

Measures for diffusion, ergodicity, & ageing

Ralf Metzler, U Potsdam & Wrocław U Science & Technology

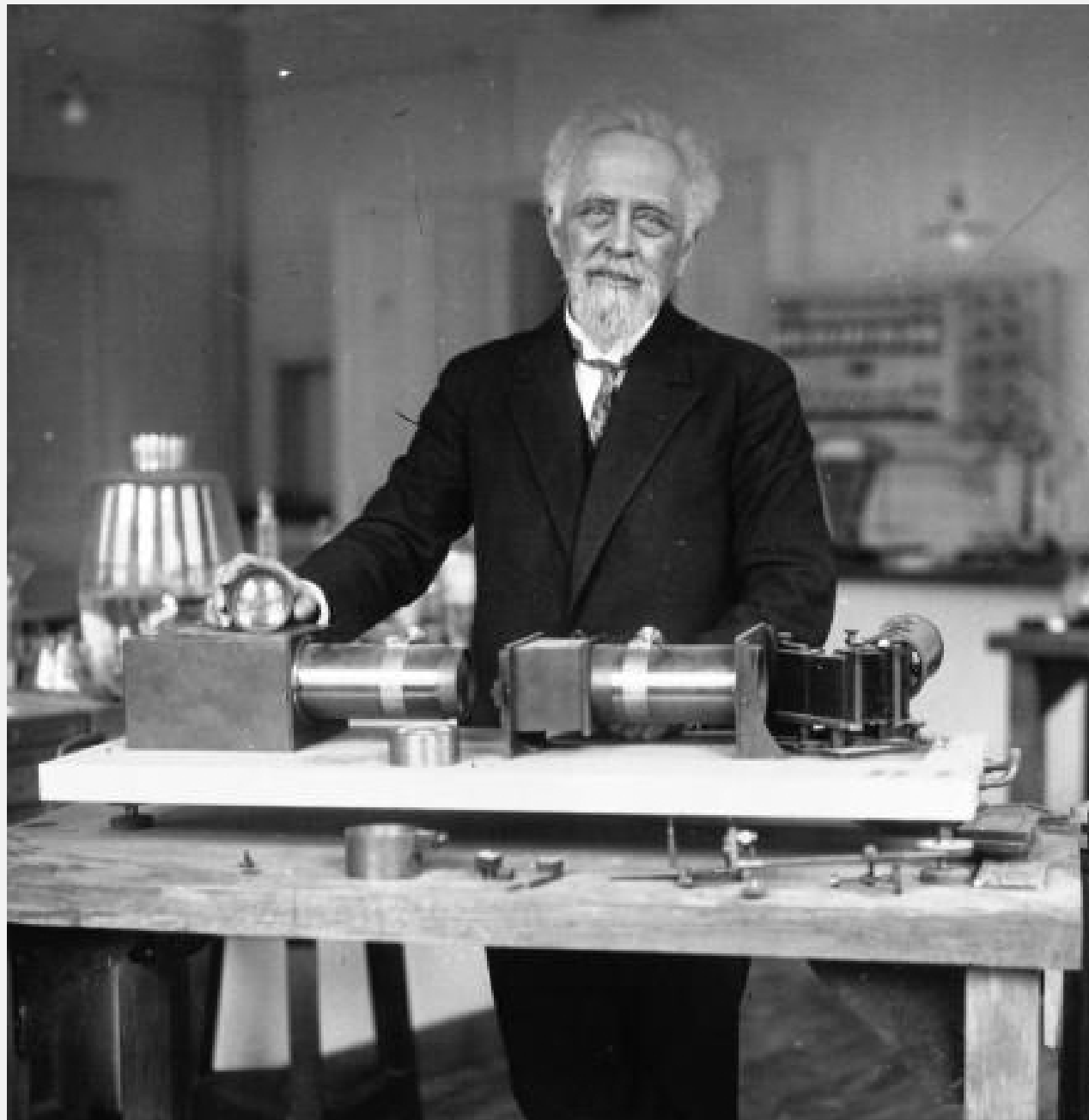
— UP Golm, 1st June 2018 —

Microscopical observations

on the particles contained in the pollen of plants; and on the general existence of active molecules in organic and inorganic bodies

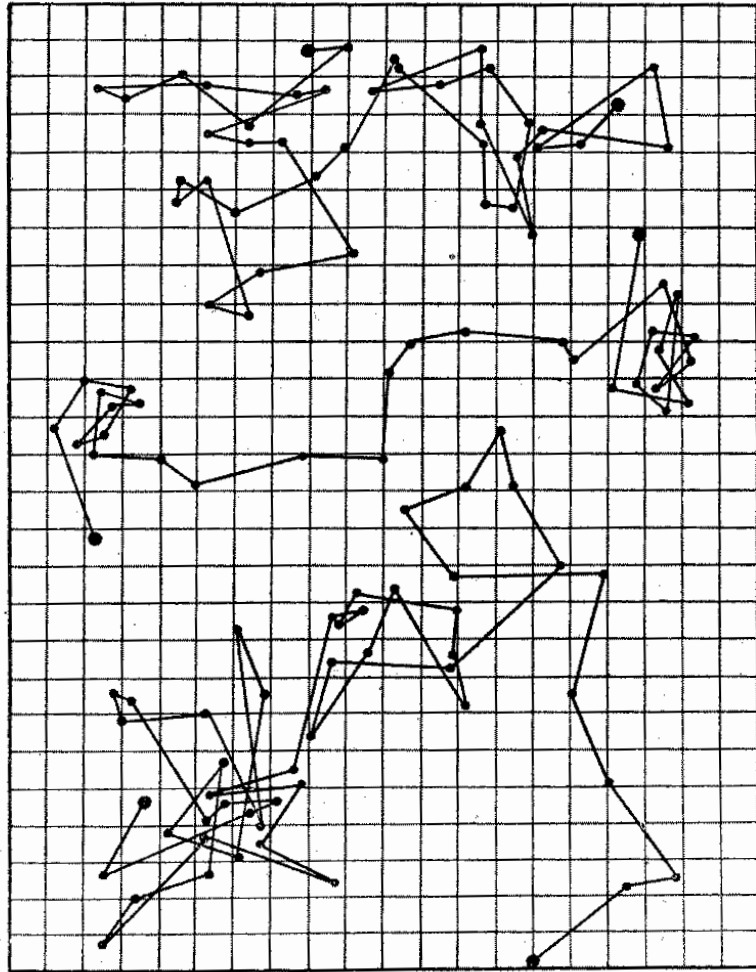
Rocks of all ages, including those in which organic remains have never been found, yielded the molecules in abundance. Their existence was ascertained in each of the constituent molecules of granite, a fragment of the Sphinx being one of the specimens examined.





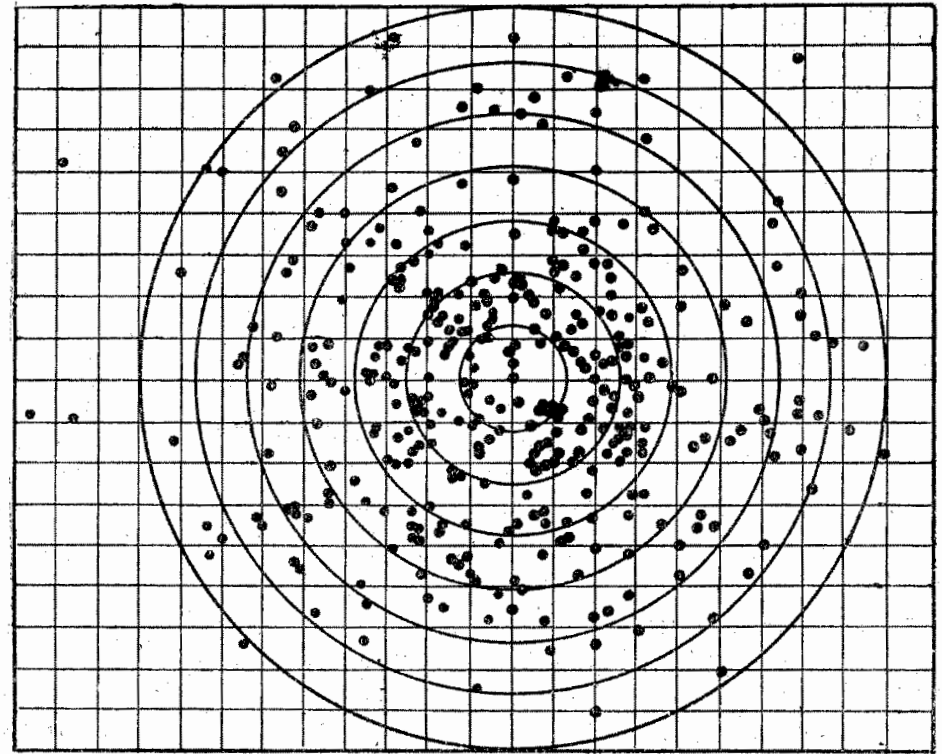
Brownian motion

Fig. 6.



$\Delta t = 30 \text{ sec}$

Fig. 7.

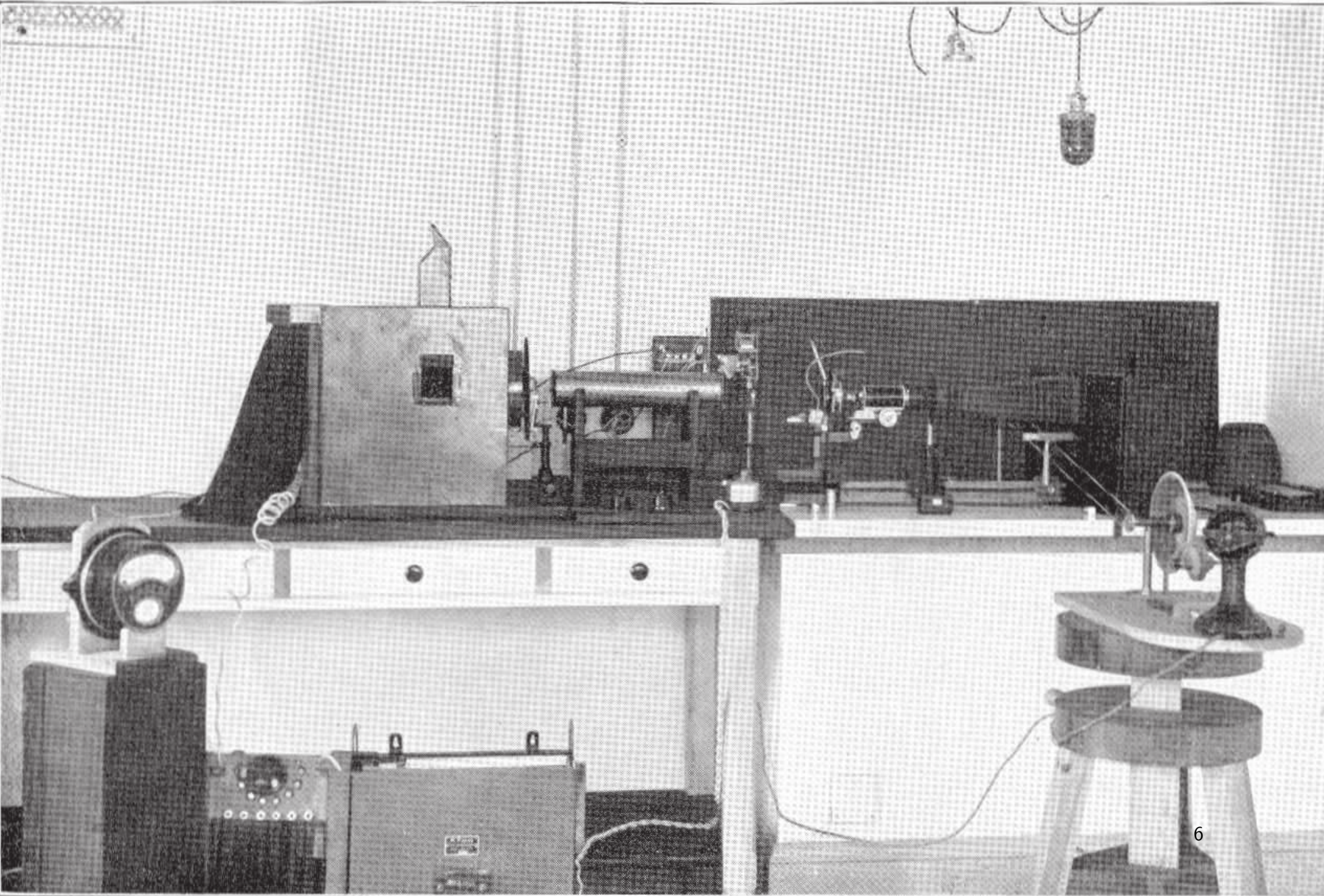


$$P(\mathbf{r}, \Delta t) = \frac{1}{(4\pi K \Delta t)^{d/2}} \exp\left(-\frac{r^2}{4K \Delta t}\right)$$

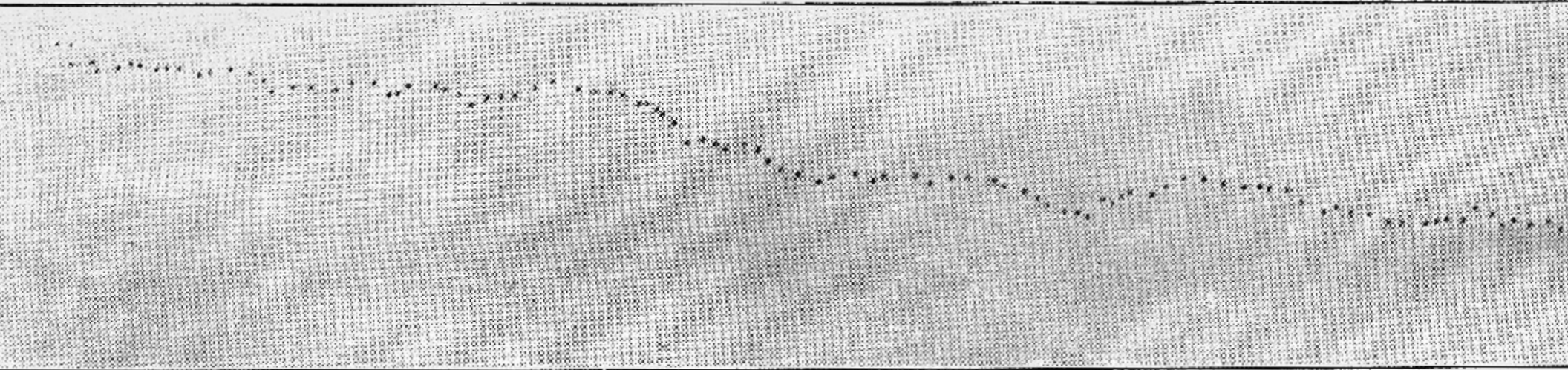
Einstein-Smoluchowski relation:

$$K = \frac{k_B T}{m \eta} = \frac{(R/N_A) T}{m \eta}$$

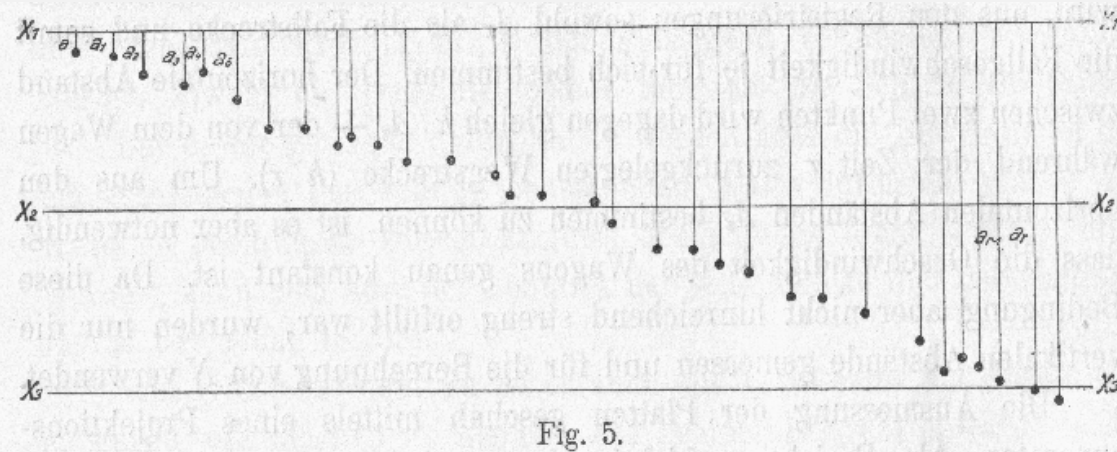




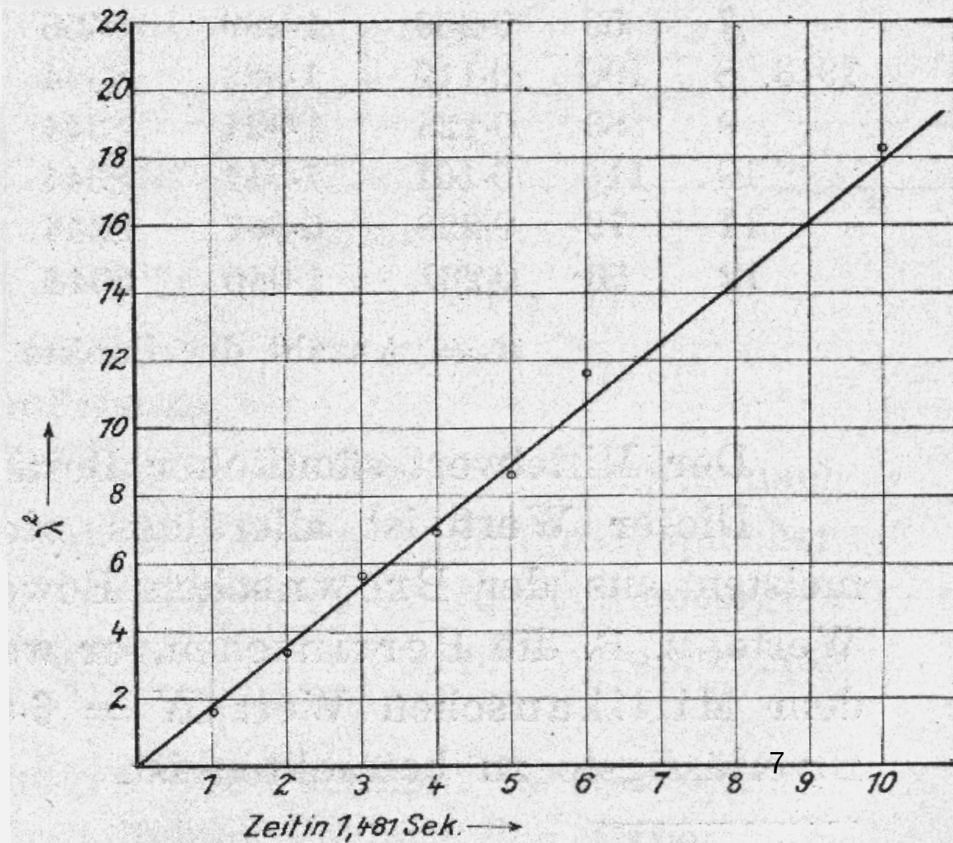
Ivar Nordlund: 100+ years of SPT with time series analysis



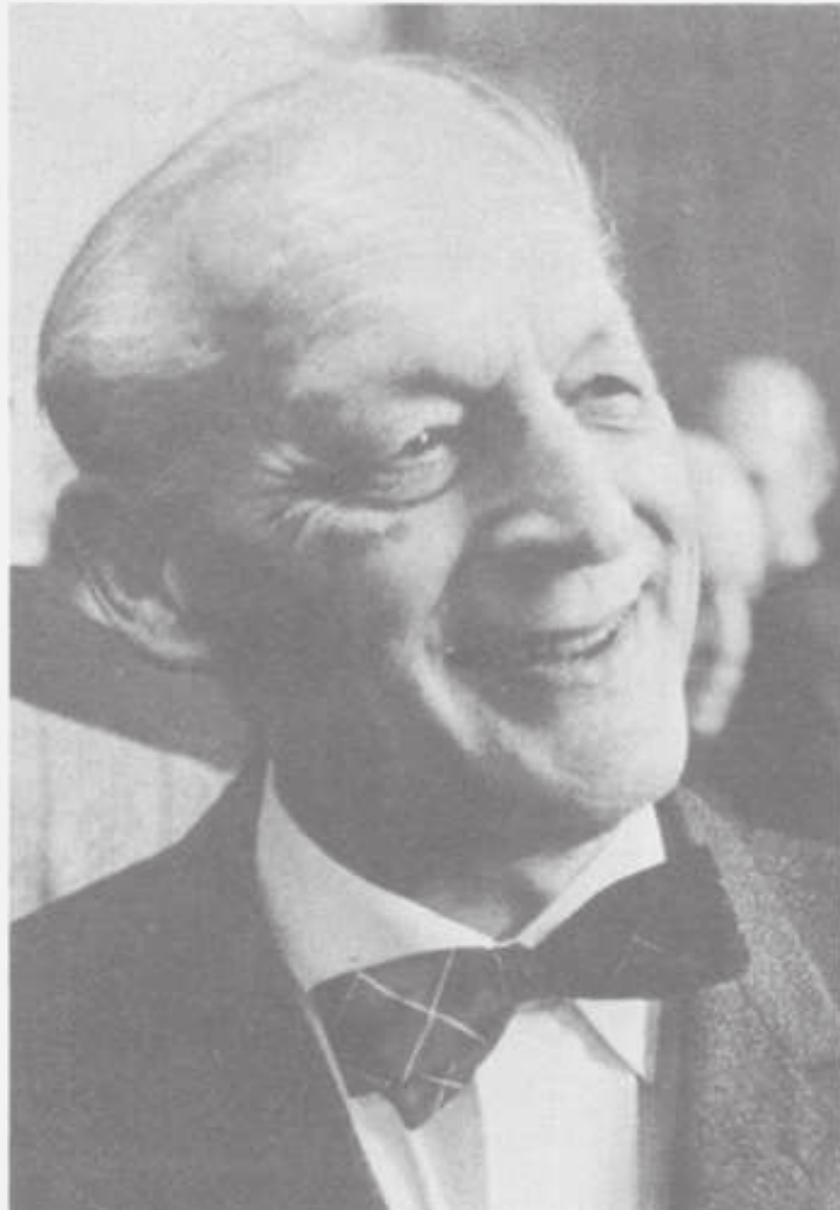
Mercury droplet in aqueous solution



I Nordlund, Z Physik (1914): $N_A = 5.91 \times 10^{23}$

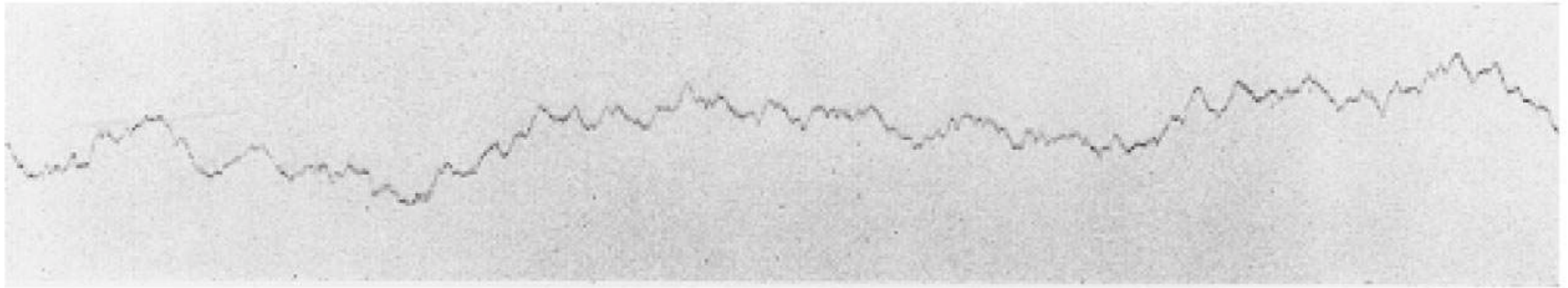


Eugen Kappler: ultimate diffusion measurements



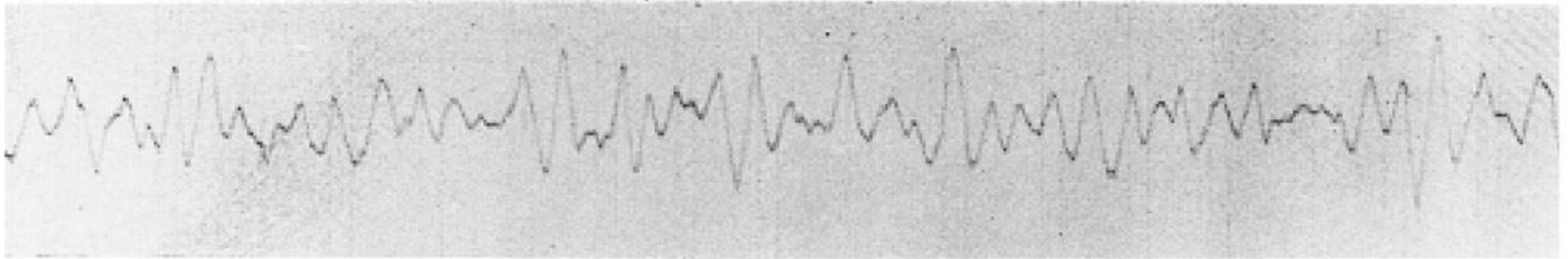
Obituary by L Reimer, Physikalische Blätter Feb 1978 pp 86

