A model of Intracellular non-Gaussian diffusion

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Motivation

- Single particle tracking experiments evidence that motion in visco-elastic media (such as the cytoplasm) can be non-Gaussian [1,5]. With other examples coming from granular media, turbulent flows, gels, this seems to be general feature of diffusion in complex media.
- Typically, distribution of increments is either purely exponential or with exponential tails.
- Several models of a tracer experiencing local changes of diffusivity treat diffusivity is as a random process [2,3].
- We propose a model of motion when diffusivity evolves as a Cox-Ingersoll-Ross process [4] that allows diffusivity to be positive and correlated in time.
- Our model encodes diffusivity dynamics with three easily interpretable parameters that are useful to further understand information about the experienced medium.

Statistical properties

- Probability density after averaging over diffusion coefficient:

$$P(x,t) = \int_{-\infty}^{\infty} dq e^{iq(x-x_0)} \left(e^{-\frac{1}{2}(\omega-1)\tau} \frac{4\omega}{(\omega+1)^2} \left(1 - \left(\frac{\omega-1}{\omega+1}\right)^2 e^{-\omega t} \right)^{-1} \right)^{\nu}$$

with $\omega = \sqrt{1+4q^2\sigma^2/a^2}$, $\tau = at$ and $\nu = a\bar{D}/\sigma^2$
It becomes Brownian in the limit $\frac{a}{\sigma} \to \infty$.

- Mean Squared Displacement:

$$\langle x_t^2 \rangle = 2\bar{D}t$$

- Fourth moment:

$$\langle x_t^4 \rangle = 12\bar{D}^2t^2 + 24\frac{\sigma^2\bar{D}}{a^3}\left(at + (e^{-at}-1)\right)$$

This is a linear Brownian-like MSD, but the underlying process is far more richer.

- Non-Gaussian Parameter

$$\frac{\langle x_t^4 \rangle}{3\langle x_t^2 \rangle^2} - 1 = \frac{2\sigma^2}{a^2\bar{D}t}\left(1 + \frac{1}{at}(e^{-at}-1)\right)$$

- Autocorrelation of squared increments ($\approx$ autocorrelation of diffusivity) in the limit $t \to \infty$

$$\langle dx_t^2 dx_{t+\tau}^2 \rangle = \begin{cases} \dfrac{12\sigma^2\bar{D}}{a} + 8\bar{D}^2 \text{ if } \tau=0 \\ \dfrac{4\sigma^2\bar{D}}{a} e^{-a\tau} \text{ else} \end{cases}$$

Diffusivity is positively correlated with exponential memory kernel

Parameters can be estimated by calculating $\langle x_t^2 \rangle$ (to get $\bar{D}$), $\langle dx_t^2 dx_{t+\tau}^2 \rangle$ (to get a) and $\langle x_t^4 \rangle$ (to get σ).

Conclusion

- Non-Gaussian features can be reproduced using this model.
- This is an ergodic generalization of Brownian motion which converges to Gaussian distribution in the long-time limit.
- The model is rich in terms of different shapes of the distribution $P(x,t)$. Parameter ν controls the shape by changing how often diffusivity can vanish.
- It is possible to estimate parameters from experimental data.

Cox-Ingersoll-Ross model of diffusivity

Consider a tracer in a complex medium with spatio-temporal fluctuations of diffusivity.
- η^{-1} time for a tracer to equilibrate with its local environment
- a^{-1} time for diffusivity to equilibrate
- dt time-step of trajectory x_t.

Under the condition $\eta^{-1} \ll dt \ll a^{-1}$, one can define diffusivity D_t as a Cox-Ingersoll-Ross process, with random fluctuations of amplitude σ around its mean $\bar{D}$.
Corresponding Langevin equation is:

$$\begin{cases} dx_t = \sqrt{2D_t}dW_t^1 \\ dD_t = a(\bar{D}-D_t)dt + \sigma\sqrt{2D_t}dW_t^2 \end{cases}$$

