau^s\rangle = \int_0^\infty dt\ t\, q_\alpha(\mathbf{r},t) = -\left(\frac{\partial}{\partial s}\tilde{q}_\alpha(\mathbf{r},s)\right)_{s=0} = \infty. \tag{22}$$

In contrast, many subdiffusing particles find a target with a finite mean time. We define the probability density $p_\alpha(t)$ for the MPST as

$$p_\alpha(t) = -\frac{\partial}{\partial t}S_\infty(t) = \rho R^d f_d'(t)\exp[-\rho R^d f_d(t)]. \tag{23}$$

The short-time asymptotic behavior of $p_\alpha(t)$ follows directly from Eq. (16):

$$p_\alpha(t) \simeq \begin{cases} \dfrac{S_d}{\Gamma\left(\frac{\alpha}{2}\right)}\rho R^{d-1}\sqrt{D_\alpha}t^{\alpha/2-1} & (\Lambda=0), \\ \dfrac{S_d}{\Gamma(\alpha)}\dfrac{\rho R^{d-1}D_\alpha}{\Lambda}t^{\alpha-1} & (\Lambda>0), \end{cases} \tag{24}$$

while the long-time asymptotic behavior is essentially stretched-exponential, with the function $f_d(t)$ given by Eqs. (18), (19), and (21). The stretched-exponential decrease of $p_\alpha(t)$ ensures the existence of all the moments of the MPST. In particular, the mean search time is

$$\langle\tau_d^{\mathrm{m}}\rangle = \int_0^\infty dt\ t\, p_\alpha(t) = \int_0^\infty dt\ \exp[-\rho R^d f_d(t)]. \tag{25}$$

In what follows, we analyze the mean search time for subdiffusion in one and three dimensions.

A. One dimension

The explicit Eq. (17) for $f_1(t)$ allows us to write the mean search time as

$$\langle\tau_1^{\mathrm{m}}\rangle = \frac{\left[\Gamma\left(1+\frac{\alpha}{2}\right)\right]^{2/\alpha}\Gamma\left(1+\frac{2}{\alpha}\right)}{(4D_\alpha\rho^2)^{1/\alpha}}T_{1,\alpha}(2\rho\Lambda), \tag{26}$$

where

$$T_{1,\alpha}(x) = \frac{1}{\Gamma\left(\frac{2}{\alpha}\right)}\int_0^\infty dz\ z^{2/\alpha-1}$$
$$\times\exp\left(-z+x\left[1-E_{\alpha/2}\left(-\frac{z\Gamma\left(1+\frac{\alpha}{2}\right)}{x}\right)\right]\right). \tag{27}$$

Note that the mean search time is independent of the size R of the target.

For small x, the function $T_{1,\alpha}(x)$ approaches a constant: $T_{1,\alpha}(0)=1$. The prefactor in Eq. (26) is therefore the mean search time for a perfectly reactive target ($\Lambda=0$). For normal diffusion ($\alpha=1$), one gets $\langle\tau_1^{\mathrm{m}}\rangle=\pi/(8D_1\rho^2)$ at $\Lambda=0$.

For large x, one has

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$$T_{1,\alpha}(x) \simeq \frac{\Gamma\left(\frac{1}{\alpha}\right)}{2\Gamma\left(\frac{2}{\alpha}\right)}\left(\frac{\Gamma(1+\alpha)}{\left[\Gamma\left(1+\frac{\alpha}{2}\right)\right]^2}\right)^{1/\alpha} x^{1/\alpha}.$$

Since corrections are of the order of $x^{1/\alpha-1/2}$, they may be significant for practical use.

