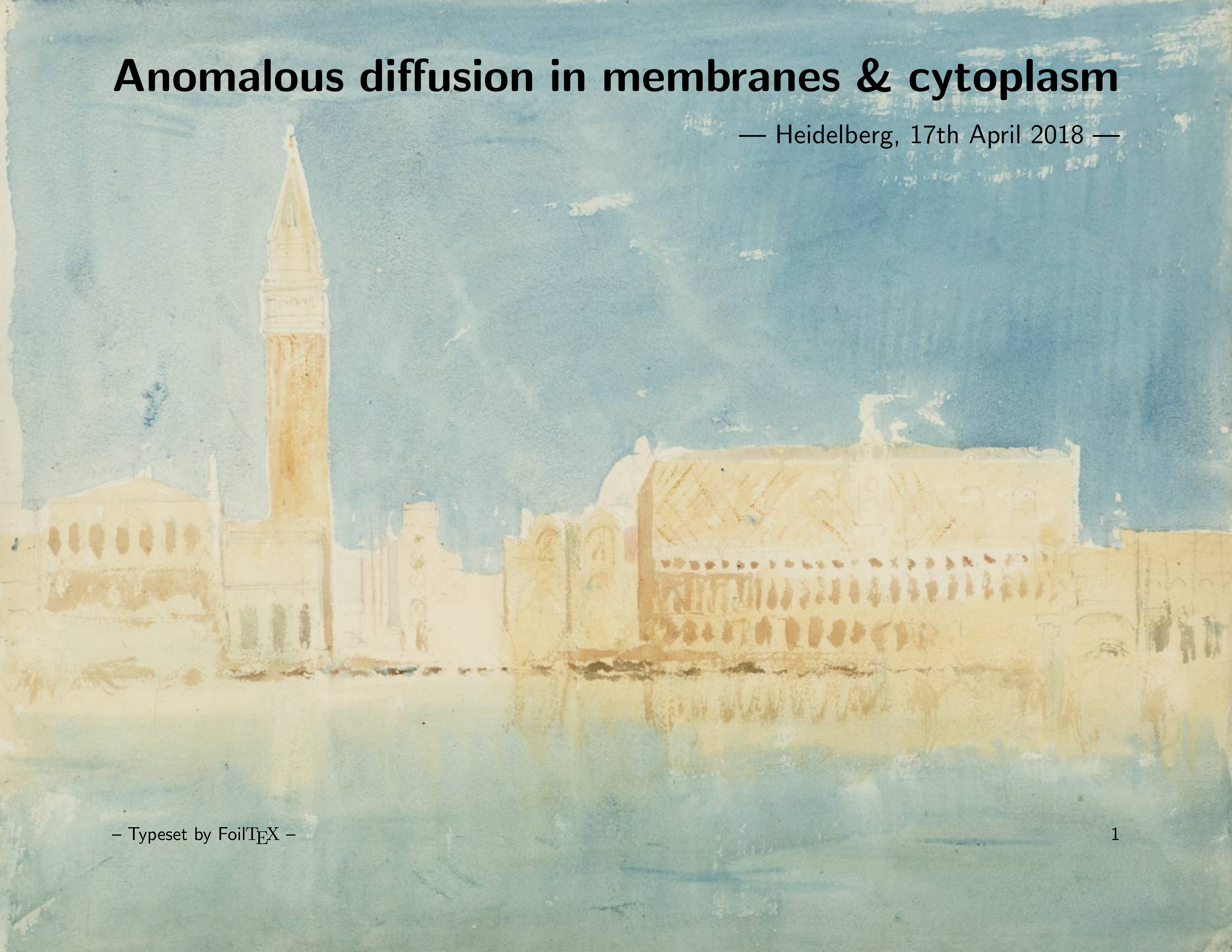
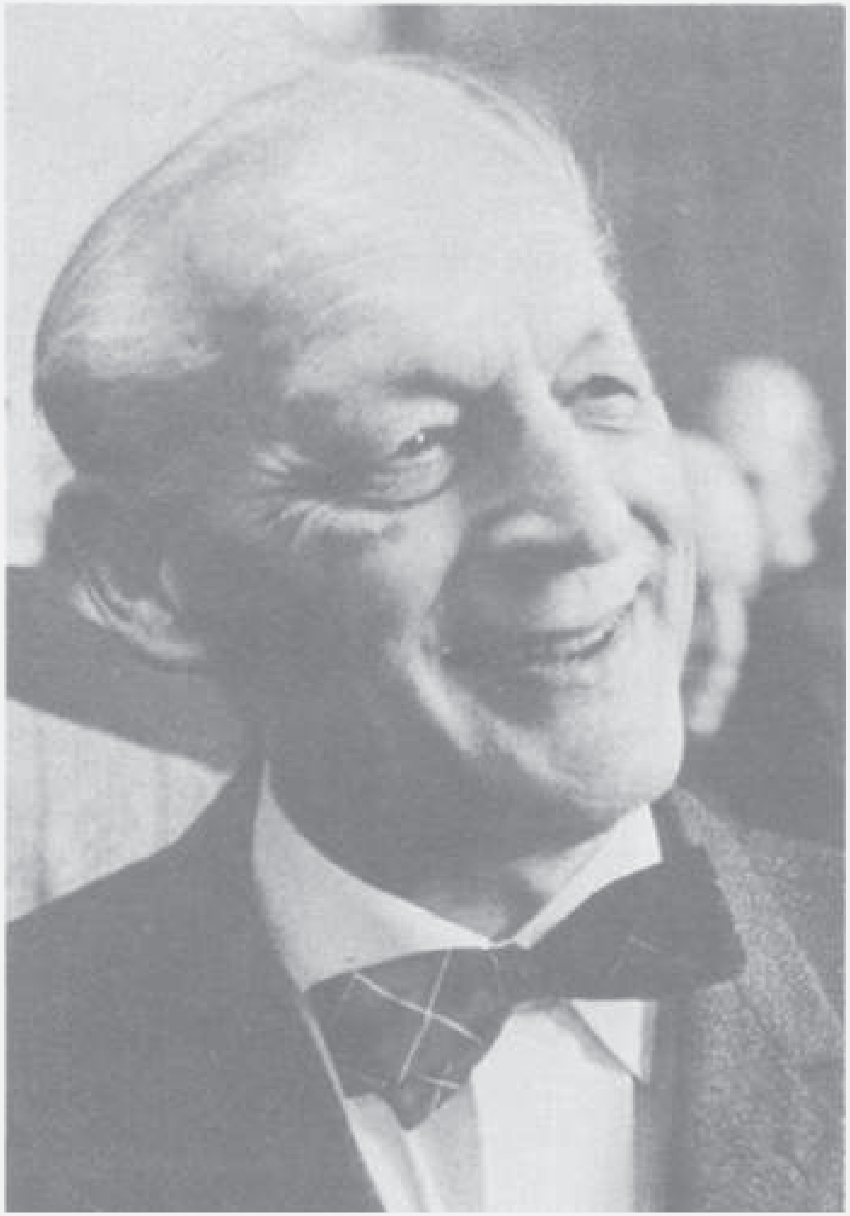


Anomalous diffusion in membranes & cytoplasm

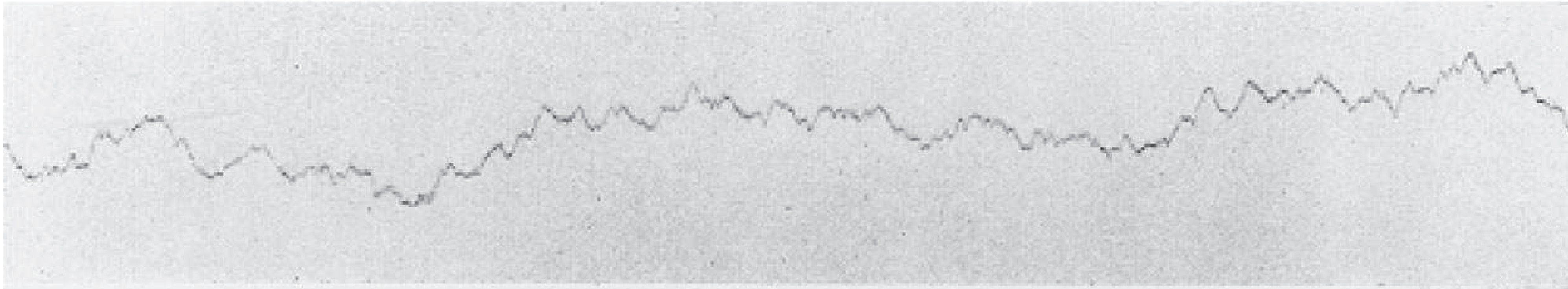
— Heidelberg, 17th April 2018 —

Eugen Kappler: ultimate diffusion measurements



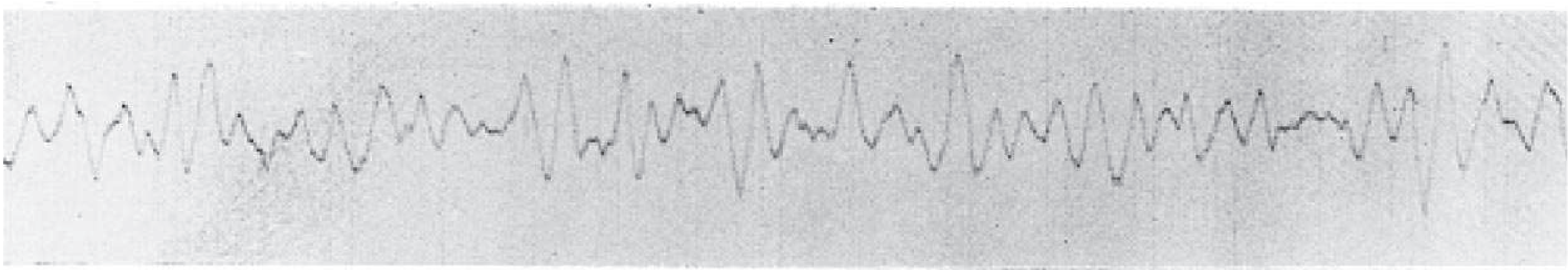
Obiturary by L Reimer, Physikalische Blätter Feb 1978 pp 86

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

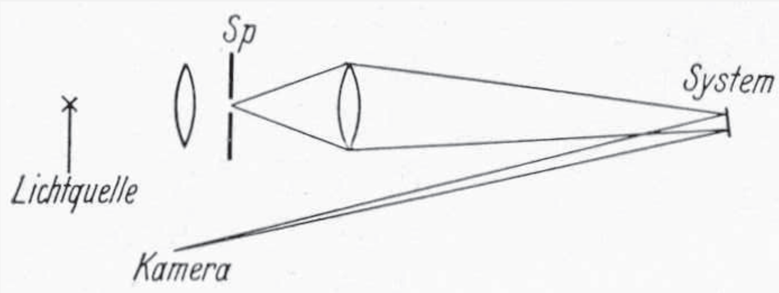


Registrieraufnahme der **Brownschen** Bewegung (natürliche Größe).
Direktionskraft $9{,}428 \cdot 10^{-9}$ abs. Einh. Trägheitsmoment $1 \cdot 10^{-7}$ abs. Einh. Abstand Spiegel–Kamera: 72,1 cm.
Zeitmarke: 30 sec $dx = 1$ mm. b) $1 \cdot 10^{-3}$ mm Hg. Temperatur 13° C

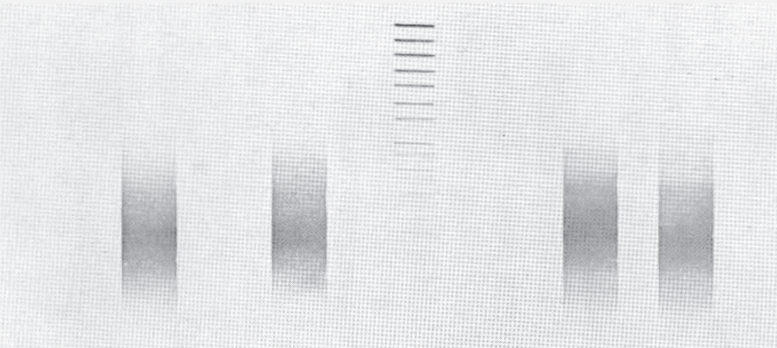
Fig. 5b

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

Brownian motion & Kappler's diffusion measurements



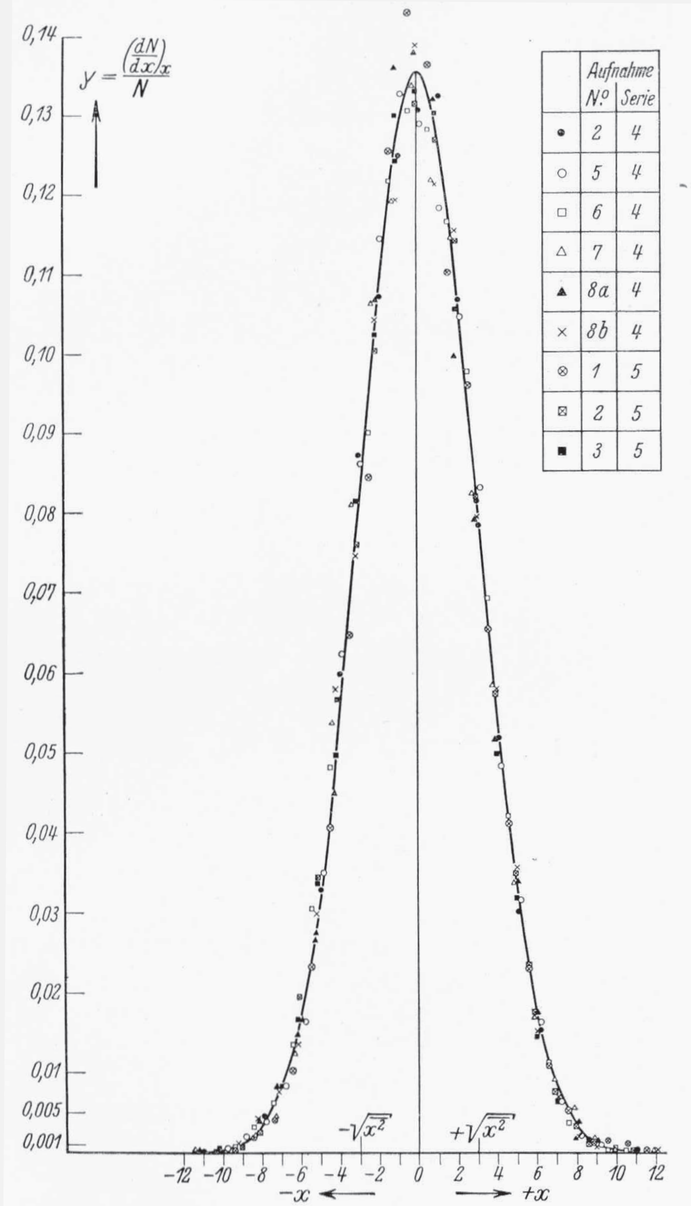
Schema der Meßanordnung
Fig. 1



Distribution @ fixed photographic plate

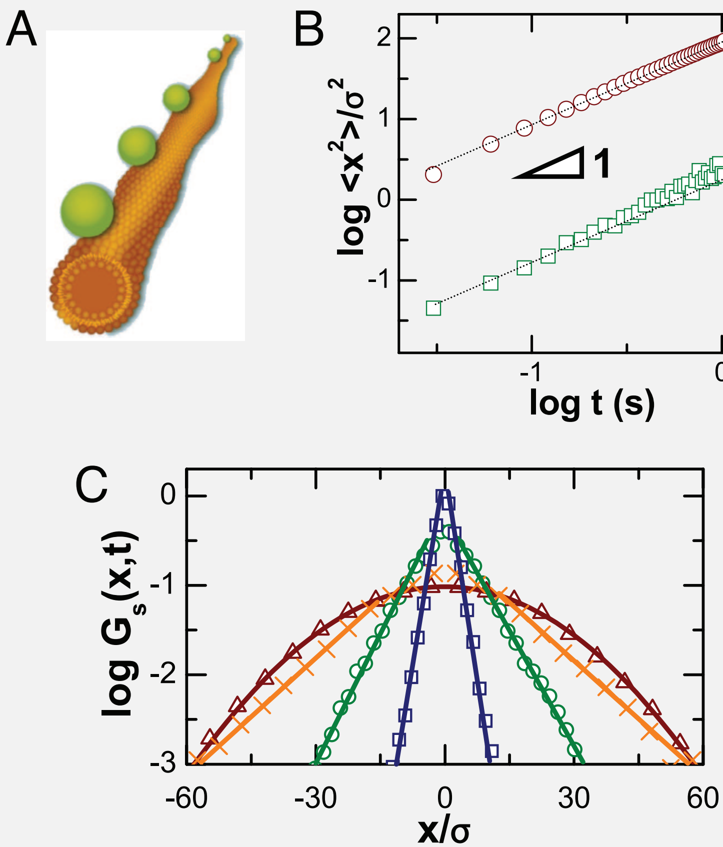
$$\langle \mathbf{r}^2(t) \rangle = 2dKt$$

