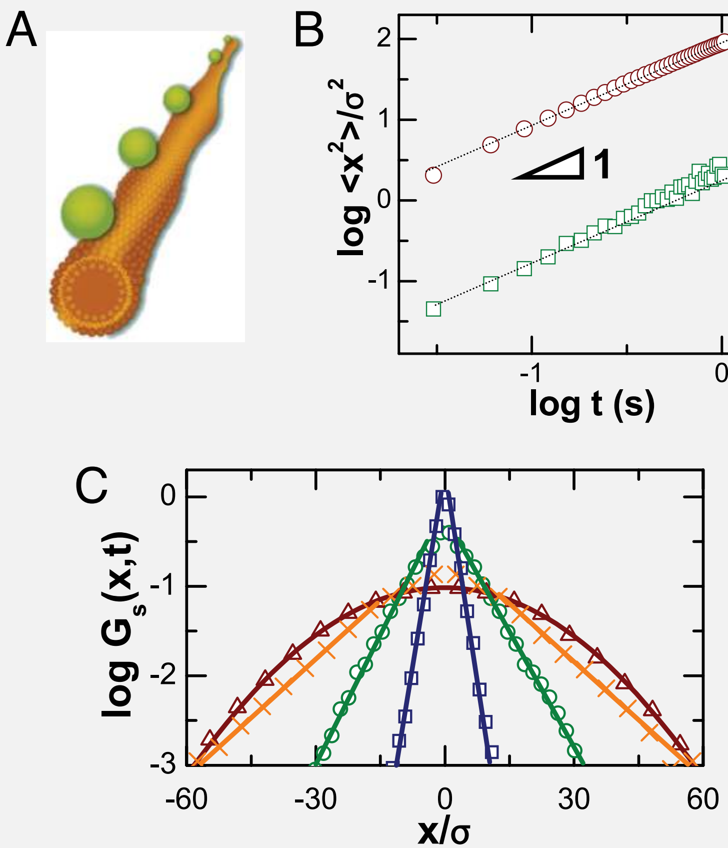
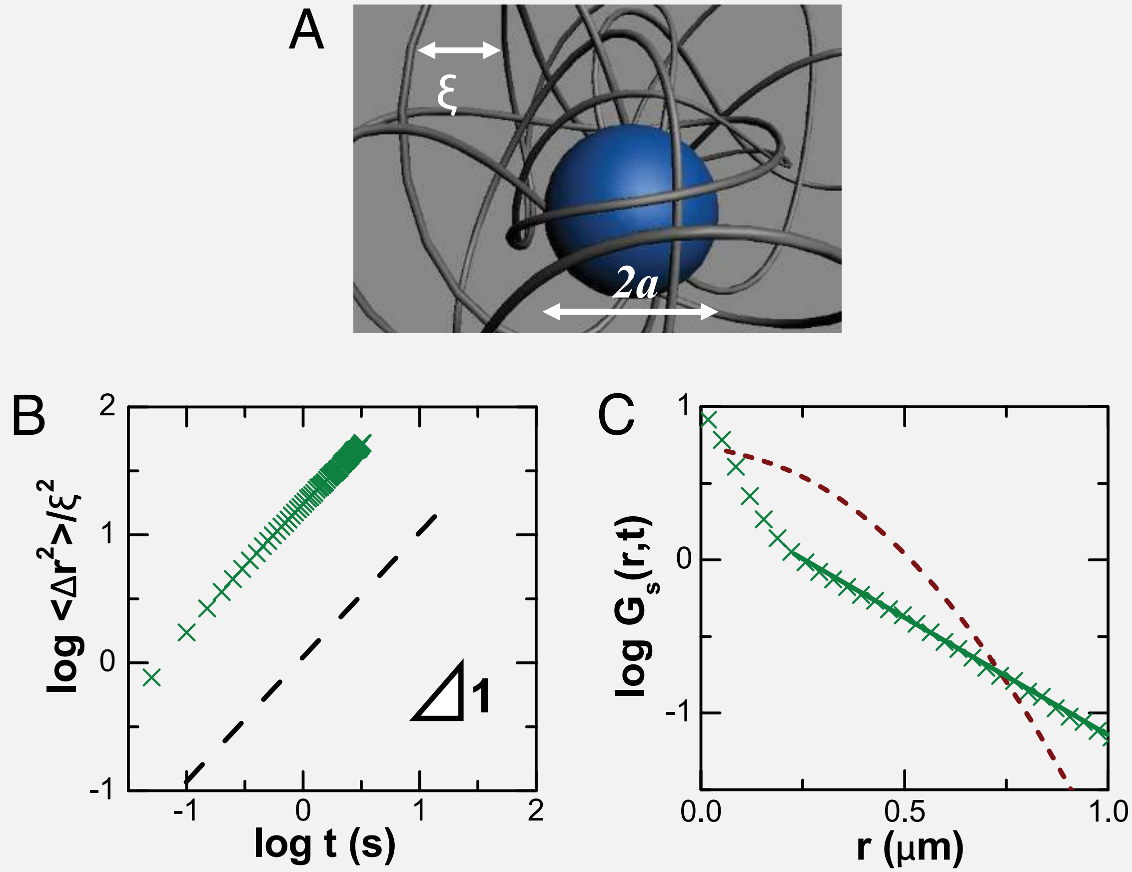
# Anomalous diffusion in membranes

— Shanghai, 2nd July 2018 —

# When Brownian diffusion is not Gaussian



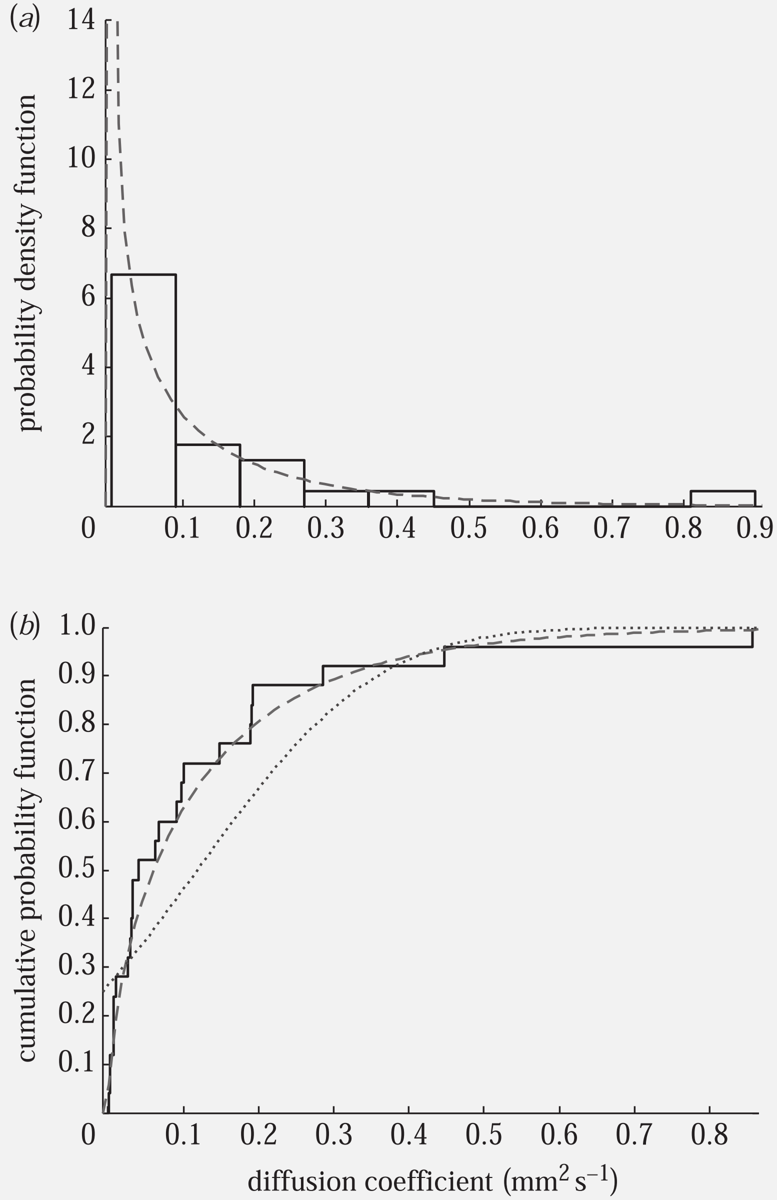




Colloidal beads diffusing on nanotubes

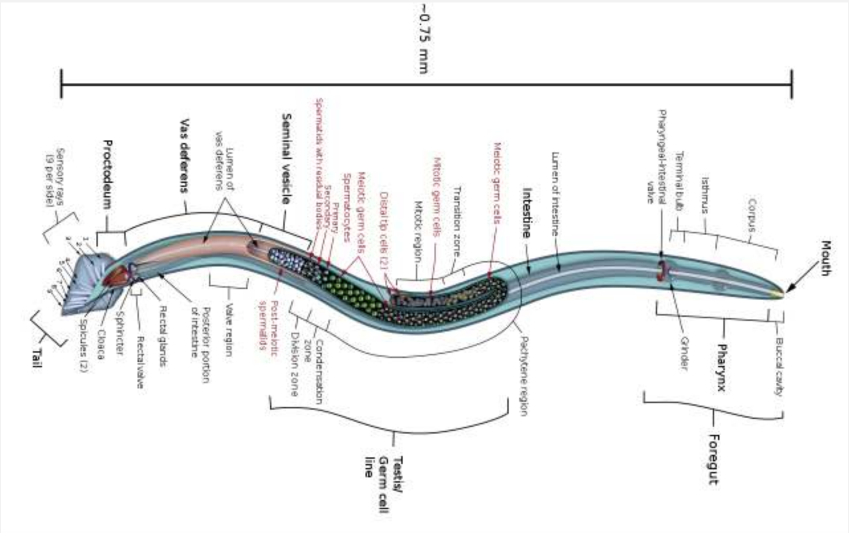
Nanospheres diffusing in entangled actin

