BINA Bar-Ilan Institute of Nanotechnology & Advanced Materials

אוניברסיטת בר-אילן
Bar-Ilan University

Summer School

on Stochastic Processes with Applications to Physics and Biophysics

September 25-28, 2017

In Acre

The Bar-Ilan Institute for Nano-technology and Advanced Materials is proud to present:
The summer school on normal and anomalous stochastic processes in Physics.
The program includes: basic introduction to the field, specific applications from the fields of single molecule tracking in the environment of the cell and stochasticity in the cell cycle.

The school is open for theoreticians and experimentalists.

Deadline for submitting applications: 1 May 2017
Participation fee of 650 NIS

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Fluctuations of Single-Particle Diffusivity in Random Environments

Eli Barkai

Bar-Ilan University

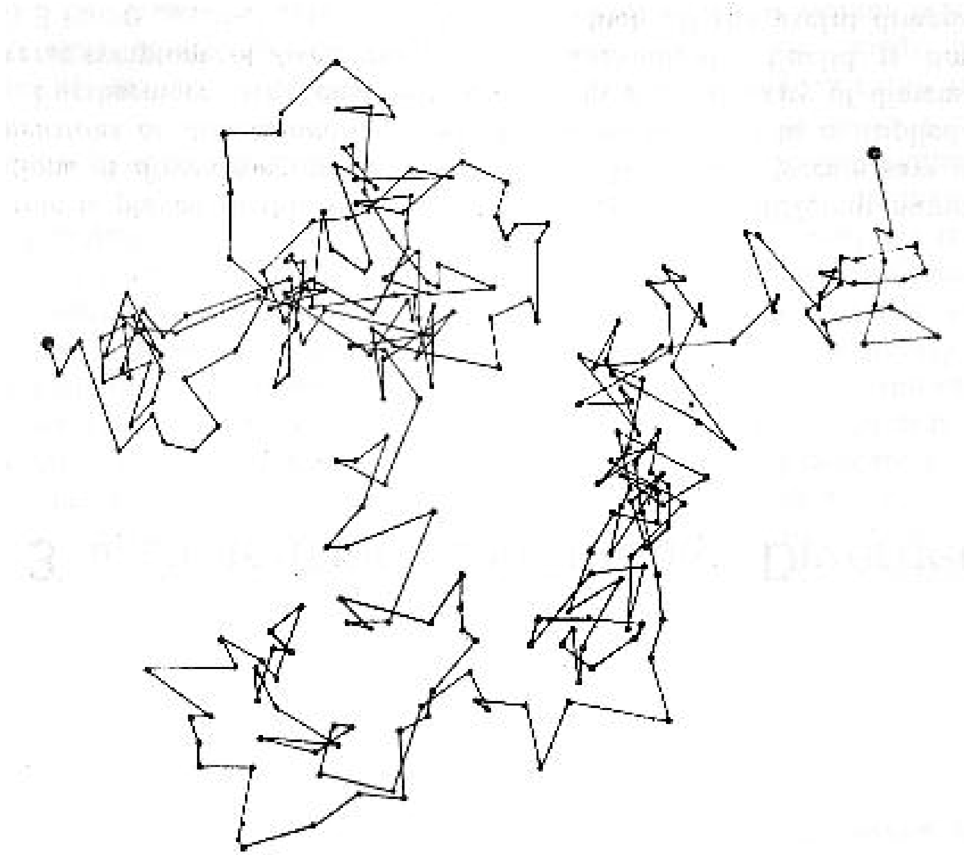
He, Burov, Metzler, EB PRL 2008. **Akimoto, EB, Saito** PRL 2016.

2017

Outline

- Disorder greatly affects diffusion.
- Time averages and ensemble averages are non-equivalent.
- Experiments: anomalous diffusion of single molecules in the cell.
- Random time scale invariant diffusion and transport coefficients.
- Quenched environment gives by far larger fluctuations of the diffusivity (compared with the annealed model).

Brownian Motion



$$\overline{\delta^2}\,(\Delta, t) = \frac{\int_0^{t-\Delta} \left[x(t'+\Delta) - x(t')\right]^2 dt'}{t-\Delta} \to 2D\Delta$$