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

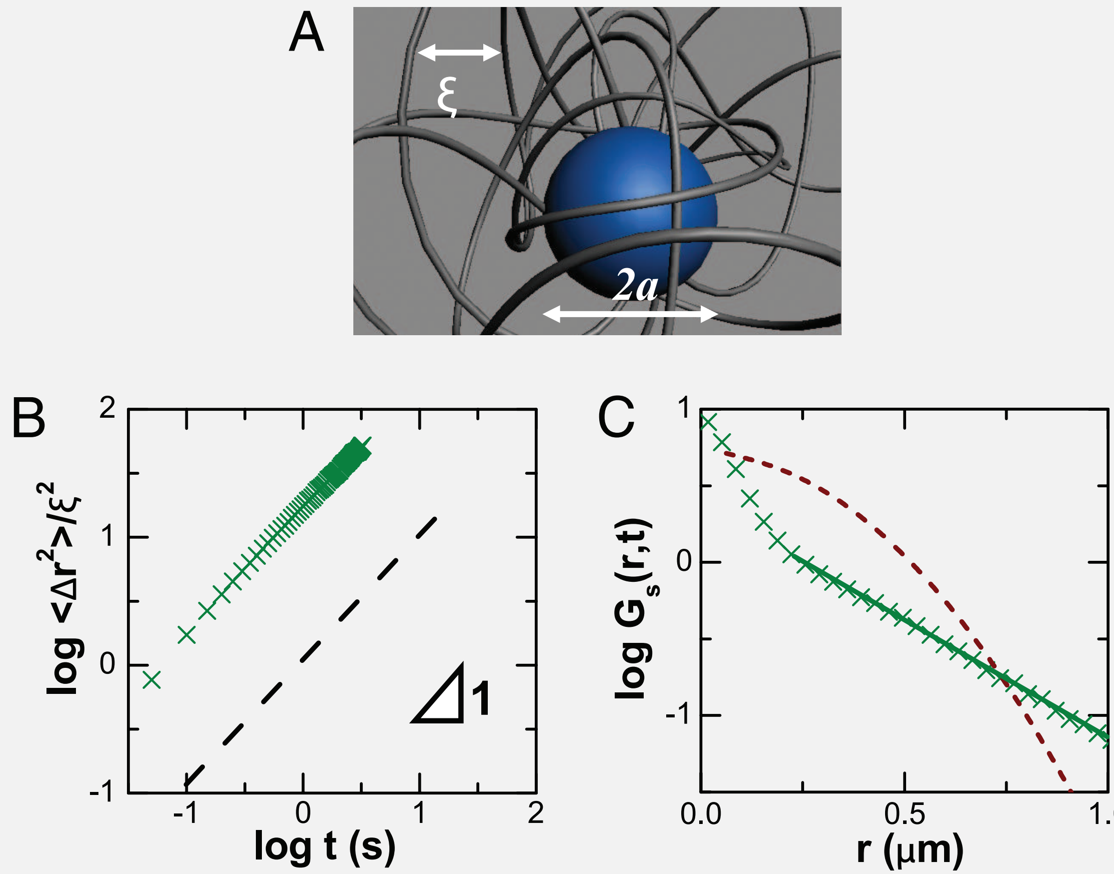


E Kappler, Ann d Physik (1931): $N_A = 60.59 \times 10^{22} \pm 1\%$

When Brownian diffusion is not Gaussian



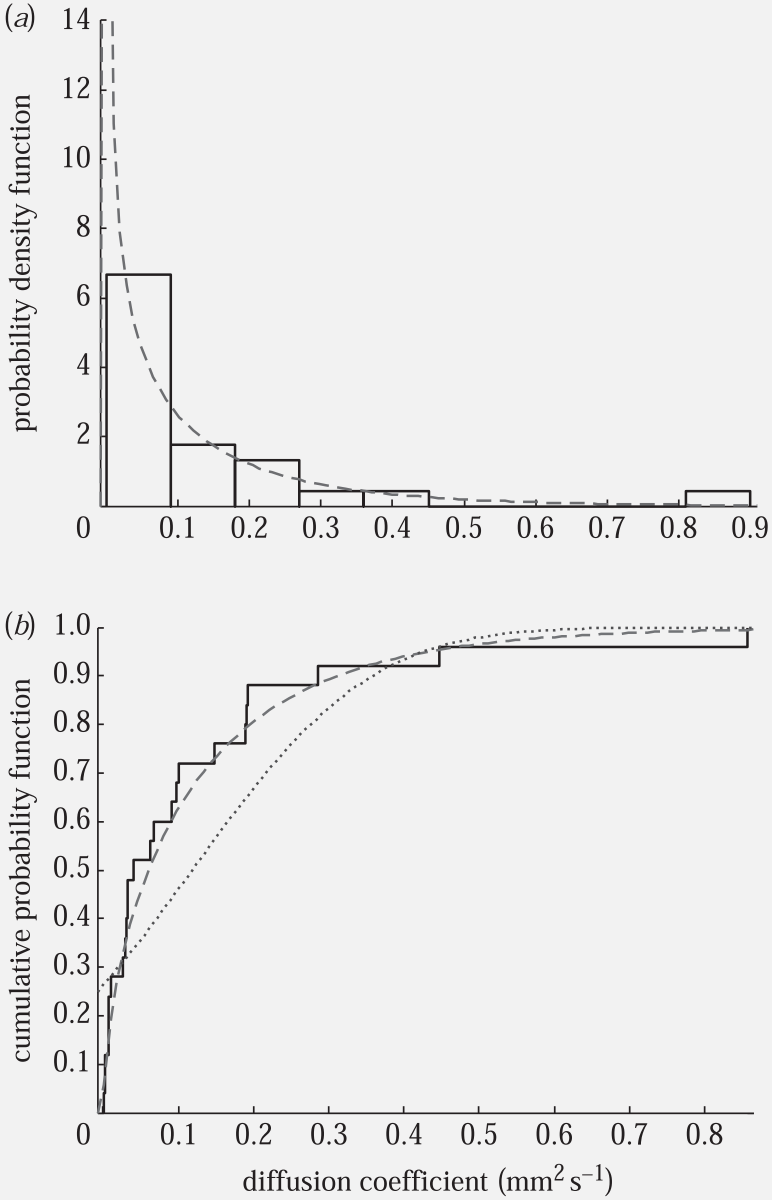
Colloidal beads diffusing on nanotubes



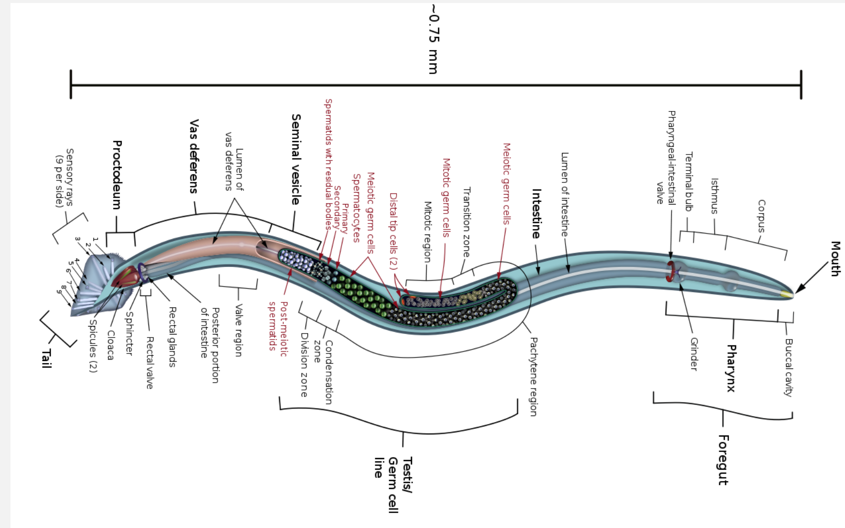
Nanospheres diffusing in entangled actin

Wang et al, PNAS (2009); Nature Mat (2012)

Heterogeneous diffusion in population of nematodes



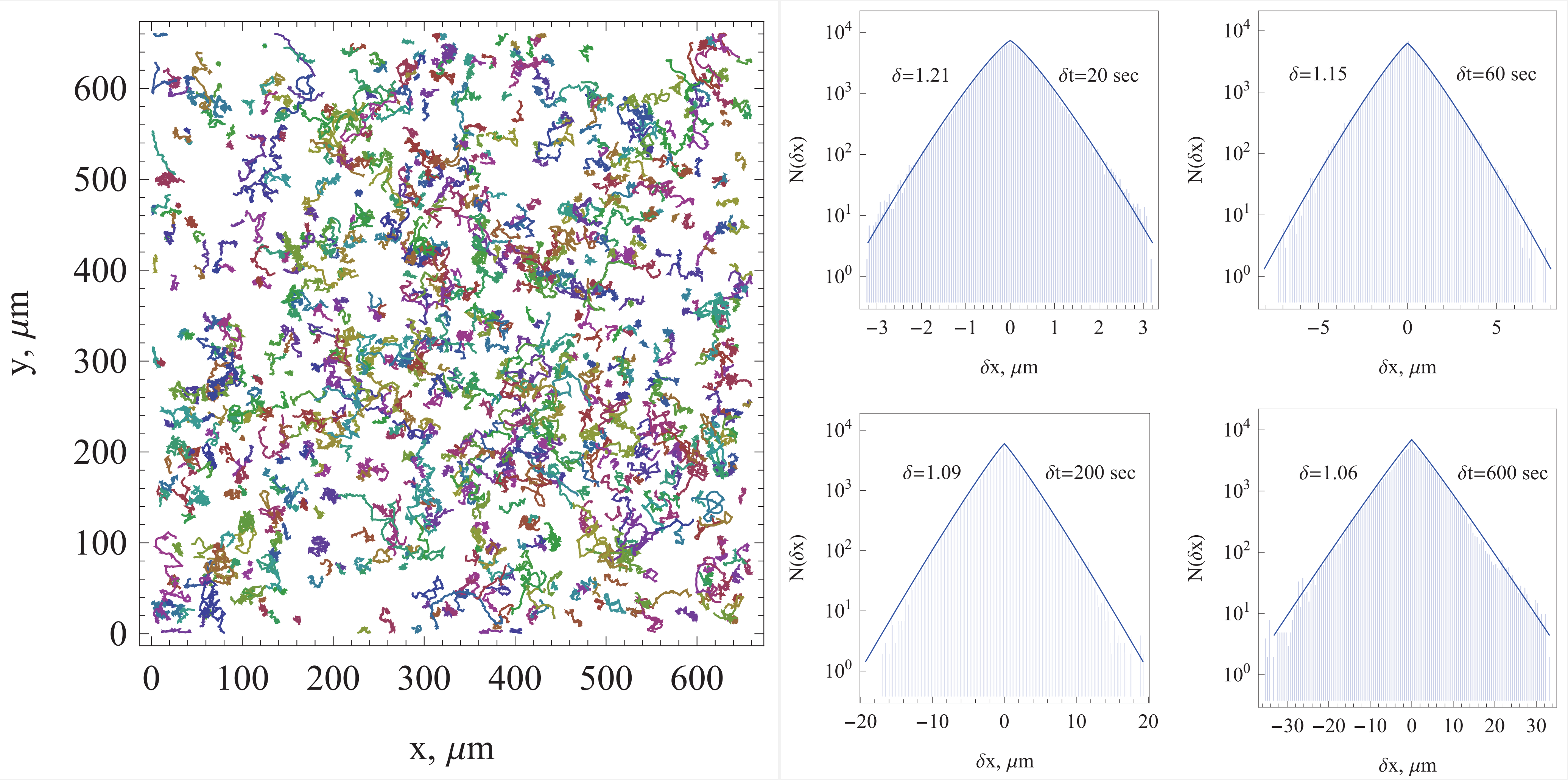
S Hapca, JW Crawford & IM Young, Roy Soc Interface (2009)



Male C. elegans nematode

Soybean cyst nematode & egg

Non-Gaussian diffusion of Dictyostelium cells



AG Cherstvy, O Nagel, C Beta & RM (2018)

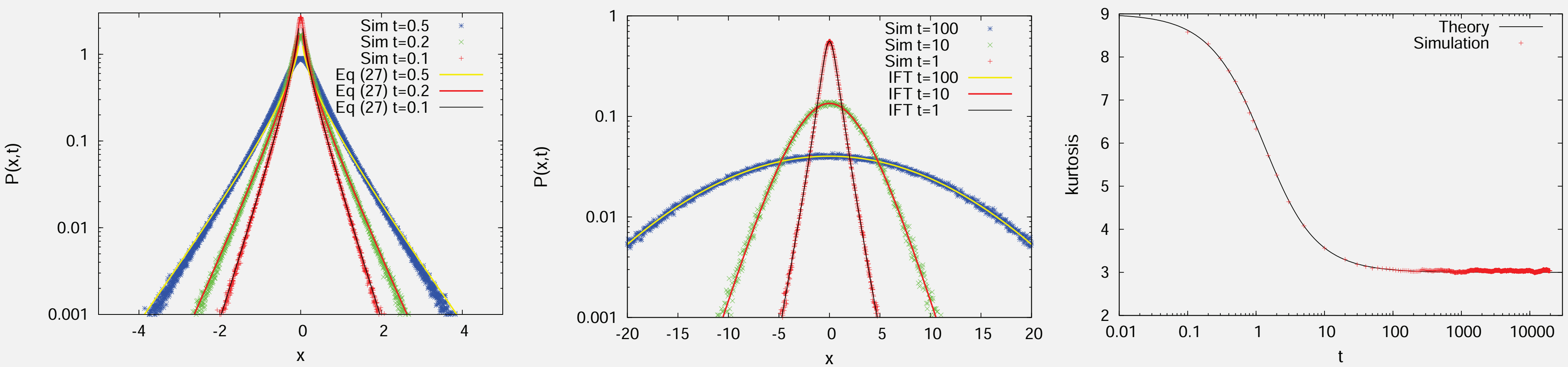
Fickian, non-Gaussian diffusion with diffusing diffusivity

