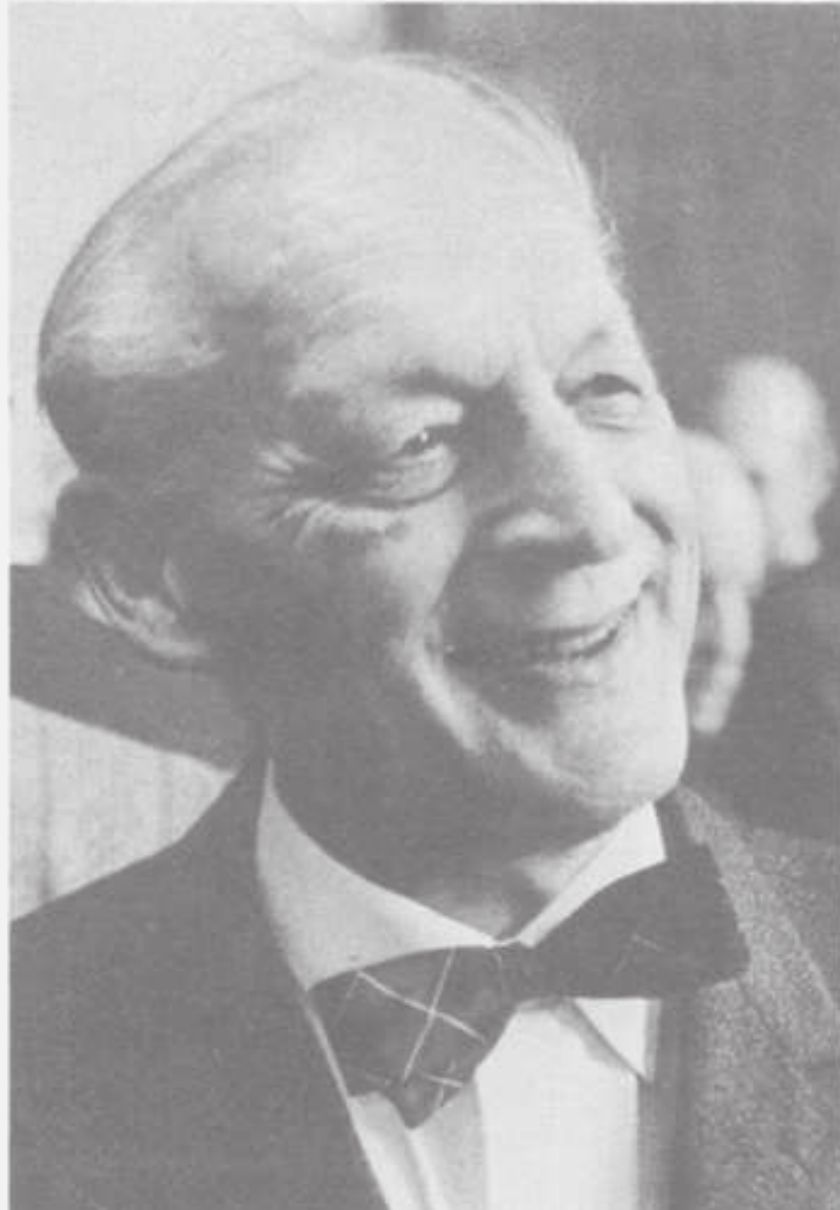


Anomalous diffusion in membranes & cytoplasm

— Heidelberg, 17th April 2018 —

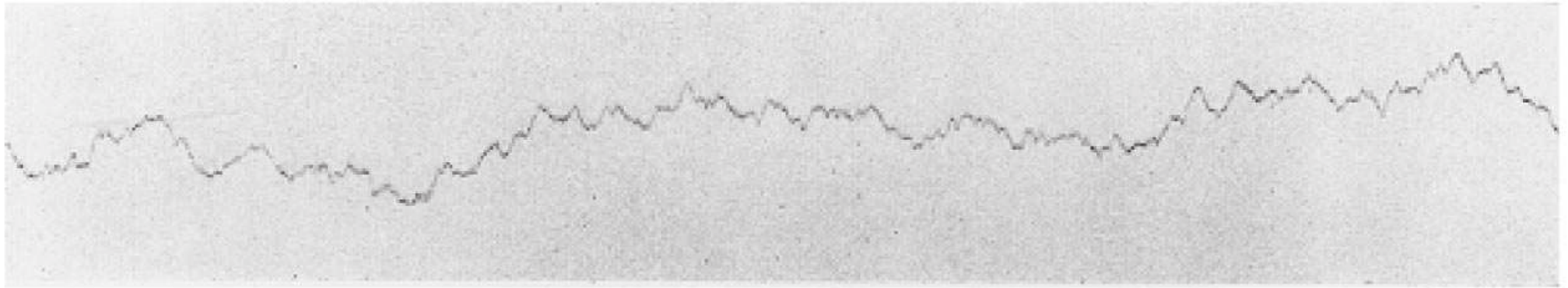


Eugen Kappler: ultimate diffusion measurements



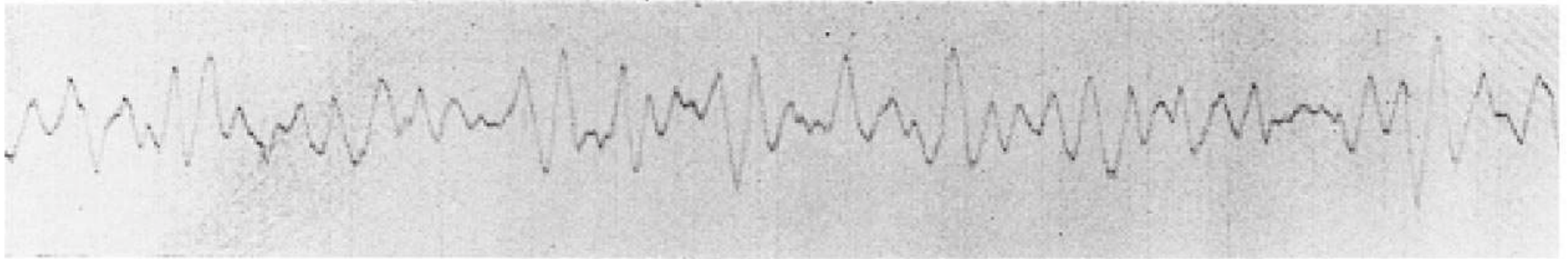
Obituary by L Reimer, Physikalische Blätter Feb 1978 pp 86

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

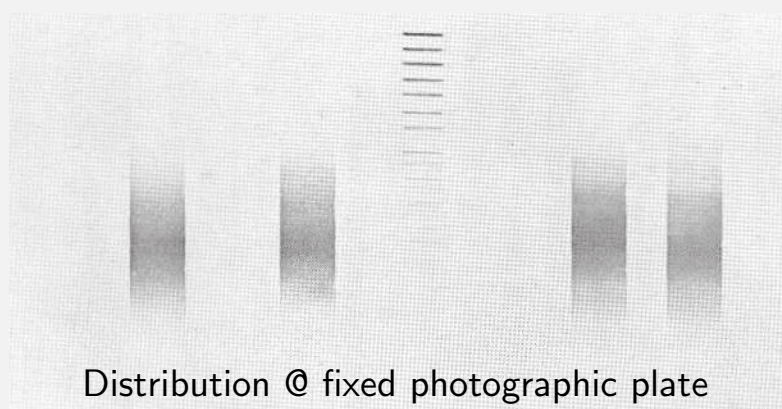
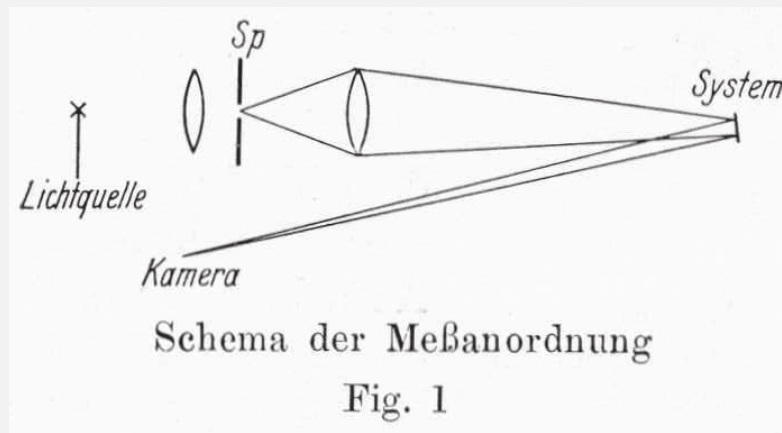
Fig. 5a



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

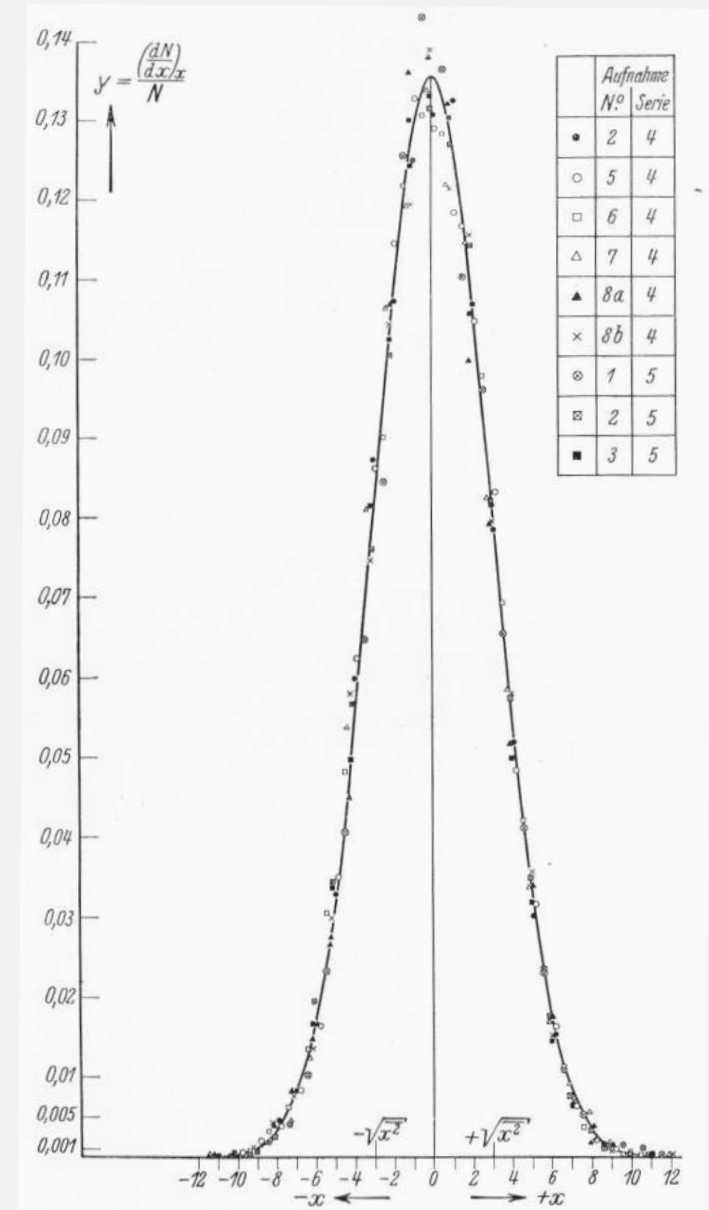
Fig. 5b

Brownian motion & Kappler's diffusion measurements



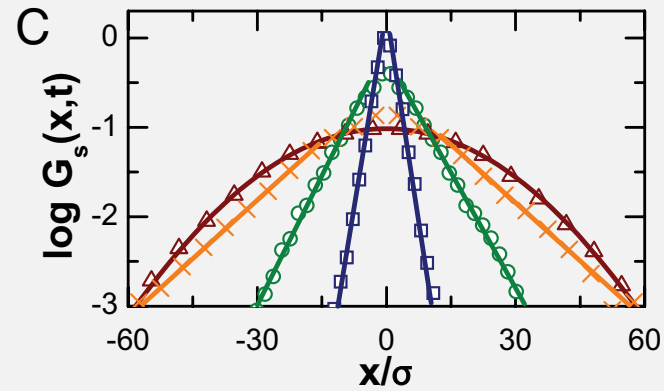
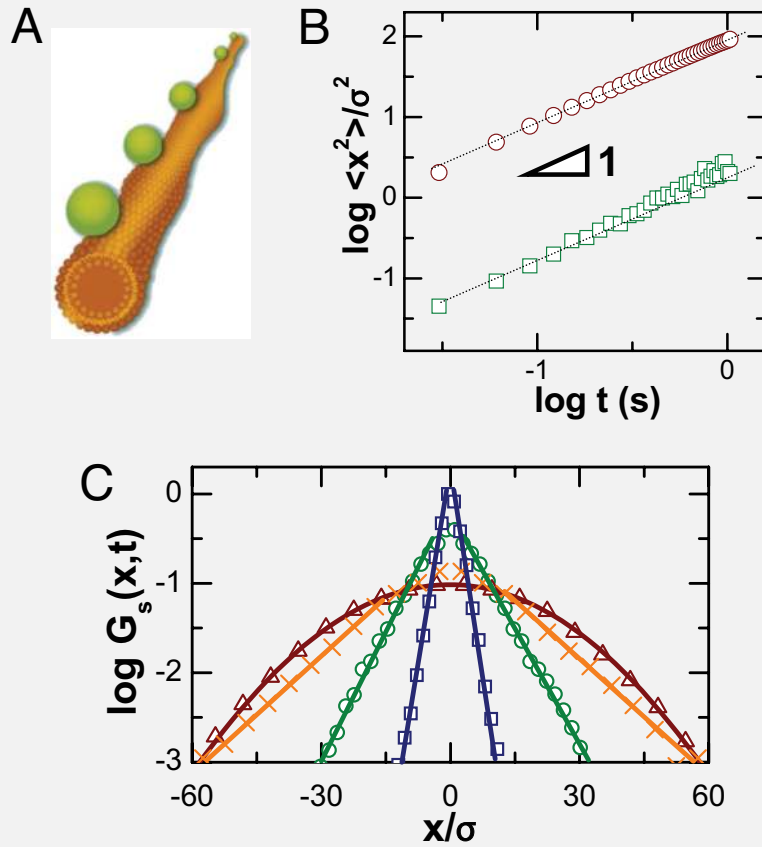
$$\langle r^2(t) \rangle = 2dKt$$