Eugen Kappler: ultimate diffusion measurements



Registrieraufnahme der Brownschen Bewegung (natürliche Größe).
Direktionskraft $9,428 \cdot 10^{-9}$ abs. Einh. Trägheitsmoment: $1 \cdot 10^{-7}$ abs. Einh. Abstand Spiegel-Kamera: 72,1 cm.
Zeitmarke: 30 sec $dx = 1$ mm. a) Atmosphärendruck. Temperatur 13° C

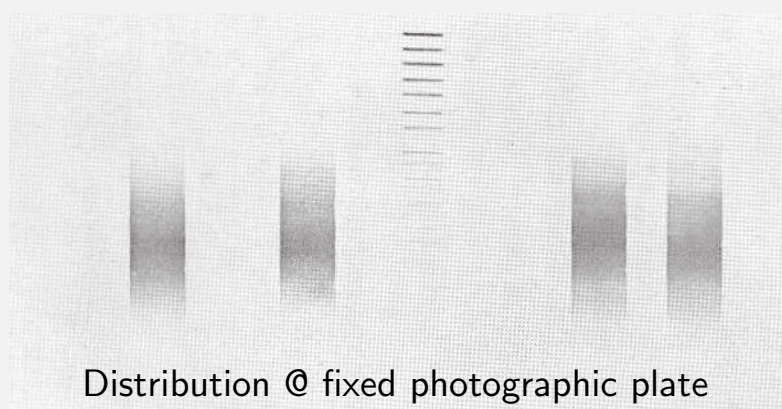
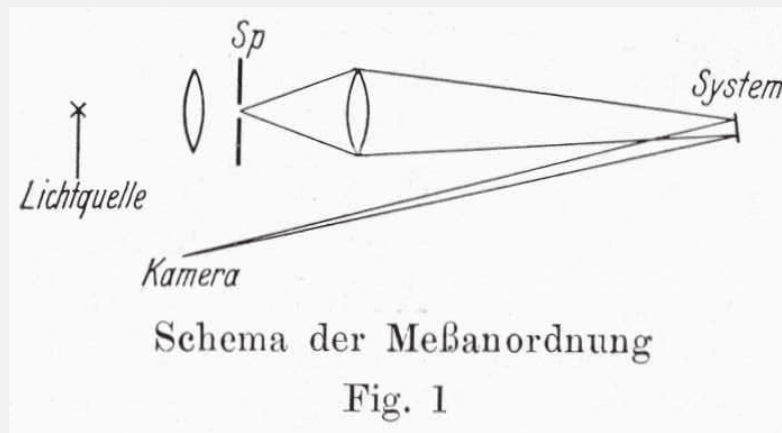
Fig. 5a



Registrieraufnahme der Brownschen Bewegung (natürliche Größe).
Direktionskraft $9,428 \cdot 10^{-9}$ abs. Einh. Trägheitsmoment $1 \cdot 10^{-7}$ abs. Einh. Abstand Spiegel-Kamera: 72,1 cm.
Zeitmarke: 30 sec $dx = 1$ mm. b) $1 \cdot 10^{-3}$ mm Hg. Temperatur 13° C

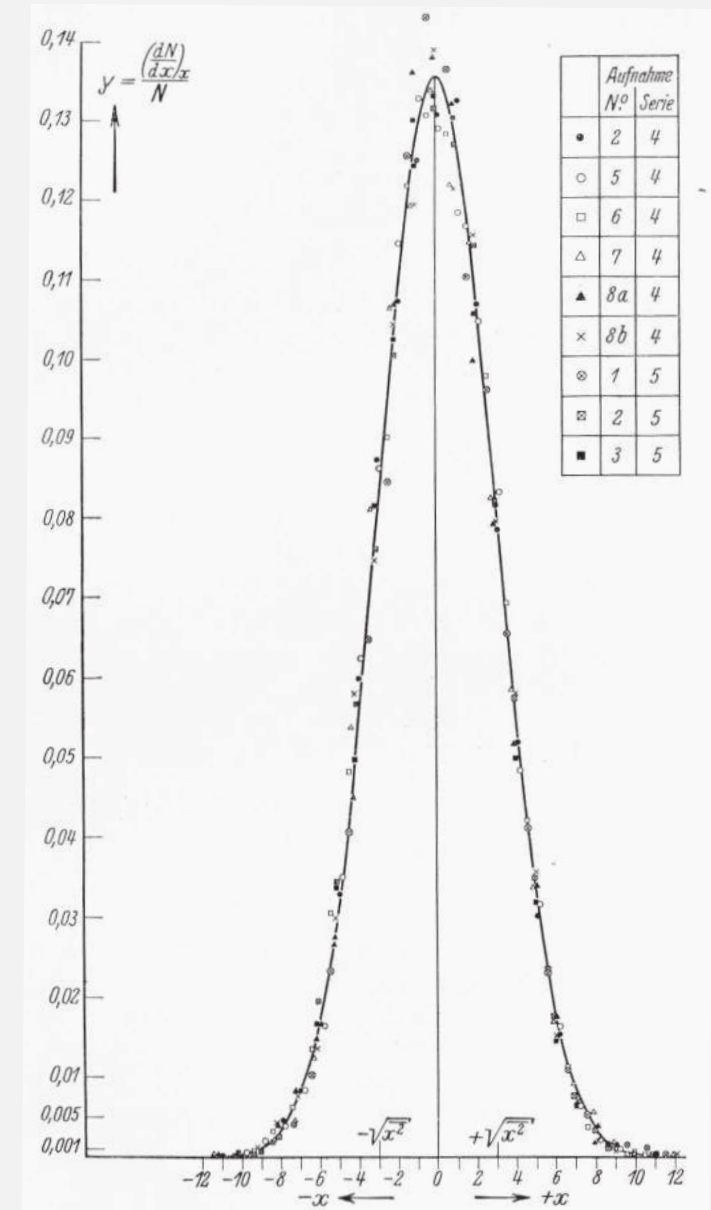
Fig. 5b

Brownian motion & Kappler's diffusion measurements



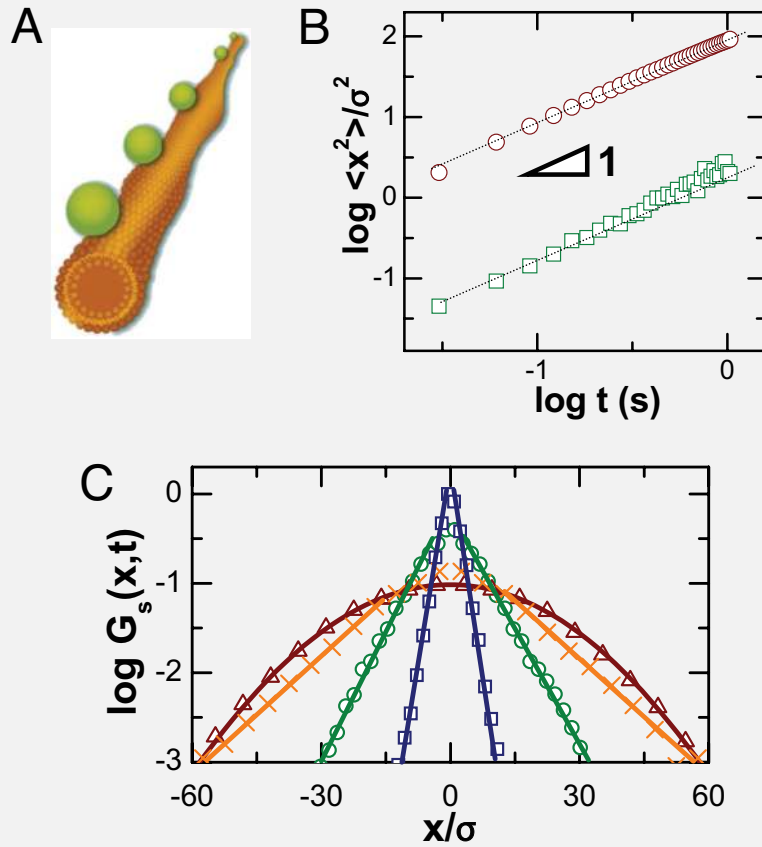
$$\langle r^2(t) \rangle = 2dKt$$

$$P(r, t) = (4\pi Kt)^{-d/2} \exp(-r^2/[4Kt])$$

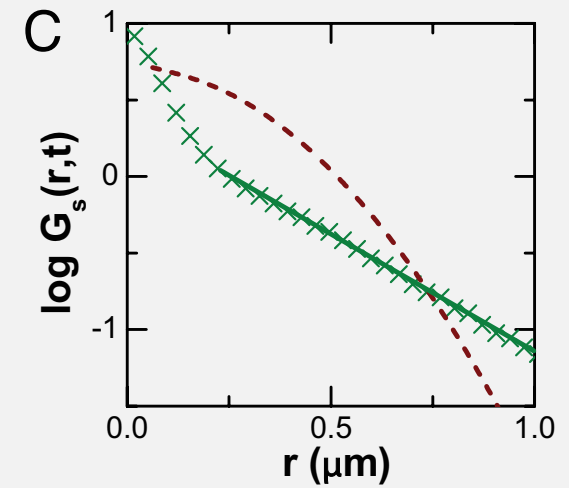
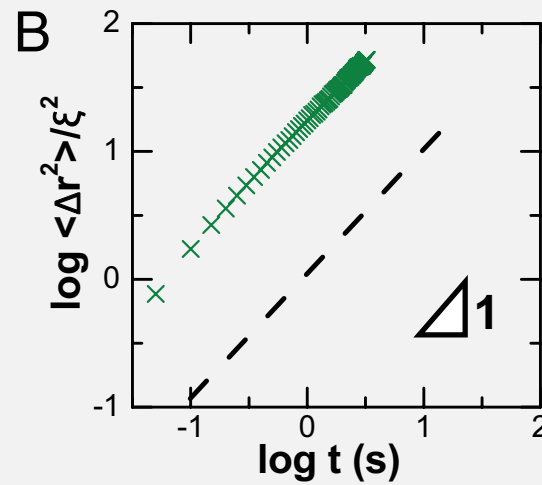
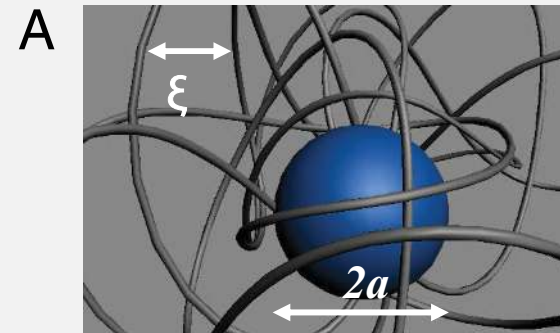


E Kappler, Ann d Physik (1931): $N_A = 60.59 \times 10^{22} \pm 1\%$

When Brownian diffusion is not Gaussian

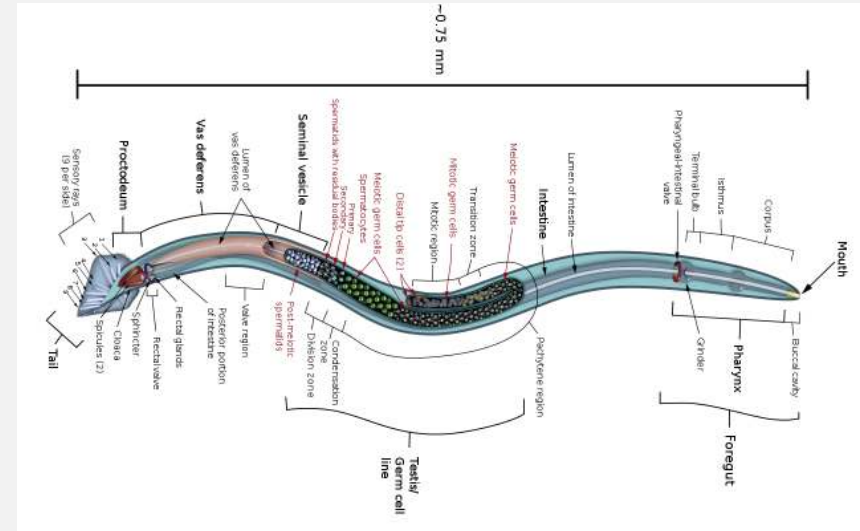
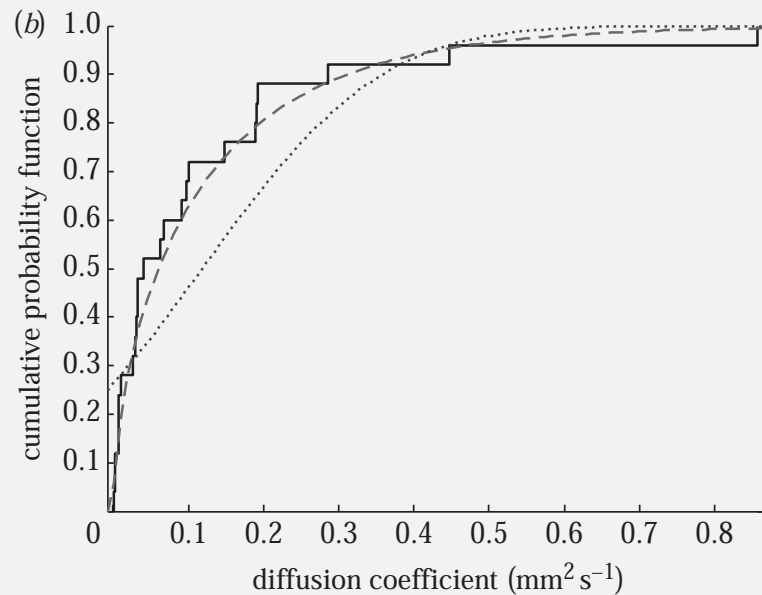
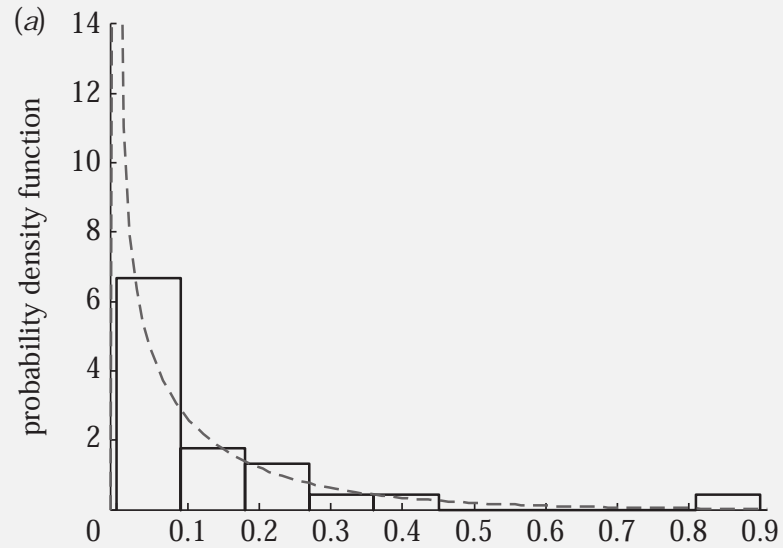


Colloidal beads diffusing on nanotubes



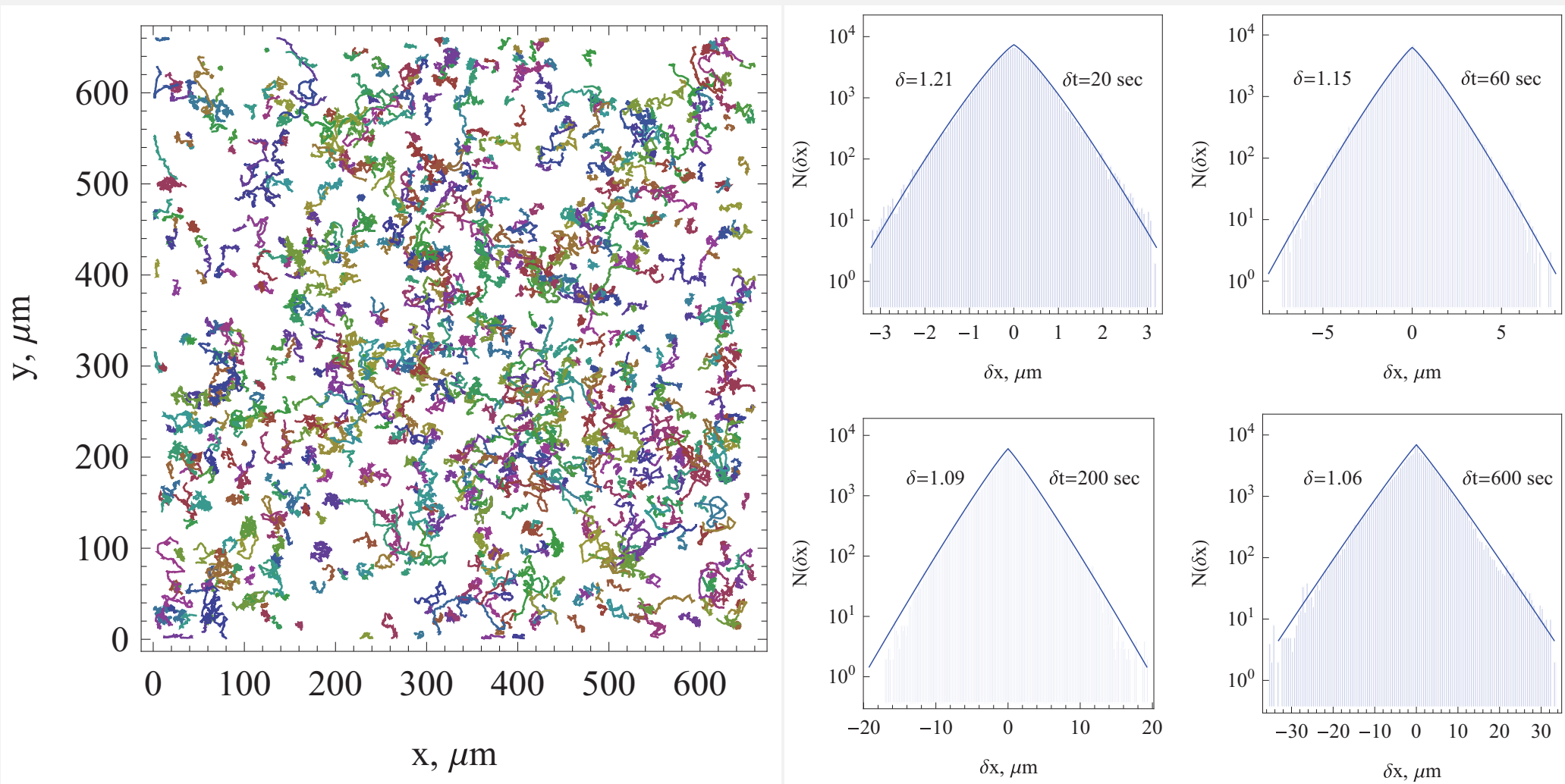
Nanospheres diffusing in entangled actin