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

# Heterogeneous diffusion in population of nematodes



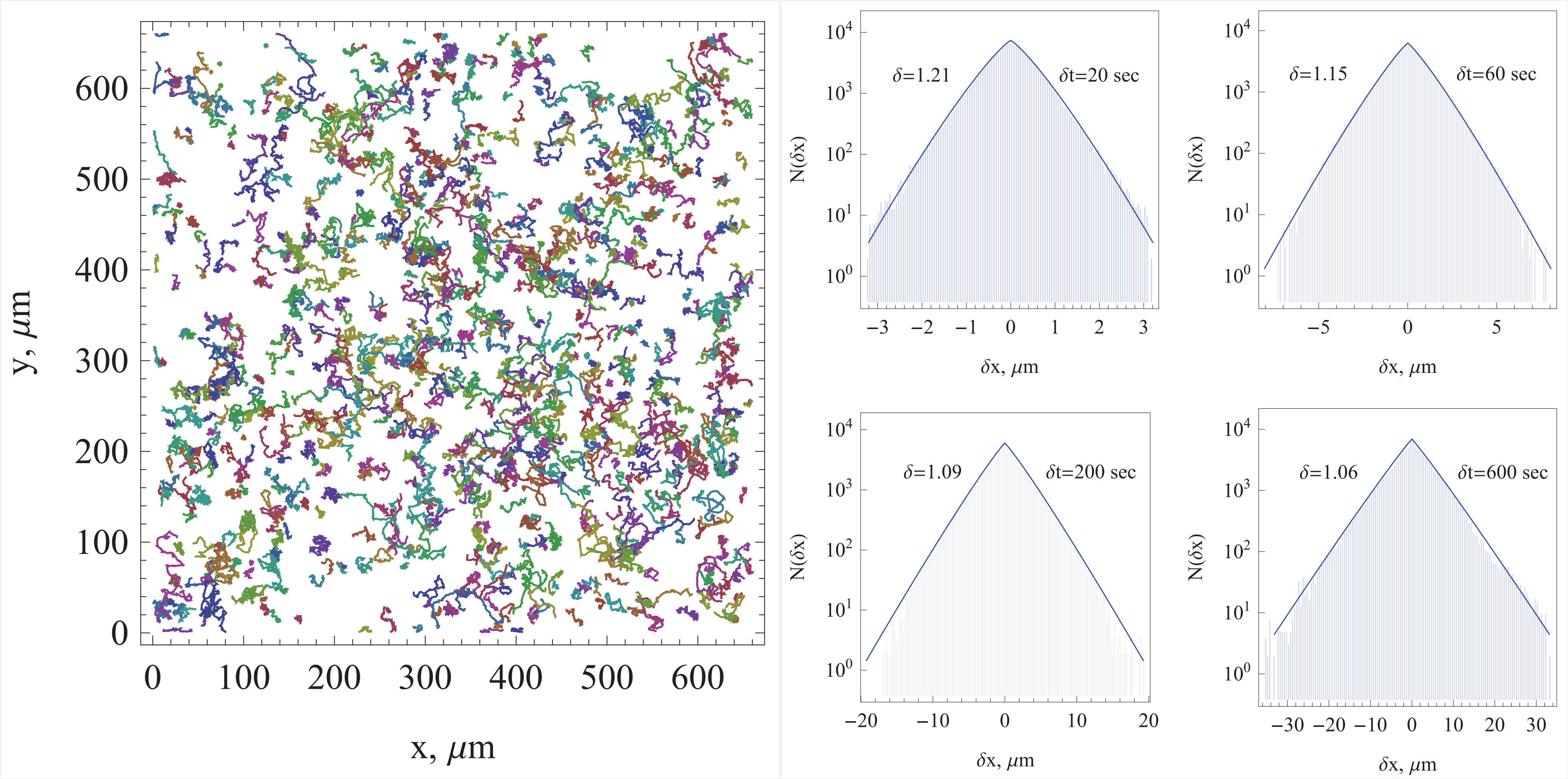

S Hapca, JW Crawford & IM Young, Roy Soc Interface (2009)




Male C. elegans nematode

Soybean cyst nematode & egg

# Non-Gaussian diffusion of Dictyostelium cells




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

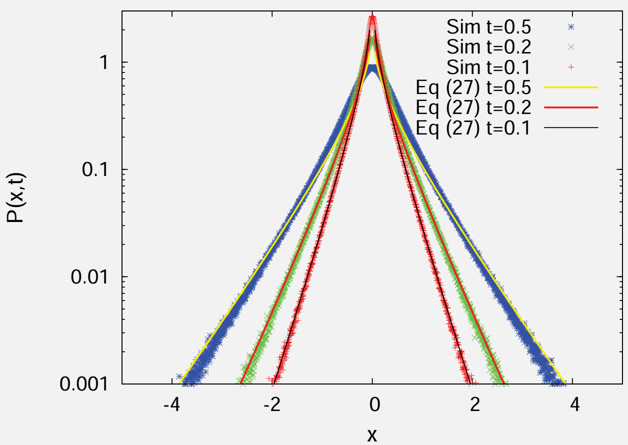
# Fickian, non-Gaussian diffusion with diffusing diffusivity

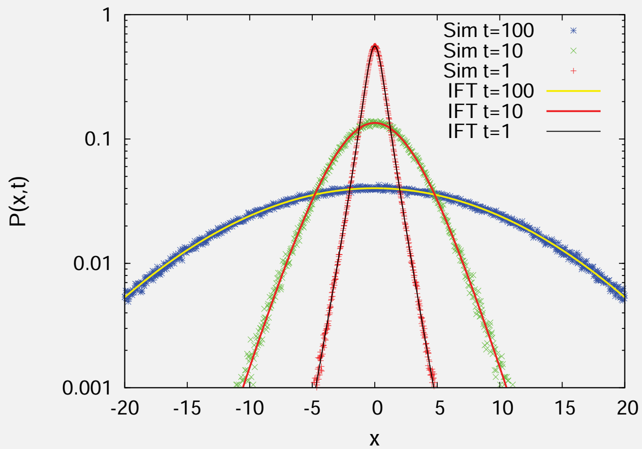
B Wang, J Kuo, SC Bae & S Granick, Nat Mat (2012): $\langle x^2(t)\rangle = 2K_1 t$, yet $P(x,t)$ non-Gaussian. Superstatistical approach $P(x,t)=\int_0^\infty G(x,t)p(D)dD$

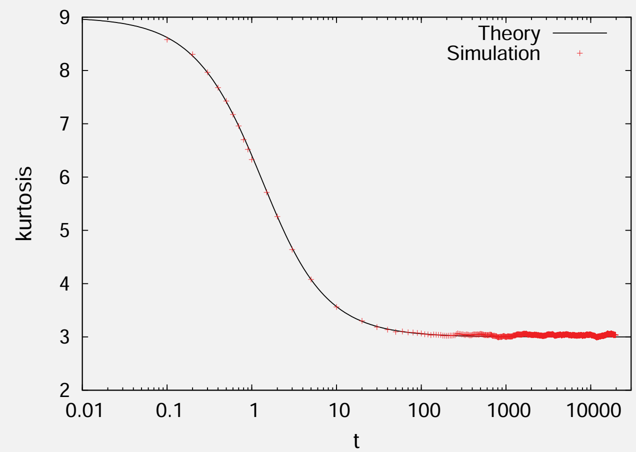
MV Chubinsky & G Slater, PRL (2014); R Jain & KL Sebastian, JPC B (2016): diffusing diffusivity

Our minimal model for diffusing diffusivity:

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

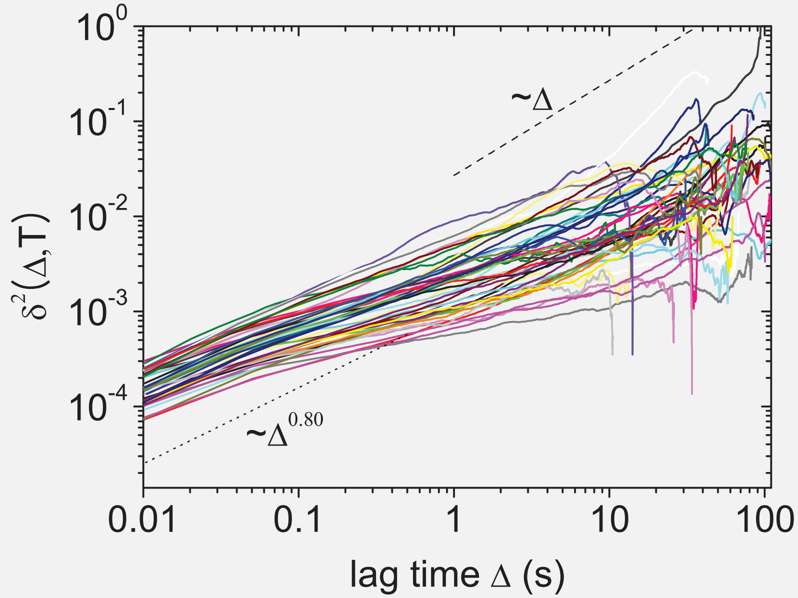


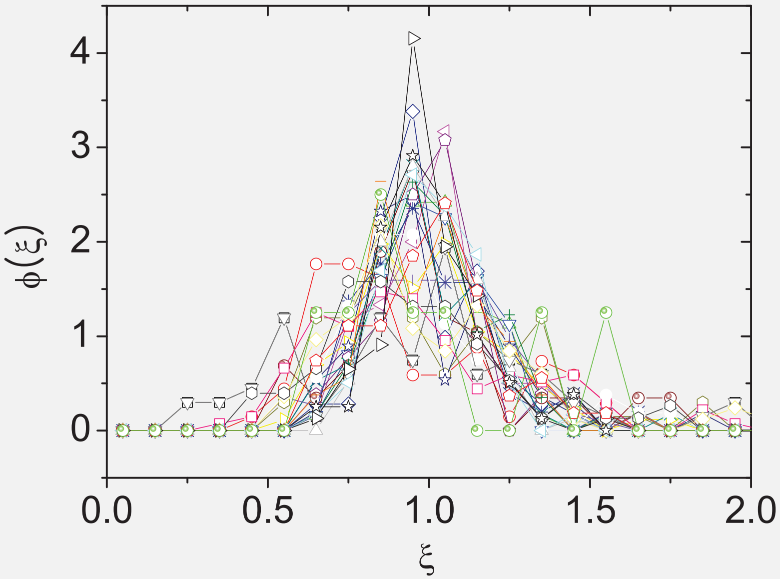




AV Chechkin, F Seno, RM & IM Sokolov, PRX (2017); generalised $\gamma(D)$: V Sposini, AV Chechkin, G Pagnini, F Seno & RM, NJP (2018)

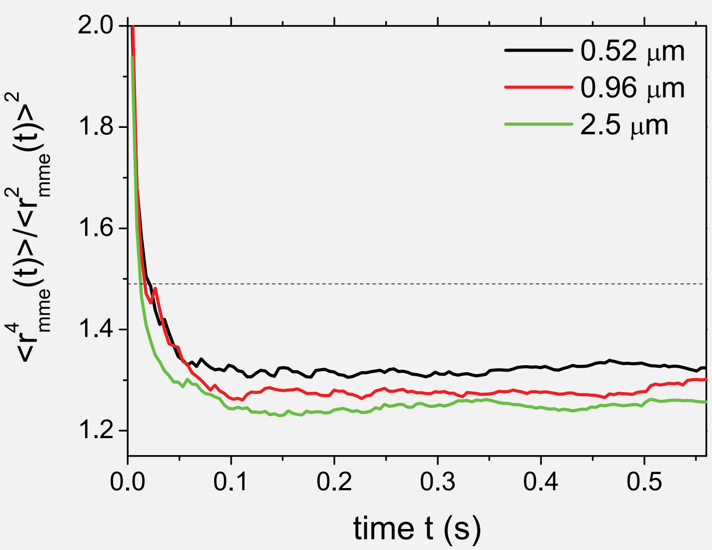
# Passive motion of submicron tracers in cells is viscoelastic

