# Anomalous diffusion in biology: fractional Brownian motion, Lévy flights

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# Outline

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

# History overview

- Diffusion is a transport phenomena that has been studied since $18^{th}$ 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

$$J = -D\frac{\partial \phi}{\partial x} \tag{1}$$

- the flux is proper to concentration change
- Second Fick's law

$$\frac{\partial \phi}{\partial t} = -\frac{\partial J}{\partial x} = D\frac{\partial^2 \phi}{\partial x^2} \tag{2}$$

- 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

$$m\ddot{x}(t) - F = 0 \tag{3}$$

- Langevin equation

$$m\ddot{x}(t) + \frac{\partial U}{\partial x} + \gamma\dot{x}(t) = \eta(t) \tag{4}$$

  - $-\frac{\partial U}{\partial x}$ - 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



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

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

- Relation between diffusion coefficient and friction

$$D = \frac{k_B T}{\gamma} \tag{6}$$

- 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 od Langevin equation is through probability distribution of the system $p(x, t)$
- for free particle we obtain diffusion equation

$$\frac{\partial p(x,t)}{\partial t} = \frac{D}{\gamma^2}\frac{\partial^2 p(x,t)}{\partial x^2}. \tag{7}$$

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

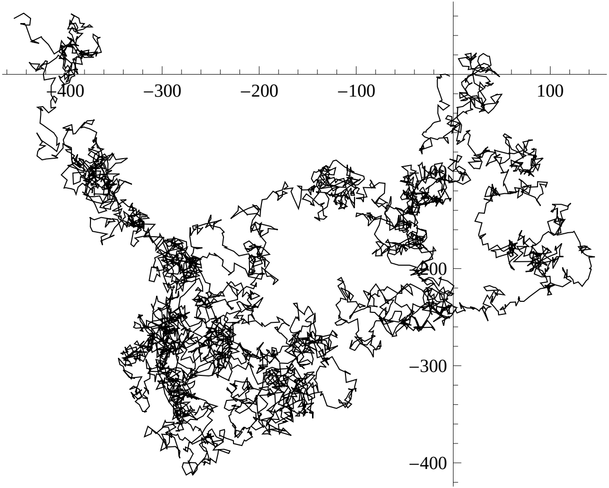
$$p(x,t) = \frac{1}{\sqrt{4\pi D t}} \exp\left(-\frac{(x-x_0)^2}{4Dt}\right) \tag{8}$$

# 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
  - $W(0) \overset{a.s.}{=} 0$
  - 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 $Var(X(t))$
  - for time: correlations $Corr(X(t), X(s))$
- 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

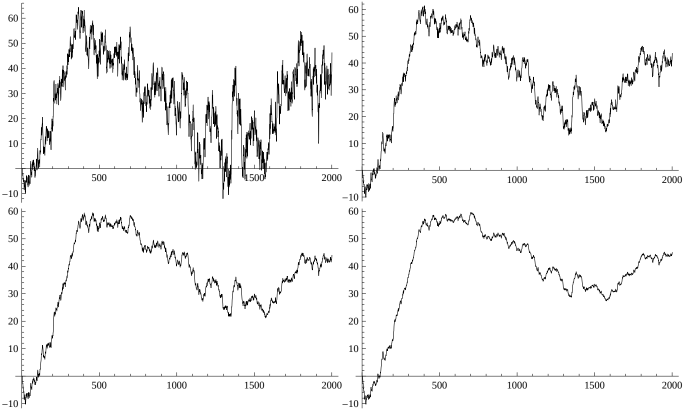
$$\mathrm{E}[W(t)W(s)] = \min\{s, t\} = \frac{1}{2}\left(s + t - |s - t|\right) \tag{9}$$

- we introduce a generalization $W_H(t)$ with the same properties, but covariance

$$E(W_H(t)W_H(s)) = \frac{1}{2}(s^{2H} + t^{2H} - |s - t|^{2H}) \tag{10}$$

- Standard deviation scales as $|\Delta W_H(t)| \propto t^H$
- 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.



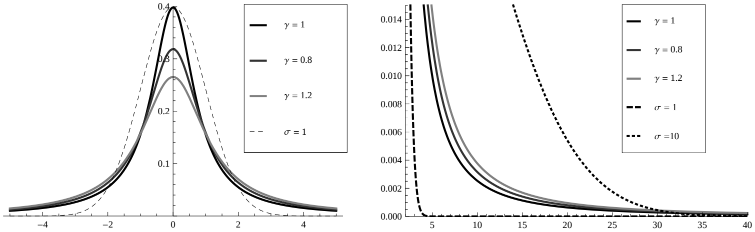
# Lévy distributions

- 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

$$L_\alpha(x) \simeq \frac{l_\alpha}{|x|^{1+\alpha}} \ \text{for} \ |x| \to \infty \tag{11}$$

  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 ($\alpha = 1$)

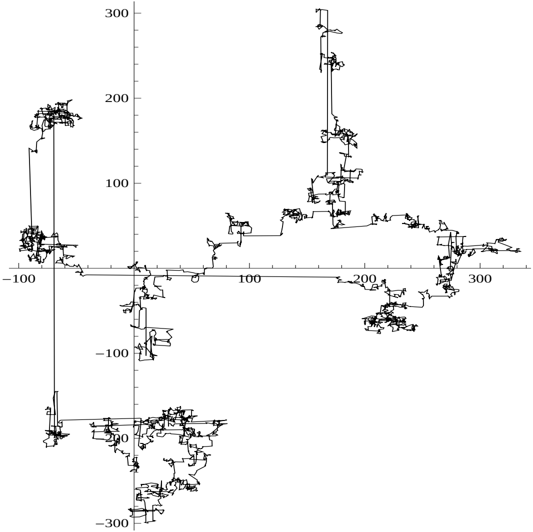


# Lévy flights

- Lévy flight $L_\alpha(t)$ is a stochastic process that the same properties as Brownian motion, but it increments have Lévy distribution
- Because of infiniteness of variance, scaling properties are expressed via sum of random variables
  - for Brownian motion: $a^{1/2}W(t) + b^{1/2}W(t) \stackrel{d}{=} (a+b)^{1/2}W(t)$
  - for Lévy flight: $a^{1/\alpha}L_\alpha(t) + b^{1/\alpha}L_\alpha(t) \stackrel{d}{=} (a+b)^{1/\alpha}L_\alpha(t)$
- $\alpha$-th fractional moment $\mathrm{E}(|X|^\alpha) = \int x^\alpha p(x)\mathrm{d}x$ of increment is equal to

