LA-UR- 09-00708

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Title: Anomalous Diffusion and Scaling in Coupled Stochastic Processes

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Intended for: Submission to Phys. Rev. Lett.

Anomalous diffusion and scaling in coupled stochastic processes

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(Dated: January 29, 2009)

Ispired by problems in biochemical kinetics, we study statistical properties of an overdamped Langevin processes with the friction coefficient depending on the state of a similar, unobserved, process. Integrating out the latter, we derive the Focker-Planck the friction coefficient of the first depends on the state of the second. Integrating out the latter, we derive the Focker-Planck equation for the probability distribution of the former. This has the form of diffusion equation with time-dependent diffusion coefficient, resulting in an anomalous diffusion. The diffusion exponent can not be predicted using a simple scaling argument, and anomalous scaling appears as well. The diffusion exponent of the Weiss-Havlin comb model is derived as a special case, and the same exponent holds even for weakly coupled processes. We compare our theoretical predictions with numerical simulations and find an excellent agreement. The findings caution against treating biochemical systems with unobserved dynamical degrees of freedom by means of standandard, diffusive Langevin descritpion.

PACS numbers: 05.10.Gg,05.20.Dd,82.39.Rt

Introduction: Single molecule kinetics has come within a reach of biophysical experiments [1–4], and theoretical and computational tools for analysis of such processes have experienced a corresponding growth [5–9]. It is clear that the combinatorially large number of microscopic steps involved in even the simplest of biochemical events makes their rigorous stochastic treatment hard. For example, gene expression, often modeled as a single-step mRNA creation, in fact, includes transcription-factor-DNA binding, polymeraze recruitment, transcriptional bubble formation, and multiple elongation steps, each of which is a complex process on its own.

Therefore, any theoretical analysis of stochastic biochemical processes necessarily involves coarse-graining: identifying a small subset of dynamical variables that are modeled explicitly, while agglomerating the rest into an effective behavior. Such coarse-grained dynamics is often modeled using the master equation, the Fokker-Planck, or the Langevin approaches, which require Markoviness (the former two) or white-noise random forcing (the latter). Both of these assumptions are, generally, flawed, and *quantitative* corrections have been worked out in certains cases [10, 11]. Less explored is the possibility that internal degrees of freedom can introduce *qualitative* differences, such as long-range temporal correlations among state transitions, or the random forcing spectrum that diverges at zero frequency.

A well-studied example shows that this is possible for a Langevin system. In Ref. [12], Weiss and Havlin have analyzed a two-dimensional diffusion model, known as the *comb* model. There diffusion along the y coordinate is unhindered, while motion along x is allowed only when $y = 0$. This results in $\langle x\rangle = 0$ and $\langle x^2\rangle \propto \sqrt{t}$, that is, in a subdiffusive, long-memory process. This model is hardly realistic in a biochemical context due to the discontinuos dependence of the diffusion coefficient on y. However, it is plausible that diffusive dynamics of a real biological or chemical variable in the state or in the physical spaces depends on unobserved, decimated variables in some other non-trivial way. For example, in a chemotaxing *E. coli*, the number of directly unobservable signaling proteins CheY-P is coupled to the distribution of times a bacterial motor rotates counterclockwise, and the bacterium swims straight. For a fixed concentration of CheY-P, the distribution is essentially exponential, resulting in a regular diffusive motion of the bacterium. But as the number of CheY-P fluctuates (diffuses in the number space), the distribution becomes a power law [13], and bacteria exhibit superdiffusive real-space motion. While not true in this particular system, the distribution of clockwise rotation times could have been strongly coupled to CheY-P as well, and, averaged over the unobserved, fluctuating CheY-P, this would have resulted in a power law distribution of times that the bacterium spends reorienting itself without forward motion, and hence in its subdiffusive motion. In both cases, neglecting the CheY-P fluctuations and describing bacterial motion as a normal diffusion is qualitatively wrong.

In this letter, we explore these types of phenomena in detail, and we derive properties of a diffusion process, for which the diffusion coefficient depends on the state of another, unobserved, variable. We show that, quite generally, such dependence leads to anomalous diffusion, suggesting that traditional stochastic approaches may fail, and that more thought should be given to modeling stochastic phenomena in complex interacing systems, in particular in biophysics.