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

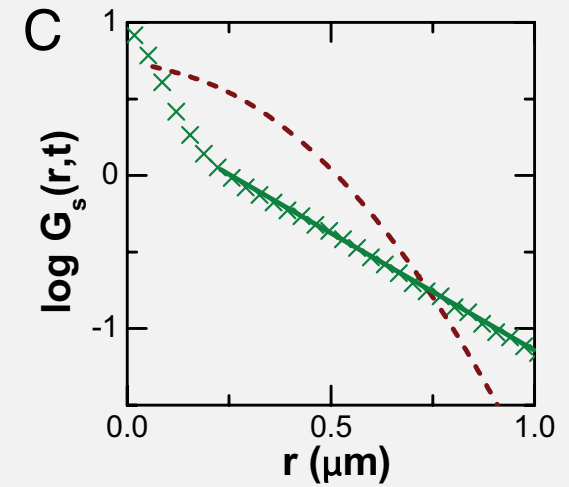
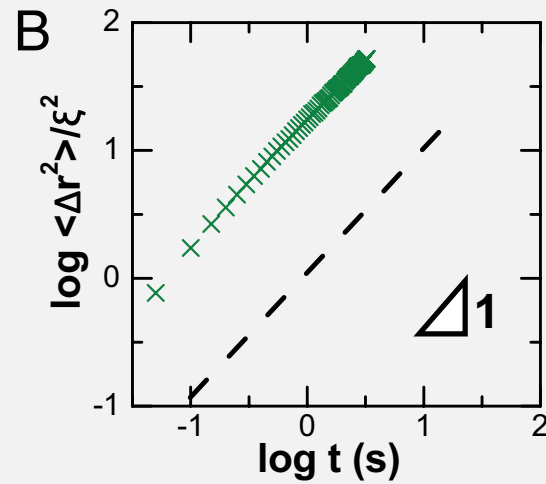
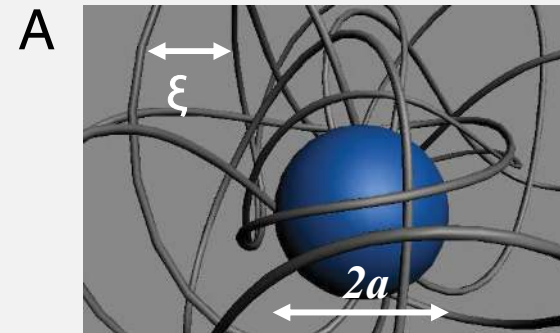


E Kappler, Ann d Physik (1931): $N_A = 60.59 \times 10^{22} \pm 1\%$

When Brownian diffusion is not Gaussian

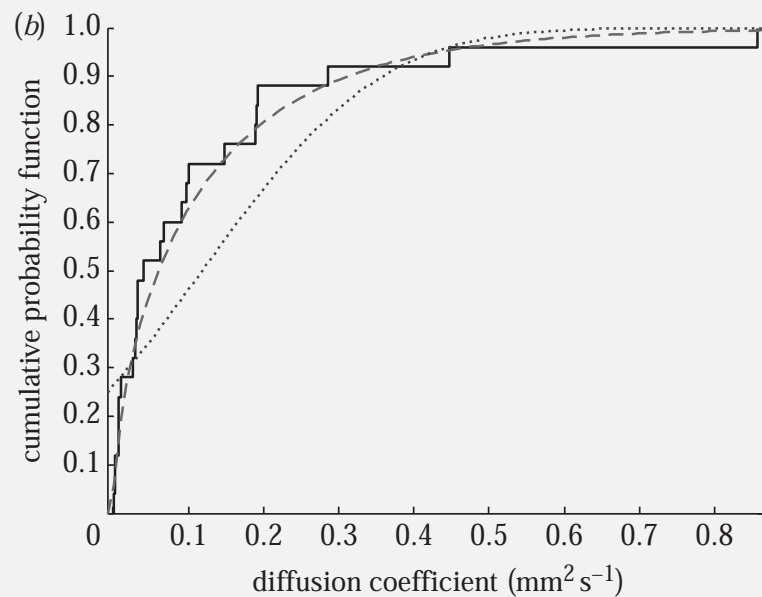
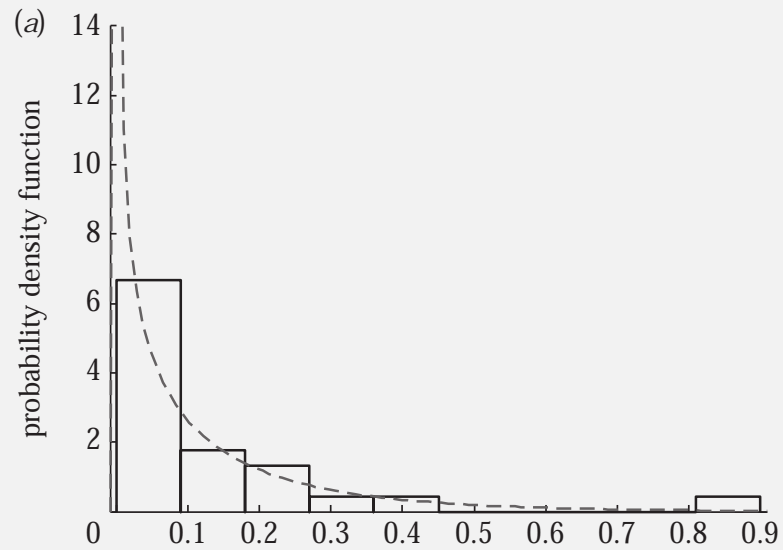


Colloidal beads diffusing on nanotubes

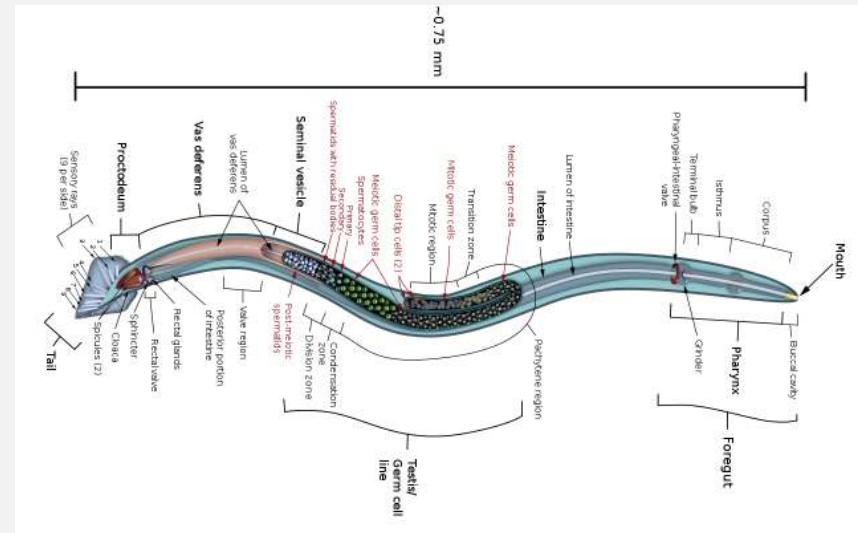


Nanospheres diffusing in entangled actin

Heterogeneous diffusion in population of nematodes



S Hapca, JW Crawford & IM Young, Roy Soc Interface (2009)

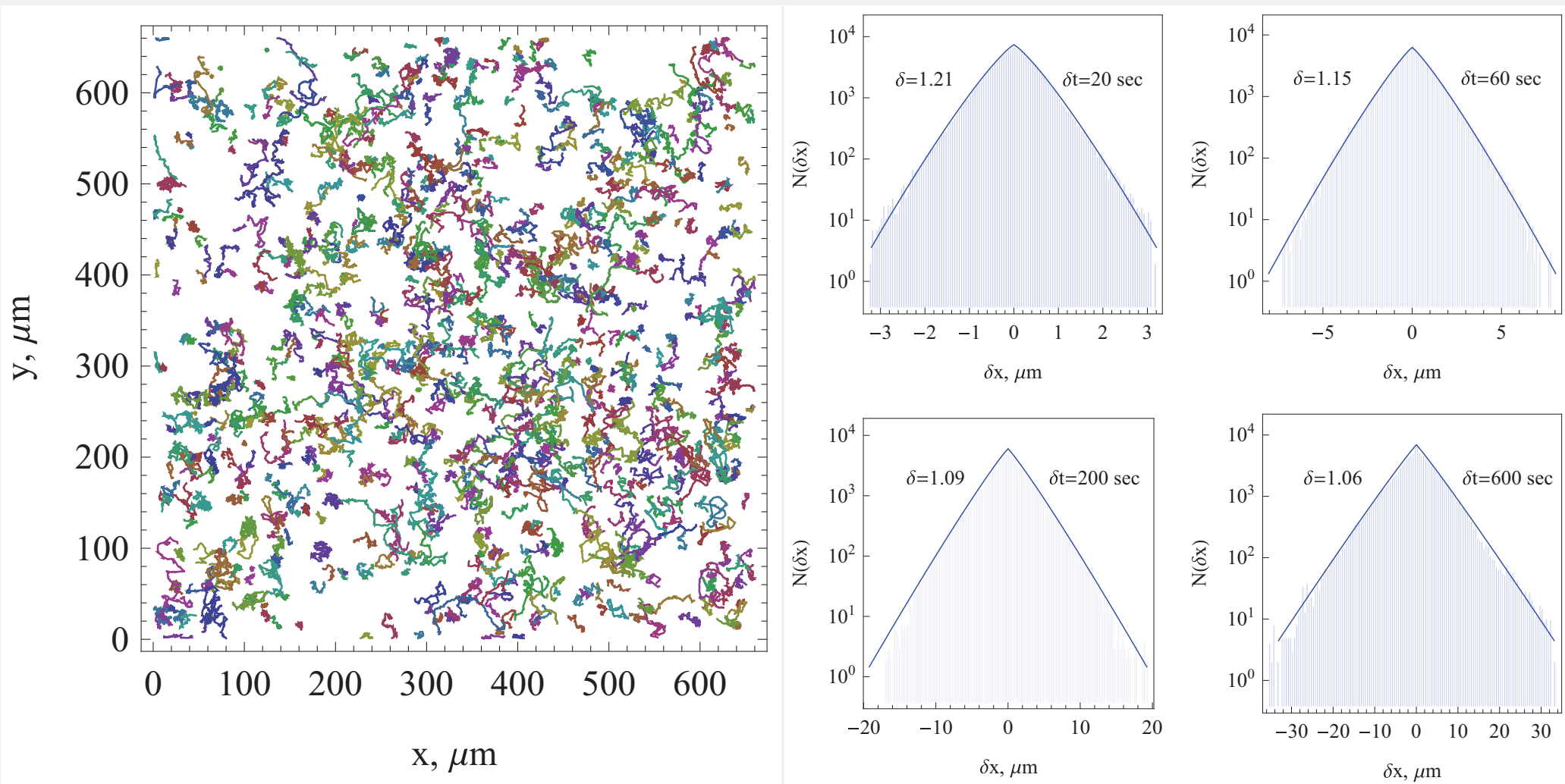


Male *C. elegans* nematode



Soybean cyst nematode & egg

Non-Gaussian diffusion of Dictyostelium cells



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 $P(x, t) = \int_0^\infty G(x, t) p(D) dD$

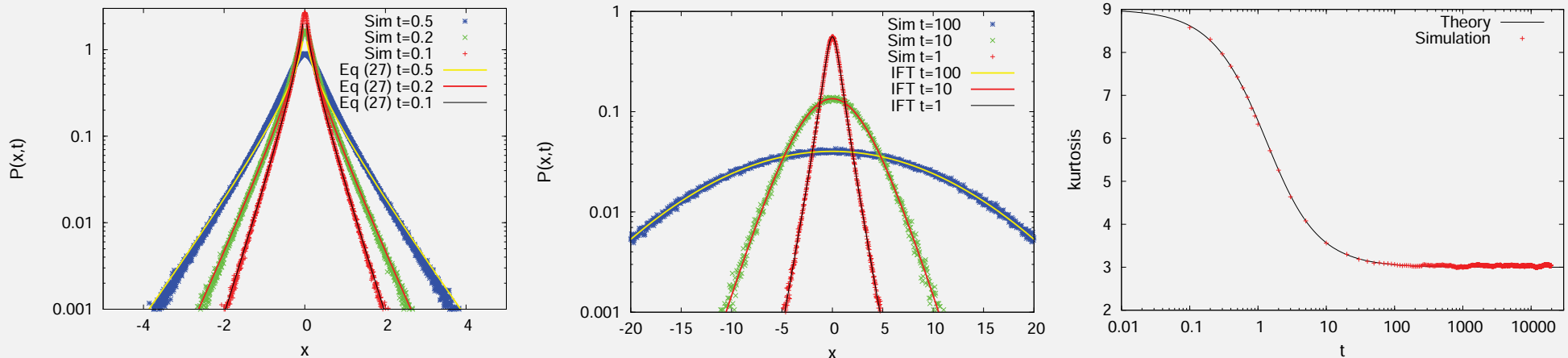
MV Chubinsky & G Slater, PRL (2014); R Jain & KL Sebastian, JPC B (2016): diffusing diffusivity

Our minimal model for diffusing diffusivity:

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

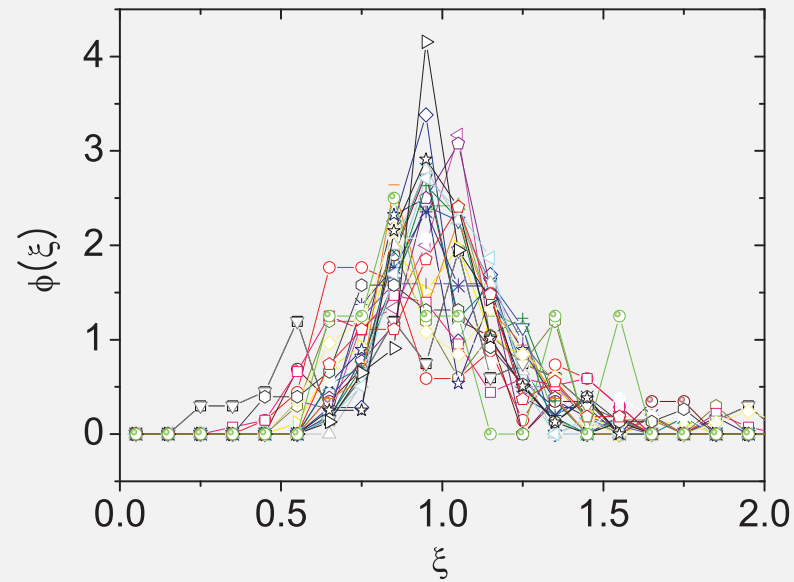
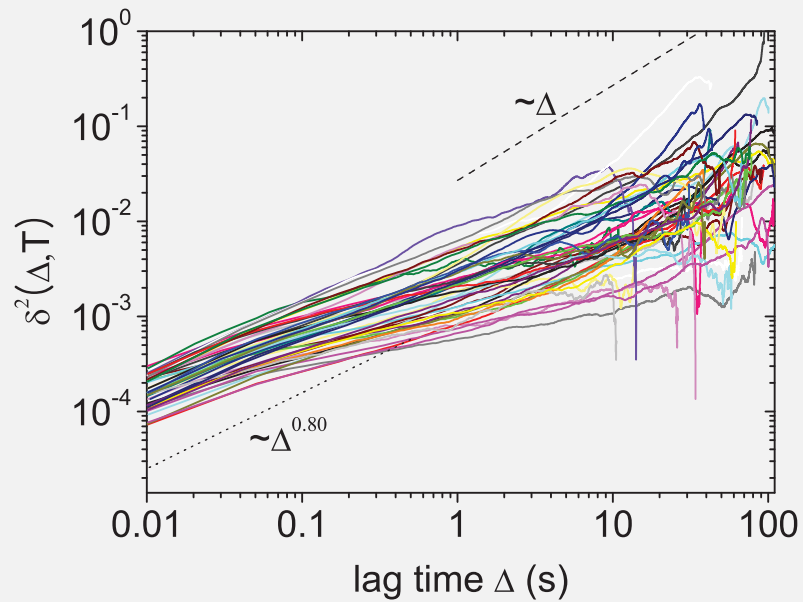
$$D(t) = y^2(t)$$

