

Identifying the interpretation in two-dimensional diffusion processes with power-law spatially dependent diffusivity

He-Chuan Liu¹, Rui-Bin Zhong¹, Jun-Feng Zhang¹, Li-Ming Fan², Peng-Cheng Li¹, and Ming-Gen Li^{1,*}

¹Department of Physics, College of Science, *Shantou University*, Shantou, Guangdong 515063, China

²College of Physical Science and Technology, *Shenyang Normal University*, Shenyang 110034, China



(Received 29 October 2025; accepted 26 January 2026; published 9 February 2026)

Heterogeneous diffusion processes (HDPs) are ubiquitous in macromolecules or submicron tracers in biological cells. The Fokker-Planck equation (FPE) provides a fundamental framework for analyzing these diffusion dynamics. However, its formulations for HDPs with spatially dependent diffusivity are not unique, which can lead to potentially divergent dynamical predictions. We investigate three conventional interpretations (Itô, Stratonovich, and Hänggi-Klimontovich) of FPEs describing two-dimensional diffusion processes with power-law spatially dependent diffusivity. Through analytical solutions of time-dependent probability density functions, which are validated by numerical simulations, we reveal significant interpretation-dependent discrepancies in several physical quantities. These include distinct temporal evolution of mean-square displacement (MSD), survival probabilities, and threshold times at which half of the particles reach a set boundary. Furthermore, we demonstrate that the mean of time-averaged MSDs varies across different interpretations, yielding distinct effective diffusion coefficients. This offers a chance to identify the applicable interpretation by comparing theoretical effective diffusion coefficients with those extracted from single-particle tracking experiments. Our findings reveal that the appropriate interpretation could depend on measurement timescales and system's parameters. We believe that these results are helpful for investigating diffusion dynamics in complex heterogeneous environments.

DOI: [10.1103/xz7y-n8w2](https://doi.org/10.1103/xz7y-n8w2)

I. INTRODUCTION

Heterogeneous diffusion processes (HDPs) with spatially dependent diffusivity are ubiquitous in many systems [1–6], such as macromolecular diffusion or submicron tracers in biological cells [7,8]. In such complex systems, the diffusivity is not constant but exhibits spatial variation arising from two primary mechanisms. First, thermodynamic inhomogeneities like temperature gradient fields and viscosity stratification modulate local diffusivity [9,10]. Second, spatial variations of diffusivity emerge from molecular crowding, cytoskeletal confinement in cells, and structural disorder inherent in systems like colloidal suspensions, actin gels, and granular materials [11]. In recent years, much effort has been devoted to investigating HDPs with spatially varying diffusivity in chemical, physical, and biological systems [12–16]. There are two main ways to analyze diffusion dynamics: Langevin stochastic differential equations governing particle trajectories, and deterministic Fokker-Planck equations (FPEs) for the time evolution of probability density functions [17,18]. While they are equivalent for homogeneous systems with

constant diffusivity, the Itô-Stratonovich dilemma arises for heterogeneous media [19–21]. This dilemma reflects that the link between the Langevin equations and FPEs is not unique, and the form of FPE depends on specific interpretation of formal integration of Langevin equation [22–24].

Although the FPE offers a fundamental framework for analyzing diffusion dynamics, the nonuniqueness of its formulations for HDPs potentially prevents getting exact dynamical predictions and leads to misleading conclusions [25–27]. This dilemma is particularly significant in biological contexts like intracellular dynamics [28,29], where the heterogeneous nature of the diffusivity requires careful identification of the FPE form. In this work, we study the role of FPE interpretations for diffusion processes in two-dimensional (2D) heterogeneous landscapes characterized by axisymmetric diffusivity [30],

$$D(x, y) = D_0 \frac{A}{A + x^2 + y^2}, \quad (1)$$

where D_0 fixes the units of the diffusivity and A is a small constant that prevents divergence. At the radial distance $r = 0$, $D(x, y) = D_0$, while for large r the diffusivity exhibits power-law scaling $D(x, y) \sim D_0/r^2$, where $r \equiv \sqrt{x^2 + y^2}$. The functional form has been widely used in studying 2D heterogeneous diffusion processes, which exhibits qualitative agreement with experimentally measured diffusivity trends for small fluorescently labeled proteins in the cytoplasm of mammalian cells (e.g., NLFK/HeLa) [31].

*Contact author: mgli@stu.edu.cn

Published by the American Physical Society under the terms of the *Creative Commons Attribution 4.0 International* license. Further distribution of this work must maintain attribution to the author(s) and the published article's title, journal citation, and DOI.

We investigate three conventional interpretations (Itô, Stratonovich, and Hänggi-Klimontovich [32,33]) of FPEs with diffusivity given by Eq. (1) [34]. By obtaining analytical solutions for the time-dependent probability density function (PDF) under each interpretation, we demonstrate that several physical quantities exhibit significant interpretation dependence. These include the mean-square displacement (MSD), survival probabilities, and threshold times at which half of the particles reach a prescribed boundary. An extensive study has systematically investigated HDPs under various spatially dependent diffusivity [35], providing analytical and numerical solutions for both MSDs and PDFs. Single-particle tracking (SPT) technology [36], which has revolutionized the field of cellular biophysics, provides a potential route to identify the appropriate interpretation [37–39]. Based on recent work by Pacheco-Pozo *et al.*, which established a framework for selecting the interpretation via SPT data in a heterogeneous system with a stepwise diffusion coefficient [28,29], we find that time-averaged MSDs and effective diffusion coefficients vary across different interpretations [40]. This provides a chance to identify the appropriate interpretation through direct comparison between theoretical effective diffusion coefficients with those obtained from SPT data. Our analysis reveals that the appropriate interpretation could depend on the measurement timescale and the system's parameters.

The paper is organized as follows: Section II revisits the nonuniqueness of FPEs for two-dimensional HDPs with spatially dependent diffusivity and presents numerical algorithms of stochastic dynamics for various interpretations. In Sec. III, we present the analytical solutions for the time-dependent PDF under each interpretation, verified by numerical results. Several physical quantities are also compared here. Here, we also show the interpretation-dependent variations in the mean of time-averaged MSDs and establish a framework for determining the appropriate interpretation from experimental datasets. The final section presents our conclusions.

II. MODEL

A. Nonunique formulations of FPE for HDP

Diffusion in 2D heterogeneous landscapes is commonly modeled by the Langevin equations with spatially dependent diffusivity [41]:

$$\frac{dx(t)}{dt} = \sqrt{2D(x, y)}\xi_x(t), \quad \frac{dy(t)}{dt} = \sqrt{2D(x, y)}\xi_y(t), \quad (2)$$

where ξ_x and ξ_y are independently white Gaussian noise with $\langle \xi_i(t_1)\xi_j(t_2) \rangle = \delta_{ij}\delta(t_1 - t_2)$ ($i, j = x, y$). The diffusivity $D(x, y)$ varies depending on the particles' position, as illustrated in Fig. 1. Note that in physical units we have $[D(r)] = [D_0/r^2] = \mu\text{m}^2\text{s}^{-1}$. While the corresponding FPE provides a powerful framework for analyzing diffusion dynamics [17,42], its formulation for heterogeneous diffusion is nonunique. This ambiguity arises from different interpretations of the stochastic integral defining particle displacement over $[t_i, t_{i+1}]$, which is $I_n(t_i, t_{i+1}) \equiv \int_{t_i}^{t_{i+1}} \sqrt{2D(x(t), y(t))}\xi_n(t)dt$ with $n \equiv (x, y)$. There are three conventional interpretations of the integration, which are

