Subdiffusion in an external potential: Anomalous effects hiding behind normal behavior

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We propose a model of subdiffusion in which an external force is acting on a particle at all times not only at the moment of jump. The implication of this assumption is the dependence of the random trapping time on the force with the dramatic change of particles behavior compared to the standard continuous time random walk model in the long time limit. Constant force leads to the transition from non-ergodic subdiffusion to ergodic diffusive behavior. However, we show this behavior remains anomalous in a sense that the diffusion coefficient depends on the external force and on the anomalous exponent. For quadratic potential we find that the system remains non-ergodic. The anomalous exponent in this case defines not only the speed of convergence but also the stationary distribution which is different from standard Boltzmann equilibrium.

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I. INTRODUCTION

Recently it has become clear that anomalous diffusion measured by a non-linear growth of the ensemble averaged mean squared displacement $\langle x^2 \rangle \sim t^{\mu}$ with the anomalous exponent $\mu \neq 1$ is as widespread and important as normal diffusion with $\mu = 1$ [1]. Subdiffusion with $\mu < 1$ was observed in many physical and biological systems such as porous media [2], glass-forming systems [3], motion of single viruses in the cell [4], cell membranes [5,6], and inside living cells [7–9]. Many examples of subdiffusive processes in biological systems can be found in recent reviews [10,11]. Nowadays new tools are available including super-resolution light optical microscopy techniques to deal with biological in vivo data which allows to monitor a large number of trajectories at the single-molecule level and at nanometre resolution [12–14]. Using these techniques it is possible to discriminate between anomalous ergodic processes where the ensemble and time averages coincide and non-ergodic processes where ensemble and time averages have different behavior [15–17]. Two important observations have been made about anomalous transport in living cells: (1) anomalous transport is usually a transient phenomenon before transition to normal diffusion or saturation due to confined space [18–20] (2) ergodic and non-ergodic processes may coexist as it was observed in plasma membrane [21].

Several models were proposed to describe ergodic and non-ergodic anomalous processes such as non-ergodic continuous time random walk (CTRW) with power-law tail waiting times, ergodic anomalous process generated by fractal structures, fractional Brownian-Langevin motion characterized by long correlations and time-dependent diffusion coefficient, and scaled Brownian motion [1,22–24]. The standard CTRW model for subdiffusion of a particle in an external field $F(x)$ randomly moving along discrete one-dimensional lattice can be described by the generalized master equation for the probability density $p(x,t)$ to find the particle at position x at time t

$$\frac{\partial p}{\partial t} = -i(x,t) + w^{+}(x-a)i(x-a,t) + w^{-}(x+a)i(x+a,t), \tag{1}$$

where a is the lattice spacing and $i(x,t)$ is the total escape rate from x

$$i(x,t) = \frac{1}{\Gamma(1-\mu)\tau_0^{\mu}} \mathcal{D}_t^{1-\mu} p(x,t). \tag{2}$$

Here τ_0 is a constant time scale and $\mathcal{D}_t^{1-\mu}$ is the Riemann-Liouville fractional derivative defined by

$$\mathcal{D}_t^{1-\mu} p(x,t) = \frac{1}{\Gamma(\mu)} \frac{\partial}{\partial t} \int_0^t \frac{p(x,\tau)}{(t-\tau)^{1-\mu}} d\tau. \tag{3}$$

The probabilities of jumping to the right $w^{+}(x)$ and to the left $w^{-}(x)$ are

$$w^{+}(x) = \tfrac{1}{2} + \beta a F(x), \quad w^{-}(x) = \tfrac{1}{2} - \beta a F(x). \tag{4}$$

Series expansion of Eq. (1) together with Eqs. (2) and (4) leads to the fractional Fokker-Planck equation (FFPE) [25,26]

$$\frac{\partial p}{\partial t} = D_{\mu} \left[\frac{\partial^2}{\partial x^2} - \beta \frac{\partial}{\partial x} F(x) \right] \mathcal{D}_t^{1-\mu} p, \tag{5}$$

where the generalized diffusion $D_{\mu} = a^2/[2\,\Gamma(1-\mu)\tau_0^{\mu}]$. The stationary solution of Eq. (5) in a confining potential is the Boltzmann distribution. There exist a huge literature on this equation [25,26] and its generalization for time-dependent forces [27–33].

One of the main assumptions in this literature, which is not always clearly stated is that, as long as a random walker is trapped at a particular point x, the external force $F(x)$ does not influence the particle. It is clear from Eq. (2) that the escape rate $i(x,t)$ does not depend on the external force $F(x)$. The force only acts at the moment of escape inducing a bias. The question is how to take into account the dependence of the escape rate on $F(x)$? To the author's knowledge this is still an open question. One of the main aims of this paper is to propose a model which deals with this problem. We find that the dependence of escape rate on force drastically changes the form of the master equation (1) and FFPE (5). We observe transient anomalous diffusion and transition from non-ergodic to normal ergodic behavior. However, we show that this seemingly normal process could be still anomalous masked by normal behavior. Our findings suggest that a closer inspection of experimental results could be necessary in order to discriminate between normal and anomalous processes.