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

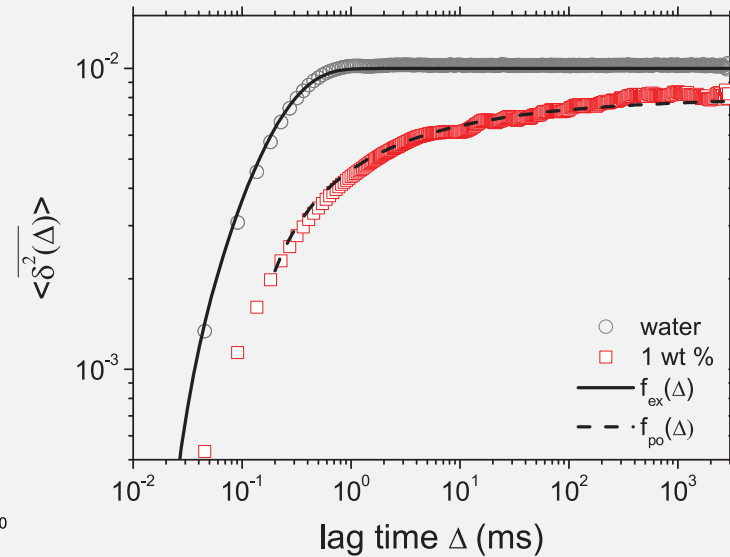
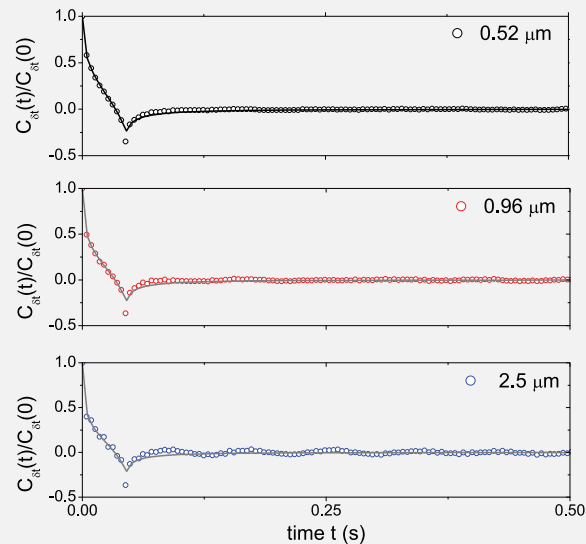
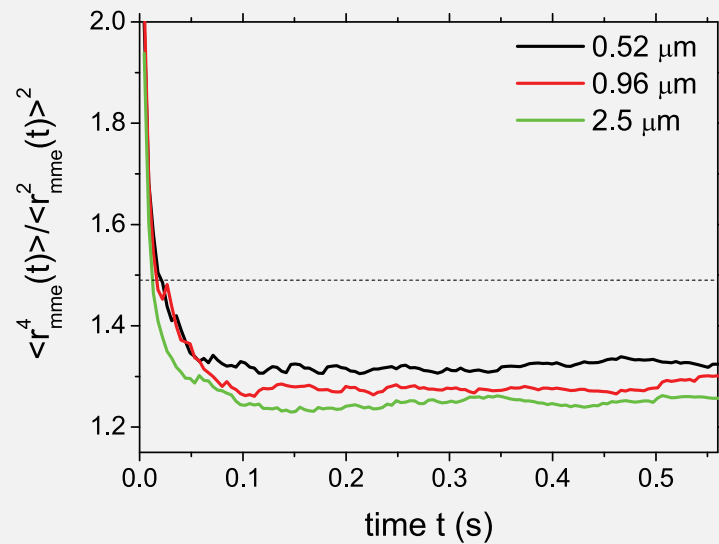


AV Chechkin, F Seno, RM & IM Sokolov, PRX (2017); generalised $\gamma(D)$: V Sposini, AV Chechkin, G Pagnini, F Seno & RM, NJP (2018) 8

Passive motion of submicron tracers in cells is viscoelastic



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



JH Jeon, . . . L Oddershede & RM, PRL (2011); JH Jeon, N Leijnse, L Oddershede & RM, NJP (2013)

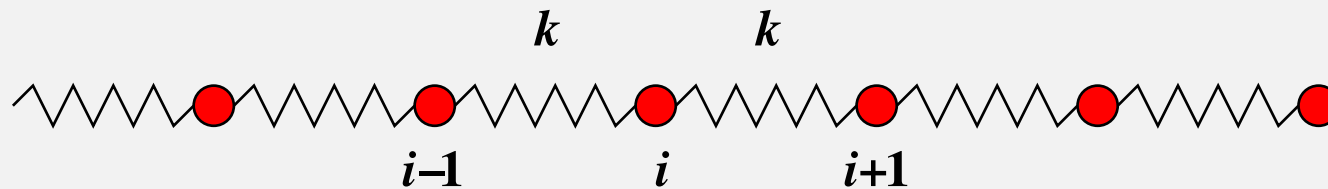
Fractional Langevin equations in viscoelastic systems

Coupled set of Markovian processes (e.g., Rouse model for polymers):

$$m_i \ddot{\mathbf{r}}_i(t) = k(\mathbf{r}_i - \mathbf{r}_{i+1}) + k(\mathbf{r}_{i-1} - \mathbf{r}_i) - \eta \dot{\mathbf{r}}_i + \sqrt{2\eta k_B T} \times \boldsymbol{\zeta}_i(t)$$

Integrating out all d.o.f. but one $\leadsto$ Generalised Langevin equation (GLE):

$$m \ddot{\mathbf{r}}(t) + \int_0^t \eta(t-t') \dot{\mathbf{r}}(t') dt' = \boldsymbol{\zeta}(t) \therefore \eta(t) = \sum_{i=1}^N a_i(k) e^{-\nu_i t} \rightarrow t^{-\alpha}$$



Kubo fluctuation dissipation theorem (in conti limit $\eta(t) \simeq t^{-\alpha}$ fractional Gaussian noise):

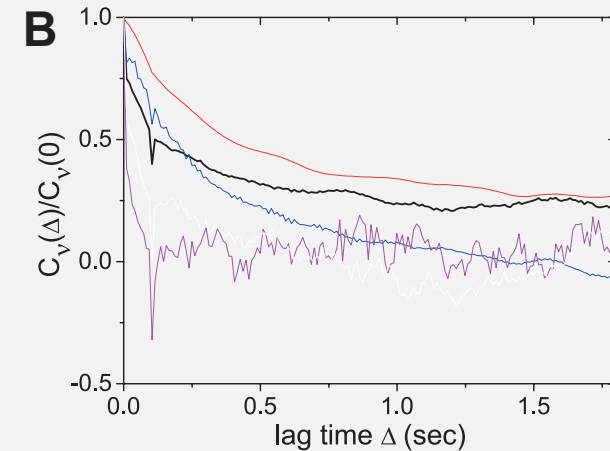
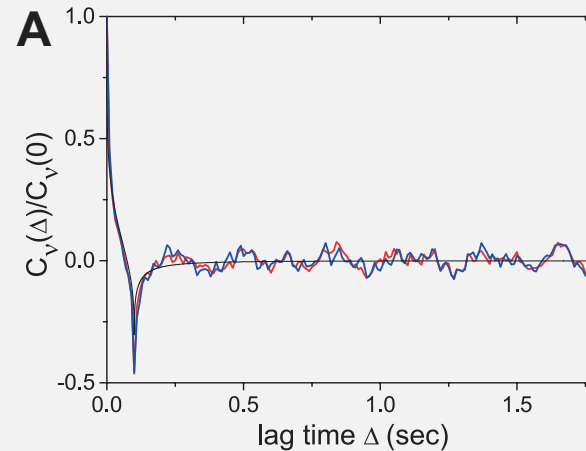
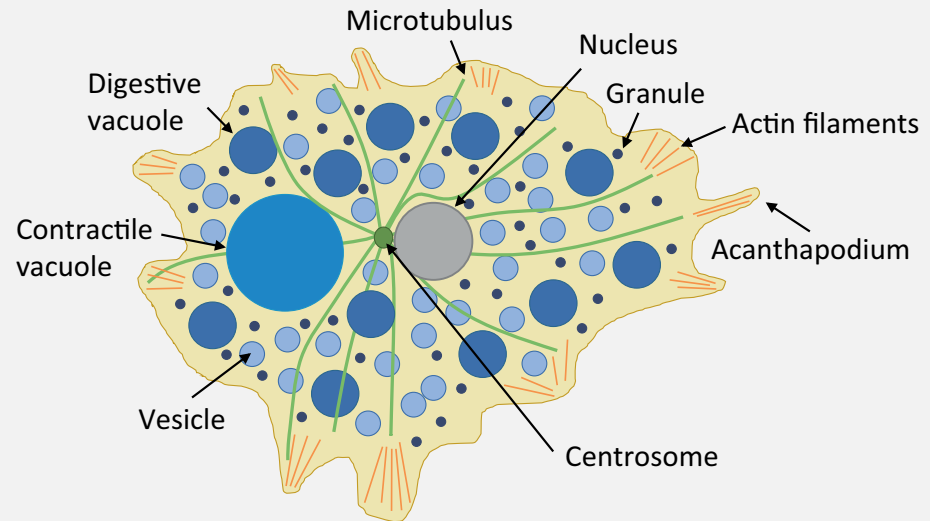
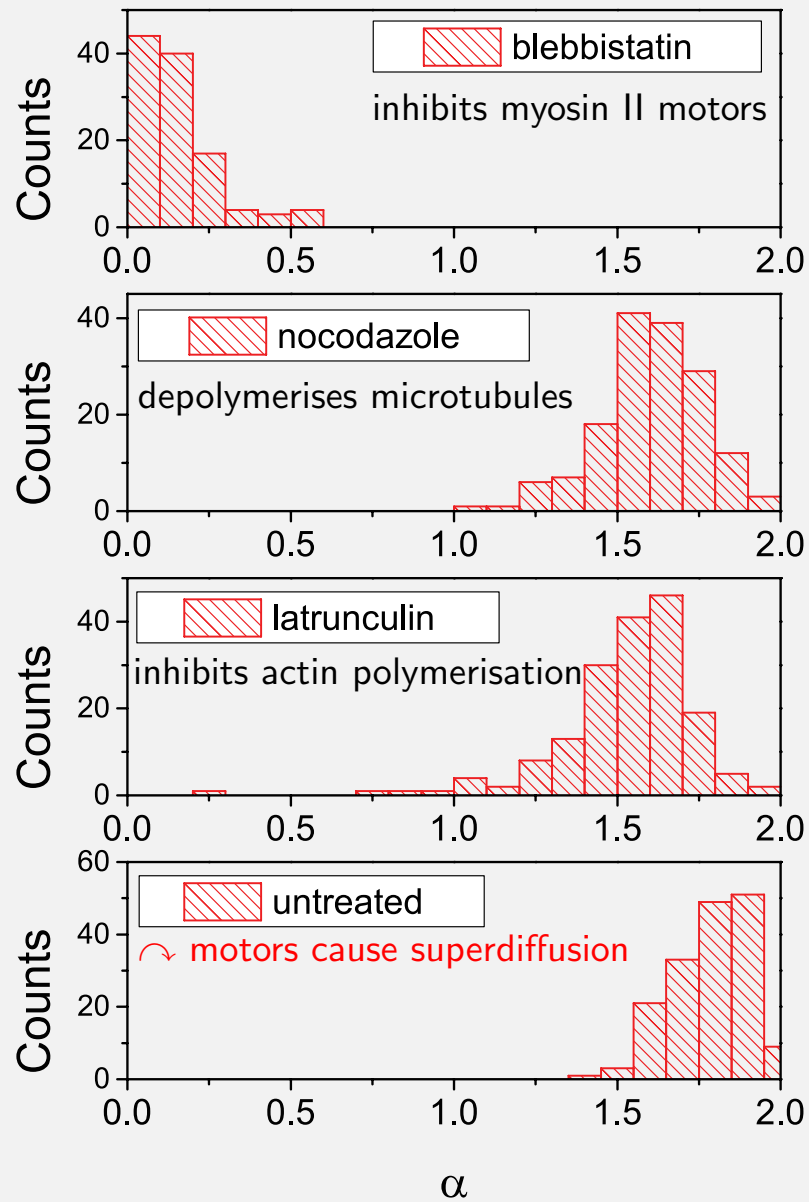
$$\langle \zeta_i(t) \zeta_j(t') \rangle = \delta_{ij} k_B T \eta(|t - t'|)$$

$\leadsto$ fractional Langevin equation. Overdamped limit: Mandelbrot's FBM

Quantum mechanics: Nakajima-Zwanzig equation using projection operators

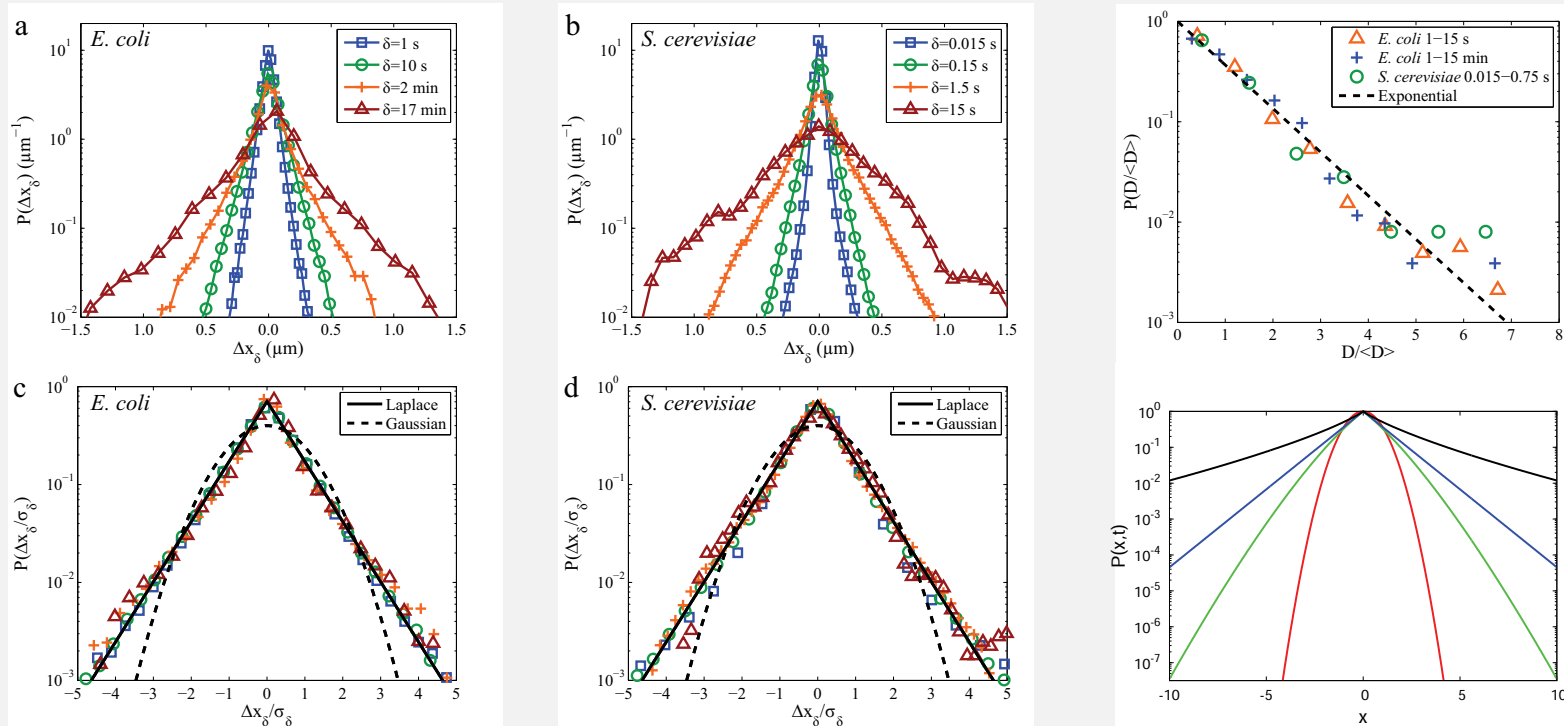
Hydrodynamics: Basset force with $\eta(t) \simeq t^{-1/2}$ due to hydrodynamic backflow