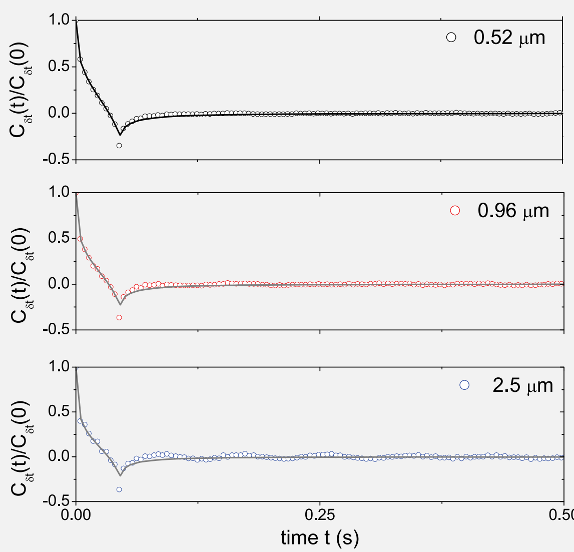


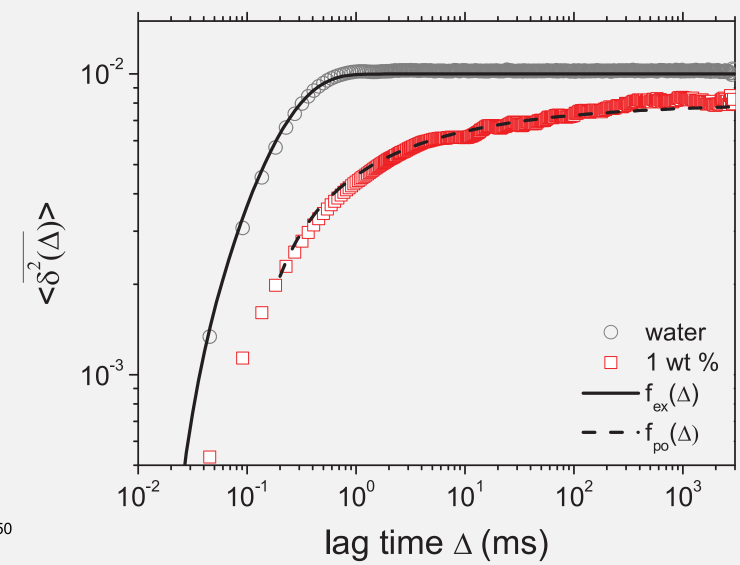




Lipid granules in living yeast cells ←

Tracer beads in wormlike micellar solution →




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

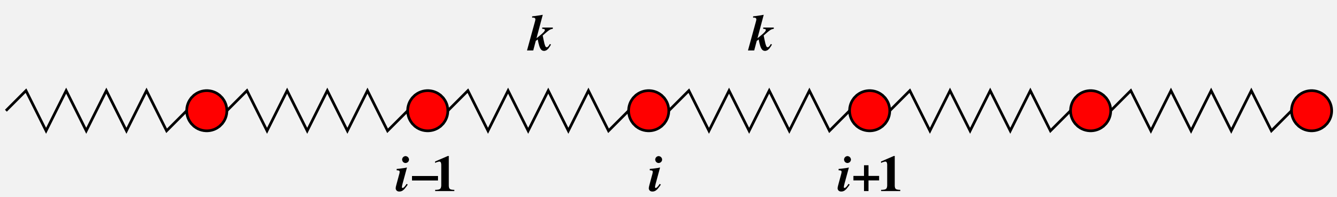
# Fractional Langevin equations in viscoelastic systems

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

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

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

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




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

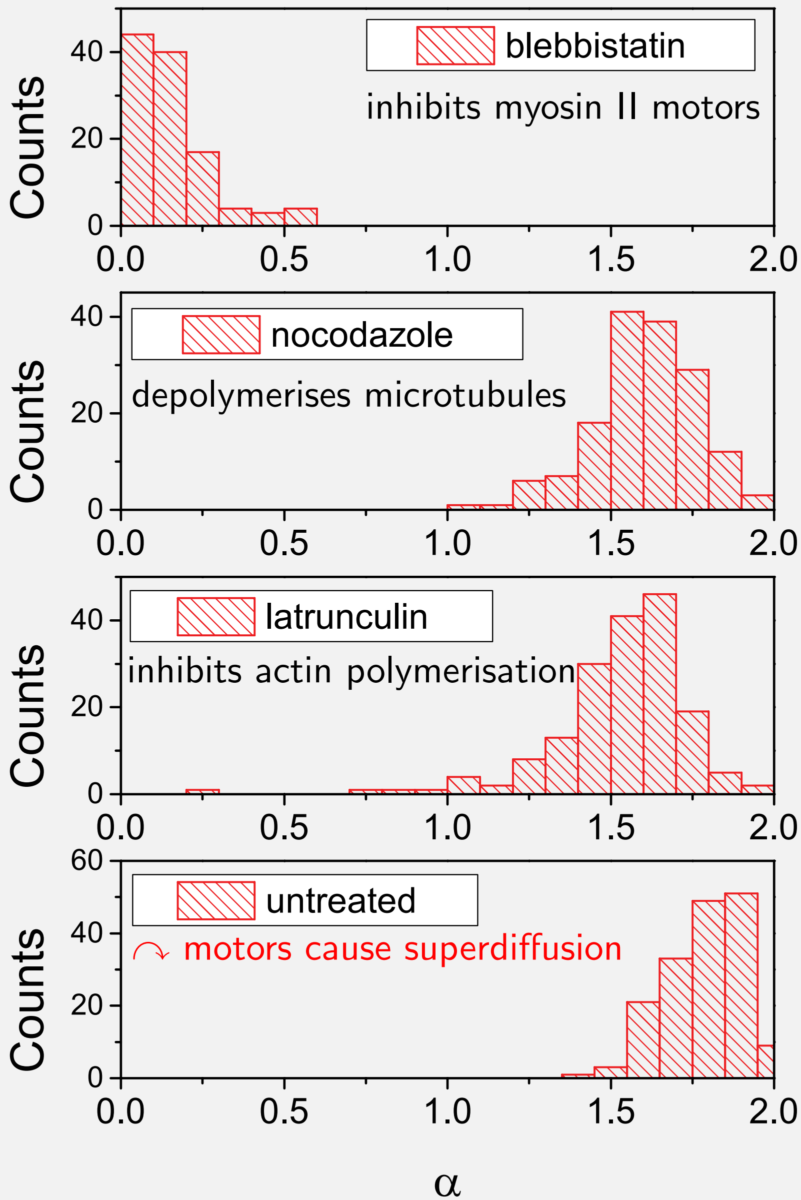
$$\langle\zeta_i(t)\zeta_j(t')\rangle=\delta_{ij}k_BT\eta(|t-t'|)$$

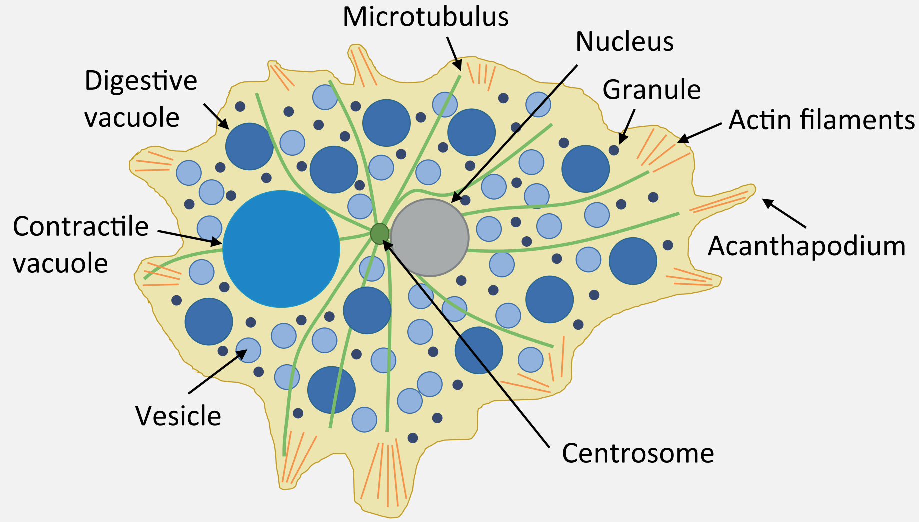
$\curvearrowright$ fractional Langevin equation. Overdamped limit: Mandelbrot's FBM

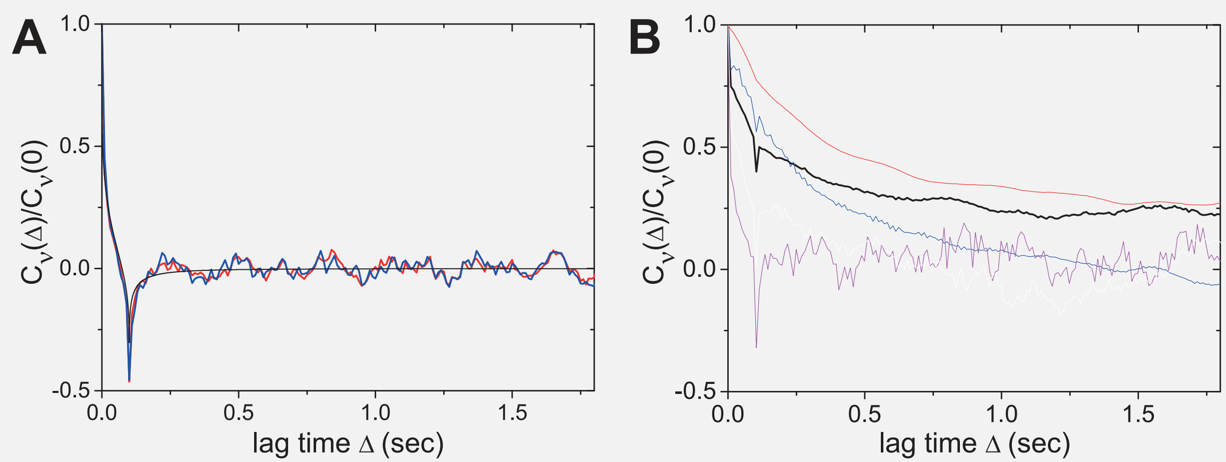
Quantum mechanics: Nakajima-Zwanzig equation using projection operators