II. RANDOM WALK MODEL

We consider a random particle moving on a one-dimensional lattice under assumption that an external force acts on a particle at all times not only at the moment of jump as in Eq. (1). The implication of this assumption is the dependence of the random trapping time on the external force [not just jumping probabilities as in Eq. (4)]. Some discussion of the situation when the external force influence the rates and jumps can be found in [27]. The influence of the time-dependent force on the non-Poisson two-state model was considered in [34]. The authors of this paper considered the dependence of the sojourn time distributions on the force.

The main physical idea behind our model is different. We assume that there exists two independent mechanisms of escaping from the point x with two different random residence times. The first mechanism is due to external force with the escape rate which we assume to be proportional to $F(x)$. The second one is the subdiffusive mechanism involving the rate inversely proportional to the residence time. The latter generates the power-law waiting time distribution with the infinite first moment.

Regarding the first mechanism, we define the jump process from the point x as follows. We assume that the rate of jump to the right $\mathbb{T}_x^+$ from x to $x+a$ is $\nu aF(x)$ when $F(x) \geqslant 0$ and the rate of jump to the left $\mathbb{T}_x^-$ from x to $x-a$ is $-\nu aF(x)$ when $F(x) \leqslant 0$. For this jump model the random waiting time T_F at the point x is defined by the exponential survival probability $\Psi_F(x,\tau)$ involving the external force $F(x)$

$$\Psi_F(x,\tau) = \Pr\{T_F > \tau\} = \exp(-\nu a|F(x)|\tau), \tag{6}$$

where ν is the intensity of jumps due to force field. For example, one can think of the escape rate $\mathbb{T}_x^+$ that is defined in terms of the potential field $U(x)$ that is $\mathbb{T}_x^+ = -\nu[U(x+a) - U(x)] > 0$, there $F(x) = -U'(x) + o(a^2)$ for $U'(x) \leqslant 0$. In this paper we consider the "weak force" case for which the rate $\nu a|F|$ is small enough such that

$$\nu a|F|\tau_0 \ll 1. \tag{7}$$

The second mechanism involves the random walk escape rate $\lambda(\tau)$. In case of Poisson random walk this rate is constant $\lambda(\tau) = \text{const}$. Here we consider the escape rate which is inversely proportional to the residence time τ

$$\lambda(\tau) = \frac{\mu}{\tau_0 + \tau}, \tag{8}$$

where τ_0 is a parameter with units of time. In this case the random waiting time T_λ at the point x is defined by the survival probability

$$\Psi_\lambda(\tau) = \Pr\{T_\lambda > \tau\} = \exp\left(-\int_0^\tau \lambda(s)ds\right). \tag{9}$$

It follows from Eqs. (8) and (9) that the survival function is

$$\Psi_\lambda(\tau) = \left(\frac{\tau_0}{\tau_0 + \tau}\right)^\mu. \tag{10}$$

The corresponding waiting time probability density function (pdf) has a power-law dependence

$$\psi_\lambda(\tau) = -\frac{d\Psi_\lambda}{d\tau} = \frac{\mu\tau_0^\mu}{(\tau_0 + \tau)^{1+\mu}}. \tag{11}$$

For $\mu < 1$ the waiting time pdf $\psi_\lambda(\tau)$ has infinite first moment which corresponds to subdiffusion.

The question now is how to implement the jumping process due to external force into the subdiffusive random walk scheme? When the random walker makes a jump to the point x, it spends some random time (residence time) before making another jump to $x+a$ or $x-a$. Let us denote this residence time T_x. The key point of our model is that we define this residence time as the minimum of two: T_λ and T_F

$$T_x = \min(T_\lambda, T_F). \tag{12}$$

For the anomalous subdiffusive case this model leads to the drastic change in the form of the fractional master equation. The main reason for this is that the external force $F(x)$ plays the role of tempering factor preventing the random walker from been trapped at point x anomalously long. To see this we notice that the survival probability corresponding to the random time T_x, $\Psi(x,\tau) = \Pr\{T_x > \tau\}$, is a product of Eqs. (6) and (10)

$$\Psi(x,\tau) = \Psi_\lambda(\tau)\Psi_F(x,\tau) = \Psi_\lambda(\tau)\exp(-\nu a|F(x)|\tau). \tag{13}$$

So, the waiting time probability density function $\psi(x,\tau) = -\partial\Psi(x,\tau)/\partial\tau$ is given by

$$\psi(x,\tau) = \psi_\lambda(\tau)\exp(-\nu a|F(x)|\tau) + \Psi_\lambda(\tau)\nu a|F(x)|\exp(-\nu a|F(x)|\tau). \tag{14}$$