Superdiffusion in supercrowded *Acanthamoeba castellani*



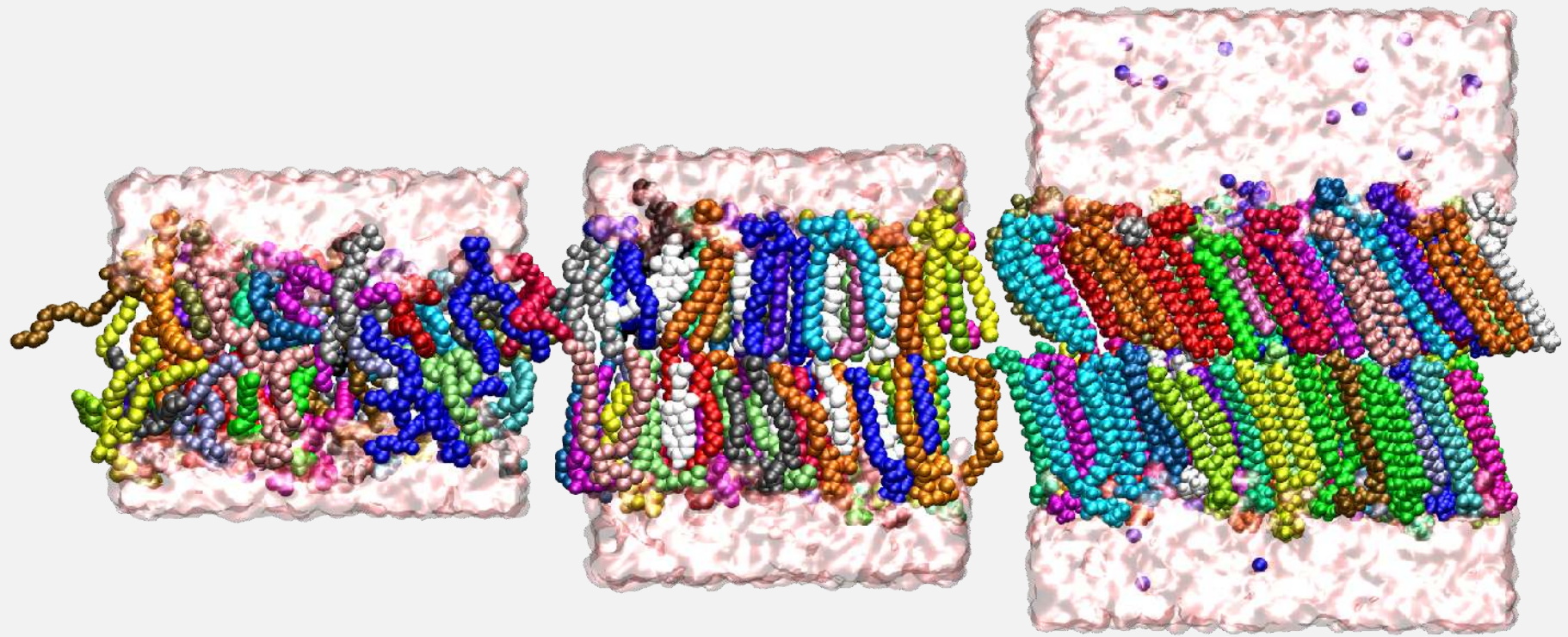
Non-Gaussian diffusion in viscoelastic systems

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)

Single lipid motion in bilayer membrane MD simulations

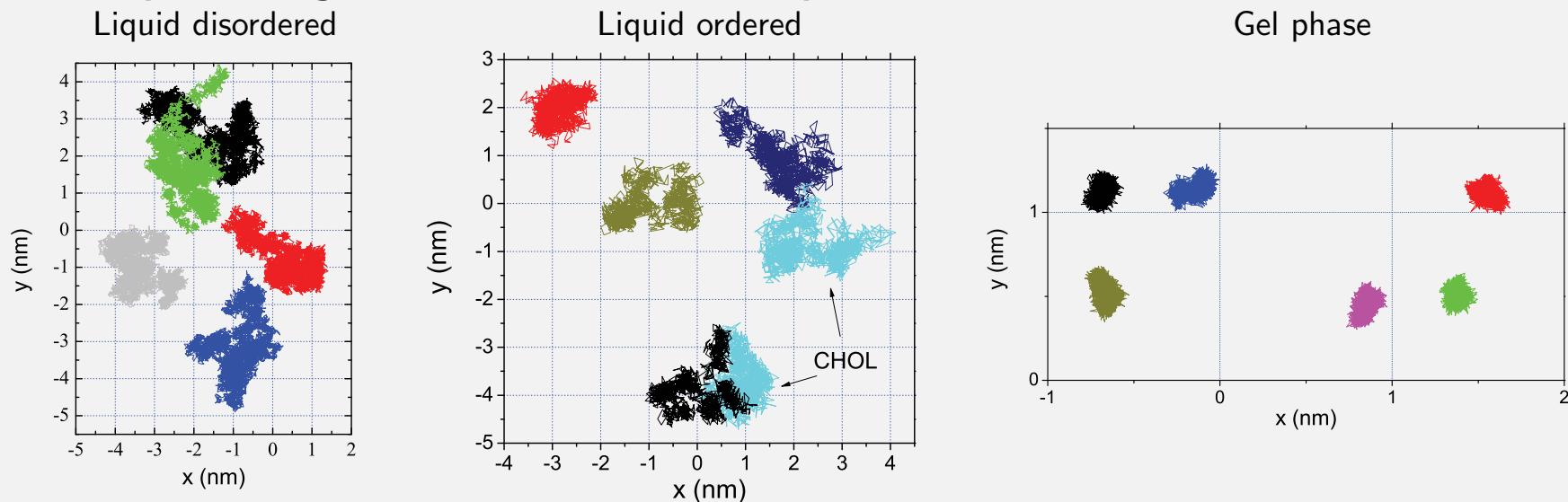


Liquid disordered

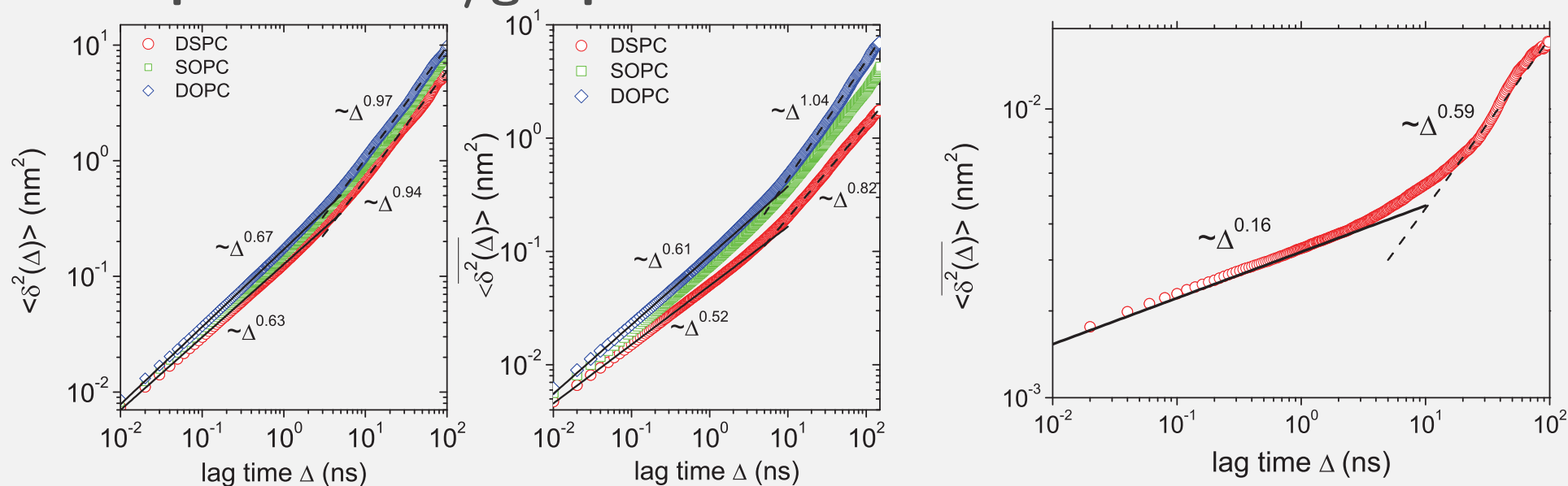
Liquid ordered

Gel phase

Sample trajectories for the lipid & cholesterol motion



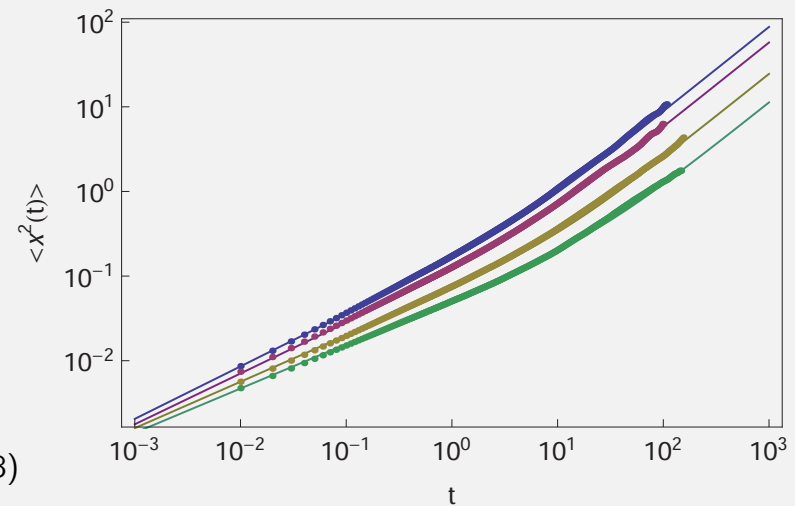
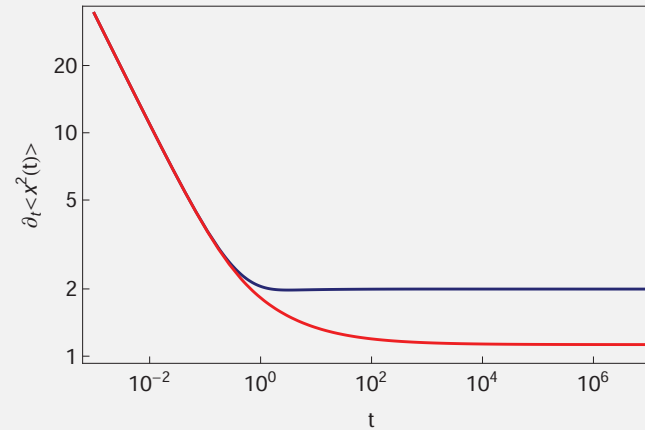
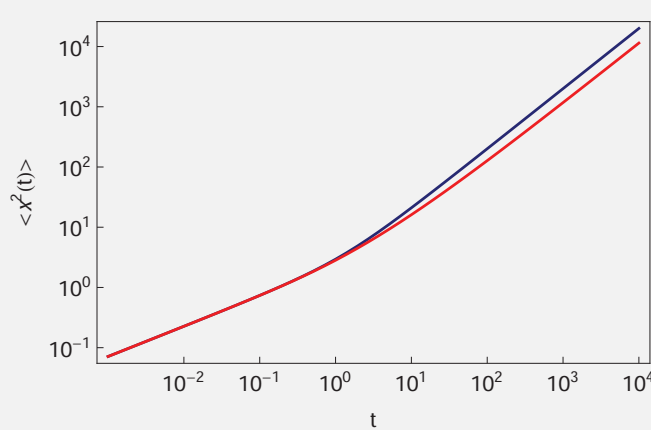
Liquid ordered/gel phases: extended anomalous diffusion



Tempered FBM & FLE motion: sub- to normal diffusion

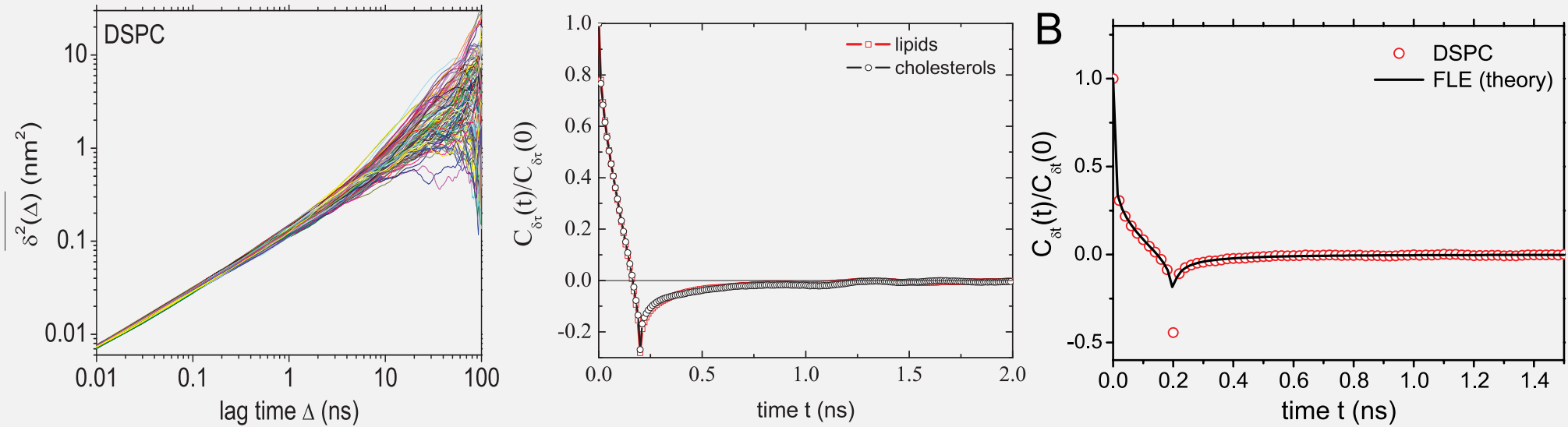
Consider tempered fGn:

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

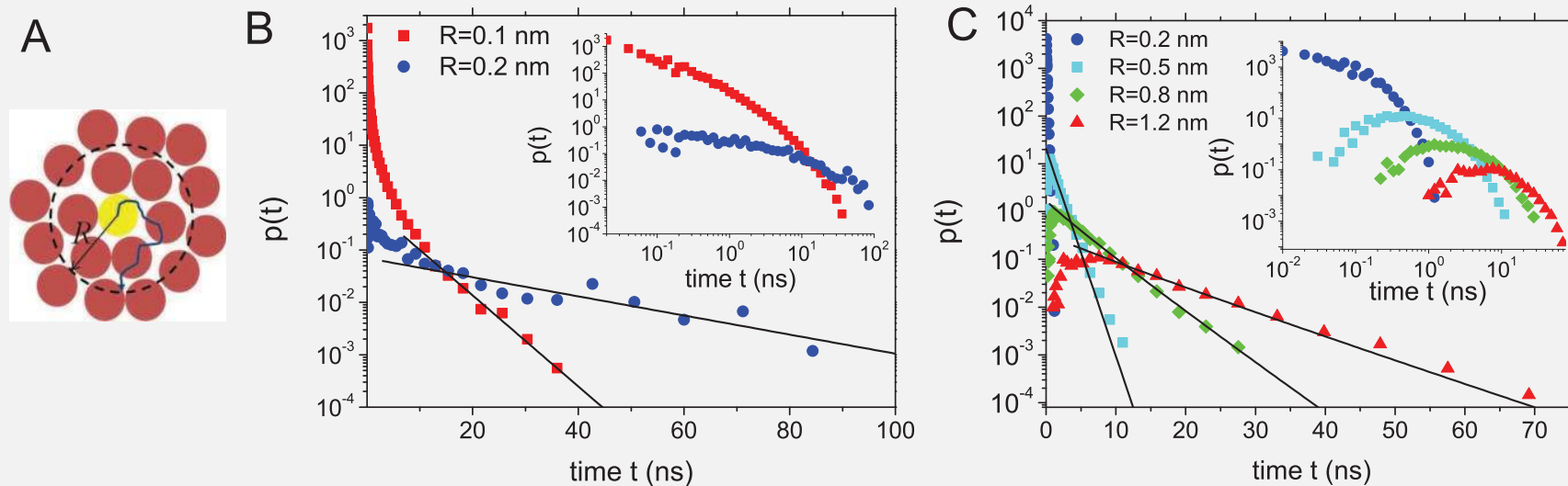


D Molina-Garcia, T Sandev, G Pagnini, AV Chechkin & RM (2018)

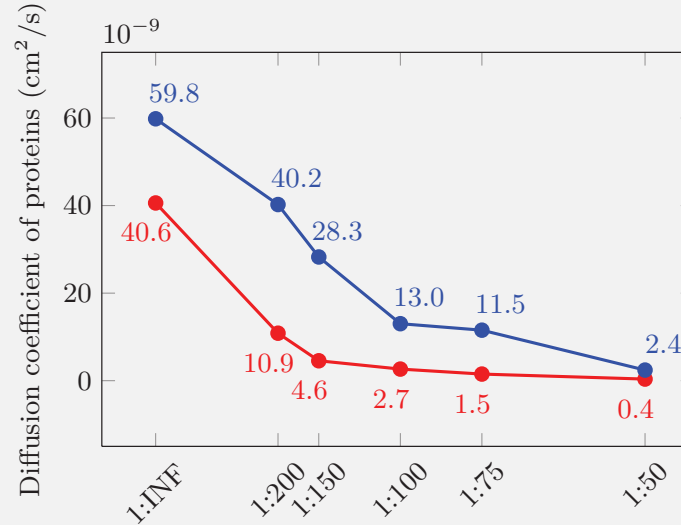
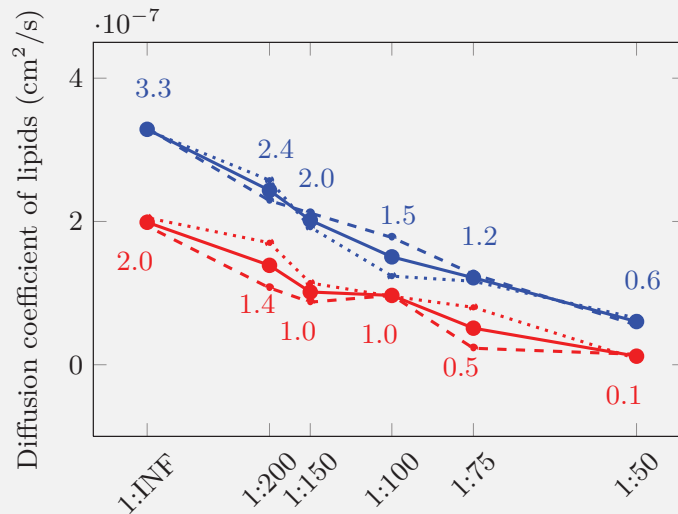
Reproducible TA MSD & antipersistent correlations



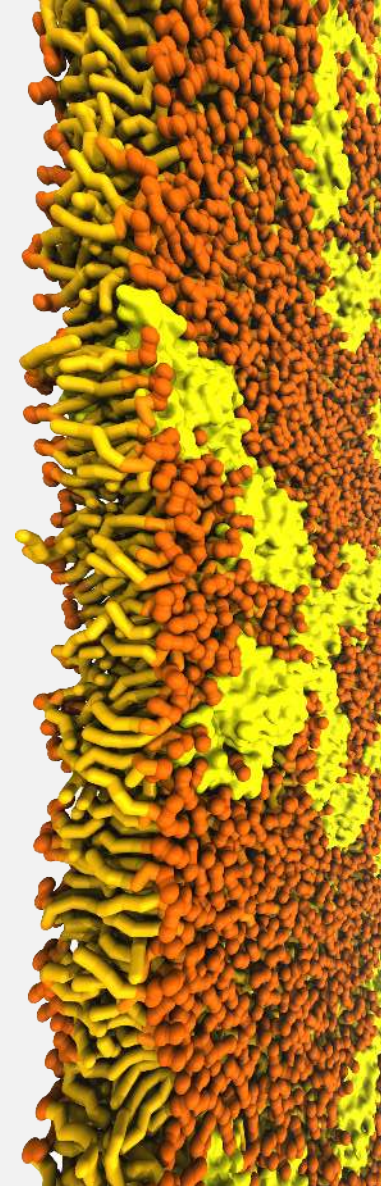
Rattling dynamics: exptl first passage PDF $\rightarrow$ FLE motion



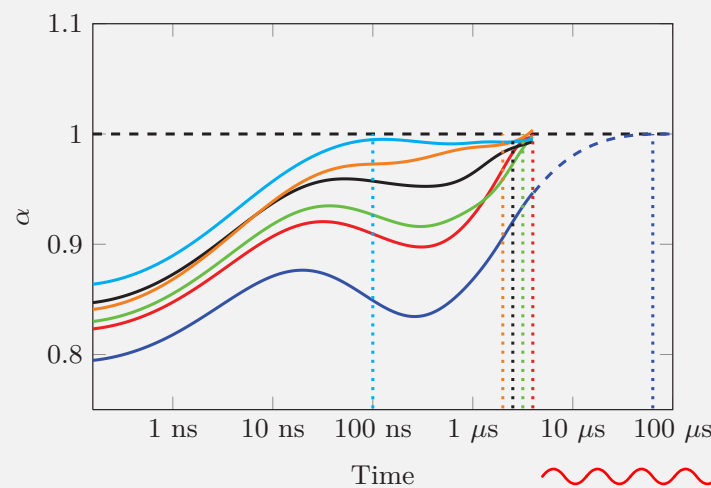
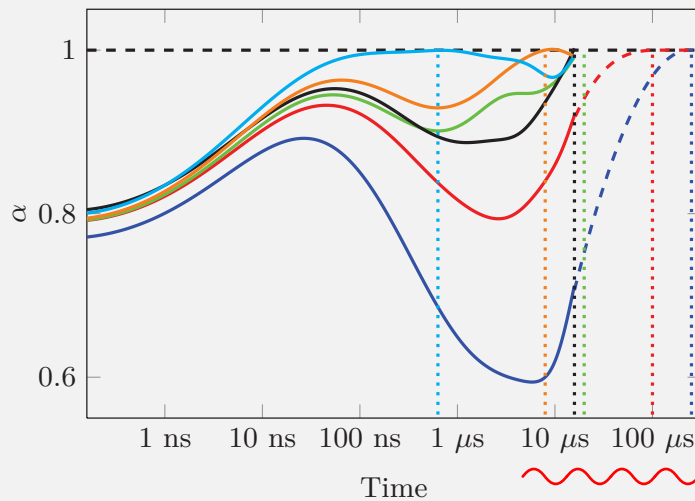
Protein crowded membranes reduce effective mobility



Blue: DLPC. Red: DPPC

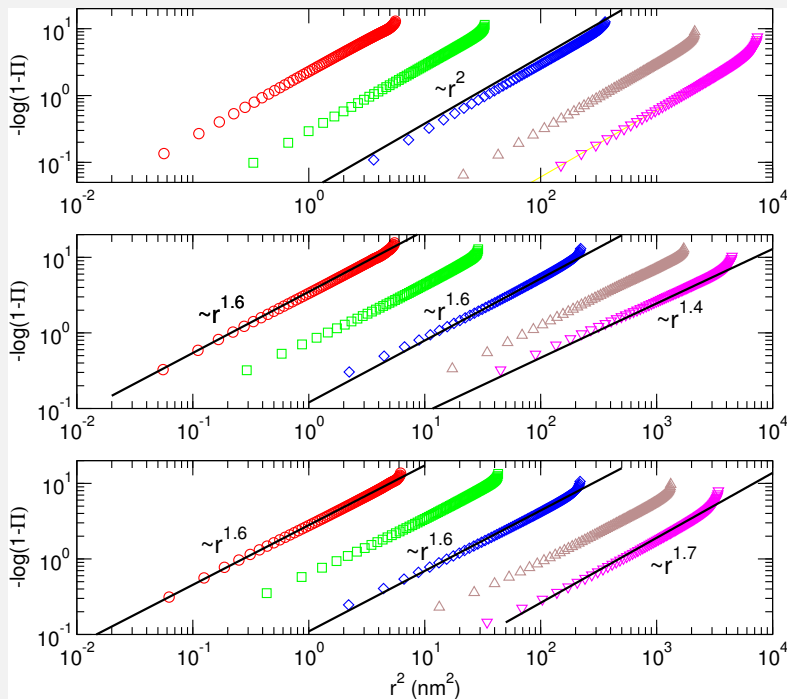
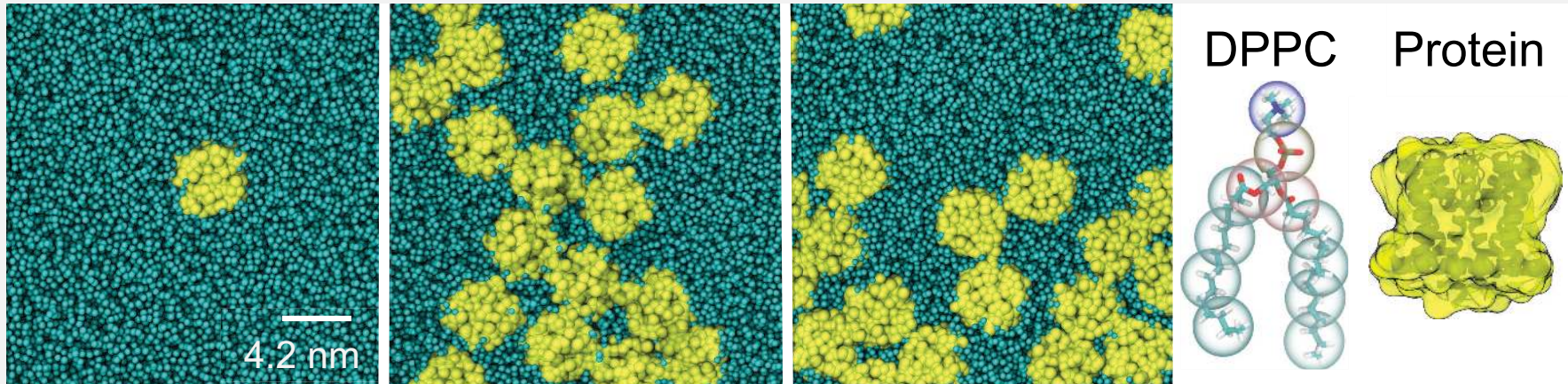


Protein crowding effects anomalous lipid diffusion



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

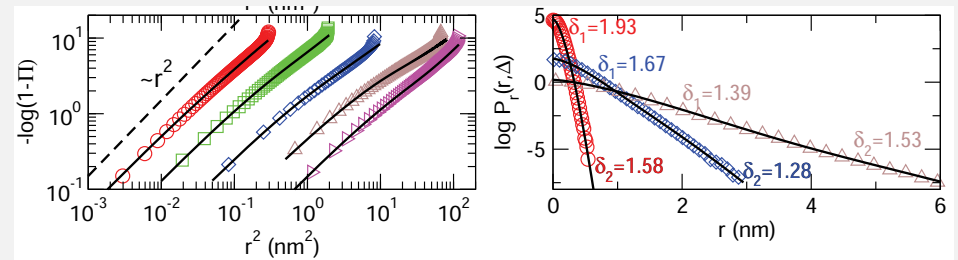
Crowding in membranes: non-Gaussian lipid/protein diffusion