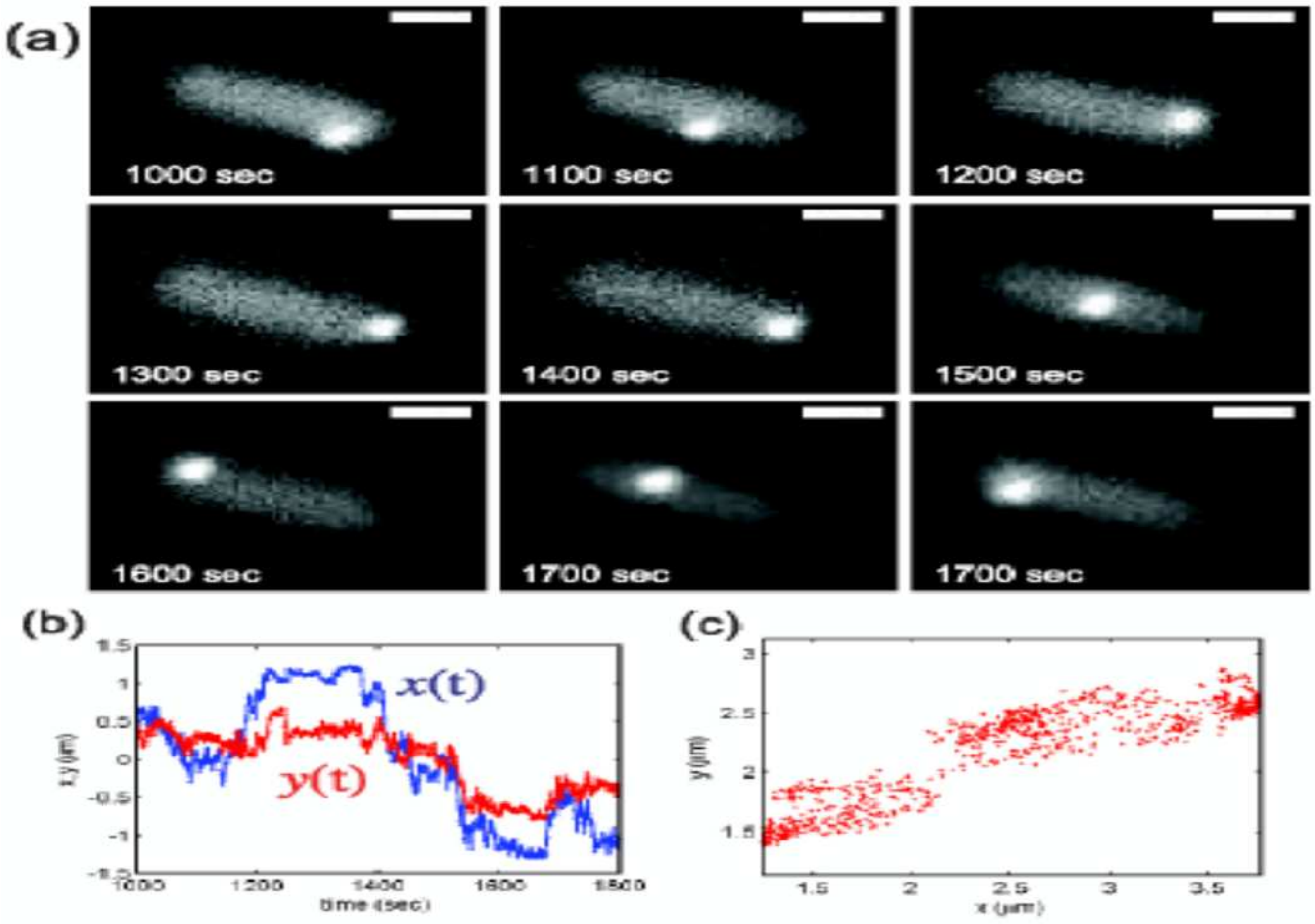
Ergodicity for Brownian particles

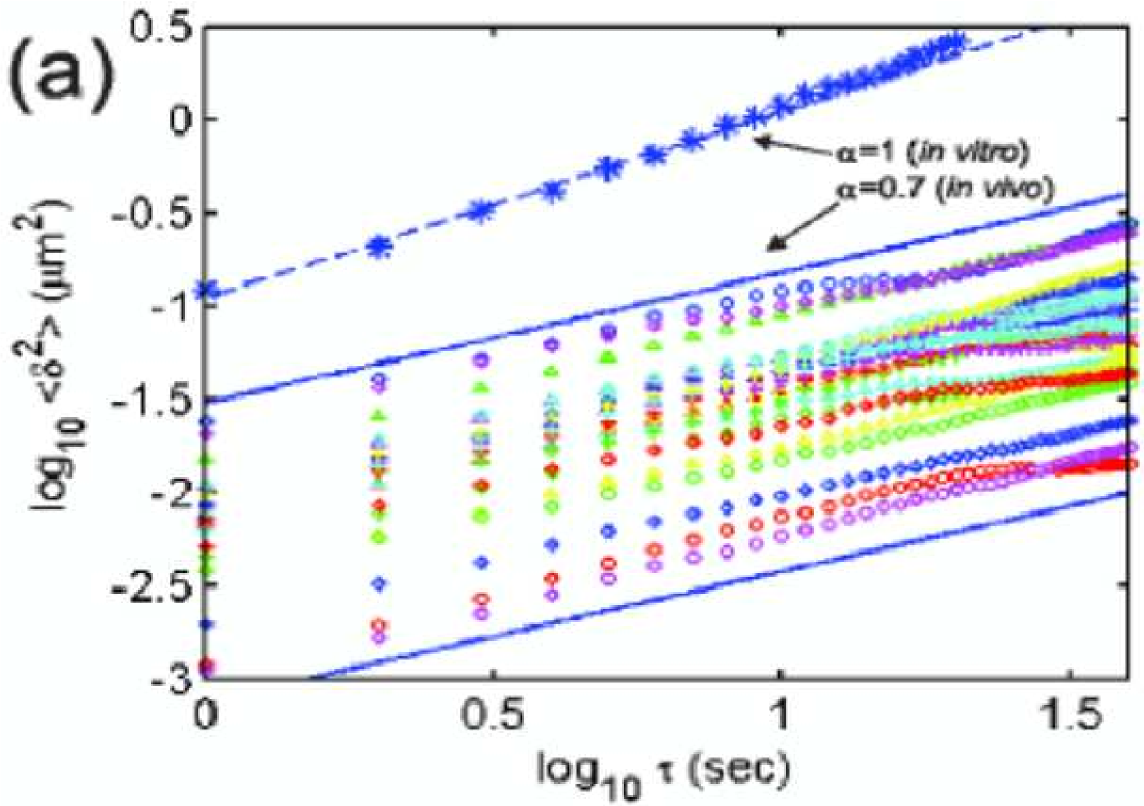
- Time averages are reproducible.
- Two measurements of $\overline{\delta^2}$ yield the same result.
- The time and ensemble averages coincide (ergodicity).

$$\overline{\delta^2} = \langle x^2 \rangle .$$

- Diffusion is normal $\delta^2 \sim \Delta$.
- Measure between $(0,t)$ and $(t,2t)$ yield same results (stationary).
- These properties are broken in single molecule experiments in cells.

mRNA diffusing in a cell Golding and Cox



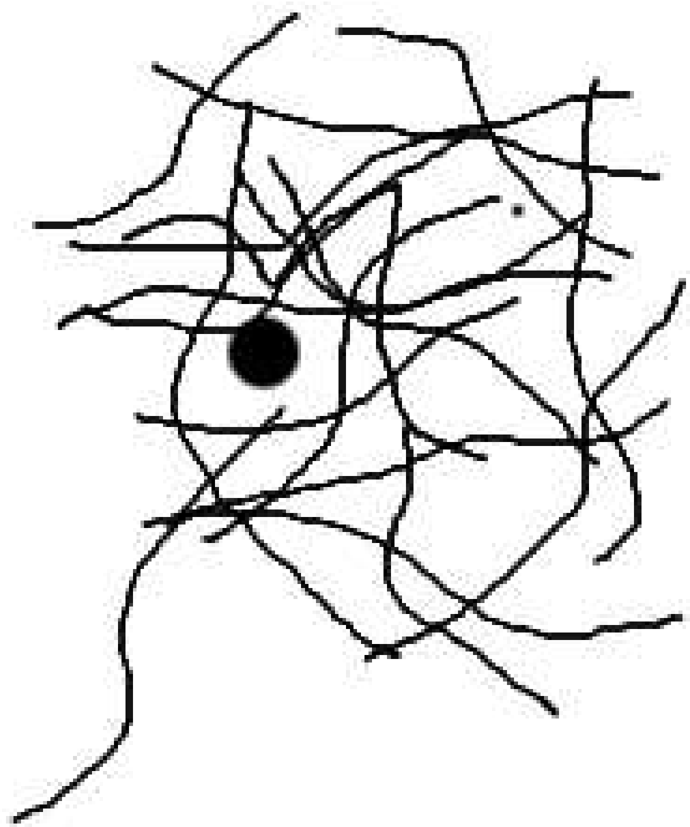


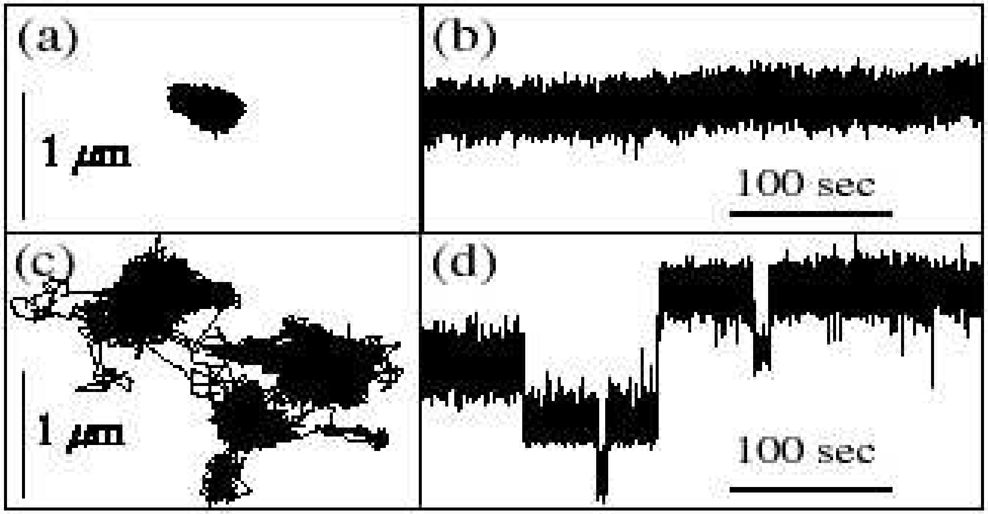
- Bronstien, ... Barkai, Garini **PRL** (2009). Anomalous diffusion and randomness of time averages is common.

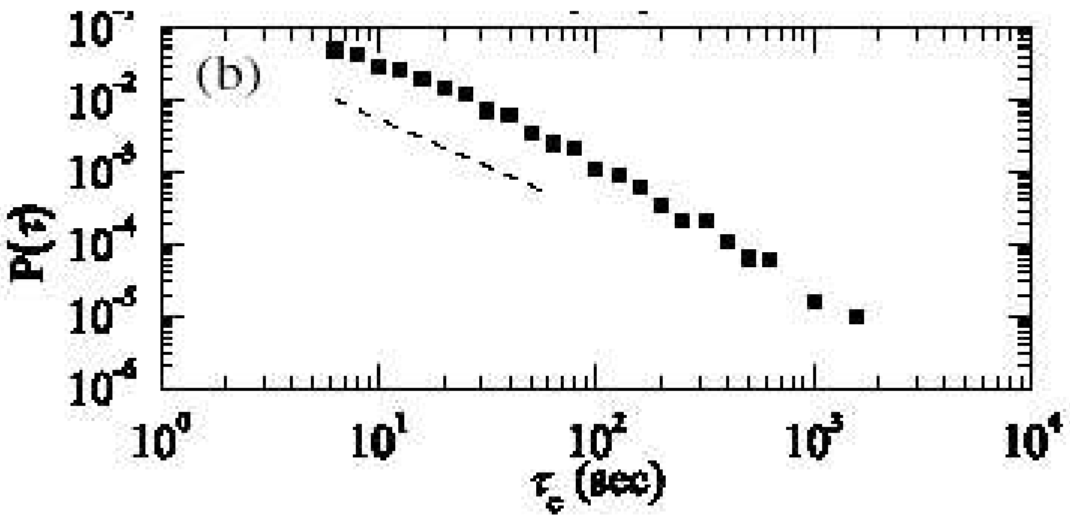
Continuous Time Random Walk (CTRW)

Dispersive Transport in Amorphous Material Scher-Montroll (1975).

Bead Diffusing in Polymer Network Weitz (2004).

