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Temporal disorder as a mechanism for spatially heterogeneous diffusion

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A fundamental issue in analyzing diffusion in heterogeneous media is interpreting the space dependence of the associated diffusion coefficient. This reflects the well-known Ito-Stratonovich dilemma for continuous stochastic processes with multiplicative noise. In order to resolve this dilemma it is necessary to introduce additional constraints regarding the underlying physical system. Here we introduce a mechanism for generating nonlinear Brownian motion based on a form of temporal disorder. Motivated by switching processes in molecular biology, we consider a Brownian particle that randomly switches between two distinct conformational states with different diffusivities. In each state the particle undergoes normal diffusion (additive noise) so there is no ambiguity in the interpretation of the noise. However, if the switching rates depend on position, then in the fast-switching limit one obtains Brownian motion with a space-dependent diffusivity. We show that the resulting multiplicative noise process is of the Ito form. In particular, we solve a first-passage time problem for finite switching rates and show that the mean first-passage time reduces to the Ito version in the fast-switching limit.

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Introduction. A fundamental issue in the theory of continuous stochastic process is how to interpret a stochastic differential equation (SDE) with multiplicative noise, for which the noise term explicitly depends on the state of the system [1,2]. This could arise, for example, in the case of nonlinear Brownian motion where the diffusivity depends on position. The interpretation of multiplicative noise is ambiguous due to the subtleties of stochastic integration, and the associated distinction between Ito and Stratonovich versions of stochastic calculus [3–5]. The different interpretations of multiplicative noise result in different versions of the corresponding Fokker-Planck (FP) equation, which describes the evolution of the distribution of sample paths. In order to select the appropriate version, additional physical constraints are required. For example, consistency of nonlinear Brownian motion with equilibrium statistical physics yields the so-called kinetic interpretation [6–8], whereas taking the white noise limit of a particle driven by colored noise generates the Stratonovich version [1]. Although this long-standing controversy appeared to be settled, there has been a recent revival of interest due to major advances in single-particle tracking experiments. One set of experiments involves the motion of a colloidal particle near a wall, where hydrodynamic interactions lead to spatial variations in the diffusion coefficient D [9–11]. The other class of experiments occurs in biophysics, where spatial variations may arise from the surrounding cellular medium or from conformational changes in the diffusing species [12–16].

In this Rapid Communication, we introduce an alternative mechanism for generating nonlinear Brownian motion based on temporal rather than spatial disorder. The basic idea is to consider a Brownian particle that randomly switches between two distinct conformational states with different diffusivities. (This type of switching is prevalent in cell biology [16,17].) In each state the particle undergoes normal diffusion (additive noise) so there is no ambiguity in the interpretation of the noise. However, if the switching rates depend on position, then in the fast-switching limit one obtains Brownian motion with a space-dependent diffusivity of the Ito form. We first show this by carrying out an adiabatic reduction of the underlying Chapman-Kolomogorov (CK) equation to obtain an Ito version of the FP equation. We then check numerically that the stationary density of the full model reduces to the stationary density of the FP equation in the fast-switching limit. One potential limitation of the adiabatic reduction is that it generates a singular partial differential equation in the fast-switching limit. Moreover, it does not give any indication of how statistical quantities of interest such as mean first-passage times (MFPTs) behave for large but finite switching rates. Therefore, we solve a first-passage time problem for the full model and determine how the MFPT converges to the Ito version in the fast-switching limit, with the latter recently calculated elsewhere [18].

Brownian motion with spatial disorder. Consider a Brownian particle diffusing in a one-dimensional (1D) domain of length L. The position of the particle $X(t)$ satisfies the SDE

$$dX(t) = \sqrt{2D(x)}dW(t), \tag{1}$$

where $D(x)$ is a position-dependent diffusivity and $W(t)$ is a Wiener process with $\langle dW(t)\rangle = 0$ and $\langle dW(t)dW(t')\rangle = \delta(t-t')dt\,dt'$. The particular example of a piecewise constant diffusivity is shown in Fig. 1(a), with $D(x) = D_{\mathrm{I}}$ for $x \in [0,l]$ and $D(x) = D_{\mathrm{II}}$ for $x \in (l,L]$. Ambiguity in the interpretation of the SDE is reflected by the form of the corresponding FP equation for the probability density $p(x,t) = p(x,t|x_0,0)$ with x_0 fixed:

$$\frac{\partial p(x,t)}{\partial t} = -\frac{\partial J(x,t)}{\partial x} = \frac{\partial}{\partial x}\left[D(x)^{\mu}\frac{\partial D(x)^{1-\mu}p(x,t)}{\partial x}\right] \tag{2}$$

for $0 \leqslant \mu \leqslant 1$. The particular choices $\mu = 0,1/2,1$ correspond, respectively, to the Ito, Stratonovich, and kinetic interpretations [3–5,18]. In the case of the piecewise constant diffusivity shown in Fig. 1(a), the associated probability flux $J(x,t)$ is continuous across the interior junction $x = l$, for all values of μ. On the other hand, $p(x,t)$ is only continuous when $\mu = 1$, while $D(x)p(x,t)$ and $\sqrt{D(x)}p(x,t)$ are continuous when $\mu = 0$ and $\mu = 1/2$, respectively. Suppose that Eq. (2) is supplemented by an absorbing boundary condition at $x = 0$ and a reflecting boundary condition at $x = L$: $p(0,t) = 0$, $J(L,t) = 0$. Following the recent analysis of first-passage

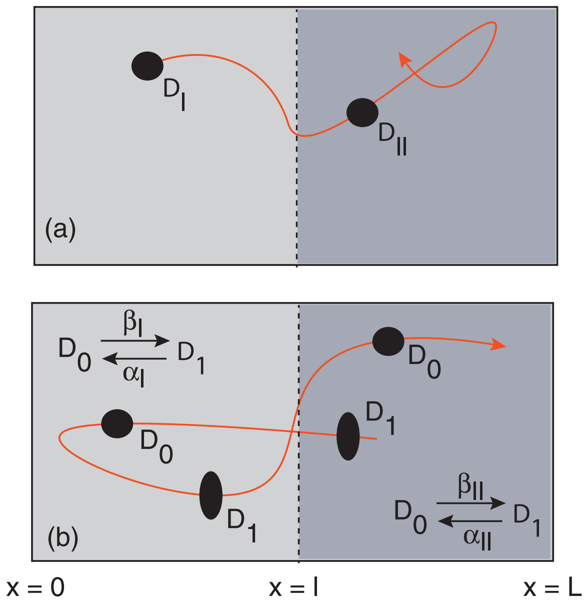

FIG. 1. Brownian motion that is heterogeneous with respect to the x coordinate, $0 \leqslant x \leqslant L$. (a) Example of spatially inhomogeneous diffusion, in which the domain is partitioned into two subdomains with different diffusivities $D_{\rm I}, D_{\rm II}$. (b) Example of temporal disorder where a Brownian particle randomly switches between two conformational states $n = 0,1$ with different diffusivities D_n. The switching rates differ in the two domains.

times in d-dimensional heterogeneous media [18], the choice of μ has a significant effect on the MFPT to be absorbed at $x = 0$.

Let $\tau(x_0)$ denote the MFPT to reach the absorbing boundary at $x = 0$, given that $X(0) = x_0$. One way to calculate the MFPT is to Laplace transform the FP equation (2) and determine the moments of the resulting flux through $x = 0$. Here we briefly describe an alternative approach based on the analysis of residence times [18,19]. Introduce the mean residence time $\tau_k(x_0), k = {\rm I,II}$ according to

$$\tau_k(x_0) = \int_{\Sigma_k} dx \int_0^\infty dt\; p(x,t|x_0,0), \tag{3}$$

with $\Sigma_{\rm I} = [0,l]$ and $\Sigma_{\rm II} = (l,L]$. The MFPT can then be expressed as the sum over the mean residence times in the different subintervals,

$$\tau(x_0) = \sum_{k={\rm I,II}} \tau_k(x_0). \tag{4}$$

Integrating Eq. (2) and using the reflecting boundary condition at $x = L$ shows that

$$J(x,t) = \int_x^L dx' \frac{\partial p(x',t)}{\partial t}.$$

Substituting the explicit expression for J and integrating with respect to x gives

$$p(x,t) = -\frac{1}{D(x)^{1-\mu}} \int_0^L \frac{dy}{D(y)^\mu} \int_y^L dx' \frac{\partial p(x',t)}{\partial t}.$$