Heterogeneous diffusion in population of nematodes

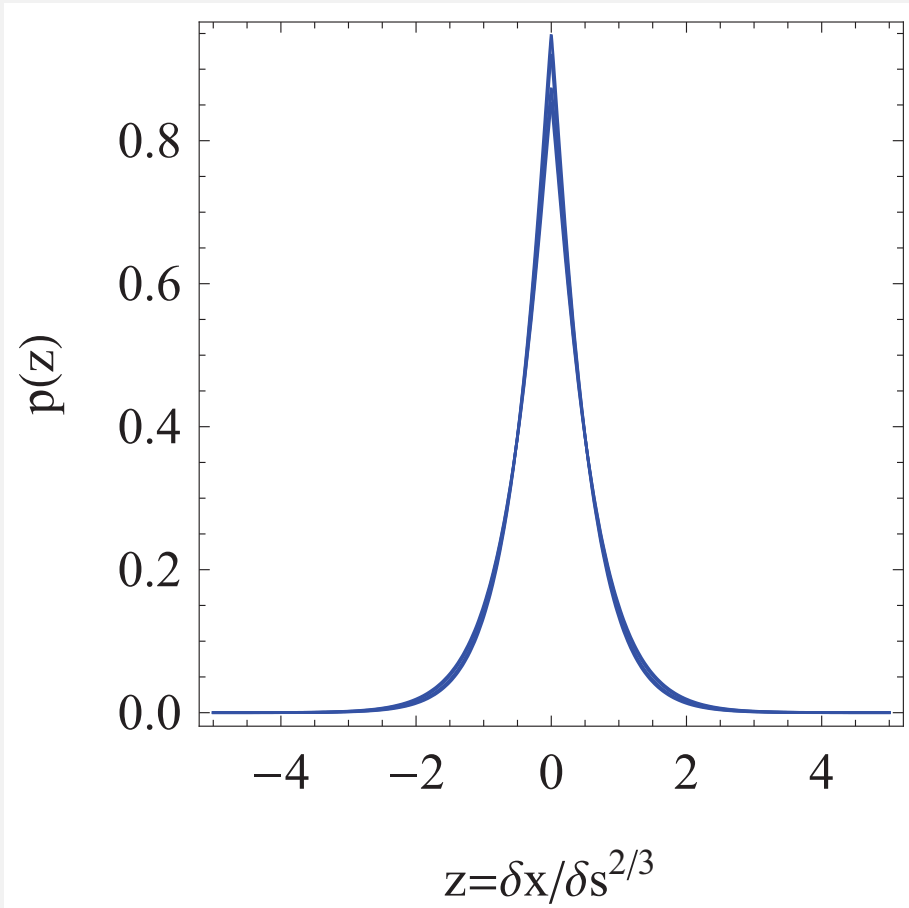
Male *C. elegans* nematode

Soybean cyst nematode & egg

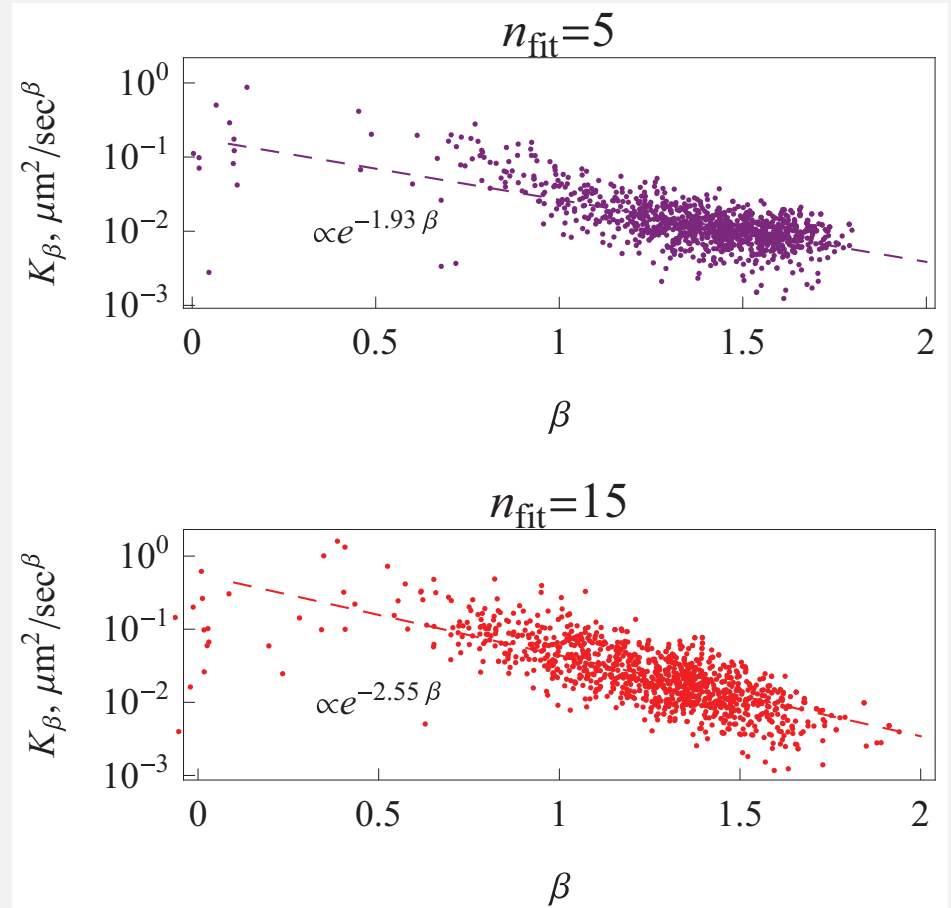
Non-Gaussian diffusion of Dictyostelium cells



Non-Gaussian diffusion of Dictyostelium cells



Similarity function



$$K_\beta \simeq \exp(-c_1\beta + c_2)$$

Fickian, non-Gaussian diffusion with diffusing diffusivity

B Wang, J Kuo, SC Bae & S Granick, Nat Mat (2012): $\langle x^2(t) \rangle = 2K_1 t$, yet $P(x, t)$ non-Gaussian. Superstatistical approach $P(x, t) = \int_0^\infty G(x, t) p(D) dD$

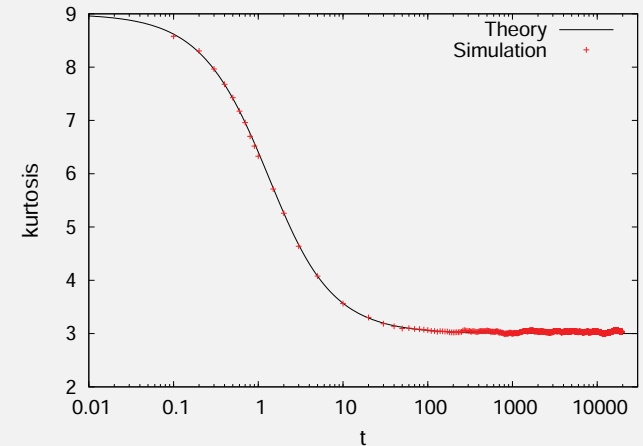
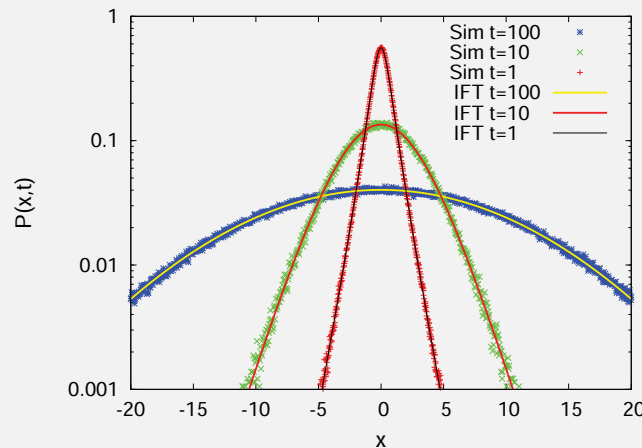
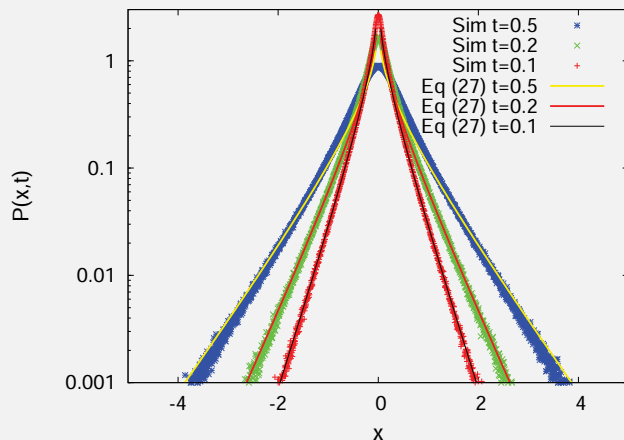
MV Chubinsky & G Slater, PRL (2014); R Jain & KL Sebastian, JPC B (2016): diffusing diffusivity

Our minimal model for diffusing diffusivity:

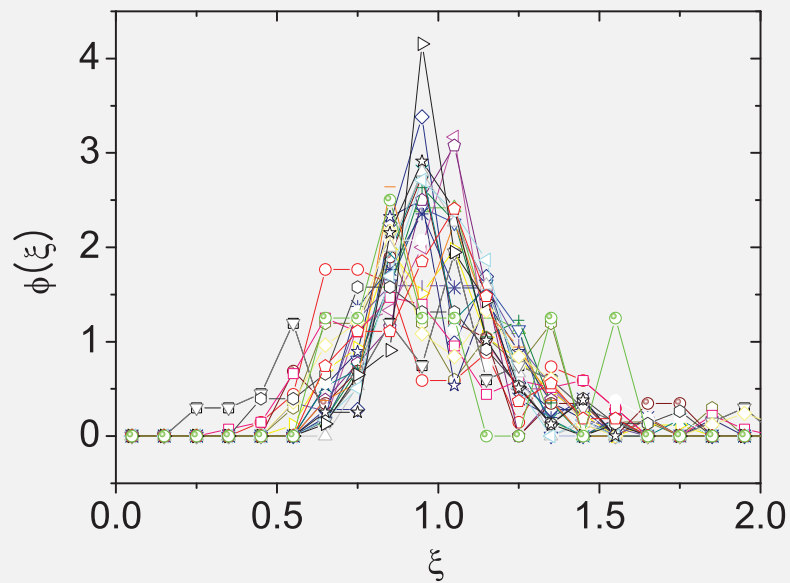
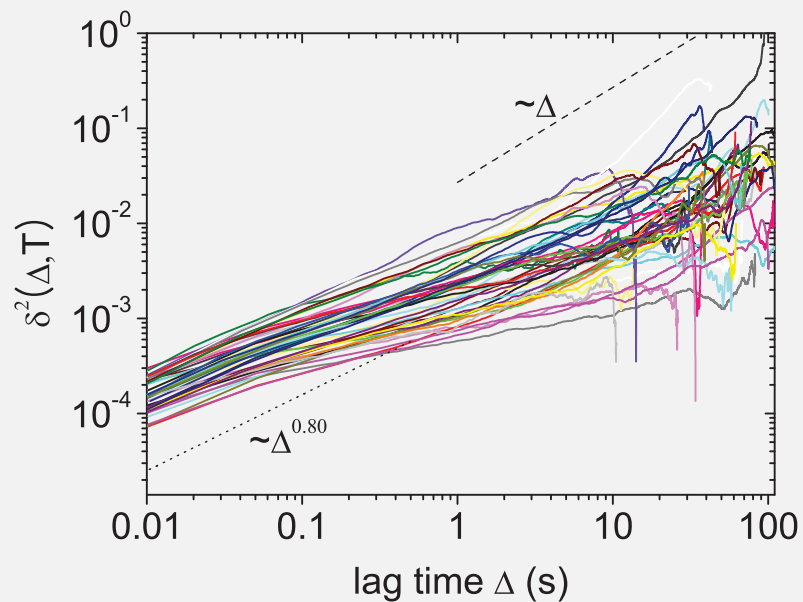
$$\dot{x}(t) = \sqrt{2D(t)}\xi(t)$$

$$D(t) = y^2(t)$$

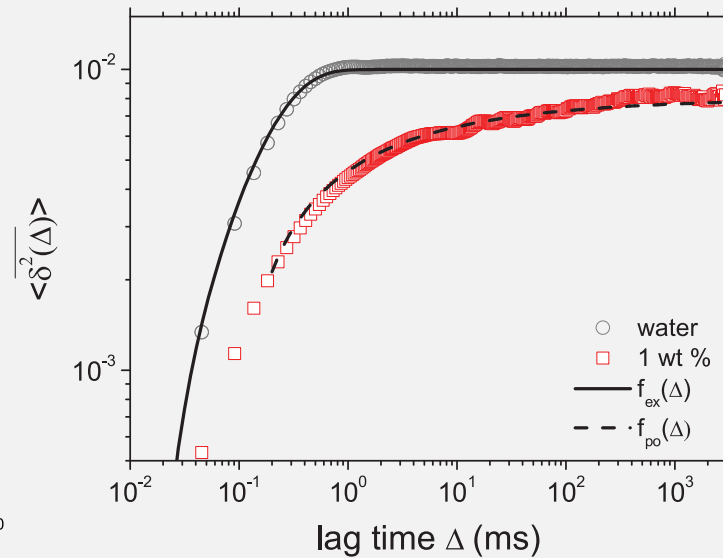
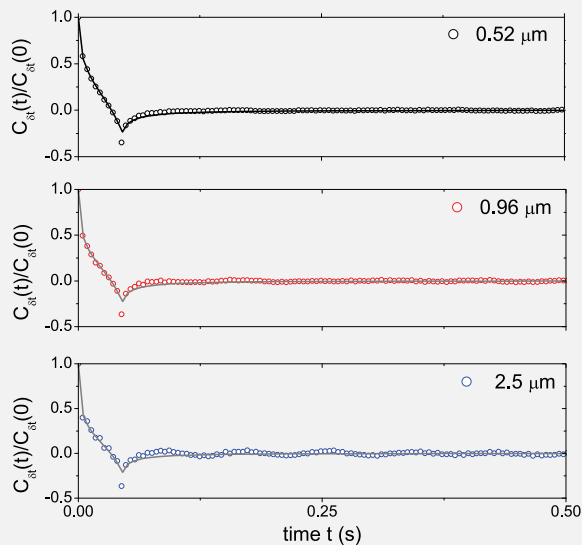
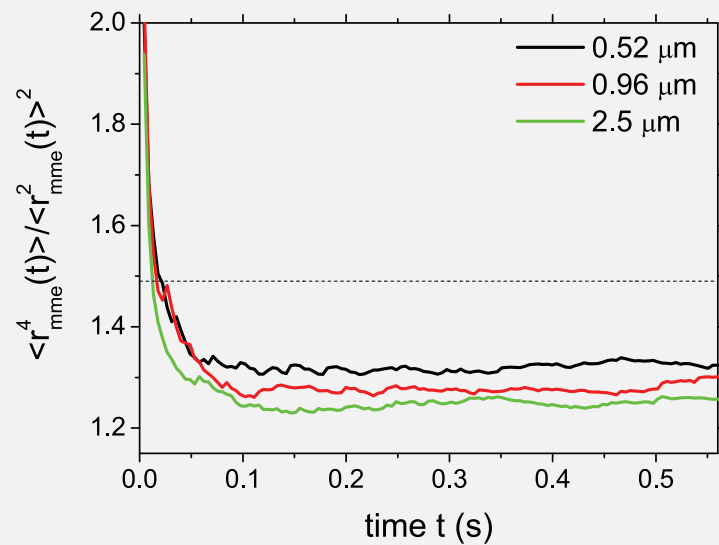
$$\dot{y}(t) = -\tau^{-1}y + \sigma\eta(t)$$



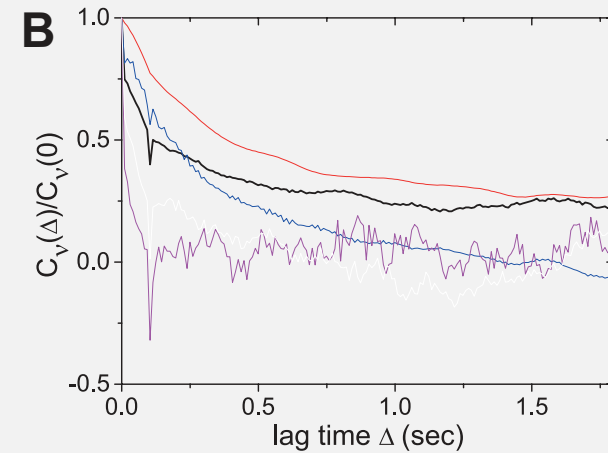
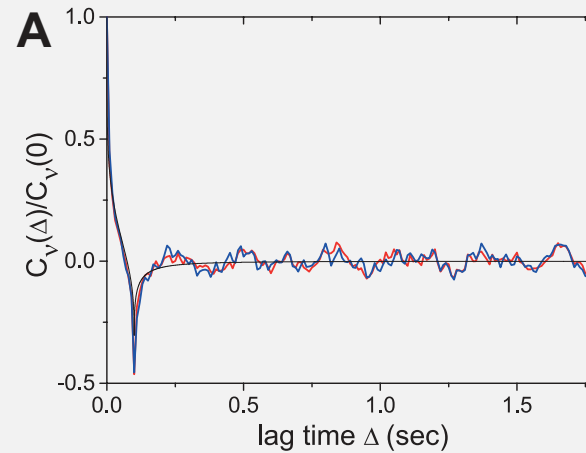
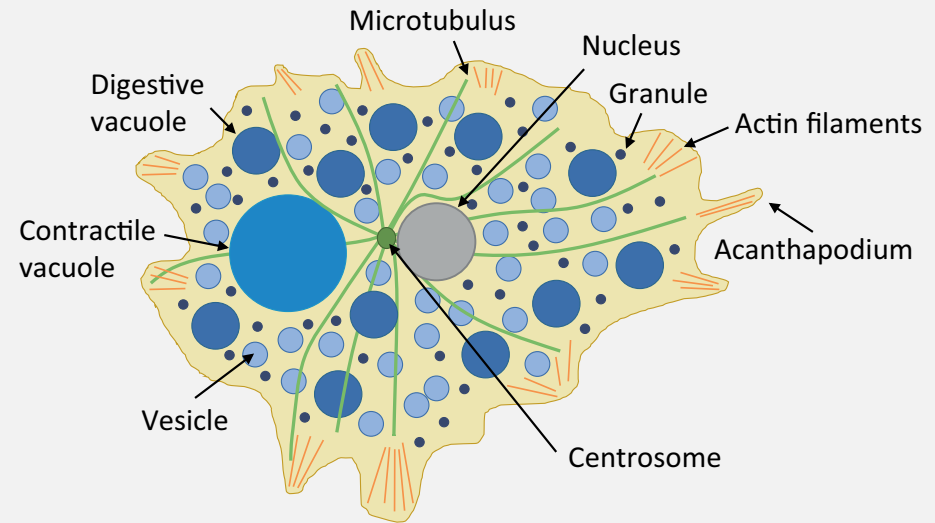
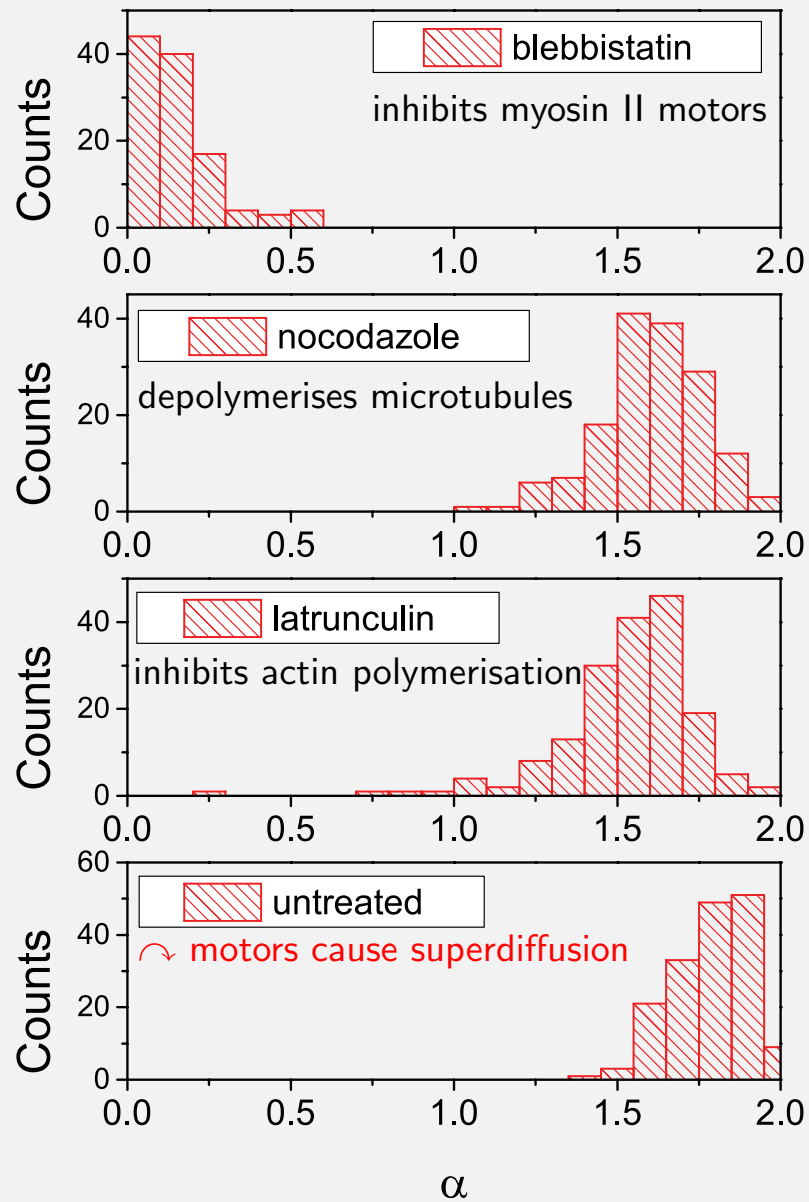
Passive motion of submicron tracers in cells is viscoelastic



Tracer beads in wormlike micellar solution $\downarrow$
Lipid granules in living yeast cells $\downarrow$

