Anomalous diffusion in biology: fractional Brownian motion, Lévy flights

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Minisymposium on fundamental aspects behind cell systems biology, Nové Hrady

22. 11. 2012
Outline

- Diffusion phenomenon
  - History
  - Different descriptions of diffusion
- Anomalous diffusion models
  - Fractional Brownian motion
  - Lévy flights
- Interesting processes exhibiting anomalous diffusion
History overview

- Diffusion is a transport phenomena that has been studied since 18th century
- First developments were done by Maxwell, Clausius, Boyle...
- 1827 - discovered Brownian motion
- The theoretical description of the Brownian motion was given by Langevin, Einstein, Smoluchowski...
- Many different approaches from different branches
- macroscopic vs microscopic approaches
Macroscopic description of diffusion

Fick’s laws

- Adolf Fick described in 1855 the diffusion by equations for concentration $\phi$
- First Fick’s law
  \[ J = -D \frac{\partial \phi}{\partial x} \]  
  \[ J \]  
  the flux is proper to concentration change  
- Second Fick’s law
  \[ \frac{\partial \phi}{\partial t} = - \frac{\partial J}{\partial x} = D \frac{\partial^2 \phi}{\partial x^2} \]  
  \[ \frac{\partial \phi}{\partial t} \]  
  time evolution is given by inhomogeneity of current
- the equation is formally the same as heat equation
Microscopic description of diffusion

Langevin equation

- Generalization of Newton’s dynamics to systems in contact with heat bath
- Newton equation
  \[ m\ddot{x}(t) - F = 0 \]  \hspace{1cm} (3)
- Langevin equation
  \[ m\ddot{x}(t) + \frac{\partial U}{\partial x} + \gamma \dot{x}(t) = \eta(t) \]  \hspace{1cm} (4)

- \(-\frac{\partial U}{\partial x}\) - external forces
- \(-\gamma \dot{x}(t)\) - friction forces
- \(\eta(t)\) - fluctuation forces with \(\langle \eta(t) \rangle = 0, \langle \eta(t)\eta(t') \rangle = 2D\delta(t - t')\)
Microscopic description of diffusion

Langevin equation

- both, friction and fluctuations are necessary, otherwise we would get nonphysical solution
- in the long time limit we get from the relation for velocity

\[ \langle v(t)^2 \rangle \simeq \frac{D}{\gamma m} \equiv \frac{k_B T}{m} \quad (5) \]

- Relation between diffusion coefficient and friction

\[ D = \frac{k_B T}{\gamma} \quad (6) \]

- for long times we get \( \langle x^2(t) \rangle \simeq t \) which means that \( |\Delta x| \simeq \sqrt{t} \)
Microscopic description of diffusion

Diffusion equation

- Alternative representation of Langevin equation is through probability distribution of the system \( p(x, t) \)
- For free particle we obtain diffusion equation

\[
\frac{\partial p(x, t)}{\partial t} = \frac{D}{\gamma^2} \frac{\partial^2 p(x, t)}{\partial x^2}.
\]  

(7)

- The equation is formally the same as Fick’s equation for concentration
- For one localized particle at time 0 we get a Gaussian function

\[
p(x, t) = \frac{1}{\sqrt{4\pi D t}} \exp \left( - \frac{(x - x_0)^2}{4Dt} \right).
\]  

(8)
Microscopic description of diffusion

Wiener stochastic process

- Another possibility is to use a formalism of stochastic processes
- **Definition:** A stochastic process \( W(t) \) (for \( t \in [0, \infty] \)) is called Wiener process, if
  - \( W(0) \equal{} 0 \)
  - for every \( t, s \) are increments \( W(t) - W(s) \) stationary process with distribution: \( W(t) - W(s) \sim \mathcal{N}(0, |t - s|) \).
  - for different values are increments not correlated.
- The Wiener process also obeys diffusion equation
- All formalisms lead to the main property of diffusion:
  \[
  |\Delta W(t)| = t^\frac{1}{2}
  \]
Diffusion in 2D
Anomalous diffusion

