

Fractional-time random walk subdiffusion and anomalous transport with finite mean residence times: Faster, not slower

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Continuous time random walk (CTRW) subdiffusion along with the associated fractional Fokker-Planck equation (FFPE) is traditionally based on the premise of random clock with divergent mean period. This work considers an alternative CTRW and FFPE description which is featured by finite mean residence times (MRTs) in any spatial domain of finite size. Transient subdiffusive transport can occur on a very large time scale τ_c which can greatly exceed mean residence time in any trap, $\tau_c \gg \langle \tau \rangle$, and even not being related to it. Asymptotically, on a macroscale transport becomes normal for $t \gg \tau_c$. However, mesoscopic transport is anomalous. Differently from viscoelastic subdiffusion no long-range anticorrelations among position increments are required. Moreover, our study makes it obvious that the transient subdiffusion and transport are faster than one expects from their normal asymptotic limit on a macroscale. This observation has profound implications for anomalous mesoscopic transport processes in biological cells because the macroscopic viscosity of cytoplasm is finite.

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I. INTRODUCTION

The subject of anomalous diffusion and transport became increasingly popular in the last two decades (see Fig. 1 in Ref. [1]) with many application fields in physics and beyond and many theoretical approaches coexisting and developed in parallel. The works by Montroll and Weiss [2], Scher and Montroll [3], and Shlesinger [4] laid the grounds for the continuous time random walk (CTRW) approach to subdiffusion based on the premise of a random distribution of the residence times spent in traps with a nonexistent mean time period between two successive spatial steps. Assuming that the residence times in traps are independently distributed and no correlations between spatial steps exist (semi-Markovian assumption), the whole process is completely characterized by a residence time distribution $\psi_i(\tau)$ in the i th trap and the probability distribution $p(k|i)$ to jump from i to another trap k . Highly dispersive subdiffusive transport with the position variance growing sublinearly, $\langle \delta x^2(t) \rangle \propto \kappa_\alpha t^\alpha$, $0 < \alpha < 1$, where κ_α is subdiffusion coefficient, emerges when the residence time distributions (RTDs) behave asymptotically as

$$\psi(\tau) \propto \tau^{-\alpha-1}. \quad (1)$$

This approach acquired enormous popularity and has been followed by numerous workers in the field [5–7]. However, there are no real processes in nature which would show this characteristic feature, i.e., infinite mean residence time (MRT) in a *finite* spatial domain. Of course, in reality it is always finite. Nevertheless, it can largely exceed a characteristic time $\tau_L \sim (L^2/\kappa_\alpha)^{1/\alpha}$ related to a finite linear size L of the medium, e.g., the width of a thin amorphous semiconductor film exhibiting akin transport properties. Then, the *approximation* of infinite mean residence time can be well justified. Asymptotically transport will be normal. However, this macroscopic normal transport regime is irrelevant on mesoscale in the corresponding amorphous media. The main advance of this work is to introduce an alternative *semi-Markovian* CTRW approach to subdiffusive transport on mesoscale featured but by finite MRT as a main premise. Moreover, we derive a modified fractional Fokker-Planck equation (MFFPE) for diffusion and transport

in an external force field in the continuous space limit, where MRT in a pointlike trap becomes *infinitely* small. Within this alternative CTRW approach MRT $\langle \tau \rangle$ in any finite spatial domain not only remains finite, but it shrinks to zero with vanishing size of the domain. Nevertheless, the corresponding residence time distribution does scale as one in Eq. (1) on a long intermediate time scale. Since in all real experiments the mean residence times are always finite, one can conjecture that some experimental observations of the law (1) along with subdiffusion, e.g., in Ref. [8], might be more consistent with our alternative description, rather than with the popular one.