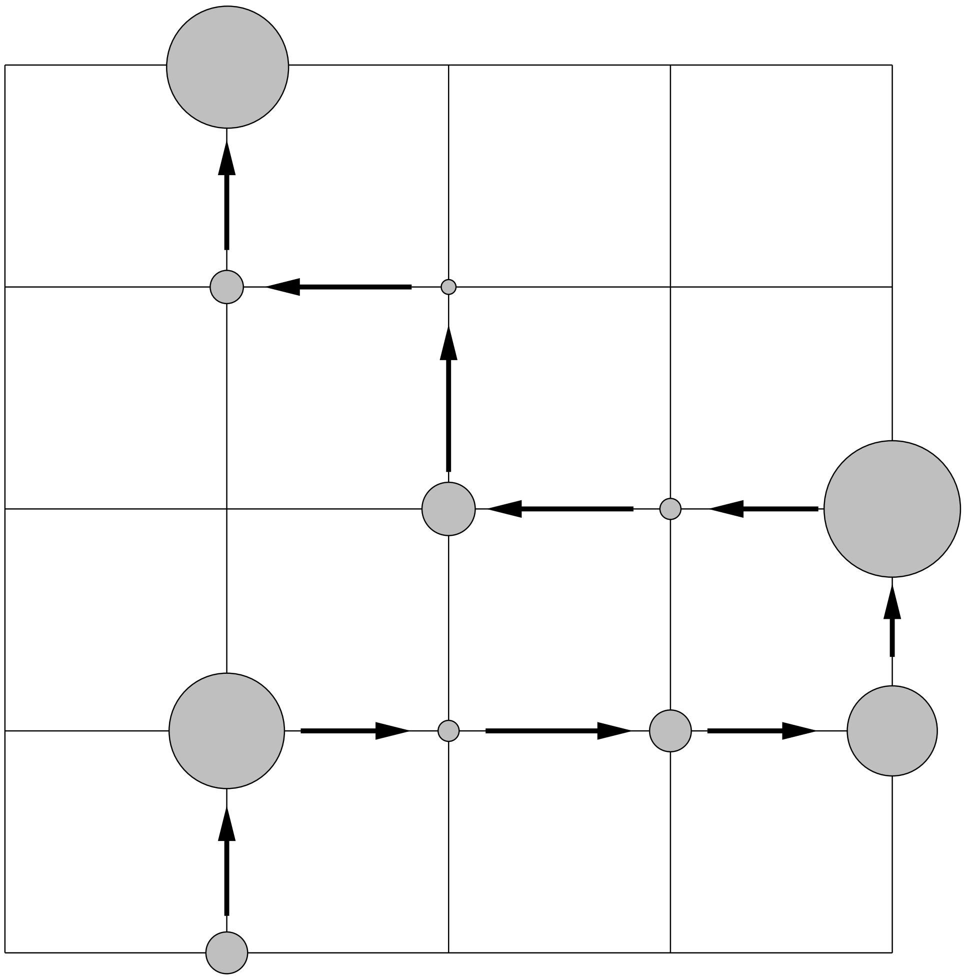


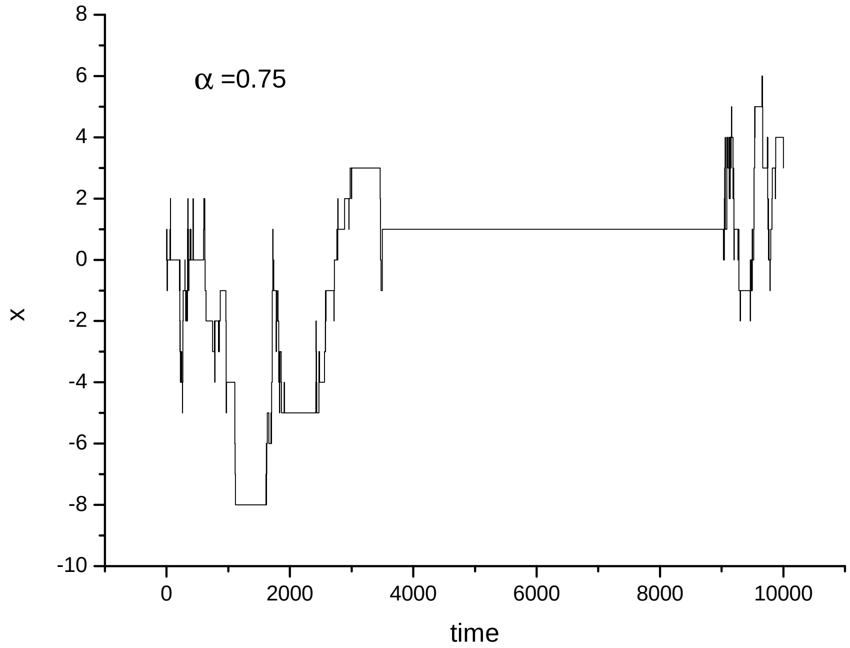




Average Waiting Time is ∞. Diffusion is anomalous $\langle r^2 \rangle \sim t^\alpha$.

CTRW: power law waiting times $\psi(t) \sim t^{-(\alpha+1)}$



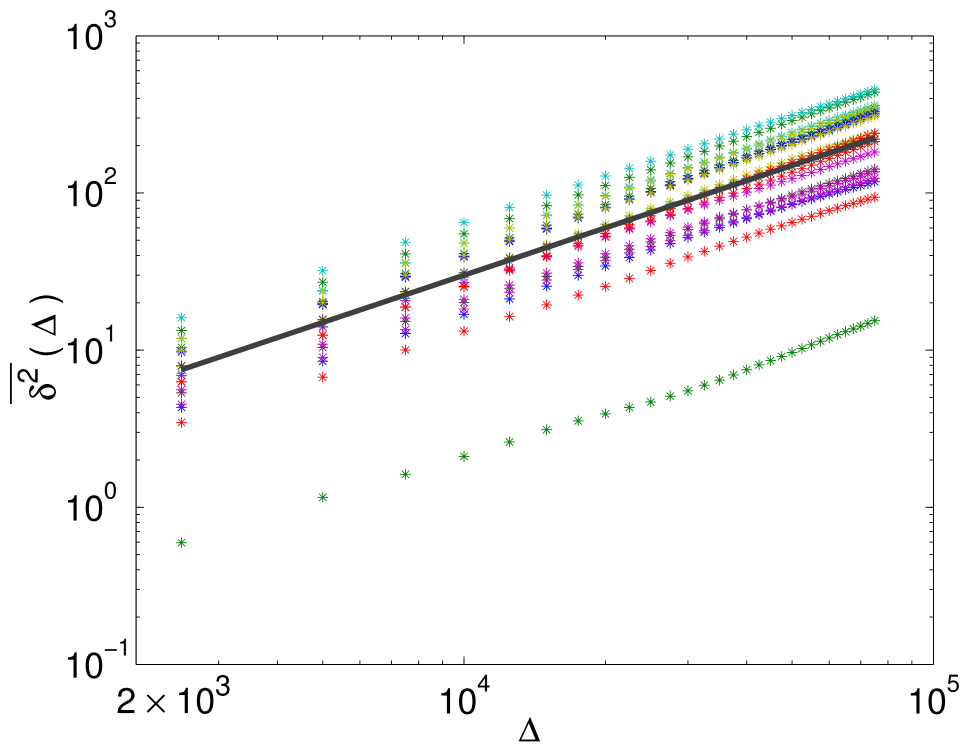


- Random walk on lattice with jumps to nearest neighbours only.
- $\psi(t) \sim t^{-1-\alpha}$ with $0 < \alpha < 1$ gives $\langle r^2 \rangle \sim t^{\alpha}$

CTRW and ergodicity breaking

- Einstein $D = \frac{\langle \delta x^2 \rangle}{2\langle \tau \rangle}$.
- Boltzmann-Gibbs: If measurement time $t >> \langle \tau \rangle$ expect ergodicity.
- Scher-Montroll: If $\langle \tau \rangle \to \infty$, $D \to 0$ and the process is sub-diffusive.
- Bouchaud: If $\langle \tau \rangle \to \infty$ expect weak ergodicity breaking.

Random Time-Scale Invariant Diffusion Constant



$$\overline{\delta^2}\left(\Delta, t\right) = \frac{\int_0^{t-\Delta}\left[x(t'+\Delta) - x(t')\right]^2 dt'}{t-\Delta}$$

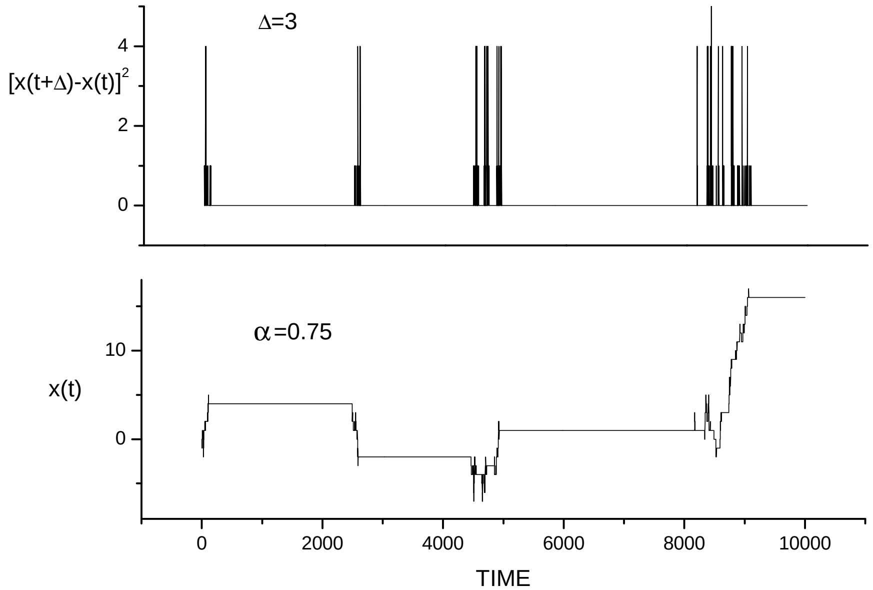
- He Burov Metzler Barkai PRL (2008), Lubelski, Sokolov, Klafter (ibid).