- For Brownian motion we can observe typical scales for space and time variables
  - for space: variance $\text{Var}(X(t))$
  - for time: correlations $\text{Corr}(X(t), X(s))$
- if these quantities do not produce characteristic quantities (standard deviation, correlation time), we observe anomalous diffusion
- for long-term correlations we observe fractional Brownian motion
- for infinite variance we observe Lévy flight
Fractional Brownian Motion

- we generalize Brownian motion by introduction of non-trivial correlations
- for Brownian motion is the covariance element
  \[ E[W(t)W(s)] = \min\{s, t\} = \frac{1}{2} (s + t - |s - t|) \]  
  (9)
- we introduce a generalization \( W_H(t) \) with the same properties, but covariance
  \[ E(W_H(t)W_H(s)) = \frac{1}{2}(s^{2H} + t^{2H} - |s - t|^{2H}) \]  
  (10)
- Standard deviation scales as \( |\Delta W_H(t)| \sim t^H \)
- for \( H = \frac{1}{2} \) we have Brownian motion, for \( H < \frac{1}{2} \) sub-diffusion, for \( H > \frac{1}{2} \) super-diffusion
Sample functions of fBM for $H=0.3, 0.5, 0.6, 0.7$. 
Lévy distributions

- Gaussian distribution has special property - it is a stable distribution
- Such distributions are limits in long time for stochastic processes driven by independent increments with given distribution
- Lévy distributions - class of stable distributions with polynomial decay

\[ L_\alpha(x) \sim \frac{l_\alpha}{|x|^{1+\alpha}} \text{ for } |x| \to \infty \quad (11) \]

for \( \alpha \in (0, 2) \)

- the variance for these distributions is infinite
- the distribution has sharper peak and fatter tails (= heavy tails)
Difference between Gaussian distribution and Cauchy distribution ($\alpha = 1$)
Lévy flights

- Lévy flight $L_\alpha(t)$ is a stochastic process that has the same properties as Brownian motion, but its increments have Lévy distribution.

- Because of infiniteness of variance, scaling properties are expressed via sum of random variables:
  - for Brownian motion: $a^{1/2} W(t) + b^{1/2} W(t) \overset{d}{=} (a + b)^{1/2} W(t)$
  - for Lévy flight: $a^{1/\alpha} L_\alpha(t) + b^{1/\alpha} L_\alpha(t) \overset{d}{=} (a + b)^{1/\alpha} L_\alpha(t)$

- $\alpha$-th fractional moment $\mathbb{E}(|X|^\alpha) = \int x^\alpha \rho(x) dx$ of increment is equal to

$$\mathbb{E}(|L_\alpha(t_1) - L_\alpha(t_2)|^\alpha) \sim |t_1 - t_2|.$$ (12)
Lévy flight in 2D
Another possibility, how to estimate the scaling exponent is power spectrum

It is the absolute value of Fourier transform

\[ P_x(\omega) = |\mathcal{F}[x](\omega)|^2 \]  \hspace{1cm} (13)

It is closely related to correlations and variance

\[ \langle (\Delta x(t))^2 \rangle \propto t^\alpha \Rightarrow P_x(\omega) \propto \frac{1}{\omega^{1+\alpha}} \] \hspace{1cm} (14)
Examples of anomalous diffusion

- **Subdiffusive behavior**
  - mRNA molecules in E. coli cells
  - Lipid granules in yeast cells
  - Cytoplasmatic molecules

- **Power law behavior**
  - Power law memory kernel for fluctuations within a single protein molecule
  - Persistent cell motion of eukaryotic cells
random motion of fluorescently labeled mRNA molecules in E. coli is measured

the track of molecules are recorded and fluctuations are calculated

the fluctuation function $\langle \delta(t)^2 \rangle$ scales with an exponent of $\alpha = 0.70 \pm 0.007$ (for 21 trajectories)

for comparison is done the measurement also in 70% glycerol, with an exponent of $\alpha = 1.04 \pm 0.03$, which corresponds to diffusion