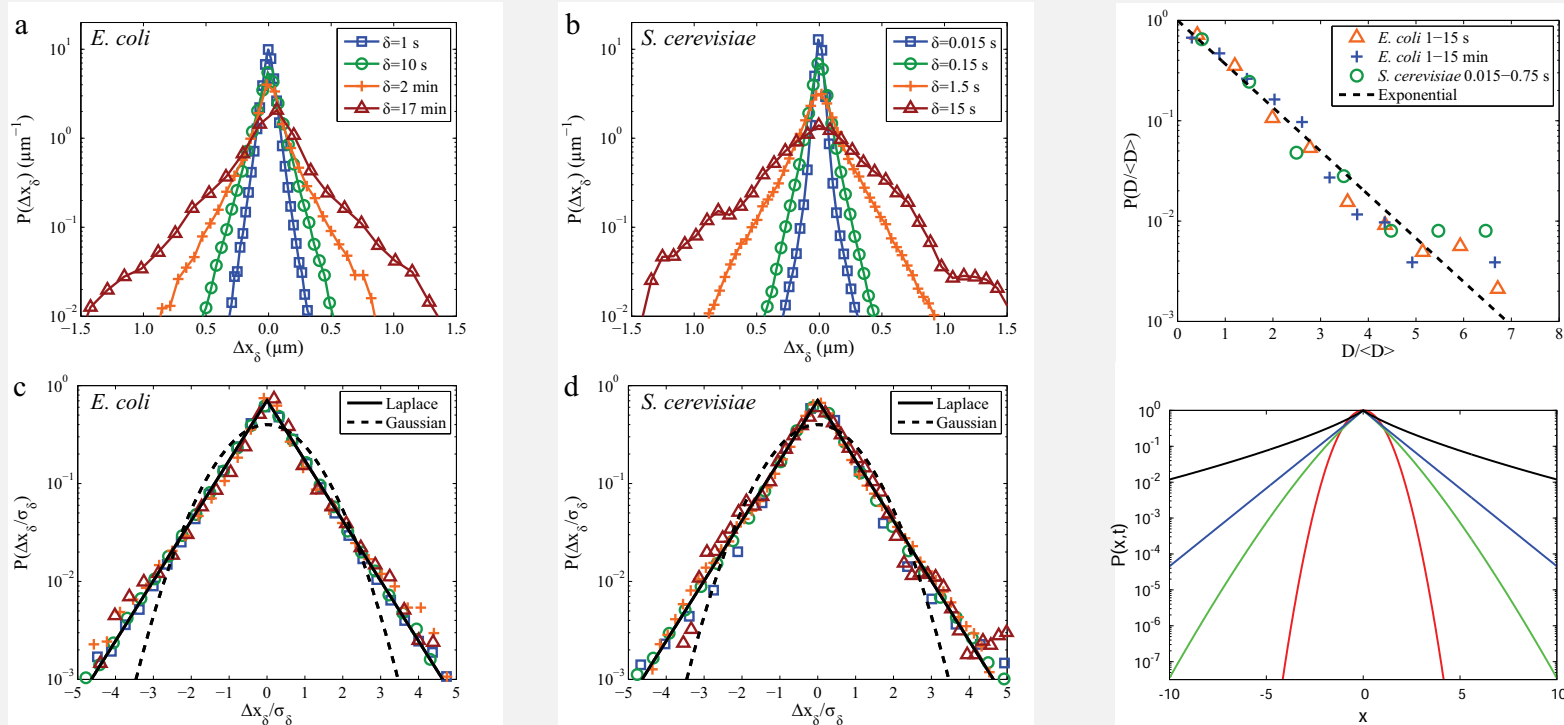


Superdiffusion in supercrowded *Acanthamoeba castellani*



Non-Gaussian diffusion in viscoelastic systems

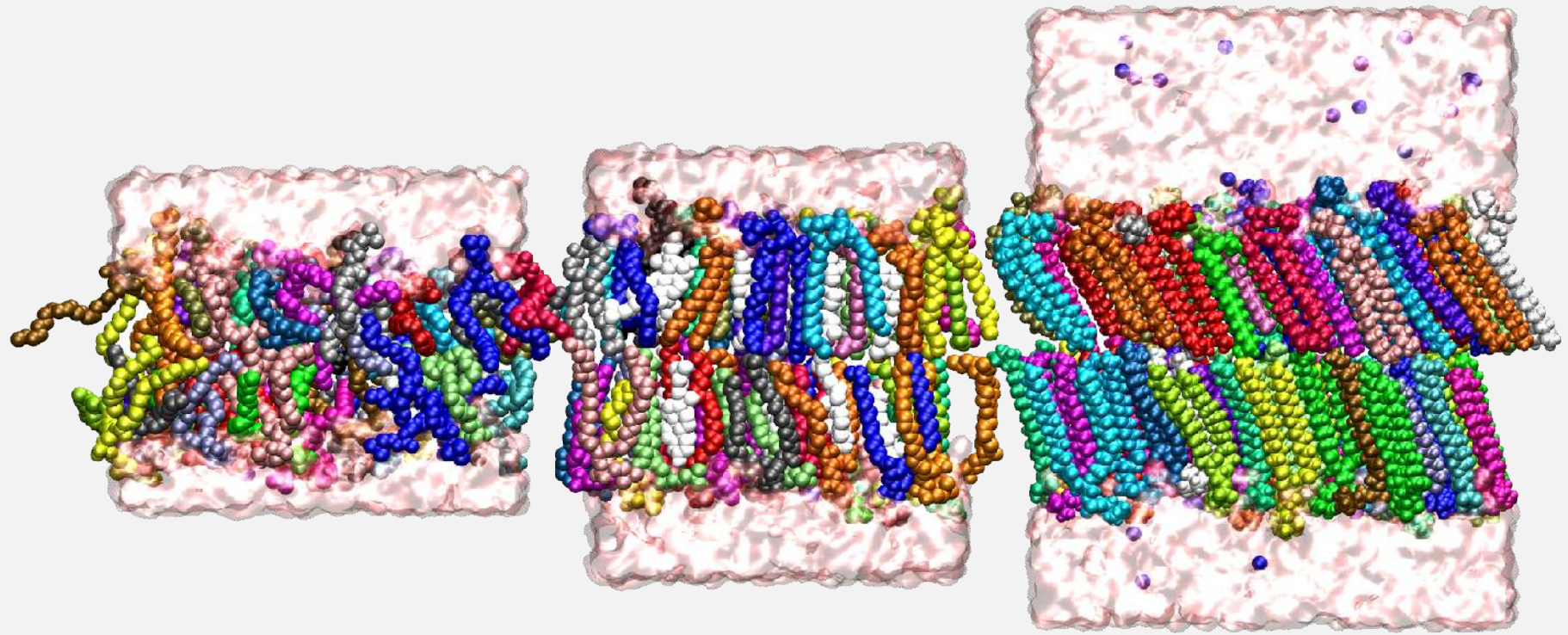
So far consensus: submicron tracer motion in cytoplasm is FBM-like, i.e., Gaussian RNA-protein particles in *E.coli* & *S.cerevisiae* perform exponential anomalous diffusion:



Modelling based on grey GLE: J Ślęzak, RM & M Magdziarz, NJP (2018)

TJ Lampo, S Stylianidou, MP Backlund, PA Wiggins & AJ Spakowitz, BPJ (2017); N&V: RM, BPJ (2017)

Single lipid motion in bilayer membrane MD simulations

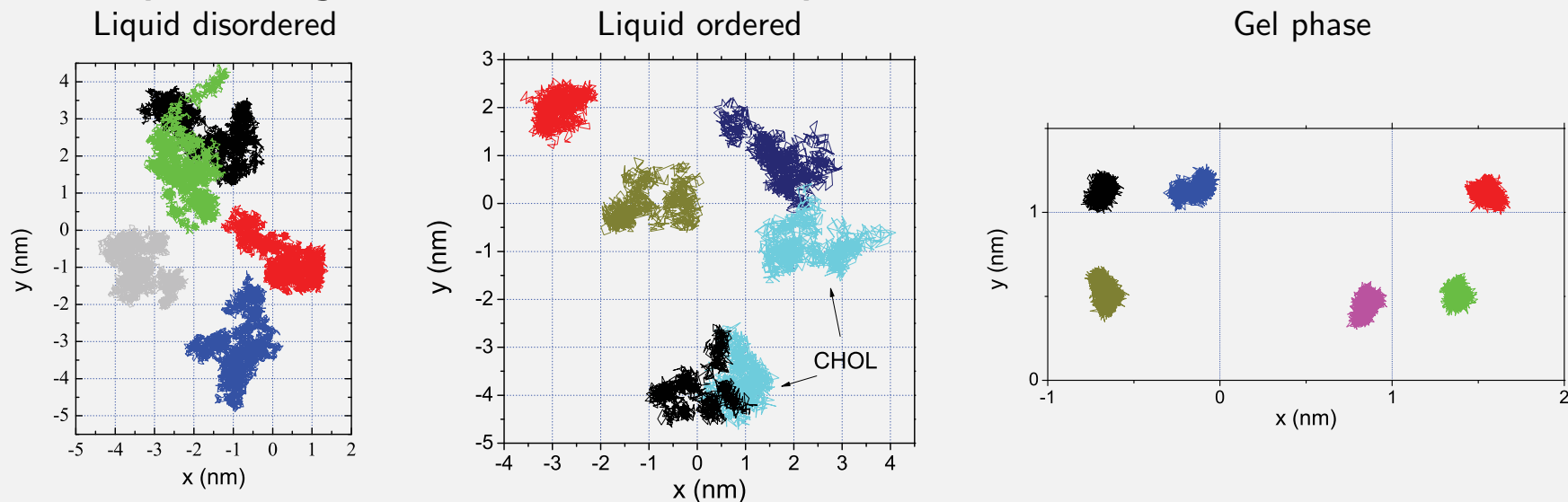


Liquid disordered

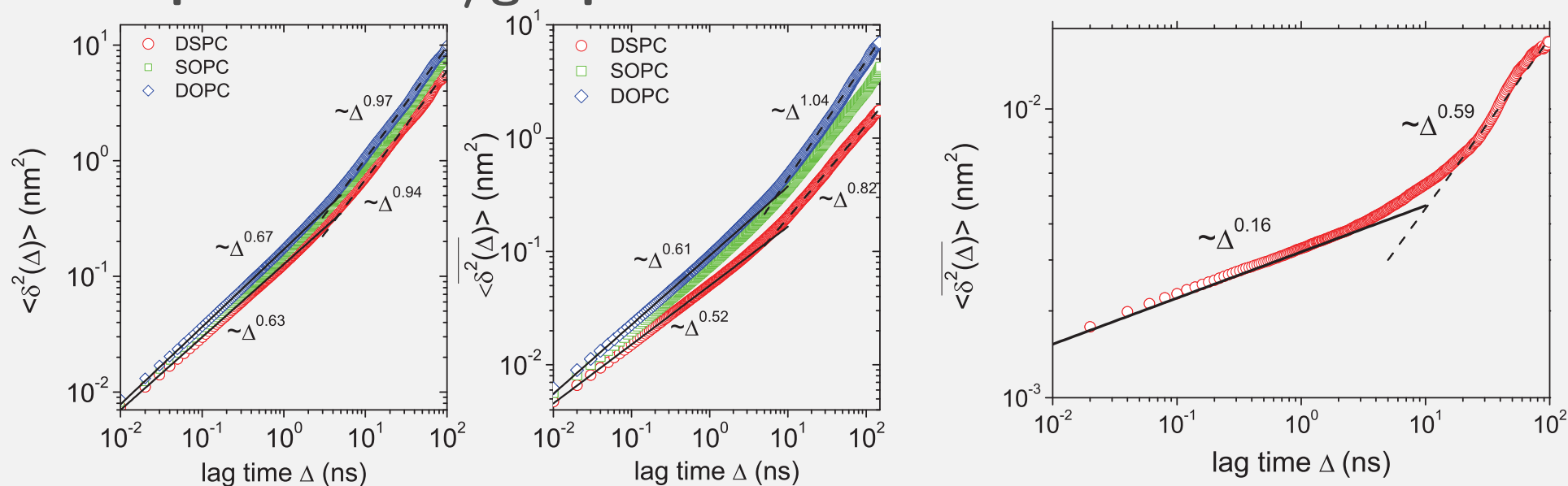
Liquid ordered

Gel phase

Sample trajectories for the lipid & cholesterol motion



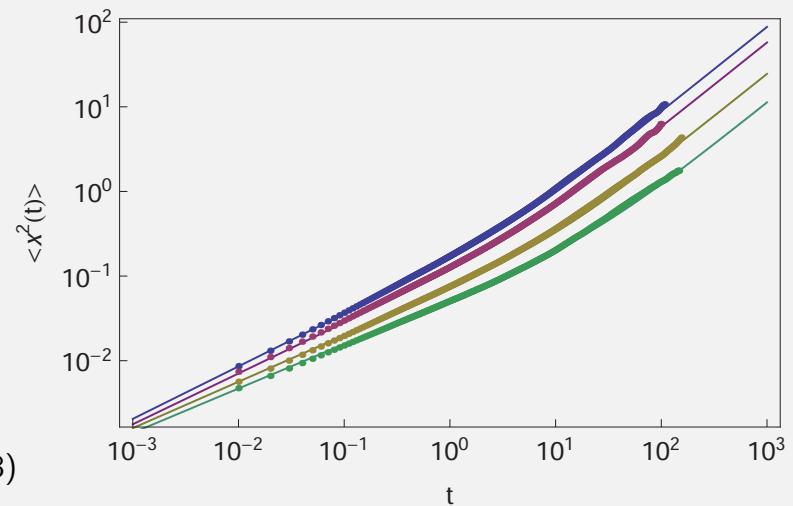
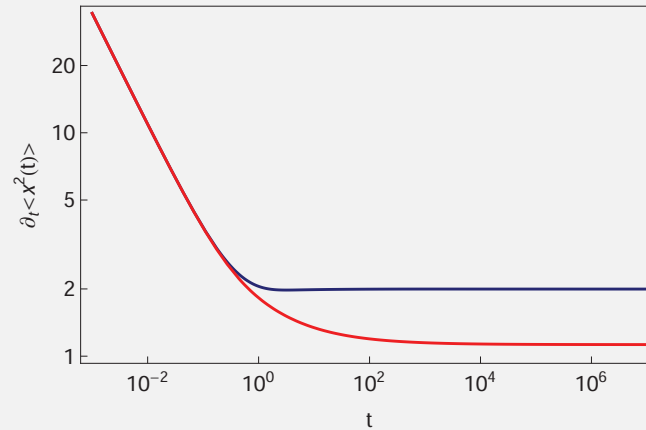
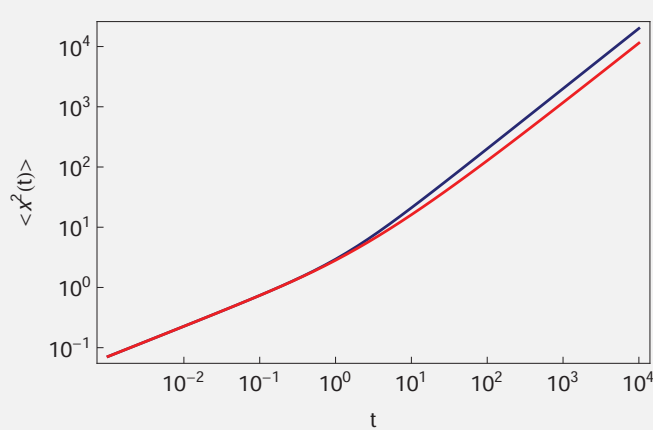
Liquid ordered/gel phases: extended anomalous diffusion



Tempered FBM & FLE motion: sub- to normal diffusion

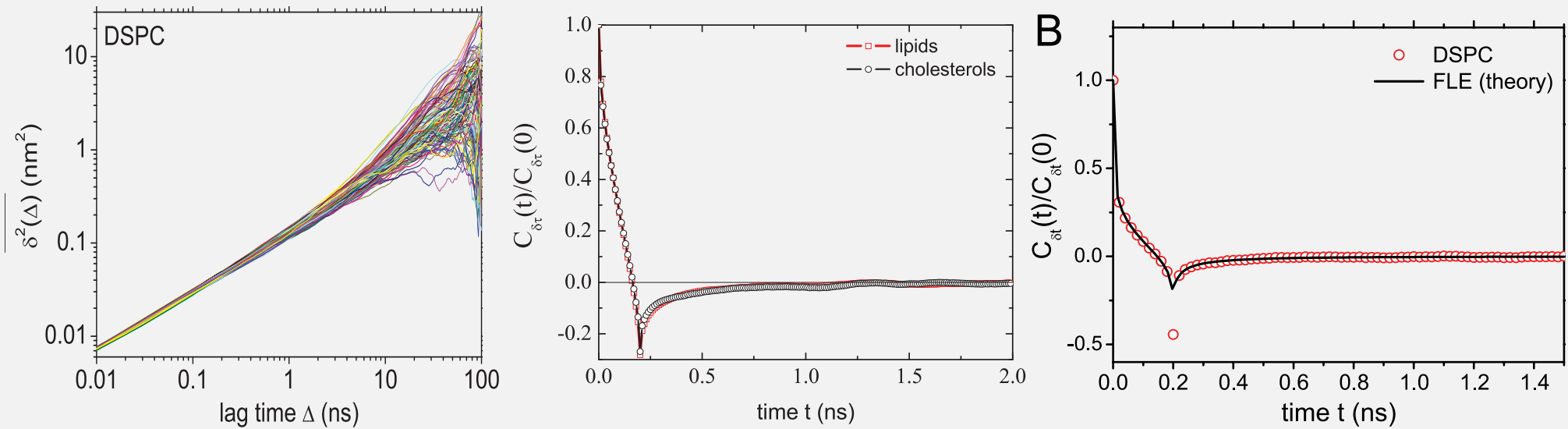
Consider tempered fGn:

$$\langle \xi(t) \xi(t + \tau) \rangle = \begin{cases} \frac{C}{\Gamma(2H-1)} \tau^{2H-2} e^{-\tau/\tau_\star} \\ \frac{C}{\Gamma(2H-1)} \tau^{2H-2} \left(1 + \frac{\tau}{\tau_\star}\right)^{-\mu} \end{cases}$$

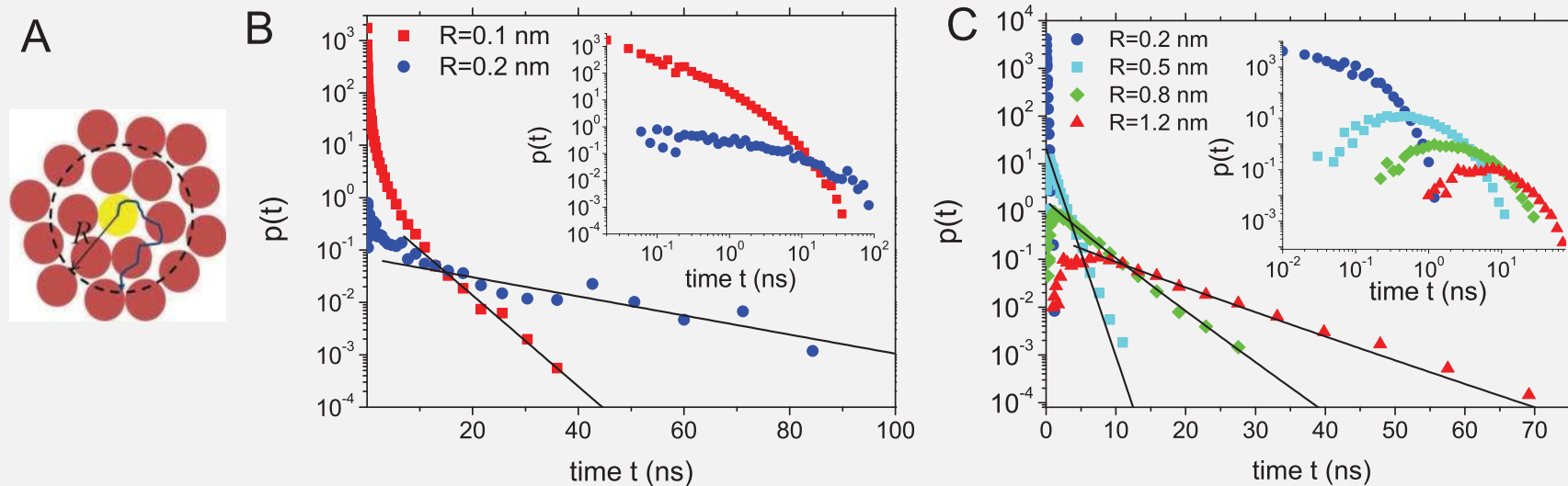


D Molina-Garcia, T Sandev, G Pagnini, AV Chechkin & RM (2018)

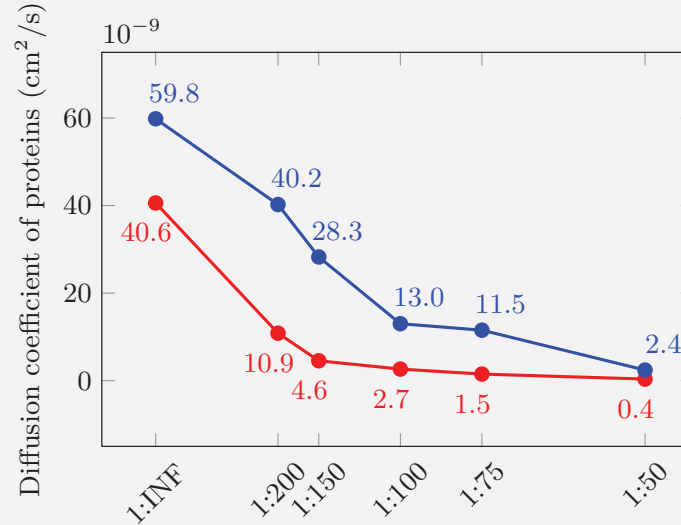
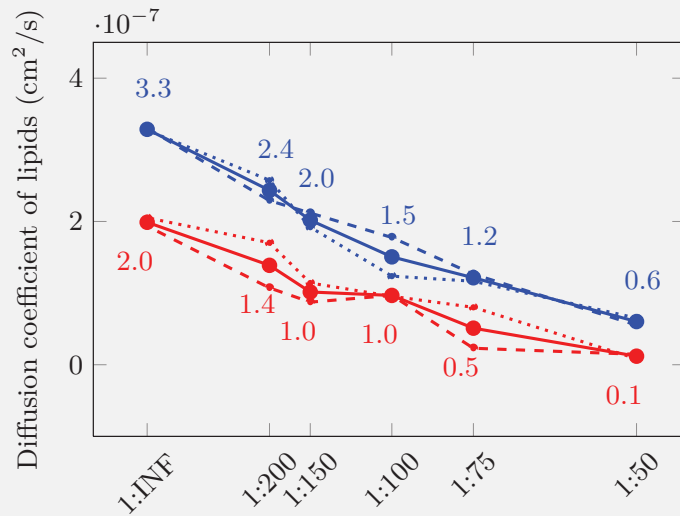
Reproducible TA MSD & antipersistent correlations



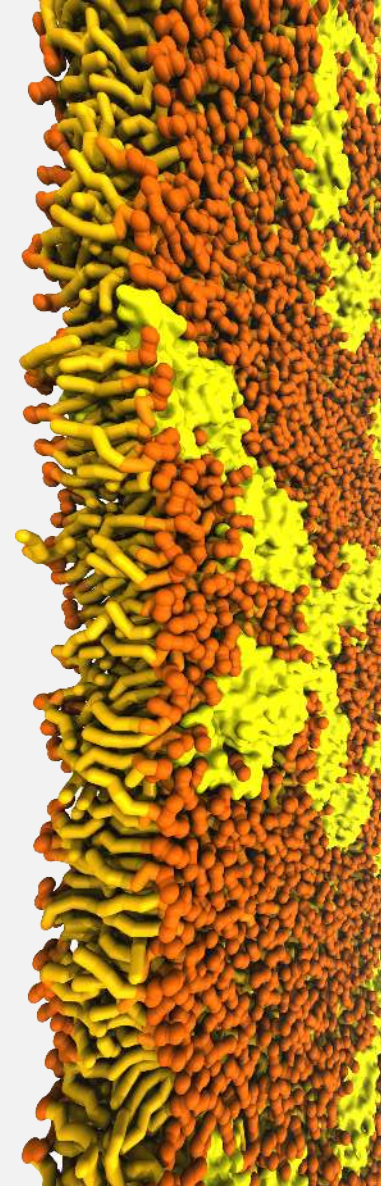
Rattling dynamics: exptl first passage PDF $\rightarrow$ FLE motion