B. Three dimensions

In three dimensions, the explicit formula (20) yields

$$\langle \tau_3^{\mathrm{m}} \rangle = \frac{\Gamma\left(\frac{1}{\alpha}\right)[\Gamma(1+\alpha)]^{1/\alpha}}{\alpha(4\pi\rho R D_\alpha)^{1/\alpha}} T_{3,\alpha}(\Lambda/R, \rho R^3), \tag{28}$$

where

$$T_{3,\alpha}(x,y) = \frac{2}{\Gamma\left(\frac{1}{\alpha}\right)[\Gamma(1+\alpha)]^{1/\alpha}} \frac{(4\pi y)^{1/\alpha}}{(1+x)^{2/\alpha}} \times \int_0^\infty dz\ z^{2/\alpha-1} \exp\left(-\frac{4\pi y}{(1+x)^3}\left[\frac{z}{\Gamma\left(1+\frac{\alpha}{2}\right)} + \frac{z^2}{\Gamma(1+\alpha)} - x\left[1 - E_{\alpha/2}(-z/x)\right]\right]\right). \tag{29}$$

1. Perfectly reactive target

For a perfectly reactive target ($\Lambda=0$ or $x=0$), Eq. (29) becomes

$$T_{3,\alpha}(0,y) = \frac{2(4\pi y)^{1/\alpha}}{\Gamma\left(\frac{1}{\alpha}\right)[\Gamma(1+\alpha)]^{1/\alpha}} \int_0^\infty dz\ z^{2/\alpha-1} \times \exp\left(-4\pi y\left[\frac{z}{\Gamma\left(1+\frac{\alpha}{2}\right)} + \frac{z^2}{\Gamma(1+\alpha)}\right]\right). \tag{30}$$

For the low density ρ of searching particles (small y), the main contribution to the integral in Eq. (30) comes from large values of z so that the linear term in z can be neglected in comparison to the quadratic one, yielding

$$T_{3,\alpha}(0,y) \simeq 1 + O(\sqrt{y}) \quad (y \to 0). \tag{31}$$

According to Eq. (28), the mean search time $\langle \tau_3^{\mathrm{m}} \rangle$ diverges as $(\rho R D_\alpha)^{-1/\alpha}$. As expected, a particle undergoing slower subdiffusive motion (smaller α) needs longer time to find a target.

For the high density ρ of searching particles (large y), the main contribution to the integral in Eq. (30) comes from small values of z so that the quadratic term z^2 can be neglected. In this case, one has

$$T_{3,\alpha}(0,y) \simeq \frac{2\Gamma\left(\frac{2}{\alpha}\right)\left[\Gamma\left(1+\frac{\alpha}{2}\right)\right]^{2/\alpha}}{\Gamma\left(\frac{1}{\alpha}\right)[\Gamma(1+\alpha)]^{1/\alpha}} (4\pi y)^{-1/\alpha}, \tag{32}$$

and the mean search time $\langle \tau_3^{\mathrm{m}} \rangle$ decreases as $(\rho R^2 \sqrt{D_\alpha})^{-2/\alpha}$. Interestingly, smaller values of α yield a faster decrease of the mean search time. In other words, slower subdiffusive motion allows for a faster search of a target. We return to this seemingly paradoxal result in Sec. III C.

A transition region between two asymptotic limits [Eqs. (31) and (32)] can be modeled by a Padé approximation

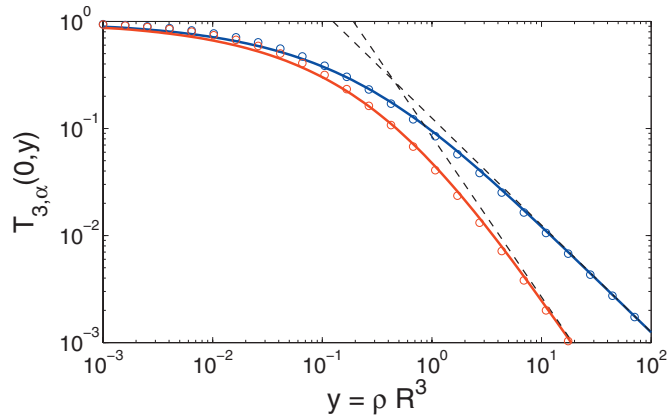

FIG. 2. The function $T_{3,\alpha}(0,y)$ for $\alpha=1$ (top curve in blue) and $\alpha=2/3$ (bottom curve in red), its asymptotic behavior [Eq. (32)] at large y (dashed lines), and Padé approximation [Eq. (33)] with $\beta=\alpha/1.5$ (circles).