Inserting this into Eq. (3) with the initial condition $p(x,0) = \delta(x - x_0)$ finally gives

$$\tau_k(x_0) = \int_{\Sigma_k} \frac{dz}{D(z)^{1-\mu}} \int_0^z \frac{dy}{D(y)^\mu} \Theta(x_0 - y). \tag{5}$$

The integrals can be evaluated explicitly: we find that

$$\tau_{\rm I}(x_0) = \begin{cases} \left[2lx_0 - x_0^2\right]/2D_{\rm I}, & \text{if } x_0 \in [0,l), \\ l^2/2D_{\rm I}, & \text{if } x_0 \in (l,L], \end{cases} \tag{6a}$$

and

$$\tau_{\rm II}(x_0) = \begin{cases} \dfrac{x_0(L-l)}{D_{\rm I}^\mu D_{\rm II}^{1-\mu}}, \text{ if } x_0 \in [0,l) \\ \dfrac{(L-l)l}{D_{\rm I}^\mu D_{\rm II}^{1-\mu}} + \dfrac{(2L - x_0 - l)(x_0 - l)}{2D_{\rm II}}, \\ \quad \text{if } x_0 \in (l,L]. \end{cases} \tag{6b}$$

As found in more general cases [18], only the residence time further away from the absorbing boundary depends on the parameter μ.

Brownian motion with temporal disorder. We now turn to an alternative formulation of heterogeneous Brownian motion based on temporal disorder [see Fig. 1(b)]. We assume that the Brownian particle switches between two conformational states labeled $n = 0,1$ according to a two-state jump Markov process $N(t) \in \{0,1\}$, with $0 \underset{\alpha}{\overset{\beta}{\rightleftharpoons}} 1$. The diffusion coefficient is taken to depend on the conformational state, that is, $D = D_n$ when $N(t) = n$. Thus, we are replacing the spatial heterogeneity in the diffusion coefficient considered in Fig. 1(a) by a temporal heterogeneity. Since the stochastic process is now additive, we no longer have to worry about the particular interpretation of the corresponding hybrid SDE,

$$dX(t) = \sqrt{2D_n}dW(t) \qquad \text{for } N(t) = n. \tag{7}$$

Given the joint Markov process $[N(t),X(t)]$ and the initial conditions $X(0) = X_0$, $N(0) = n_0$, introduce the probability density $p_n(x,t|x_0,n_0,0)$ that the particle is at $X(t) = x$ and in conformational state $N(t) = n$ at time t. The probability density p evolves according to the forward differential CK equation [1,17]

$$\frac{\partial p_n(x,t)}{\partial t} = D_n \frac{\partial^2 p_n(x,t)}{\partial x^2} + \sum_{m=0,1} A_{nm}(x) p_m(x,t), \tag{8}$$

(after dropping the explicit dependence on initial conditions). Here $\mathbf{A}(x)$ is the matrix generator

$$\mathbf{A}(x) = \begin{pmatrix} -\beta(x) & \alpha(x) \\ \beta(x) & -\alpha(x) \end{pmatrix},$$

and we have allowed for the possibility that the transition rates α,β are position dependent. Note, however, that this spatial heterogeneity does not result in multiplicative noise, at least in the case of finite switching rates. If x were fixed at some value x_*, then the resulting discrete Markov process for $p_n(t) = p_n(x_*,t)$ would have a unique stationary distribution $\rho_n(x_*)$ with $p_n(t) \to \rho_n(x_*)$ in the limit $t \to \infty$ and

$$\rho_0(x) = \frac{\alpha(x)}{\alpha(x) + \beta(x)}, \qquad \rho_1(x) = 1 - \rho_0(x). \tag{9}$$

Consider the averaged diffusion coefficient

$$\overline{D}(x) = \sum_{n=0,1} \rho_n(x) D_n. \tag{10}$$

Intuitively speaking, one would expect the hybrid SDE (7) to reduce to the SDE

$$dX(t) = \sqrt{2\overline{D}(x)}dW(t) \tag{11}$$

in the fast-switching limit $\alpha(x),\beta(x) \to \infty$. For the Markov chain then undergoes many jumps over a small time interval Δt during which $\Delta x \approx 0$, and thus the relative frequency of the two discrete states n is approximately $\rho_n(x)$. This suggests that temporal disorder can lead to spatially heterogeneous diffusion. In order to determine the correct interpretation of the resulting multiplicative noise process, we carry out a quasi-steady state or adiabatic reduction of the CK equation (8). The first step is to fix the time scale by setting $\tau \equiv \min_n\{L^2/D_n\} = 1$. The fast-switching limit can be implemented by rescaling the transition rates according to $\alpha,\beta \to \alpha/\varepsilon,\beta/\varepsilon$, with $\alpha,\beta = O(1)$, and taking $\varepsilon \to 0$.