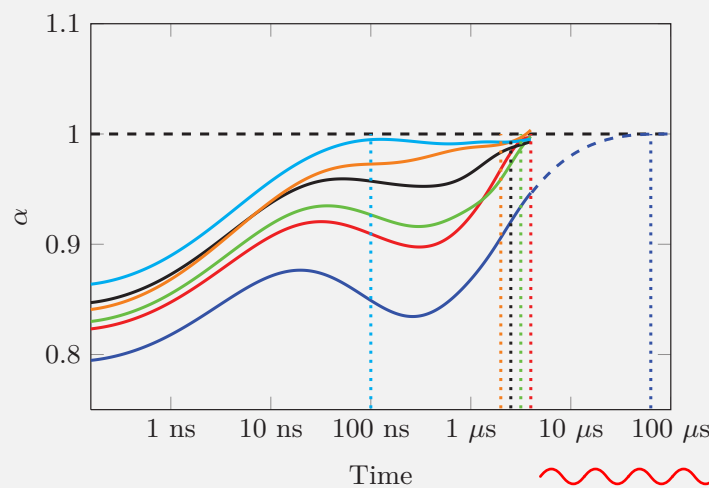
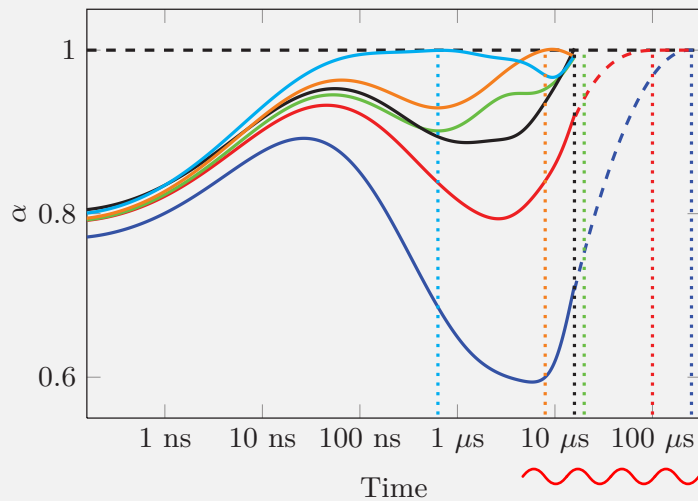
Protein crowded membranes reduce effective mobility



Blue: DLPC. Red: DPPC

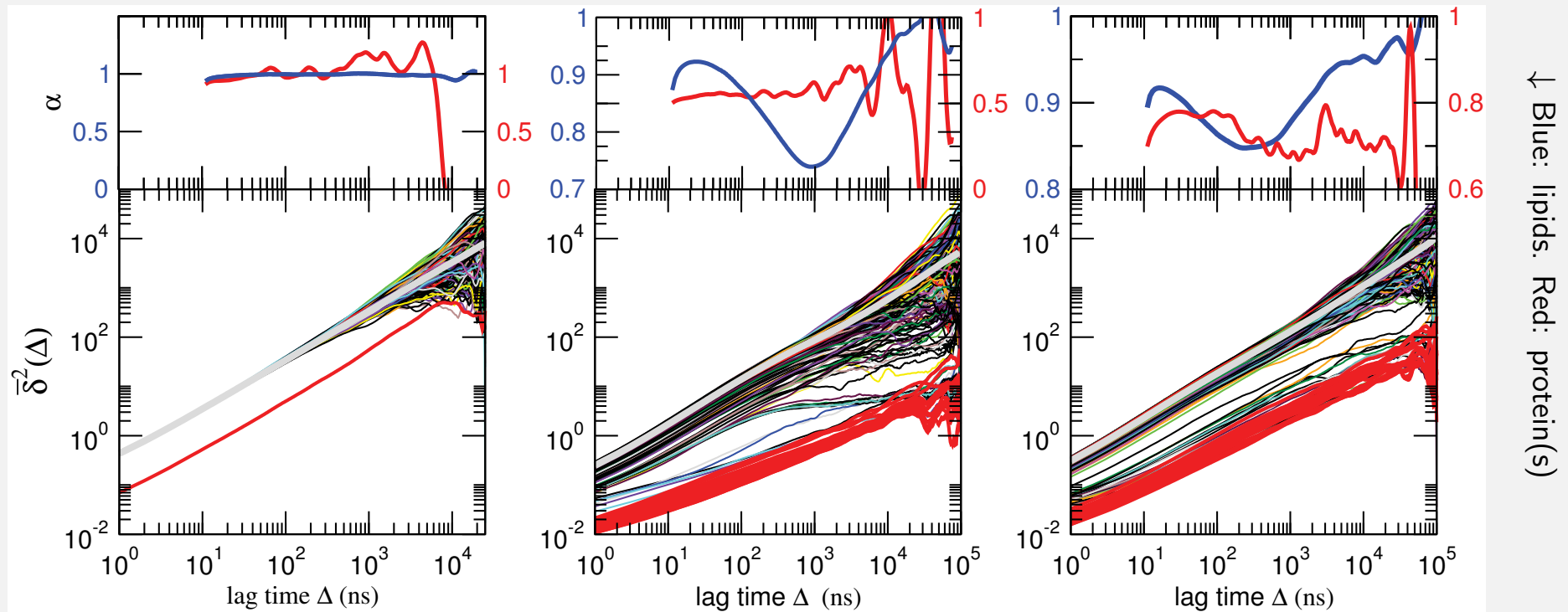


Protein crowding effects anomalous lipid diffusion



Left: DPPC (protein-aggregating) case. Right: DLPC protein non-aggregating case.

Crowding in membranes increases dynamic heterogeneity



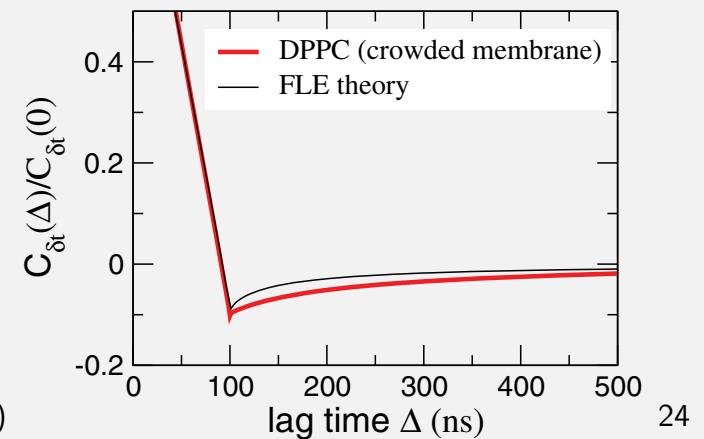
Single NaK channel

DLPC (non-aggregating)

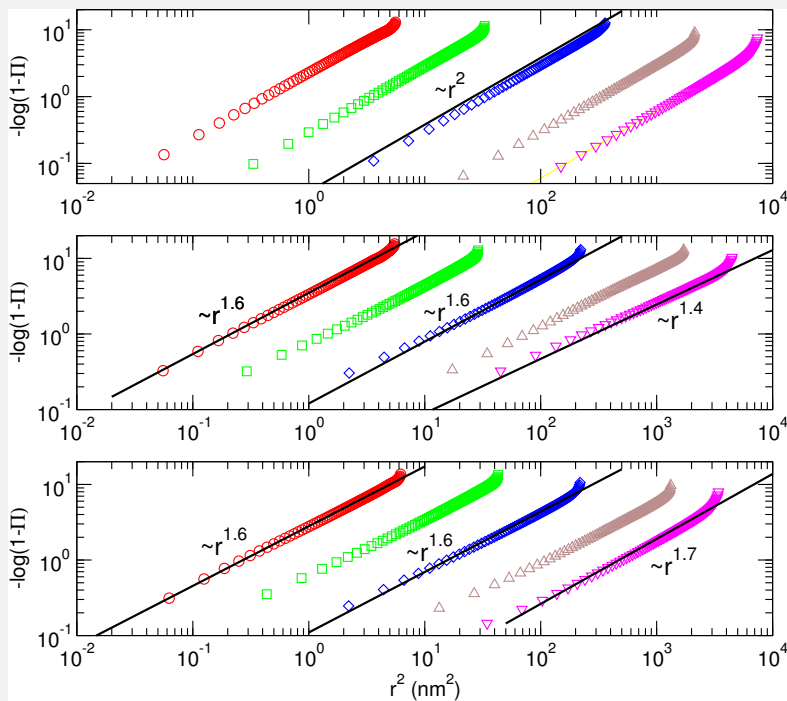
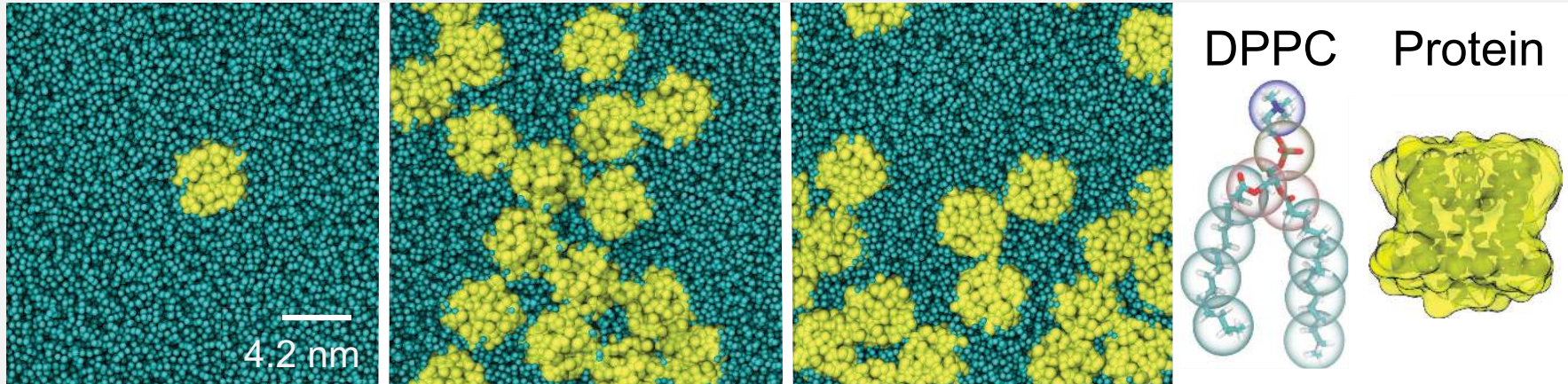
DPPC (aggregating)

Lipids & proteins behave quite differently

Increment correlation no longer simple FBM $\rightarrow$



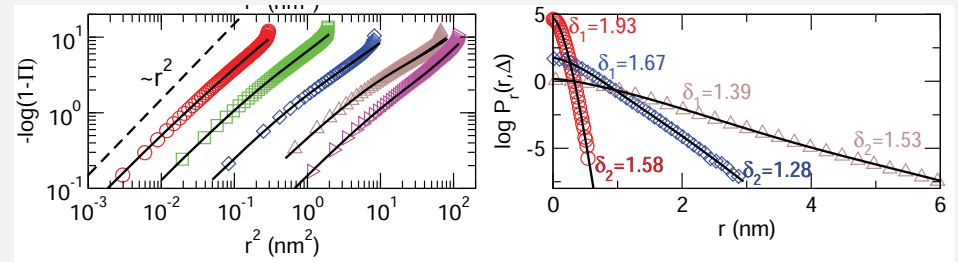
Crowding in membranes: non-Gaussian lipid/protein diffusion



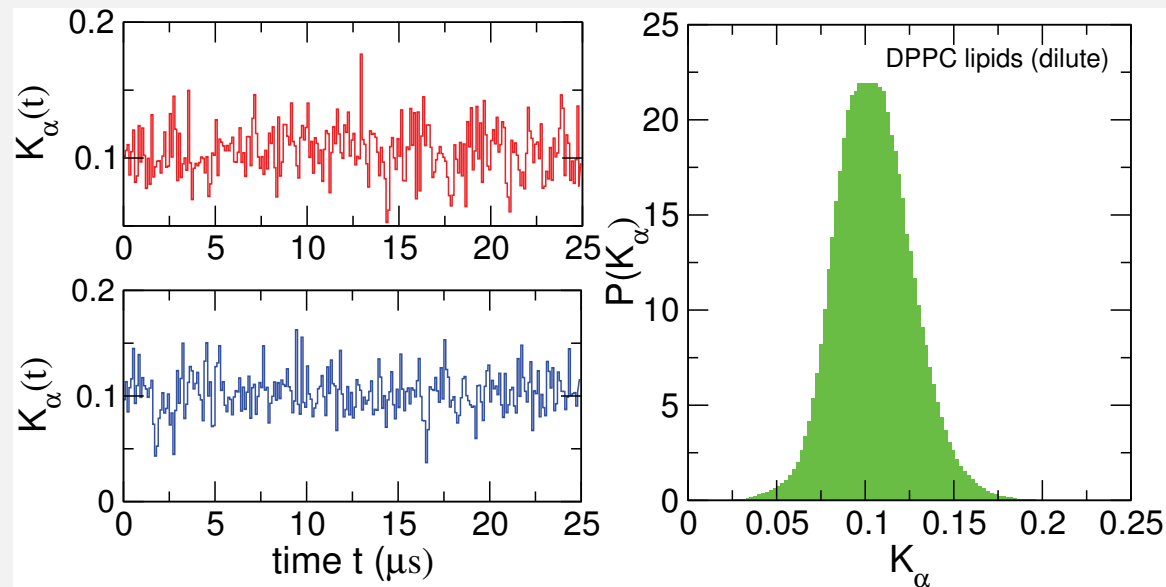
Dilute membrane: $P(r, t)$ Gauss

Crowded membrane ($\delta \approx 1.3 \dots 1.7$):

$$P(r, t) \propto \exp \left(- \left[\frac{r}{ct^{\alpha/2}} \right]^\delta \right)$$

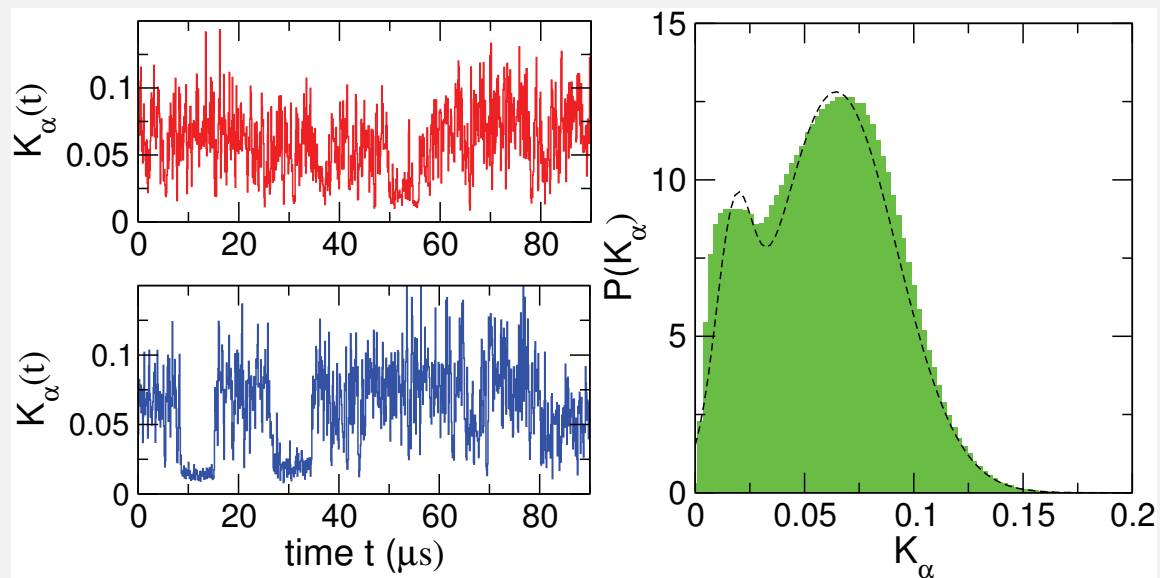


Crowding in membranes increases dynamic heterogeneity



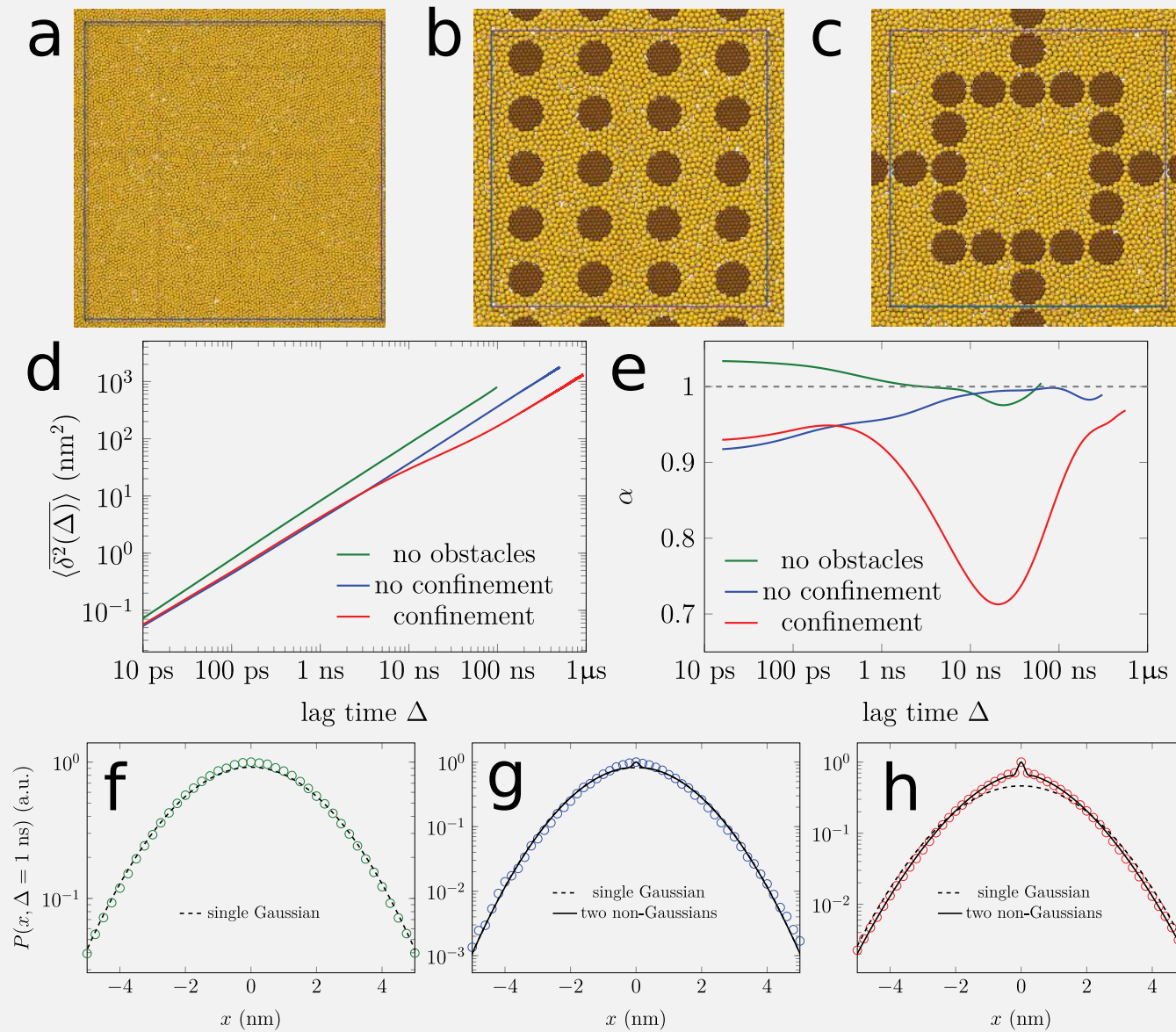
Diffusivity(t) for two lipids

Lipid diffusivity, dilute membrane

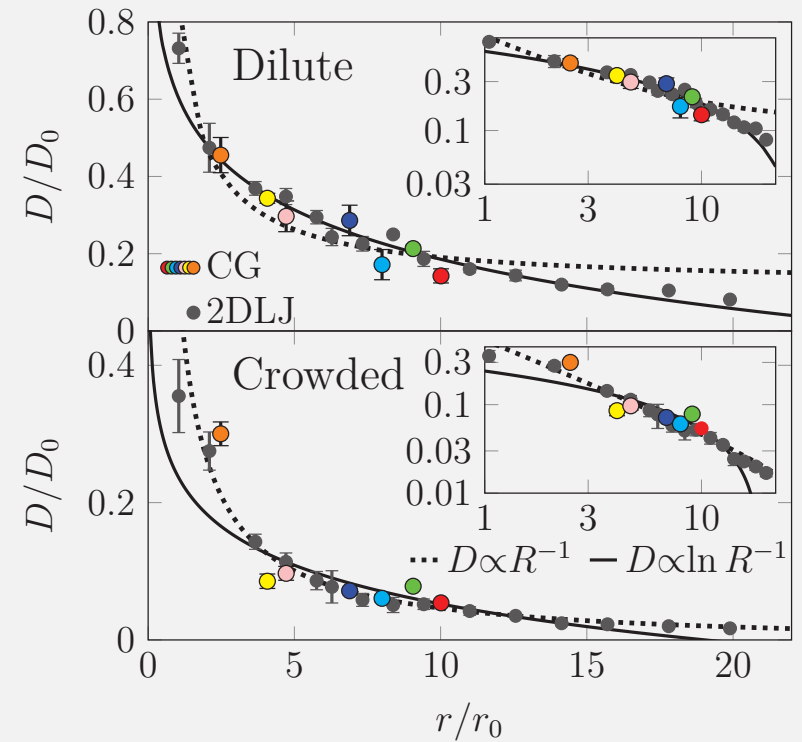
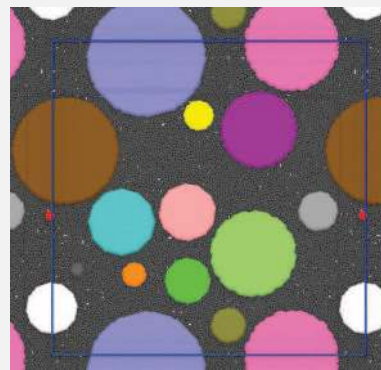
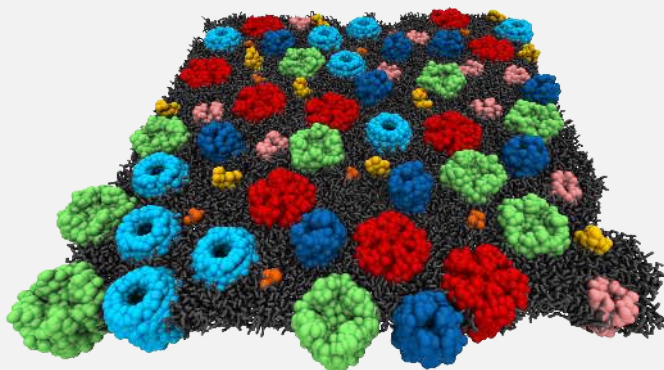
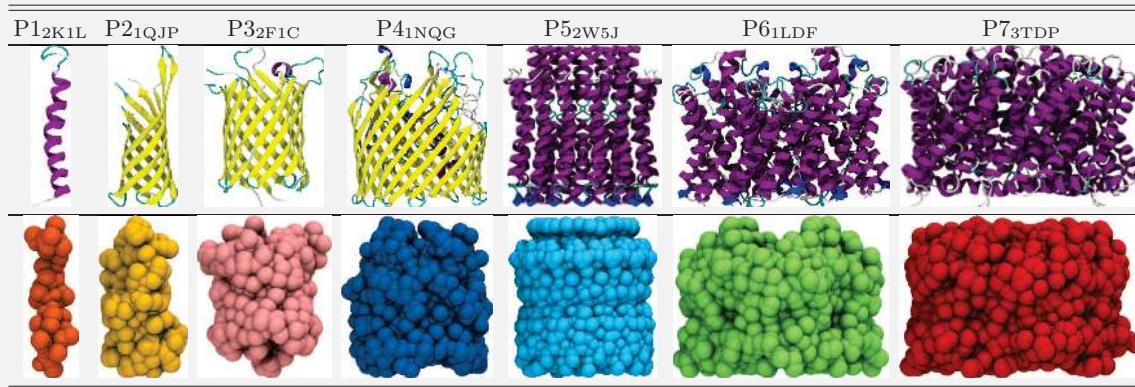