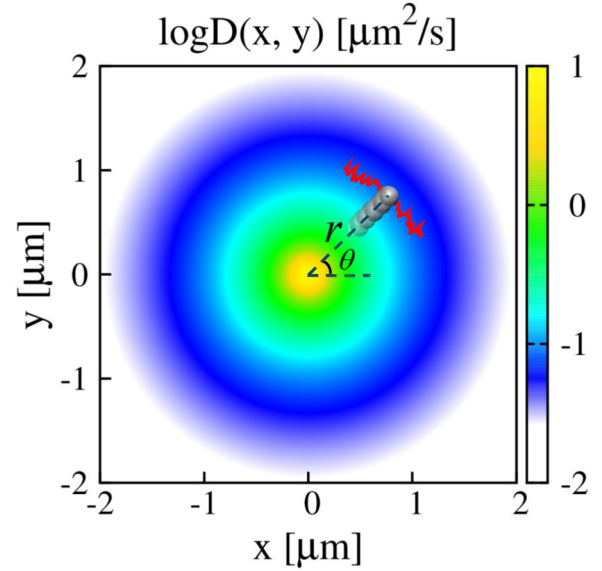


FIG. 1. Schematic diagram of particle (indicated in gray dots) moving in 2D heterogeneous diffusivity landscape (logarithmic scale), driven by random noise (indicated in red arrows). The parameter settings used are $D_0 = 10 \mu\text{m}^4/\text{s}$ and $A = 0.01$.

given by

$$\begin{aligned} I_n(t_i, t_{i+1}) &\simeq \sqrt{2D(x(t_i), y(t_i))} \int_{t_i}^{t_{i+1}} \xi_n(s)ds \quad (\text{I}), \\ &\times \sqrt{2D\left(\frac{x(t_i) + x(t_{i+1})}{2}, \frac{y(t_i) + y(t_{i+1})}{2}\right)} \\ &\times \int_{t_i}^{t_{i+1}} \xi_n(s)ds \quad (\text{S}), \\ &\times \sqrt{2D(x(t_{i+1}), y(t_{i+1}))} \int_{t_i}^{t_{i+1}} \xi_n(s)ds \quad (\text{HK}). \end{aligned} \quad (3)$$

These interpretations correspond to evaluating $D(x, y)$ at different points when the particle moves during the infinitesimal time step. Specifically, Itô's description (I) uses the value at the beginning of the time step and Stratonovich's one (S) takes the value of the average at the initial and end points, but Hänggi-Klimontovich's interpretation (HK) uses the value at the end of the time step.

After a straightforward derivation, the corresponding FPE can be written as

$$\begin{aligned} \frac{\partial P(x, y, t)}{\partial t} &= \sum_{i=1}^2 \frac{\partial}{\partial x_i} \left\{ D^\alpha(x, y) \frac{\partial}{\partial x_i} \right. \\ &\times [D^{1-\alpha}(x, y)P(x, y, t)] \left. \right\} \quad (x_1 \equiv x; x_2 \equiv y), \end{aligned} \quad (4)$$

with $\alpha = 0, 0.5, 1$ for the Itô, Stratonovich, and Hänggi-Klimontovich interpretations (this assignment is adhered to hereon after), and $P(x, y, t)$ denotes the time-dependent PDF of the particle's position (x, y) at time t . Under polar

coordinate transformation, $x = r \cos \theta$, $y = r \sin \theta$, where r represents the distance from the origin and θ the angle (see Fig. 1), one has

$$\frac{\partial^2 f}{\partial x^2} + \frac{\partial^2 f}{\partial y^2} = \frac{\partial^2 f}{\partial r^2} + \frac{1}{r} \frac{\partial f}{\partial r} + \frac{1}{r^2} \frac{\partial^2 f}{\partial \theta^2}, \quad (5)$$

$$\frac{\partial f}{\partial x} \frac{\partial g}{\partial x} + \frac{\partial f}{\partial y} \frac{\partial g}{\partial y} = \frac{\partial f}{\partial r} \frac{\partial g}{\partial r} + \frac{1}{r^2} \frac{\partial f}{\partial \theta} \frac{\partial g}{\partial \theta}, \quad (6)$$

where f and g are arbitrary functions. For $\alpha = 0$ (the Itô interpretation), Eq. (4) reads

$$\frac{\partial P(x, y, t)}{\partial t} = \left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} \right) [D(x, y)P(x, y, t)]. \quad (7)$$

By using equality (5), Eq. (7) in polar coordinates is given by

$$\begin{aligned} \frac{\partial P(r, \theta, t)}{\partial t} &= \frac{1}{r} \frac{\partial}{\partial r} \left\{ r \frac{\partial}{\partial r} [D(r)P(r, \theta, t)] \right\} \\ &+ \frac{1}{r^2} \frac{\partial^2}{\partial \theta^2} [D(r)P(r, \theta, t)]. \end{aligned} \quad (8)$$

Under axial symmetry ($\partial P(r, \theta, t)/\partial \theta = 0$), we get

$$\frac{\partial P(r, t)}{\partial t} = \frac{1}{r} \frac{\partial}{\partial r} \left\{ r \frac{\partial}{\partial r} [D(r)P(r, t)] \right\}. \quad (9)$$

For $\alpha = 0.5$, Eq. (4) in Stratonovich interpretation is expressed as

$$\begin{aligned} \frac{\partial P(x, y, t)}{\partial t} &= \frac{\partial \sqrt{D(x, y)}}{\partial x} \frac{\partial [\sqrt{D(x, y)}P(x, y, t)]}{\partial x} \\ &+ \frac{\partial \sqrt{D(x, y)}}{\partial y} \frac{\partial [\sqrt{D(x, y)}P(x, y, t)]}{\partial y} \\ &+ \sqrt{D(x, y)} \left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} \right) [\sqrt{D(x, y)}P(x, y, t)]. \end{aligned} \quad (10)$$

With equalities (5) and (6), Eq. (10) is rewritten by

$$\begin{aligned} \frac{\partial P(r, \theta, t)}{\partial t} &= \frac{1}{r} \frac{\partial}{\partial r} \left\{ r \sqrt{D(r)} \frac{\partial [\sqrt{D(r)}P(r, \theta, t)]}{\partial r} \right\} \\ &+ \frac{1}{r^2} \frac{\partial \sqrt{D(r)}}{\partial \theta} \frac{\partial [\sqrt{D(r)}P(r, \theta, t)]}{\partial \theta} \\ &+ \frac{\sqrt{D(r)}}{r^2} \frac{\partial^2}{\partial \theta^2} [\sqrt{D(r)}P(r, \theta, t)]. \end{aligned} \quad (11)$$

The axial symmetry condition gives

$$\frac{\partial P(r, t)}{\partial t} = \frac{1}{r} \frac{\partial}{\partial r} \left\{ r \sqrt{D(r)} \frac{\partial [\sqrt{D(r)}P(r, t)]}{\partial r} \right\}. \quad (12)$$

With $\alpha = 1$, Eq. (4) in the Hänggi-Klimontovich interpretation is

$$\begin{aligned} \frac{\partial P(x, y, t)}{\partial t} &= D(x, y) \left(\frac{\partial^2 P}{\partial x^2} + \frac{\partial^2 P}{\partial y^2} \right) + \frac{\partial D(x, y)}{\partial x} \frac{\partial P(x, y, t)}{\partial x} \\ &+ \frac{\partial D(x, y)}{\partial y} \frac{\partial P(x, y, t)}{\partial y}. \end{aligned} \quad (13)$$

Substituting Eqs. (5) and (6) into Eq. (13) yields

$$\begin{aligned} \frac{\partial P(r, \theta, t)}{\partial t} &= \frac{1}{r} \frac{\partial}{\partial r} \left[r D(r) \frac{\partial P(r, \theta, t)}{\partial r} \right] \\ &+ \frac{1}{r^2} \frac{\partial D(r)}{\partial \theta} \frac{\partial P(r, \theta, t)}{\partial \theta} + \frac{D(r)}{r^2} \frac{\partial^2 P(r, \theta, t)}{\partial \theta^2}. \end{aligned} \quad (14)$$