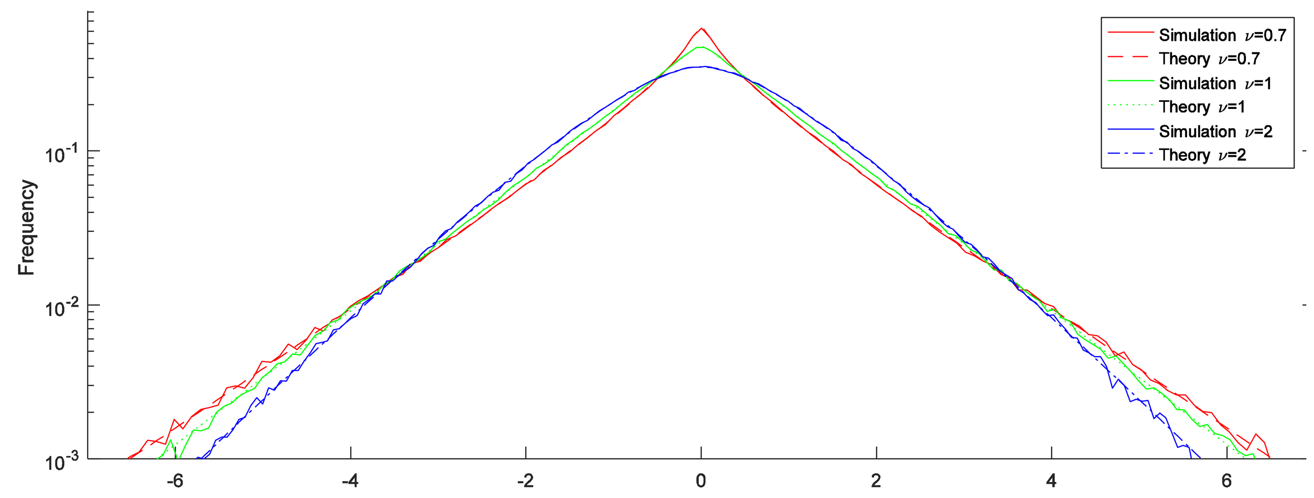
In any case $P(D_t \geq 0) = 1$, i.e., diffusivity remains positive, and it becomes strictly positive, $P(D_t > 0) = 1$, if $a\bar{D} > \sigma^2$

Forward Fokker-Planck equation:

$$\frac{\partial}{\partial t}P(x,D,t|x_0,D_0) = a\frac{\partial}{\partial D}[(\bar{D}-D)P] + D\frac{\partial^2}{\partial x^2}P + \sigma^2\frac{\partial^2}{\partial D^2}[DP]$$