The model: Our model is described by two variables x and y, which may represent, in particular, concentrations of two interacting chemical species. Particles of both species can be created and destroyed, which results in an overdumped diffusive motion of the system in the concentration space (we disregard the directional drift for simplicity, but it can be reintronduced easily). Just like in the original comb model [12], we assume that the difusion of x is y-dependent. That is,

$$\frac{dy}{dt} = \frac{1}{\gamma_y}\eta\left(t\right), \tag{1}$$

$$\frac{dx}{dt} = \frac{C\left(y\right)}{\gamma_x}\xi\left(t\right). \tag{2}$$

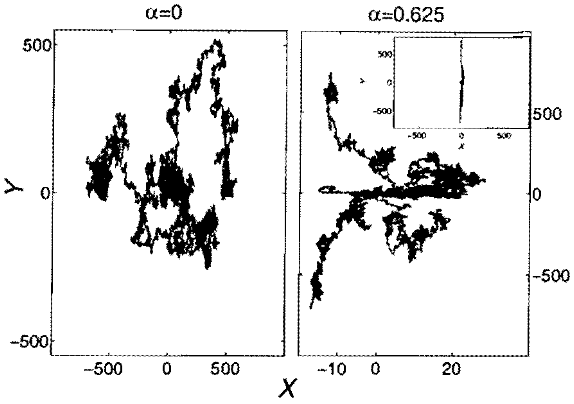

Figure 1: Typical diffusive trajectories for $C(y) = 1/(1+|Ay|^{\alpha})$ and $D_x = D_y = \gamma_x = \gamma_y = 1$, ilustrating suppression of diffusion in x. The left panel shows the case of $\alpha = 0$, namely decoupled Langevin processes. The right panel shows $\alpha = 0.625$, when $\overline{\langle x(t)^2\rangle} \sim \sqrt{t}$. The inset on the right shows x and y scaled equally.

Here γ_x, γ_y are the effective friction coefficients (assumed to be homogeneous) corresponding to x, y and $\eta(t)$ and $\xi(t)$ are independent, zero-mean white noise forces such that

$$\begin{aligned} \langle \eta(t)\,\eta(t')\rangle &= 2D_y\gamma_y^2\delta(t-t') \\ \langle \xi(t)\,\xi(t')\rangle &= 2D_x\gamma_x^2\delta(t-t') \end{aligned} \tag{3}$$

The Focker-Planck equations for the probability distribution functions (PDFs) of x and y can be derived. The PDF of y is that of normal diffusion

$$p(y,t|y_0,0) = \frac{1}{\sqrt{4\pi D_y t}} e^{-\frac{(y-y_0)^2}{4D_y t}}, \tag{4}$$

where the initial condition is $y(t=0) = y_0$. The PDF of x is more complicated due to the dependence on y, satisfying

$$\frac{\partial p(x,t)}{\partial t} = D(t)\,\frac{\partial^2 p(x,t)}{\partial x^2}. \tag{5}$$

In the equation above we introduced the notation $D(t) \equiv D_x\overline{C^2(y)}$ and $\overline{\cdots}$ stands for the ensemble-average over y. Since $\overline{C^2(y)}$ is time dependent, we see that $p(x)$ obeys the diffusion equation with a time dependent diffusion coefficient.

It is also possible to derive directly the equation describing the dynamics of the mean square displacement $\langle x(t)^2\rangle$, where $\langle\cdots\rangle$ stands for the average over the white noises η and ξ. We start by writing the formal solution for $x(t)$ as

$$x(t) = \frac{1}{\gamma_x}\int_0^t C(y(t'))\,\xi(t')\,dt'. \tag{6}$$

Multiplying Eq. (2) by $2x(t)$, given by Eq. (6), yields

$$\frac{dx(t)^2}{dt} = \frac{2C(y)}{\gamma_x^2}\xi(t)\int_0^t C(y(t'))\,\xi(t')\,dt'. \tag{7}$$

Averaging over the noise $\xi(t)$ yields the dynamics of the mean squared displacement of x conditional on $y(t)$,

$$\frac{d\langle x(t)^2\,|y(t)\rangle}{dt} = 2D_x C(y(t))^2. \tag{8}$$

To get the marginal expectation $\overline{\langle x(t)^2\rangle}$, we now average the conditional expectation over y, distributed as in Eq. (4):

$$\frac{d\overline{\langle x(t)^2\rangle}}{dt} = 2D(t) = \frac{2D_x}{\sqrt{4\pi D_y t}}\int_{-\infty}^{\infty} e^{-\frac{(y-y_0)^2}{4D_y t}}\,C(y(t))^2 dy. \tag{9}$$

The function $C(y)$ may take different forms for different systems. The simplest case is when the dynamics of x is independent of y and $C(y) = C = \text{const.}$ Substituting this in Eq. (9) yields the expected trivial result $\overline{\langle x^2\rangle} = 2D_x C^2 t$.