Note that this pdf is different from the standard one involving exponential tempering factor [35]. In our case the tempering is more complex. It has two terms and depends on the external force. Because of the independence of two mechanisms, in our model the rate of jumps $\mathbb{T}_x^+$ to the right from x to $x+a$ and the rate of jumps $\mathbb{T}_x^-$ to the left from x to $x-a$ can be written as the sum

$$\mathbb{T}_x^+ = \begin{cases} \omega^+(x)\lambda(\tau) + \nu aF(x), & F(x) \geqslant 0, \\ \omega^+(x)\lambda(\tau), & F(x) < 0 \end{cases} \tag{15}$$

and

$$\mathbb{T}_x^- = \begin{cases} \omega^-(x)\lambda(\tau), & F(x) \geqslant 0, \\ \omega^-(x)\lambda(\tau) - \nu aF(x), & F(x) < 0. \end{cases} \tag{16}$$

Although it is straightforward to consider general $\omega^+(x)$ and $\omega^-(x)$, for simplicity in what follows we consider $\omega^+(x) = \omega^-(x) = 1/2$. In our model the asymmetry of random walk occurs only from the force dependent rates. Let us explain the main idea of Eqs. (15) and (16). The external force $F(x) \geqslant 0$ increases the subdiffusive rate of jumps to the right and does not change the subdiffusive rate of jumps to the left. The essential property of Eqs. (15) and (16) is that the rate $\lambda(\tau)$ depends on the residence time variable τ. This dependence makes any model involving the probability density $p(x,t)$ non-Markovian. For the Markov case with $F(x) = 0$, λ^{-1} has a meaning of the mean residence time. When the parameter $\nu = 0$ and the rates are $\mathbb{T}_x^+ = w^+(x)\lambda(\tau)$, $\mathbb{T}_x^- = w^-(x)\lambda(\tau)$, we obtain the standard fractional Fokker-Planck equation (5). Notice that Eq. (12) is consistent with the expression for the effective escape rate $\mathbb{T}_x^+ + \mathbb{T}_x^-$ as a sum of two rates $\lambda(\tau) + \nu a|F(x)|$. Similar situation has been considered in [36].

Markovian model

As an illustration let us consider a Markovian model for which the rate of escape $\lambda(x,\tau)$ is independent of the residence time τ with the constant rate $\lambda(\tau) = \text{const}$. It follows from Eqs. (15) and (16) and the assumption $w^+ = w^- = 1/2$ that the master equation for the probability density $p(x,t)$ takes the form

$$\frac{\partial p}{\partial t} = -\lambda p(x,t) + \lambda p(x-a,t)/2 + \lambda p(x+a,t)/2 + \Phi, \tag{17}$$

where

$$\Phi = \begin{cases} -\nu a F(x) p(x,t) + \nu a F(x-a) p(x-a,t), & F \geqslant 0, \\ \nu a F(x) p(x,t) - \nu a F(x+a) p(x+a,t), & F < 0. \end{cases} \tag{18}$$

Here we put $\tau_0 = 1$ assume that and $F(x)$ and $F(x+a)$ have the same sign for small values of a. We expand the right-hand side of a master equation (17) to second order in jump size a and obtain the advection-diffusion equation

$$\frac{\partial p(x,t)}{\partial t} = -\nu a^2 \frac{\partial}{\partial x}[F(x)p] + \frac{\lambda a^2}{2}\frac{\partial^2 p}{\partial x^2} + o(a^2). \tag{19}$$

One can see that the dependence of the escape rate from the external force $F(x)$ leads only to the advection term. When the force $F(x) = -\partial U(x)/\partial x$ and $\nu = \lambda/(2k_B T)$ (here k_B is the Boltzmann constant and T is the temperature), the stationary solution is given by Boltzmann equilibrium

$$p_{st}(x) = N e^{-\frac{U(x)}{k_B T}}, \tag{20}$$

with some normalization constant N. In the non-Markovian case we expect essential modifications of the governing equations with the stationary solution different from standard Boltzmann equilibrium.

III. GENERALIZED MASTER AND FRACTIONAL DIFFUSION EQUATION

Now we derive corresponding generalized master and fractional diffusion equations for the case involving the rates (15) and (16). We use structured probability density function $\xi(x,t,\tau)$ with the residence time τ as an auxiliary variable. This density gives the probability that the particle position $X(t)$ at time t is at the point x and its residence time T_x at point x is in the interval $(\tau,\tau+d\tau)$. The density $\xi(x,t,\tau)$ obeys the balance equation

$$\frac{\partial \xi}{\partial t} + \frac{\partial \xi}{\partial \tau} = -[\mathbb{T}_x^+(x,\tau) + \mathbb{T}_x^-(x,\tau)]\xi. \tag{21}$$

We consider only the case when the residence time of random walker at $t=0$ is equal to zero, so the initial condition is

$$\xi(x,0,\tau) = p_0(x)\delta(\tau), \tag{22}$$

where $p_0(x)$ is the initial density. The boundary condition in terms of residence time variable ($\tau = 0$) can be written as [37]

$$\xi(x,t,0) = \int_0^t \mathbb{T}_x^+(x-a,\tau)\xi(x-a,t,\tau)d\tau + \int_0^t \mathbb{T}_x^-(x+a,\tau)\xi(x+a,t,\tau)d\tau. \tag{23}$$