With $\partial P(r, \theta, t)/\partial \theta = 0$, Eq. (14) can be simplified by

$$\frac{\partial P(r, t)}{\partial t} = \frac{1}{r} \frac{\partial}{\partial r} \left[r D(r) \frac{\partial P(r, t)}{\partial r} \right]. \quad (15)$$

Combining Eqs. (9), (12), and (15), the radial FPE in the various interpretations can be expressed as [43]

$$\frac{\partial P(r, t)}{\partial t} = \frac{1}{r} \frac{\partial}{\partial r} \left\{ r D^\alpha(r) \frac{\partial}{\partial r} [D^{1-\alpha}(r)P(r, t)] \right\}. \quad (16)$$

B. Numerical algorithms of Eq. (2) for various interpretations

In the simulation, Eq. (2) is discretized using a time step Δt , $t_i = i\Delta t$, $i = 0, 1, 2, \dots$, $x(t_i) \equiv x_i$, and $y(t_i) \equiv y_i$ are discretized correspondingly. The stochastic integrals $\int_{t_i}^{t_{i+1}} \xi_x(t) dt = \sqrt{\Delta t} \psi_i$ and $\int_{t_i}^{t_{i+1}} \xi_y(t) dt = \sqrt{\Delta t} \varphi_i$ represent an increase in the Wiener process with Δt variance. The sets $\{\psi_i\}$ and $\{\varphi_i\}$ denote mutually independent Gaussian random numbers with zero mean and unit variance.

According to Eq. (3), the Itô interpretation of the stochastic integral is $I_n(t_i, t_{i+1}) \simeq \sqrt{2D(x(t_i), y(t_i))} \int_{t_i}^{t_{i+1}} \xi_n(s) ds$, where $n = (x, y)$. The stochastic Euler algorithm for the iterative integration of Eq. (2) reads

$$x_{i+1} = x_i + \sqrt{2D(x_i, y_i) \Delta t} \psi_i, \quad (17)$$

$$y_{i+1} = y_i + \sqrt{2D(x_i, y_i) \Delta t} \varphi_i.$$

The Stratonovich interpretation corresponds to $I_n(t_i, t_{i+1}) \simeq \sqrt{2D(\frac{x_i+x_{i+1}}{2}, \frac{y_i+y_{i+1}}{2})} \int_{t_i}^{t_{i+1}} \xi_n(s) ds$. By employing Heun's method [44], the iteration scheme reads

$$x_i^{(1)} = x_i + \sqrt{2D(x_i, y_i) \Delta t} \psi_i,$$

$$y_i^{(1)} = y_i + \sqrt{2D(x_i, y_i) \Delta t} \varphi_i,$$

$$x_{i+1} = x_i + \frac{1}{2} (\sqrt{2D(x_i, y_i) \Delta t} + \sqrt{2D(x_i^{(1)}, y_i^{(1)}) \Delta t}) \psi_i,$$

$$y_{i+1} = y_i + \frac{1}{2} (\sqrt{2D(x_i, y_i) \Delta t} + \sqrt{2D(x_i^{(1)}, y_i^{(1)}) \Delta t}) \varphi_i. \quad (18)$$

The Hänggi-Klimontovich interpretation of the integral $I_n(t_i, t_{i+1}) \simeq \sqrt{2D(x_{i+1}, y_{i+1})} \int_{t_i}^{t_{i+1}} \xi_n(s) ds$. An iterative semi-implicit Euler stochastic algorithm is used to solve Eq. (2) yielding [45,46]

$$x_{i+1} = x_i + \sqrt{2D(x_{i+1}, y_{i+1}) \Delta t} \psi_i,$$

$$y_{i+1} = y_i + \sqrt{2D(x_{i+1}, y_{i+1}) \Delta t} \varphi_i. \quad (19)$$

III. RESULTS

A. Probability density function, $P(r, t)$

We systematically investigate the solution $P(r, t)$ in different interpretations by solving Eq. (16) with Eq. (1). For $\alpha = 0$,

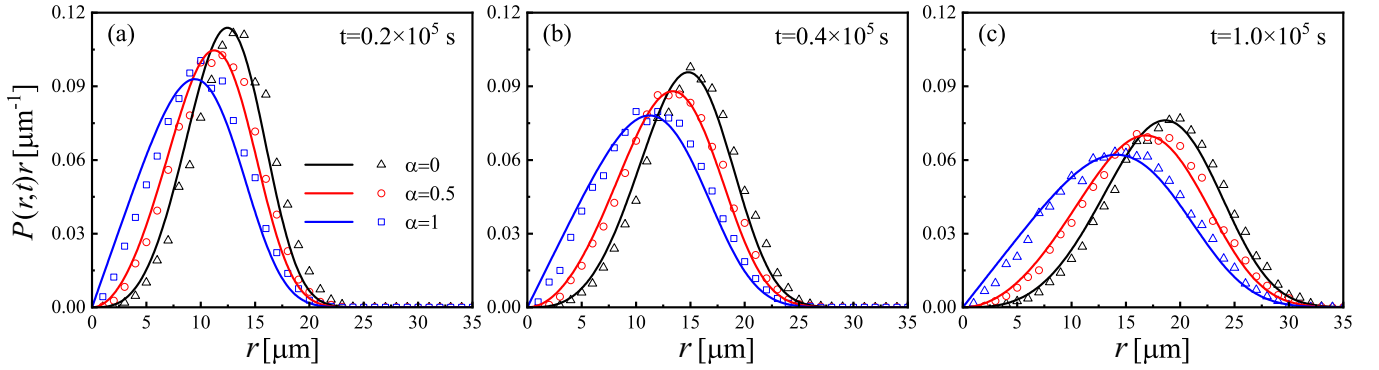


FIG. 2. Comparison of analytical and numerical results of $P(r, t)r$ for different interpretations. The analytical results (solid lines) are calculated from Eq. (34). Color symbols represent data taken from Langevin simulations of Eq. (2) with Eq. (1) by using the algorithms given by Eqs. (17)–(19) with time step 1 s and 10^4 trajectories. Parameter settings used are same as for Fig. 1.

we start from Eq. (9). Let $q_1 \equiv \frac{1}{2}r^2$ ($q_1 \geq 0$); we obtain

$$\frac{\partial}{\partial r} = r \frac{\partial}{\partial q_1} = \sqrt{2q_1} \frac{\partial}{\partial q_1}. \quad (20)$$

Inserting Eq. (20) into Eq. (9) yields

$$\frac{\partial P(q_1, t)}{\partial t} = \frac{\partial}{\partial q_1} \left\{ 2D_0 A q_1 \frac{\partial}{\partial q_1} [(2q_1)^{-1} P(q_1, t)] \right\}, \quad (21)$$

where $D(r) \simeq D_0 A r^{-2} = D_0 A (2q_1)^{-1}$ has been used. Setting $W(q_1, t) \equiv (2q_1)^{-1} P(q_1, t)$ and

$$\frac{\partial q_2}{\partial q_1} = 2q_1, \quad \frac{\partial}{\partial q_1} = \frac{\partial q_2}{\partial q_1} \frac{\partial}{\partial q_2} = 2q_1 \frac{\partial}{\partial q_2}, \quad (22)$$

Eq. (21) becomes

$$\frac{\partial W}{\partial t} = \frac{\partial}{\partial q_2} \left[4D_0 A q_2 \frac{\partial W}{\partial q_2} \right]. \quad (23)$$

With the particle's motion starting at the origin, a few studies [19,47] have derived the solution of Eq. (23) given by

$$W(q_2, t) = \frac{1}{4D_0 A t} \exp \left[-\frac{q_2}{4D_0 A t} \right]. \quad (24)$$