Lipid diffusivity, crowded membrane

Confinement in argon system shows geometric origin



Geometry-induced violation of Saffman-Delbrück relation



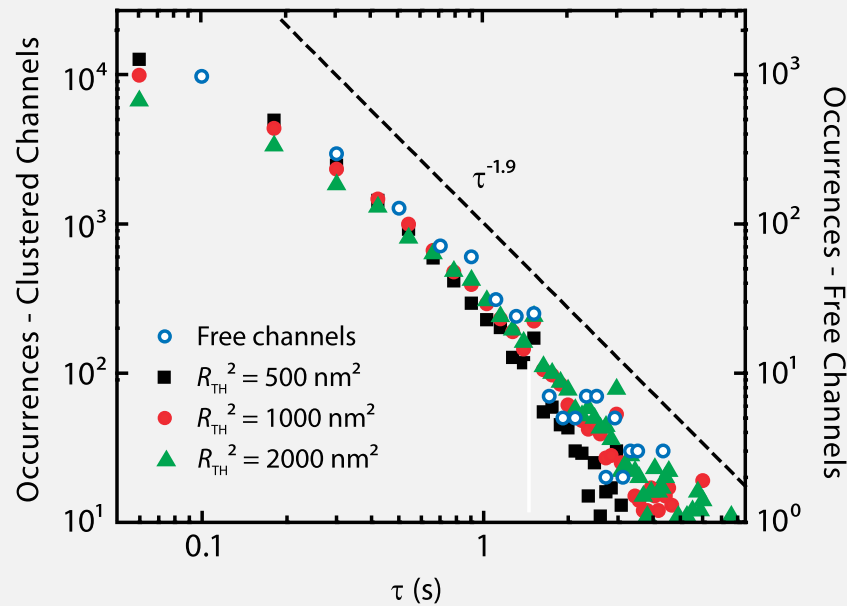
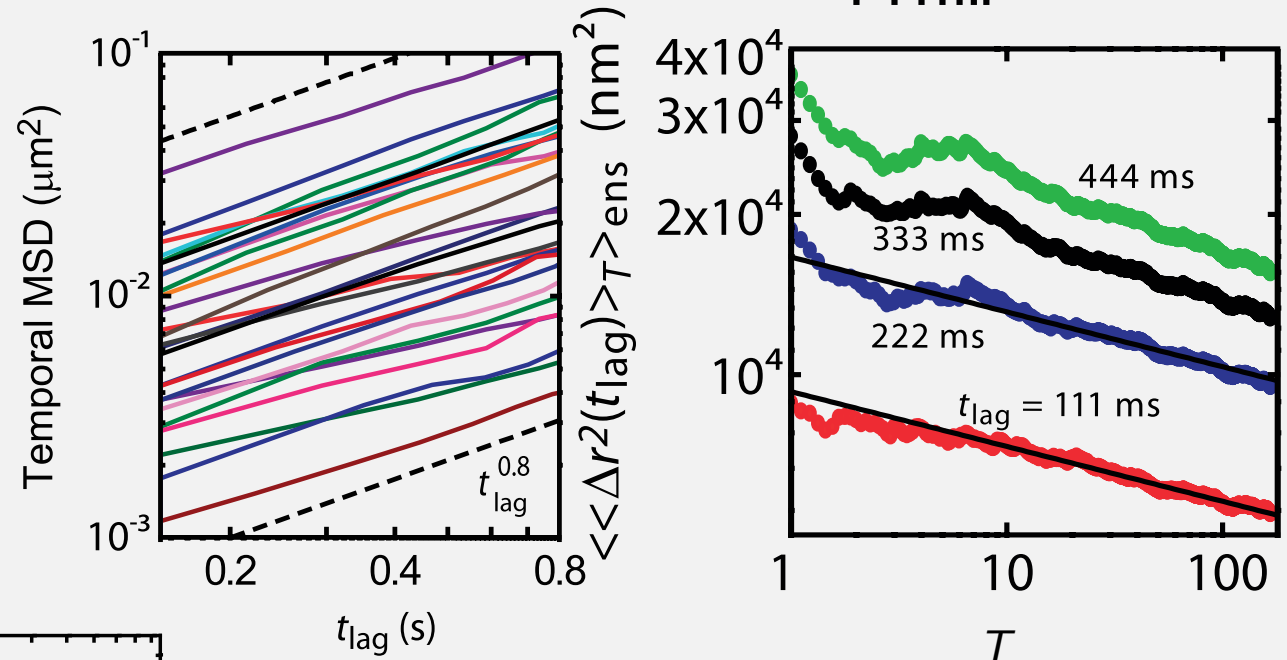
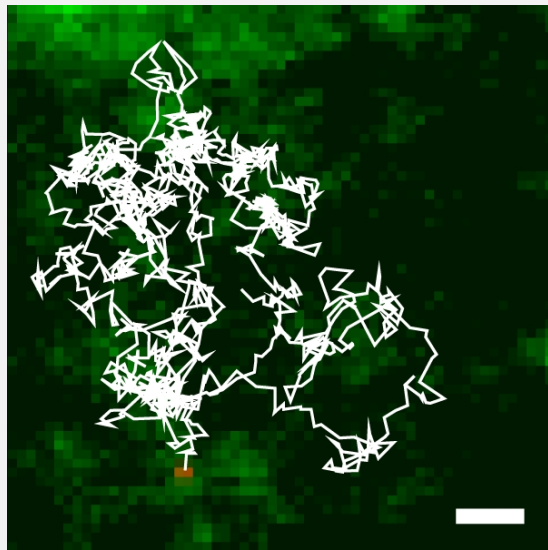
Dilute system: Saffman-Delbrück law

$$D(R) \simeq \log(1/R)$$

Crowded membrane & 2DLJ discs:

$$D(R) \simeq 1/R$$

CTRW-like motion of Ka channels in plasma membrane



$$\psi(\tau) \simeq \tau^{-1-\alpha} \text{ scale free}$$

$$\overline{\delta^2(\Delta)} \text{ apparently random}$$

$$\overline{\delta^2(\Delta)} \neq \langle \mathbf{r}^2(\Delta) \rangle \text{ WEB}$$

Time averaged MSD & weak ergodicity breaking (WEB)

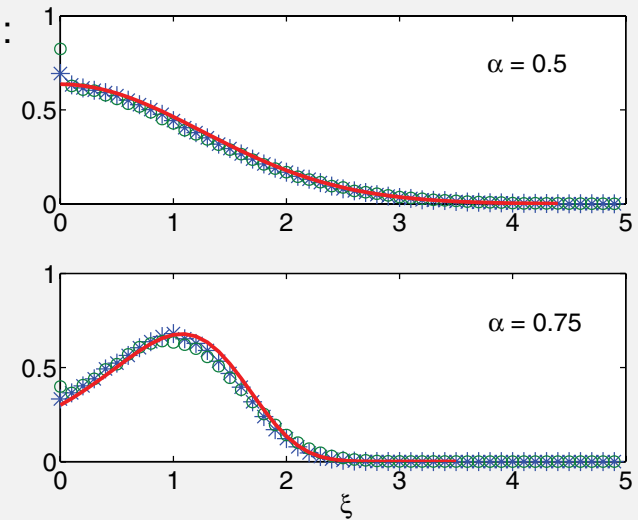
Time averaged MSD $\simeq \Delta$ is pseudo-Brownian and ageing ($\langle x^2(t) \rangle \simeq K_\alpha t^\alpha$):

$$\langle \overline{\delta^2(\Delta)} \rangle \sim \frac{1}{N} \sum_i^N \overline{\delta_i^2(\Delta)} \sim \frac{2dK_\alpha}{\Gamma(1+\alpha)} \frac{\Delta}{T^{1-\alpha}} \quad \therefore \quad K_\alpha \equiv \frac{\langle \delta \mathbf{r}^2 \rangle}{2\tau^\alpha}$$

Amplitude distribution $\overline{\delta^2}$ of trajectories ($\xi \equiv \overline{\delta^2} / \langle \overline{\delta^2} \rangle$):

$$\phi_\alpha(\xi) \sim \frac{\Gamma^{1/\alpha}(1+\alpha)}{\alpha \xi^{1+1/\alpha}} L_\alpha^+ \left(\frac{\Gamma^{1/\alpha}(1+\alpha)}{\xi^{1/\alpha}} \right)$$

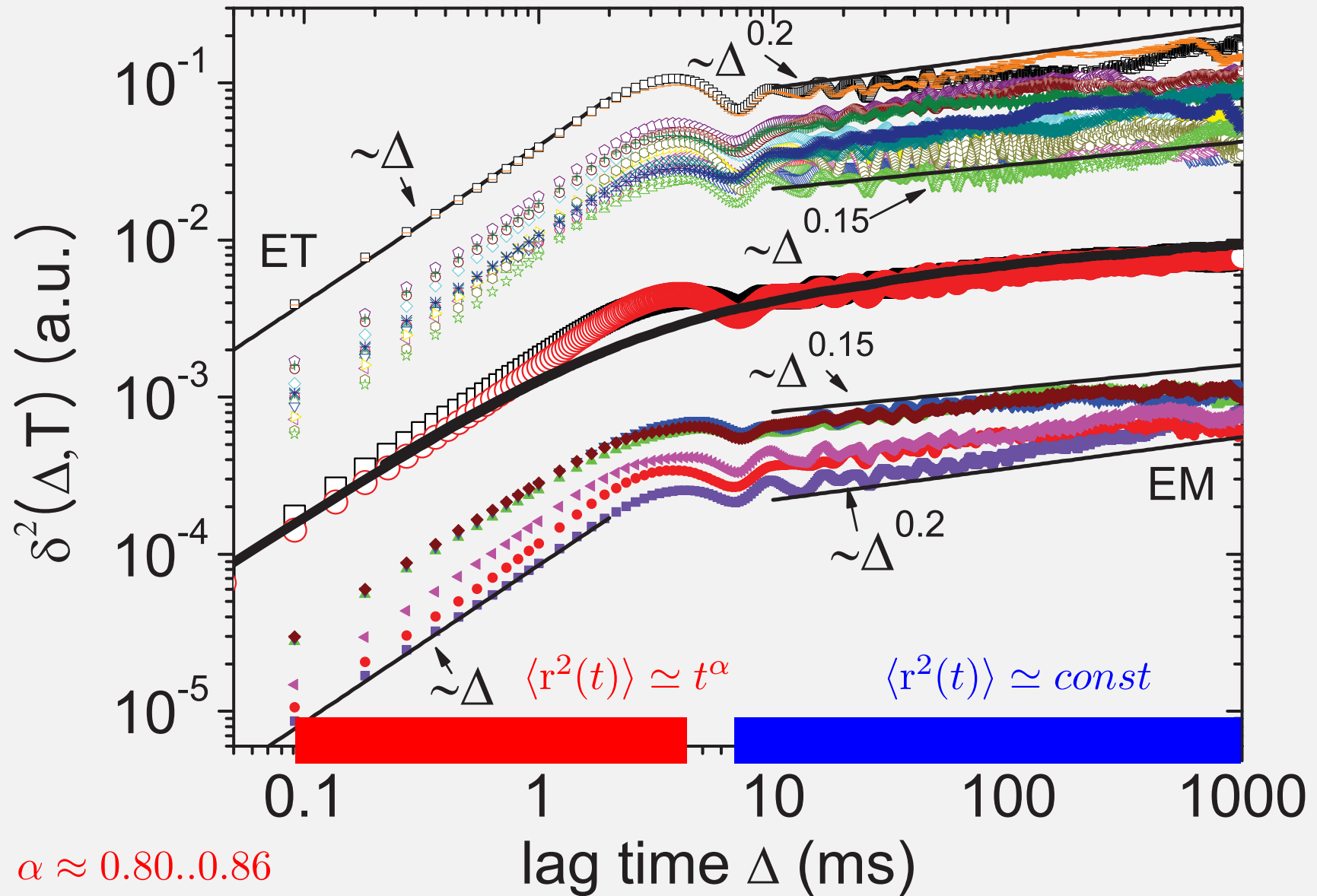
$$\phi_{1/2}(\xi) = \frac{2}{\pi} \exp \left(-\frac{\xi^2}{\pi} \right); \quad \phi_1(\xi) = \delta(\xi - 1)$$



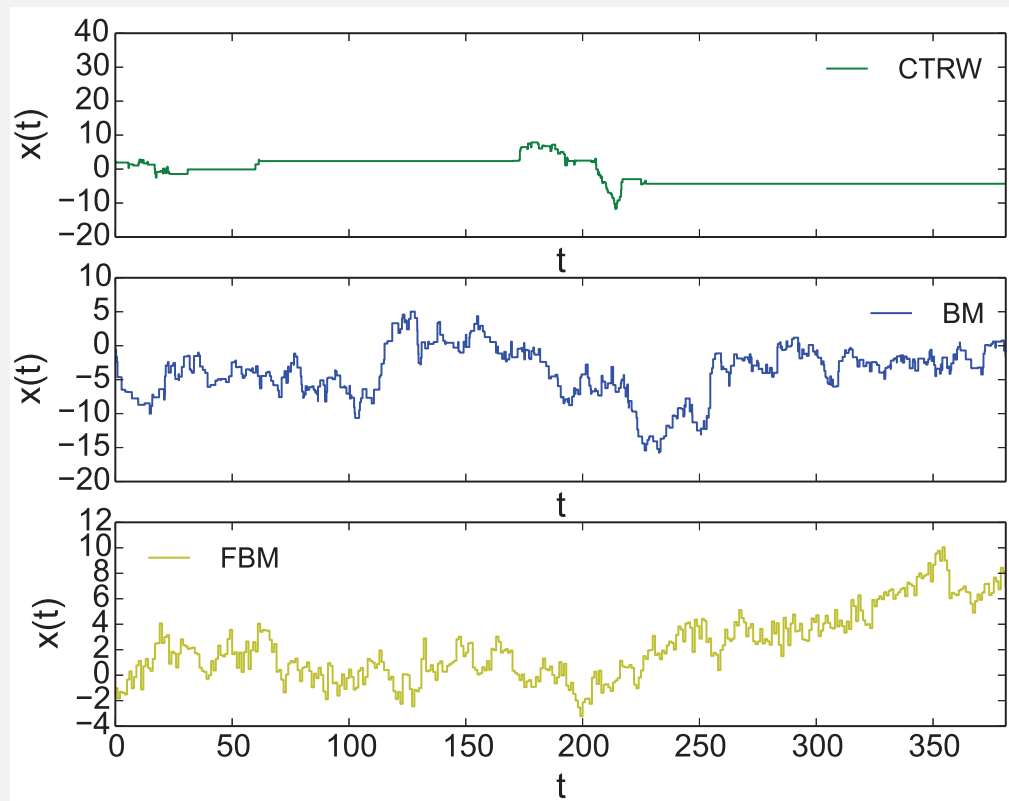
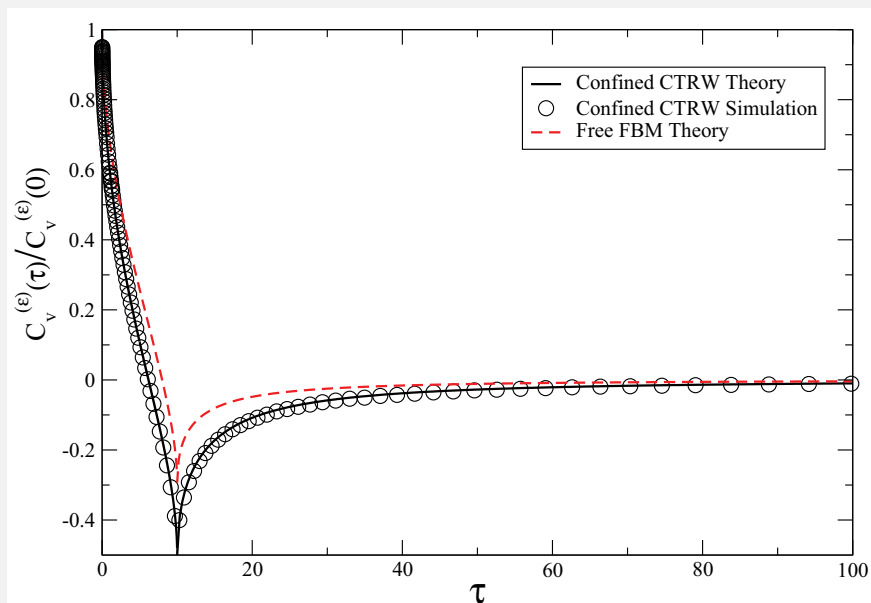
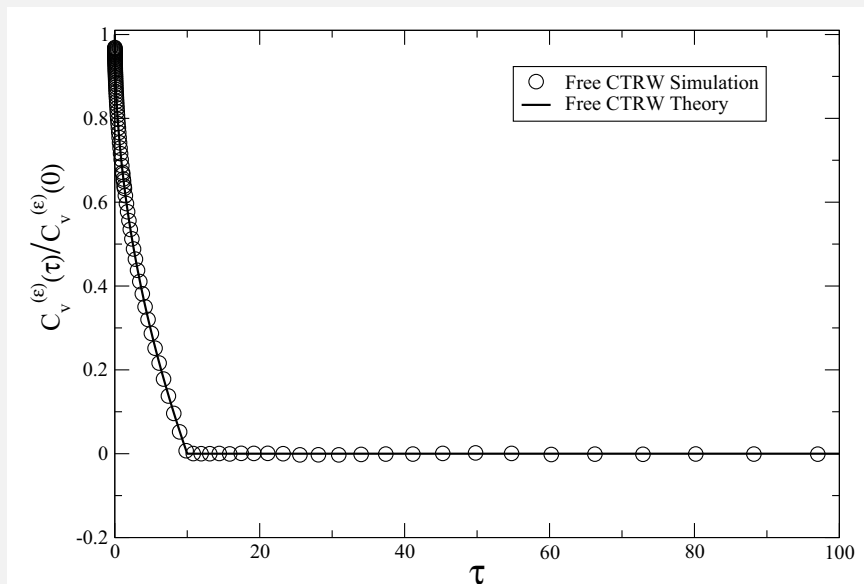
Confinement does not effect a plateau ($\langle x^2(t) \rangle \simeq \text{const}(T)$):

$$\langle \overline{\delta^2(\Delta)} \rangle \sim \left(\langle x^2 \rangle_B - \langle x \rangle_B^2 \right) \frac{2 \sin(\pi\alpha)}{(1-\alpha)\alpha\pi} \left(\frac{\Delta}{T} \right)^{1-\alpha}; \quad \frac{1}{(K_\alpha \lambda_1)^{1/\alpha}} \ll \Delta \ll T$$

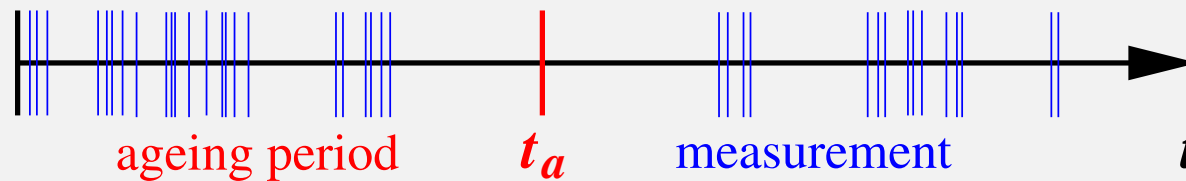
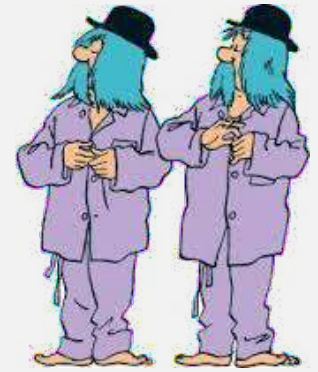
Granule subdiffusion in harmonic optical tweezer potential



A caveat when using the increment correlator



Ageing effects in single trajectory time averages

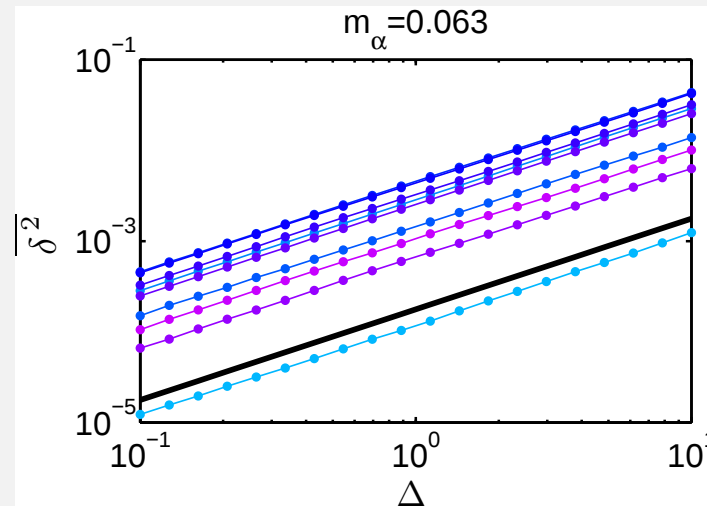
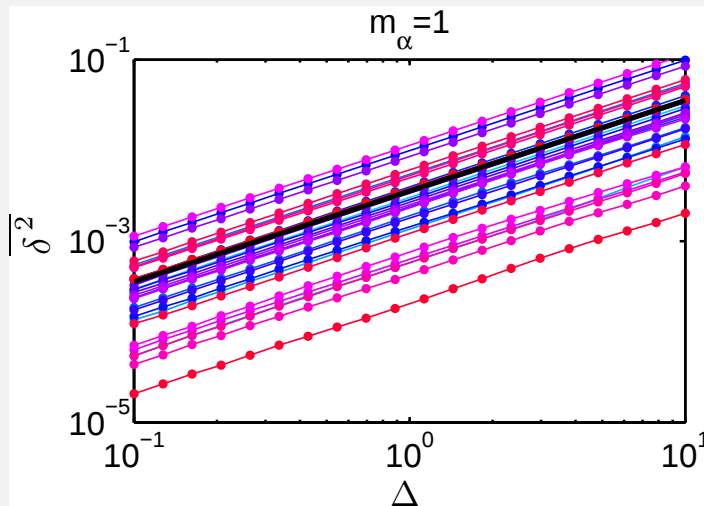