For small but nonzero ε, one can use an adiabatic approximation to reduce the CK equation (8) to a corresponding FP equation for the total probability density $p(x,t) = \sum_{n=0,1} p_n(x,t)$ [1,20,21]. The basic steps are as follows. First, decompose the probability density p_n as

$$p_n(x,t) = p(x,t)\rho_n(x) + \varepsilon w_n(x,t),$$

where $\sum_n w_n(x,t) = 0$. Substituting this decomposition into Eq. (8), summing both sides with respect to n, and using $\sum_n A_{nm}(x) = 0$ yields an equation for p,

$$\frac{\partial p}{\partial t} = \frac{\partial^2 \overline{D}(x)p}{\partial x} + \varepsilon \sum_{n=0,1} D_n \frac{\partial^2 w_n}{\partial x^2}. \tag{12}$$

Next we use Eq. (12) to eliminate $\partial p/\partial t$ in the expanded version of Eq. (8). Introducing the asymptotic expansion $w_n \sim w_n^{(0)} + \varepsilon w_n^{(1)} + O(\varepsilon^2)$ and collecting the $O(1)$ terms then yields an equation for $w_n^{(0)}$, which has a unique solution on imposing the condition $\sum_n w_n^{(0)}(x,t) = 0$. Finally, setting $w_n = w_n^{(0)}$ in Eq. (12) shows that to $O(\varepsilon)$, p evolves according to the fourth-order equation

$$\frac{\partial p}{\partial t} = \frac{\partial^2}{\partial x^2}[\overline{D}(x)p] + \varepsilon \frac{\partial^2}{\partial x^2}\left(\sum_m B_m(x)\frac{\partial^2 \rho_m(x)p}{\partial x^2}\right) + \varepsilon \frac{\partial^2}{\partial x^2}\left(C(x)\frac{\partial^2 \overline{D}(x)p}{\partial x^2}\right) \tag{13}$$

with $B_m(x) = \sum_{n=0,1} D_n A^\dagger_{nm}(x) D_m$ and $C(x) = \sum_{n,m=0,1} D_n A^\dagger_{nm}(x)\rho_m(x)$. Here $\mathbf{A}^\dagger$ is the pseudoinverse of $\mathbf{A}$. It follows that in the fast-switching limit $\varepsilon \to 0$, the CK equation (8) reduces to an FP equation of the Ito form with effective space-dependent diffusivity $\overline{D}(x)$. We illustrate convergence to the Ito form in Fig. 2 by plotting the stationary density for different choices of $\alpha(x)$ and $\beta(x)$.

It is clear from the above analysis that the fast-switching limit is singular due to the presence of the fourth-order terms in Eq. (13). Therefore, we further investigate this limit by calculating the MFPT to be absorbed at $x = 0$ in the special case of finite, piecewise constant transition rates: $\alpha(x),\beta(x) = \alpha_{\rm I},\beta_{\rm I}$ for $x \in [0,l]$ and $\alpha(x),\beta(x) = \alpha_{\rm II},\beta_{\rm II}$ for $x \in (l,L]$. It follows from Eq. (10) that $\overline{D}(x)$ reduces to the piecewise diffusion coefficient of Fig. 1(a), with