Substituting $q_2 = q_1^2$, we get $P(q_1, t) = 2q_1 W(q_1, t) = 2q_1 / (4D_0 A t) \exp[-q_1^2 / (4D_0 A t)]$. With $q_1 = r^2/2$, we have

$$P(r, t) = \frac{r^2}{4D_0 A t} \exp \left[-\frac{r^4}{16D_0 A t} \right]. \quad (25)$$

For $\alpha = 0.5$, we solve Eq. (12). Using the same method as for $\alpha = 0$, Eq. (12) can be rewritten as

$$\frac{\partial P(q_1, t)}{\partial t} = D_0 A \frac{\partial}{\partial q_1} \sqrt{2q_1} \frac{\partial (\sqrt{2q_1})^{-1} P(q_1, t)}{\partial q_1}. \quad (26)$$

Setting $Q(q_1, t) = (\sqrt{2q_1})^{-1} P(q_1, t)$ and

$$\frac{\partial q_2}{\partial q_1} = \sqrt{2q_1}, \quad \frac{\partial}{\partial q_1} = \frac{\partial q_2}{\partial q_1} \frac{\partial}{\partial q_2} = \sqrt{2q_1} \frac{\partial}{\partial q_2}, \quad (27)$$

we obtain

$$\frac{\partial Q}{\partial t} = \frac{\partial}{\partial q_2} 3^{\frac{2}{3}} D_0 A q_2^{\frac{2}{3}} \frac{\partial Q}{\partial q_2}. \quad (28)$$

The solution of Eq. (28) is given by

$$Q(q_2, t) = \frac{(D_0 A t)^{-3/4}}{2\Gamma[3/4]} \exp \left[-\frac{3^{4/3} q_2^{4/3}}{16D_0 A t} \right]. \quad (29)$$

The function $\Gamma[\alpha]$ is the Gamma function defined by $\Gamma[\alpha] \equiv \int_0^\infty t^{\alpha-1} e^{-t} dt$. With $q_2 = \int \sqrt{2q_1} dq_1 = (2q_1)^{3/2}/3$, we have $P(q_1, t) = \sqrt{2q_1} Q(q_1, t)$,

$$P(q_1, t) = \frac{(D_0 A t)^{-3/4}}{2\Gamma[3/4]} \sqrt{2q_1} \exp \left[-\frac{4q_1^2}{16D_0 A t} \right]. \quad (30)$$

Substituting $r = \sqrt{2q_1}$,

$$P(r, t) = \frac{(D_0 A t)^{-3/4}}{2\Gamma[3/4]} r \exp \left[-\frac{r^4}{16D_0 A t} \right]. \quad (31)$$

For $\alpha = 1$, we solve Eq. (15). Following the same processes for $\alpha = 0$, Eq. (15) is rewritten as

$$\frac{\partial P(q_1, t)}{\partial t} = D_0 A \frac{\partial^2 P(q_1, t)}{\partial q_1^2}, \quad (32)$$

which has the formal solution $P(q_1, t) = 1/\sqrt{\pi D_0 A t} \exp[-q_1^2 / (4D_0 A t)]$. Substituting $r = \sqrt{2q_1}$ yields

$$P(r, t) = \frac{1}{\sqrt{\pi D_0 A t}} \exp \left(-\frac{r^4}{16D_0 A t} \right). \quad (33)$$

Thus,

$$P(r, t) = \begin{cases} \frac{r^2}{4D_0 A t} \exp \left(-\frac{r^4}{16D_0 A t} \right), & \alpha = 0, \\ \frac{(D_0 A t)^{-3/4}}{2\Gamma[3/4]} r \exp \left(-\frac{r^4}{16D_0 A t} \right), & \alpha = 0.5, \\ \frac{1}{\sqrt{\pi D_0 A t}} \exp \left(-\frac{r^4}{16D_0 A t} \right), & \alpha = 1. \end{cases} \quad (34)$$

Figure 2 displays the radial evolution of $P(r, t)r$ at different times. As shown in Fig. 2, slight deviations exist between the numerical results and analytical solutions. These discrepancies arise mainly from two factors. First, the analytical solutions are obtained from the FPE under a simplified framework that neglects higher-order terms. Second, the numerical results naturally incorporate errors due to the discrete simulation of stochastic differential equations, including those from finite time step size and accumulated round-off errors. These deviations reflect the approximations inherent in the

TABLE I. Results of several physical quantities for three different interpretations: Itô ($\alpha=0$), Stratonovich ($\alpha=0.5$), and Hänggi-Klimontovich ($\alpha=1$). The incomplete gamma function $\gamma(s, p) \equiv \int_0^p t^{s-1} e^{-t} dt$ and error function $\text{erf}[s] \equiv (2/\sqrt{\pi}) \int_0^s e^{-t^2} dt$ are employed in analytical solutions, with $\gamma^{-1}(\cdot)$ and $\text{erf}^{-1}[\cdot]$ denoting their inverses.

α	0	0.5	1
$\langle r^2(t) \rangle$	$2\sqrt{\pi D_0 A t}$	$\frac{\Gamma[1/4]\sqrt{D_0 A t}}{\Gamma[3/4]}$	$4\sqrt{\frac{D_0 A t}{\pi}}$
$\lim_{t \rightarrow \infty} \langle r^2(t) \rangle$	$3.54\sqrt{D_0 A t}$	$2.96\sqrt{D_0 A t}$	$2.26\sqrt{D_0 A t}$
$S(t)$	$1 - \exp(-\frac{R^4}{16D_0 A t})$	$\frac{\gamma(\frac{3}{4}, \frac{R^4}{16D_0 A t})}{\Gamma[3/4]}$	$\text{erf}[\frac{R^2}{4\sqrt{D_0 A t}}]$
$\lim_{t \rightarrow \infty} S(t)$	$0.063 \frac{R^4}{D_0 A t}$	$0.14 (\frac{R^4}{D_0 A t})^{\frac{3}{4}}$	$0.28 (\frac{R^4}{D_0 A t})^{\frac{1}{2}}$
$t_{1/2}$	$\frac{1}{16 \ln 2 D_0 A} R^4$	$\frac{1}{16 D_0 A \gamma^{-1}(\frac{3}{4}, \frac{1}{2} \Gamma[\frac{3}{4}])} R^4$	$\frac{1}{16 D_0 A [\text{erf}^{-1}(0.5)]^2} R^4$
$\lim_{R \rightarrow \infty} t_{1/2}$	$\frac{0.09}{D_0 A} R^4$	$\frac{0.138}{D_0 A} R^4$	$\frac{0.275}{D_0 A} R^4$

theoretical model and the standard limitations of the numerical approach, rather than any fundamental inconsistencies. All results remain in good qualitative agreement and illustrate that different formulations of FPE with the same $D(r)$ given by Eq. (1) could lead to different solutions $P(r, t)$.

B. Several interpretation-dependent observables

We show that the interpretation-dependent solutions $P(r, t)$ in Eq. (34) induce three distinct physical observables. First, MSD has become a standard statistical method to quantify diffusive properties of heterogeneous systems [48,49], which is defined by

$$\langle r^2(t) \rangle = \int_0^\infty r^2 P(r, t) r dr, \quad (35)$$

where $\langle \cdot \rangle$ represents the ensemble averaging. Second, to describe the probability that particles continue to exist without being absorbed or decaying, the survival probability $S(t)$ has been widely used. In diffusion problems, such as particles moving within a circular domain bounded by outer boundaries, $S(t)$ is obtained by integrating the probability density

over the domain:

$$S(t) = \int_0^R P(r, t) r dr, \quad (36)$$

where R denotes the radius of the outer boundary. Third, the threshold time $t_{1/2}$ at which half of the fastest particles reach the set boundary is determined by

$$\int_0^R P(r, t) r dr|_{t=t_{1/2}} = \frac{1}{2}. \quad (37)$$

This threshold behavior is relevant in biological contexts, such as modeling population dispersal or the spread of viral epidemics [50].