II. THEORY

The key modification in this alternative is to consider the residence time distribution in the i th trap which is characterized by the Laplace-transformed survival probability

$$\tilde{\Phi}_i(s) = \frac{1}{s + \sum_{j=0}^N r_{\alpha_j, i} s^{1-\alpha_j}}, \quad (2)$$

where $\alpha_0 = 1$ and $0 < \alpha_j < 1$ for $j = 1, 2, \dots, N$. By noting that $\tilde{\psi}_i(s) = 1 - s\tilde{\Phi}_i(s)$, the corresponding residence time distribution $\psi_i(\tau)$ can be represented as a sum over $N + 1$ independent escape channels, $\psi_i(\tau) = \sum_{j=0}^N \psi_{ji}(\tau)$, with the Laplace-transformed $\psi_{ji}(\tau)$ reading

$$\tilde{\psi}_{ji}(s) = r_{\alpha_j, i} s^{1-\alpha_j} \tilde{\Phi}_i(s). \quad (3)$$

This justifies (see also below) naming the quantities $r_{\alpha_j, i}$ the fractional rates. One of them, $r_{1, i} = r_{\alpha_0, i}$ is just the normal rate corresponding to $\alpha_0 = 1$. The presence of such a fast escape route from any trap is a crucial point yielding a finite MRT, $\langle \tau_i \rangle = \tilde{\Phi}_i(0) = 1/r_{1, i}$ in the trap i . This is because the particle can go either via any slow route, or through the fast one which defines the MRT.

This expression (2) can be derived as follows. Let us consider first a single escape channel. The escape is governed by a random fractional clock with the Mittag-Leffler survival probability $\tilde{\Phi}_{j, i}(\tau) = E_{\alpha_j}(-r_{\alpha_j, i} \tau^{\alpha_j})$. Here, $E_\alpha(z) = \sum_{n=0}^{\infty} z^n / \Gamma(\alpha n + 1)$ is the Mittag-Leffler function [9], which

is a generalization of the exponential function, $E_1(z) = \exp(z)$. For $\alpha_0 = 1$, survival probability decays exponentially. The probability density of the time intervals between two successive escape events is (subindexes are temporally omitted for clarity) $\psi(\tau) = -d\Phi(\tau)/d\tau$. The Laplace-transformed probability to have n independent escape events within the time interval $[0, t]$ is $\tilde{p}(n, s) = [\tilde{\psi}(s)]^n \tilde{\Phi}(s)$. From this it is easy to obtain the Laplace-transformed mean number of escape events $\langle \tilde{n}(s) \rangle = \sum_{n=1}^{\infty} n \tilde{p}(n, s)$. Straightforward calculations yield

$$\langle \tilde{n}(s) \rangle = \left(\frac{1}{\tilde{\Phi}(s)} - s \right) \frac{1}{s^2}. \quad (4)$$

Furthermore, the Laplace-transformed Mittag-Leffler survival probability is $\tilde{\Phi}(s) = 1/(s + r_\alpha s^{1-\alpha})$. This in Eq. (4) yields $\langle \tilde{n}(s) \rangle = r_\alpha s^{-1-\alpha}$ or $\langle n(t) \rangle = r_\alpha t^\alpha / \Gamma(1 + \alpha)$. Now the last steps: Having $N + 1$ independent escape channels acting in parallel, it is obvious that $\langle \tilde{n}(s) \rangle = \sum_{j=0}^N \langle \tilde{n}_j(s) \rangle = \sum_{j=0}^N r_{\alpha_j} s^{-1-\alpha_j}$. The use of this result in Eq. (4) yields (2) upon restoring subindex i .

The MRT is thus finite in our model, due to the presence of a fast escape channel, but its variance is not bounded, $\langle \delta\tau_i^2 \rangle = \infty$, reflecting the presence of anomalously slow pathways. Similar happens, e.g., if the particle can escape out of the anomalous CTRW subdiffusion domain being injected on the normal radiation boundary which it can either leave with normal rate immediately or penetrate further inside the anomalous domain [10]. Even more strikingly, by doing the continuous space limit below we shall consider the limit $\langle \tau_i \rangle \rightarrow 0$. Here lies the principal difference of our subdiffusive CTRW model from a popular one dominating currently over this research domain. The simplest representative of this class of models is ($N = 1$)

$$\tilde{\Phi}_i(s) = \frac{\langle \tau_i \rangle}{1 + (\tau_c s)^{1-\alpha} + s \langle \tau_i \rangle}, \quad (5)$$

where τ_c is a cutoff time which is equal for all traps and defines the maximal time range of subdiffusion. For $\alpha = 1/2$ this expression can be easily inverted to the time domain and expressed in terms of a combination of the error function and power-law functions. Generally, it can be inverted in terms of a sum of Mittag-Leffler functions [9]. It is not difficult to show that for $\langle \tau_i \rangle \ll \tau \ll \tau_c$, $\psi_i(\tau)$ exhibits precisely the same scaling behavior as one in Eq. (1). Asymptotically for $\tau \gg \tau_c$ it is but a different power law, $\psi_i(\tau) \propto \tau^{\alpha-3}$, ensuring that the MRT is finite. Apart from this, initially for $\tau \ll \langle \tau_i \rangle$, $\psi(\tau) \propto \tau^{-1+\alpha}$. All in all, our RTD exhibits three different interchanging power laws even in the simplest case of $N = 1$, providing a rather rich model.