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

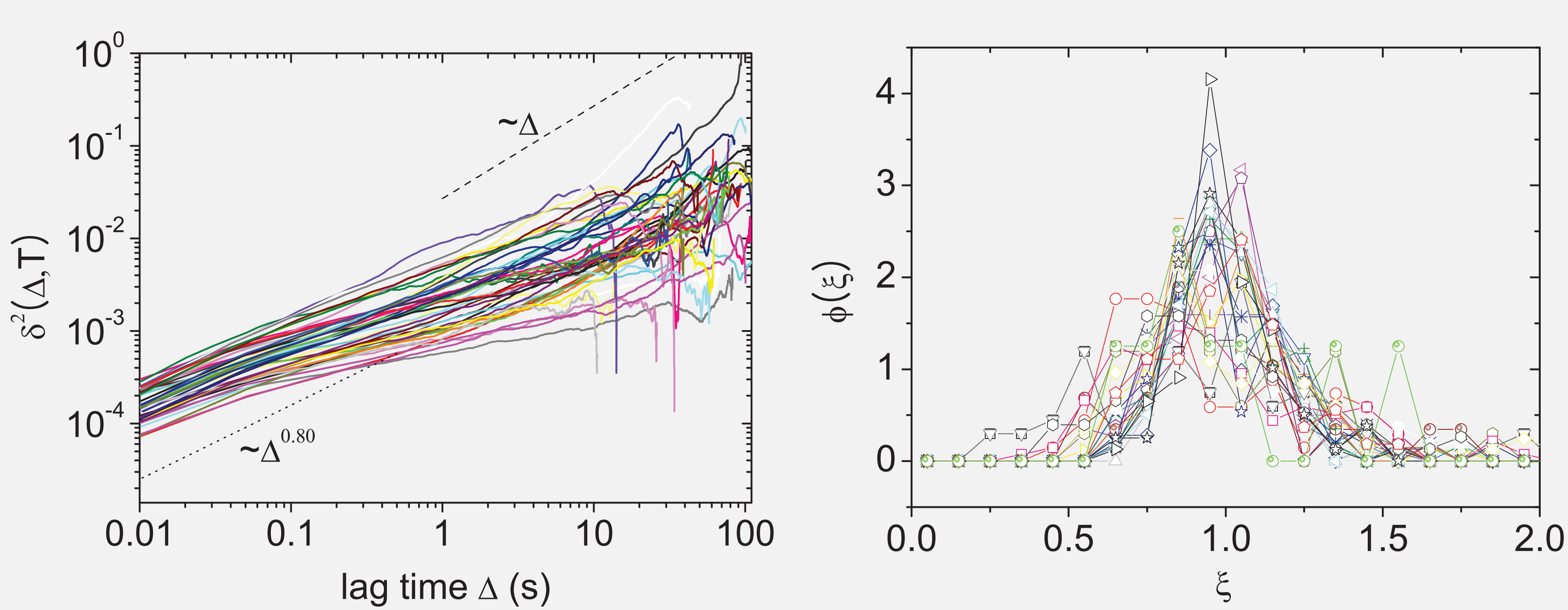
Our minimal model for diffusing diffusivity:

$$\dot{x}(t) = \sqrt{2D(t)}\xi(t)$$
$$D(t) = y^2(t)$$
$$\dot{y}(t) = -\tau^{-1}y + \sigma\eta(t)$$



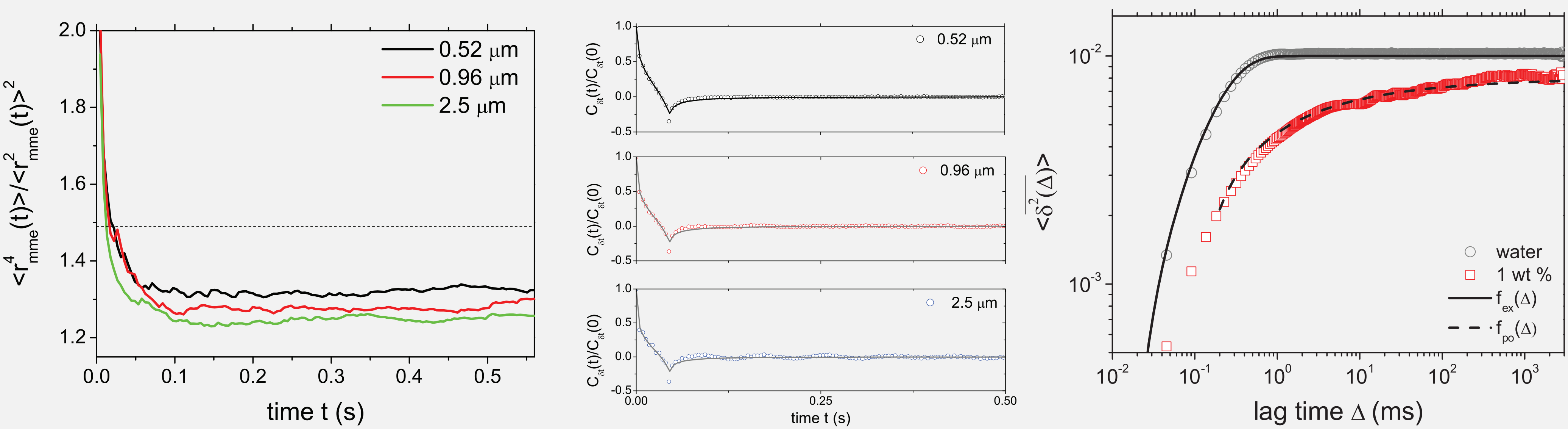
AV Chechkin, F Seno, RM & IM Sokolov, PRX (2017); generalised $\gamma(D)$: V Sposini, AV Chechkin, G Pagnini, F Seno & RM, NJP (2018)

Passive motion of submicron tracers in cells is viscoelastic



Lipid granules in living yeast cells ↓

Tracer beads in wormlike micellar solution ↓



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

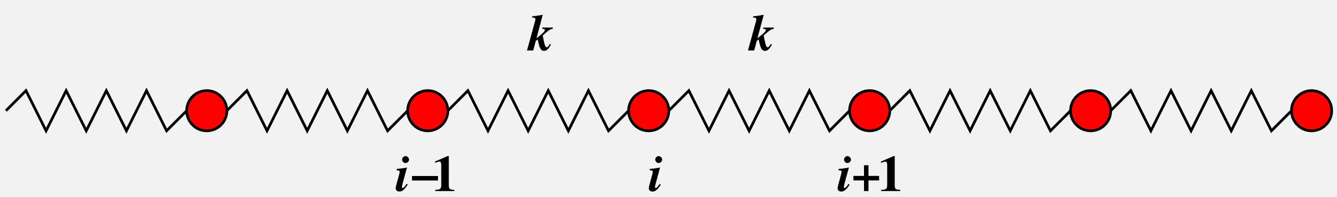
Fractional Langevin equations in viscoelastic systems

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 $\curvearrowright$ Generalised Langevin equation (GLE):

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



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

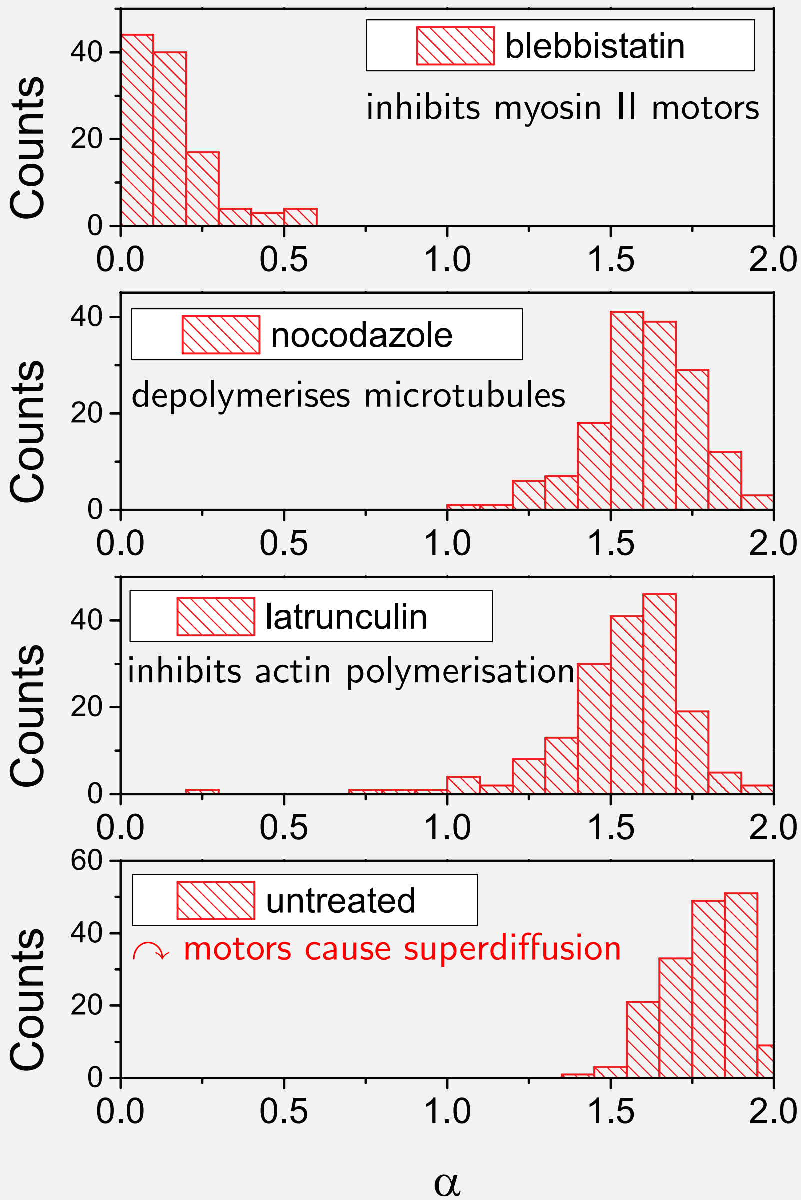
$$\langle\zeta_i(t)\zeta_j(t')\rangle = \delta_{ij}k_B T\eta(|t-t'|)$$

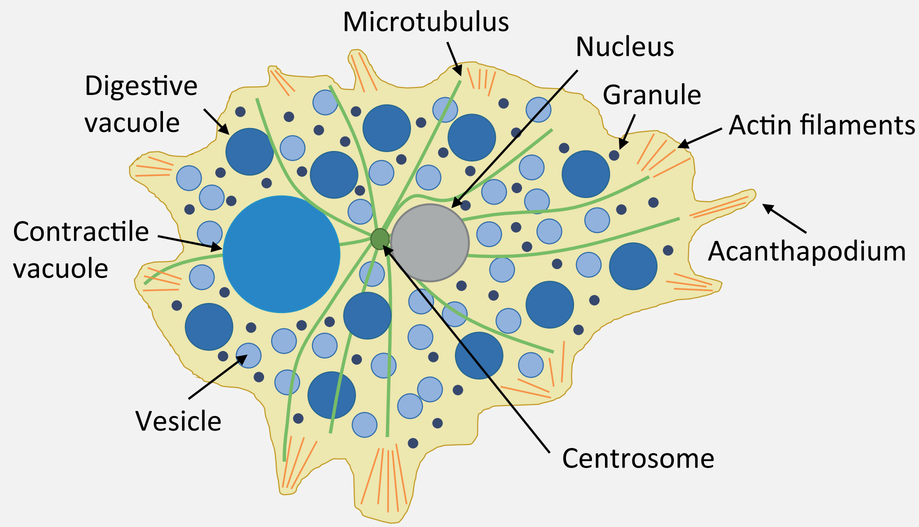
$\curvearrowright$ fractional Langevin equation. Overdamped limit: Mandelbrot's FBM

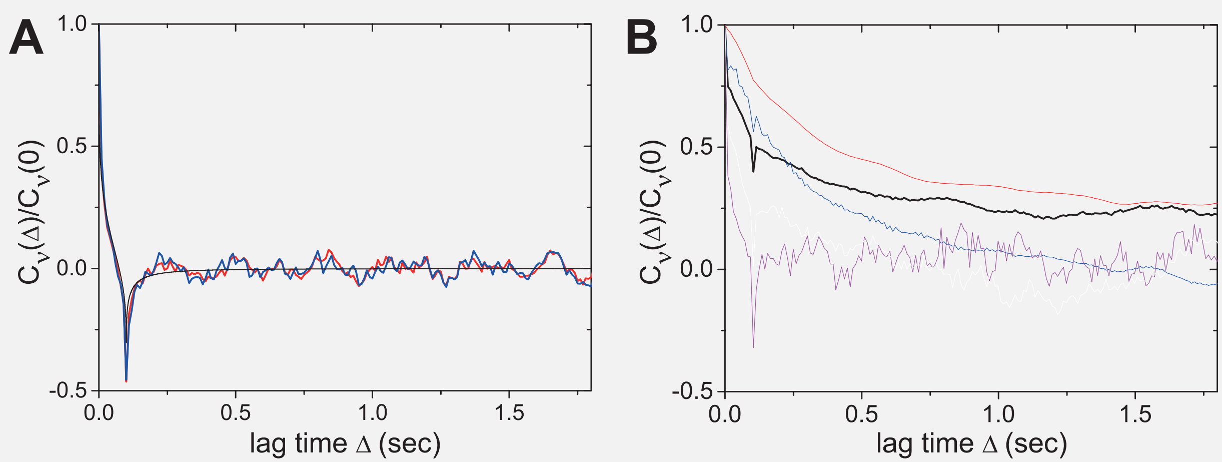
Quantum mechanics: Nakajima-Zwanzig equation using projection operators

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

Superdiffusion in supercrowded Acanthamoeba castellani



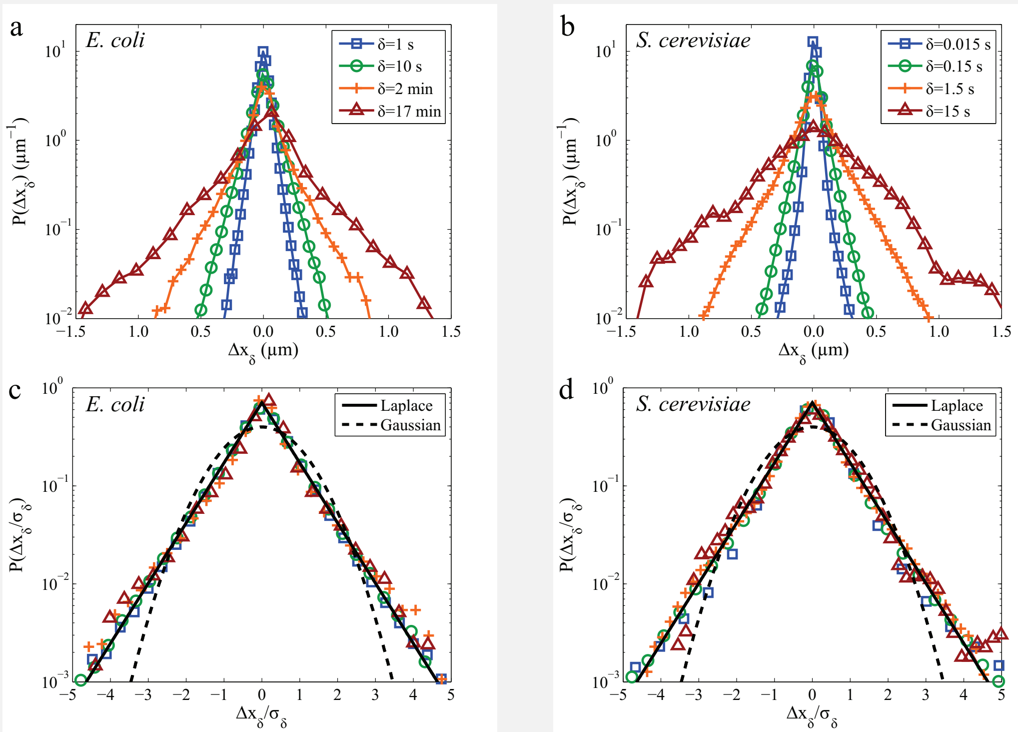


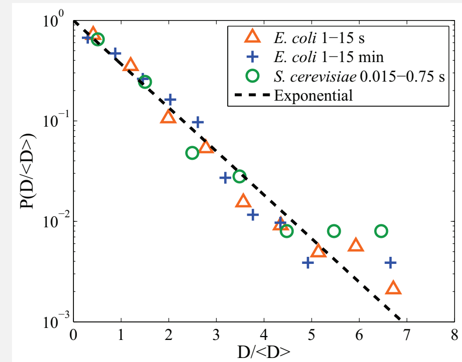


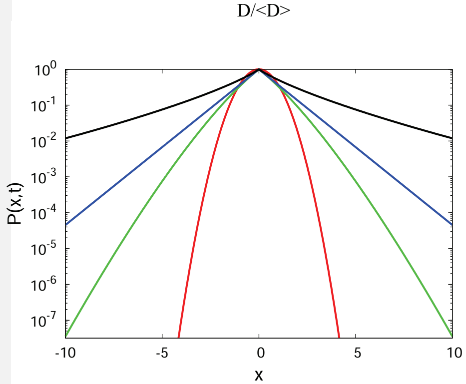
JF Reverey, J-H Jeon, H Bao, M Leippe, RM & C Selhuber-Unkel, Sci Rep (2015)