Anomalous Seems Normal

$$\langle \overline{\delta^2} \rangle \sim \frac{2D_\alpha}{\Gamma(1+\alpha)} \frac{\Delta}{t^{1-\alpha}}$$

- Normal diffusion $\langle \overline{\delta^2} \rangle = 2D\Delta$.
- For anomalous diffusion $D(t) \sim \frac{d\langle x^2 \rangle}{dt} \sim t^{\alpha-1}$.
- Aging effect $\langle \overline{\delta}^2 \rangle$ decreases when measurement time increases.

Fluctuations of the time average $\overline{\delta^2}$

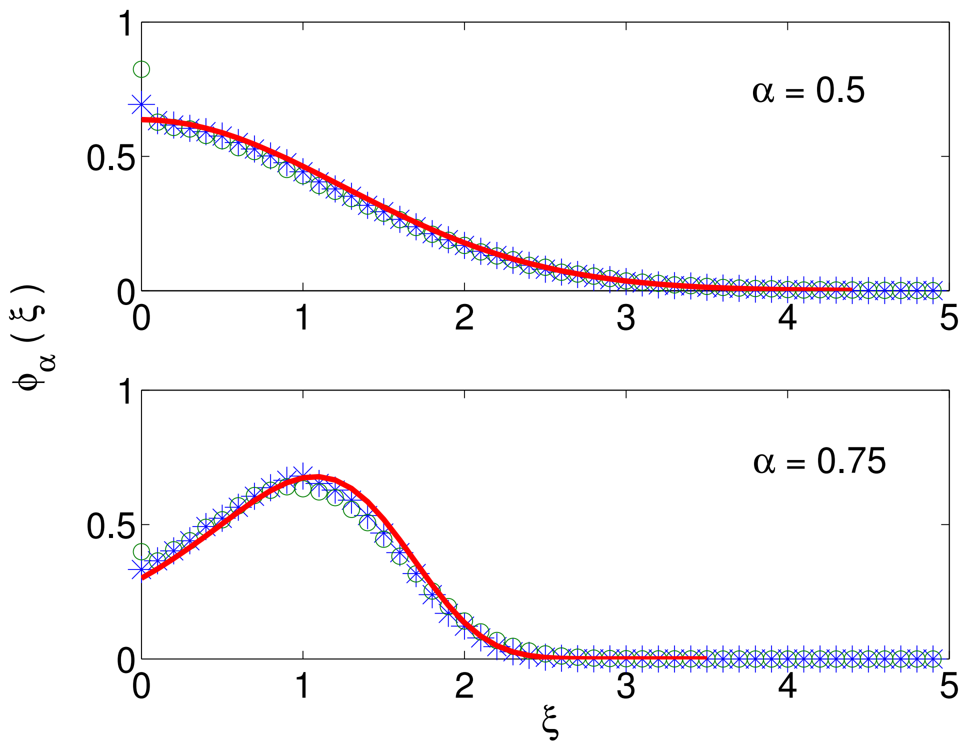


$\overline{\delta^2} \sim \frac{s}{t}$ number of jumps in $(0,t)$ is s.

Most of measurement time $[x(t'+\Delta)-x(t')]^2 = 0$ due to long trapping.

Distribution of $\overline{\delta^2}$

$$\xi = \frac{s}{\langle s \rangle} = \frac{\overline{\delta^2}}{\langle \overline{\delta^2} \rangle}, \qquad \lim_{t\to\infty} \phi_\alpha(\xi) = \frac{\Gamma^{1/\alpha}(1+\alpha)}{\alpha \xi^{1+1/\alpha}} l_\alpha \left[\frac{\Gamma^{1/\alpha}(1+\alpha)}{\xi^{1/\alpha}} \right].$$



Finite size effect is important: Anomalous again

$$\langle \overline{\delta^2} \rangle = \frac{\int_0^{t-\Delta} \left[\langle x^2(t'+\Delta)\rangle + \langle x^2(t')\rangle - 2\langle x(t'+\Delta)x(t')\rangle \right] dt}{t-\Delta}.$$

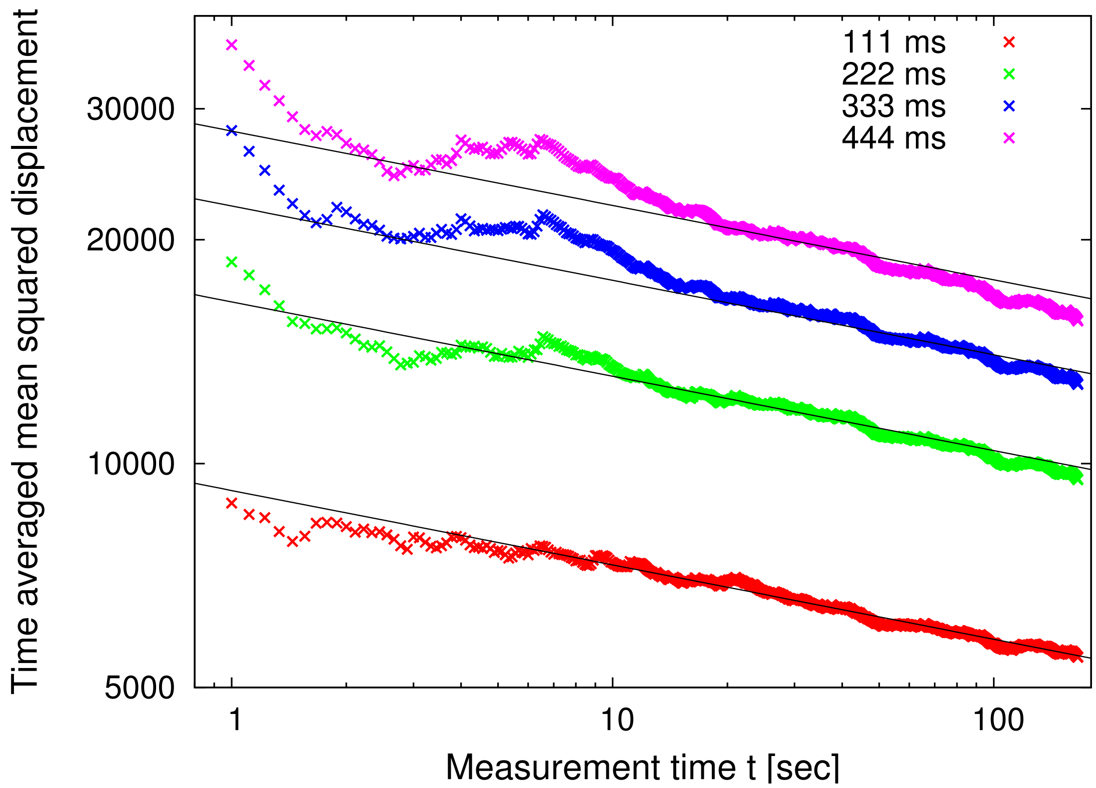
- We consider the fractional Fokker-Planck dynamics in a binding field $V(x)$
- If $\langle x \rangle_B = 0$ namely $V(x) = V(-x)$.

$$\langle x(t_1)x(t_2)\rangle \sim \langle x^2 \rangle_B \frac{B(t_1/t_2, \alpha, 1-\alpha)}{\Gamma(\alpha)\Gamma(1-\alpha)}.$$

$$\boxed{\langle \overline{\delta^2} \rangle \sim \langle x^2 \rangle_B \tfrac{2\sin(\alpha\pi)}{(1-\alpha)\alpha\pi} \left(\tfrac{\Delta}{t}\right)^{1-\alpha}}$$

- Neusius, Sokolov, Smith (PRE) 2009. Burov, Metzler, Barkai (PNAS) 2010.

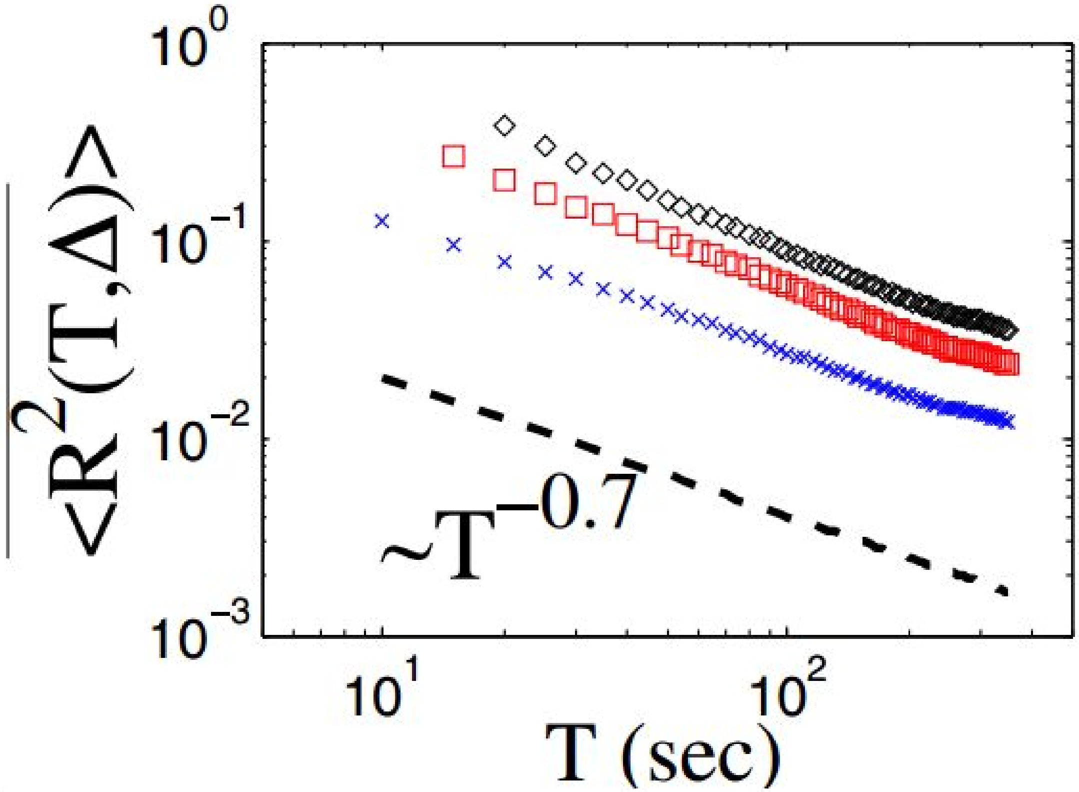
Aging effect (Diego Krpaf's experiment)