It should be mentioned that the considered model is different from another scheme proposed earlier to describe transient subdiffusion which is based on the truncated (tempered) residence time distributions [11,12]. In the case of tempered RTDs, all the moments of RTDs are finite, and not only the first one. Furthermore, the resulting Fokker-Planck description is different from one given below (it has a different memory kernel). Moreover, the analytical expression for the particle variance describing transient subdiffusion is different from one in Eq. (14) (see below, even for $F \rightarrow 0$). Our description allows for a direct comparison both with the experimental

results parametrized in the form of Eq. (19) and with an alternative way to describe transient subdiffusion based on the generalized Langevin equation (see below). This is an important feature.

Next, let us consider the generalized master equation (GME) for the CTRW on the lattice $x_i = i\Delta x$ ($i \in Z$) with a discretization step Δx and nearest neighbor jumps only, characterized by the jump probabilities $q_i^+ = p(i+1|i)$ and $q_i^- = p(i-1|i)$ obeying $q_i^+ + q_i^- = 1$. The corresponding GME reads [13]

$$\dot{P}_i(t) = \int_0^t \{K_{i-1}^+(t-t')P_{i-1}(t') + K_{i+1}^-(t-t')P_{i+1}(t') - [K_i^+(t-t') + K_i^-(t-t')]P_i(t')\} dt', \quad (6)$$

where the Laplace transform of the kernel $K_i^\pm(t)$ is related to the Laplace transform of the residence time distribution (RTD) by $\tilde{K}_i^\pm(s) = q_i^\pm \tilde{\psi}_i(s) / \tilde{\Phi}_i(s)$, which for the considered model yields

$$\tilde{K}_i^\pm(s) = q_i^\pm \left(r_{1,i} + \sum_{j=1}^N r_{\alpha_j,i} s^{1-\alpha_j} \right). \quad (7)$$

One can also define forward and backward fractional rates as $r_{\alpha_j,i}^\pm = q_i^\pm r_{\alpha_j,i}$, accordingly, with $r_{\alpha_j,i} = r_{\alpha_j,i}^+ + r_{\alpha_j,i}^-$, and rewrite the GME (6) in the form of a fractional master equation

$$\dot{P}_i(t) = \sum_{j=0}^N {}_0\hat{D}_t^{1-\alpha_j} \{r_{\alpha_j,i-1}^+ P_{i-1}(t) + r_{\alpha_j,i+1}^- P_{i+1}(t) - [r_{\alpha_j,i}^+ + r_{\alpha_j,i}^-] P_i(t)\}, \quad (8)$$

where

$${}_t\hat{D}_t^\gamma f(t) := \frac{1}{\Gamma(1-\gamma)} \frac{\partial}{\partial t} \int_{t_0}^t dt' \frac{f(t')}{(t-t')^\gamma}, \quad (9)$$

with $0 < \gamma < 1$ defines the fractional Riemann-Liouville derivative acting on some function $f(t)$ [6].

Furthermore, let us consider an additional potential field $V(x)$ which influences the jumping rates as follows:

$$r_{\alpha_j,i}^\pm = [\kappa_{\alpha_j} / (\Delta x)^2] \exp[-\beta(V_{i\pm 1/2} - V_i)], \quad (10)$$

where κ_{α_j} has the meaning of a (generally) anomalous diffusion coefficient, and $\beta = 1/(k_B T)$ is inverse temperature. The form (10) ensures that the Boltzmann equilibrium condition $r_{\alpha_j,i-1}^+ / r_{\alpha_j,i}^- = \exp[\beta(V_{i-1} - V_i)]$ is satisfied for any $V(x)$ and our description is thermodynamically consistent. Using a finite difference operator $\Delta/\Delta x$, $\Delta P(x, t)/\Delta x := [P(x + \Delta x/2, t) - P(x - \Delta x/2, t)]/\Delta x$, one can rewrite the GME (8) for the considered model as

$$\dot{P}(x_i, t) = \left(\kappa_1 + \sum_{j=1}^N \kappa_{\alpha_j} {}_0\hat{D}_t^{1-\alpha_j} \right) \times \frac{\Delta}{\Delta x} \left(e^{-\beta V(x_i)} \frac{\Delta}{\Delta x} e^{\beta V(x_i)} P(x_i, t) \right), \quad (11)$$

where we have explicitly singled out the fast transition channel which is present between any two localized states and acting in parallel to all other ultraslow channels.