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:



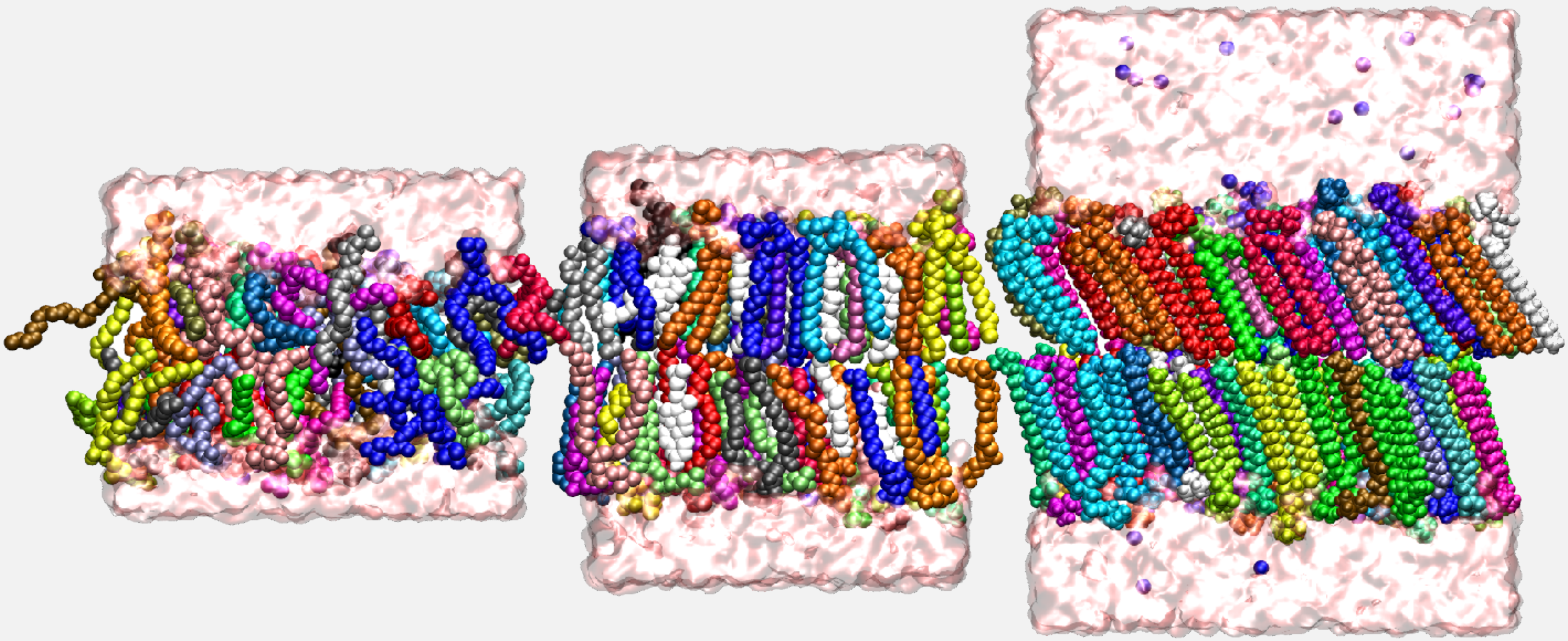




Modelling based on grey GLE: J Ślezak, RM & M Magdziarz, NJP (2018)

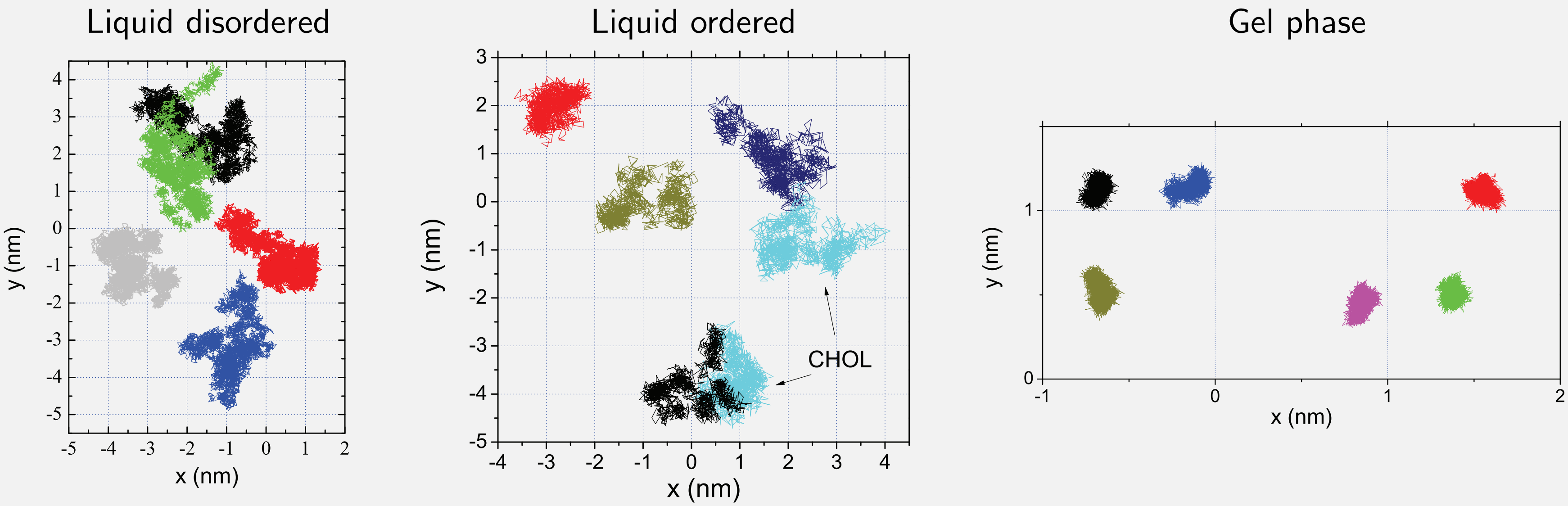
TJ Lampo, S Stylianidou, MP Backlund, PA Wiggins & AJ Spakowitz, BPJ (2017); N&V: RM, BPJ (2017)

Single lipid motion in bilayer membrane MD simulations

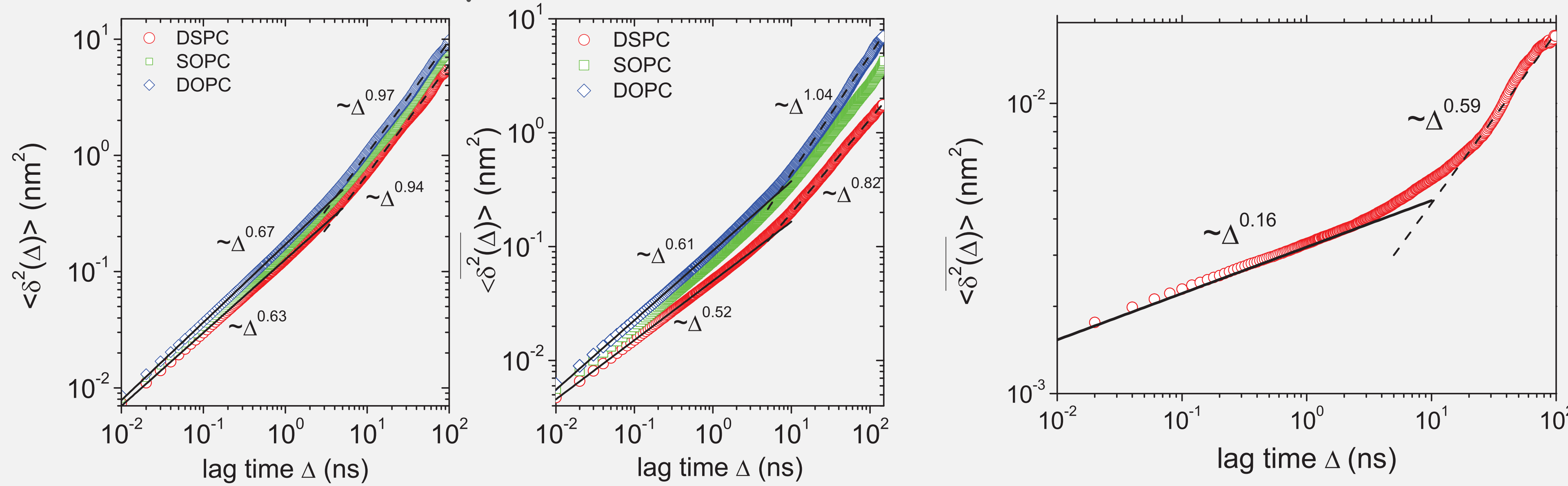


J-H Jeon, H Martinez-Seara Monne, M Javanainen & RM, PRL (2012)

Sample trajectories for the lipid & cholesterol motion



Liquid ordered/gel phases: extended anomalous diffusion

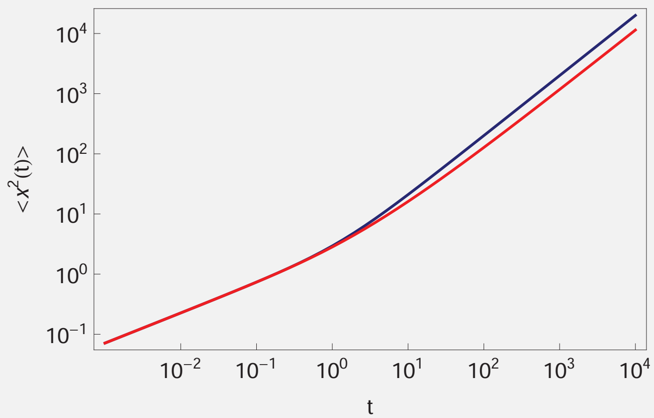


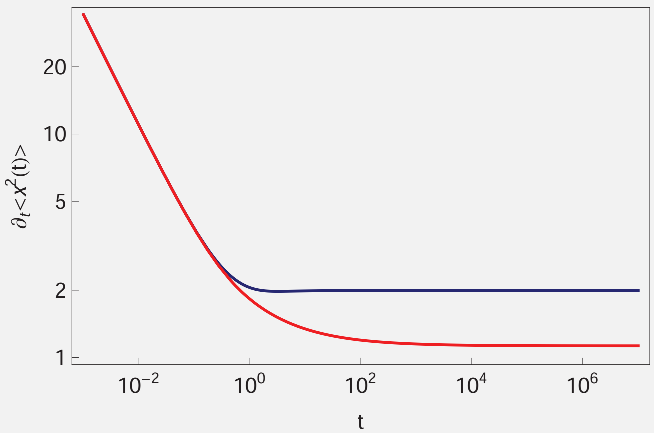
J-H Jeon, H Martinez-Seara Monne, M Javanainen & RM, PRL (2012)

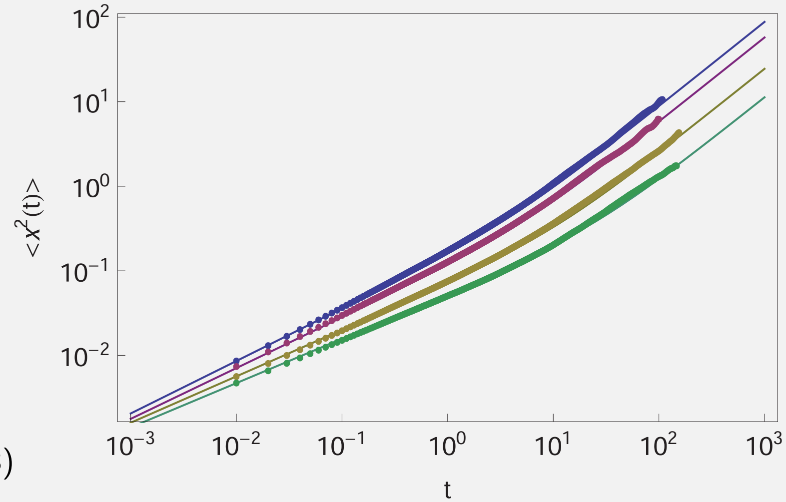
Tempered FBM & FLE motion: sub- to normal diffusion

Consider tempered fGn:

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

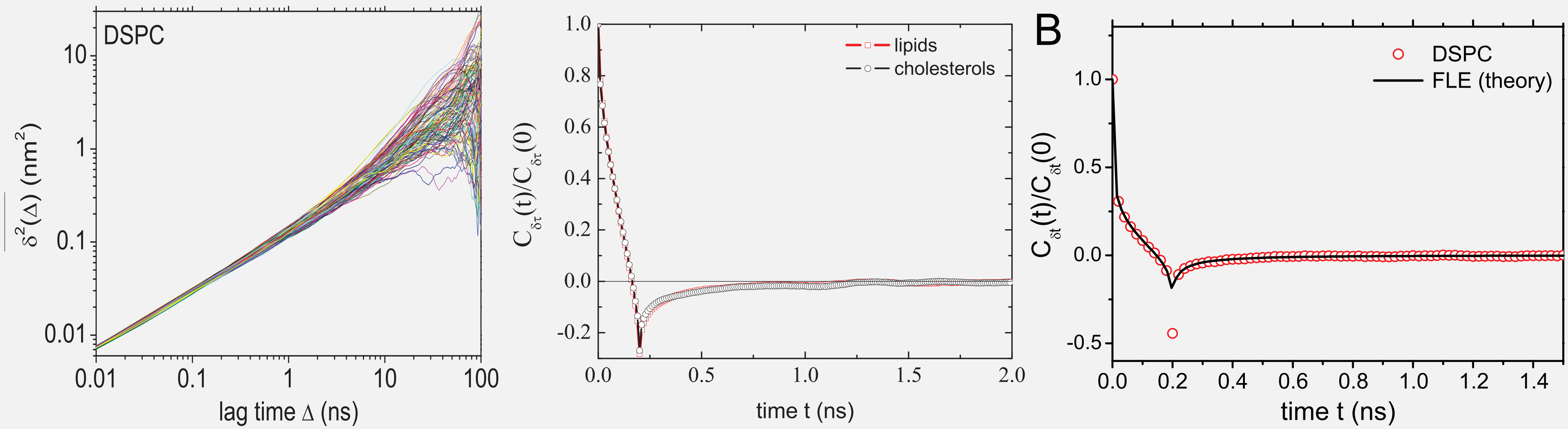




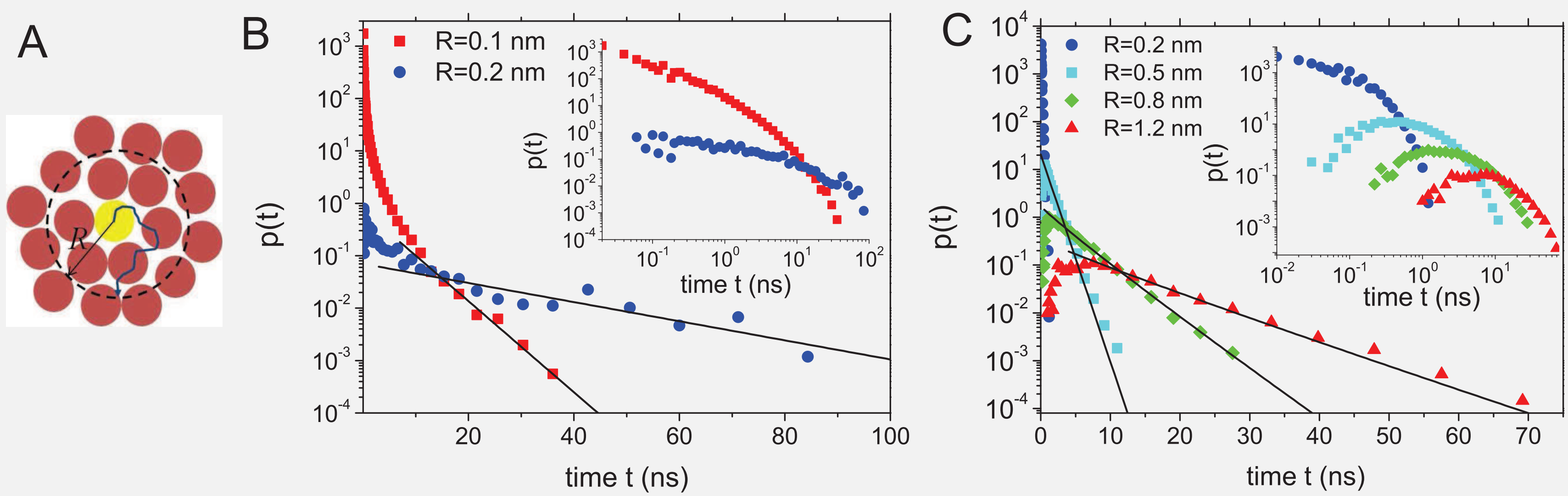


D Molina-Garcia, T Sandev, G Pagnini, AV Chechkin & RM (2018)