$$\mathrm{E}(|L_\alpha(t_1) - L_\alpha(t_2)|^\alpha) \sim |t_1 - t_2|. \tag{12}$$

# Lévy flight in 2D



# Power Spectrum

- Another possibility, how to estimate the scaling exponent is power spectrum
- it is the absolute value of fourier transform

$$P_x(\omega) = |\mathcal{F}[x](\omega)|^2 \tag{13}$$

- it is closely related to correlations and variance

$$\langle(\Delta x(t))^2\rangle \propto t^\alpha \Rightarrow P_x(\omega) \propto \frac{1}{\omega^{1+\alpha}} \tag{14}$$

# 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

# Physical Nature of Bacterial Cytoplasm

Ido Golding and Edward C. Cox. Physical nature of bacterial cytoplasm.

*Phys Rev Lett*, 96, 2006

- 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

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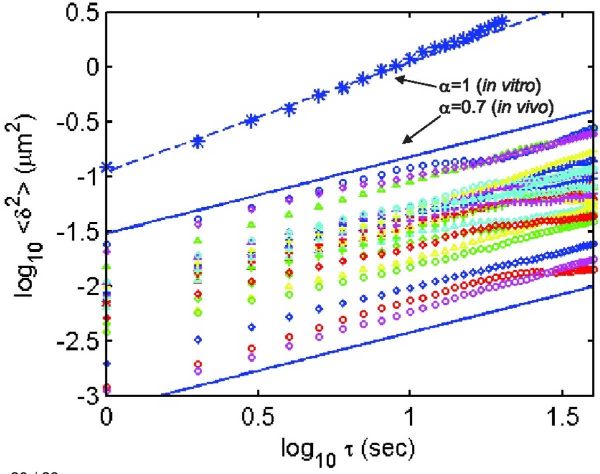

# Anomalous Diffusion in Living Yeast Cells

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

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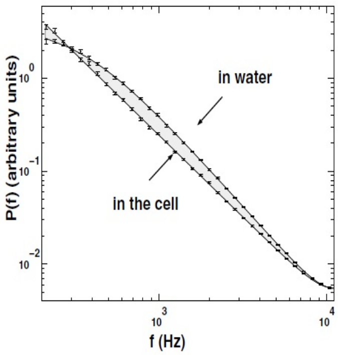


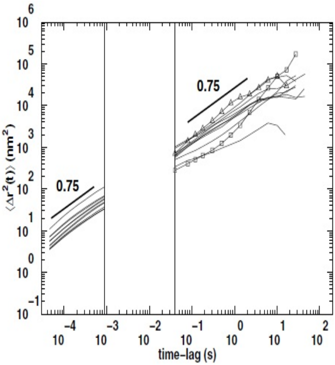

# Anomalous Subdiffusion Is a Measure for Cytoplasmic Crowding in Living Cells

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 coefficienty $D(t) = \Gamma t^{\alpha-1}$ and obtain correlation function

$$C(\tau) \simeq \frac{1 + fe^{-\tau/\tau_C}}{1 + (\tau/\tau_D)^\alpha} \tag{15}$$

- for different different masses and hydrodynamic radii were different $\alpha$'s obtained, but $\alpha < 1$ in all cases

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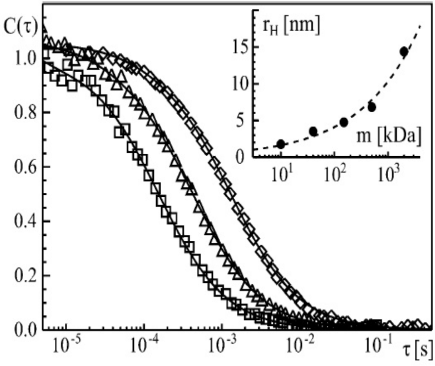

# Power law within protein molecules

X. Sunney Xie et al. Observation of a power-law memory kernel for fluctuations within a single protein molecule.
*Phys Rev Lett*, 94, 2005

- 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

$$m\ddot{x}(t) = -\zeta \int_0^t \mathrm{d}\tau K(\tau)\dot{x}(\tau) - \frac{\mathrm{d}U}{\mathrm{d}x} + F(t) \qquad (16)$$

- 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 ($\sim 10min$) 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

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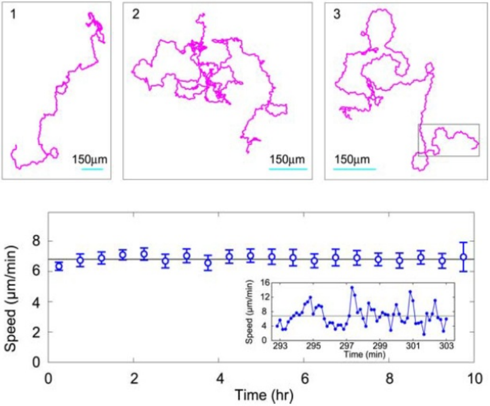

# Summary

- 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

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Thank you for attention!