$$T_{3,\alpha}(0,y) \simeq \left(1 + \left[(4\pi y)^{1/\alpha} \frac{\Gamma\left(\frac{1}{\alpha}\right)[\Gamma(1+\alpha)]^{1/\alpha}}{2\Gamma\left(\frac{2}{\alpha}\right)\left[\Gamma\left(1+\frac{\alpha}{2}\right)\right]^{2/\alpha}}\right]^\beta\right)^{-1/\beta}, \tag{33}$$

where β is an adjustable parameter. For an empirical value $\beta=\alpha/1.5$, the Padé approximation is accurate within 10%. Figure 2 presents $T_{3,\alpha}(0,y)$ as a function of $y=\rho R^3$ for $\alpha=1$ (normal diffusion) and $\alpha=2/3$ (subdiffusion). The asymptotic formulas (31) and (32) and the Padé approximation [Eq. (33)] are shown for comparison. It is worth stressing that the Padé formula (33) is an empirical approximation. At the same time, this approximation correctly describes, both qualitatively and quantitatively, the behavior of the mean MPST. For practical purposes, it helps to avoid a numerical computation of the integral in Eq. (30).

Note that for normal diffusion ($\alpha=1$), the Mittag–Leffler function $E_{1/2}(z)$ can be written in terms of the complementary error function $\mathrm{erfc}(z)$ as $E_{1/2}(z)=e^{z^2}\,\mathrm{erfc}(-z)$, from which one gets an explicit form

$$T_{3,1}(0,y) = 1 - \sqrt{4\pi y}\, e^{4y}\, \mathrm{erfc}(2\sqrt{y}).$$

2. Partially reactive target

For a partially reactive target ($\Lambda>0$ or $x>0$), four asymptotic regimes with small/large values of x and y can be distinguished. Since $T_{3,\alpha}(x,y)$ has a finite limit as $x\to 0$, the behavior for small x is similar to that for $x=0$ from the previous subsection. For large x, one obtains

$$T_{3,\alpha}(x,y) \simeq x^{1/\alpha}. \tag{34}$$

This asymptotic result is also valid for any $x>0$ in the limit $y\to\infty$. Figure 3 shows $T_{3,\alpha}(x,y)$ for $\alpha=1$ and $\alpha=2/3$ and its asymptotic behavior at large x.

A Padé approximation between small and large values of x reads as

$$T_{3,\alpha}(x,y) \simeq T_{3,\alpha}(0,y)\left(1 + \left[\frac{x^{1/\alpha}}{T_{3,\alpha}(0,y)}\right]^\beta\right)^{1/\beta}. \tag{35}$$

The adjustable parameter β may depend on α and the second variable y. Numerical computations show that β is close to α

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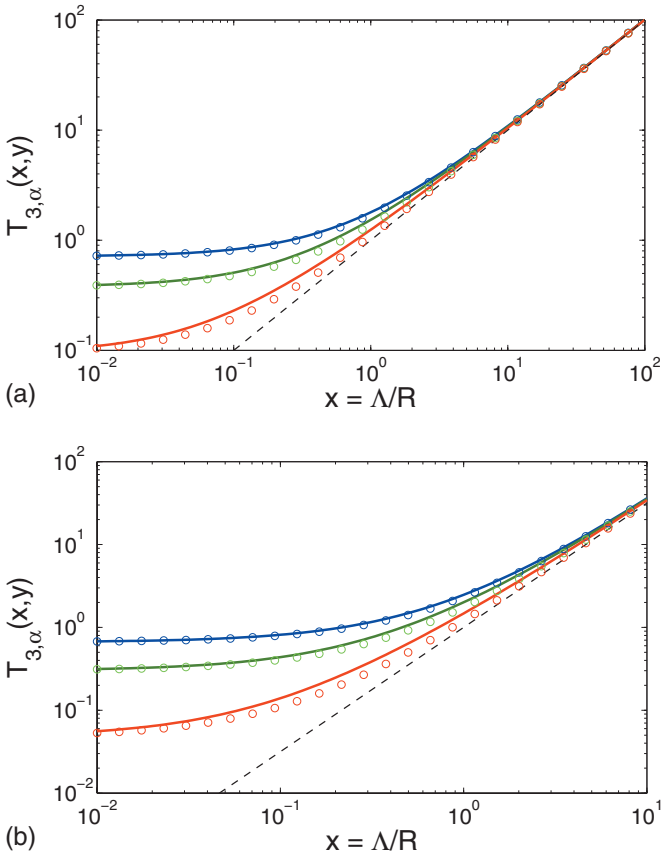