Reproducible TA MSD & antipersistent correlations

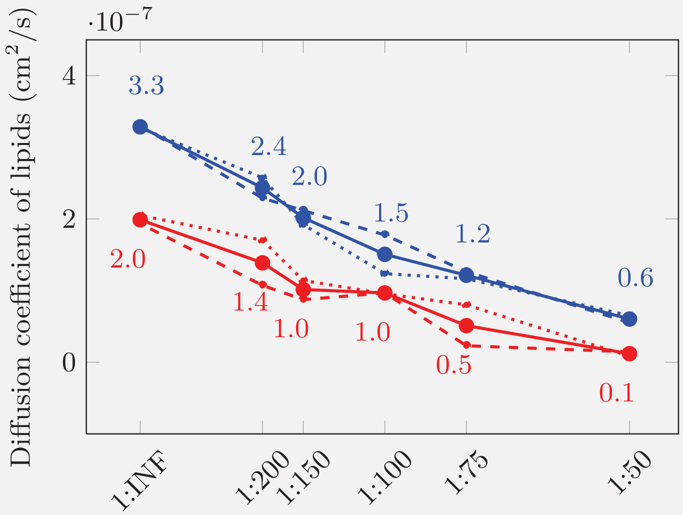


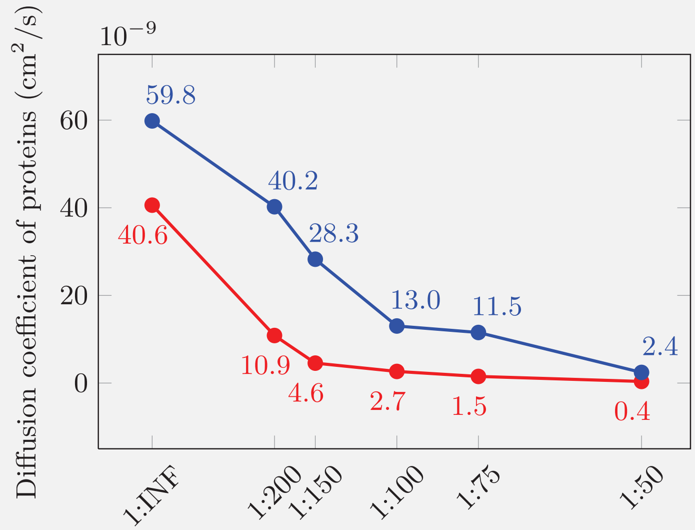
Rattling dynamics: exptl first passage PDF ↷ FLE motion



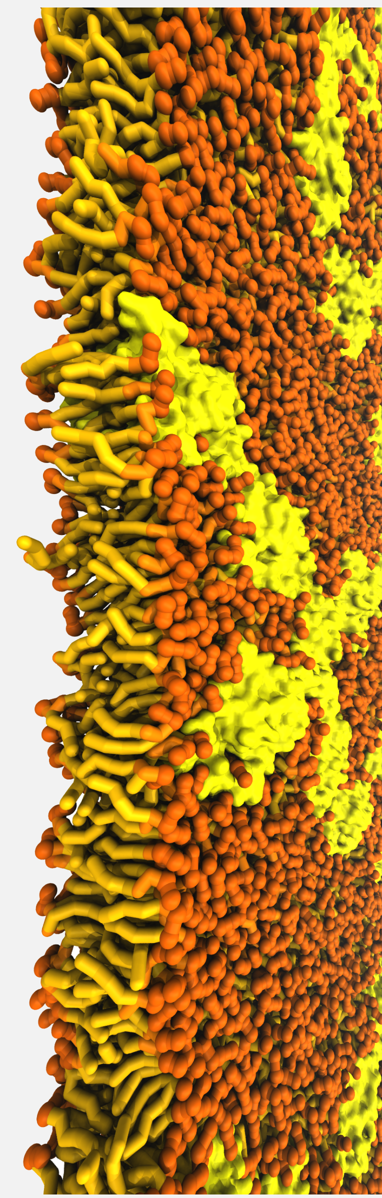
D Molina-Garcia, T Sandev, G Pagnini, AV Chechkin & RM (2018)

Protein crowded membranes reduce effective mobility

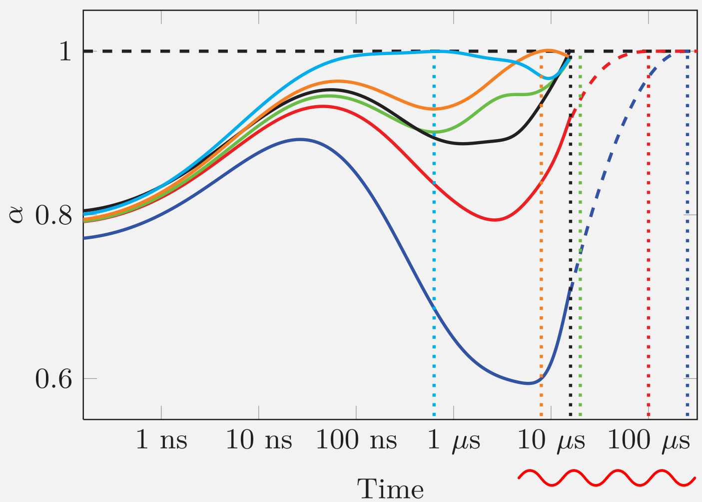


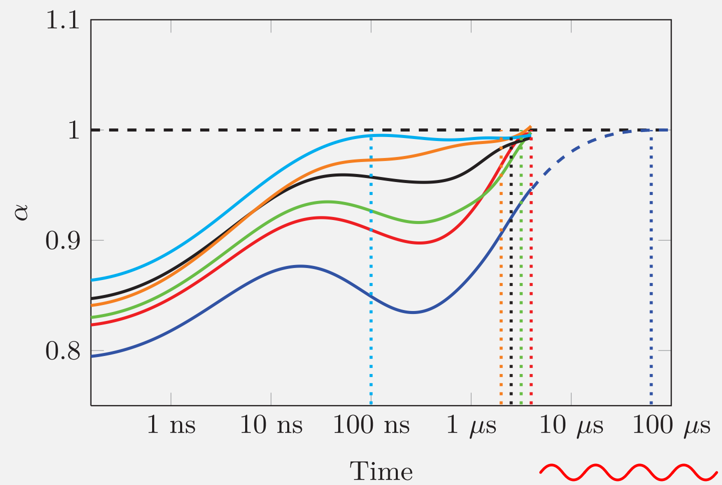


Blue: DLPC. Red: DPPC



Protein crowding effects anomalous lipid diffusion

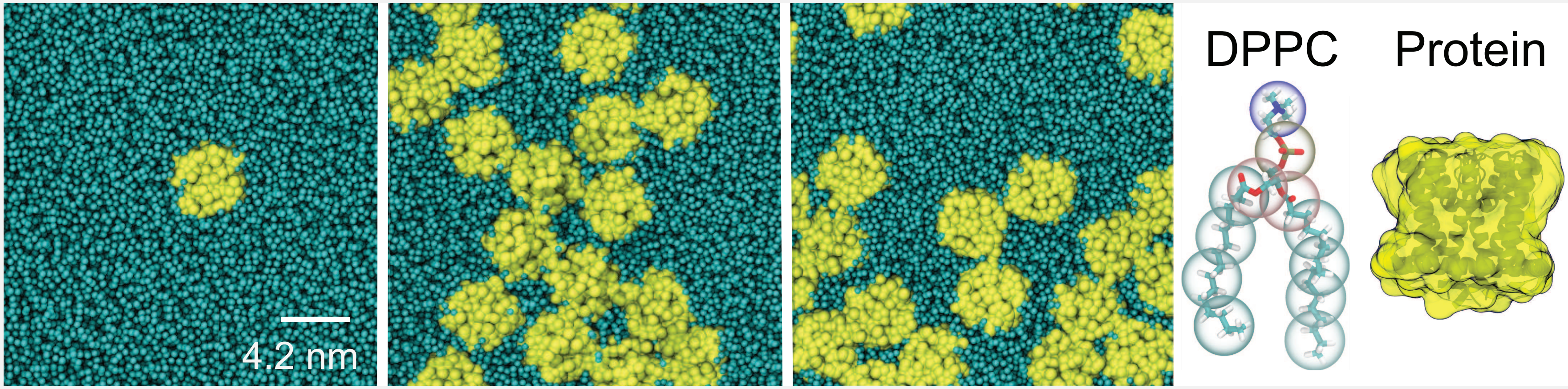


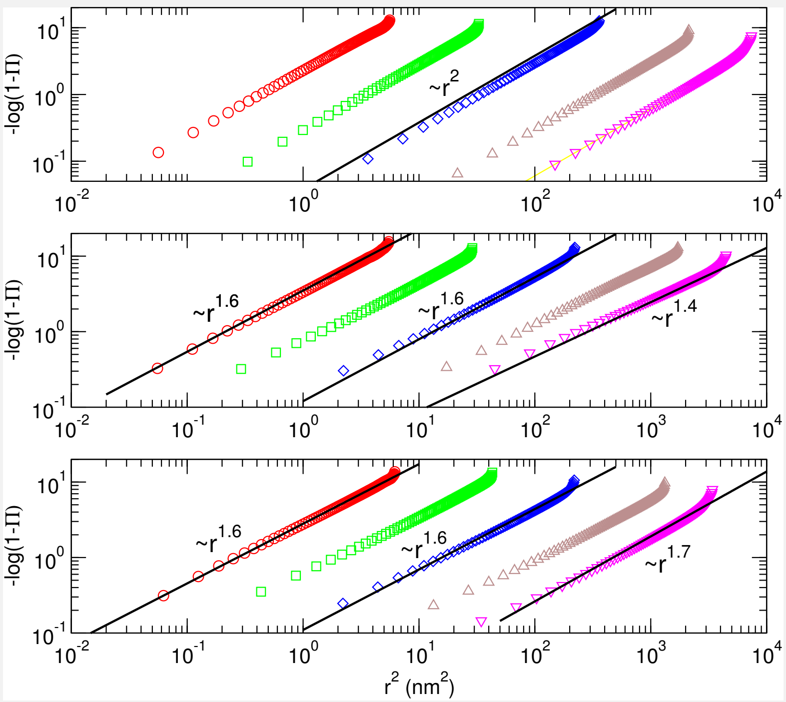


Left: DPPC (protein-aggregating) case. Right: DLPC protein non-aggregating case.

M Javanainen, H Hammaren, L Monticelli, JH Jeon, RM & I Vattulainen, Faraday Disc (2013)

Crowding in membranes: non-Gaussian lipid/protein diffusion

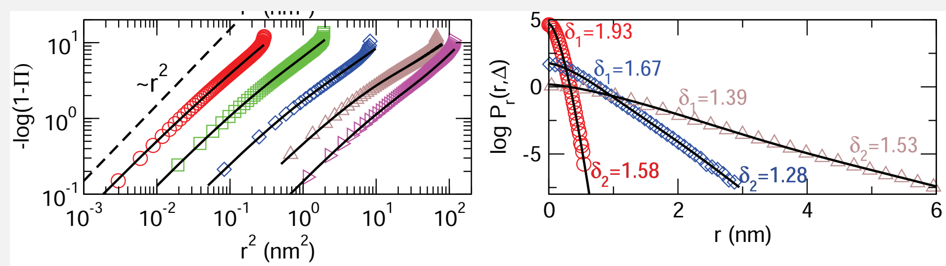




Dilute membrane: $P(r,t)$ Gauss

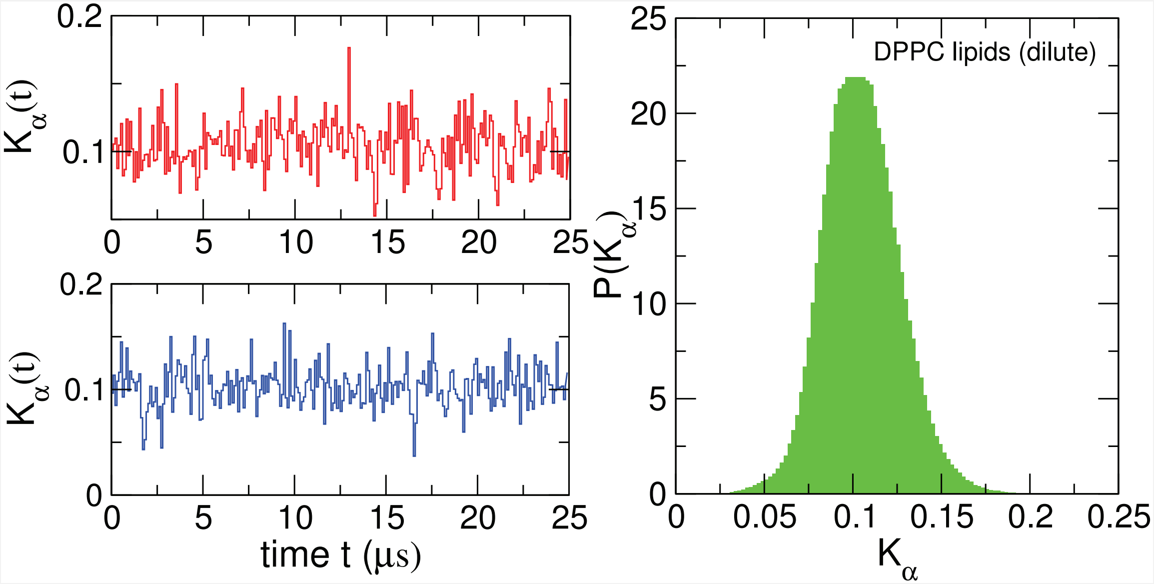
Crowded membrane ($\delta \approx 1.3 \dots 1.7$):