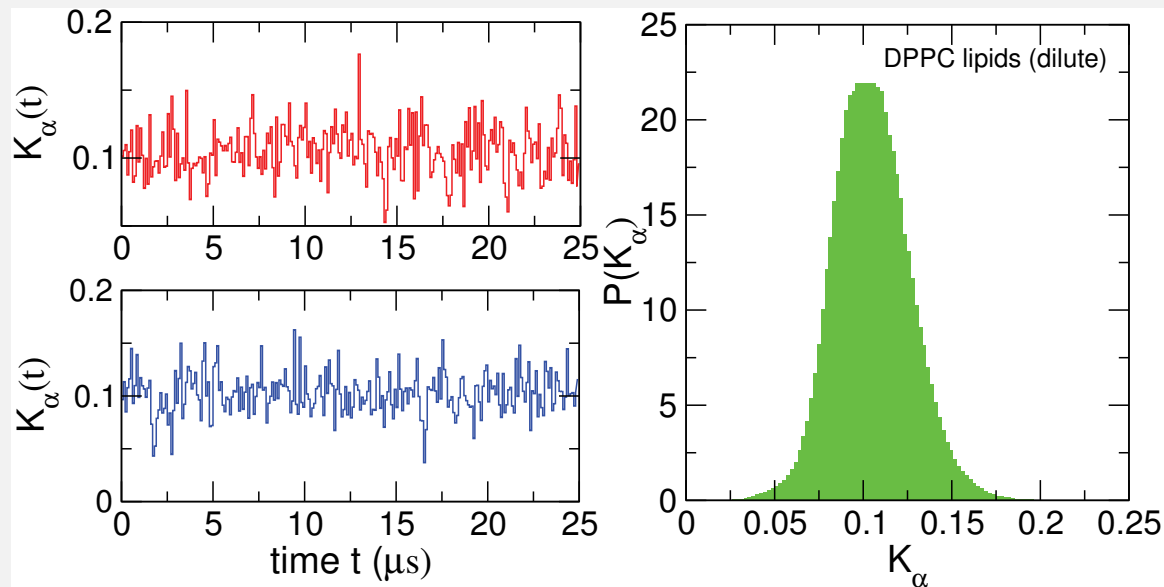
Dilute membrane: $P(r, t)$ Gauss

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

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

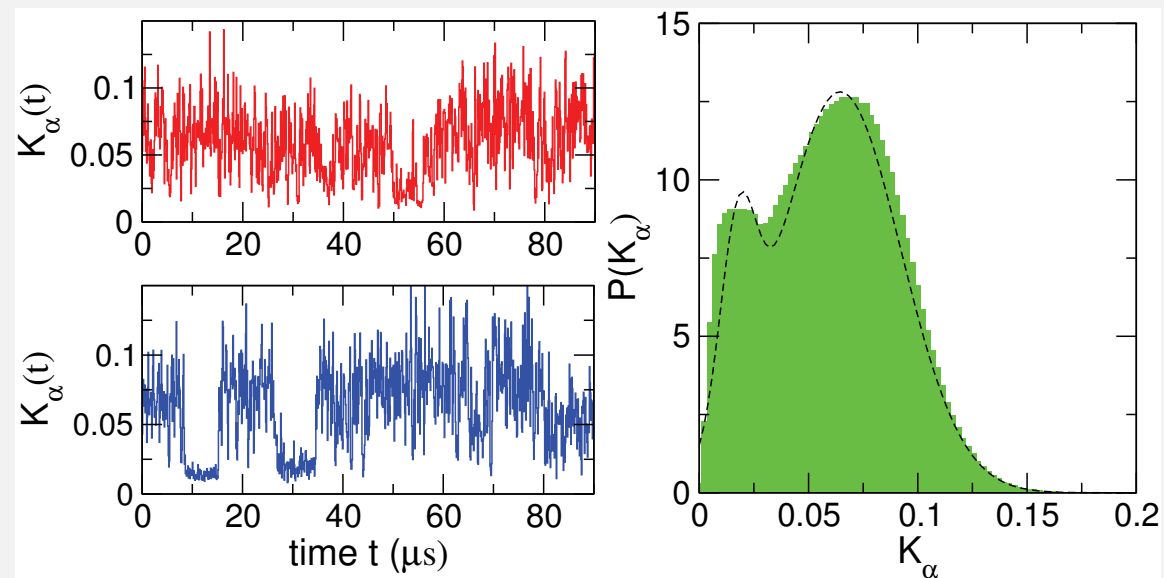


Crowding in membranes increases dynamic heterogeneity



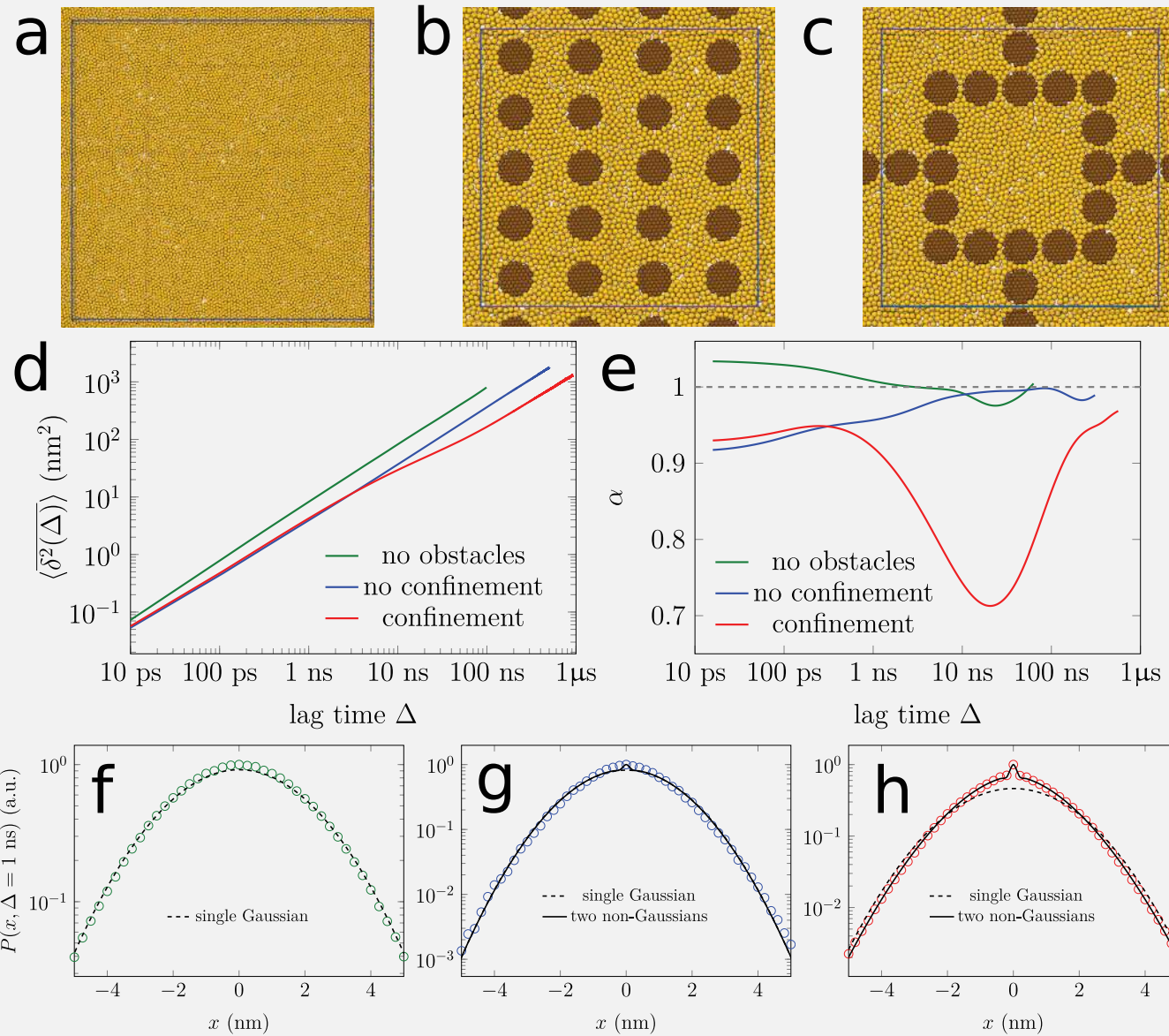
Diffusivity(t) for two lipids

Lipid diffusivity, dilute membrane

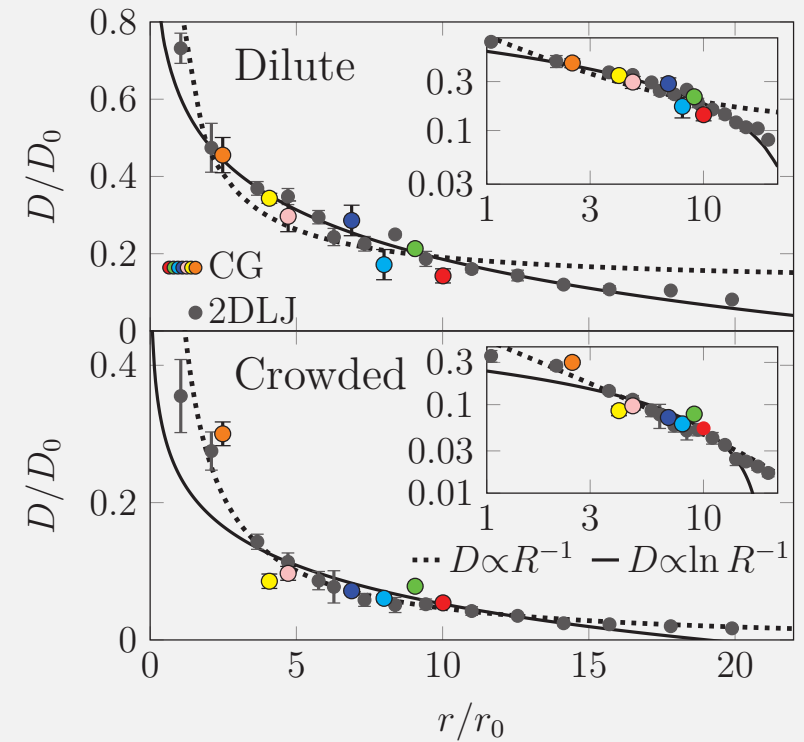
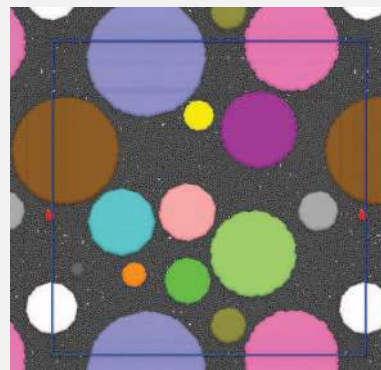
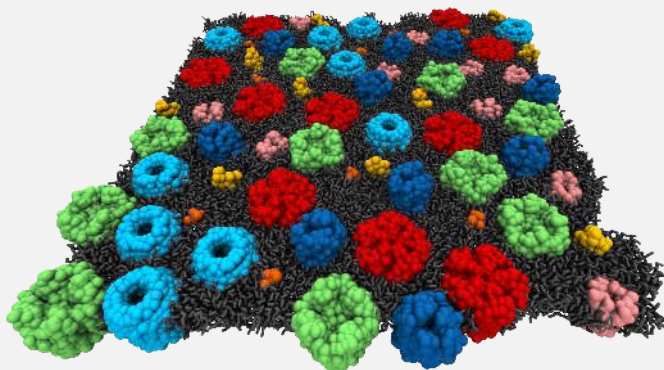
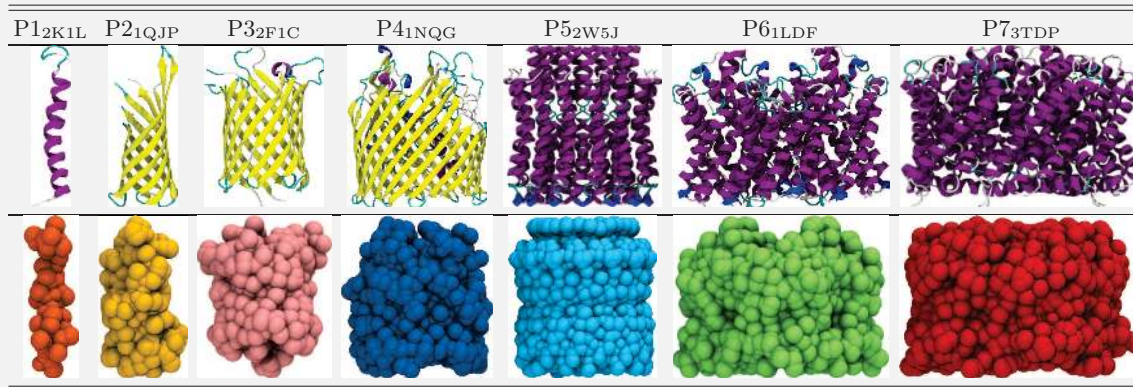


Lipid diffusivity, crowded membrane

Confinement in argon system shows geometric origin



Geometry-induced violation of Saffman-Delbrück relation



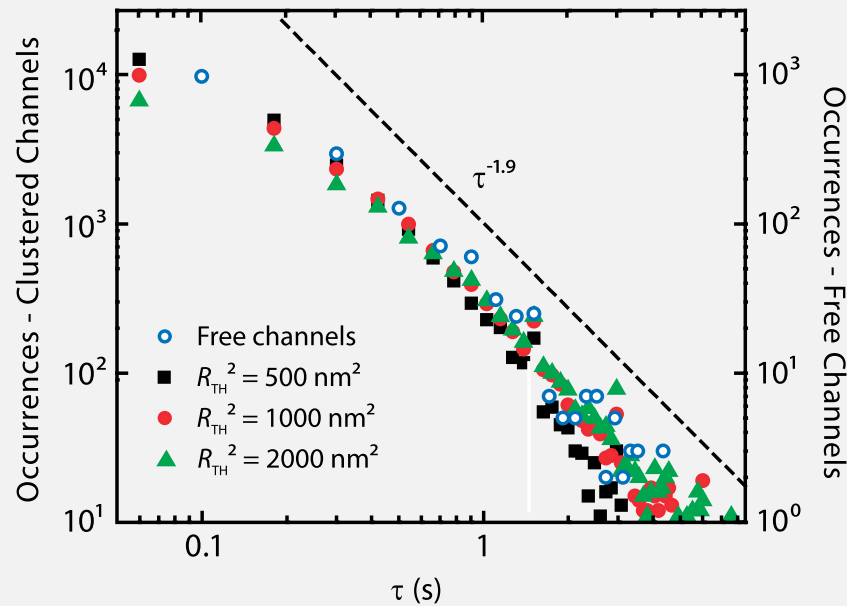
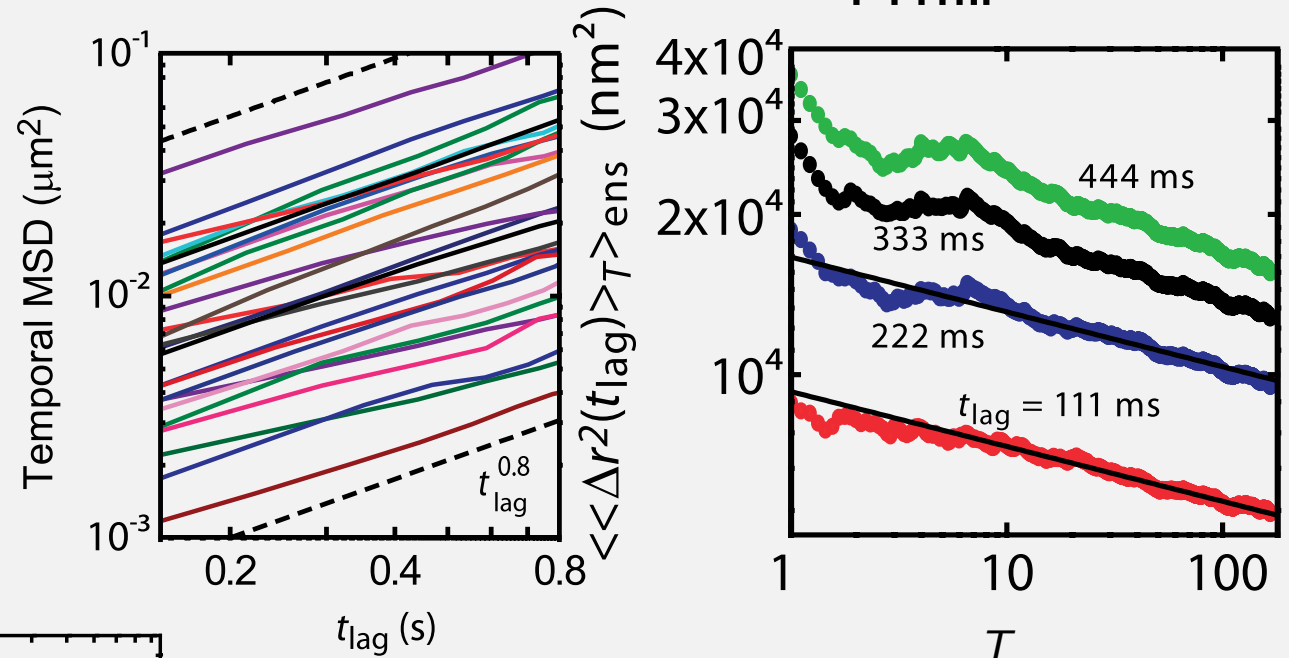
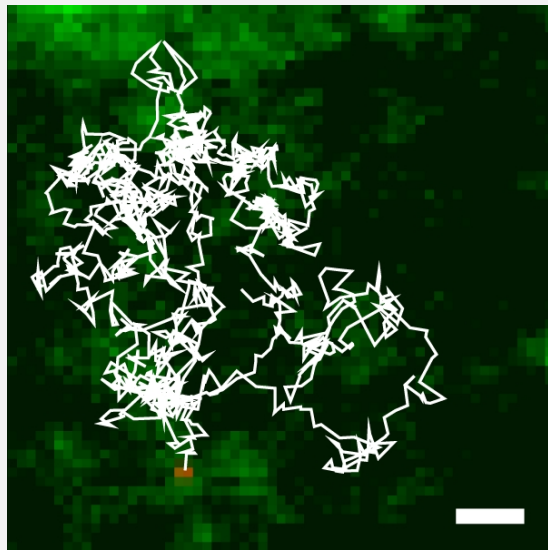
Dilute system: Saffman-Delbrück law