Ageing mean squared displacement ($\Lambda(z) = (1 + z)^\alpha - z^\alpha$)

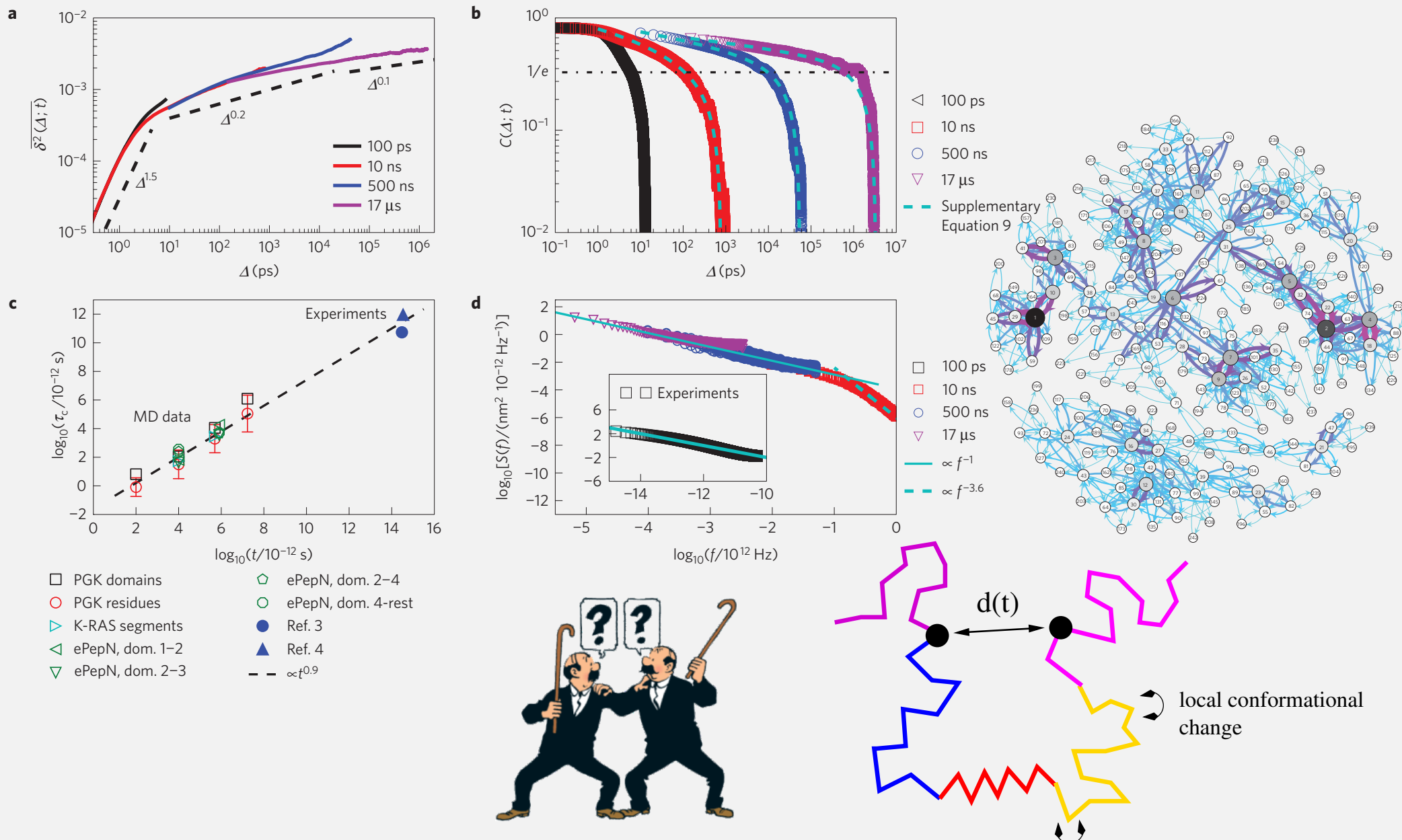
$$\left\langle \overline{\delta^2(\Delta)} \right\rangle_a = \frac{\Lambda_\alpha(t_a/T) g(\Delta)}{\Gamma(1 + \alpha) T^{1-\alpha}} \Leftrightarrow \langle x^2(t) \rangle_a \simeq \begin{cases} t^\alpha, & t_a \ll t \\ t_a^{\alpha-1} t, & t_a \gg t \end{cases}$$

Probability to make at least one step during $[t_a, t_a + T]$: *population splitting*

$$m_\alpha(T/t_a) \simeq (T/t_a)^{1-\alpha}, \quad T \ll t_a$$

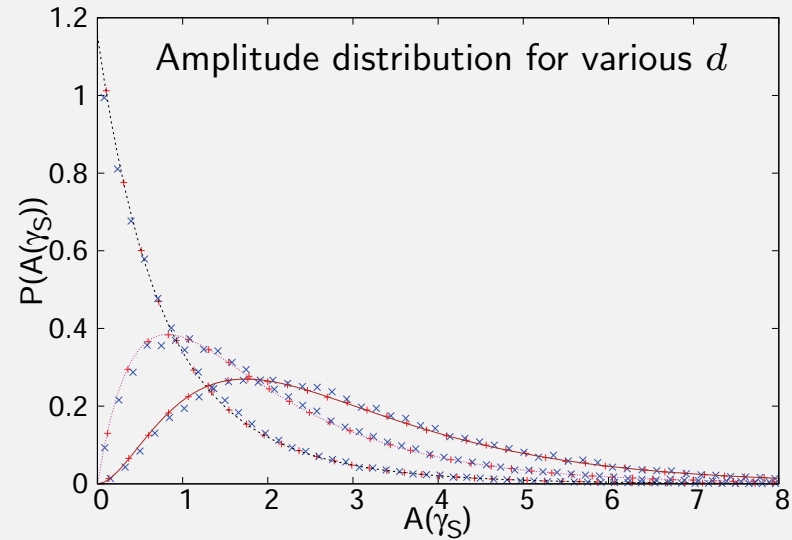
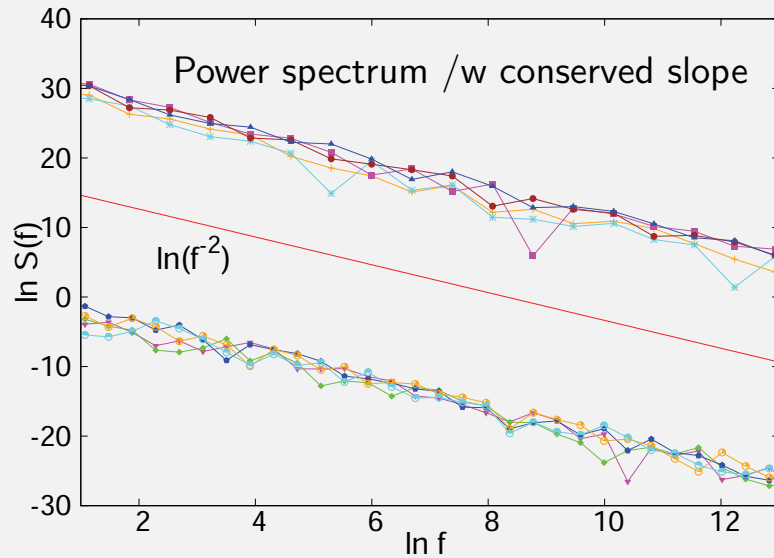


Self-similar internal protein dynamics: 13 decades of ageing

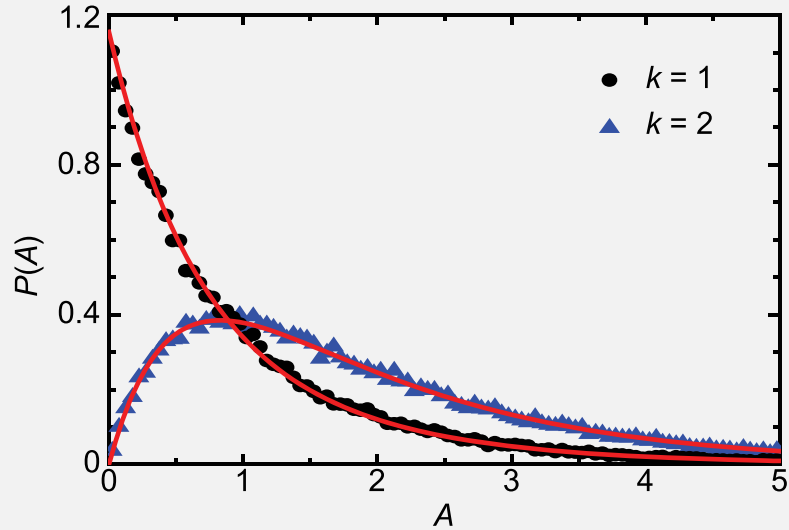
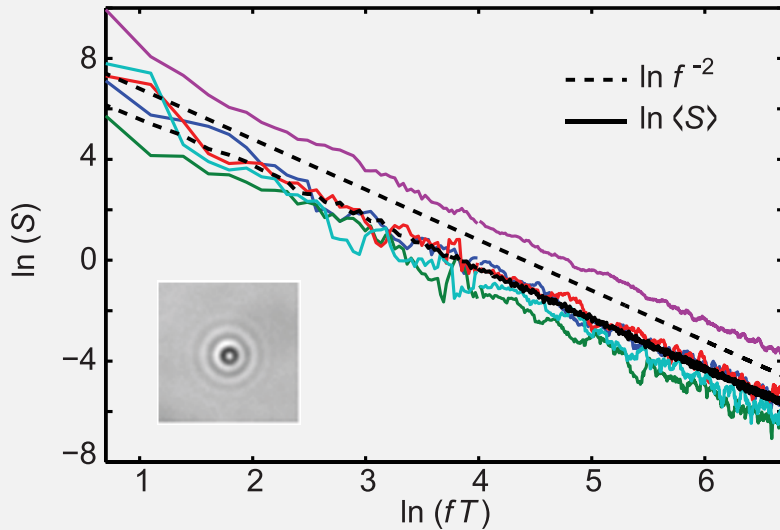


X Hu, L Hong, MD Smith, T Neusius, X Cheng & JC Smith, Nature Phys (2016); N&V RM Nature Phys (2016)

Power spectral density of a single Brownian trajectory

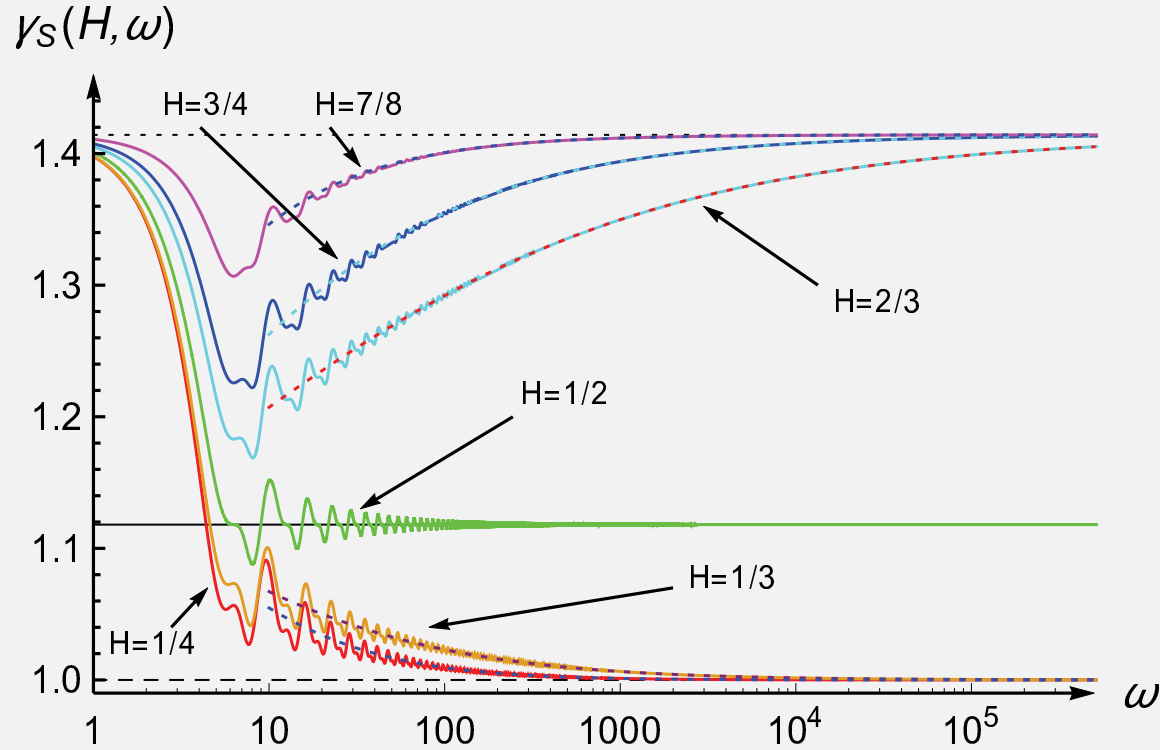


Theory



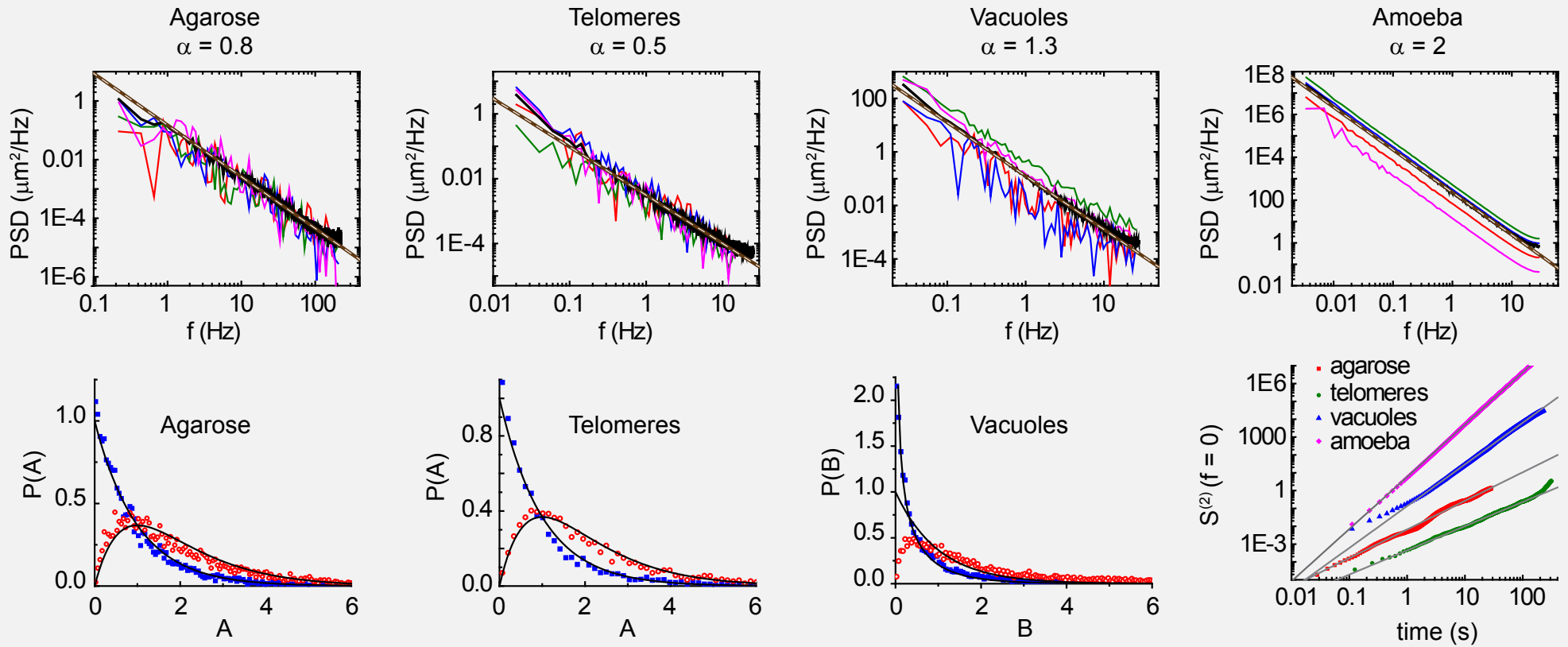
Experiment

Power spectral density of a single FBM trajectory

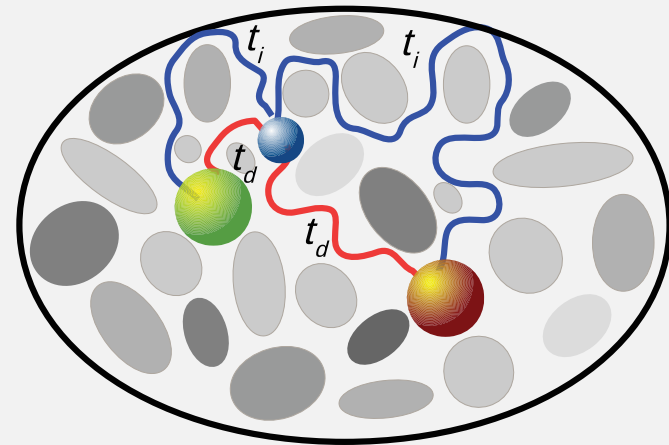
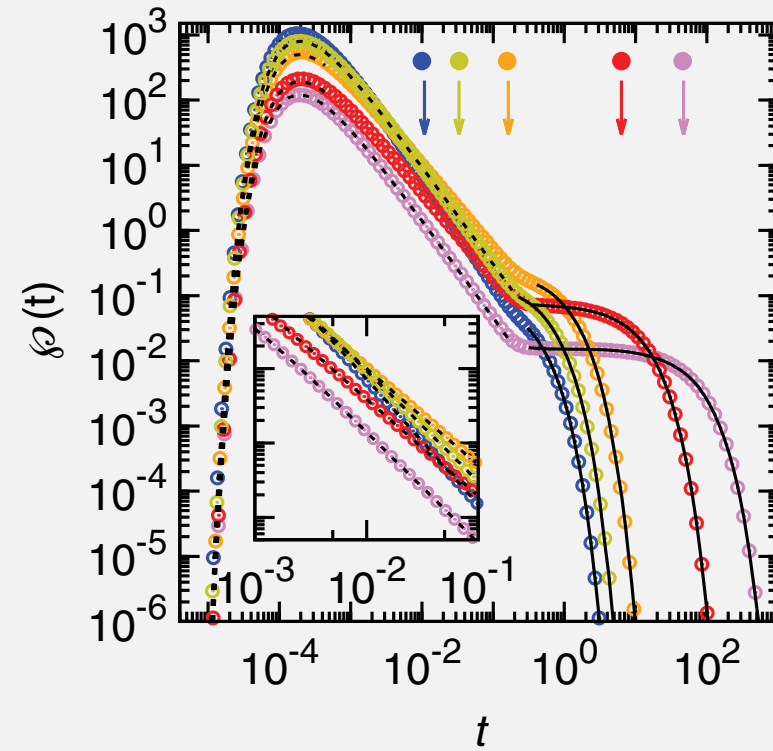
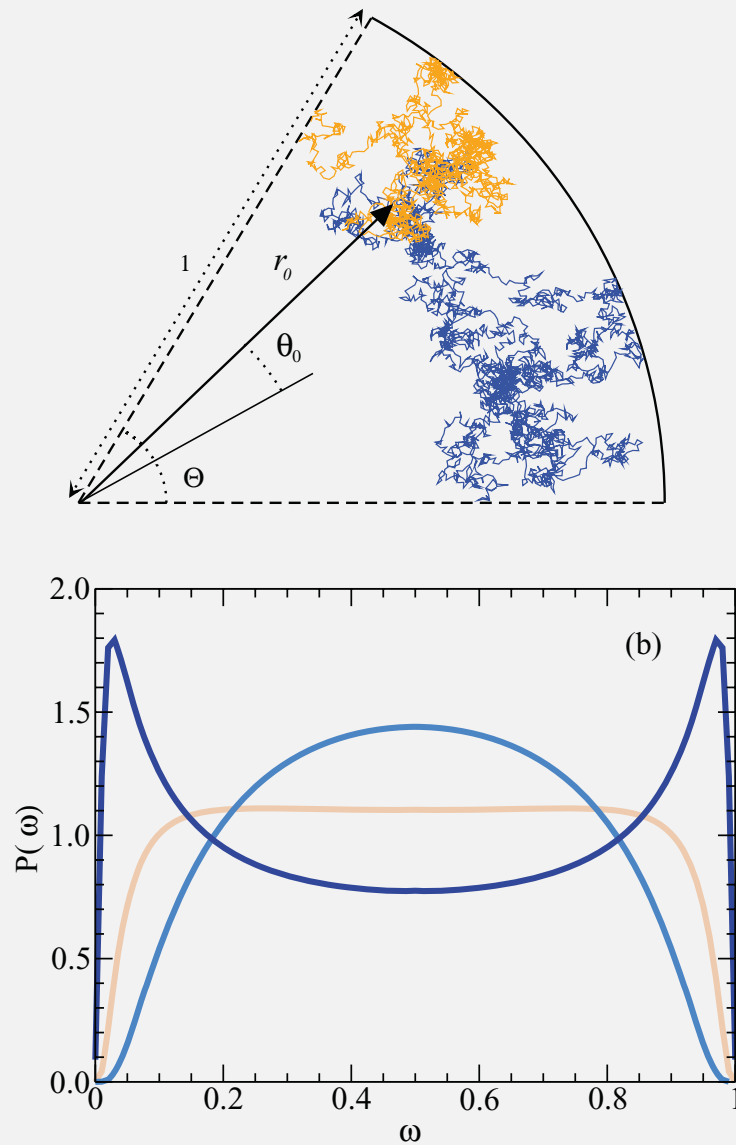


$$\gamma = \frac{(\langle S_T^2(f) \rangle - \langle S_T(f) \rangle^2)^{1/2}}{\langle S_T(f) \rangle}$$