Substituting Eq. (34) into Eqs. (35)–(37) yields explicit expressions for the MSD $\langle r^2(t) \rangle$, survival probability $S(t)$, and threshold time $t_{1/2}$ under each interpretation, which are shown in Table I. These physical quantities exhibit distinct interpretation-dependent behaviors. As shown in Fig. 3(a), the MSD data under different interpretations vary considerably. In Fig. 3(b), the survival probability of particles that start from the origin and diffuse toward the set boundary under different interpretations follows different scaling, given by $S(t) \simeq t^{-1}$ ($\alpha = 0$), $S(t) \simeq t^{-3/4}$ ($\alpha = 0.5$), and $S(t) \simeq t^{-1/2}$ ($\alpha = 1$). Figure 3(c) shows the trend of the threshold time $t_{1/2}$ with the boundary radius R under these three different interpretations. All interpretations present a scaling relation $t_{1/2} \propto R^4$, yet with distinct prefactors reflecting interpretation-dependent increase rates.

C. Stratified effective diffusion coefficient

As shown in Sec. III B, fundamental physical observables including MSD, survival probability, and threshold time $t_{1/2}$ exhibit interpretation-dependent dynamics under different interpretations. This indicates that we need to choose the interpretation cautiously to avoid erroneous predictions of system behavior. To identify the appropriate interpretation for 2D heterogeneous diffusion processes governed by Eq. (2) with Eq. (1), we turn to SPT methodology. This is motivated by recent works by Pacheco-Pozo *et al.*, which established a framework for selecting the interpretation via SPT in a heterogeneous system with a stepwise diffusivity [28,29]. The central observable in SPT experiments is the mean of the

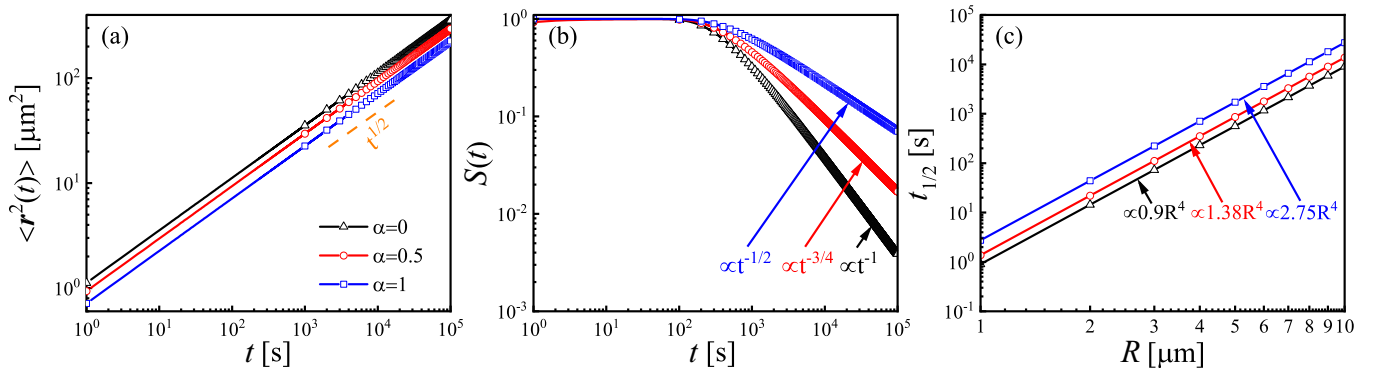


FIG. 3. Comparison of several physical observables calculated from Table I under different interpretations: (a) the time-dependent MSD $\langle r^2(t) \rangle$, (b) survival probability $S(t)$, where $R = 5 \mu\text{m}$, and (c) threshold time $t_{1/2}$. Parameter settings used are same as for Fig. 1.

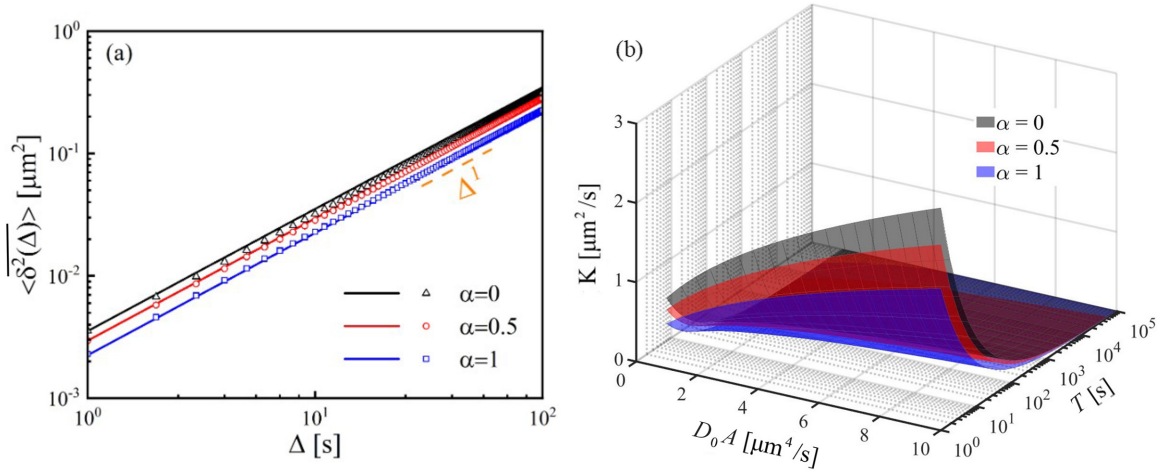


FIG. 4. (a) Comparison of analytical and numerical results of the mean of time-averaged MSD under three interpretations. Solid lines calculated from Eq. (39) denote analytical results. Color symbols denote numerical results of Eq. (2) with Eq. (1). Parameter settings used are $T = 10^5$ s, and others are the same as for Fig. 1. (b) Stratified effective diffusion coefficients calculated from Eq. (40) in the three interpretations for various T and D_0A .

time-averaged MSD, $\overline{\langle \delta^2(\Delta) \rangle}$ [51–54], which is defined by

$$\overline{\langle \delta^2(\Delta) \rangle} = \frac{1}{T - \Delta} \int_0^{T-\Delta} [\langle r^2(t + \Delta) \rangle - \langle r^2(t) \rangle] dt, \quad (38)$$

where T is the total trajectory length, which sets the time window over which the time-averaged MSD is evaluated across different temporal regimes, and $\Delta \ll T$ the lag time [55,56]. This quantity is often suitable for the experiment with a limited number of trajectories. Substituting $\langle r^2(t) \rangle$ under different interpretations into Eq. (38) yields

$$\overline{\langle \delta^2(\Delta) \rangle} \simeq \begin{cases} 2\sqrt{\pi D_0 A} \frac{\Delta}{\sqrt{T}}, & \alpha = 0, \\ \frac{\Gamma[1/4]\sqrt{D_0 A}}{\Gamma[3/4]} \frac{\Delta}{\sqrt{T}}, & \alpha = 0.5, \\ \frac{4\sqrt{D_0 A}}{\sqrt{\pi}} \frac{\Delta}{\sqrt{T}}, & \alpha = 1. \end{cases} \quad (39)$$