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



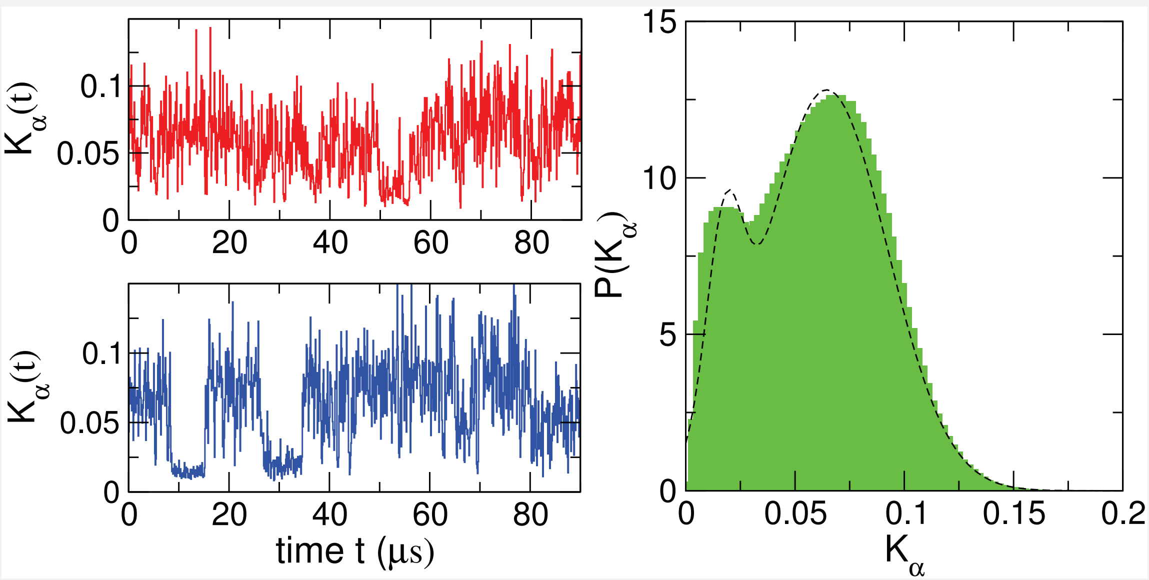
J-H Jeon, M Javanainen, H Martinez-Seara, RM & I Vattulainen, PRX (2016); compare Faraday Disc (2013)

Crowding in membranes increases dynamic heterogeneity



Diffusivity(t) for two lipids

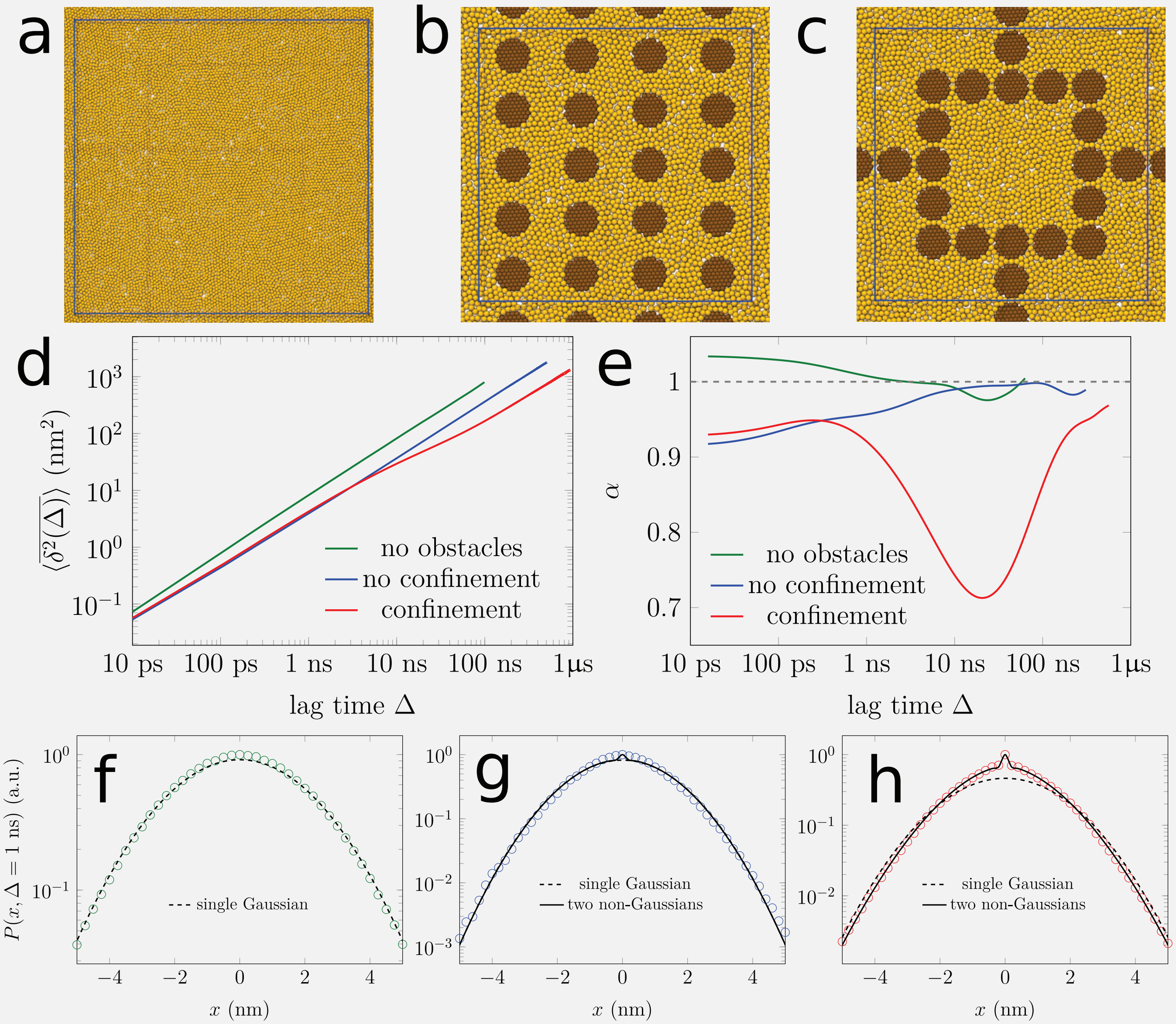
Lipid diffusivity, dilute membrane



Lipid diffusivity, crowded membrane

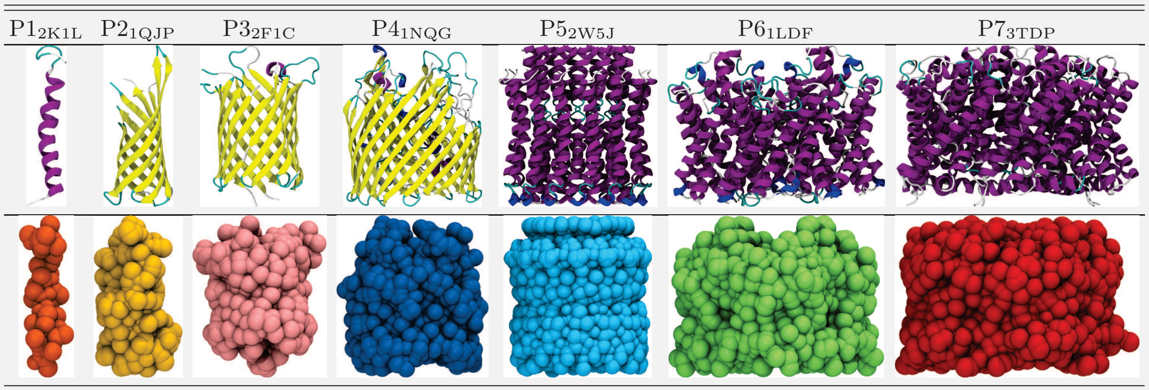
J-H Jeon, M Javanainen, H Martinez-Seara, RM & I Vattulainen, PRX (2016); compare Faraday Disc (2013)

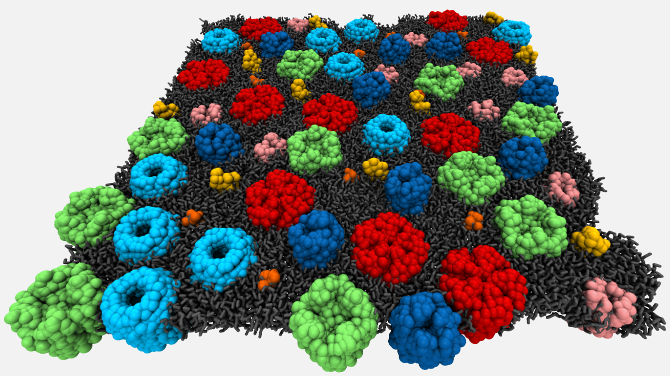
Confinement in argon system shows geometric origin

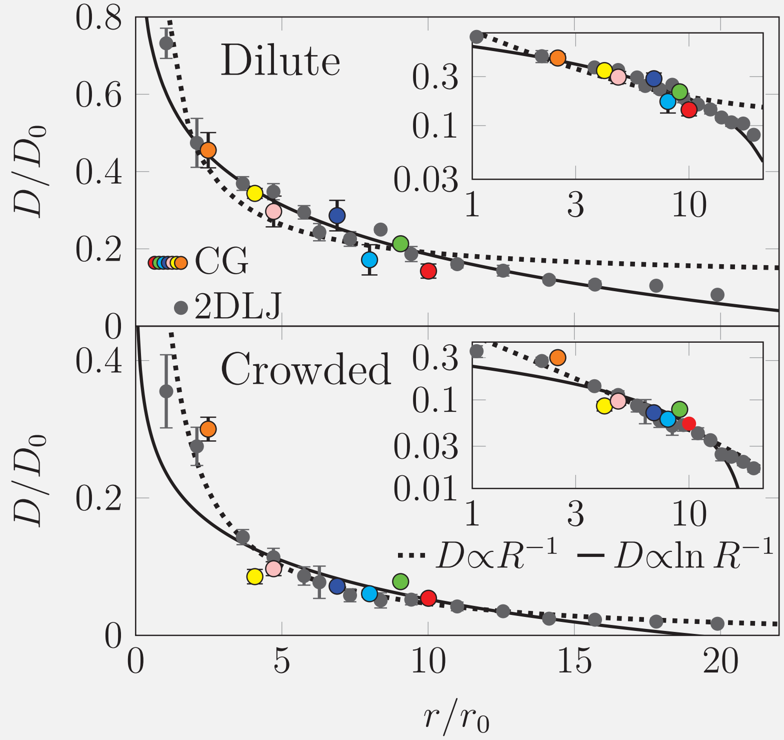


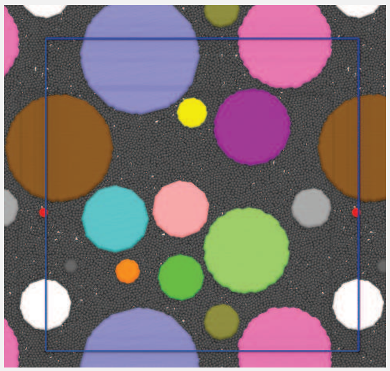
J-H Jeon, M Javanainen, H Seara Monne, RM & I Vattulainen, PRX (2016)

Geometry-induced violation of Saffman-Delbrück relation









Dilute system: Saffman-Delbrück law

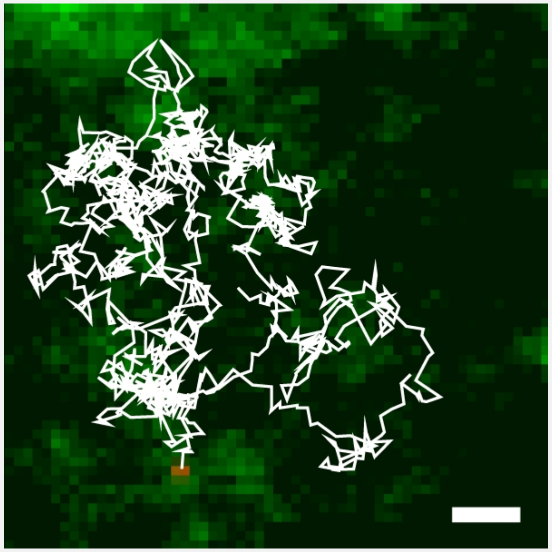
$$D(R) \simeq \log(1/R)$$

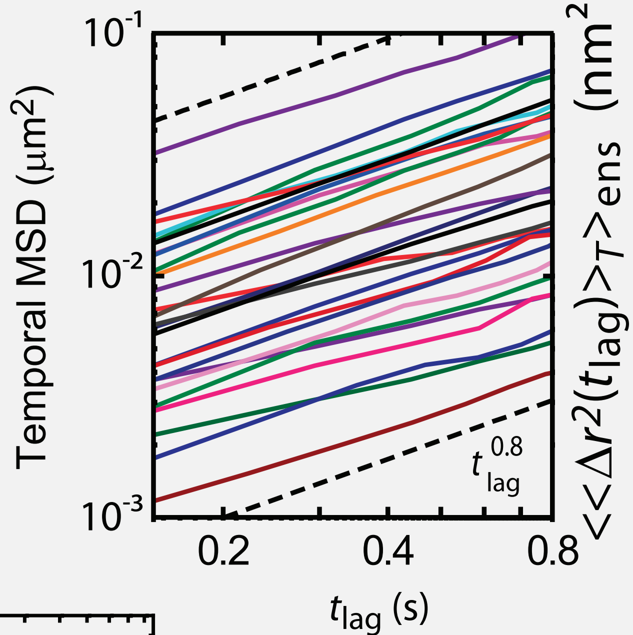
Crowded membrane & 2DLJ discs:

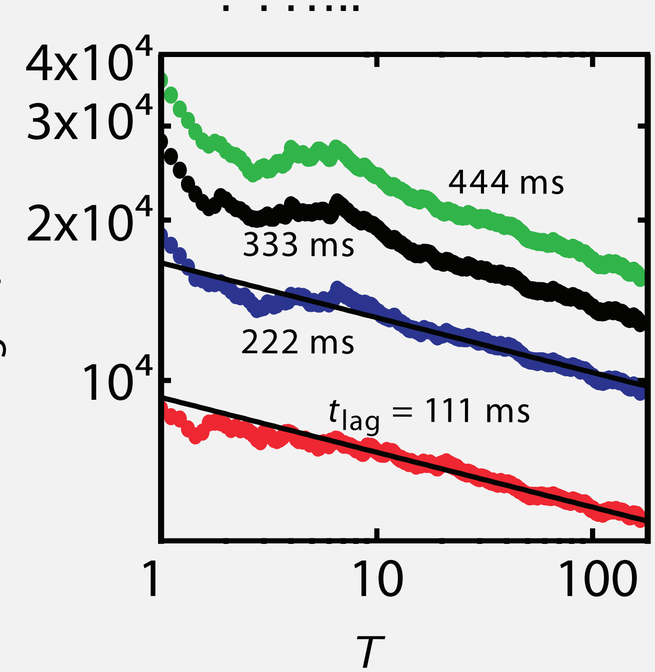
$$D(R) \simeq 1/R$$

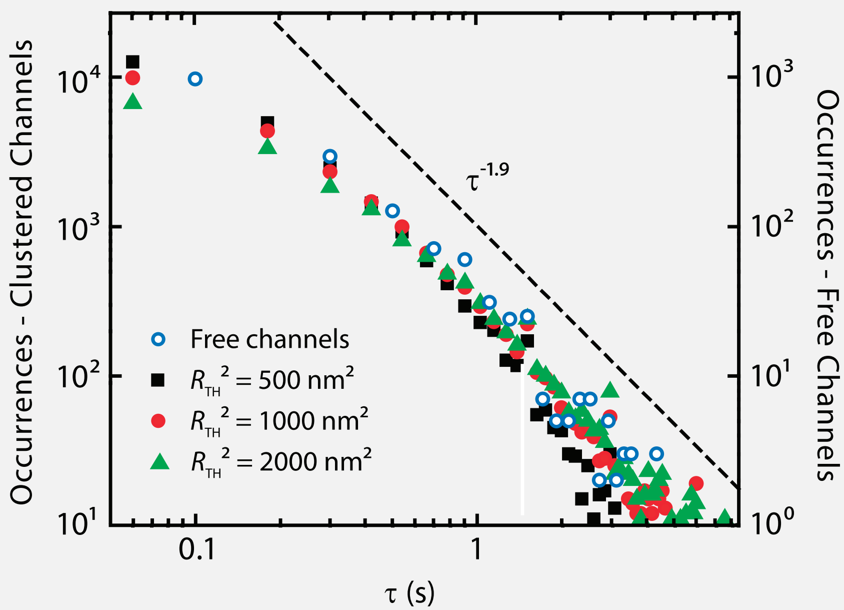
M Javanainen, H Seara Monne, RM & I Vattulainen, JPC Lett (2017)