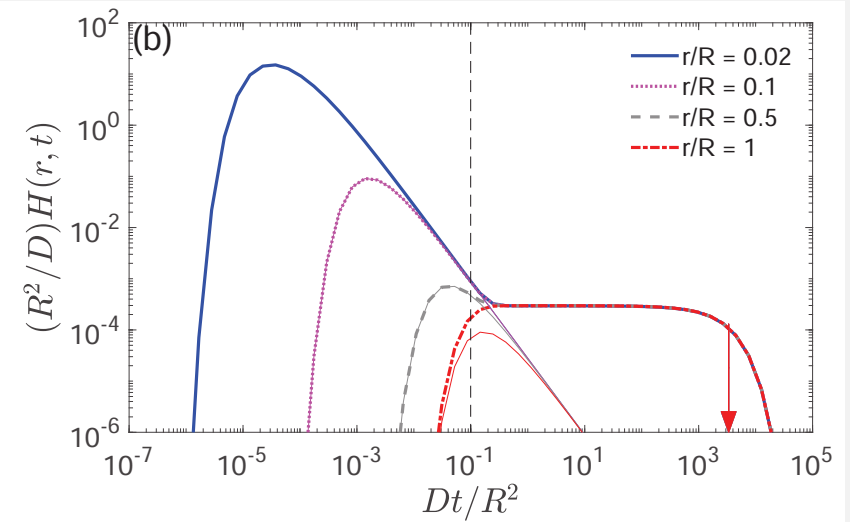
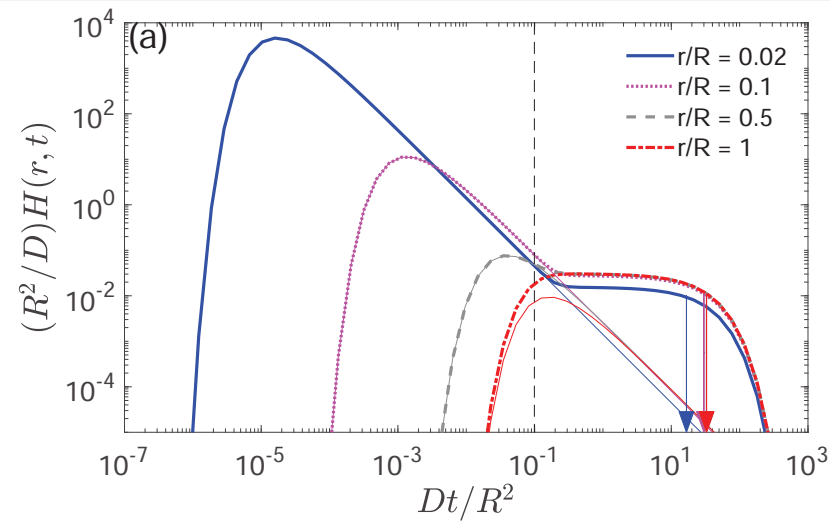
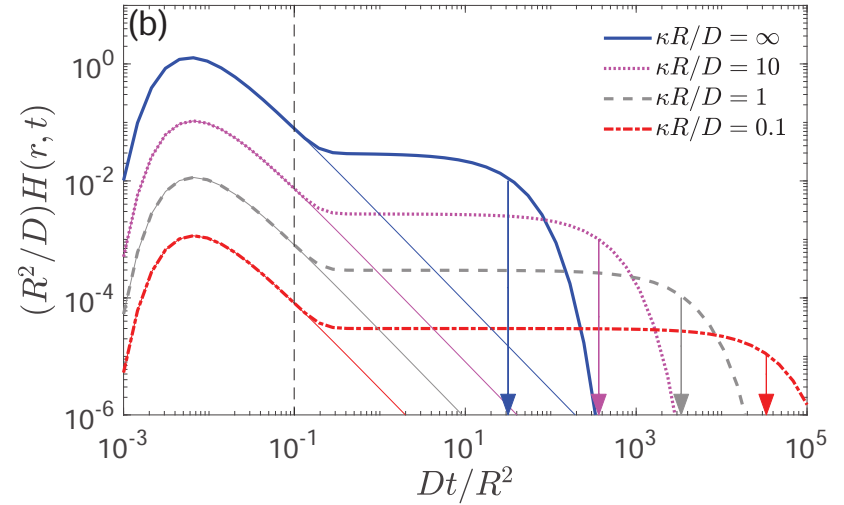
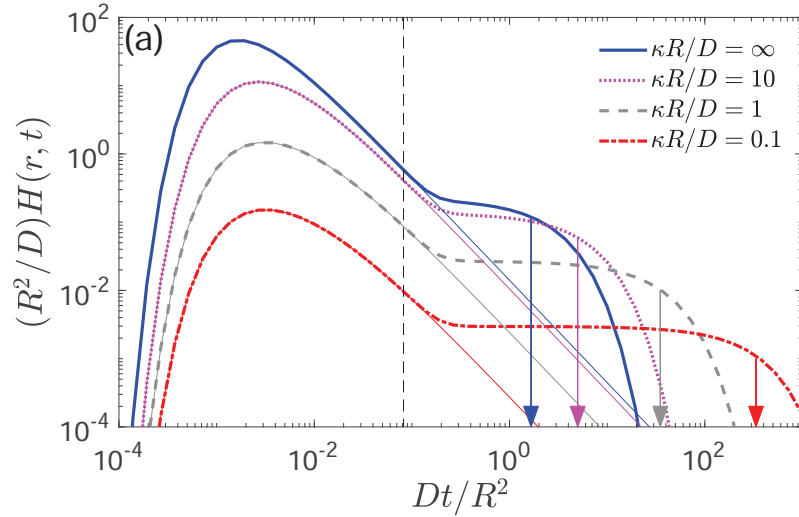
Power spectral density of a single FBM trajectory



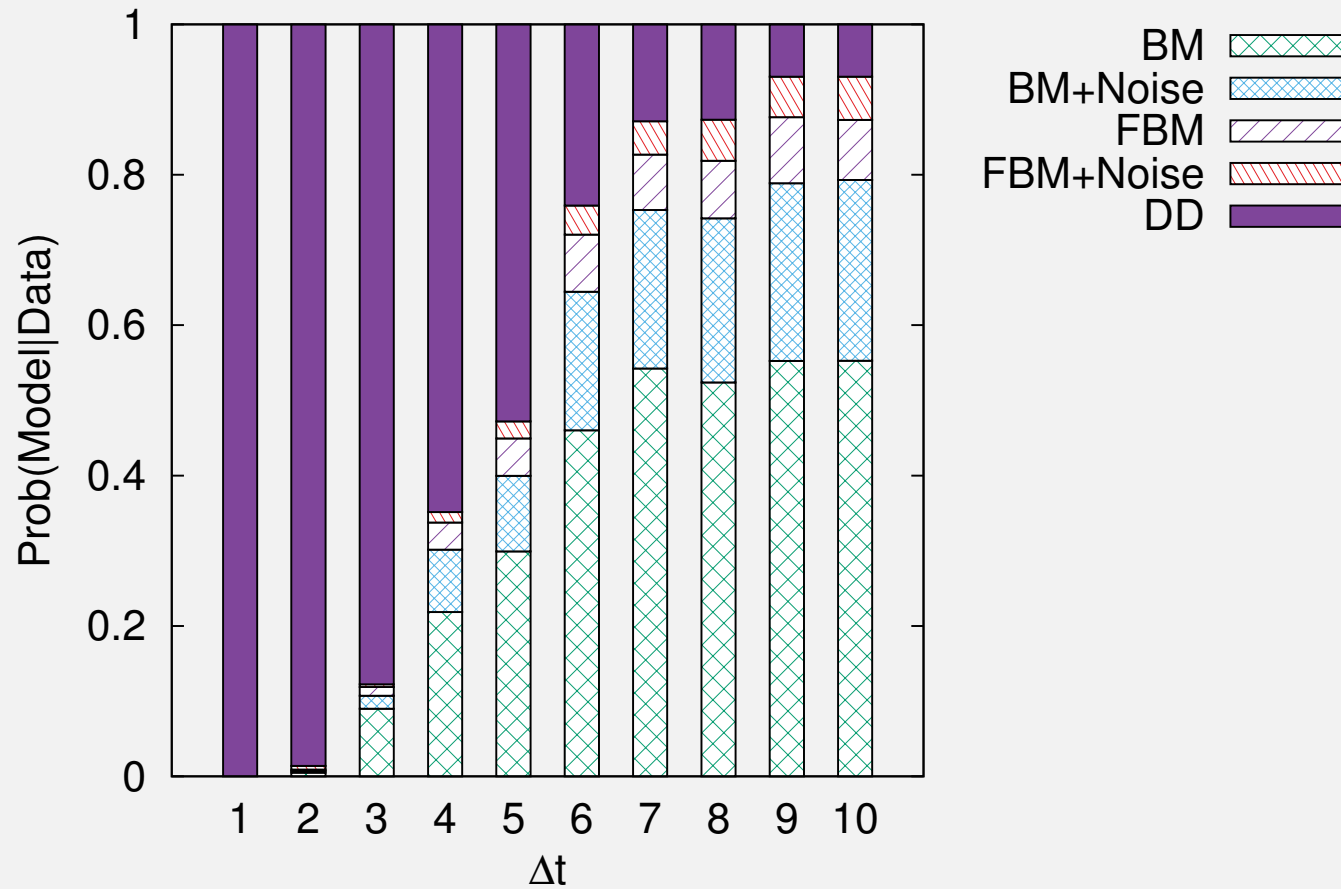
First-past-the-post: few-encounter limit & geometry control



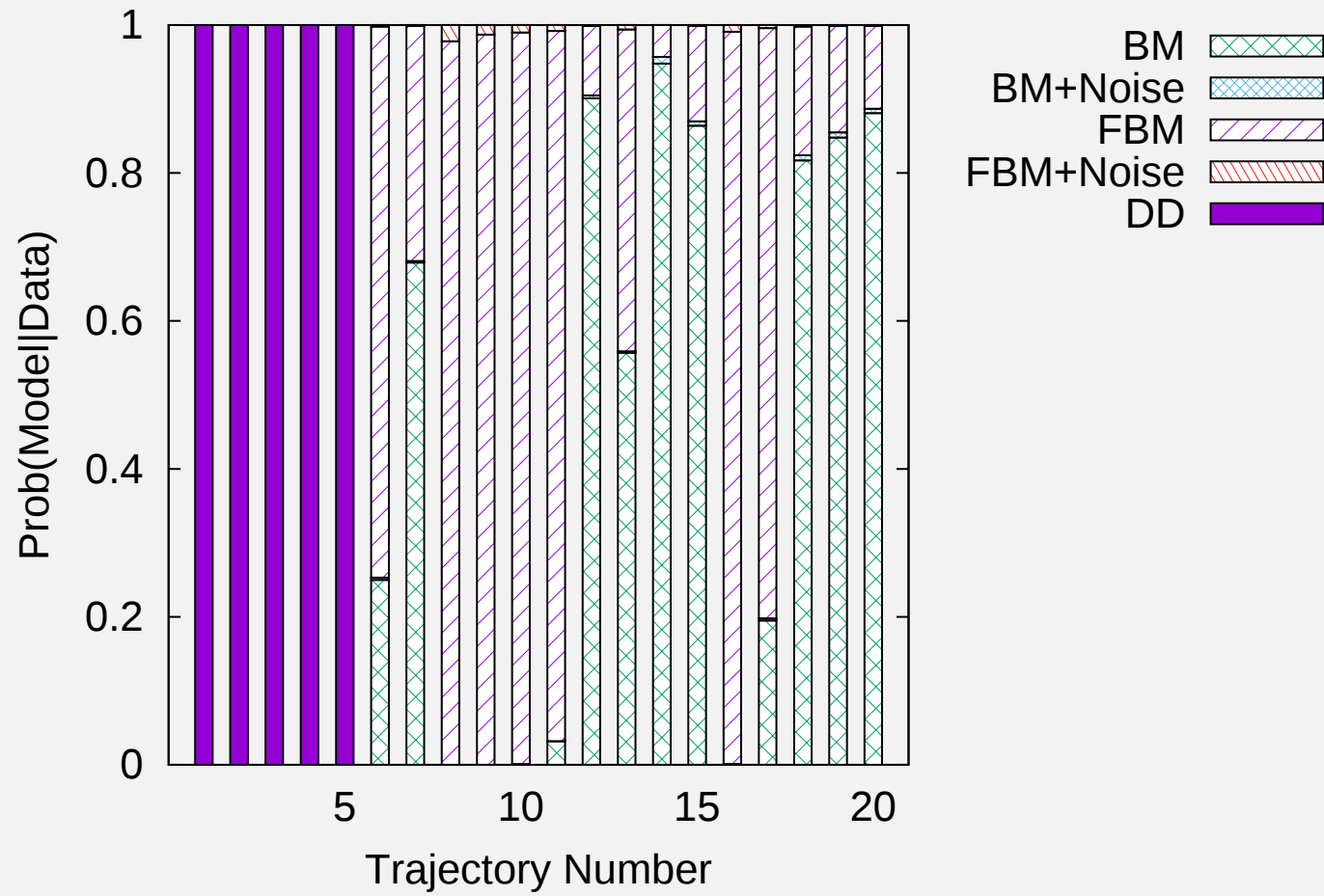
Geometry control, defocusing, & finite target reactivity



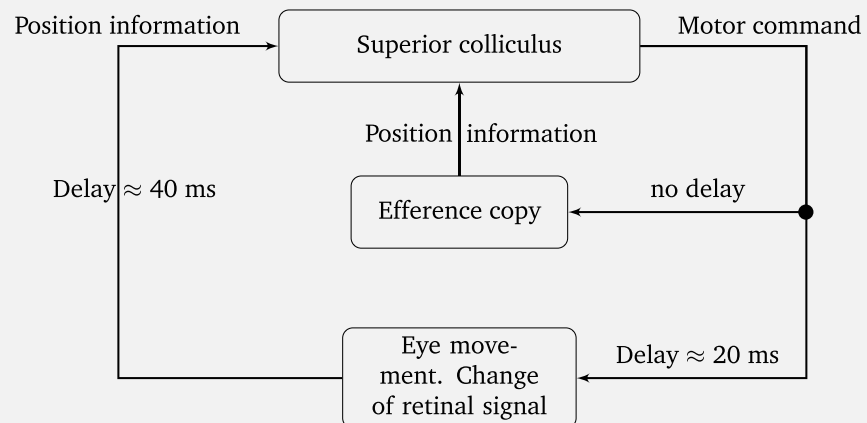
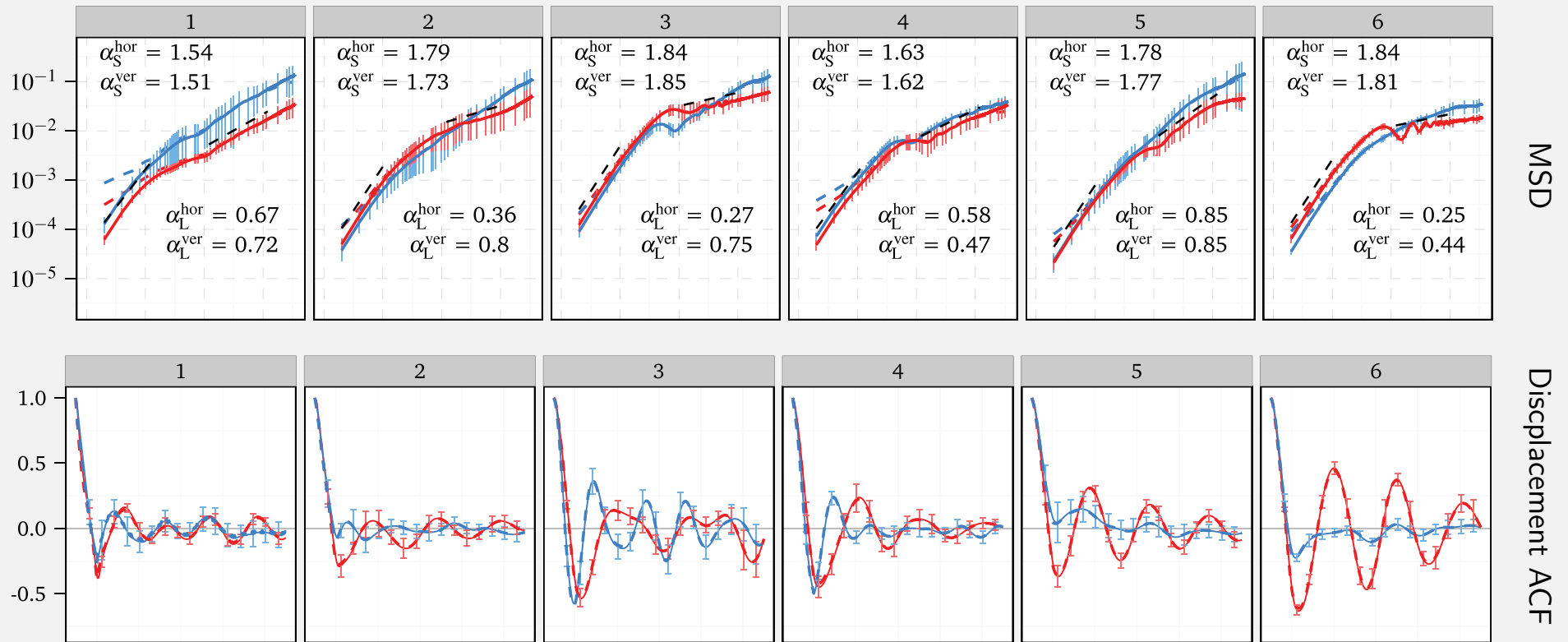
Maximum likelihood implementation of diffusing diffusivity



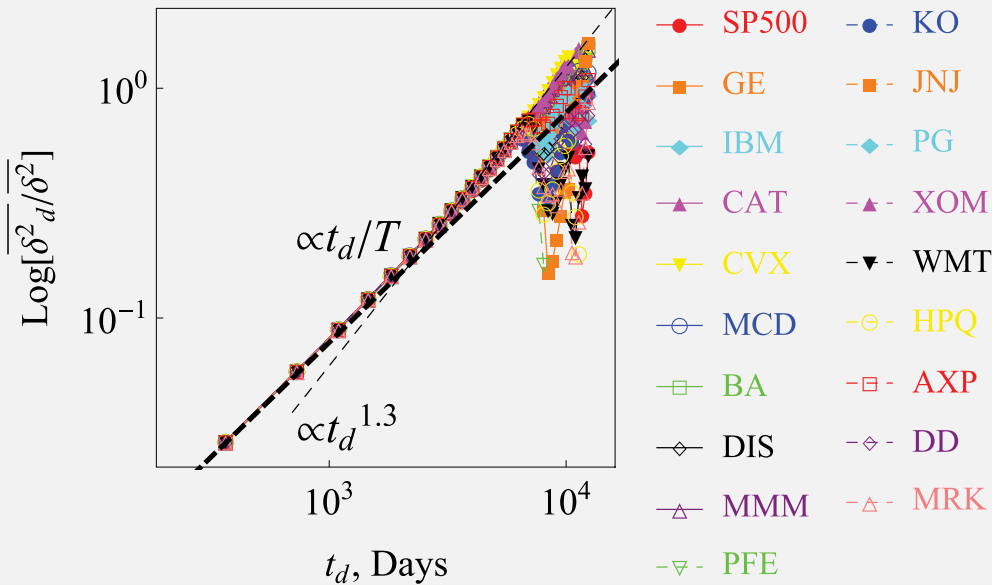
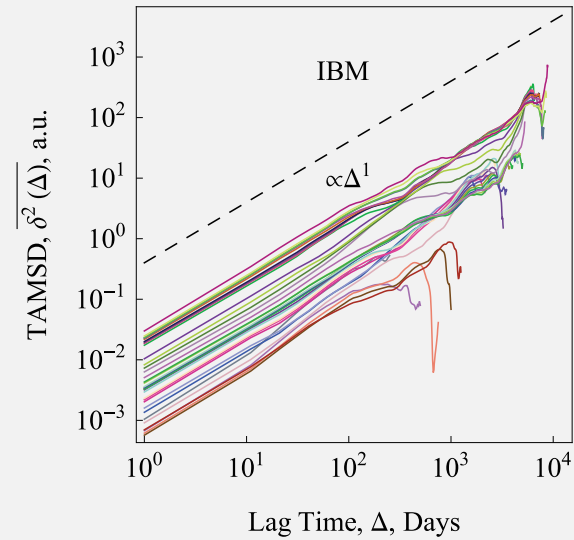
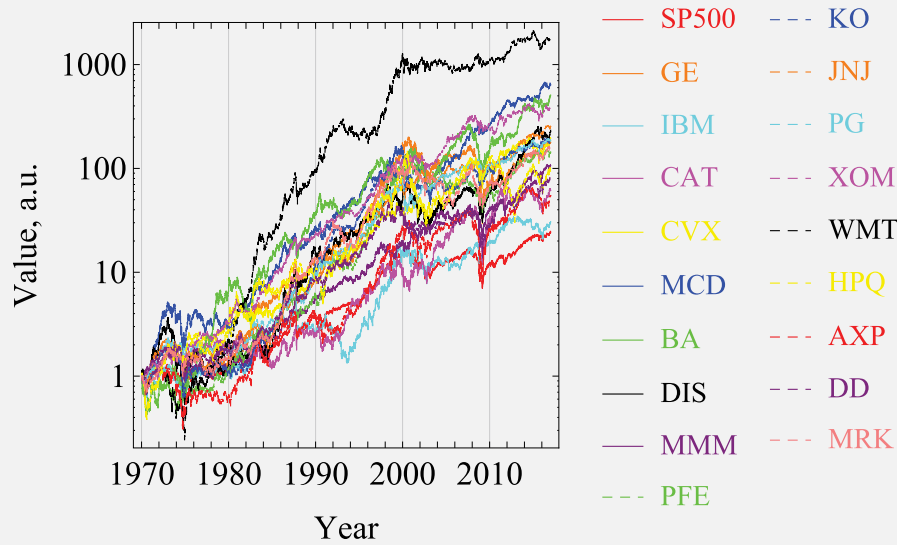
Application to mucin data



Stochasticity of fixational eye movements



Time averages & ageing in financial market time series



$$dX(t) = \mu X(t)dt + \sigma X(t)dW(t)$$

$$\overline{\delta_d^2(\Delta)} = \frac{\int_{t_d}^{T-\Delta} [X(t+\Delta) - X(t)]^2 dt}{T - t_d - \Delta}$$

$$\sim \frac{\Delta}{T - t_d} X_0^2 \left(e^{\sigma^2 T} - e^{\sigma^2 t_d} \right)$$

$$\log \left[\frac{\langle \overline{\delta_d^2(\Delta, t_d)} \rangle}{\langle \overline{\delta^2(\Delta)} \rangle} \right] \sim t_d/T$$

Overview articles

- I Single particle manipulation & tracking:
C Nørregaard, RM, CM Ritter, K Berg-Sørensen & LB Oddershede,
Chem Rev **117**, 4342 (2017)

- II Anomalous diffusion models, WEB & ageing:
RM, JH Jeon, AG Cherstvy & E Barkai, Phys Chem Chem Phys **16**,
24128 (2014)

- III Ageing renewal theory:
JHP Schulz, E Barkai & RM, Phys Rev X **4**, 011028 (2014)

- IIII Anomalous diffusion in membranes:
RM, JH Jeon & AG Cherstvy, Biochimica et Biophysica Acta - Biomem-
branes **1858**, 2451 (2016)

- IIII Polymer translocation:
V Palyulin, T Ala-Nissila & RM, Soft Matter **10**, 9016 (2014)