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

# Superdiffusion in supercrowded Acanthamoeba castellani



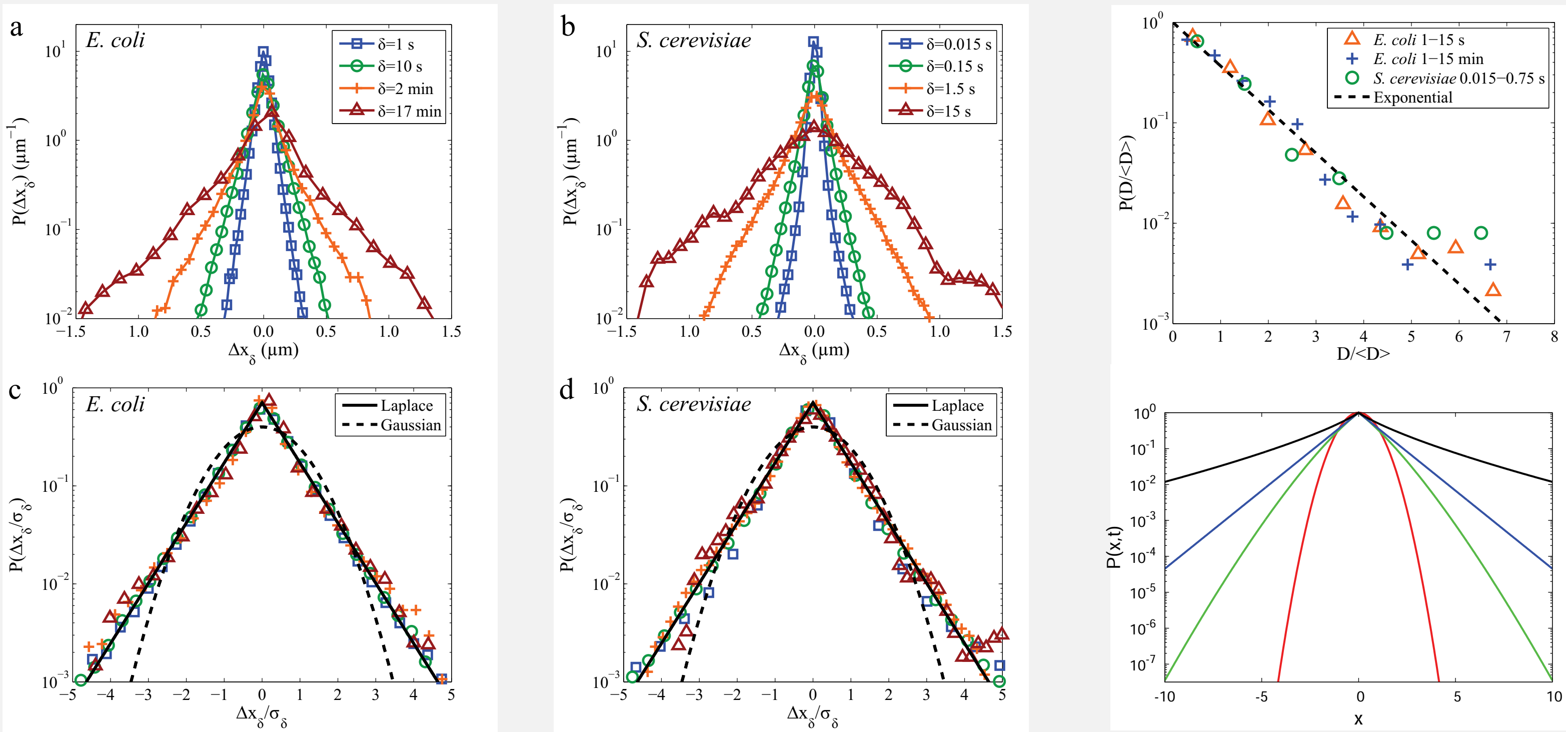




JF Reverey, J-H Jeon, H Bao, M Leippe, RM & C Selhuber-Unkel, Sci Rep (2015)

# Non-Gaussian diffusion in viscoelastic systems

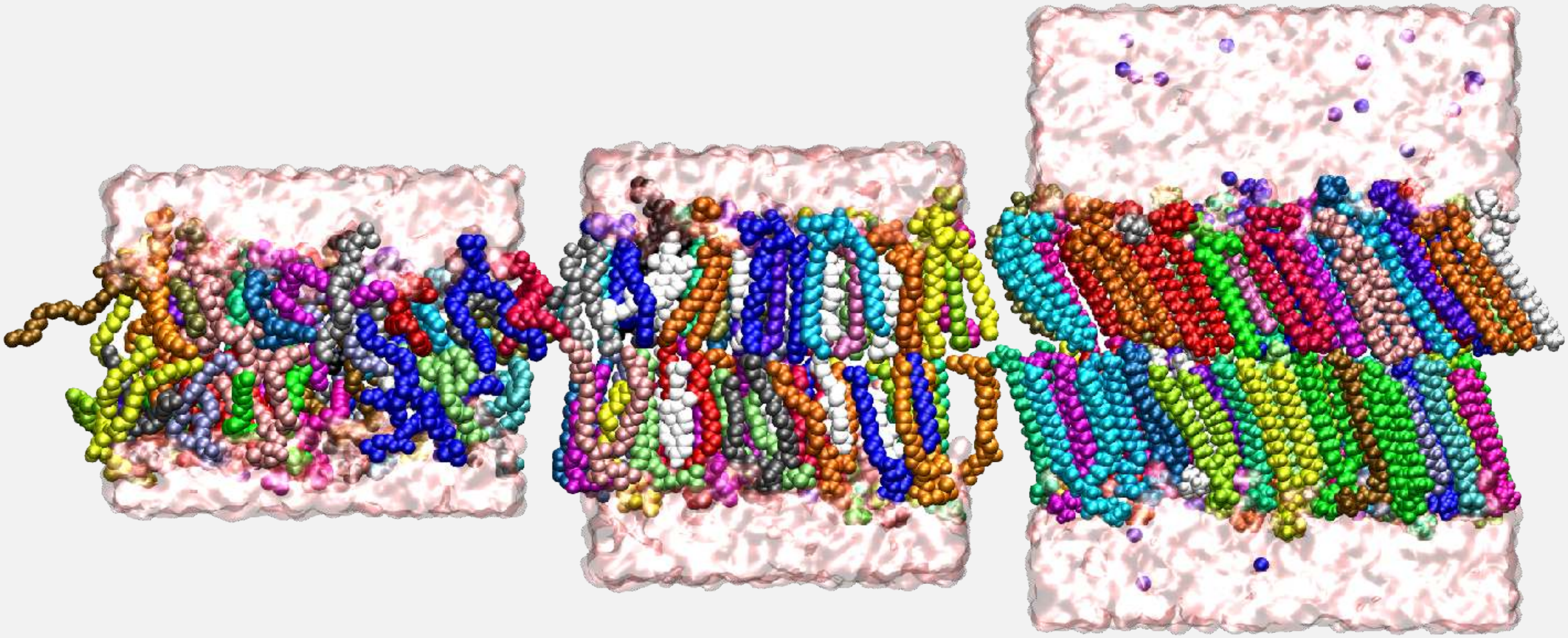
So far consensus: submicron tracer motion in cytoplasm is FBM-like, i.e., Gaussian
RNA-protein particles in E.coli & S.cerevisiae perform exponential anomalous diffusion:




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)

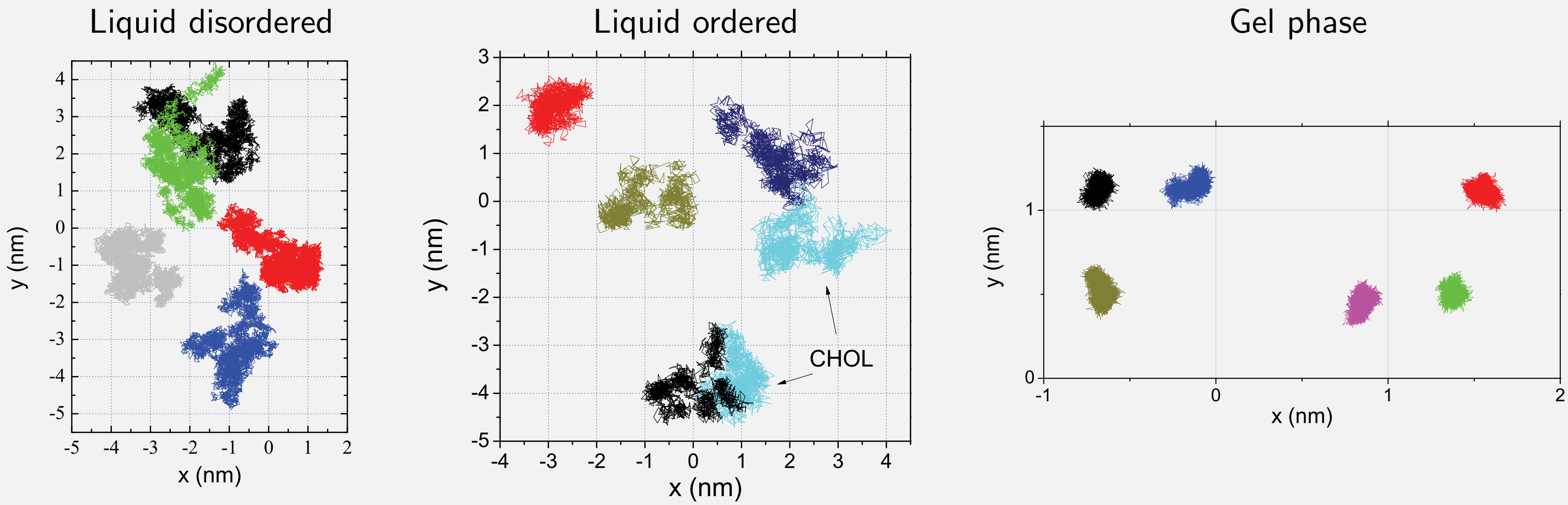
# Single lipid motion in bilayer membrane MD simulations