FIG. 3. The function $T_{3,\alpha}(x,y)$ for $\alpha=1$ (top plot) and $\alpha=2/3$ (bottom plot) with $y=0.01$ (top curve in blue), $y=0.1$ (middle curve in green), and $y=1$ (bottom curve in red). The asymptotic behavior [Eq. (34)] at large x is shown by dashed line, and the Padé approximation [Eq. (35)] with $\beta=\alpha$ is shown by circles.

for small y and then β slowly decreases with an increase of y. We stress again that the Padé formula (35) is merely a convenient empirical approximation. For $\beta=\alpha=1$, the function $T_{3,1}(x,y)$ is simply approximated by the sum of $T_{3,1}(0,y)$ and $x=\Lambda/R$ which can be interpreted as contributions to the mean search time from two search stages, namely, detection and recognition of the target. A similar result was reported for the exit time from a spherical domain.[61]

C. Other dimensions

The asymptotic behavior of the mean MPST in the limit of large density ρ can be derived for any d. In this limit, the contribution to the integral in Eq. (25) comes from small times t so that the asymptotic formula (16) for $f_d(t)$ can be used to obtain

$$\langle \tau_d^{\mathrm{m}} \rangle \simeq \begin{cases} \dfrac{\Gamma\left(1+\frac{2}{\alpha}\right)\left[\Gamma\left(1+\frac{\alpha}{2}\right)\right]^{2/\alpha}}{(S_d\sqrt{D_\alpha}\rho R^{d-1})^{2/\alpha}} & (\Lambda=0), \\ \dfrac{\Gamma\left(1+\frac{1}{\alpha}\right)[\Gamma(1+\alpha)]^{1/\alpha}}{(S_d D_\alpha \rho R^{d-1}/\Lambda)^{1/\alpha}} & (\Lambda>0). \end{cases} \tag{36}$$

For smaller α, the mean MPST decreases with ρ *faster*, i.e., slower subdiffusive motion allows for a faster search.

A qualitative explanation of the "paradox" which was mentioned in Sec. III B relies in the short-time asymptotic behavior [Eq. (16)]. If one introduces a time scale t_0 as

$$t_0 = \begin{cases} \left(\dfrac{R}{\sqrt{D_\alpha}}\dfrac{\Gamma\left(1+\frac{\alpha}{2}\right)}{S_d}\right)^{2/\alpha} & (\Lambda=0), \\ \left(\dfrac{\Lambda R}{D_\alpha}\dfrac{\Gamma(1+\alpha)}{S_d}\right)^{1/\alpha} & (\Lambda>0), \end{cases}$$

then $f_d(t)\simeq(t/t_0)^{\alpha/2}$ for $\Lambda=0$ and $f_d(t)\simeq(t/t_0)^{\alpha}$ for $\Lambda>0$. For any fixed time t in the region $t<t_0$, $f_d(t)$ as a function of α is larger for smaller α, while the function $e^{-\rho R^d f_d(t)}$ is smaller for smaller α. The integral of the latter function from 0 to t_0 which provides the major contribution to the mean search time in the high density limit, is smaller for smaller α.

IV. CONCLUSION

A recognition phase was introduced to the classical target search problem through Robin boundary condition on the target boundary. Each time when a target is found, a subdiffusing particle may either "recognize" it and stop the searching process, or leave the target unrecognized and continue to search. The recognition phase may account for a finite reaction rate in many chemical or biochemical reactions. Although the problem is formulated for arbitrary target shape, we focused on spherical targets. The rotation invariance allowed us to derive explicit formulas for the Laplace transform of the probability density $q_\alpha(\mathbf{r},t)$ of the single-particle search time. The short and long-time asymptotic behaviors of this density were analyzed. The mean SPST is known to be infinite.