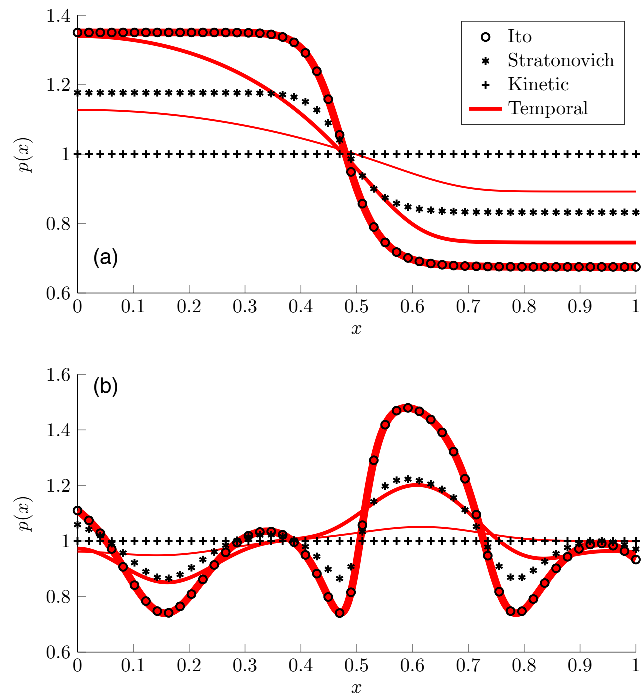

FIG. 2. Equilibrium probability density for heterogeneous Brownian motion in the unit interval. The temporal disorder density converges in the fast-switching limit to the spatial disorder density with an Ito interpretation rather than Stratonovich or kinetic. The red curves were found by numerically solving Eq. (8) at steady state, with thicker curves for smaller values of ε. The black markers were found by numerically solving Eq. (2) at steady state for $\mu = 0$, 1/2, or 1. (a) $D_0 = 1$ and $D_1 = 2$ and the switching rates for the red curves are $\alpha(x) = 1/2^{15}$ and $\beta(x) = x^{15}$ so that ρ_0,ρ_1 in Eq. (9) are Hill functions. The diffusion coefficient for the black markers is the corresponding $\overline{D}(x)$ in Eq. (10). (b) $D_0 = 1$ and $D_1 = 2$ and the switching rates for the red curves are $\alpha(x) = \cos(x/0.05) + 1$ and $\beta(x) = \sin(x/0.125) + 1$. The diffusion coefficient for the black markers is the corresponding $\overline{D}(x)$ in Eq. (10).

$$D_{\rm I} = \frac{\alpha_{\rm I} D_0 + \beta_{\rm I} D_1}{\alpha_{\rm I} + \beta_{\rm I}}, \quad D_{\rm II} = \frac{\alpha_{\rm II} D_0 + \beta_{\rm II} D_1}{\alpha_{\rm II} + \beta_{\rm II}}. \tag{14}$$

We wish to determine how it converges to the MFPT $\tau(x_0) = \tau_{\rm I}(x_0) + \tau_{\rm II}(x_0)$, with the residence times given by Eqs. (6a) and (6b) in the limit $\varepsilon \to 0$, and if it is consistent with the Ito form ($\mu = 0$).

Calculation of MFPT for temporal disorder. Introduce the survival probability

$$S_m(x_0,t) = \sum_{n=0,1} \int_0^L p(x,n,t|x_0,m,0)dx.$$

Introducing the corresponding FPT density $f_m(x_0,t) = -dS_m(x_0,t)/dt$, we can define the conditional MFPT $\tau_m(x_0)$ as $\tau_m(x_0) = \int_0^\infty t f_m(x_0,t)dt = \int_0^\infty S_m(x_0,t)dt$. Using the backward CK equation for $q_m(x_0,t) = p(n,x,t|x_0,m,t)$ one finds that

$$D_m \frac{d^2\tau_m(x_0)}{dx^2} + \frac{1}{\varepsilon}\sum_{n=0,1} A_{nm}(x_0)\tau_n(x_0) = -1. \tag{15}$$

The boundary conditions are $\tau_m(0) = 0$ and $\tau_m'(L) = 0$. We wish to solve Eq. (15) for the piecewise constant transition rates illustrated in Fig. 1(b), for which Eq. (15) takes the explicit form

$$D_0\tau_0''(x_0) + \frac{\beta_k}{\varepsilon}[\tau_1(x_0) - \tau_0(x_0)] = -1 \tag{16a}$$

$$D_1\tau_1''(x_0) + \frac{\alpha_k}{\varepsilon}[\tau_0(x_0) - \tau_1(x_0)] = -1, \quad x_0 \in \Sigma_k \tag{16b}$$

for $k = \mathrm{I,II}$. It is convenient to rewrite these equations in terms of the sums and differences $\Delta = \tau_0 - \tau_1$ and $S = \tau_0 + \tau_1$:

$$\Delta''(x_0) - \frac{\Gamma_k^+}{\varepsilon}\Delta(x_0) = -\gamma_-, \tag{17a}$$

$$S''(x_0) - \frac{\Gamma_k^-}{\varepsilon}\Delta(x_0) = -\gamma_+, \qquad x \in \Sigma_k, \tag{17b}$$

where

$$\Gamma_k^{\pm} = \frac{D_1\beta_k \pm D_0\alpha_k}{D_0 D_1}, \qquad \gamma_{\pm} = \frac{D_1 \pm D_0}{D_0 D_1}.$$