We solve Eq. (21) by the method of characteristics for $\tau < t$:

$$\xi(x,t,\tau) = \xi(x,t-\tau,0)e^{-\int_0^\tau \lambda(\tau)d\tau - \nu a|F(x)|\tau}. \tag{24}$$

The structural density ξ can be rewritten in terms of the survival function Eq. (9) and the integral arrival rate

$$j(x,t) = \xi(x,t,0)$$

as

$$\xi(x,t,\tau) = j(x,t-\tau)\Psi_\lambda(x,\tau)e^{-\nu a|F(x)|\tau}, \quad \tau < t. \tag{25}$$

Our purpose now is to derive the master equation for the probability density

$$p(x,t) = \int_0^{t^+} \xi(x,t,\tau)d\tau. \tag{26}$$

Let us introduce the integral escape rate to the right $i^+(x,t)$ and the integral escape rate to the left $i^-(x,t)$ as

$$i^\pm(x,t) = w^\pm(x)\int_0^{t^+} \lambda(\tau)\xi(x,t,\tau)d\tau. \tag{27}$$

We should note that the integration with respect to the residence time τ in Eqs. (26) and (27) involves the upper limit $\tau = t$, where we have a singularity due to the initial condition (22). Then the boundary conditions (23) can be written in a simple form:

$$j(x,t) = i^+(x-a,t) + i^-(x+a,t) + \begin{cases} \nu a F(x-a)p(x-a,t), & F \geqslant 0, \\ -\nu a F(x+a)p(x+a,t), & F < 0. \end{cases} \tag{28}$$

It follows from Eqs. (22), (25), and (27) that

$$i^\pm(x,t) = \int_0^t \psi^\pm(x,\tau)j(x,t-\tau)e^{-\nu a|F(x)|\tau}d\tau + \psi^\pm(x,t)p_0(x)e^{-\nu a|F(x)|t}, \tag{29}$$

where

$$\psi^\pm(x,\tau) = w^\pm(x)\psi_\lambda(\tau) = w^\pm(x)\lambda(\tau)\Psi_\lambda(\tau). \tag{30}$$

Substitution of Eqs. (22) and (25) to Eq. (26), gives

$$p(x,t) = \int_0^t \Psi_\lambda(\tau)j(x,t-\tau)e^{-\nu a|F(x)|\tau}d\tau + \Psi_\lambda(t)p_0(x)e^{-\nu a|F(x)|t}. \tag{31}$$

The balance equation for probability density $p(x,t)$ can be written as

$$\frac{\partial p}{\partial t} = -i^+(x,t) - i^-(x,t) + j(x,t) - \nu a|F(x)|p. \tag{32}$$

Let us find a closed equation for $p(x,t)$ by finding the formulas for the integral rates $i^\pm(x,t)$ and $j(x,t)$ in terms of density $p(x,t)$. We apply the Laplace transform $\hat{f}(s) = \int_0^\infty f(\tau)e^{-s\tau}d\tau$ to Eqs. (29) and (31), and obtain

$$\hat{\imath}^{\pm}(x,s) = \hat{\psi}^{\pm}(x,s+\nu a|F(x)|)[\hat{\jmath}(x,s)+p_0(x)]$$

and

$$\hat{p}(x,s) = \hat{\Psi}_\lambda(s+\nu a|F(x)|)[\hat{\jmath}(x,s)+p_0(x)].$$

From these two equations we find

$$\hat{\imath}^{\pm}(x,s) = \frac{\hat{\psi}^{\pm}(x,s+\nu a|F(x)|)}{\hat{\Psi}_\lambda(s+\nu a|F(x)|)}\hat{p}(x,s). \tag{33}$$

Applying the inverse Laplace transform and using the shift theorem we obtain

$$i^{\pm}(x,t) = \int_0^t K^{\pm}(x,t-\tau)e^{-\nu a|F(x)|(t-\tau)}p(x,\tau)d\tau,$$

where $K^+(x,t)$ and $K^-(x,t)$ are the memory kernels defined by Laplace transforms

$$\hat{K}^{\pm}(x,s) = \frac{\hat{\psi}^{\pm}(x,s)}{\hat{\Psi}_\lambda(s)}. \tag{34}$$

A. Generalized fractional diffusion equation

Now we derive the generalized fractional diffusion equation for subdiffusion that is for $\lambda(\tau)$ given by Eq. (8). For simplicity we consider

$$w^+ = w^- = 1/2. \tag{35}$$

It is straightforward to generalize to non-homogeneous systems by considering space dependent $\lambda(x,\tau)$ and space dependent anomalous exponent $\mu(x)$, this case we consider elsewhere [38,39]. The waiting time probability density functions Eq. (30) are

$$\psi^{\pm}(\tau) = \frac{1}{2}\psi_\lambda(\tau) = \frac{1}{2}\frac{\mu\tau_0^\mu}{(\tau_0+\tau)^{1+\mu}}. \tag{36}$$