In the continuous space limit $\Delta x \rightarrow 0$ with constant κ_{α_j} , Eq. (11) yields the following generalization of the fractional Fokker-Planck equation (FFPE) of Refs. [6,14–16]:

$$\frac{\partial P(x,t)}{\partial t} = \left(\kappa_1 + \sum_{j=1}^N \kappa_{\alpha_j} {}_0\hat{D}_t^{1-\alpha_j} \right) \times \frac{\partial}{\partial x} \left(e^{-\beta V(x)} \frac{\partial}{\partial x} e^{\beta V(x)} P(x,t) \right). \quad (12)$$

The generalization consists primarily in the presence also of a normal diffusion term along with the anomalous diffusion contributions. Notice that it was not only obtained from the CTRW possessing finite MRT in each trap but even in the limit $\langle \tau_i \rangle \propto (\Delta x)^2 / \kappa_1 \rightarrow 0$, so that the MRT in any spatial domain of a finite size is obviously finite. For $N = 1$, and in the limit $\kappa_1 \rightarrow 0$ it reduces to the original FFPE of works [14,15]. In the same limit, but for $N = 2$ it reduces to the modified FFPE of Ref. [17]. Generally, Eq. (12) belongs to the class of distributed order fractional kinetic equations [17,18]. The Fokker-Planck equation with memory introduced in Ref. [12] does not belong to this class.

A. Simplest case of one normal and one anomalously slow transition channel

In the following, we consider the simplest case of $N = 1$, with finite κ_1 and $\kappa_\alpha = \kappa_1 \tau_c^{1-\alpha}$ with a very large τ_c . The key point is that for $t \ll \tau_c$ the normal diffusion term is negligible and the dynamics is subdiffusive, whereas the mean residence time in any finite spatial domain is finite. Here lies a profound, striking difference with the earlier approach. For $t \gg \tau_c$, the normal diffusion contribution dominates the transport, which becomes asymptotically normal. However, the biased subdiffusion changes asymptotically into superdiffusion (see below) because the variance of residence times is infinite.

Our focus is now on an intermediate subdiffusive regime. Considering the mean displacement under the constant force F , the solution of Eq. (12) yields

$$\begin{aligned} \langle \delta x(t) \rangle &= Ft/\eta_1 + Ft^\alpha / [\eta_\alpha \Gamma(1 + \alpha)] \\ &= \frac{F\tau_c}{\eta_1} \left[\frac{t}{\tau_c} + \frac{1}{\Gamma(1 + \alpha)} \left(\frac{t}{\tau_c} \right)^\alpha \right], \end{aligned} \quad (13)$$

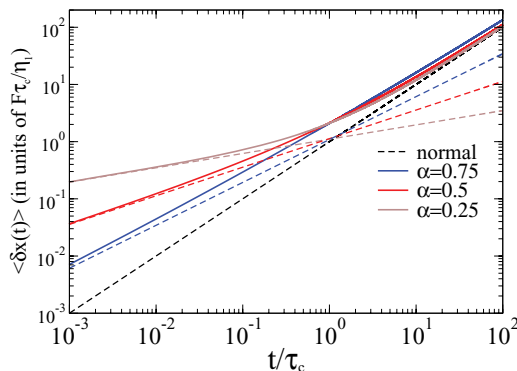


FIG. 1. (Color online) Anomalous transport which asymptotically becomes normal.