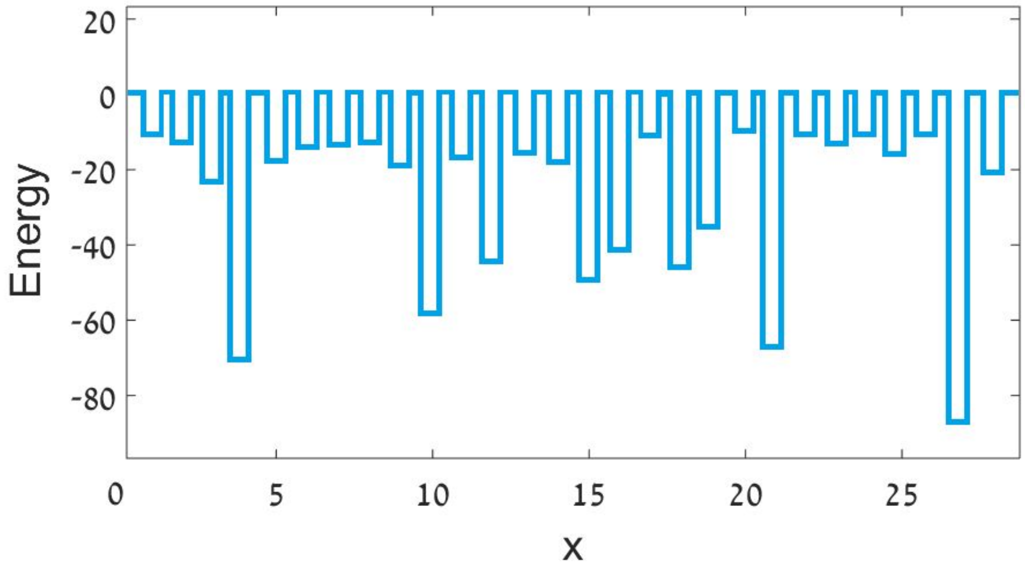
- The older you get the slower you are
- Channel protein molecules on a membrane.
- Weigel $\cdots$ Krapf PNAS (2011).

Three more experiments showing aging MSD

- Receptor Motion in Living Cells **Manzo... Garcia Parajo** PRX (2015).
- Insulin granule in pancreatic cell **Tabei ... Scherer** PNAS (2013).
- Myosin motors in filament system **Burov ... Dinner** PNAS (2013).



Quenched trap model



$\tau_i = \exp(E_x/k_B T)$ and E_x IID RV.

Exponential density of states $\rho(E) = \exp(-E/T_g)/T_g$

Sojourn time PDF $\psi(\tau) \sim \tau^{-(1+T/T_g)}$

Ergodic properties of the quenched trap model

- For a finite system of size L the largest waiting time is finite. It is determined by the deepest trap.

- Quenched trap model is ergodic when we take $t \to \infty$ before $L \to \infty$.

- Quenched model exhibits non self averaging.

Non ergodicity mimics inhomogeneity (SOKOLOV)

How to quantify the fluctuations of the quenched model?

Annealed versus quenched models. Where are fluctuations larger?

Is Mittag-Leffler statistics universal?

Role of initial conditions? equilibrium versus non equilibrium initial state.

Role of dimension $d = 2$ is critical.

Distribution of diffusion constant

- The size of the system is crucial

$$\langle \overline{\delta^2} \rangle_{dis} = 2 \frac{\Gamma\left(\alpha^{-1}\right)}{\alpha\Gamma\left(1-\alpha\right)^{1/\alpha} L^{1/\alpha - 1}} \Delta.$$

- Starting from thermal initial conditions, periodic boundary conditions, the ensemble average MSD is

$$\langle r^2 \rangle_{eq} = \frac{t}{\sum_i \tau_i / L}.$$

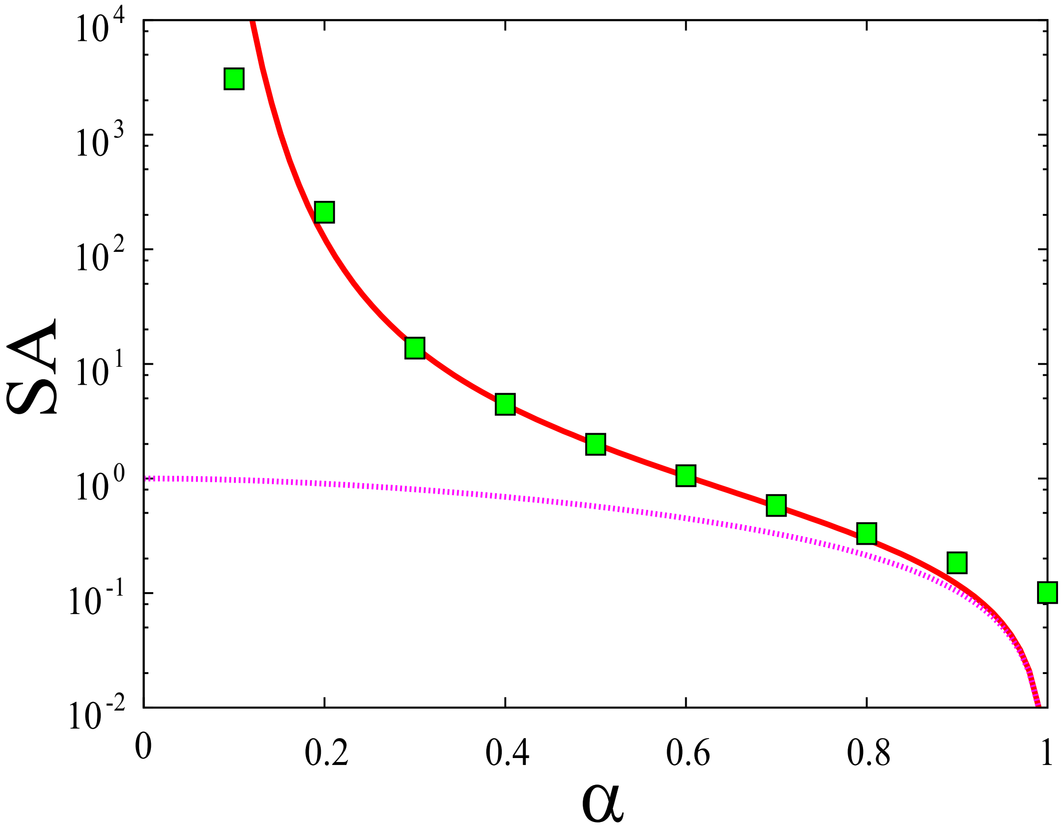
- The SA parameter

$$SA = \frac{\langle \overline{\mathcal{O}}^2 \rangle_{dis} - \langle \overline{\mathcal{O}} \rangle_{dis}^2}{\langle \overline{\mathcal{O}} \rangle_{dis}^2}.$$