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

Crowded membrane & 2DLJ discs:

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

CTRW-like motion of Ka channels in plasma membrane

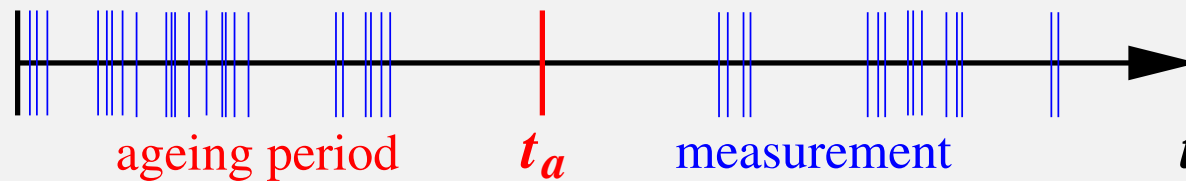
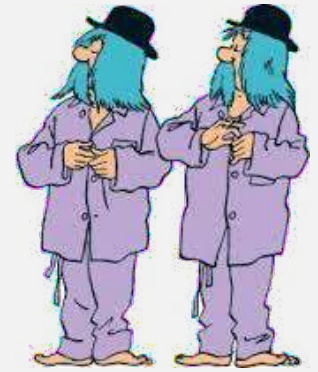


$$\psi(\tau) \simeq \tau^{-1-\alpha} \text{ scale free}$$

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

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

Ageing effects in single trajectory time averages

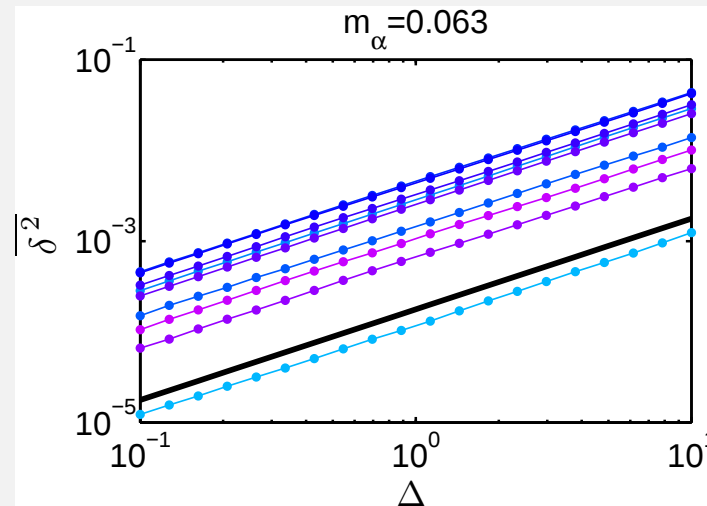
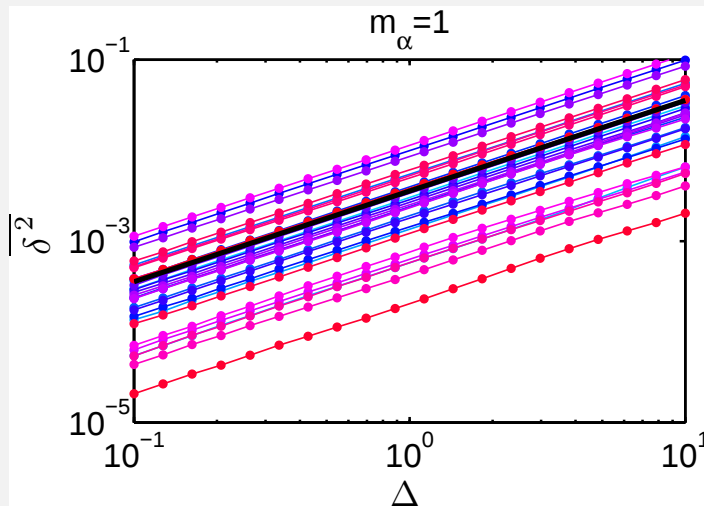


Ageing mean squared displacement ($\Lambda(z) = (1 + z)^\alpha - z^\alpha$)

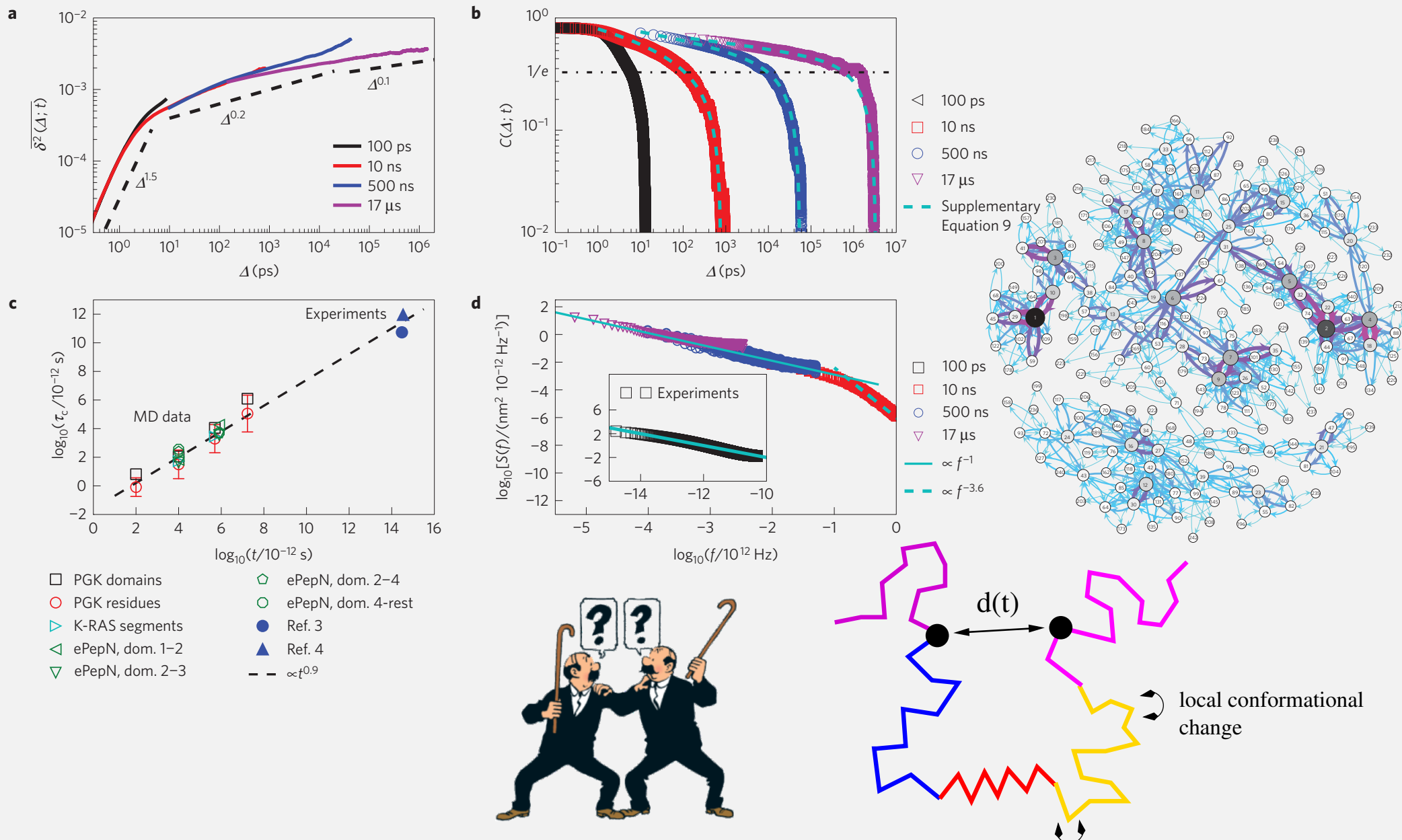
$$\left\langle \overline{\delta^2(\Delta)} \right\rangle_a = \frac{\Lambda_\alpha(t_a/T) g(\Delta)}{\Gamma(1 + \alpha) T^{1-\alpha}} \Leftrightarrow \langle x^2(t) \rangle_a \simeq \begin{cases} t^\alpha, & t_a \ll t \\ t_a^{\alpha-1} t, & t_a \gg t \end{cases}$$

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

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

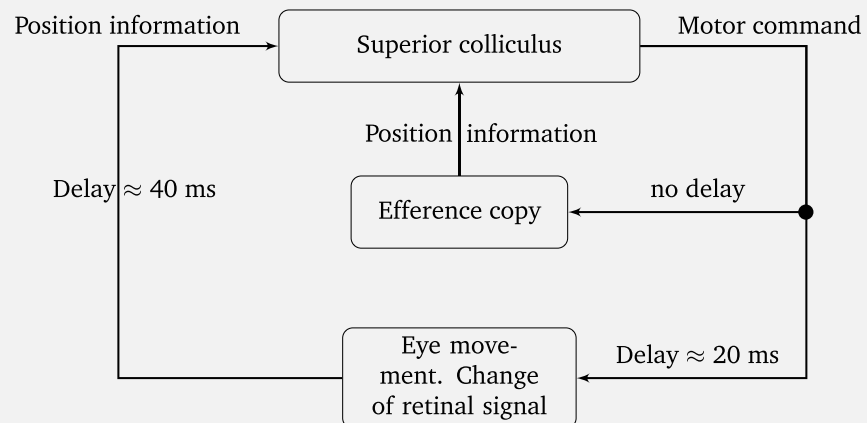
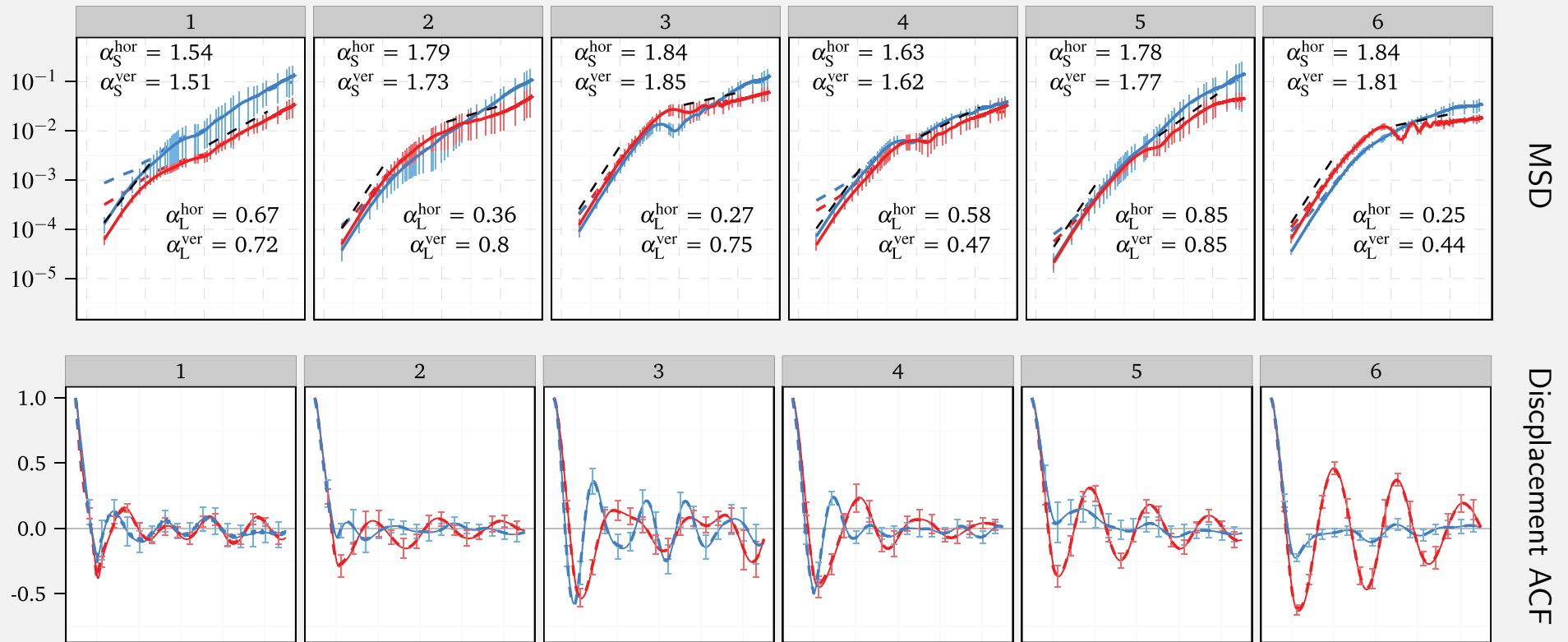