The situation is different when many independent subdiffusing particles search simultaneously for the same target. We obtained explicit formulas for the probability density of the MPST for subdiffusion in one and three dimensions. We computed the mean multiple-particles search time and studied its dependence on the reaction rate (the length Λ), the density of particles ρ, and the exponent α characterizing subdiffusion. As expected, lower density or smaller reaction rate (larger Λ) lead to a longer search. In turn, in the limit of high density ρ, the particles undergoing slower subdiffusive motion (smaller α) find a target faster. This seemingly paradoxal result can be explained by the short-time asymptotic behavior of the probability density of the MPST.

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[1] A. Szabo, K. Schulten, and Z. Schulten, J. Chem. Phys. 72, 4350 (1980).
[2] G. H. Weiss, J. Stat. Phys. 42, 3 (1986).
[3] H. Sano and M. Tachiya, J. Chem. Phys. 71, 1276 (1979).
[4] M. Tachiya, Radiat. Phys. Chem. 21, 167 (1983).
[5] A. V. Barzykin and M. Tachiya, J. Chem. Phys. 99, 9591 (1993).
[6] M. Coppey, O. Bénichou, R. Voituriez, and M. Moreau, Biophys. J. 87, 1640 (2004).
[7] S. B. Yuste, G. Oshanin, K. Lindenberg, O. Bénichou, and J. Klafter, Phys. Rev. E 78, 021105 (2008).
[8] K. Bénichou and V. Sheinman, Phys. Rev. Lett. 103, 138102 (2009).
[9] M. Tolić-Nørrelykke and O. Thon, Phys. Rev. Lett. 93, 078102 (2004).