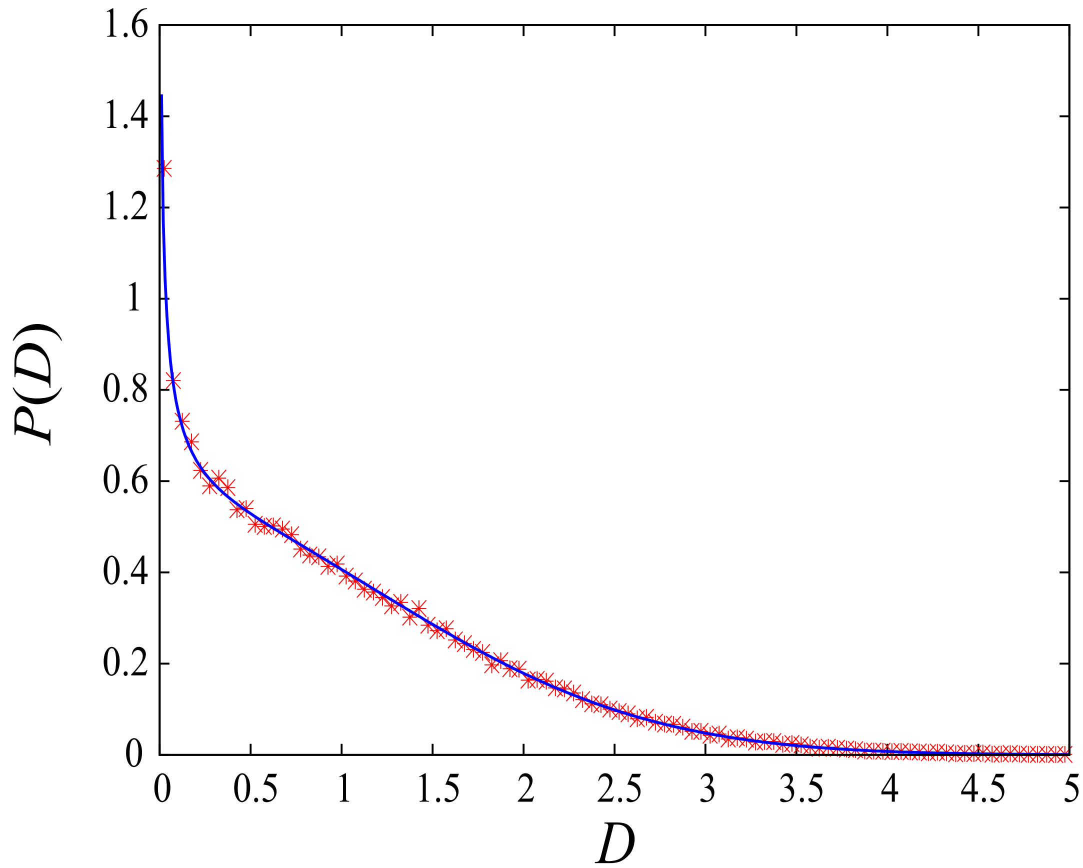
- The EB parameter

$$EB = \frac{\langle \overline{\mathcal{O}}^2 \rangle - \langle \overline{\mathcal{O}} \rangle^2}{\langle \overline{\mathcal{O}} \rangle^2}.$$

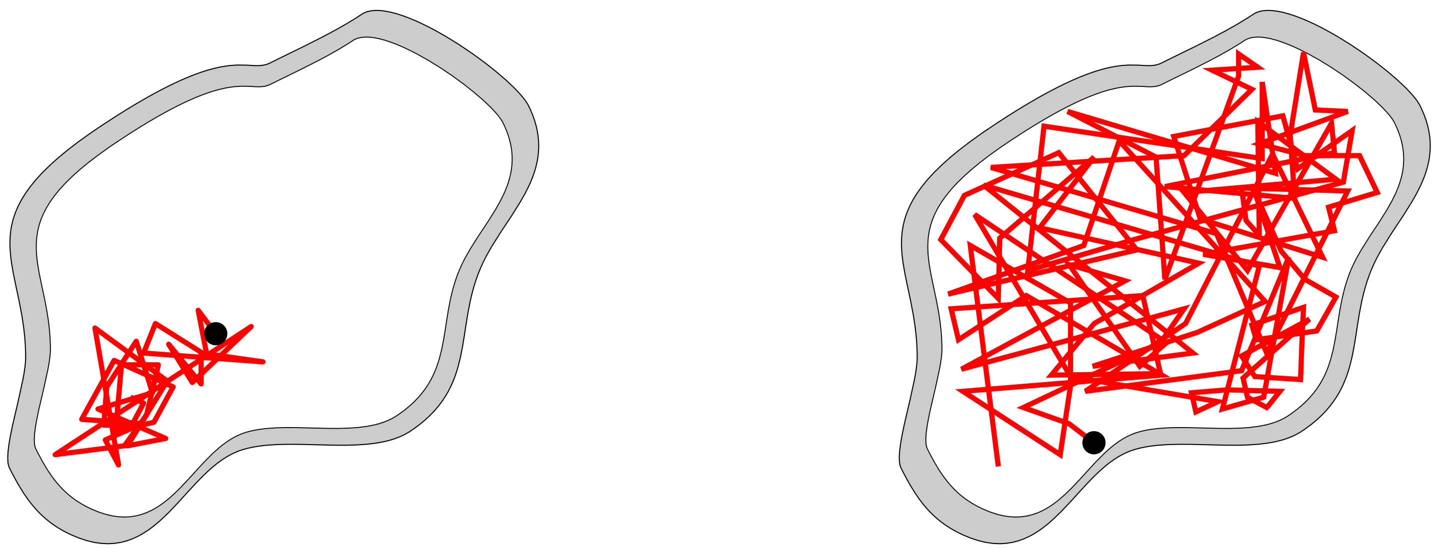
SA versus EB parameters



Distribution of diffusivities $\alpha = 2/3$, $\langle D \rangle = 1$



Local and Global Measurements

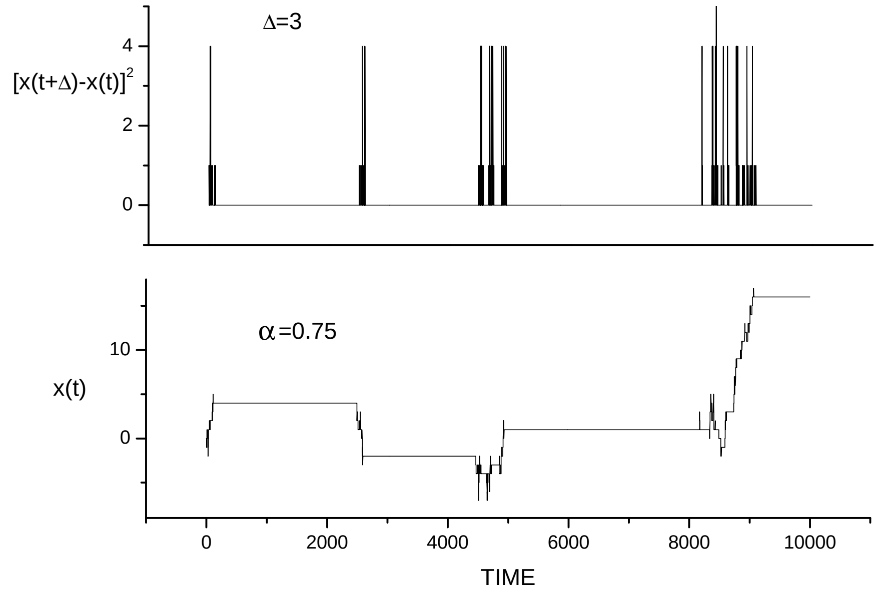


- Brownian motion: Local = global measurements, when $\Delta << L^2/D$.
- CTRW: Local $\neq$ global measurements.
  Both age and exhibit ergodicity breaking.
- Quenched model: Local measurements age (like annealed case).
  Global measurement exhibit a diffusivity decreasing with system, super large fluctuations, and non self averaging.

Open problems and some further subtle points

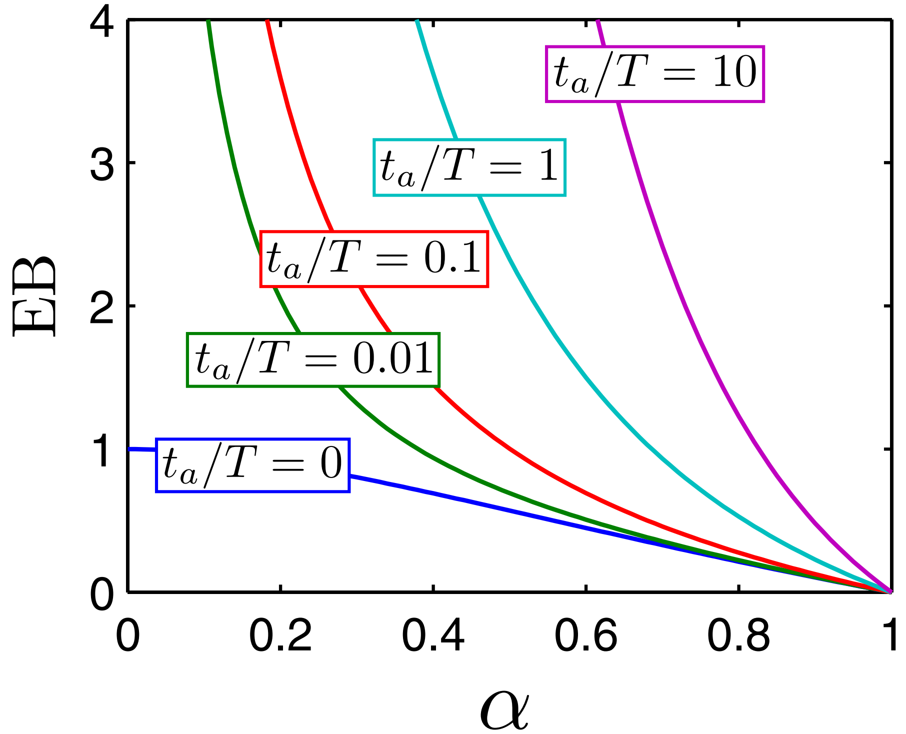
- Population splitting.
- Aging initial conditions in CTRW.
- Noise and EB.