where the normal, η_1 , and fractional, η_α , frictional coefficients are related to the corresponding diffusion coefficients by standard, $\eta_1 = k_B T / \kappa_1$, and generalized, $\eta_\alpha = k_B T / \kappa_\alpha$, Einstein relations, respectively. Figure 1 displays this solution for three different values of α along with one and the same normal diffusion asymptotics for $t \gg \tau_c$ and three different initial $t \ll \tau_c$ asymptotics. One can conclude that the motion remains subdiffusive for the most time and can be characterized by a time-dependent power exponent $\alpha_{\text{eff}}(t)$ which gradually changes from α for $t \ll \tau_c$ to $\alpha = 1$ for $t \gg \tau_c$. Even more strikingly, in the subdiffusive regime the transport is as a matter of fact faster than its normal diffusion asymptotics. Indeed, already the structure of the generalized master equation (6) says that in the Markovian approximation $P_i(t') \approx P_i(t)$, only the normal rate term contributes asymptotically, $t \rightarrow \infty$. This is because the terms in the integral of the memory kernel $\int_0^t K_i^\pm(t') dt'$, which correspond to the anomalous rate contributions, tend to zero with increasing the upper limit t like $1/t^{1-\alpha_j}$ being always positive. Initially these terms, however, profoundly contribute to making the overall transport faster than its normal asymptotics. Notice that this interpretation is opposite to that suggested in Ref. [18] for diffusion, which we consider shortly: The transport obviously slows down in the course of time and does not accelerate.

For the displacement variance $\langle \delta x^2(t) \rangle = \langle x^2(t) \rangle - \langle \delta x(t) \rangle^2$, which characterizes diffusion, after some algebra we obtain

$$\begin{aligned} \langle \delta x^2(t) \rangle &= 2\kappa_1 t + 2\kappa_\alpha t^\alpha / \Gamma(1 + \alpha) \\ &+ \left(\frac{F\tau_c}{\eta_1} \right)^2 \left\{ \frac{2(1 - \alpha)}{\Gamma(2 + \alpha)} \left(\frac{t}{\tau_c} \right)^{1+\alpha} \right. \\ &\left. + \left[\frac{2}{\Gamma(1 + 2\alpha)} - \frac{1}{\Gamma^2(1 + \alpha)} \right] \left(\frac{t}{\tau_c} \right)^{2\alpha} \right\}. \end{aligned} \quad (14)$$

Taking into account the generalized Einstein relation, it is seen immediately that a linear fluctuation-response relation $\langle \delta x(t) \rangle = [F/(2k_B T)] \langle \delta x^2(t) \rangle_{F=0}$ is satisfied, between the “fluctuation” $\langle \delta x^2(t) \rangle_{F=0}$ in the absence of driving force F , and the “response” $\langle \delta x(t) \rangle$ to it. In the subdiffusive transport regime restricted by $t \ll \tau_c$,

$$\begin{aligned} \langle \delta x(t) \rangle &\approx Ft^\alpha / [\eta_\alpha \Gamma(1 + \alpha)], \\ \langle \delta x^2(t) \rangle &\approx 2\kappa_\alpha t^\alpha / \Gamma(1 + \alpha), \end{aligned} \quad (15)$$

i.e., the variance $\langle \delta x^2(t) \rangle$ behaves subdiffusively also in the presence of bias F , like the mean displacement in Fig. 1. This is in a striking contrast with the standard CTRW and FFPE subdiffusion based on the premise of infinite mean residence times. In the latter case, $\langle \delta x^2(t) \rangle_{F \neq 0} \propto Ft^{2\alpha}$, for a sufficiently large F , or asymptotically, similar to the last term in Eq. (14). Therefore, our theory is closer to what one intuitively expects for normal transport, sharing this normal feature also with the alternative generalized Langevin equation (GLE) approach to subdiffusion which we shall discuss shortly.

Within the presented modified theory the large time asymptotic behavior of the variance in the presence of bias is also rather unusual. Obviously for $F \neq 0$ and $t \gg \tau_c$, the main contribution in Eq. (14) is superdiffusive, $\langle \delta x^2(t) \rangle_{F \neq 0} \propto Ft^{1+\alpha}$. The explanation of this is the following. Even if the random clock governing subdiffusion in our case does possess

a mean value, its variance is but infinite and in accordance with Ref. [1] (see the Appendix therein) determines the displacement variance in the case of *biased* diffusion. Unbiased diffusion remains nevertheless asymptotically normal. Such a combination of normal transport and superdiffusion was found recently in numerical simulations of normal Langevin dynamics in near critically biased washboard potentials in the presence of frozen disorder for a parameter regime [19]. In this respect it is worth mentioning that hopping diffusion in disordered potentials is equivalent within the mean-field (effective medium) approximation to a CTRW [5]. This provides one of the physical justifications for the CTRW phenomenological approach.