A key insight from our results concerns the ergodic character of the process. Using the definition of the ergodicity-breaking parameter [57], we explicitly calculated the ratio $\mathcal{EB}(\Delta) \equiv \overline{\langle \delta^2(\Delta) \rangle} / \langle r^2(\Delta) \rangle$. Based on MSD results in Table I and Eq. (39), we find that this ratio is identical for all three interpretations, which is equivalent to $(\Delta/T)^{1/2}$. This invariance demonstrates that the fundamental ergodic properties of the HDP remain unchanged regardless of the interpretation chosen. Besides, the universal $T^{-1/2}$ scaling of the mean of the time-averaged MSD, which is independent of the stochastic interpretation, reflects a distinctive feature of the present HDP model with static spatial disorder. This behavior contrasts with other anomalous diffusion frameworks. For instance, within the continuous-time random walk model, the scaling with T is nonuniversal and depends on the waiting time exponent [58]. These different $\langle \delta^2(\Delta) \rangle$ produce different effective diffusion

coefficients $K \equiv \overline{\langle \delta^2(\Delta) \rangle} / (4\Delta)$, which is given by

$$K = \begin{cases} \frac{\sqrt{\pi D_0 A}}{2\sqrt{T}}, & \alpha = 0, \\ \frac{\Gamma[1/4]\sqrt{D_0 A}}{4\Gamma[3/4]\sqrt{T}}, & \alpha = 0.5, \\ \frac{\sqrt{D_0 A}}{\sqrt{\pi T}}, & \alpha = 1. \end{cases} \quad (40)$$

Equations (39) and (40) reveal interpretation-dependent disparities in both the mean of the time-averaged MSD and effective diffusion coefficients, as visualized in Fig. 4. The interpretation-dependent variations in the mean of time-averaged MSDs generate stratified effective diffusion coefficients. For fixed parameters D_0A and T , distinct interpretations yield divergent values of effective diffusion coefficients, K . This implies that we may identify the appropriate interpretation by comparing theoretical effective diffusion coefficients with those extracted from SPT experiments.

D. Parameter-dependent interpretation choice

Based on the above discussion, we propose a promising method to identify appropriate interpretation in heterogeneous systems through SPT. For a given heterogeneous diffusion system, the effective diffusion coefficient obtained from SPT trajectories is given by

$$K_{\text{exp}} \equiv \sum_{l=1}^N \overline{\delta_l^2(\Delta)} / (4N\Delta), \quad (41)$$

where N denotes the number of tracking trajectories. We suppose that we use Eq. (2) with Eq. (1) to model the system; we could get various theoretical effective diffusion coefficients K_{the}^α calculated from Eq. (40), where the superscript α denotes different interpretations. By comparing K_{the}^α with K_{exp} , the appropriate interpretation can be identified for which K_{the}^α is closest to K_{exp} . To directly reflect the relative deviation between K_{the}^α and K_{exp} , we define a dimensionless parameter,

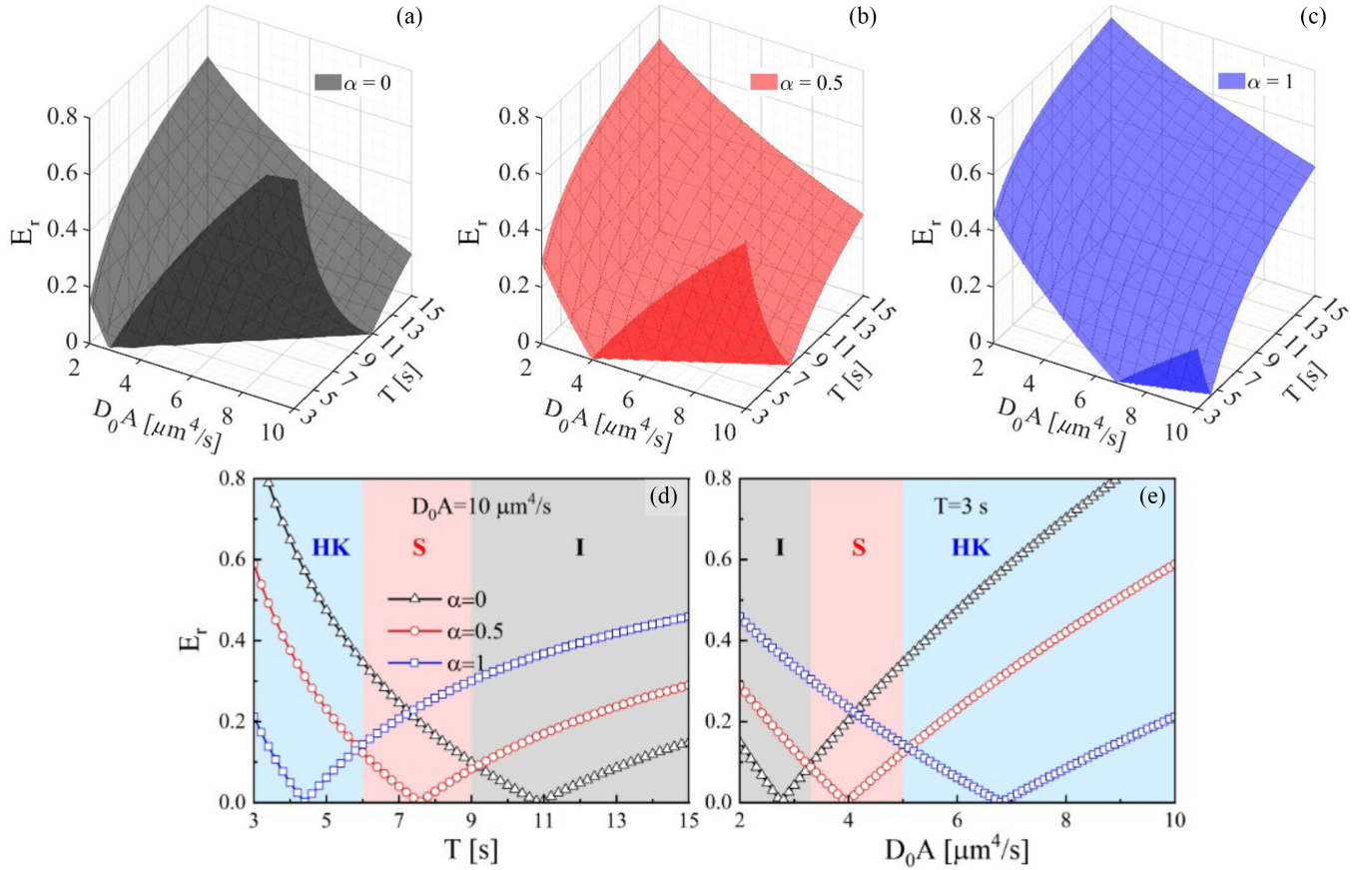


FIG. 5. (a)–(c) Dependence of $E_r = |K_{\text{the}}^\alpha - K_{\text{exp}}|/K_{\text{exp}}$ on total trajectory length T and D_0A in the three interpretations. Here, $K_{\text{exp}} = 0.85 \mu\text{m}^2/\text{s}$ is employed and K_{the}^α is calculated from Eq. (40). Vertical slices of E_r at $D_0A = 10 \mu\text{m}^4/\text{s}$ and $T = 3 \text{ s}$ are shown in panels (d) and (e), respectively.

given by

$$E_r \equiv \frac{|K_{\text{the}}^\alpha - K_{\text{exp}}|}{K_{\text{exp}}}. \quad (42)$$

The optimal interpretation satisfies $\alpha = \min\{E_r(\alpha)\}$, $\alpha \in \{0, 0.5, 1\}$, where $\min\{\dots\}$ denotes the minimum value.