We can now proceed by first solving for $\Delta(x_0)$ and then $S(x_0)$. In the interval $x_0 \in [0,l)$ we find that

$$\Delta_{\mathrm{I}}(x_0) = \left[\left(A - \frac{\varepsilon\gamma_-}{\Gamma_{\mathrm{I}}^+}\right)e^{\lambda_{\mathrm{I}}x_0} - Ae^{-\lambda_{\mathrm{I}}x_0}\right] + \frac{\varepsilon\gamma_-}{\Gamma_{\mathrm{I}}^+}, \tag{18a}$$

$$S_{\mathrm{I}}(x_0) = \frac{\Gamma_{\mathrm{I}}^-}{\Gamma_{\mathrm{I}}^+}\left[\left(A - \frac{\varepsilon\gamma_-}{\Gamma_{\mathrm{I}}^+}\right)e^{\lambda_{\mathrm{I}}x_0} - Ae^{-\lambda_{\mathrm{I}}x_0}\right] - \frac{x_0^2}{2D_{\mathrm{I}}} + Bx_0 - \frac{\varepsilon\gamma_-}{\Gamma_{\mathrm{I}}^+}\frac{\Gamma_I^-}{\Gamma_{\mathrm{I}}^+}, \tag{18b}$$

where $\lambda_k \equiv \sqrt{\Gamma_k^+/\epsilon}$ and $\Gamma_k^-\gamma_-/\Gamma_k^+ - \gamma_+ = -D_k^{-1}$ for $k = \mathrm{I,II}$, and we have imposed the boundary conditions $\tau_m(0) = 0$. Similarly, in the interval $x_0 \in (l,L)$,

$$\Delta_{\mathrm{II}}(x_0) = \widehat{A}[e^{\lambda_{\mathrm{II}}x_0} + e^{-\lambda_{\mathrm{II}}x_0}]. \tag{18c}$$

$$S_{\mathrm{II}}(x_0) = \frac{\Gamma_{\mathrm{II}}^-}{\Gamma_{\mathrm{II}}^+}\widehat{A}[e^{\lambda_{\mathrm{II}}x_0} + e^{-\lambda_{\mathrm{II}}x_0}] - \frac{[L-x_0]^2}{2D_{\mathrm{II}}} + \widehat{B}, \tag{18d}$$

where we have imposed the boundary conditions $\tau_m'(L) = 0$. There are four unknown constants $A,\widehat{A},B,\widehat{B}$, which are determined by imposing continuity and flux conservation at $x_0 = l$: $\Delta_{\mathrm{I}}(l) = \Delta_{\mathrm{II}}(l)$, $S_{\mathrm{I}}(l) = S_{\mathrm{II}}(l)$, and $\Delta_{\mathrm{I}}'(l) = \Delta_{\mathrm{II}}'(l)$, $S_{\mathrm{I}}'(l) = S_{\mathrm{II}}'(l)$.

We are particularly interested in the fast-switching limit $\varepsilon \to 0$. In this case, $A \to \varepsilon\gamma_-/\Gamma_I^+ \to 0$ and $\widehat{A} \to 0$ so, to leading order in ε, $\Delta_k(x_0) \sim 0$ for $k = \mathrm{I,II}$, and

$$S_{\mathrm{I}}(x_0) \sim -\frac{x_0^2}{2D_{\mathrm{I}}} + Bx_0, \tag{19a}$$

$$S_{\mathrm{II}}(x_0) \sim -\frac{[L-x_0]^2}{2D_{\mathrm{II}}} + \widehat{B}. \tag{19b}$$