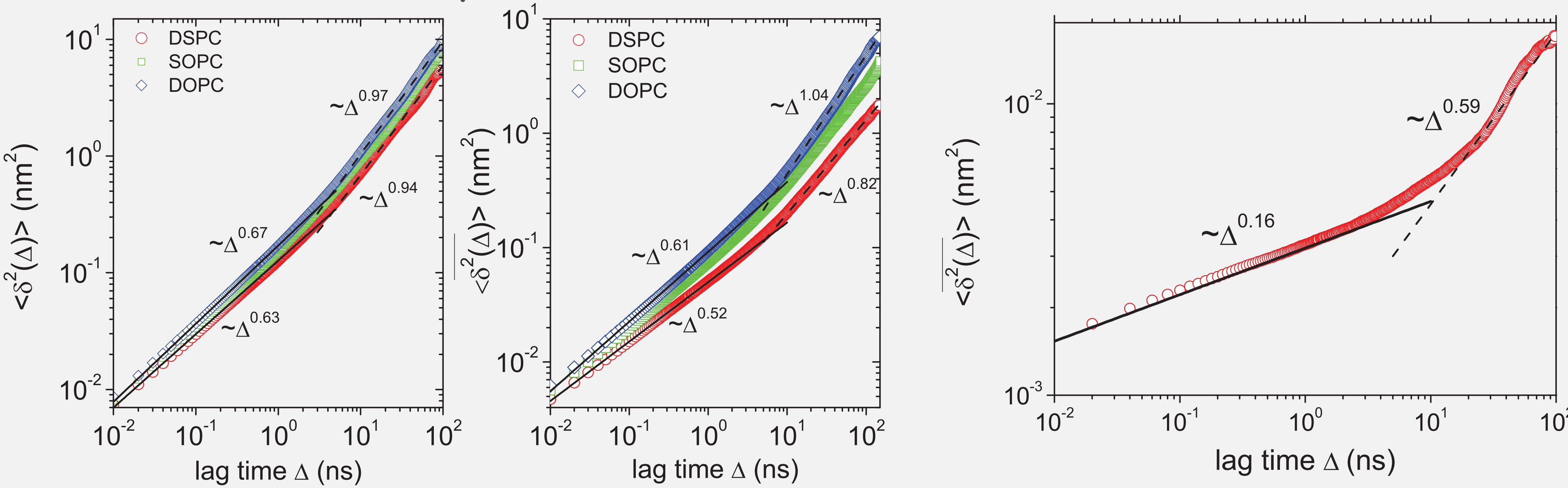
Liquid disordered　　Liquid ordered　　Gel phase

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

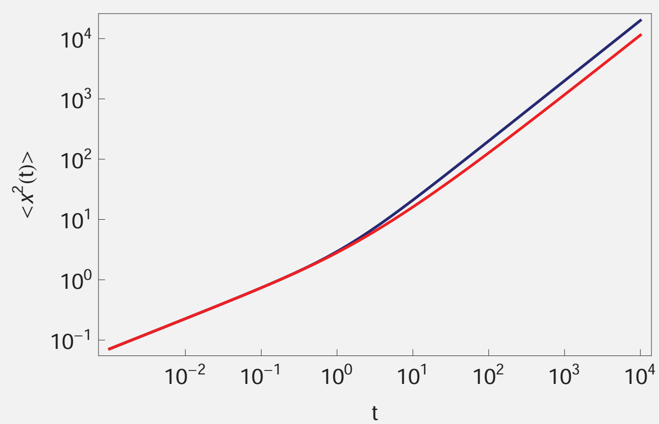


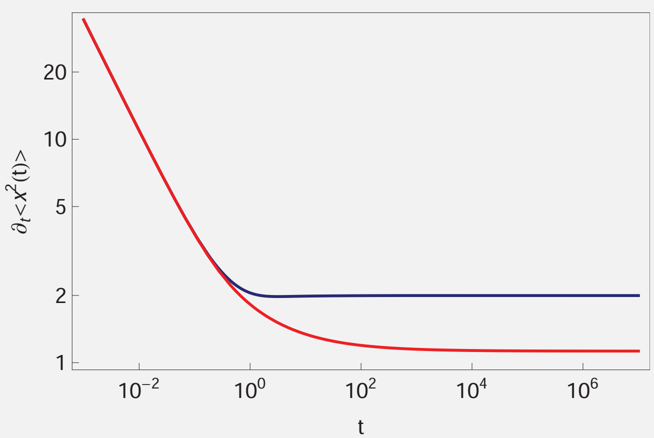

J-H Jeon, H Martinez-Seara Monne, M Javanainen & RM, PRL (2012)

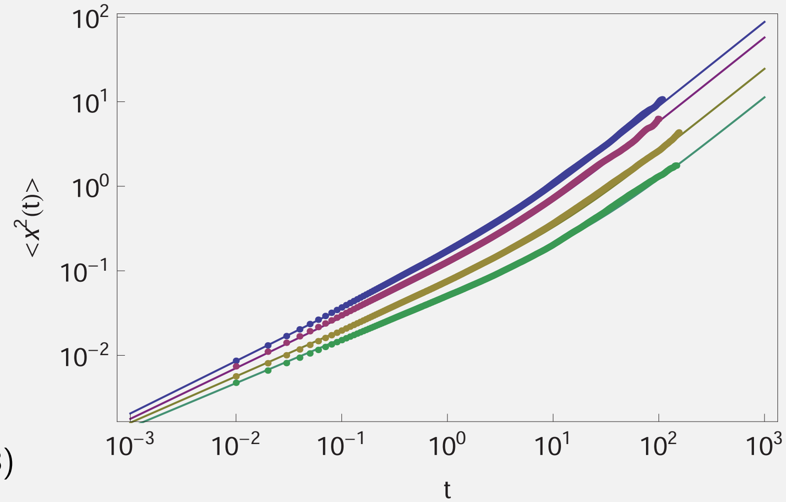
# Tempered FBM & FLE motion: sub- to normal diffusion

Consider tempered fGn:

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

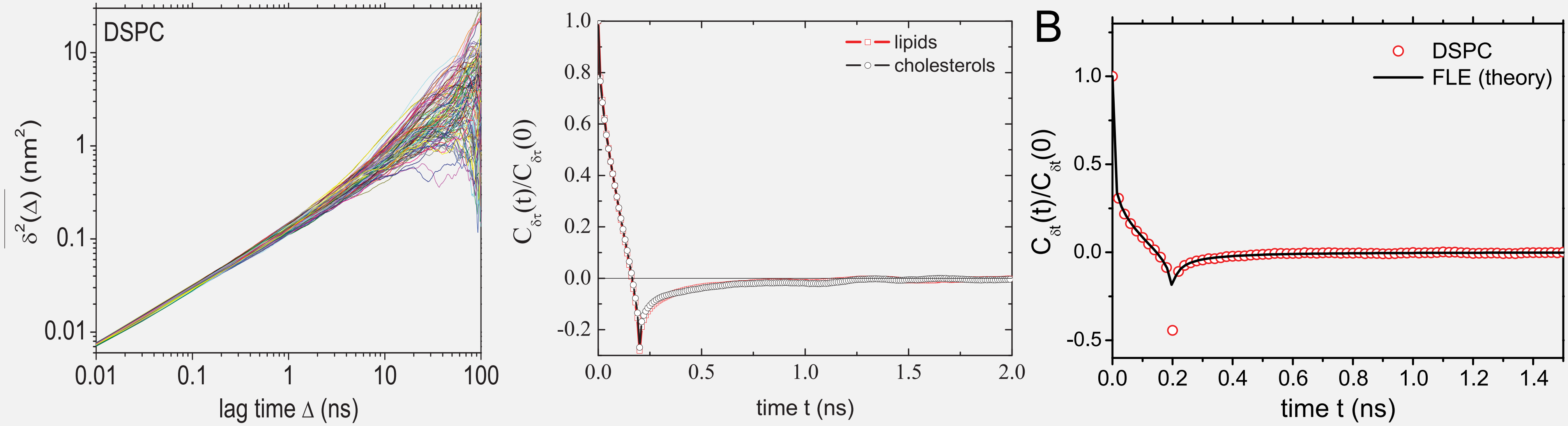


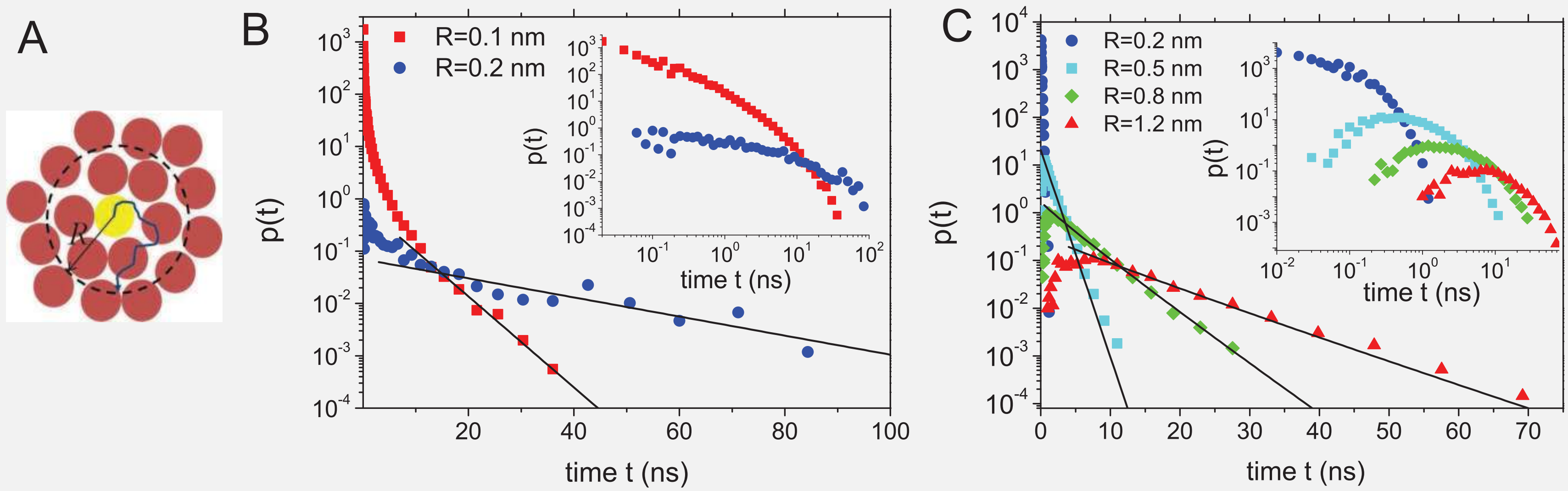




D Molina-Garcia, T Sandev, G Pagnini, AV Chechkin & RM (2018)