Another scenario is that x can evolve in time only for a given value of y, which resembles the original comb model of Weiss and Havlin [12]. Indeed, substituting $C(y(t))^2 = C\delta(y-y_1)$ (C is a constant with length units, and $\delta(y)$ is the Dirac delta function) into Eq. (9), we get

$$\frac{d\overline{\langle x(t)^2\rangle}}{dt} = \frac{2D_x C}{\sqrt{4\pi D_y t}} e^{-\frac{(y_1-y_0)^2}{4D_y t}}, \tag{10}$$

which, for $t \gg (y_1-y_0)^2/(4D_y)$, gives $\overline{\langle x(t)^2\rangle} \sim \sqrt{t}$ in agreement with [12]. Similarly, if $C(y)$ falls off exponentially at $y \longrightarrow \infty$, the same sub-diffusion exponenet is recovered.

A more interesting case is when, at large y, $C(y)$ falls off, but not too fast. We consider a power law form, namely

$$C(y(t)) = \frac{1}{1+|Ay|^{\alpha}}, \tag{11}$$

were A is a constant with the units of inverse length, and α is a dimensionless parameter. Typical diffusive trajectories with this $C(y)$, $A = 1$, and $\alpha = 0, 0.625$ are shown in Fig. 1.

Assuming that the behavior of $C(y)$ for large y (i.e., $C(y) \sim |y|^{-\alpha}$) dominates the $t \longrightarrow \infty$ dynamics of $\overline{\langle x(t)^2\rangle}$, a simple scaling argument suggests that $\overline{\langle x(t)^2\rangle} \sim t^{1-\alpha}$. However, this is clearly wrong for large α, suggesting that $\overline{\langle x(t)^2\rangle}$ must pick up an anomalous scaling due to the $y \longrightarrow 0$ properties of $C(y)$. In what follows, we derive the long time behavior of $\overline{\langle x(t)^2\rangle}$ in a more rigorous way.

Equation (9) with $C(y)$ as in Eq. (11) gives

$$\frac{d\overline{\langle x(t)^2\rangle}}{dt} = \frac{2D_x}{\sqrt{\pi}}\int_{-\infty}^{\infty} \frac{e^{-\left(\frac{y-y_0}{\sqrt{4D_y t}}\right)^2}}{\left[1+\left(\sqrt{4D_y t}\,|Ay|\right)^{\alpha}\right]^2}\,dy. \tag{12}$$

For $\frac{y_0}{\sqrt{4D_yt}} \ll 1$, we rewrite the above equation as

$$\frac{d\overline{\langle x(t)^2\rangle}}{dt} = \frac{4D_x}{\sqrt{\pi}}\left\{\int_0^{\frac{1}{A\sqrt{4D_yt}}} \frac{e^{-y^2}}{\left[1+\left(\sqrt{4D_yt}Ay\right)^{\alpha}\right]^2}dy \right.$$
$$\left. + \int_{\frac{1}{A\sqrt{4D_yt}}}^{\infty} \frac{e^{-y^2}}{\left[1+\left(\sqrt{4D_yt}Ay\right)^{\alpha}\right]^2}dy\right\}. \quad (13)$$

In the first integral, we approximate the integrand as a constant for $t \to \infty$, and, in the second integral, we neglect 1 compared to $\left(\sqrt{4D_yt}\,|Ay|\right)^{\alpha}$, thus obtaining

$$\frac{d\overline{\langle x^2\rangle}}{dt} \approx \frac{2D_X}{A\sqrt{\pi D_yt}} + \frac{2D_xt^{-\alpha}}{\left(4A^2D_y\right)^{-\alpha}\sqrt{\pi}}\Gamma\left(\frac{1}{2}-\alpha, \frac{1}{4A^2D_yt}\right), \quad (14)$$

where $\Gamma(a,b) \equiv \int_b^{\infty}\tau^{a-1}e^{-\tau}d\tau$ is the incomplete Gamma function. Integrating Eq. (14) over t results in the long time behavior of $\overline{\langle x(t)^2\rangle}$

$$\overline{\langle x(t)^2\rangle} \sim D_1\sqrt{t} + D_2t^{1-\alpha}. \quad (15)$$

where $D_{1,2}$ are constants depending on the model parameters D_x, D_y, α and A. This implies that, for $\alpha < 1/2$, the long time behavior is dominated by $\overline{\langle x(t)^2\rangle} \sim t^{1-\alpha}$, as the scaling argument suggests. However, for $\alpha > 1/2$, the scaling argument breaks and $\overline{\langle x(t)^2\rangle} \sim \sqrt{t}$. Note that when the $C(y)$ falls faster than $1/\sqrt{y}$, the diffusion exponent is exactly as for the comb model, in which the dynamics of x is limited to $y = 0$.

