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Stochastic fractal behavior in concentration fluctuation and fluorescence correlation spectroscopy

Hong Qian[a,b,*], Gary M. Raymond[b], James B. Bassingthwaighte[b]

[a] Department of Applied Mathematics, University of Washington, Seattle, WA 98195, USA
[b] Department of Bioengineering, University of Washington, Seattle, WA 98195, USA

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Abstract

Fluctuations in the concentration of Brownian particles in one and two dimensions, or any reasonable measurement of the concentration such as in fluorescence correlation spectroscopy, is shown to be a stochastic fractal with a long tail. Being singular at $\omega = 0$, the power spectrum of the fluctuation $S(\omega) \sim \omega^{-1/2}$ for diffusion in one dimension, $\sim \log \omega$ in two dimensions, but non-singular in three dimensions. This discovery provides one simple physical mechanism for possible long-memory fractal behavior, and its implications to various biological processes are discussed. © 1999 Elsevier Science B.V. All rights reserved.

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1. Introduction

Long-tail kinetics in biophysics are often considered to be evidence for complex physical processes [1]. In terms of Fourier analysis, the power spectrum of a long-tail (long-memory) process is singular when the frequency f goes to zero: $S(f) \sim f^{-\alpha}$ where α is usually between 0 and 1. This behavior is also known as a stochastic fractal or the power-law [2,3]. The fractal descriptions of natural phenomena have been found to be useful in many branches of science, but there are only a few cases where the fractal behavior has been interpreted in terms of physical mechanism. More mechanistic models are required before fractal theory can be regarded as a fundamental model in physics and biology [4]. One model for a stochastic fractal is Brownian motion, whose trajectories exhibit fractal geometry. A generalization of Brownian motion to strongly correlate (long-memory) random processes is *fractional Brownian motion* (fBm) [3,5,6]. The construction of fBm pioneered by Mandelbrot and van Ness [7] gives a wide range of power-law scaling, but the definition is only a mathematical one. It is not clear how a long-memory stochastic fractal can arise physically from a diffusion-like motion. In this note we show that a natural physical process associated with diffusion, the concen-

* Corresponding author.

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tration fluctuation, also known as the Smoluchowski process [8], exhibits a long-memory fractal behavior in one and two dimensions. In biophysics, one encounters such processes in Fluorescence Correlation Spectroscopy (FCS) [9–11]. However, the implications of the present result is much broader; it applies to all biological processes with random-walk like fluctuations.

A long-memory fractal process has its power spectrum $S(\omega)$ singular at $\omega = 0$ with the asymptotic relation $S(\omega) \sim \omega^{1-2H}$, where $\omega = 2\pi f$. The exponent H, the Hurst coefficient, is between 1 and 0.5 [3]. We show that the concentration fluctuations have a Hurst coefficient of 0.75 in one dimension and 0.5^{+} in two dimensions (the meaning of '$^{+}$' will become clear later). More interestingly, the concentration fluctuations can be observed through various measurement devices, and in general these measurements will all exhibit the same long-tail behavior. This result provides a possible mechanistic model for a range of long-tail processes with simple and sound mathematics. It shows that long-tail kinetics need not necessarily be associated with complex biological processes. Concentration fluctuation is also an easy stochastic process to simulate on a computer; hence the current result provides an algorithm for numerically generated stochastic fractals.

2. Analysis of the Smoluchowski process

In 1959, Kac [8] presented an interesting stochastic process associated with Brownian motion of particles in a container. The problem was originally studied by Smoluchowski to explain the experimental observation of Svedberg [11] on the fluctuation of concentration. In 1972, Magde et al. [9] developed FCS which provides an optical measurement for concentration fluctuations of fluorescent molecules in solution. In developing a theory for FCS, Elson and Magde [10] discovered that the autocorrelation function (being more precise, the autocovariance function) of the fluctuation has a long algebraic tail:

$$\rho_\nu(\tau) = \frac{\rho_\nu(0)}{(1+\tau/\tau_0)^{\nu/2}} \qquad (1)$$

where $\nu = 1, 2, 3$ for Brownian motion in one, two, and three dimensions, respectively. Therefore, for $\nu = 1$ and 2 the Smoluchowski process has a long memory since $\int_0^\infty \rho_\nu(\tau)\mathrm{d}\tau$ diverges [3,5].