## Reproducible TA MSD & antipersistent correlations

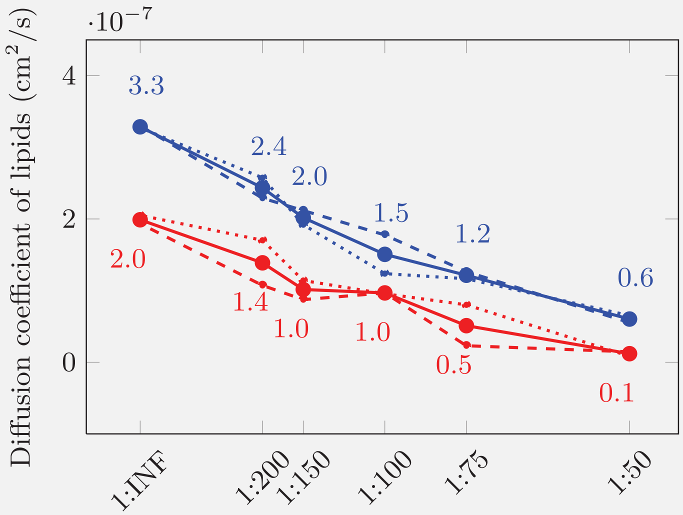


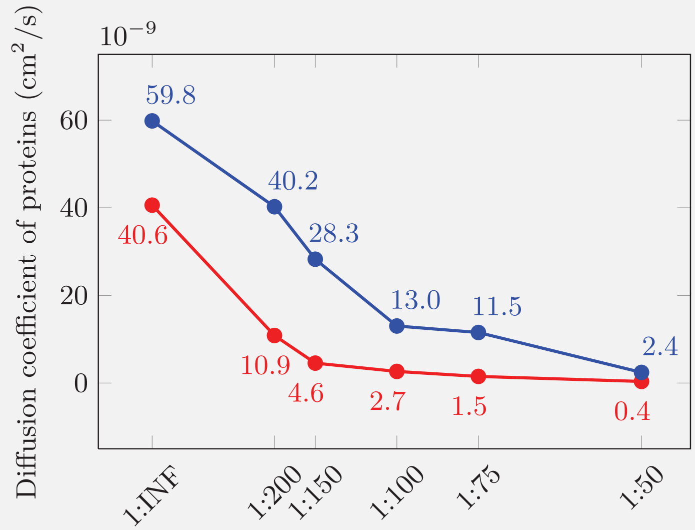

## Rattling dynamics: exptl first passage PDF $\curvearrowright$ FLE motion



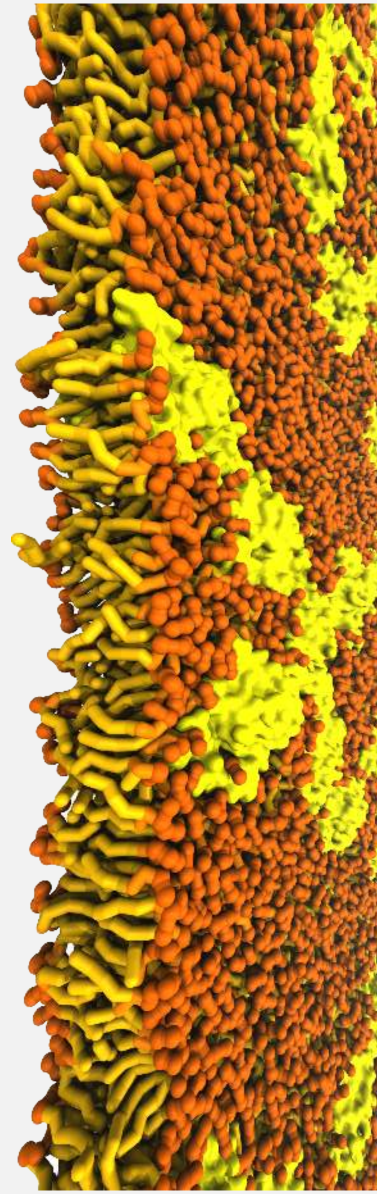

D Molina-Garcia, T Sandev, G Pagnini, AV Chechkin & RM (2018)

# Protein crowded membranes reduce effective mobility

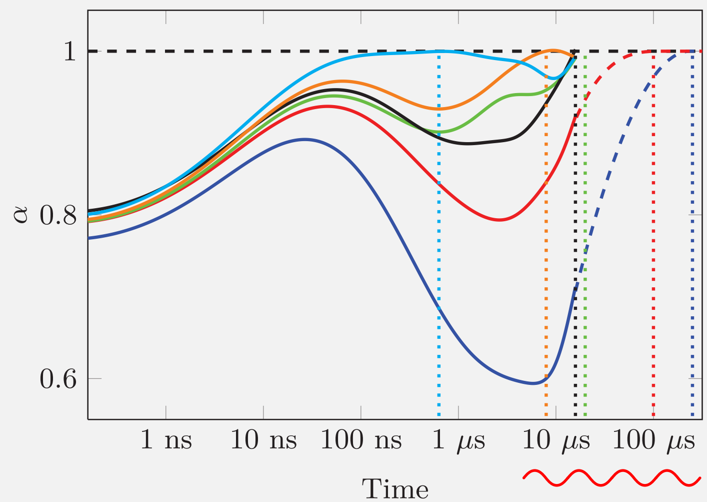


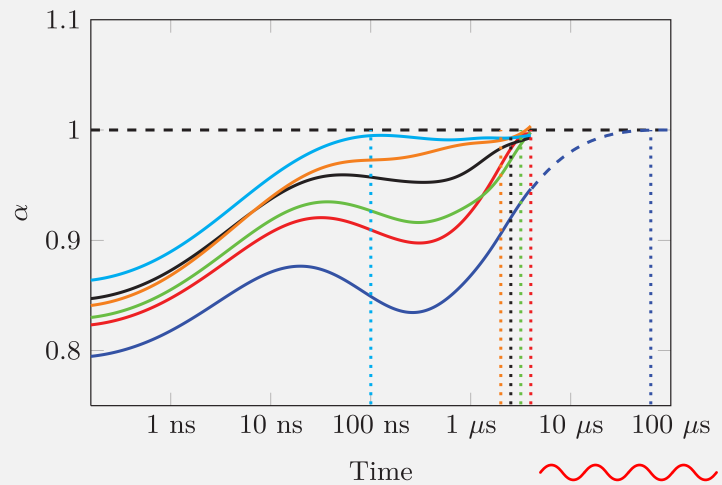




Blue: DLPC. Red: DPPC



# Protein crowding effects anomalous lipid diffusion

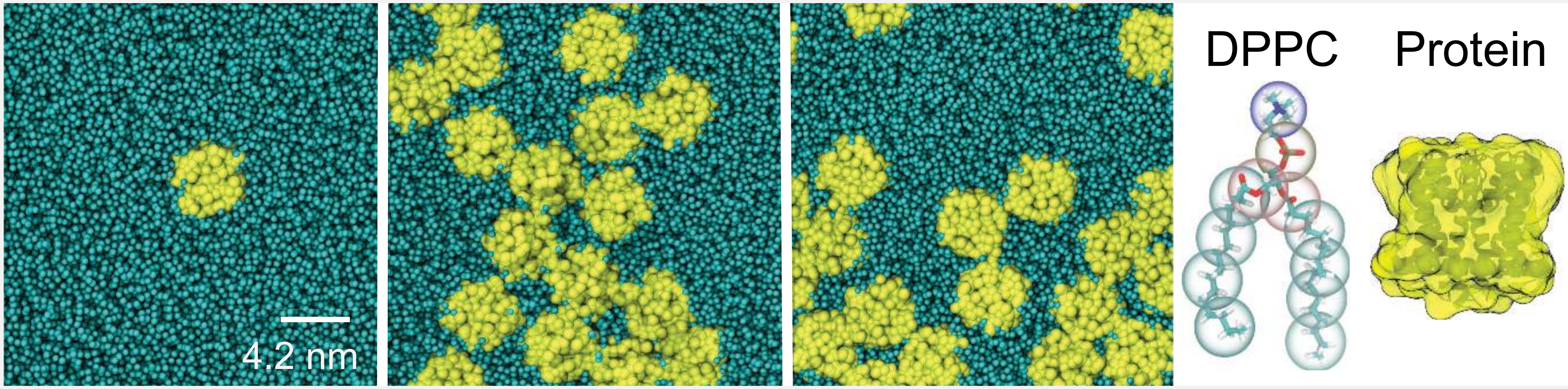


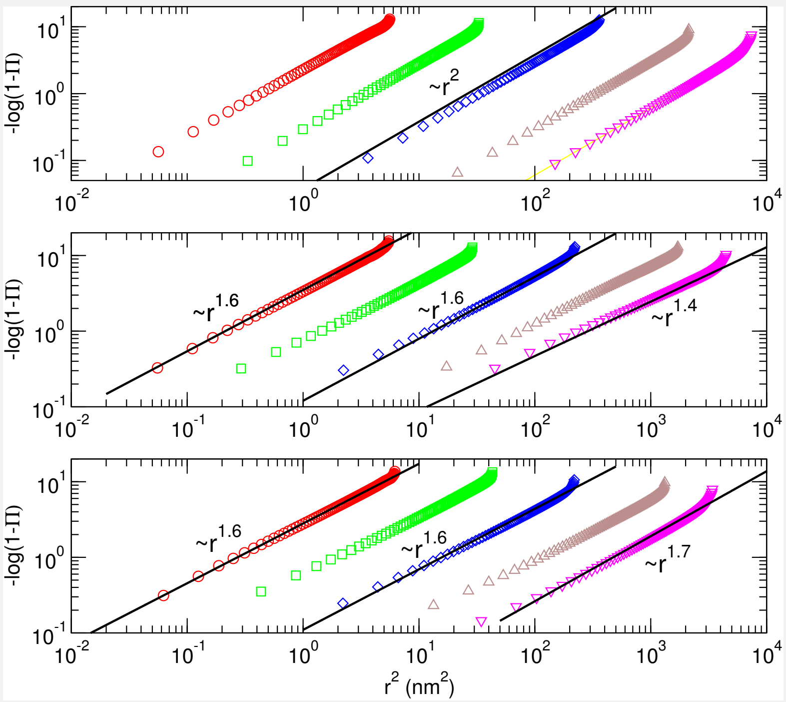




Left: DPPC (protein-aggregating) case. Right: DLPC protein non-aggregating case.

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

# Crowding in membranes: non-Gaussian lipid/protein diffusion

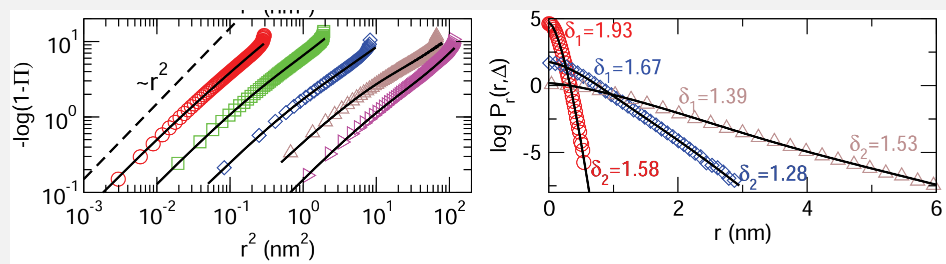



Dilute membrane: $P(r,t)$ Gauss

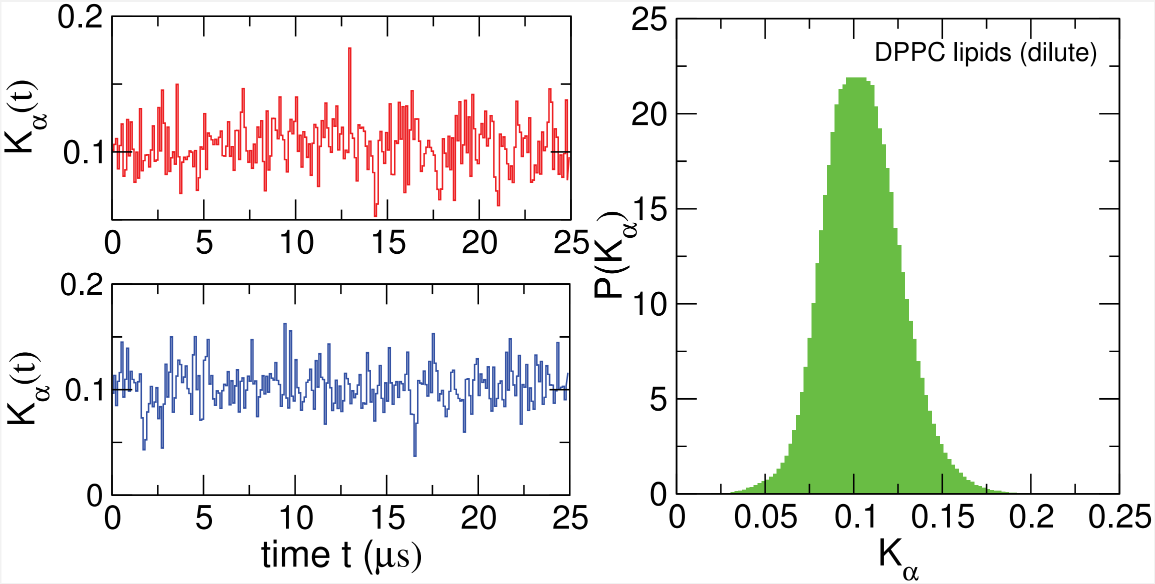
Crowded membrane ($\delta \approx 1.3 \ldots 1.7$):