B. Comparison with alternative GLE approach

Let us compare now the considered modification of CTRW subdiffusional transport phenomenology with even more normal GLE description of subdiffusion [20–23]. Here, all the moments of the residence time distribution in any finite-size spatial domain are finite [22]. Such a GLE approach is intrinsically based on the phenomenon of viscoelasticity [24,26] with long-range correlations in the Brownian particle displacements. Here, the physical origin of subdiffusion is entirely different from one in the semi-Markovian CTRW [22,23]. Stochastic dynamics is described by the overdamped GLE [20,21]

$$\int_0^t \eta(t-t') \dot{x}(t') dt' = -\frac{\partial V(x,t)}{\partial x} + \xi(t), \quad (16)$$

where thermal force $\xi(t)$ is (i) Gaussian, (ii) unbiased on average, and (iii) obeys the fluctuation-dissipation relation

$$\langle \xi(t) \xi(t') \rangle = k_B T \eta(|t-t'|) \quad (17)$$

at the environmental temperature T . The inertial effects are completely neglected, similar to the above CTRW description. Macroscopic power-law models of viscoelasticity were introduced in 1936 by Gemant [24,25] as a generalization of the Maxwell model [26] with an exponentially decaying viscoelastic memory kernel. One of Gemant's macroscopic models having relation to our present work corresponds to the memory friction

$$\tilde{\eta}(s) = \frac{\eta_1}{1 + (s\tau_c)^{1-\alpha}}, \quad (18)$$

in the Laplace space. For $t \ll \tau_c$, $\eta(t)$ can be approximated by $\eta(t) \approx \eta_\alpha / [\Gamma(1-\alpha)t^\alpha]$, with $\eta_\alpha = \eta_1 \tau_c^{\alpha-1}$ and its asymptotic decay for $t \gg \tau_c$ is another power law, $\eta(t) \propto t^{\alpha-2}$, ensuring that $\tilde{\eta}(0) = \eta_1$ is finite. This GLE model with the memory kernel (18) for $f(x) = F = \text{const}$ yields again exactly the same solution (13) for the mean displacement and a modified (with $F \rightarrow 0$, the first line only remains) solution (14) for the variance [27]. It must be emphasized that GFFPE (12) with $N = 1$ does not present a master equation counterpart of the GLE (16) with the memory kernel (18), as they have physically (and mathematically, too) totally different origins. Both approaches share, however, a prominent feature that the mean residence time in any finite spatial domain is finite.

This ensures, for example, that the asymptotic response of the corresponding anomalous dynamics to time-periodic

perturbations is finite. However, these asymptotical responses in both models can also be different in some details, reflecting different physics. For example, it has been recently shown that the traditional CTRW subdiffusion based on infinite MRTs displays an asymptotically dying response to periodic fields [28] which is at odds with most experimental data on an anomalous dielectric response, and nevertheless agrees with some [29]. Normally, the anomalous response exhibits aging behavior. However, the response normally decays not to zero, but to some finite value. The response to periodic fields can serve to distinguish among different underlying physical mechanisms. A generalization of the presented here modified CTRW and FFPE model to time-dependent fields is not a trivial matter at all. It is left for a separate study.

III. APPLICATION TO BIOLOGICAL SUBDIFFUSION

For subdiffusion restricted by the time scale $t < \tau_c$ and spatial scale $x < L \sim (\kappa_\alpha \tau_c^\alpha)^{1/2}$ it is not easy to distinguish between two different models discussed here, if to study only the mean displacement and the displacement variance. They display a very similar transient behavior. Calculation of the velocity autocorrelation function as, e.g., in Ref. [30] can clearly prove that the viscoelastic mechanism is at work, or statistical analysis of single trajectories [31] can help to make the distinction. The common feature is, however, that in both cases the transient transport is *faster* than the asymptotically normal one, and the transient subdiffusion is faster than asymptotically normal diffusion in the unbiased case. The results on mRNA molecule subdiffusion in bacterial cells [32] seem consistent with this paradoxical conclusion [27]. Moreover, the experimental results on subdiffusion of the colloidal gold particles having a typical size of proteins with radius $R = 2.5$ nm in cytoplasm of living cells [33] delivers a further clear confirmation. Indeed, in Ref. [33] experimental results were parametrized as

$$\langle \delta x^2(t) \rangle = 2D\tau_D \left[\frac{t}{\tau_D} + \left(\frac{t}{\tau_s} \right)^\alpha \right]. \quad (19)$$