Age and noise matter



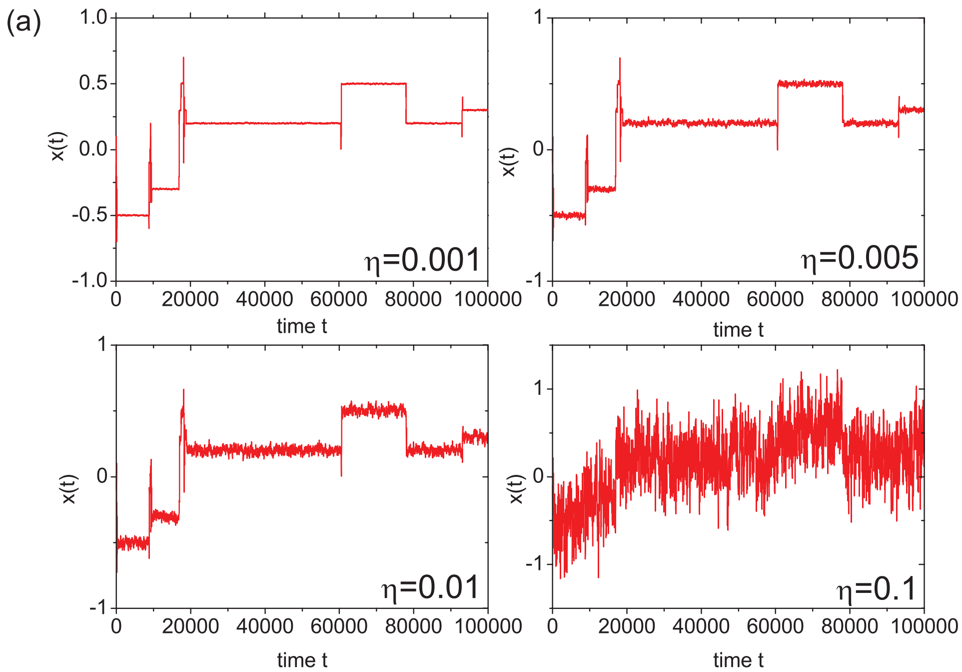
- start at time t_a? Observe population splitting $T << t_a$.
- Add noise? crucial for time averages.

Timing of start of measurement matters



$$EB = 2\alpha \frac{B([1+t_a/T]^{-1}; 1+\alpha, \alpha)}{[1-(1+T/t_a)^{-\alpha}]^2} - 1.$$

For time averages noise matters



$$\langle r^2 \rangle \sim t^{\alpha} + \text{const}$$
$$\langle \overline{\delta^2} \rangle \sim \Delta / t^{1-\alpha} + \text{const}$$

Future work

So far over damped limit, no velocity.

Scale invariant velocity correlation functions $\langle v(t)v(t+\tau)\rangle$ we generalize the Green-Kubo relation (simple).

Let $\langle r^2\rangle \sim t^\alpha$ and $\langle v^2\rangle \sim t^\beta$.

Then $\langle\overline{\delta^2}\rangle \sim t^\beta \Delta^{\alpha-\beta}$.

Aging exponent has a clear physical meaning, but is it physical?

Green-Kubo Relation

- Green-Kubo relation between diffusion constant and velocity correlation function

$$\langle x^2 \rangle = 2Dt$$

$$D = \int_0^\infty d\tau \langle v(t+\tau) v(t) \rangle .$$

- In our case $D \to \infty$ or $D \to 0$.

- What then?

Scaling Green-Kubo relation

- For non stationary processes, exhibiting aging,

$$\langle v(t+\tau)v(t)\rangle = \mathcal{C}t^{\alpha-2}\phi\left(\frac{\tau}{t}\right).$$

- Then $\langle x^2(t)\rangle = 2D_\alpha t^\alpha$ with

$$D_\alpha = \frac{\mathcal{C}}{\alpha}\int_0^\infty ds \frac{\phi(s)}{(1+s)^\alpha}.$$

- This relation is valid for a process starting at $t=0$.
- Applications: blinking quantum dots, atoms in optical lattices, active transport, coupled CTRWs.

Dechant, Lutz, Kessler Barkai **PRX** (2014)

Scaling Green-Kubo for the time average

$$\langle\overline{\delta^2}\rangle \sim \frac{2c_1 C}{(\beta+1)(\alpha-\beta-1)(\alpha-\beta)} t^{\beta}\Delta^{\alpha-\beta}.$$

Here only small argument behavior of the correlation function enters. Unlike the ensemble average.

$$\phi_{EA}\left(\frac{\tau}{t}\right) \sim c_1 \left(\frac{\tau}{t}\right)^{-2+\alpha-\beta}.$$

The measurement of time average MSD does not provide information on the ensemble average diffusion constant D_α (CTRW is an exception!).

Summary

- In disordered system diffusivity remains random and depends on the measurement protocol.

- In equilibrium, for closed system, fluctuations of quenched system far exceed the annealed case.

- Aging effect is experimentally observed, $\overline{\delta^2}$ decreases with measurement time t and increases with lag time Δ.

- For quenched systems the measurement time ageing is replaced with system size reduction of the diffusivity.

Refs. and THANKS

- Popular reviews:
- Barkai, Garini and Metzler *Strange Kinetics of Single Molecules in the Cell* **Physics Today** 65(8), 29 (2012).
- Metzler, Jeon, Cherstvy, and Barkai *Anomalous diffusion models and their properties: non-stationarity, non-ergodicity and ageing at the centenary of single particle tracking* **Physical Chemistry Chemical Physics 16** (44), 24128 - 24164 (2014).
- Theory:
- Akimoto, EB, Saito *Universal Fluctuations of Single-Particle Diffusivity in Quenched Environment* **Phys. Rev. Lett. 117**, 180602 (2016).

More ref.

- J.-H. Jeon, EB, R. Metzler *Noisy continuous time random walks* **The Journal of Chemical Physics 139**, 121916 (2013)

- A. Dechant, E. Lutz, D. Kessler, EB *Scaling Green-Kubo relation and application to three aging systems*. **Physical Review X 4**, 011022 (2014).

- P. Meyer, EB, and H. Kantz *Scale invariant Green-Kubo relation for time averaged diffusivity* arXiv:1708.09634 [cond-mat.stat-mech]

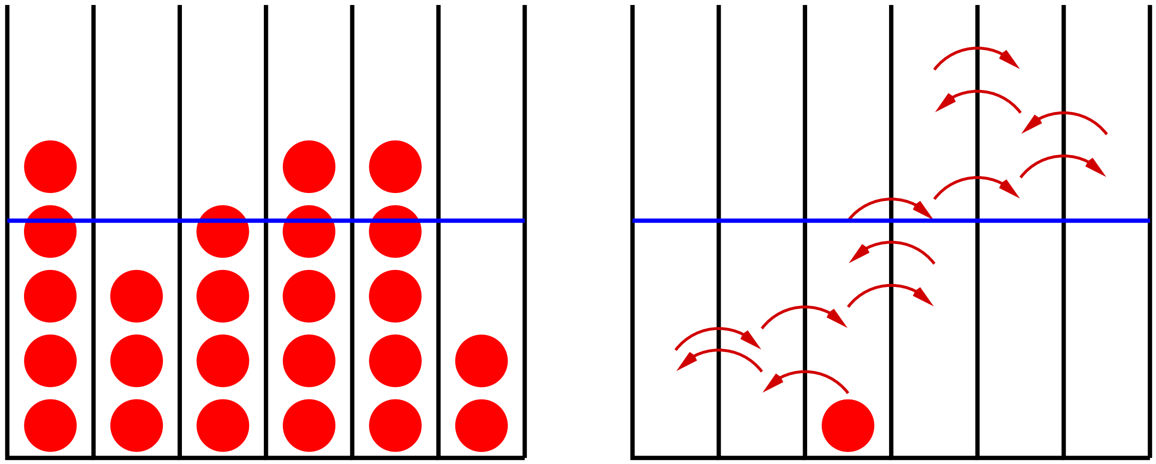
More ref.

- Experiments:

- Bronstein, Israel, Kepten, Mai, Shav-Tal, Barkai, Garini *Transient Anomalous Diffusion of Telomeres in the Nucleus of Mammalian Cells* **Phys. Rev. Lett. 103**, 018102 (2009).

- Jeon, Tejedor, Burov, Barkai, Selhuber-Unkel, Berg-Sorensen, Oddershede, and Metzler *In vivo anomalous diffusion and weak ergodicity breaking of lipid granules* **Phys. Rev. Lett. 106**, 048103 (2011).

Ergodicity in equilibrium



$$\langle \mathcal{O} \rangle = \int \mathcal{O}(x)\mu(dx) \equiv \overline{\mathcal{O}} = \lim_{t\to\infty} \frac{1}{t}\int_0^t \mathcal{O}(t')dt'$$

For example $\overline{x} = \langle x \rangle$.

Weak Ergodicity Breaking in CTRW

$$\overline{\mathcal{O}} = \sum_x \overline{p}_x \mathcal{O}_x$$

$\overline{p}_x = t_x/t$ the occupation fraction

$\mathcal{O}_x$ value of the observable in state x.

ergodicity $\overline{p}_x \to P_x^{eq}$.