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



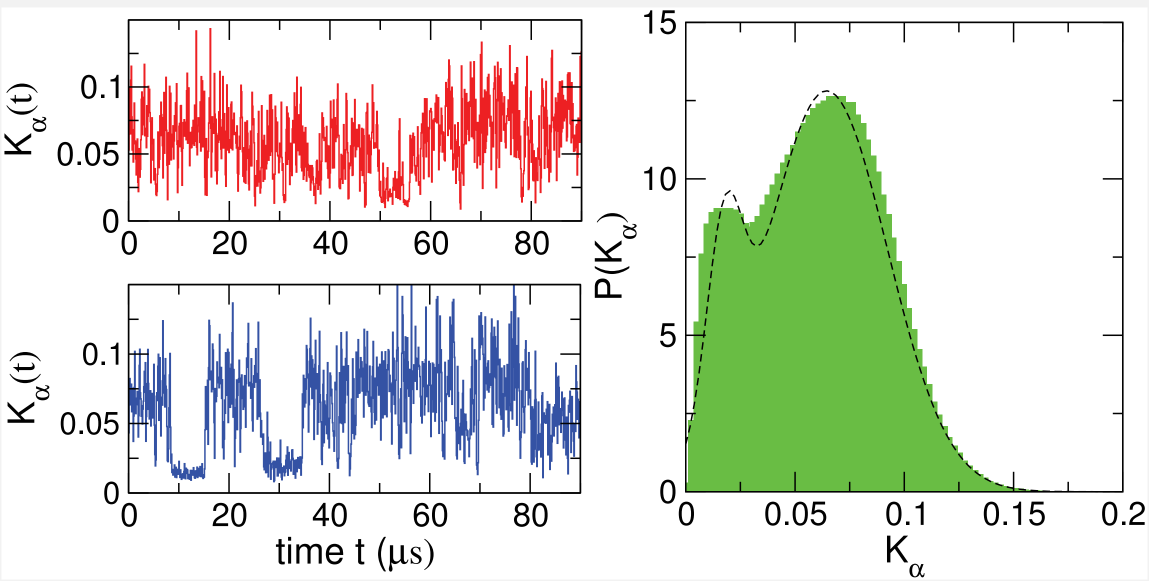

J-H Jeon, M Javanainen, H Martinez-Seara, RM & I Vattulainen, PRX (2016); compare Faraday Disc (2013)

# Crowding in membranes increases dynamic heterogeneity




Diffusivity$(t)$ for two lipids

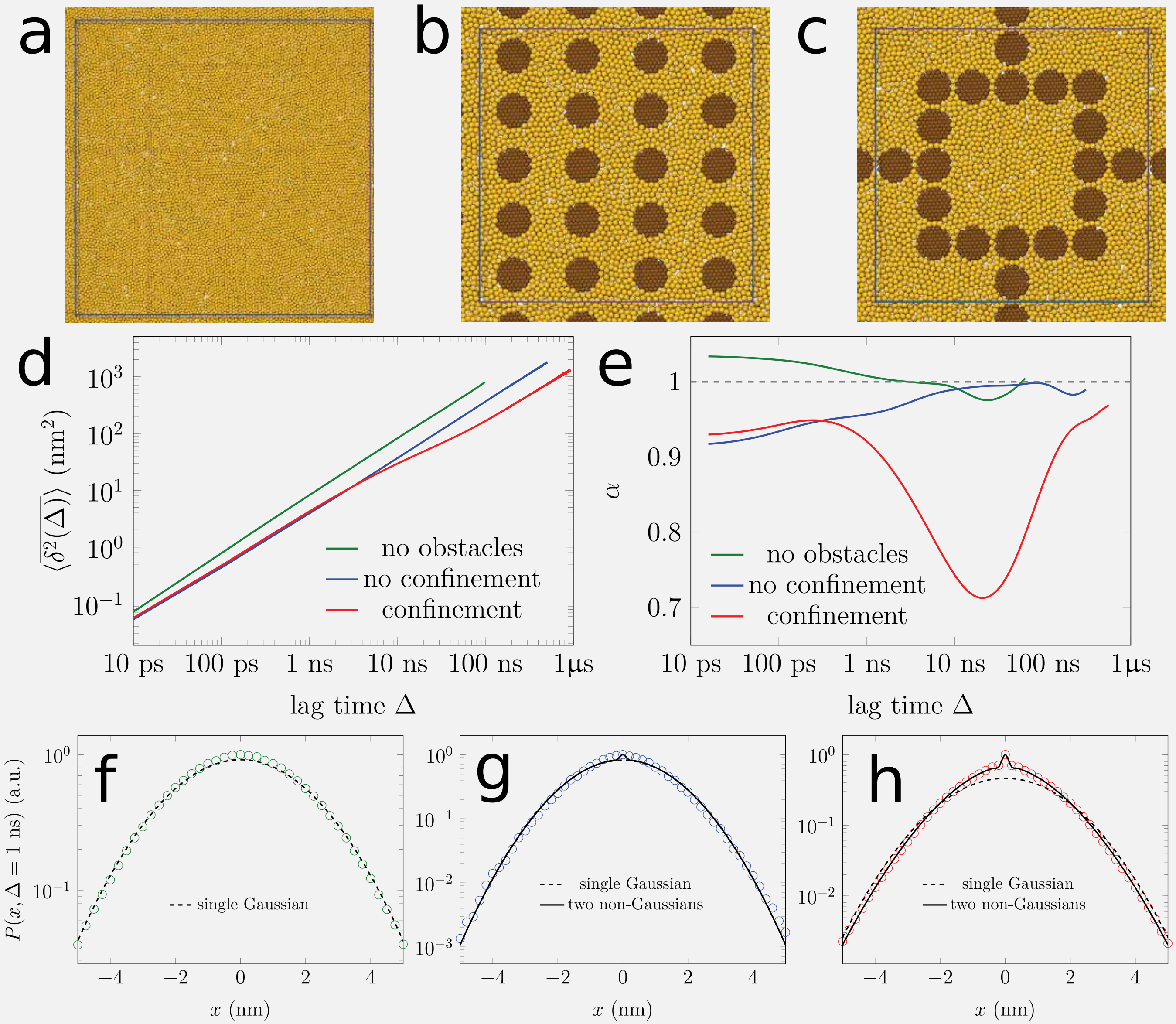
Lipid diffusivity, dilute membrane




Lipid diffusivity, crowded membrane

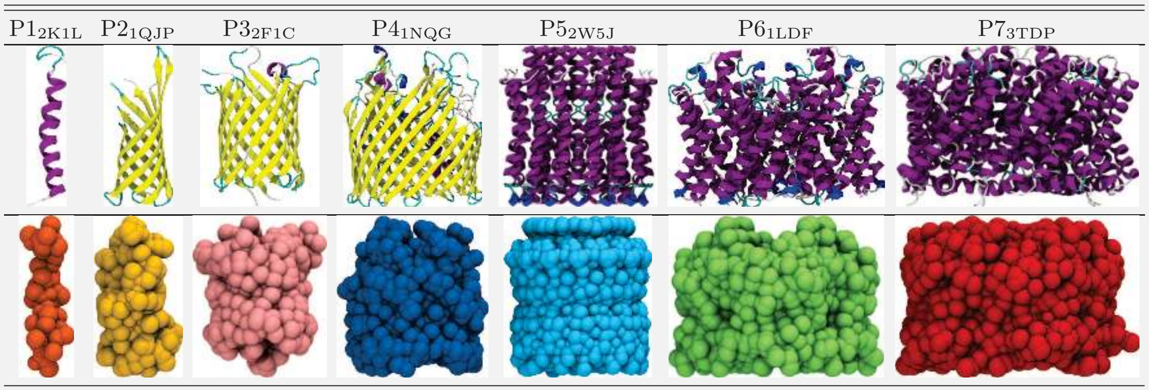
J-H Jeon, M Javanainen, H Martinez-Seara, RM & I Vattulainen, PRX (2016); compare Faraday Disc (2013)

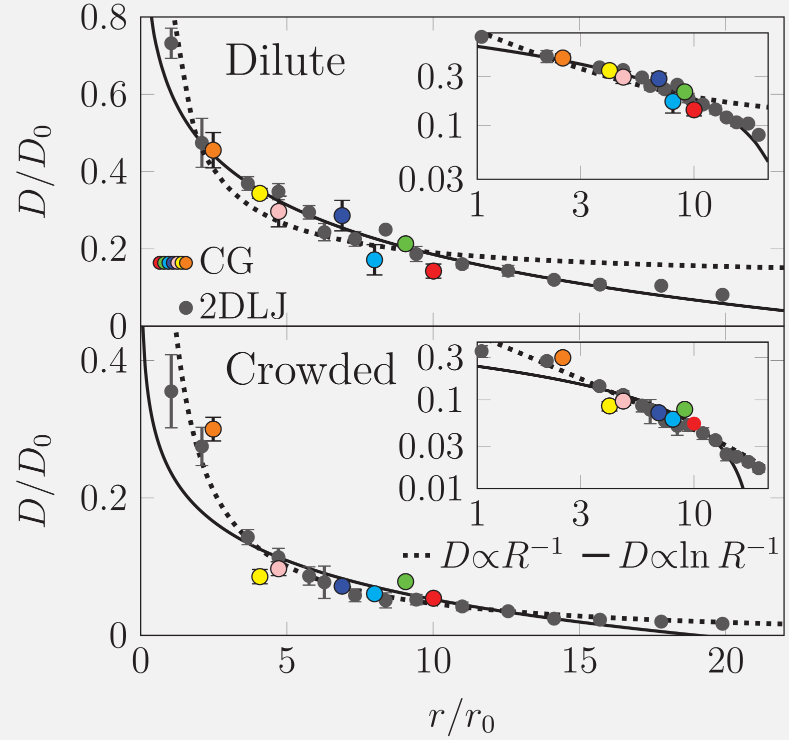
# Confinement in argon system shows geometric origin