The Laplace transform of the waiting time densities (36) can be found from $\psi_\lambda(\tau)$ Eq. (11) using the Tauberian theorem

$$\hat{\psi}_\lambda(s) \simeq 1 - gs^\mu, \quad s\to 0$$

with

$$g = \Gamma(1-\mu)\tau_0^\mu. \tag{37}$$

From Eq. (34) we obtain the Laplace transforms

$$\hat{K}^{\pm}(s) \simeq \frac{s^{1-\mu}}{2g}, \quad s\to 0. \tag{38}$$

Therefore, the integral escape rates to the right $i^+(x,t)$ and to the left $i^-(t)$ in the subdiffusive case are

$$i^{\pm} = e^{-\nu a|F(x)|t}\mathcal{D}_t^{1-\mu}[p(x,t)e^{\nu a|F(x)|t}]/(2g). \tag{39}$$

By introducing the total integral escape rate

$$i(x,t) = i^+(x,t) + i^-(x,t), \tag{40}$$

and expanding the right-hand side of Eq. (32) to second order in jump size a we obtain the following fractional equation:

$$\frac{\partial p}{\partial t} = -a^2\nu\frac{\partial}{\partial x}[F(x)p(x,t)] + \frac{a^2}{2}\frac{\partial^2 i}{\partial x^2}, \tag{41}$$

which using Eq. (39) leads to the main equation of the paper—the generalized fractional diffusion equation:

$$\frac{\partial p}{\partial t} = \frac{\partial^2}{\partial x^2}\left[D_\mu e^{-\nu a|F(x)|t}\mathcal{D}_t^{1-\mu}[p(x,t)e^{\nu a|F(x)|t}]\right] - a^2\nu\frac{\partial}{\partial x}[F(x)p(x,t)]. \tag{42}$$

We should note that Eq. (42) does not involve the standard subdiffusive limit $a\to 0,\tau_0\to 0$ such that $D_\mu = a^2/[2\Gamma(1-\mu)\tau_0^\mu]$ remains constant. This fractional equation describes the transition from an intermediate subdiffusion to an asymptotically normal advection-diffusion transport. Within the time scale T_1 for which $\tau_0/T_1 \ll 1$ and $\nu a|F|T_1 \ll 1$ we have the intermediate subdiffusive regime, while for T_2 with $\nu a|F|T_2 \gg 1$ we obtain normal diffusion. This implies that $\nu a|F|\tau_0 \ll 1$. Numerical simulations (see below) confirms that Eq. (11) is a good approximation for the master equation.

Equation (42) is fundamentally different from the classical FFPE (5) because it involves the external force in both terms on the right-hand side. One can see that the force $F(x)$ not only determines the advection term as in Eq. (5), but also plays the role of tempering parameter through the factor $e^{\nu a|F(x)|t}$. Similar factor occurs in subdiffusive equation with the death or evanescent process [40,41]. However, here we consider the system with constant total number of particle.

B. Constant force

First we consider linear potential which results in a constant force. We assume $F>0$. The generalized fractional diffusion equation Eq. (42) in this case simplifies to

$$\frac{\partial p}{\partial t} = e^{-\nu aFt}\frac{\partial^2}{\partial x^2}\left[D_\mu\mathcal{D}_t^{1-\mu}[p(x,t)e^{\nu aFt}]\right] - a^2\nu F\frac{\partial}{\partial x}[p(x,t)]. \tag{43}$$

Applying simultaneously Laplace and Fourier transforms $\mathcal{L}\{f(t)\} = \hat{f}(s) = \int_0^\infty f(\tau)e^{-s\tau}d\tau$, $\mathcal{F}\{f(x)\} = \tilde{f}(k) = \int_{-\infty}^\infty f(x)e^{-ikx}dx$, and using the Laplace transform of the fractional derivative $\mathcal{L}\{\mathcal{D}_t^{1-\mu}f(t)\} = s^{1-\mu}\hat{f}(s)$ for $0<\mu<1$, the solution of this equation reads

$$\hat{\tilde{p}}(k,s) = \frac{1}{s + k^2D_\mu(s+\nu aF)^{1-\mu} + ikFa^2\nu}. \tag{44}$$

Here we use the initial condition $p(x,0) = \delta(x)$, which has the Fourier transform $\tilde{p}(k) = 1$. Taking the limit $s\to 0$ and $k\to 0$ which corresponds to the long time and large distance limit, we get

$$\hat{\tilde{p}}(k,s) = \frac{1}{s + k^2D_\mu(\nu aF)^{1-\mu} + ikFa^2\nu}. \tag{45}$$

The inverse Fourier-Laplace transform of Eq. (45) is the solution of the diffusion-advection equation

$$\frac{\partial p}{\partial t} = D_F\frac{\partial^2}{\partial x^2}p(x,t) - v\frac{\partial}{\partial x}p(x,t). \tag{46}$$

Of course, the solution of this equation is a celebrated Gaussian density with the diffusion coefficient and advection velocity given by

$$D_F = D_\mu (\nu a F)^{1-\mu}, \quad v = \nu F a^2. \tag{47}$$

However, note that in our case the long-time limit is drastically different from the standard Fokker-Planck equation because both advection and diffusion coefficients depend on the external force. This is another example how anomalous effects are hiding behind the seemingly normal behavior.