Self-similar internal protein dynamics: 13 decades of ageing



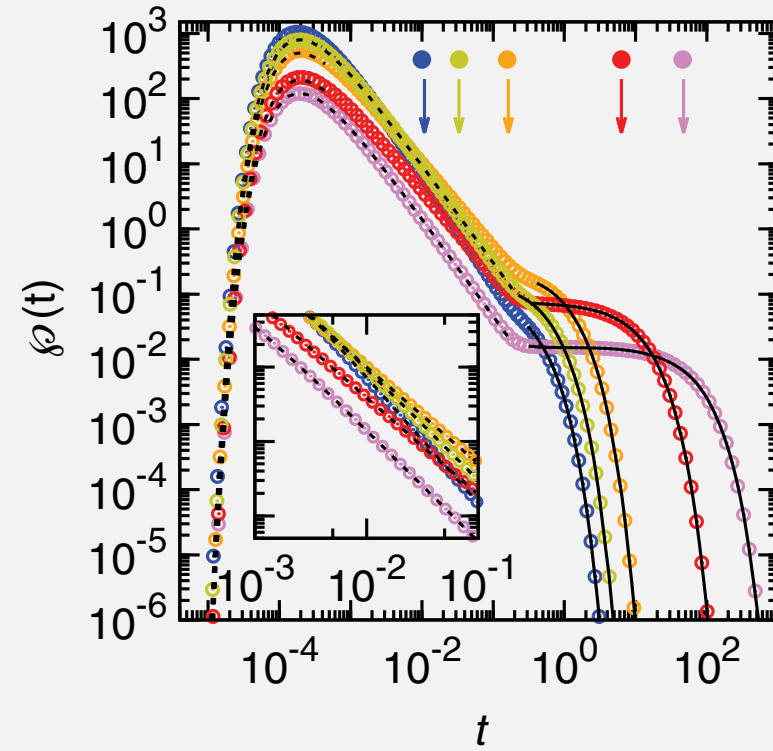
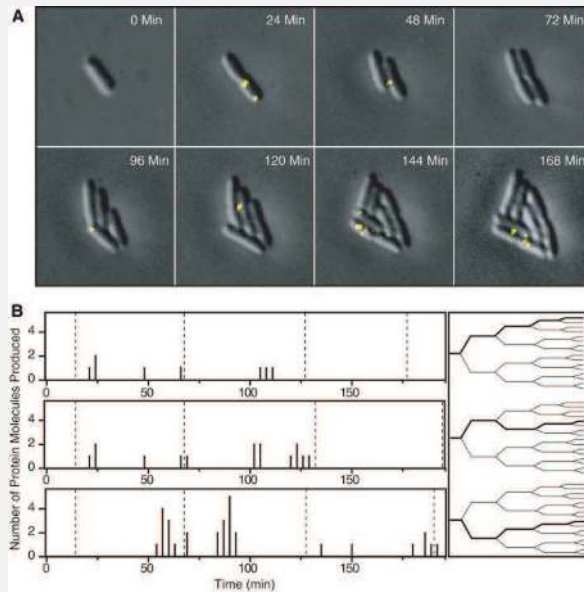
X Hu, L Hong, MD Smith, T Neusius, X Cheng & JC Smith, Nature Phys (2016); N&V RM Nature Phys (2016)

Stochasticity of fixational eye movements

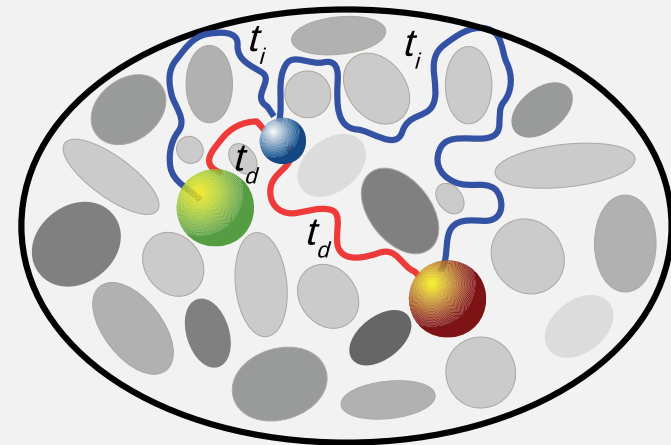
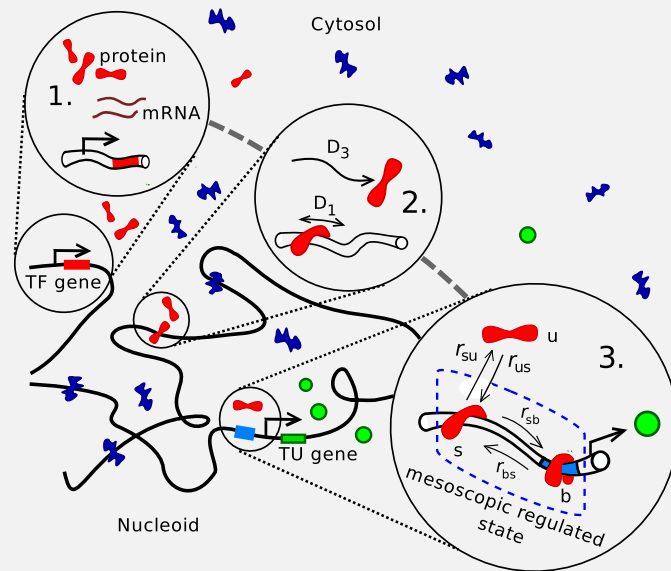


First-past-the-post: few-encounter limit in cell signalling

Yu et al, Science (2006)

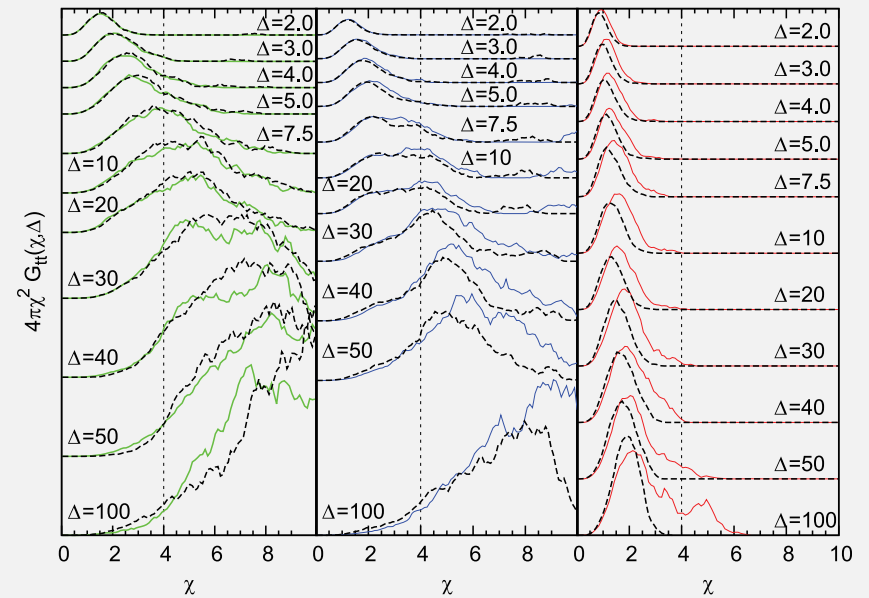
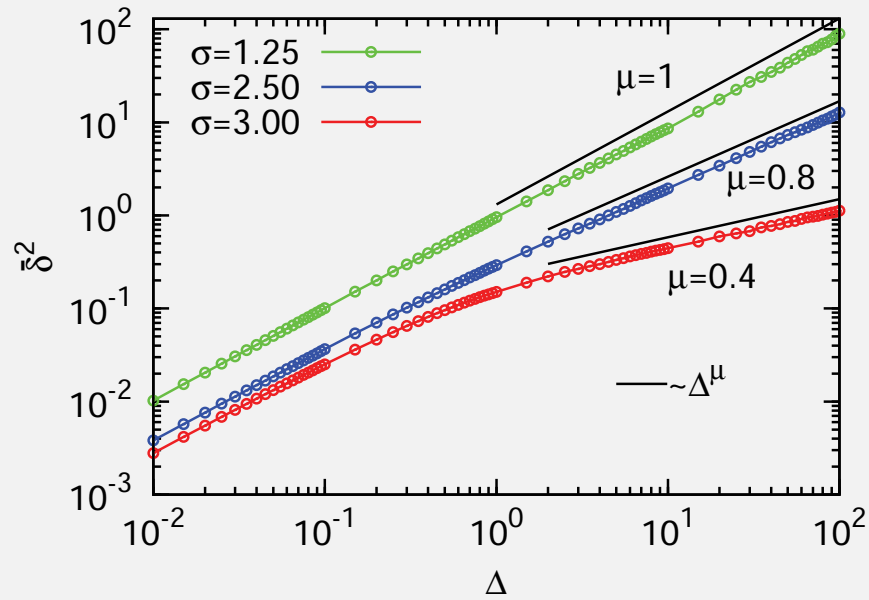
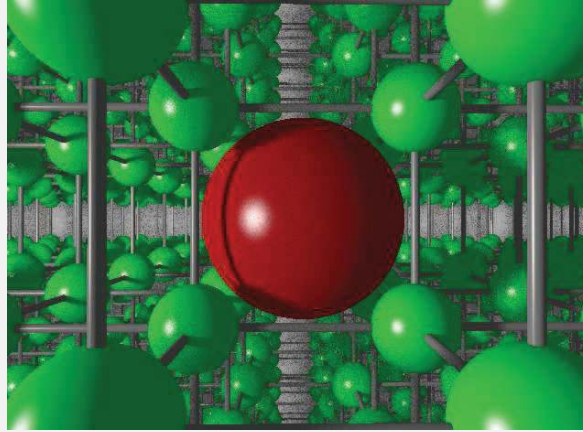


O Pulkkinen & RM, PRL (2013)

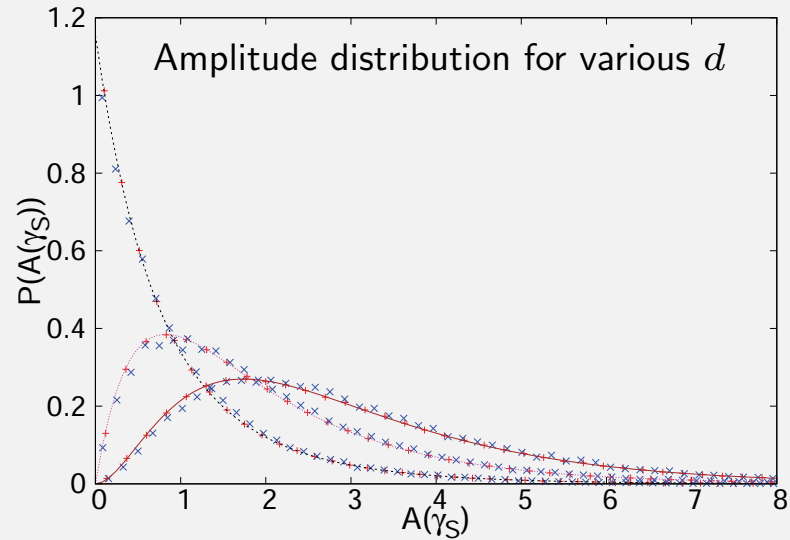
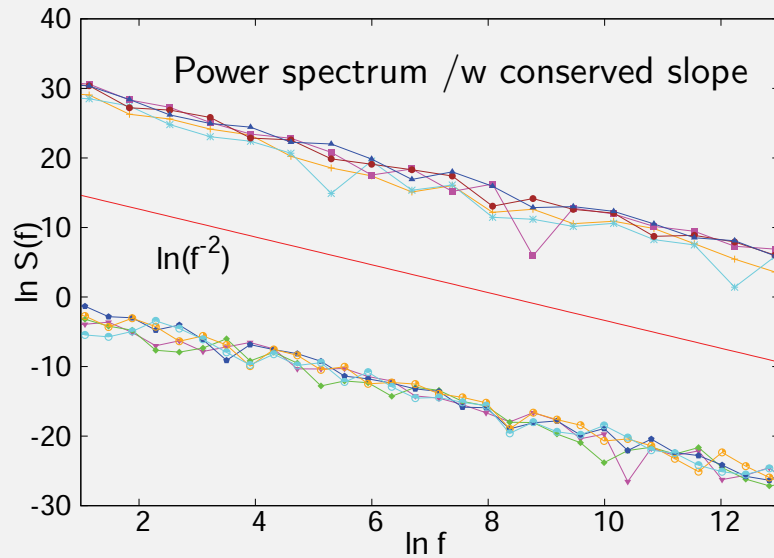


A Godec & RM, PRX (2016); Sci Rep (2016)

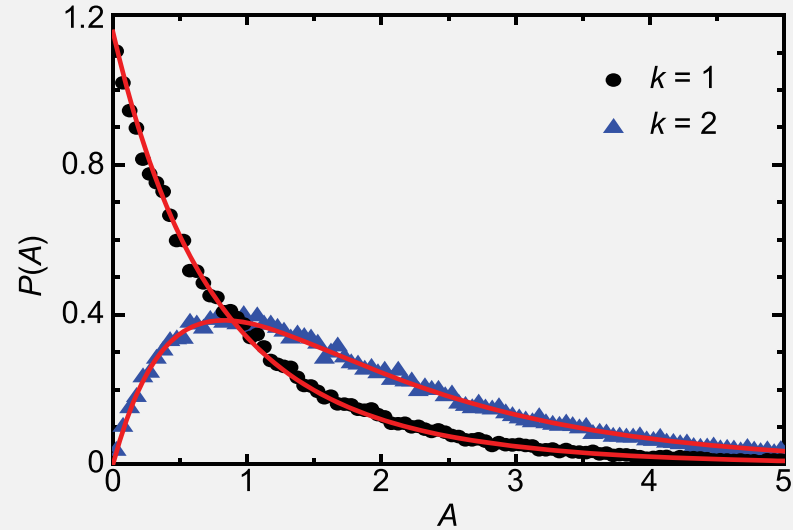
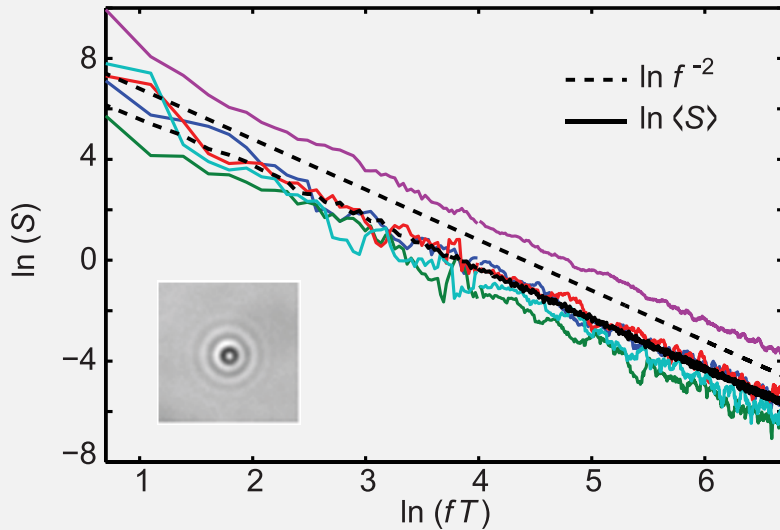
Tracer diffusion in flexible Morse spring gel



Power spectral density of a single Brownian trajectory



Theory



Experiment

Journal of Physics A's new Biological Modelling section

Journal of Physics A
Mathematical and Theoretical

Biological Modelling

For anything interesting too mathematical or not general enough for other journals

Suggestions for topical reviews & special issues welcome

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 - Biomembranes **1858**, 2451 (2016)

IIII Polymer translocation:

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