The case of $\alpha = \frac{1}{2}$ is special since the result of the integral can't be expressed in terms of the incomplete Gamma function. Here Eq. (13) may be written as

$$\frac{d\overline{\langle x(t)^2\rangle}}{dt} = \frac{4D_x}{\sqrt{\pi}}\int_0^{\infty} \frac{e^{-y^2}}{\left[1+\left(\sqrt{4D_yt}^{1/2}\,|Ay|\right)\right)^{1/2}\right]^2}dy$$
$$= G^{5\,4}_{4\,5}\left(\frac{1}{4A^2D_yt}\,\middle|\,\begin{matrix}-\frac{1}{4},0,\frac{1}{4},\frac{1}{2}\\ 0,0,\frac{1}{4},\frac{1}{2},\frac{3}{4}\end{matrix}\right) \sim \frac{\ln t}{\sqrt{t}}, \quad (16)$$

where G denotes the Meijer G function [14]. The leading order term of the mean square displacement is then

$$\overline{\langle x(t)^2\rangle} \sim \sqrt{t}\ln t. \quad (17)$$

So far we cosidered only situations. in which the motion of x was slowed at large y, but we can also consider the opposite scenarios, when large y promotes diffusion in x, as in [13]:

$$C(y(t)) = y^{\beta}, \beta > 0. \quad (18)$$

Now from Eq. (9), we get

$$\frac{d\overline{\langle x(t)^2\rangle}}{dt} = \frac{2D_x}{\sqrt{\pi}}\left(4D_yt\right)^{\beta}\int_{-\infty}^{\infty} e^{-\left(y-\frac{y_0}{\sqrt{4D_yt}}\right)^2}y^{2\beta}dy. \quad (19)$$

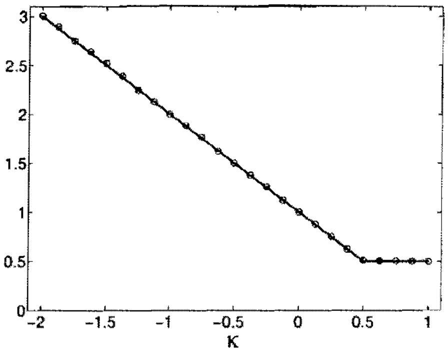

Figure 2: Leading order diffusion exponent ν defined by $\overline{\langle x(t)^2\rangle} \sim t^{\nu}$ for the coupled stochastic processes model with different types of coupling between the diffusion of x and y, measured by the exponent κ. For the case of hindered diffusion of x (see Eq. (11)), $\kappa = \alpha$, while for the enhanced diffusion (see Eq. (18)), $\kappa = -\beta$. Numerical simulations (points) and theoretical predictions (line) agree well for both scenarios.

Taking the long time limit yields $d\overline{\langle x(t)^2\rangle}/dt \sim t^{\beta}$, and

$$\overline{\langle x(t)^2\rangle} \sim t^{\beta+1}. \quad (20)$$

To confirm our analytical results, we performed numerical simulations for the different cases considered above. In Fig. 2, we present a comparison of the diffusion exponent ν (defined by $\overline{\langle x(t)^2\rangle} \sim t^{\nu}$) versus the coupling parameter κ (for the subdiffusion scenario Eq. (11), $\kappa = \alpha$, and for the superdiffusion scenario Eq. (18), $\kappa = -\beta$) between simulation and analytical results. The simulation dynamics was according to Eqs. (1, 2), with $\gamma_{x,y} = 1$, $D_{x,y} = 1$ and $dt = 1$. We averaged the results over 10^4 trajectories, each of length $10^7 \ldots 10^8 dt$.