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[10] M. Weiss, M. Elsner, F. Kartberg, and T. Nilsson, Biophys. J. **87**, 3518 (2004).
[11] I. Golding and E. C. Cox, Phys. Rev. Lett. **96**, 098102 (2006).
[12] J.-P. Bouchaud and A. Georges, Phys. Rep. **195**, 127 (1990).
[13] R. Metzler and J. Klafter, Phys. Rep. **339**, 1 (2000).
[14] G. M. Zaslavsky, Phys. Rep. **371**, 461 (2002).
[15] S. Havlin and D. Ben-Avraham, Adv. Phys. **51**, 187 (2002).
[16] R. Kimmich, Chem. Phys. **284**, 253 (2002).
[17] R. Metzler and J. Klafter, J. Phys. A **37**, R161 (2004).
[18] S. Redner, *A Guide to First-Passage Processes* (Cambridge University Press, Cambridge, England, 2001).
[19] B. D. Hughes, *Random Walks and Random Environments* (Clarendon, Oxford, 1995).
[20] D. Holcman, A. Marchewka, and Z. Schuss, Phys. Rev. E **72**, 031910 (2005).
[21] P. E. Levitz, D. S. Grebenkov, M. Zinsmeister, K. Kolwankar, and B. Sapoval, Phys. Rev. Lett. **96**, 180601 (2006).
[22] S. Condamin, O. Bénichou, and M. Moreau, Phys. Rev. Lett. **95**, 260601 (2005).
[23] S. Condamin, O. Bénichou, and M. Moreau, Phys. Rev. E **72**, 016127 (2005).
[24] S. Condamin, O. Bénichou, V. Tejedor, R. Voituriez, and J. Klafter, Nature (London) **450**, 77 (2007).
[25] D. S. Grebenkov, Phys. Rev. E **76**, 041139 (2007).
[26] R. C. Lua and A. Y. Grosberg, Phys. Rev. E **72**, 061918 (2005).
[27] S. B. Yuste and K. Lindenberg, Phys. Rev. E **76**, 051114 (2007).
[28] S. Condamin, O. Bénichou, and J. Klafter, Phys. Rev. Lett. **98**, 250602 (2007).
[29] S. Condamin, V. Tejedor, R. Voituriez, O. Bénichou, and J. Klafter, Proc. Natl. Acad. Sci. U.S.A. **105**, 5675 (2008).
[30] F. C. Collins and G. E. Kimball, J. Colloid Sci. **4**, 425 (1949).
[31] B. Sapoval, Phys. Rev. Lett. **73**, 3314 (1994).
[32] D. S. Grebenkov, in *Focus on Probability Theory*, edited by L. R. Velle (Nova Science Publishers, New York, 2006), pp. 135–169.
[33] A. Singer, Z. Schuss, A. Osipov, and D. Holcman, SIAM J. Appl. Math. **68**, 844 (2008).
[34] D. S. Grebenkov, M. Filoche, and B. Sapoval, Phys. Rev. E **73**, 021103 (2006).
[35] M. Filoche and B. Sapoval, Eur. Phys. J. B **9**, 755 (1999).
[36] D. S. Grebenkov, M. Filoche, and B. Sapoval, Eur. Phys. J. B **36**, 221 (2003).
[37] M. Felici, M. Filoche, C. Straus, T. Similowski, and B. Sapoval, Respir. Physiol. Neurbiol. **145**, 279 (2005).
[38] D. S. Grebenkov, Fractals **14**, 231 (2006).
[39] D. S. Grebenkov, Rev. Mod. Phys. **79**, 1077 (2007).
[40] J. M. Schurr, Biophys. J. **10**, 717 (1970).
[41] G. Seisenberger, M. U. Ried, T. Endres, H. Büning, M. Hallek, and C. Bräuchle, Science **294**, 1929 (2001).
[42] T. Chou and M. R. D'Orsogna, J. Chem. Phys. **127**, 105101 (2007).
[43] G. Wilemski and M. Fixman, J. Chem. Phys. **58**, 4009 (1973).
[44] D. Holcman and Z. Schuss, J. Chem. Phys. **122**, 114710 (2005).
[45] K. R. Brownstein and C. E. Tarr, Phys. Rev. A **19**, 2446 (1979).
[46] E. Barkai, R. Metzler, and J. Klafter, Phys. Rev. E **61**, 132 (2000).
[47] E. Barkai, Phys. Rev. E **63**, 046118 (2001).
[48] M. M. Meerschaert and H.-P. Scheffler, J. Appl. Probab. **41**, 623 (2004).
[49] S. G. Samko, A. A. Kilbas, and O. I. Marichev, *Fractional Integrals and Derivatives: Theory and Applications* (Gordon and Breach, Amsterdam, 1993).
[50] A. A. Kilbas, H. M. Srivastava, and J. J. Trujillo, *Theory and Applications of Fractional Differential Equations*, Mathematics Studies Series, Vol. 204 (Elsevier, Amsterdam, 2006).
[51] K. Seki, M. Wojcik, and M. Tachiya, J. Chem. Phys. **119**, 2165 (2003).
[52] J. D. Eaves and D. R. Reichman, J. Phys. Chem. B **112**, 4283 (2008).
[53] J. Sung and R. J. Silbey, Phys. Rev. Lett. **91**, 160601 (2003).
[54] M. A. Lomholt, I. M. Zaid, and R. Metzler, Phys. Rev. Lett. **98**, 200603 (2007).
[55] A. N. Borodin and P. Salminen, *Handbook of Brownian Motion: Facts and Formulae* (Birkhauser Verlag, Berlin, 1996).
[56] M. E. Muller, Ann. Math. Stat. **27**, 569 (1956).
[57] L. H. Zheng and Y. C. Chiew, J. Chem. Phys. **90**, 322 (1989).
[58] S. B. Lee, I. C. Kim, C. A. Miller, and S. Torquato, Phys. Rev. B **39**, 11833 (1989).
[59] D. S. Grebenkov, Phys. Rev. Lett. **95**, 200602 (2005).
[60] D. S. Grebenkov, A. A. Lebedev, M. Filoche, and B. Sapoval, Phys. Rev. E **71**, 056121 (2005).
[61] D. S. Grebenkov, "Subdiffusion in a bounded domain with a partially absorbing/reflecting boundary," Phys. Rev. E (in print).

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