Formally, the Smoluchowski process is defined as follows [12]. Let $\mathbf{B}(t)$ be the position of Brownian particle with correlation

$$\langle \mathbf{B}(t)\mathbf{B}(s)\rangle = 2\nu D \min(t,s)$$

where D is the diffusion coefficient, $\langle\cdot\rangle$ is the ensemble average, and $\min(t,s)$ denotes the smaller value between t and s. Let $\mathbf{B}_1, \mathbf{B}_2, \ldots, \mathbf{B}_N$ be N identical, independent Brownian particles. The stochastic process

$$\mathbf{Z}(t) = \sum_{n=1}^{N} I(\mathbf{B}_k(t)) \qquad (2)$$

is called a Smoluchowski process. Function $I(\mathbf{x})(\mathbf{x} \in R^\nu)$ defines the measurement for the Brownian particles $\{\mathbf{B}_k\}$. If $I(\mathbf{x})$ is the characteristic function of a region Ω in ν-dimensional space, i.e.

$$I(\mathbf{x}) = \begin{cases} 1 & \mathbf{x} \in \Omega \\ 0 & \mathbf{x} \notin \Omega \end{cases}$$

then $\mathbf{Z}(t)$ is simply the number of particles in Ω at time t, a counting process. In FCS $I(\mathbf{x}) = \exp(-|\mathbf{x}|^2/2\sigma^2)$ which is determined by a focused laser, and Elson and Magde [10] have found that the autocorrelation function

$$\langle \Delta\mathbf{Z}(t)\Delta\mathbf{Z}(t+\tau)\rangle = \rho_\nu(\tau) = \frac{\rho_\nu(0)}{(1+\tau/\tau_0)^{\nu/2}} \qquad (3)$$

where $\Delta\mathbf{Z}(t) = \mathbf{Z}(t) - \langle\mathbf{Z}(t)\rangle$, $\tau_0 = \sigma^2/4D$.

If we subject the autocorrelation functions in Eq. (3) to the usual power spectral analysis, we immediately conclude that the power spectra for $\nu = 1$ and 2 are singular at $\omega = 0$:

$$S_\nu(\omega) = \int_{-\infty}^{\infty} \rho_\nu(|t|)e^{-i\omega t}\mathrm{d}t = 2\int_0^\infty \rho_\nu(t)\cos(\omega t)\mathrm{d}t \qquad (4)$$

More specifically, for $\nu = 1$ we have [13]:

$$S_1(\omega) = 2\int_0^{\infty} \frac{\cos(\omega t)}{(1+t/\tau_0)^{1/2}}\mathrm{d}t$$

$$= 2\tau_0 \int_1^{\infty} x^{-1/2}\cos(\omega\tau_0(x-1))\mathrm{d}x$$

$$= 2\tau_0\left\{\cos(\omega\tau_0)\int_1^{\infty} x^{-1/2}\cos(\omega\tau_0 x)\mathrm{d}x + \sin(\omega\tau_0)\int_{\infty}^{1} x^{-1/2}\sin(\omega\tau_0 x)\mathrm{d}x\right\}$$

$$= 2\tau_0(\omega\tau_0)^{-1/2}\left\{\cos(\omega\tau_0)\int_{\omega\tau_0}^{\infty} y^{-1/2}\cos(y)\mathrm{d}y + \sin(\omega\tau_0)\int_{\omega\tau_0}^{\infty} y^{-1/2}\sin(y)\mathrm{d}y\right\}$$

$$\sim \sqrt{2\pi\tau_0}\,\omega^{-1/2} \quad (\omega \to 0^+)$$

where the curly bracket converges to a constant $\sqrt{\pi/2}$. Similarly, for $\nu = 2$ we have:

$$S_2(\omega) = 2\int_0^{\infty} \frac{\cos(\omega t)}{1+t/\tau_0}\mathrm{d}t$$

$$\sim -2\tau_0\cos(\omega\tau_0)\ln(\omega\tau_0) \; (\omega \to 0^+)$$

$$= -2\tau_0\ln(\omega)$$

Therefore we find that in two dimensions, the power spectrum has a logarithmic singularity when $\omega \to 0$ for positive ω. Since $\ln(\omega)$ diverges slower than any power of ω, it has no corresponding Hurst coefficient. We therefore use 0.5^+ to denote this logarithmic behavior.