It has been confirmed that Eq. (1) qualitatively agrees with the trends of small fluorescently labeled proteins in the cytoplasm. In the tracking experiments of subdiffusive population of viruses in the cells, previous studies have found that 57 of the trajectories exhibited normal diffusion, with diffusion coefficients ranging from 0.4 to 1.3 $\mu\text{m}^2/\text{s}$. The mean of the diffusion coefficient is $K_{\text{exp}} = 0.85 \mu\text{m}^2/\text{s}$ [59]. Figures 5(a)–5(c) show the dimensionless parameter E_r as a function of total trajectory length T and the parameter D_0A . Note that the parameter T reflects the temporal range used in fitting the time-averaged MSD. The stochastic interpretation itself is independent of any observational duration. The dependence of E_r on T and D_0A serves as an indicator for which interpretation yields the best fit of the observed data, not a change in the underlying physical interpretation. For instance, with $D_0A = 10 \mu\text{m}^4/\text{s}$, the optimal interpretation shifts from Hänggi-Klimontovich to Stratonovich to Itô as T increases [Fig. 5(d)]. A similar transition occurs as a function of D_0A at fixed $T = 3 \text{ s}$ [Fig. 5(e)]. Such transitions between interpretations, controlled by varying specific physical

parameters (e.g., noise correlation time), have been observed in systems like electrical circuits where colored multiplicative noise appears [25]. All these findings emphasize the need for cautious interpretations of FPE for heterogeneous diffusion. This method proposed here might be helpful for determining the appropriate interpretation by comparing theoretical and experimentally measured effective diffusion coefficients with those obtained from SPT data.

IV. CONCLUSION

The aim of this study was to investigate the role and identification of three conventional interpretations (Itô, Stratonovich, and Hänggi-Klimontovich) of Fokker-Planck equations describing diffusion processes in 2D heterogeneous landscapes. The conclusion and outlook of the study are given as follows:

(1) Through analytical solutions and numerical simulations of Fokker-Planck equations with power-law spatially dependent diffusivity, we observed significant interpretation-dependent discrepancies across several physical quantities. These include mean-square displacement, survival probabilities, and threshold times at which half of particles reach set boundaries. The distinct solutions of the time-dependent probability density function under different interpretations should account for these results.

(2) We found that the mean of time-averaged mean-square displacement, a central observable in single-particle tracking, manifests as interpretation differences in effective diffusion coefficients. Motivated by this observation, we proposed a method to identify the interpretation through comparison with diffusion coefficients measured from single-particle tracking experiments. By applying to the tracking experiments, we reveal that the appropriate interpretation may depend on measurement timescales and system's intrinsic parameters.

(3) While our model addresses spatially heterogeneous environments, realistic biological systems exhibit full spatiotemporal diffusivity variations. Extending this framework to spatiotemporal diffusivity will establish a predictive theoretical foundation for modeling intracellular transport dynamics and analyzing anomalous transport in complex media [60–62].

ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (Grant No. 12405041), the Guangdong Basic and Applied Basic Research Foundation (No. 2025A1515010709 and No. 2025A1515011278), STU Scientific Research Initiation (Grant No. NTF23014), STU-GTIIT Joint Research (Grant No. 2024LKSG02), and Special projects in key fields of ordinary universities (Grant No. 2024ZDZX1020).

DATA AVAILABILITY

The data that support the findings of this article are not publicly available. The data are available from the authors upon reasonable request.

-
- [1] Y. J. Liang, W. Wang, R. Metzler, and A. G. Cherstvy, Anomalous diffusion, nonergodicity, non-Gaussianity, and aging of fractional Brownian motion with nonlinear clocks, *Phys. Rev. E* **108**, 034113 (2023).
 - [2] W. Wang, A. G. Cherstvy, H. Kantz, R. Metzler, and I. M. Sokolov, Time averaging and emerging nonergodicity upon resetting of fractional Brownian motion and heterogeneous diffusion processes, *Phys. Rev. E* **104**, 024105 (2021).
 - [3] V. Sposini, S. Nampoothiri, A. Chechkin, E. Orlandini, F. Seno, and F. Baldovin, Being heterogeneous is advantageous: Extreme Brownian non-Gaussian searches, *Phys. Rev. Lett.* **132**, 117101 (2024).
 - [4] W. Wang, A. G. Cherstvy, X. Liu, and R. Metzler, Anomalous diffusion and nonergodicity for heterogeneous diffusion processes with fractional Gaussian noise, *Phys. Rev. E* **102**, 012146 (2020).
 - [5] A. G. Cherstvy, S. Thapa, C. E. Wagner, and R. Metzler, Non-Gaussian, non-ergodic, and non-Fickian diffusion of tracers in mucin hydrogels, *Soft Matter* **15**, 2526 (2019).
 - [6] Y. Xu, X. Liu, Y. Li, and R. Metzler, Heterogeneous diffusion processes and nonergodicity with Gaussian colored noise in layered diffusivity landscapes, *Phys. Rev. E* **102**, 062106 (2020).
 - [7] T. A. Waigh and N. Korabel, Heterogeneous anomalous transport in cellular and molecular biology, *Rep. Prog. Phys.* **86**, 126601 (2023).
 - [8] K. Sakamoto, T. Akimoto, M. Muramatsu, M. S. Sansom, R. Metzler, and E. Yamamoto, Heterogeneous biological membranes regulate protein partitioning via fluctuating diffusivity, *PNAS Nexus* **2**, pgad258 (2023).
 - [9] L. S. Ferreira, F. L. Metz, and P. Barucca, Random matrix ensemble for the covariance matrix of Ornstein-Uhlenbeck processes with heterogeneous temperatures, *Phys. Rev. E* **111**, 014151 (2025).
 - [10] M. G. Li and J. D. Bao, Resonance behavior for the dynamical friction of a system in a trapping potential, *Phys. Rev. Res.* **4**, 043058 (2022).
 - [11] L. M. Xiang, K. Chen, R. Yan, W. Li, and K. Xu, Single-molecule displacement mapping unveils nanoscale heterogeneities in intracellular diffusivity, *Nat. Methods* **17**, 524 (2020).
 - [12] A. G. Cherstvy and R. Metzler, Ergodicity breaking and particle spreading in noisy heterogeneous diffusion processes, *J. Chem. Phys.* **142**, 144105 (2015).
 - [13] Q. Xuan, F. Du, T. J. Wu, and G. R. Chen, Emergence of heterogeneous structures in chemical reaction-diffusion networks, *Phys. Rev. E* **82**, 046116 (2010).
 - [14] L. Menon and C. Anteneodo, Random search with resetting in heterogeneous environments, *Phys. Rev. E* **110**, 054111 (2024).
 - [15] M. G. Li, M. Hu, L. M. Fan, J. D. Bao, and P. C. Li, Quantifying the energy landscape in weakly and strongly disordered frictional media, *J. Chem. Phys.* **160**, 024903 (2024).
 - [16] M. G. Li, L. M. Fan, and J. D. Bao, Power-law frictional landscapes induce anomalous diffusion, *Physica A* **597**, 127249 (2022).
 - [17] H. Risken, *The Fokker-Planck Equation: Methods of Solution and Applications* (Springer, Berlin, 1989).
 - [18] K. S. Fa, Solution of Fokker-Planck equation for a broad class of drift and diffusion coefficients, *Phys. Rev. E* **84**, 012102 (2011).
 - [19] O. Farago and N. Grønbech-Jensen, Langevin dynamics in inhomogeneous media: Re-examining the Itô-Stratonovich dilemma, *Phys. Rev. E* **89**, 013301 (2014).
 - [20] G. Volpe and J. Wehr, Effective drifts in dynamical systems with multiplicative noise: A review of recent progress, *Rep. Prog. Phys.* **79**, 053901 (2016).
 - [21] I. M. Sokolov, Itô, and Stratonovich, Hänggi and all the rest: The thermodynamics of interpretation, *Chem. Phys.* **375**, 359 (2010).
 - [22] M. G. Li, R. Xing, L. M. Fan, M. Hu, J. D. Bao, and P. C. Li, On the interpretation of mean-square displacement in heterogeneous systems, *New J. Phys.* **26**, 093024 (2024).
 - [23] J. M. Sancho, Brownian colloidal particles: Itô, Stratonovich, or a different stochastic interpretation, *Phys. Rev. E* **84**, 062102 (2011).
 - [24] A. Bhattacharyay, Brownian motion near a wall: The dilemma of Itô or Stratonovich, *J. Phys. A: Math. Theor.* **58**, 213001 (2025).
 - [25] G. Pesce, A. McDaniel, S. Hottovy, J. Wehr, and G. Volpe, Stratonovich-to-Itô transition in noisy systems with multiplicative feedback, *Nat. Commun.* **4**, 2733 (2013).