A simple linear regression to $\log\overline{\langle x(t)^2\rangle} = \nu\log t + \text{const}$ was performed to estimate ν. Since the standard parameter errors obtained for the regressions were negligible, the error bars of ν were estimated from the variability of the fitted values as we changed the domain of t, for which the fits was performed. Fig. 2 shows a clear agreement between our theoretical results and the simulations. Note that in certain cases the convergence to the leading behavior of $\overline{\langle x(t)^2\rangle}$ as $t \to \infty$ is slow since the difference between the exponents of the leading and the subleading terms is small. This slowness determined the lengths of the simulations.

Time Averaged Mean Square Displacement: There are many models of anomalous diffusion, including time dependent friction coefficient in the Langevin equation, continuous time random walk (CTRW) [15], fractional Brownian dynamics [16] and fractional Langevin dynamics [17–19], Langevin dynamics with colored noise [20], to name a few. For a new model resulting in an anomalous diffusion, it is important to see if it can be reduced to one of these more familiar constructions. For example, the $t \to \infty$ behavior of the original comb model is equivalent to CTRW [21], with power law tails of the distribution of the times between successive jumps along x. However, in our model, the analogy is not as straightforward since the continous dynamics of y induces temporal correlations among successive motions along x.

To understand the relation of the coupled diffusion model to the others in the literature, we note that all of them yield the same behavior for the *ensemble* averaged mean square displacement (MSD) in the long time limit. However, they still differ from each other at short times and even in the long time behavior of *time* averaged quantities (for example the CTRW exhibits ergodicity breaking [22]). In particular, the time averaged MSD (TAMSD) is an important property (It is the TAMSD that is observable in typical single molecule diffusion experiments in biological systems [4, 23], and the number of recorded trajectories is usually insufficient to estimate ensemble averages).

$$\overline{\delta^2}(\Delta,t)=\frac{1}{t-\Delta}\int\limits_0^{t-\Delta}\left[x\left(\tau+\Delta\right)-x\left(\tau\right)\right]^2d\tau. \qquad (21)$$

For CTRW, the TAMSD is a random quantity and even its ensemble average still exhibits aging, depending on the measurement duration t in Eq. (21) [24]. On the contrary, for the fractional Brownian and Langevin dynamics, the TAMSD converges to the ensemble average MSD for long times [25].

We investigated the behavior of the TAMSD in our model with repressive coupling numerically. We find that, when the scaling argument holds, namely for $\alpha \leq 1/2$ (see Eq. 11), the TAMSD is not a random quantity, but it still shows aging, as we would expect for Langevin dynamics with a time dependent friction. On the other hand, when $\alpha \geq 1/2$, and the diffusion exponent is $1/2$, the TAMSD is similar to that of the CTRW. In Fig. 3, we show the TAMSD for $\alpha = 0.75$ and $\alpha = 0.25$. For $\alpha = 0.25$, the TAMSD lines converge as the time grows, while for $\alpha = 0.75$, the lines remain random. This is a clear indication of ergodicity breaking in our model for $\alpha > 0.5$. Further, this analysis suggests that the coupled diffusion stands as its own class among other anomalous diffusion models, exhibiting time-dependent diffusion coefficient Langevin dynamics for certain forms of coupling, and some aspects of ergodicity-braking CTRW for the others.

Discussion: In this leter, we itroduced a model of coupled diffusive processes, where the diffusion of the observed variable x is coupled to the value of a hidden variable y. We showed that the dynamics of x exhibits anomalous diffusion even for *arbitrarily weak coupling* between the variables. Depending on the nature of the interaction, the motion of x can be sub- or super-diffusive (and even super-ballistic as is the case of frictionless particle subject to white noise). Further, even for an arbitrary strong repressive xy coupling, the x diffusion exponent ν is limited from below by $\frac{1}{2}$ (anomalous scaling), so that full localization of x is impossible. Even though the long-time ensemble-averaged behavior of the model is similar to that of many others describing anomalous diffusion, the model does not reduce to either one of them, exhibiting an effective time-dependent diffusion coefficient, aging, and ergodicity breaking for different values of its parameters.

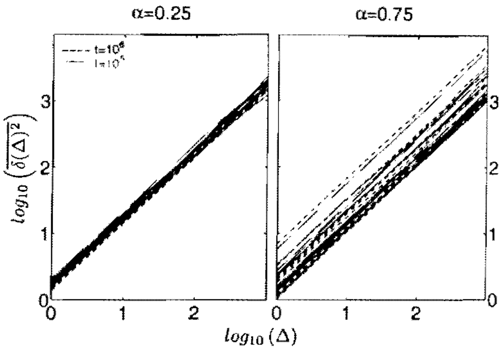

Figure 3: The time averaged mean square displacement $\overline{\delta^2}(\Delta,t)$ for $\alpha = 0.25, 0.75$ (left and right panels, respectively). All other dynamical parameters are the same as for the previous figures. We used 20 trajectories each of duration 10^5 (solid lines, red color online) and 20 trajectories of duration 10^6 (dashed lines, blue online). For $\alpha = 0.25$, the TAMSD over differen trajectories converge as the measurement time increases. However, for $\alpha = 0.75$, there is no such convergence, just like for CTRW. In both cases, the ensemble average of the TAMSD decrease as the measurement time increases, indicating aging.