The asymptotics for the power spectrum of FCS can be generalized to any measurement device characterized by a function $I(\mathbf{x})$. In the case of one dimension:

$$S_1(\omega) \sim \frac{\omega^{-1/2}}{\sqrt{4D}}\int_{-\infty}^{\infty} I(x)\mathrm{d}x \quad (\omega \to 0^+) \tag{6}$$

This can be shown as the follows. The autocorrelation function

$$\rho_1(t) = \langle I(0)I(t)\rangle = \int_{-\infty}^{\infty} I(x)P(x,t)\mathrm{d}x \tag{7}$$

where $P(x,t)$ is the conditional probability of $\mathbf{B}(t) = x$ when $\mathbf{B}(0) = 0$. That is:

$$P(x,t) = \frac{1}{\sqrt{4\pi Dt}}e^{-(x^2/4Dt)} \tag{8}$$

which is the solution of the diffusion equation

$$\frac{\partial P(x,t)}{\partial t} = D\frac{\partial^2 P(x,t)}{\partial x^2} \tag{9}$$

with the initial condition $P(x,0) = \delta(x)$. Fourier transforming Eq. (7) gives the power spectrum

$$S_1(\omega) = \int_{-\infty}^{\infty} \rho_1(|t|)e^{-i\omega t}\mathrm{d}t$$

$$= \int_{-\infty}^{\infty}\mathrm{d}t\int_{-\infty}^{\infty} I(x)P(x,|t|)e^{-i\omega t}\mathrm{d}x$$

$$= \int_{-\infty}^{\infty}\mathrm{d}t\int_{-\infty}^{\infty} I(x)[P(x,|t|) - P(0|t|)]e^{-i\omega t}\mathrm{d}x + \int_{-\infty}^{\infty}\mathrm{d}t\int_{-\infty}^{\infty} I(x)P(0,|t|)e^{-i\omega t}\mathrm{d}x \tag{10}$$

Now note that the first double integral is absolutely convergent since

$$\int_{-\infty}^{\infty} |I(x)||P(x,|t|) - P(0,|t|)|\mathrm{d}x \sim \int_{-\infty}^{\infty} \frac{\pi x^2|I(x)|}{(4\pi D|t|)^{3/2}}\mathrm{d}x$$

when $t \to \infty$. The second double integral in Eq. (10), when $\omega \to 0$, asymptotically approaches

$$\int_{-\infty}^{\infty}\mathrm{d}tP(0,|t|)e^{-i\omega t}\int_{-\infty}^{\infty} I(x)\mathrm{d}x$$

which leads to Eq. (6).

Similarly, for $\nu = 2$, we have in polar coordinates

$$
\begin{aligned}
S_2(\omega) &= \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} I(r)P(r,|t|)e^{-i\omega t}4\pi r\,\mathrm{d}r\,\mathrm{d}t \\
&= \int_{-\infty}^{\infty}\mathrm{d}t\int_{-\infty}^{\infty} I(r)[P(r|t|) \\
&\quad -P(0,|t|)]e^{-i\omega t}4\pi r\,\mathrm{d}r \\
&\quad +\int_{-\infty}^{\infty}\mathrm{d}t\int_{-\infty}^{\infty} I(r)P(0,|t|)e^{-i\omega t}4\pi r\,\mathrm{d}r \\
&\sim \int_{-\infty}^{\infty} P(0,|t|)e^{-i\omega t}\,\mathrm{d}t\int_{-\infty}^{\infty} I(r)4\pi r\,\mathrm{d}r \\
&= -\frac{\ln\omega}{4\pi D}\int_{-\infty}^{\infty} I(r)4\pi r\,\mathrm{d}r \quad (\omega \to 0^+)
\end{aligned}
$$

Therefore, we have shown that the fractal characteristics of the Smoluchowski processes are independent of the choice of the measurement function $I(\mathbf{x})$. Different choices in $I(\mathbf{x})$, however, give different prefactors for the power law.