Reasons: a) power law distributions, b) time-dependent viscosity c) time correlations
Physical Nature of Bacterial Cytoplasm


Phys Rev Lett, 96, 2006
Anomalous Diffusion in Living Yeast Cells

Iva Marija Tolic’-Norrelykke et al. Anomalous diffusion in living yeast cells. 
Phys Rev Lett, 93, 2004

- the movement of lipid granules in the living yeast cell is investigated
- the track is recorded by two methods:
  - Optical tweezer - short times ($\sim 10^{-4}$ s), measures frequency
  - Multiple particle tracking - video based, longer times ($\sim 10^{-1} – 10^2$ s)
- The results were for diffusion in the cell $\alpha = 0.737 \pm 0.003$ for OT, $\alpha = 0.70 \pm 0.03$ for MPT, about 1 in water
- Possible reasons: granules are embedded in a protein polymer network or mechanically coupled to other structures
Anomalous Diffusion in Living Yeast Cells


Phys Rev Lett, 93, 2004
Anomalous Subdiffusion Is a Measure for Cytoplasmic Crowding in Living Cells

Matthias Weiss et al. Anomalous subdiffusion is a measure for cytoplasmic crowding in living cells. 

Biophys J, 87, 2004

- cytoplasmatic molecules were investigated by fluorescence correlation spectroscopy
- autocorrelation function was measured
- we suppose a diffusion coefficient $D(t) = \Gamma t^{\alpha-1}$ and obtain correlation function

$$C(\tau) \approx \frac{1 + fe^{-\tau/\tau_C}}{1 + (\tau/\tau_D)^{\alpha}}$$  \hspace{1cm} (15)

- for different different masses and hydrodynamic radii were different $\alpha$’s obtained, but $\alpha < 1$ in all cases
Anomalous Subdiffusion Is a Measure for Cytoplasmic Crowding in Living Cells

Matthias Weiss et al. Anomalous subdiffusion is a measure for cytoplasmic crowding in living cells.

*Biophys J*, 87, 2004
Power law within protein molecules


- Fluctuations between fluorescein-tyrosine pair were monitored by photoinduced electron transfer
- System can be described by generalized Langevin equation, where we assume non-trivial autocorrelation function

\[
m\ddot{x}(t) = -\zeta \int_0^t d\tau K(\tau) \dot{x}(\tau) - \frac{dU}{dx} + F(t)
\]  

(16)

- For memory kernel \( K(t) \) was measured power decay

\[K(t) \sim t^{-0.51 \pm 0.07}\]
Persistent Cell Motion in the Absence of External Signals

Liang Li et al. *Persistent cell motion in the absence of external signals: a search strategy for eukaryotic cells.*

*PLoS ONE, 2008*

- motion of whole eukaryotic cells is investigated in the environment with no external signals
- it has been shown that the movement is not a simple random walk
- it has persistent behavior in smaller time scales, in larger time scales (∼ 10 min) it becomes a random walk motion
- the movement seems to be more complex than simple wiener process or Lévy flight
- cells are able to reach the target very efficiently
Persistent Cell Motion in the Absence of External Signals

Liang Li et al. Persistent cell motion in the absence of external signals:// a search strategy for eukaryotic cells.

*PLoS ONE, 2008*
Summary

- Diffusion is an important phenomena in biological systems
- It can be described through different formalisms
- Brownian motion can be generalized in a few different ways - fBM, Lévy flight
- There are examples of subdiffusion and power laws in cell systems and biology
Ido Golding and Edward C. Cox.
Physical nature of bacterial cytoplasm.

Liang Li et al.
Persistent cell motion in the absence of external signals:// a search strategy for eukaryotic cells.

Iva Marija Tolic’-Norrelykke et al.
Anomalous diffusion in living yeast cells.

Matthias Weiss et al.
Anomalous subdiffusion is a measure for cytoplasmic crowding in living cells.

X. Sunney Xie et al.
Observation of a power-law memory kernel for fluctuations within a single protein molecule.

Thank you for attention!