Transition from subdiffusive density at short times to Gaussian density in the long-time limit occurs since the external force acts as a tempering factor which introduces a cut-off to the power-law waiting time distribution. However the difference of our generalized fractional equation from known fractional Fokker-Planck equation is that in our case the tempering is more complex [see Eq. (14)]. It has two terms and depends on the external force. Numerical results of Sec. IV confirms our theoretical predictions.

C. Stationary solution in a confining potential

In a confining potential the system attains equilibrium. To derive the equation for the stationary solution we write the escape rate $i(x,t)$ in Laplace form

$$\hat{i}(x,s) = \frac{(s + \nu a|F(x)|)^{1-\mu}}{g}\hat{p}(x,s), \tag{48}$$

take the limit $s \to 0$ corresponding to $t \to \infty$, and obtain the stationary escape rate

$$i_{st}(x) = \frac{(\nu a|F(x)|)^{1-\mu}}{g} p_{st}(x), \tag{49}$$

where the stationary density is defined in a standard way $p_{st}(x) = \lim_{s\to 0} s\,\hat{p}(x,s)$. Taking the time derivative in Eq. (41) to zero and substituting Eq. (49) we obtain the stationary advection-diffusion equation

$$-a^2\nu\frac{d}{dx}[F(x)p_{st}(x)] + \frac{d^2}{dx^2}[D_F(x)p_{st}(x)] = 0, \tag{50}$$

where the effective diffusion coefficient is

$$D_F(x) = D_\mu(\nu a|F(x)|)^{1-\mu}. \tag{51}$$

Integrating Eq. (50) and taking into account that the flux of the particles is zero we obtain

$$-a^2\nu F(x)p_{st}(x) + \frac{d}{dx}[D_F(x)p_{st}(x)] = 0. \tag{52}$$

An interesting property of Eq. (51) is that the effective diffusion coefficient $D_F(x)$ depends on the external force and anomalous exponent. This fact implies that the Boltzmann distribution is no longer a stationary solution of Eq. (52). For the quadratic potential $U(x) = \kappa x^2/2$ with $F(x) = -\kappa x$, we find that for large x the stationary density $p_{st}(x)$ has the form

$$p_{st}(x) \sim \exp(-A|x|^{1+\mu}), \tag{53}$$

where $A > 0$ is a constant (details are given in the next section). One can see that the form of stationary density is determined by the anomalous exponent μ. In this case the particles spread further compared to the Boltzmann case. The reason is the dependence of the effective diffusion constant $D_F(x)$ on force $F(x)$. Note that for the subdiffusive fractional Fokker-Planck equation (5) the anomalous exponent only determines the slow power law relaxation rate, while the stationary density converges to Boltzmann equilibrium which does not depend on μ.

IV. NUMERICAL RESULTS

We consider two particular cases: (1) constant force F corresponding to the linear potential and (2) the quadratic potential $U(x) = \kappa x^2/2$ both in the infinite domain. We concentrate on the behavior of the density function $p(x,t)$, the mean $\langle x(t)\rangle$ and the variance $\sigma(t) = \langle x^2\rangle - \langle x\rangle^2$ calculated using an ensemble of trajectories from the initial distribution $p(x,0) = \delta(x)$. We also calculate the time averaged variance of a single trajectory of length T, $\sigma_T(\Delta,T) = \delta^2(\Delta,T) - [\delta(\Delta,T)]^2$, where $\delta^n(\Delta,T) = \int_0^{T-\Delta}[x(t+\Delta) - x(t)]^n dt/(T-\Delta)$, $n = 1,2$. This quantity become a standard tool to assess ergodic properties of a system been equivalent to its ensemble averaged counterpart only for ergodic case.

When the external force F is constant, we observe the transition from subdiffusion at short times to seemingly normal diffusion at long times (see Sec. III B). The density function changes from the distinct subdiffusive shape for short times to the Gaussian propagator at longer times. This transition is confirmed numerically and shown in the inset of Fig. 1. The ensemble averaged variance $\sigma(t)$ grows as a power-law for short times, $\sigma(t) \sim t^\eta$, and transition to a normal diffusive linear growth $\sigma(t) \sim 2D_F t$ for longer times. However, in this case the diffusion coefficient D_F given by Eq. (47) depends on the force F and anomalous exponent μ. We conclude that although the variance $\sigma(t)$ is linearly proportional to time,