- [26] G. Volpe, L. Helden, T. Brettschneider, J. Wehr, and C. Bechinger, Influence of noise on force measurements, *Phys. Rev. Lett.* **104**, 170602 (2010).
- [27] T. Brettschneider, G. Volpe, L. Helden, J. Wehr, and C. Bechinger, Force measurement in the presence of Brownian noise: Equilibrium-distribution method versus drift method, *Phys. Rev. E* **83**, 041113 (2011).
- [28] A. Pacheco-Pozo, I. M. Sokolov, R. Metzler, and D. Krapf, Heterogeneous diffusion in an harmonic potential: The role of the interpretation, *New J. Phys.* **27**, 064602 (2025).
- [29] A. Pacheco-Pozo, M. Balcerek, A. Wylomska, K. Burnecki, I. M. Sokolov, and D. Krapf, Langevin equation in heterogeneous landscapes: How to choose the interpretation, *Phys. Rev. Lett.* **133**, 067102 (2024).
- [30] A. G. Cherstvy, A. V. Chechkin, and R. Metzler, Particle invasion, survival, and non-ergodicity in 2D diffusion processes with space-dependent diffusivity, *Soft Matter* **10**, 1591 (2014).
- [31] T. Kühn, T. O. Ihala, J. Hyväluoma, N. Dross, S. F. Willman, J. Langowski, M. Vihinen-Ranta, and J. Timonen, Protein diffusion in mammalian cell cytoplasm, *PLoS One* **6**, e22962 (2011).
- [32] Y. L. Klimontovich, Nonlinear Brownian motion, *Phys. Usp.* **37**, 737 (1994).
- [33] Y. L. Klimontovich, *Statistical Physics* (Nauka, Moscow, 1982).
- [34] B. Øksendal, *Stochastic Differential Equations: An Introduction with Applications* (Springer, Berlin, 2013).
- [35] M. Heidernätsch, On the diffusion in inhomogeneous systems, Ph.D. thesis, 2015.
- [36] Muñoz-Gil, *et al.*, Quantitative evaluation of methods to analyze motion changes in single-particle experiments, *Nat. Commun.* **16**, 6749 (2025).
- [37] C. Manzo and M. F. Garcia-Parajo, A review of progress in single particle tracking: From methods to biophysical insights, *Rep. Prog. Phys.* **78**, 124601 (2015).
- [38] X. S. Xie, P. J. Choi, G.-W. Li, N. K. Lee, and G. Lia, Single-molecule approach to molecular biology in living bacterial cells, *Annu. Rev. Biophys.* **37**, 417 (2008).
- [39] H. Shen, L. J. Tauzin, R. Baiyasi, W. Wang, N. Moringo, B. Shuang, and C. F. Landes, Single particle tracking: From theory to biophysical applications, *Chem. Rev.* **117**, 7331 (2017).
- [40] S. Giordano and R. Blossey, Effective diffusion constant of stochastic processes with spatially periodic noise, *Phys. Rev. E* **110**, 044123 (2024).
- [41] D. Breoni, H. Löwen, and R. Blossey, Active noise-driven particles under space-dependent friction in one dimension, *Phys. Rev. E* **103**, 052602 (2021).
- [42] N. Leibovich and E. Barkai, Infinite ergodic theory for heterogeneous diffusion processes, *Phys. Rev. E* **99**, 042138 (2019).
- [43] G. Vaccaro, C. Antoine, and J. Talbot, First-passage times in d -dimensional heterogeneous media, *Phys. Rev. Lett.* **115**, 240601 (2015).
- [44] T. C. Gard, *Introduction to Stochastic Differential Equations* (Dekker, New York, 1988).
- [45] P. Hänggi, Connection between deterministic and stochastic descriptions of nonlinear systems, *Helv. Phys. Acta* **53**, 491 (1980).
- [46] B. Lindner, The diffusion coefficient of nonlinear Brownian motion, *New J. Phys.* **9**, 136 (2007).
- [47] S. Regev, N. Grønbech-Jensen, and O. Farago, Isothermal Langevin dynamics in systems with power-law spatially dependent friction, *Phys. Rev. E* **94**, 012116 (2016).
- [48] R. Metzler, J. H. Jeon, and A. G. Cherstvy, Non-Brownian diffusion in lipid membranes: Experiments and simulations, *Biochim. Biophys. Acta: Biomembranes* **1858**, 2451 (2016).
- [49] I. M. Sokolov, Models of anomalous diffusion in crowded environments, *Soft Matter* **8**, 9043 (2012).
- [50] T. G. Mattos, C. Mejía-Monasterio, R. Metzler, and G. Oshanin, First passages in bounded domains: When is the mean first passage time meaningful? *Phys. Rev. E* **86**, 031143 (2012).
- [51] W. Wang, A. G. Cherstvy, R. Metzler, and I. M. Sokolov, Restoring ergodicity of stochastically reset anomalous-diffusion processes *Phys. Rev. Res.* **4**, 013161 (2022).
- [52] A. Sabri, X. Xu, D. Krapf, and M. Weiss, Elucidating the origin of heterogeneous anomalous diffusion in the cytoplasm of mammalian cells, *Phys. Rev. Lett.* **125**, 058101 (2020).
- [53] E. Barkai, Y. Garini, and R. Metzler, Strange kinetics of single molecules in living cells, *Phys. Today* **65**(8), 29 (2012).
- [54] T. Neusius, I. M. Sokolov, and J. C. Smith, Subdiffusion in time-averaged, confined random walks, *Phys. Rev. E* **80**, 011109 (2009).
- [55] Y. He, S. Burov, R. Metzler, and E. Barkai, Random time-scale invariant diffusion and transport coefficients, *Phys. Rev. Lett.* **101**, 058101 (2008).
- [56] S. Burov, J. H. Jeon, R. Metzler, and E. Barkai, Single particle tracking in systems showing anomalous diffusion: The role of weak ergodicity breaking, *Phys. Chem. Chem. Phys.* **13**, 1800 (2011).
- [57] A. Godec and R. Metzler, Finite-time effects and ultraweak ergodicity breaking in superdiffusive dynamics, *Phys. Rev. Lett.* **110**, 020603 (2013).
- [58] R. Metzler, J.-H. Jeon, A. G. Cherstvy, and E. Barkai, Anomalous diffusion models and their properties: Non-stationarity, non-ergodicity, and ageing at the centenary of single particle tracking, *Phys. Chem. Chem. Phys.* **16**, 24128 (2014).
- [59] G. Seisenberger, M. U. Ried, T. Endreß, H. Buning, M. Hallek, and C. Brauchle, Real-time single-molecule imaging of the infection pathway of an adeno-associated virus, *Science* **294**, 1929 (2001).
- [60] T. Akimoto, J.-H. Jeon, R. Metzler, T. Miyaguchi, T. Uneyama, and E. Yamamoto, Anomalous statistics in the Langevin equation with fluctuating diffusivity: From Brownian yet non-Gaussian diffusion to anomalous diffusion and ergodicity breaking, *arXiv:2509.12571*.
- [61] T. Akimoto and E. Yamamoto, Distributional behaviors of time-averaged observables in the Langevin equation with fluctuating diffusivity: Normal diffusion but anomalous fluctuations, *Phys. Rev. E* **93**, 062109 (2016).
- [62] M. Kimura and T. Akimoto, Non-Markovian effects of conformational fluctuations on the global diffusivity in Langevin equation with fluctuating diffusivity, *J. Chem. Phys.* **159**, 055102 (2023).