3. Some mathematical issues

The stationarity of the Smoluchowski processes is achieved in the following sense: we consider N particles in a given container, and then let the size of the container tend to infinity at the same time $N \to \infty$, but keep the total concentration constant. In this limit, we have a stationary Smoluchowski process with Poisson distribution [8].

Many current models for long-memory, such as fractional auto-regressive, integrated, moving average (FARIMA) processes, are non-Markovian [3]. The Smoluchowski processes, however, can be Markovian. To see this, take one-dimensional $I(x) = \exp(-x^2/2\sigma^2)$ as an example. We can define the Browian motion in the half-space $x \geq 0$. with a reflecting boundary at $x = 0$. It is obvious, from the symmetry, that the Smoluchowski process is unchanged. However, now the mapping from x to $I(x)$ is monotonic and invertible. Since the Brownian motion $\mathbf{B}_t$ is Markovian, so is $I(\mathbf{B}_t)$.

4. Discussion

It is important to point out that the long memory of the Smoluchowski process in one and two dimensions is intimately related to Polya's theorem which states that the probability of returning is unity for random walks in one and two dimensions [14,15]. Heuristically, diffusion processes in one and two dimensions tend to come back constantly where they are originated, while in three dimensions and higher they are more likely to move away and 'never come back'. This leads to a much longer correlation in time in the local concentration of the diffusing particles in one and two dimensions.

The present result is not limited to the molecular diffusion in an aqueous solution. Brownian motion as a model is ubiquitous in physics and biology; many physical and biological processes are Brownian motions in one and two dimensions. Therefore, we expect that the Smoluchowski process will play an important role in understanding various other fractal processes. Even though we have only defined Smoluchowski processes rigorously in terms of concentration fluctuations, its implication to biochemistry and biology should not be overlooked. For example, the chemical concentration fluctuation contributes significantly to the receptor activation in bacterial chemotaxis [16], olfactory perception [17], and random walks underlie the firing of neurons [18]. Hence one expects that the long tail fractal behavior is inherent in many biological and neural processes [19]. It can be shown that when driven by a correlated long-memory Gaussian noise, a Langevin type equation defines a stochastic process which has all the long-memory characteristics of the correlated noise.[1] Therefore, if one can identify a few underlying, mechanistic fractal processes, one can understand many other related processes exhibiting fractal behavior.

The power spectrum of a long-memory stochastic process is known as the $1/f$ noise in con-

[1] Let's use the fractional Gaussian noise as the correlated long-memory noise for driving a Langevin equation. The solution of the Langevin equation is related to the driving force, in the frequency domain, by an exponential low-pass filter. Hence, the solution of the equation has a similar singularity at zero frequency as that of the random force: the two stochastic processes share same fractal characteristics with identical Hurst coefficient.

densed matter physics [20]. The fundamental mechanism of this fascinating phenomenon is still unclear. One of the proposed mechanisms is a *series kinetic process* in which many steps with comparable rates before a particular transition that affects the measured variables happens. In other words, it can be treated as a one-dimensional random walk [21]. Our result on the two-dimensional Smoluchowski process also indicates that not all the long memory processes having power spectra of type $f^{-\alpha}$. The logarithmic $-\log(f)$, with experimental uncertainty, could be mistaken as having any α between 0 and ∞, depending on the low frequency cutoff.

In the early 1970s, algebraic long-tails in the time correlation of the velocity of Brownian particles were intensely studied [22,23]. It has been shown, based on hydrodynamic theory and the Boltzmann equation, that the velocity correlation functions in general do not decay exponentially. Therefore, these studies have gone beyond the traditional theory of Brownian motion which assumes an exponential velocity correlation function [24]. Our present analysis, on the other hand, has shown that the long-tail kinetics can rise even in the traditional diffusion theory. In fact, Eq. (9) assumes the velocity time correlation function being a Dirac-δ function. Therefore, the present result is also applicable to a wide class of processes which are diffusion-like but do not have a hydrodynamic basis, such as olfactory perception and firing of neurons.

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