CTRW-like motion of Ka channels in plasma membrane









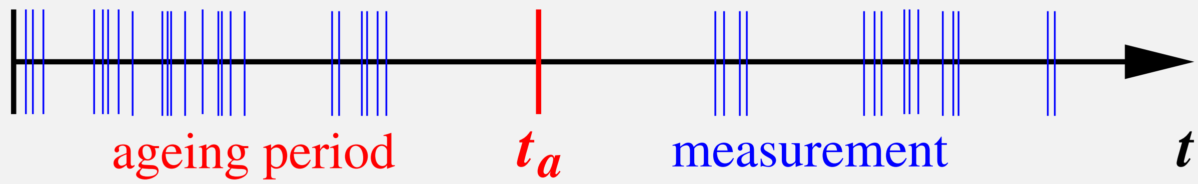
$\psi(\tau) \simeq \tau^{-1-\alpha}$ scale free

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

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

AV Weigel, B Simon, MM Tamkun & D Krapf, PNAS (2011)

Ageing effects in single trajectory time averages

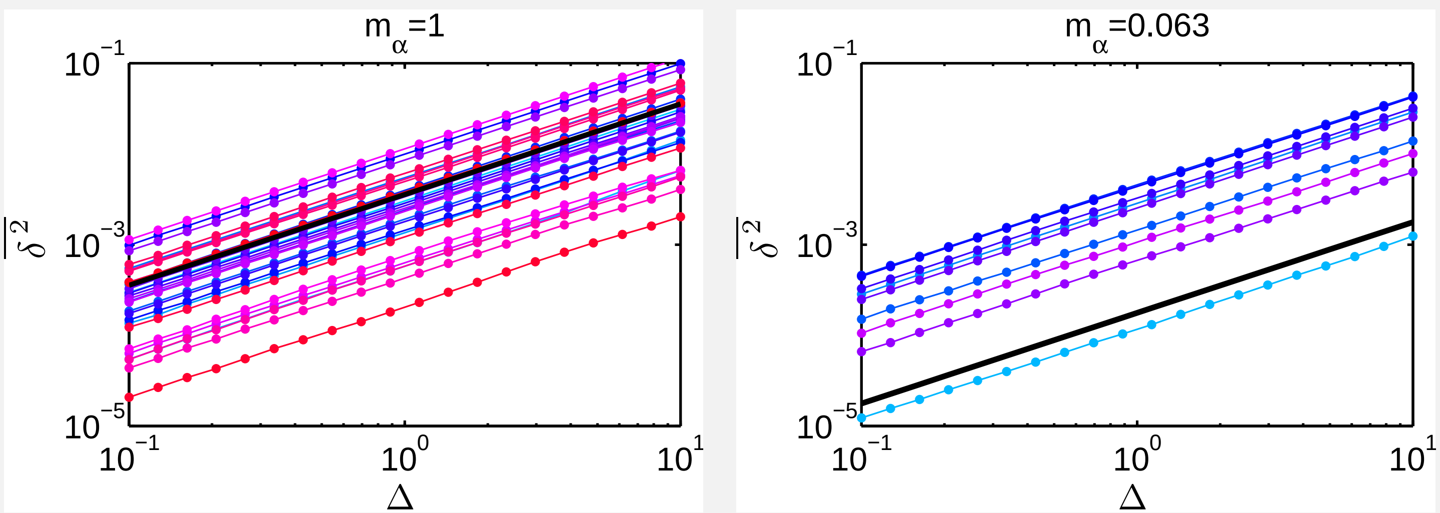


Ageing mean squared displacement ($\Lambda(z)=(1+z)^\alpha-z^\alpha$)

$$\left\langle\overline{\delta^2(\Delta)}\right\rangle_a=\frac{\Lambda_\alpha(t_a/T)}{\Gamma(1+\alpha)}\frac{g(\Delta)}{T^{1-\alpha}}\qquad\not\Leftrightarrow\qquad\langle x^2(t)\rangle_a\simeq\begin{cases}t^\alpha, & t_a\ll t\\ t_a^{\alpha-1}t, & t_a\gg t\end{cases}$$

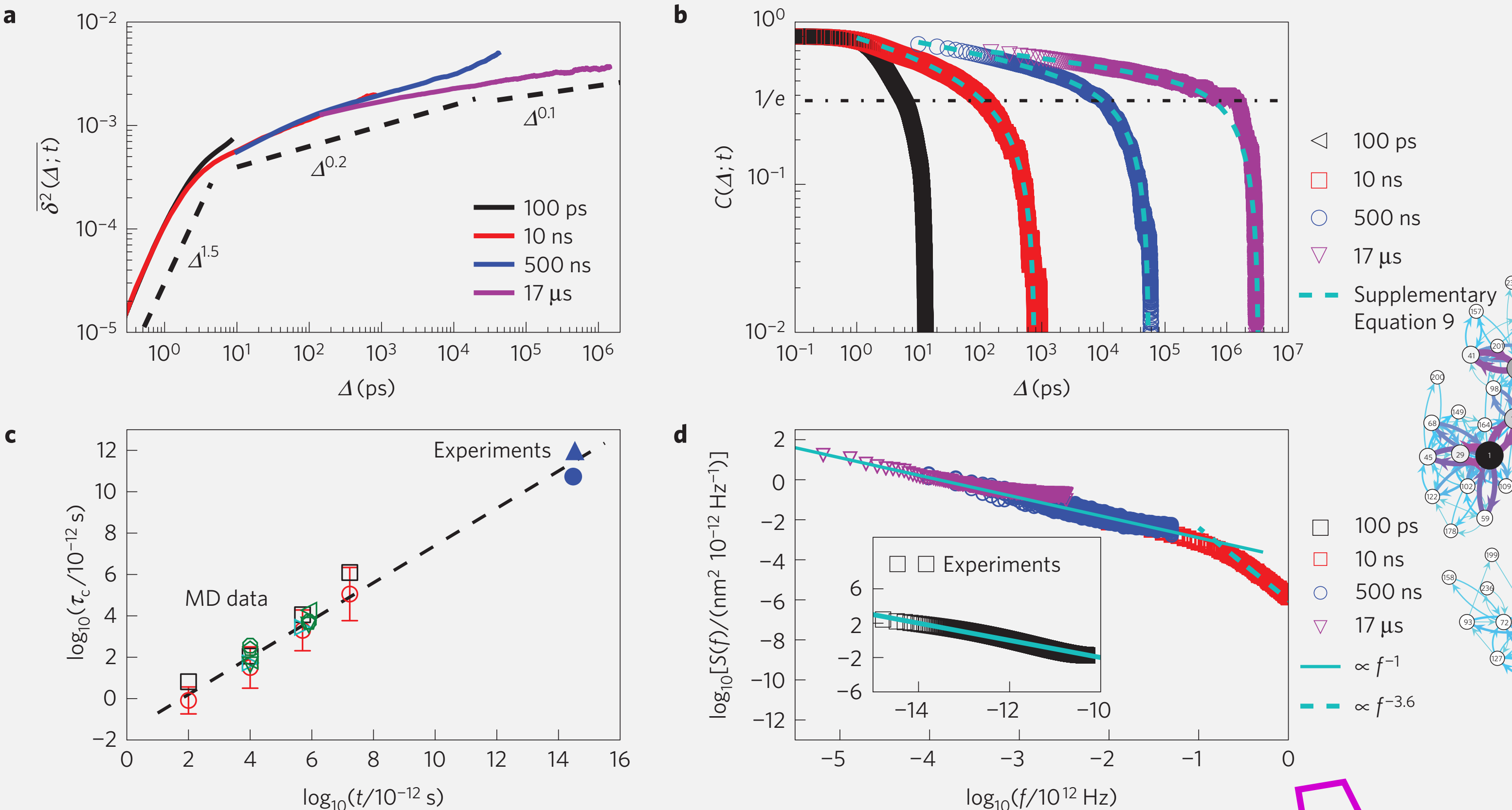
Probability to make at least one step during $[t_a,t_a+T]$: *population splitting*

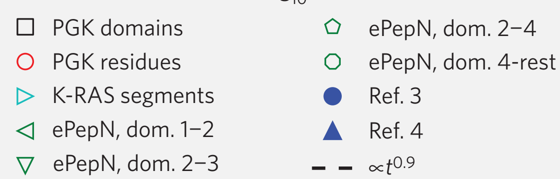
$$m_\alpha(T/t_a)\simeq(T/t_a)^{1-\alpha},\ \ T\ll t_a$$

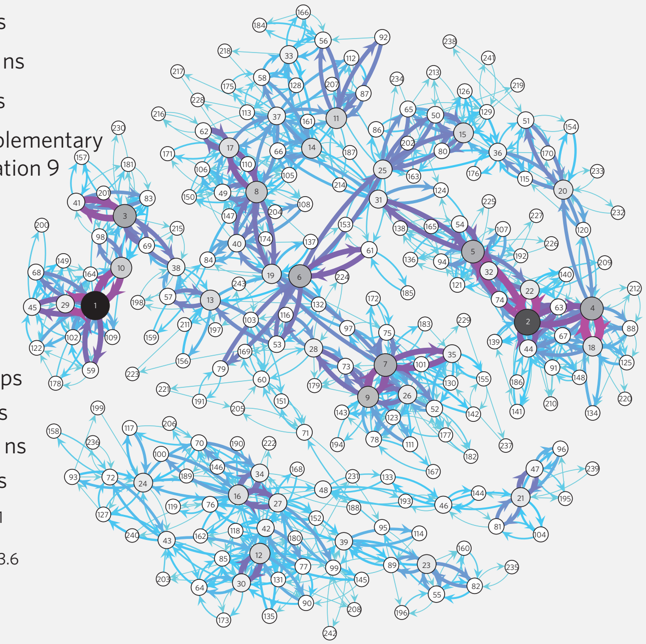


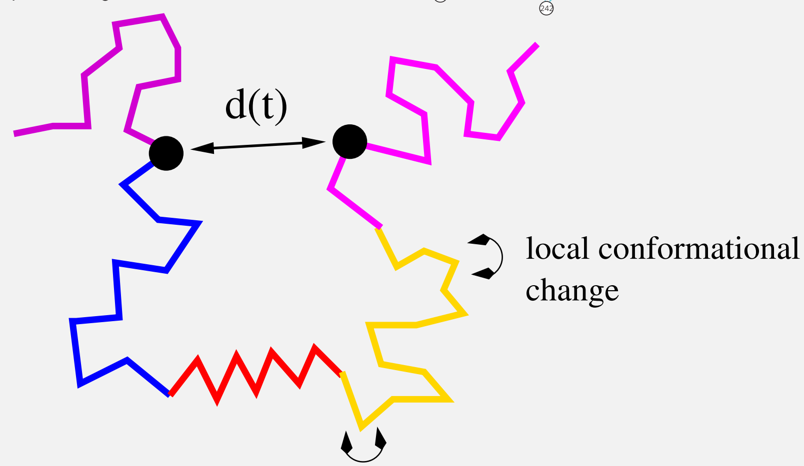
J Schulz, E Barkai & RM, PRL (2013), PRX (2014)

Self-similar internal protein dynamics: 13 decades of ageing









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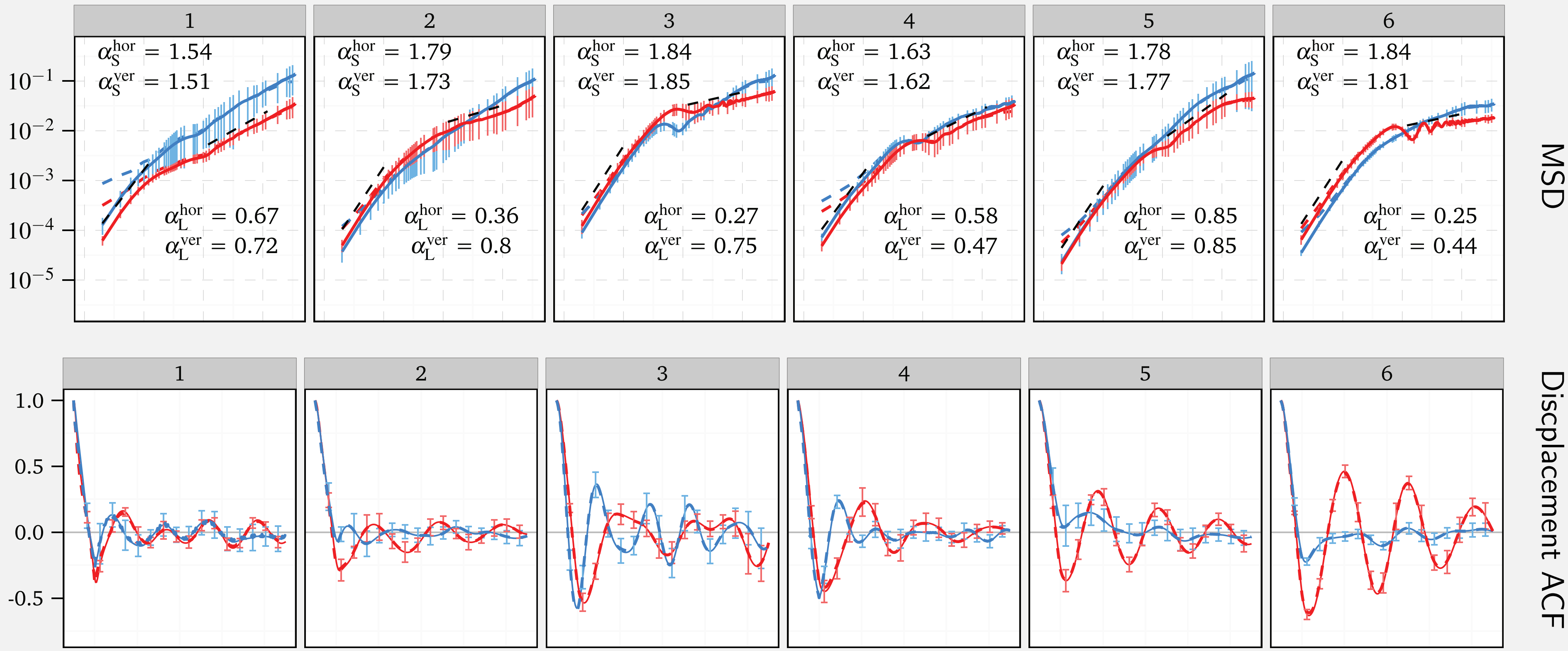
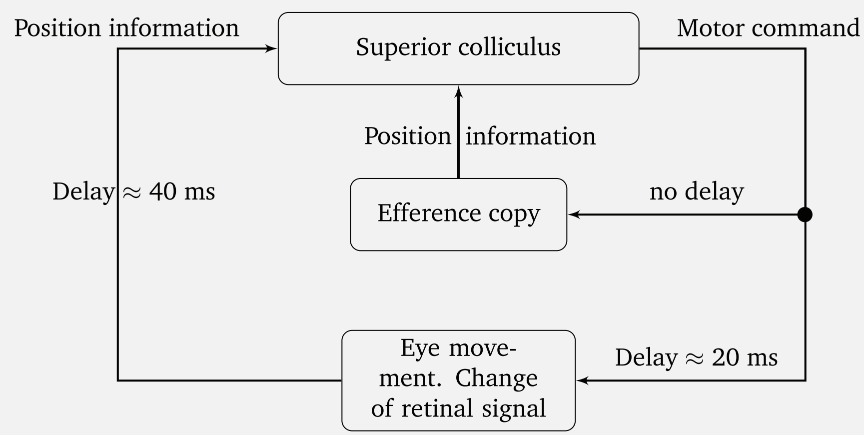
Stochasticity of fixational eye movements