The anomalous scaling and the ergodicity breaking appear in the model for the coupling parameter $\alpha > 1/2$, when the long-time behavior of the model is similar to that of the comb model. This is because, for $\alpha < 1/2$, motion of particles away from $y = 0$ contributes substantially to the ensemble averaged MSD of x. On the other hand, for $\alpha > 1/2$, only motion near $y = 0$ is important.

While important in its own right, the coupled diffusion model raises its most important questions in the biological domain. Unobservable dynamical quantities can lead to anomalous diffusion in *E. coli* chemotaxis [13], or in *mRNA* diffusion in cells [4]. Further, some of the best established models of cellular regulation involve coarse-graining of dynamical variables. For example, for the *lac* operon in *E. coli*, dynamics of the lac repressor itself is an unobservable variable [26]. But this is coupled to the speed of production of the lactose permease and the lactose-utilizing ezyme β-galacosidase and, through them, to the import and the degradation of lactose in the cell. Since even arbitrary weak such couplings may lead to anomalous diffusion, it begs the question whether relying on the field-dominating Langevin or master equation analysis of stochasticity of the *lac* repressor, as well as other regulatory circuits, such as the λ-phage [5, 9], *marRAB* [1], and others, is warranted.

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[1] C. C. Guet et al., Nucleic Acids Research **36**, e73 (2008).
[2] B. P. English et al., Nature Chemical Biology **2**, 87 (2006).
[3] C.-B. Li, H. Yang, and T. Komatsuzaki, Proc. Natl. Ac. Sci. USA **105**, 536 (2008).

[4] I. Golding and E. C. Cox, Phys. Rev. Lett. **96**, 098102 (2006).

[5] H. H. McAdams and A. Arkin, Annu. Rev. Biophys. Biomol. Struct. 27, 199 (1998).

[6] J. Paulsson, Nature **427**, 415 (2004).

[7] N. Sinitsyn, N. Hengartner, and I. Nemenman, submitted to Proc. Nat. Ac. Sci. (2008).

[8] M. Sasai and P. G. Wolynes, Proc. Natl. Ac. Sci. USA **100**, 2374 (2003).

[9] E. Aurell and K. Sneppen, Phys. Rev. Lett. **88**, 048101 (2002).

[10] I. V. Gopich and A. Szabo, J. Chem. Phys. **124**, 154712 (2006).

[11] N. A. Sinitsyn and I. Nemenman, EPL 77, 58001 (2007).

[12] G. H. Weiss and S. Havlin, Physica A **134**, 474 (1986).

[13] E. Korobkova et al., Nature **428**, 574 (2004,).

[14] S. Wolfram, *The mathematica Book* (Cambridge University press, Cambridge, 1999), 4th ed.

[15] H. Sher and E. W. Montroll, Phys. Rev. B **12**, 2455 (1975).

[16] B. B. Mandelbrot and J. W. van Ness, SIAM Review **10**, 422 (1968).

[17] W. Min et al., Phys. Rev. Lett. **94**, 198302 (2005).

[18] I. Goychuk and P. Hanggi, Phys. Rev. Lett. **99**, 200601 (2007).

[19] S. Burov and E. Barkai, Phys. Rev. Lett. **100**, 070601 (2008).

[20] R. Muralidhar et al., Physica A **167**, 539 (1990).

[21] J. P. Bouchaud and A. Georges, Phys. Rep. **195**, 127 (1990).

[22] G. Bel and E. Barkai, Phys. Rev. Lett. **94**, 240602 (2005).

[23] I. M. Tolic-Norrelykke et al., Phys. Rev. Lett. **93**, 078102 (2004).

[24] Y. He et al., Phys. Rev. Lett. **101**, 058101 (2008).

[25] W. Deng and E. Barkai, Phys. Rev. E **79**, 011112 (2009).

[26] D. Dreisigmeyer et al., IET Systems Biology **2**, 293 (2008).