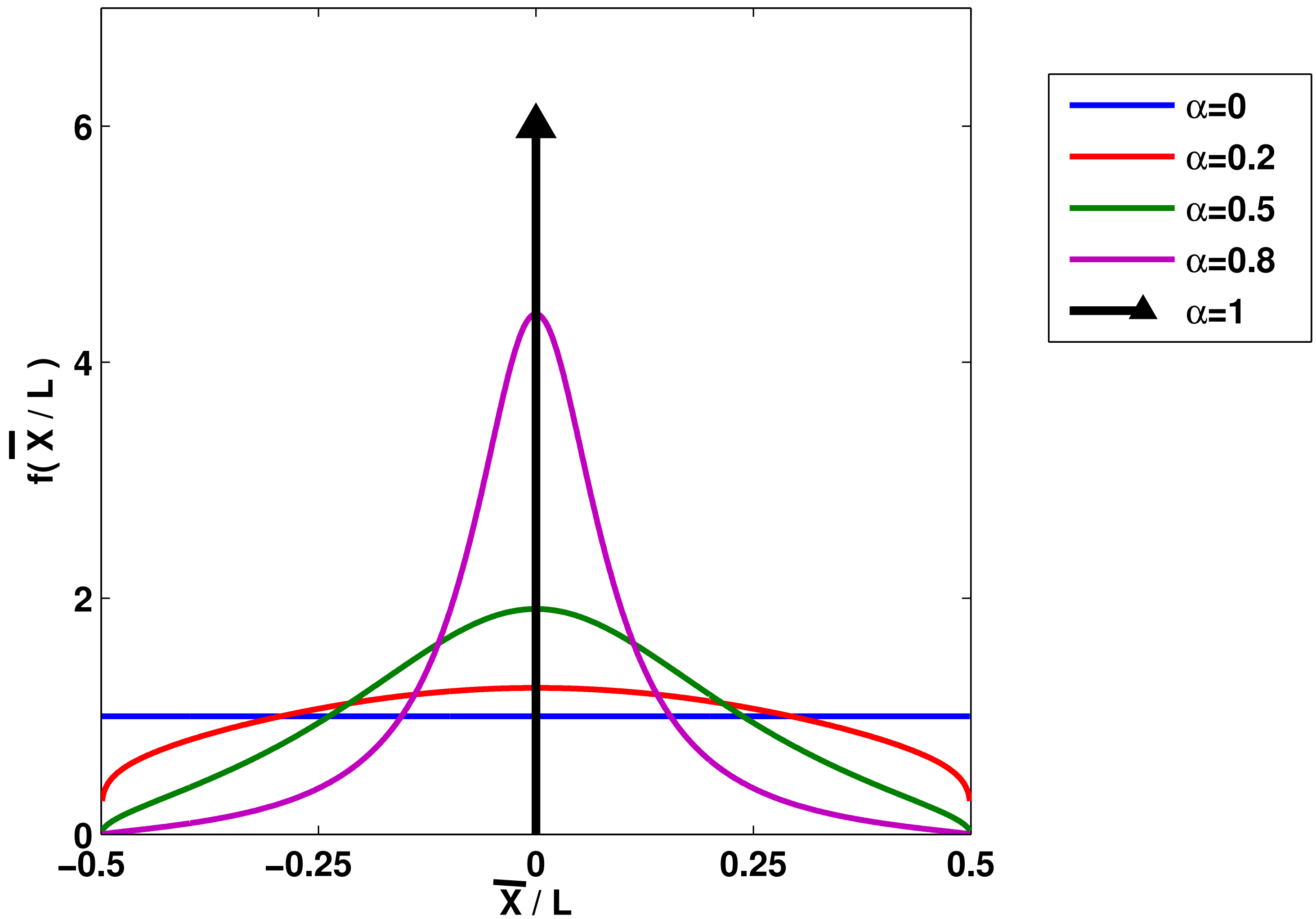
$$f_\alpha\left(\overline{\mathcal{O}}\right) = -\frac{1}{\pi}\lim_{\epsilon\to 0} \text{Im} \frac{\sum_{x=1}^{L} P_x^{eq}\left(\overline{\mathcal{O}} - \mathcal{O}_x + i\epsilon\right)^{\alpha-1}}{\sum_{x=1}^{L} P_x^{eq}\left(\overline{\mathcal{O}} - \mathcal{O}_x + i\epsilon\right)^{\alpha}}.$$

Ergodicity if $\alpha \to 1$

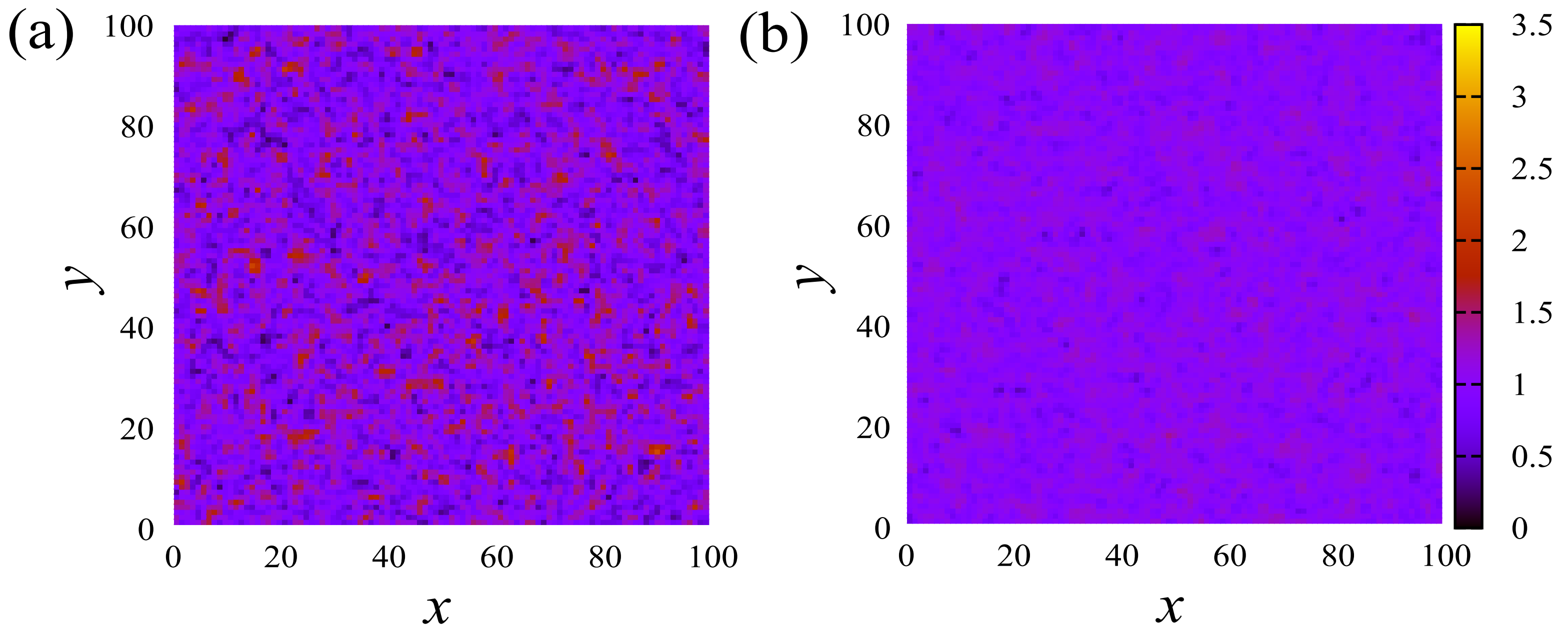
$$f_{\alpha=1}\left(\overline{\mathcal{O}}\right) = \delta\left(\overline{\mathcal{O}} - \langle\mathcal{O}\rangle\right).$$

Rebenshtok, Barkai **PRL 99 210601 (2007)**

PDF of $\overline{X}$ UNBIASED CTRW



Diffusion maps



Fractional Fokker Planck vs Fractional Brownian Motio

- Fractional Fokker Planck Equation (non-ergodic, non stationary)

$$\frac{\partial^\alpha}{\partial t^\alpha} P(x,t) = L_{fp} P(x,t)$$

Physical picture: trap model, CTRW.

- Fractional Langevin equation (ergodic, stationary)

$$m\ddot{x} + m\gamma_a \frac{\partial^{\alpha-1}}{\partial t^{\alpha-1}} \dot{x}(t) + U'(x) = F_{noise}(t)$$

Physical picture: single file diffusion, certain polymer models.

- Deng, Barkai **PRE 79** 011112 (2009).
- Metzler, Barkai, Klafter **PRL** *82*, 3563 (1999).

And what about active super diffusion?

- Certain active processes in cell exhibit super diffusion $\overline{\delta^2} \sim \Delta^{\xi}$ and $\xi > 1$.
- Lévy walks and fractional Brownian motions are models of such behaviour.
- The time average MSD remains random when average sojourn time diverges. Froemberg EB **PRE** 87 030104(R) (2013).