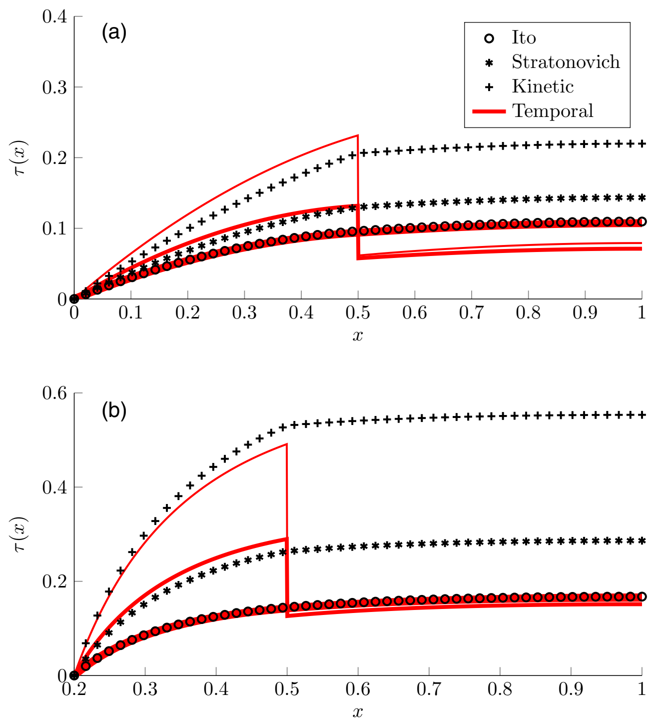

FIG. 3. Mean first-passage time for heterogeneous Brownian motion in (a) 1D and (b) 3D. The temporal disorder MFPT converges in the fast-switching limit to the spatial disorder MFPT with an Ito interpretation rather than Stratonovich or kinetic. (a) The red curves correspond to the analytical solution to Eq. (16), with thicker curves for smaller values of ε. The black markers correspond to Eqs. (6a) and (6b) (with $\mu = 0$, 1/2, or 1). We take $D_0 = 1$, $D_1 = 10$, $L = 1$, $l = 1/2$, $\alpha_{\mathrm{I}} = 10$, $\beta_{\mathrm{I}} = 1$, $\alpha_{\mathrm{II}} = 1$, and $\beta_{\mathrm{II}} = 10$, and D_{I} and D_{II} according to Eq. (10). (b) The plots give the MFPT to reach a ball of radius 0.2 in 3D. The red curves correspond to the analytical solution to the 3D analog of Eq. (16), with thicker curves for smaller values of ε. The black markers correspond to the 3D analog of Eqs. (6a) and (6b) (see [18]). The parameters are the same as the top panel.

If we now impose the boundary conditions at $x_0 = l$, we recover the MFPT of the spatially heterogeneous medium given by Eqs. (6a) and (6b) for $\mu = 0$. We show this convergence in the top panel of Fig. 3.

We can extend this analysis to higher dimensions and calculate the MFPT to reach a ball of radius $\delta > 0$ in the center of the d-dimensional sphere with a reflecting condition at radius $L > \delta$. The only change is the differential operators in Eq. (16) are modified according to $\frac{d^2}{dx^2} \to \frac{d^2}{dx^2} + \frac{d-1}{x}\frac{d}{dx}$, and the absorbing boundary condition is imposed at δ, $\tau_m(\delta) = 0$. Carrying out this calculation shows that this higher-dimensional MFPT with temporal disorder converges in the fast-switching limit to the MFPT with spatial disorder with an Ito interpretation (see [18] for the higher-dimensional MFPTs with spatial disorder). We show this convergence in Fig. 3 for dimension three.

Discussion. We have shown that the natural interpretation of nonlinear Brownian motion in a spatially heterogeneous medium is given by Ito when the underlying heterogeneity arises from a particle rapidly switching between different conformational states with distinct diffusivities. There are a number of examples in molecular biology where switching between different diffusive states can occur. For example, protein receptors undergoing lateral diffusion in the plasma membrane are continually interacting with scaffolding proteins that can significantly alter their mobility [22]. Another example is the intermittent nature of intracellular transport, whereby vesicles switch between ballistic transport mediated by molecular motors moving along cytoskeletal tracks and diffusion in the cytoplasm [23,24]. Our mechanism for spatially heterogeneous diffusion would apply to these cases if the switching rates are relatively fast and are space dependent. Finally, although for simplicity we focused on 1D models and pure diffusion, it would be possible to consider higher-dimensional diffusion and to include drift terms. The reduction of the corresponding d-dimensional CK equation could lead to an FP equation with anisotropic diffusion [25].

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