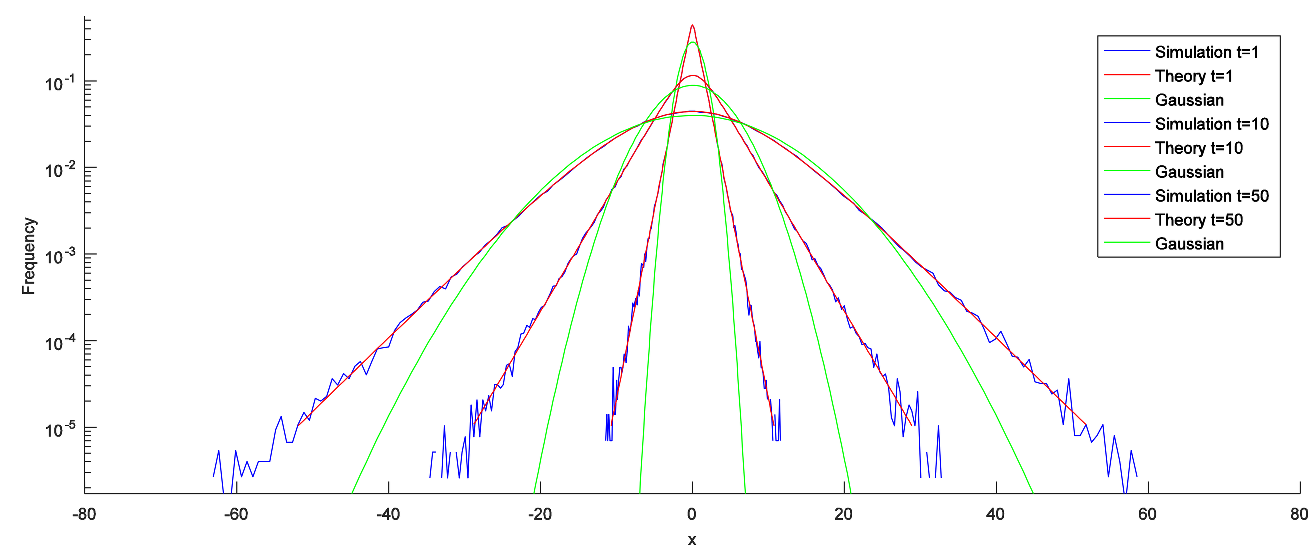
Numerical Results

- The parameter $\boldsymbol{\nu = a\bar{D}/\sigma^2}$ controls the shape of the distribution



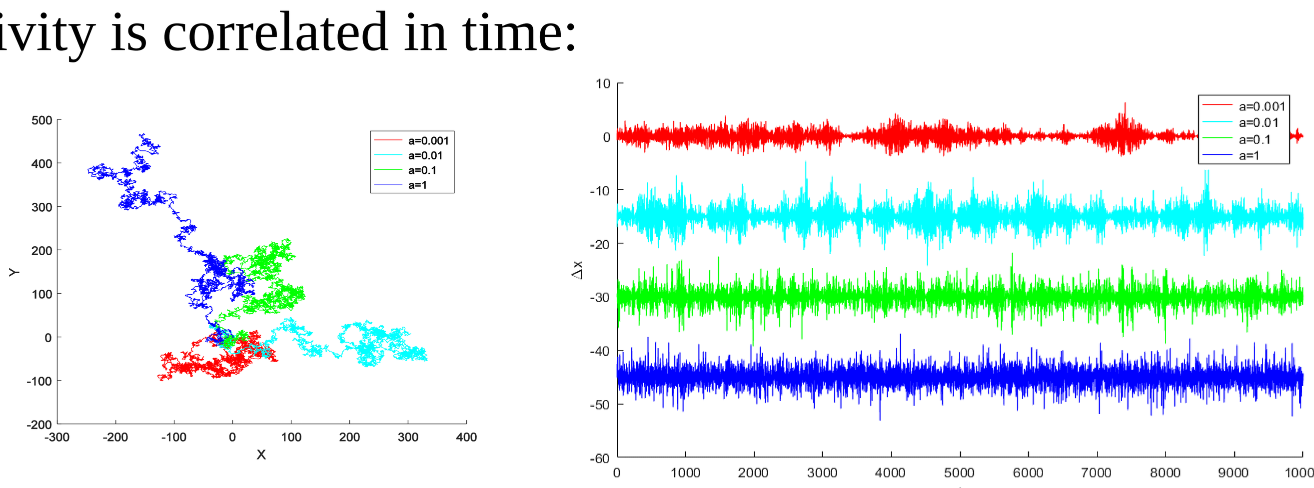
(blue) Gaussian at small x and exponential tail, $P(D_t = 0) = 0$
(green) Almost pure Exponential, $P(D_t = 0) > 0$
(red) Sub-Exponential, $P(D_t = 0) > 0$

- Non-Gaussian behavior can be tuned to last at long time t:



P(x,t) for parameters $a = 0{,}1$, $\bar{D} = 1$ and $\sigma = a^{1/2}$, for $t = [1,10,50]$. Theory (red) and simulation (blue) match perfectly, whereas Gaussian fit (green) illustrates non-Gaussianity.

- Diffusivity is correlated in time:



(left) Example of trajectories with $\nu = 1$ and varying memory a^{-1}. (right) Increments of trajectories on X axis. Parameter a clearly affects the envelop of the noise, as seen by autocorrelation of squared increments.

References

[1] Wang et al. - PNAS (2008)
[2] M.Chubinsky, G.Slater - PRL (2014)
[3] Chechkin et al. - PRX (2017)
[4] Cox et al. – Econometrica (1985)
[5] Götz et al., submitted
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