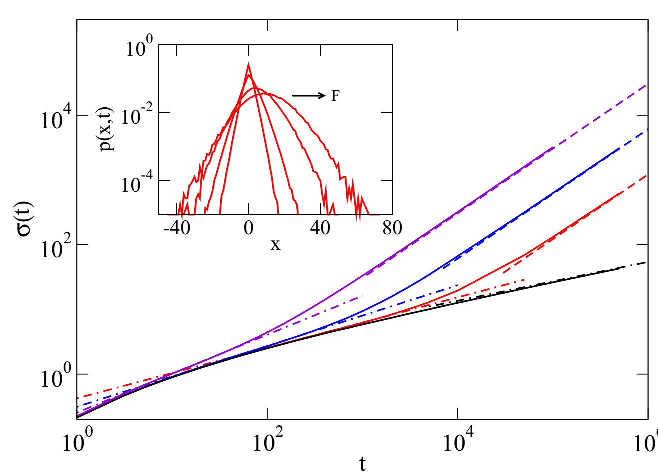

FIG. 1. (Color online) Variance $\sigma(t) = \langle x^2\rangle - \langle x\rangle^2$ of ensemble calculated with $\mu = 0.3$ and $p(x,0) = \delta(x)$. In all simulations we use $\nu = 1$, $a = 0.1$, and $\tau_0 = 1$. For $F = 0$ (lowest curve) the variance grows as $D_\mu t^\mu$ (dashed-dotted line) in the limit $t \to \infty$. Constant force $F = 0.0001$, $F = 0.001$, and $F = 0.01$ (curves from bottom to top on the RHS of the figure) leads to the transition from subdiffusive behavior for short times to normal diffusion in the long time limit, $\sigma \to 2D_F t$ (dashed lines), with D_F given by Eq. (47). Intermediate asymptotic of the variance is fitted by the power-law (dashed-dotted lines, see the text). The inset shows transition of densities from subdiffusive form for short times to the Gaussian shape for long times caused by the constant force $F = 0.0001$. Densities were calculated at $t = 10^3$, 10^4, 5×10^4, and 10^5.

this dependence reveals the anomalous nature of the process even in the limit $t \to \infty$. Numerical calculations confirms the analytical result for the diffusion coefficient Eq. (47) (see Fig. 1). Second observation is that the power-law behavior at short times involves the exponent $\eta(F) > \mu$ which depends on force F. For $\mu = 0.3$ they are estimated to be $\eta \approx 0.39$ for $F = 0.0001$, $\eta \approx 0.47$ for $F = 0.001$, and $\eta \approx 0.6$ for $F = 0.01$. This can be interpreted as an enhancement of subdiffusion coursed by the constant force. Such enhancement should be taken into account in the analysis of biological experiments where subdiffusion usually appears as transient before the transition to the normal diffusion [10]. For the large value of F the exponent η tends to one while in the small force limit $\eta \to \mu$. The time averaged variance calculated for constant force grows linearly $\sigma_T(\Delta,T) \sim \Delta$ (see Fig. 2). After averaging over different trajectories, it grows with the coefficient $2D_F$ which is equal to the ensemble average value. This shows that the non-ergodic subdiffusive system (without no force) becomes ergodic one under the action of the constant external force.

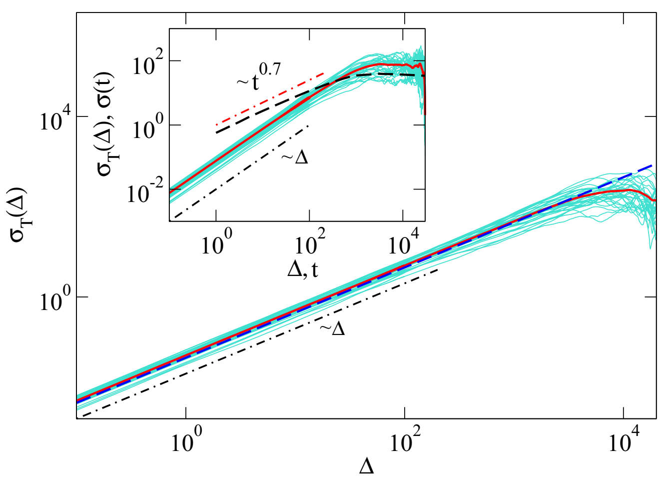

FIG. 2. (Color online) Main figure: The action of the constant force $F = 0.001$. Time-averaged variance $\sigma_T(\Delta,T)$ calculated for 30 individual trajectories each of a length $T = 3 \times 10^4$ (each curve corresponds to a single trajectory) with $\mu = 0.7$. Bold solid curve (red) represents the average over 30 trajectories. The time averaged variance is proportional to the time lag $\sigma_T(\Delta,T) \sim \Delta$ as indicated by dashed-dotted line. The dashed (blue) line represents the long time asymptotic of the ensemble averaged variance and is given by $2D_F t$ with D_F defined by Eq. (47) (see the text). The equality between the time and the ensemble averaged variance reflects the ergodic behavior of the system under the action of constant external force. Inset: Contrast this with the behavior in the quadratic potential $U(x) = \kappa x^2/2$ with $\kappa = 0.001$. Each individual curve corresponds to the time averaged variance of a single trajectory with $\mu = 0.7$. The bold solid (red) line represents average over 30 trajectories. The dashed (black) curve is the numerically calculated ensemble averaged variance. For small t the variance has power-law behavior $\sigma(t) \sim t^{\mu}$ and in the long time limit it saturates due to the confined space. The time averaged variance is proportional to the time lag $\sigma_T(\Delta,T) \sim \Delta$ (as indicated by dashed-dotted line) before it also saturates to a different than the ensemble averaged variance value. This indicates that the behavior of the system in the quadratic potential is non-ergodic.