Comparison with our model yields $\tau_c = [\Gamma(1+\alpha)\tau_D/\tau_s^\alpha]^{1/(1-\alpha)}$, $\kappa_1 = D$, and $\kappa_\alpha = D\tau_c^{1-\alpha}$. The experimental values of α , τ_D , and τ_s can be found for various cells in Ref. [33]. The corresponding asymptotic normal diffusion coefficient is $D = r_0^2/(4\tau_D)$, where $r_0 = 0.21$ μm is the microscope aperture size [33]. From this we can obtain κ_1 , κ_α , and τ_c (see Table I). For gold beads of this size in water $\kappa_{1,\text{water}} = 90$ $\mu\text{m}^2/\text{s}$. Therefore, from the experimental values of κ_1 in the cytoplasm of selected eukaryotic cells (possessing cytoskeleton) one can conclude that the cytoplasm is about $\kappa_{1,\text{water}}/\kappa_1 \sim 750$ times more viscous than water and about two times less viscous than glycerol. On the maximal time scale of experimental data in Ref. [33], which is about 1 s, the particles subdiffuse much faster than one would expect from the normal diffusion in such a viscous environment. This paradoxical and overlooked fact should be taken into account in any discussion of the influence of transient subdiffusion on living processes as it appears that subdiffusion can bring only advantages, contrary to some common expectations [27].

In this respect, GLE subdiffusion can provide additional advantages over semi-Markovian CTRW subdiffusion in the

TABLE I. Parameters derived from experimental data.

Cell	α	τ_D (ms)	τ_s (ms)	τ_c (s)	κ_1 ($\mu\text{m}^2/\text{s}$)	κ_α ($\mu\text{m}^2/\text{s}^\alpha$)
HeLa	0.51	91	0.271	30.3	0.121	0.644
THLE	0.48	89	0.329	16.7	0.124	0.536
HepG2	0.52	88	0.767	37.6	0.125	0.715
HeLa + 500 mM sucrose	0.66	92	0.954	2875	0.119	0.931

case of a three-dimensional search of a target (e.g., a binding site for regulatory protein on a gene promoter). The solution of Eqs. (16)–(18) in the limit $\tau_c \rightarrow \infty$ [34] is the fractional Brownian motion (fBm) by Kolmogorov [35] and Mandelbrot and van Ness [36]. The fractal Hausdorff dimension of its trajectories occupying 3D space is $d_H = 2/\alpha$, for $2/3 < \alpha < 1$, and $d_H = 3$ for $0 < \alpha \leq 2/3$ [37]. Hence, for $\alpha \leq 2/3$ the fBm fills densely in the three-dimensional Euclidean space. Therefore, on the time scale $t < \tau_c$ and the corresponding spatial scale the GLE subdiffusion can help dramatically to find even the smallest targets. This remarkable property is because of antipersistence of fBm increments [37]. On the contrary, subdiffusive semi-Markovian CTRW trajectories have the same $d_H = 2$ as normal Brownian motion in 3D because increments are independent and abnormal behavior stems from a very broad residence time distribution and not from the antipersistence. For the diffusion in the plane the situation changes since both the normal and the anomalously slow (either GLE or CTRW) Brownian motions have the same $d_H = 2$, which coincides with Euclidean dimension of the embedding space, independently of α . Here, no addi-

tional advantages can be provided by the GLE subdiffusion. The same is valid also for a 1D diffusional search and corresponding diffusion-limited reactions. Nevertheless, transient subdiffusion remains faster on mesoscale than one expects for normal diffusion in a fluidlike medium of large macroscopic viscosity, independently of underlying physical mechanisms.

IV. CONCLUSION

The author is confident that the modified CTRW and FFPE theory of mesoscopic subdiffusive transport considered in this work presents a viable alternative to the traditional one. It shares more similarities with viscoelastic subdiffusion and should be taken seriously as an ample modeling framework with attractive physical features and clear experimental relevance.

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