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

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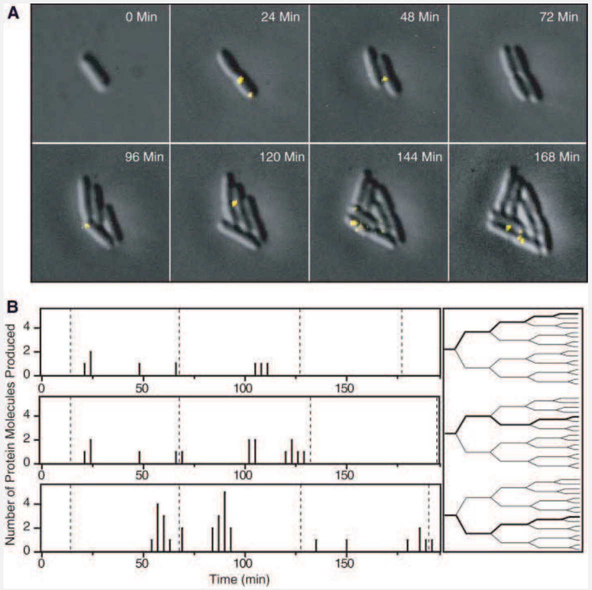

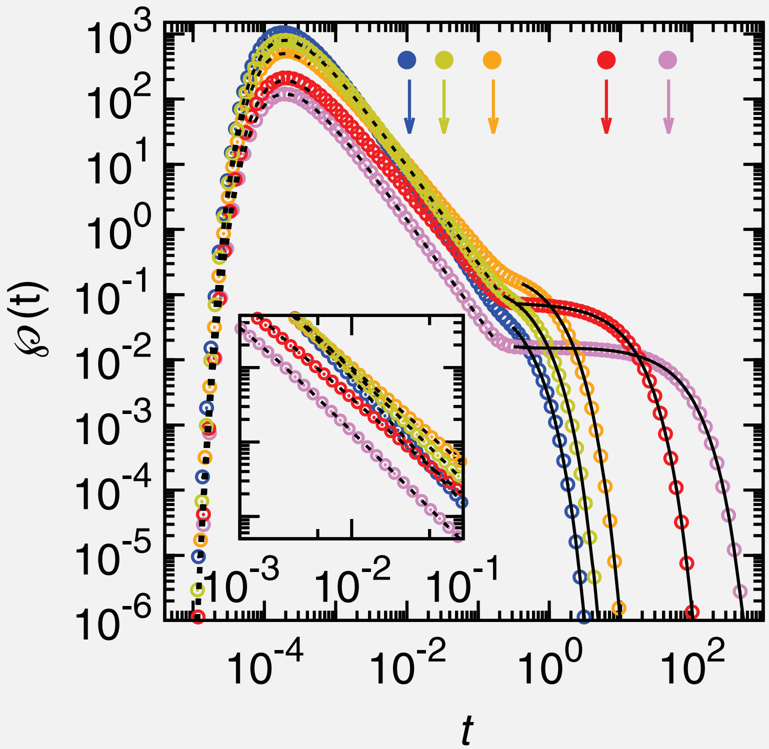

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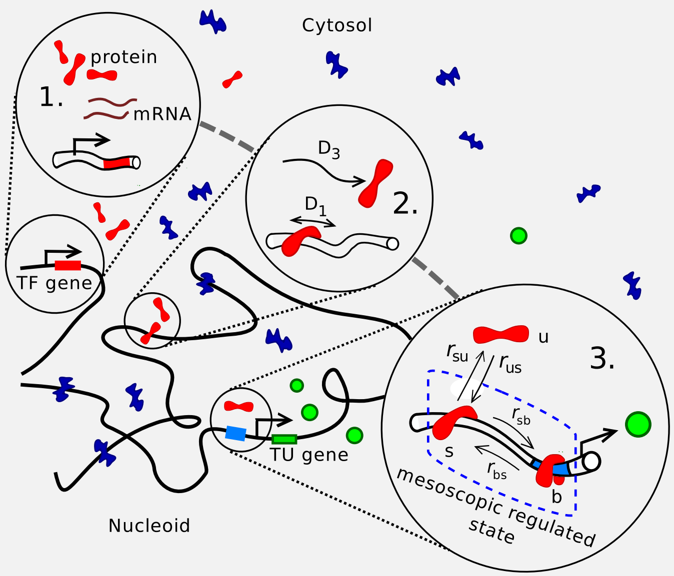

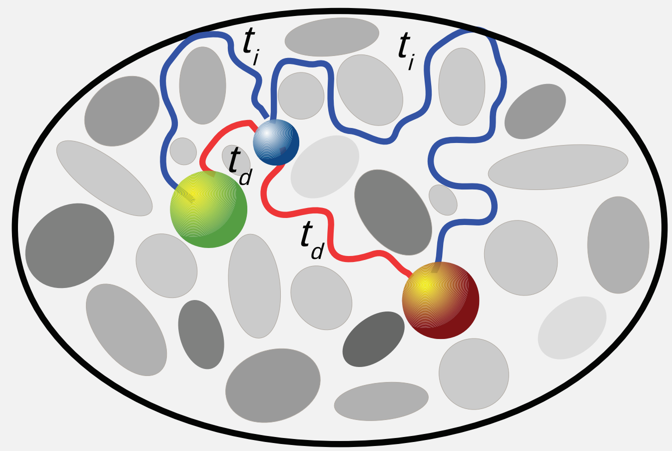

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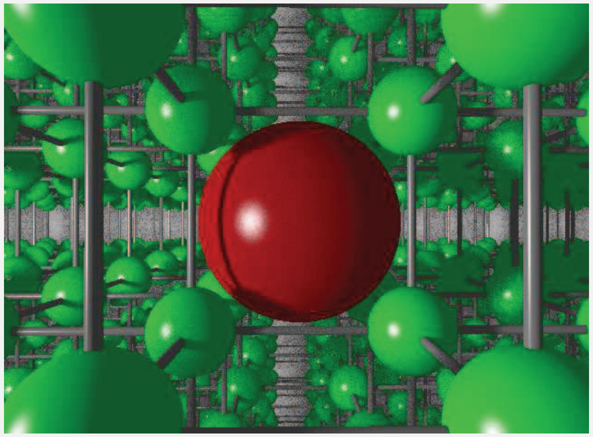
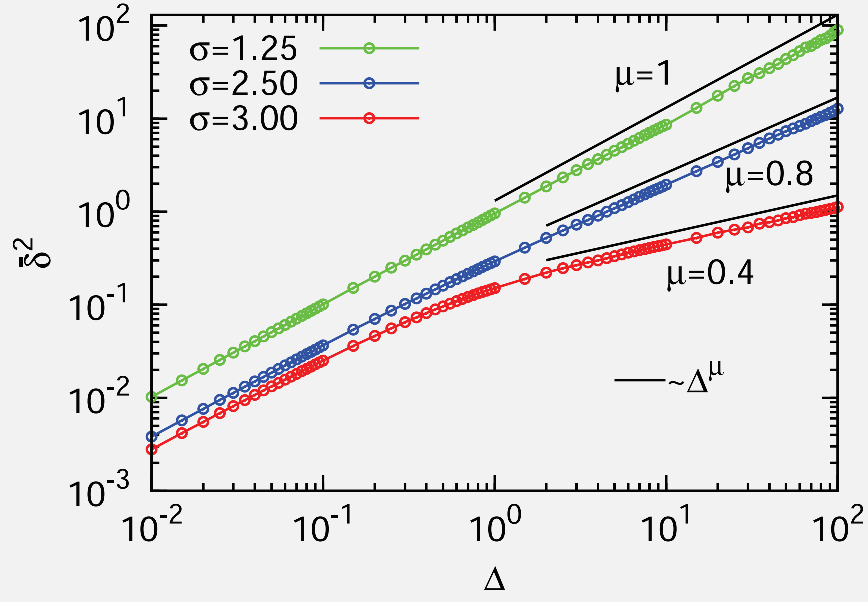
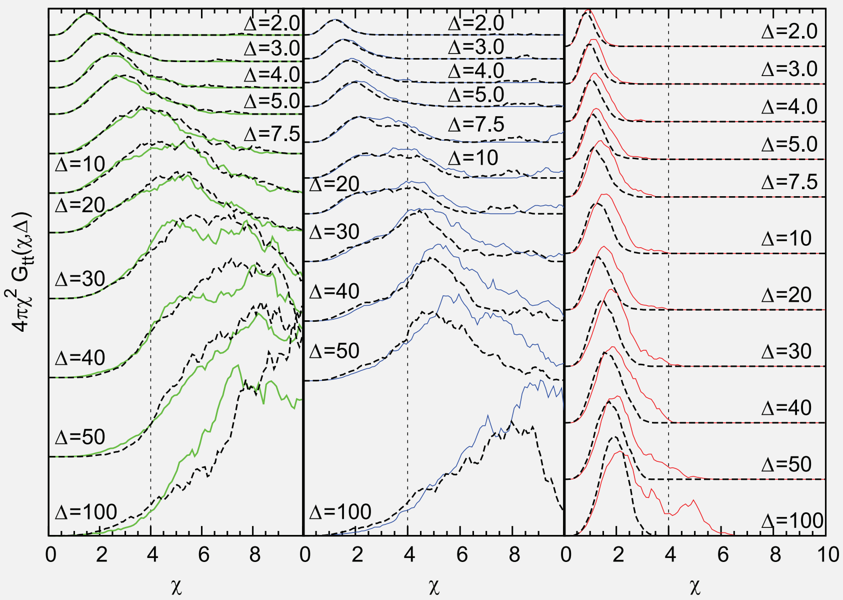
Tracer diffusion in flexible Morse spring gel







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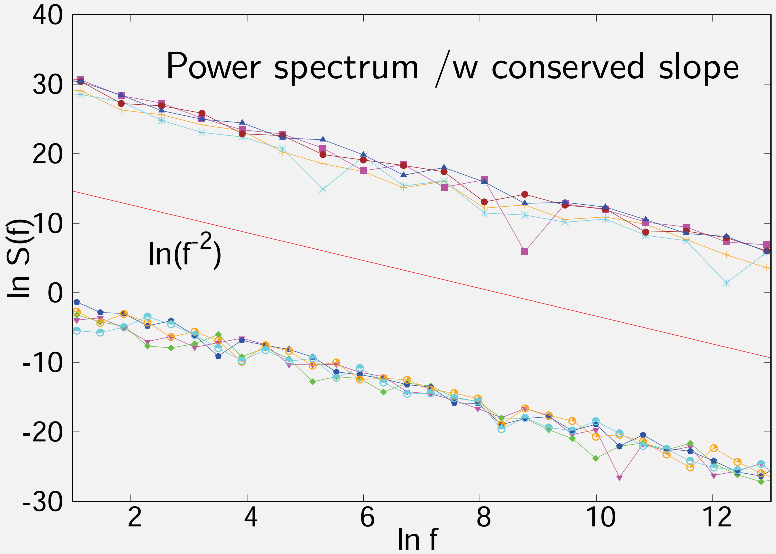
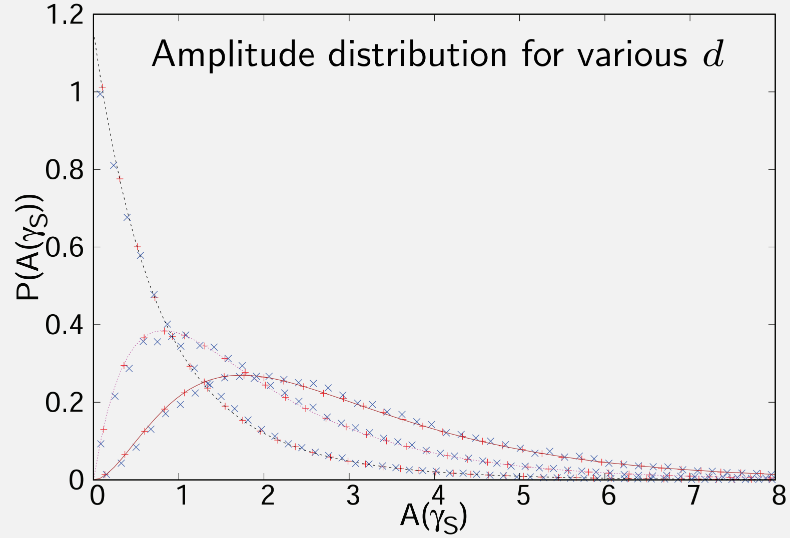
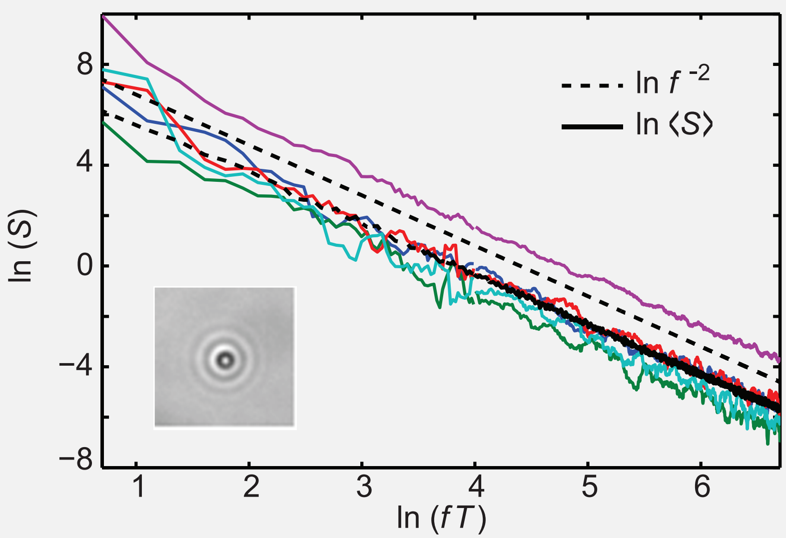
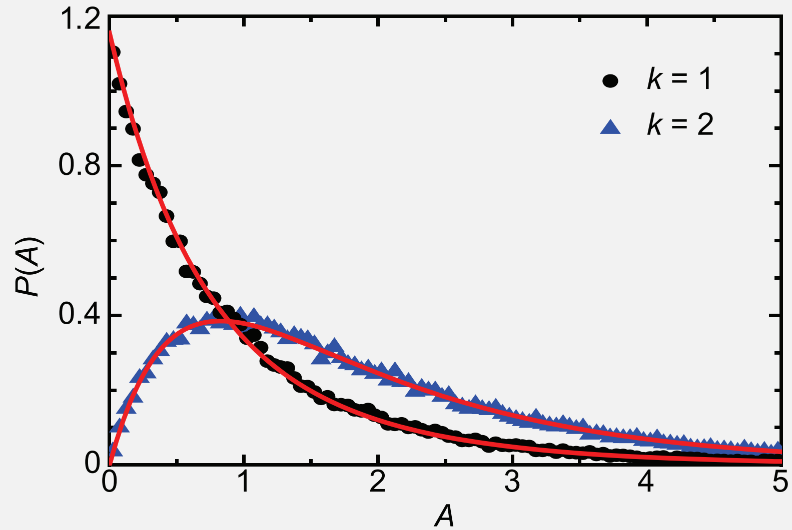
Power spectral density of a single Brownian trajectory





Theory





Experiment

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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)

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