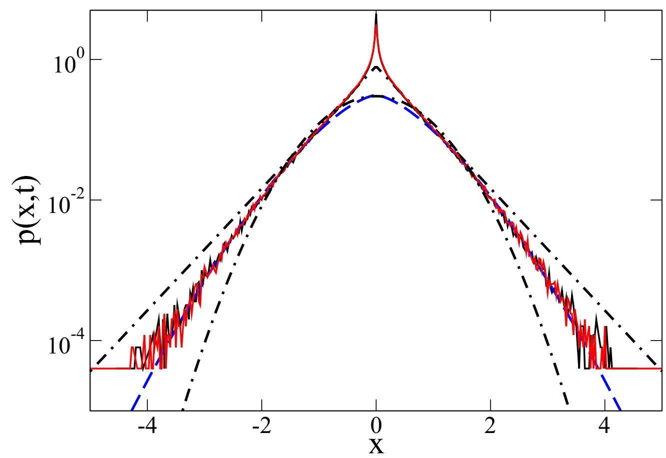

FIG. 3. (Color online) Density $p(x,t)$ in the quadratic potential $U(x) = kx^2$, $k = 0.001$ calculated with the anomalous exponent $\mu = 0.5$ at time $t = 10^5$ and $t = 10^6$. Two densities overlap indicating convergence to stationary solution p_{st}. Clearly p_{st} is non-Boltzmann and is well described (accept for the central part) by the long-wave asymptotic Eq. (52) shown by the dashed line. To distinguish the form of the stationary solution $\exp(-A|x|^{1+\mu})$, we show the Boltzmann equilibrium $\exp(-Bx^2)$ and the function $\exp(-C|x|)$ (dashed-dotted curves) to guide the eye (A,B,C are positive constants). Note that the central part of p_{st} has distinct cusp at $x = 0$ where the force vanishes.

Now we consider the quadratic potential $U(x) = \kappa x^2/2$. Again we calculate the time averaged variance and compare it with the ensemble averaged variance (inset of Fig. 2). For small t the ensemble averaged variance has the power-law behavior $\sigma(t) \sim t^{\mu}$ and in the long-time limit it saturates due to the confined space. The time averaged variance is proportional to the time lag $\sigma_T(\Delta,T) \sim \Delta$ before it also saturates to a different than the ensemble averaged variance value. This indicates that the behavior of the system in the quadratic potential becomes again non-ergodic despite the tempering affect of the force. The reason for this is that the tempering effect of the external force in our case is more complex than standard tempering and depends on force [see Eq. (14)]. Opposite to the constant force, in quadratic potential the tempering effect of the force becomes position dependent. This complex behavior is also reflected in the shape of the stationary density which is not given by Boltzmann density. Numerical simulations of the stationary density are in good agreement with analytical result Eq. (53) (see Fig. 3).

V. CONCLUSIONS

We have presented a model of anomalous subdiffusive transport in which the force acts on the particle at all times not only at the moment of jump. This leads to the dependence of jumping rate on the force with the dramatic change of particles behavior compared to the standard CTRW model. We have derived a new type of fractional diffusion equation which is fundamentally different from the classical fractional Fokker-Planck equation. In our model the force $F(x)$ not only appears in the drift term as in Eq. (5), but also determines the structure of the diffusion term controlling the spread of particles. The constant external force leads to the natural tempering of the broad waiting time distribution and, as a result, to the transition to a seemingly normal diffusion (linear growth of the mean squared displacement) and equivalence of the time and ensemble averages. However, this may lead to a wrong conclusion in analyses of experimental results on transient subdiffusion [10] that the process is normal for large times. We have found that contrary to normal diffusion process in the external force field, the diffusion coefficient depends on the force and anomalous exponent. This fact implies that the Boltzmann distribution is no longer stationary solution. External perturbations and noise fluctuations are not separable which reflects the non-Markovian nature of the process even for large times.

Our results would be possible to test in experiments, for example, by considering a bead which is moving subdiffusively in an actin network. The motion of such a bead is very well described by a continuous time random walk type of dynamics with power law waiting time distribution caused by trapping of the bead inside network "cages" [42]. Force-measurements could be realized by using optical trap and tweezers which are the nano-tools capable of performing such measurements on individual molecules and organelles within the living cell [14] or by applying an external electromagnetic force and using magnetic bead. When the force is constant the dependence of the measures diffusion coefficient on the strength of the force would reveal the predicted power-law behavior $F^{1-\mu}$. For quadratic potential it could be possible to retrieve the form of the stationary profile (53) with the slow decay compared to Boltzmann distribution for large x.

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