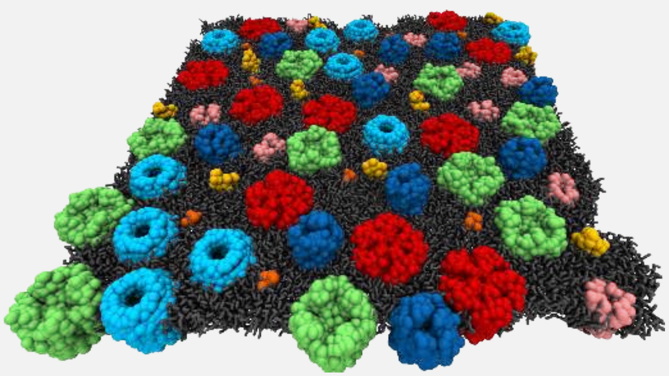


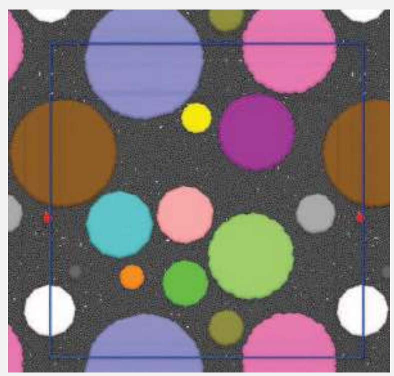

J-H Jeon, M Javanainen, H Seara Monne, RM & I Vattulainen, PRX (2016)

# Geometry-induced violation of Saffman-Delbrück relation





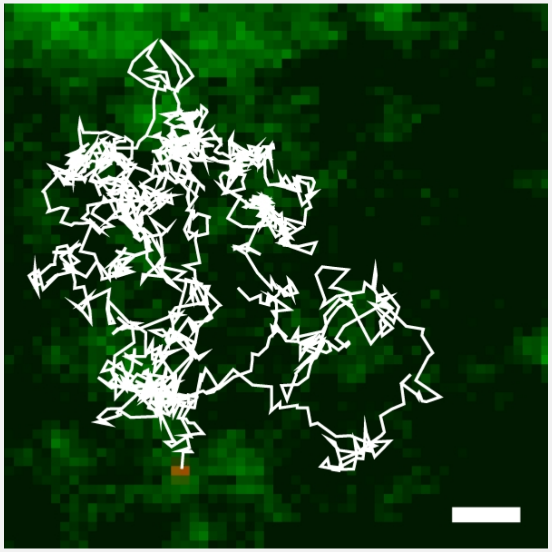
Dilute system: Saffman-Delbrück law

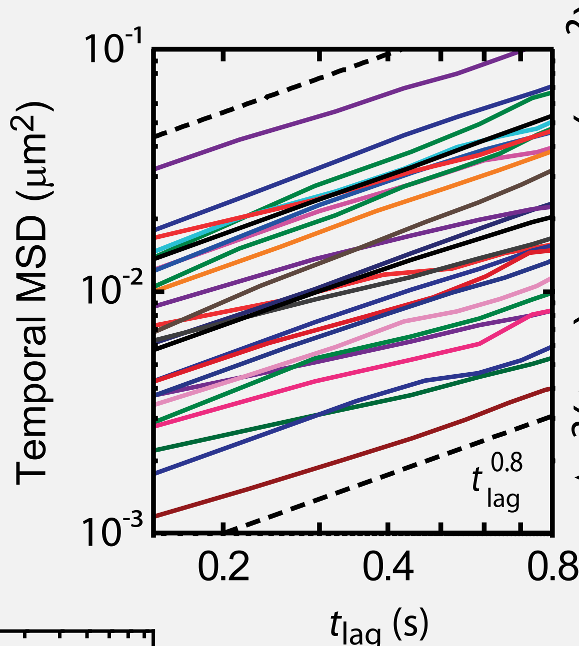
$$D(R) \simeq \log(1/R)$$

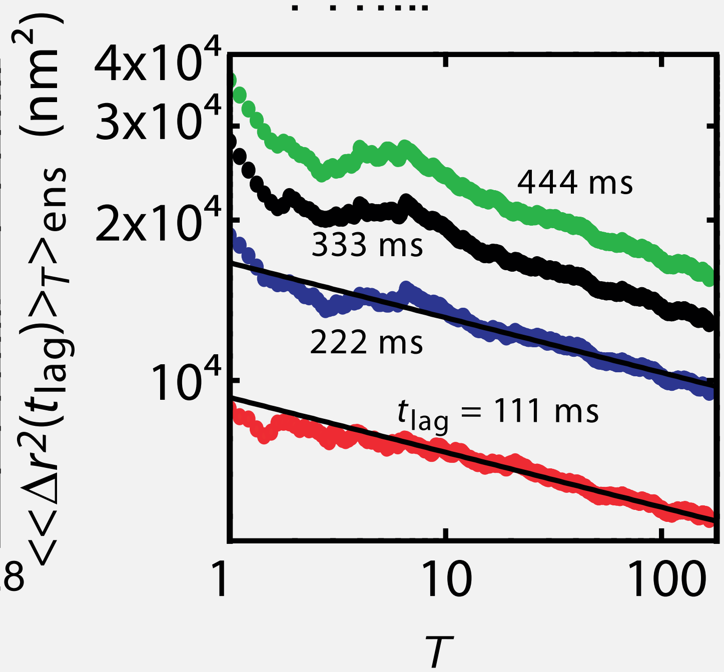
Crowded membrane & 2DLJ discs:

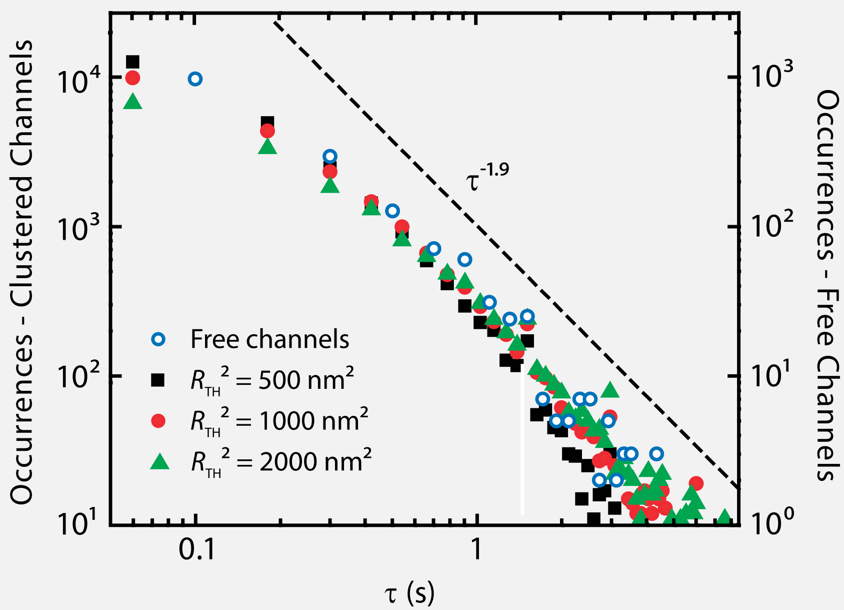
$$D(R) \simeq 1/R$$

# CTRW-like motion of Ka channels in plasma membrane





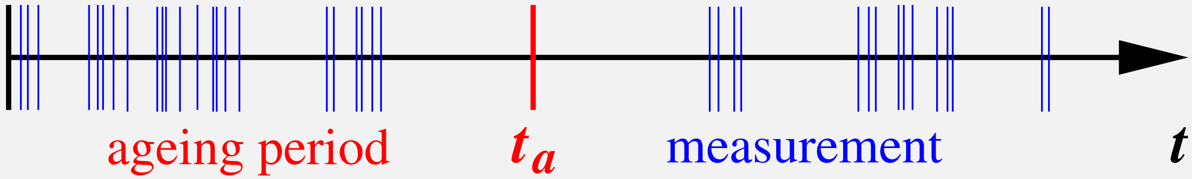

$\psi(\tau) \simeq \tau^{-1-\alpha}$ scale free

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

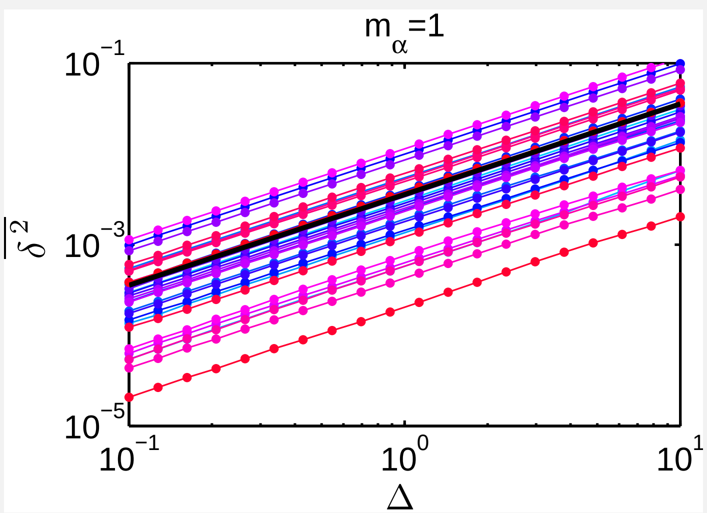


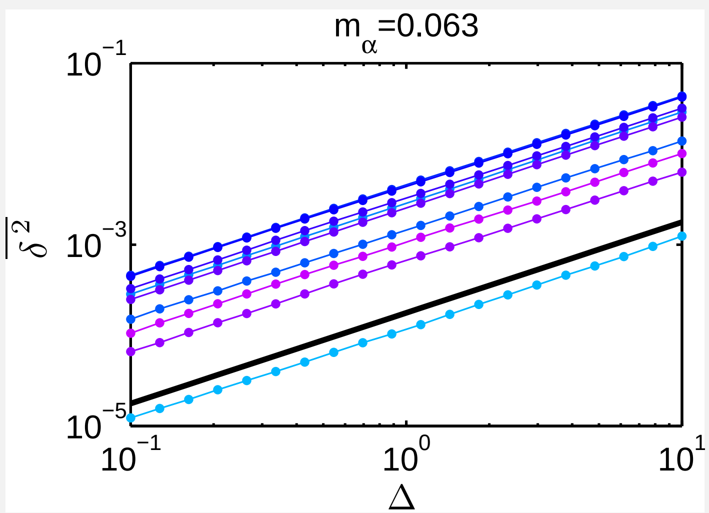

Ageing mean squared displacement ($\Lambda(z)=(1+z)^\alpha - z^\alpha$)

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

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

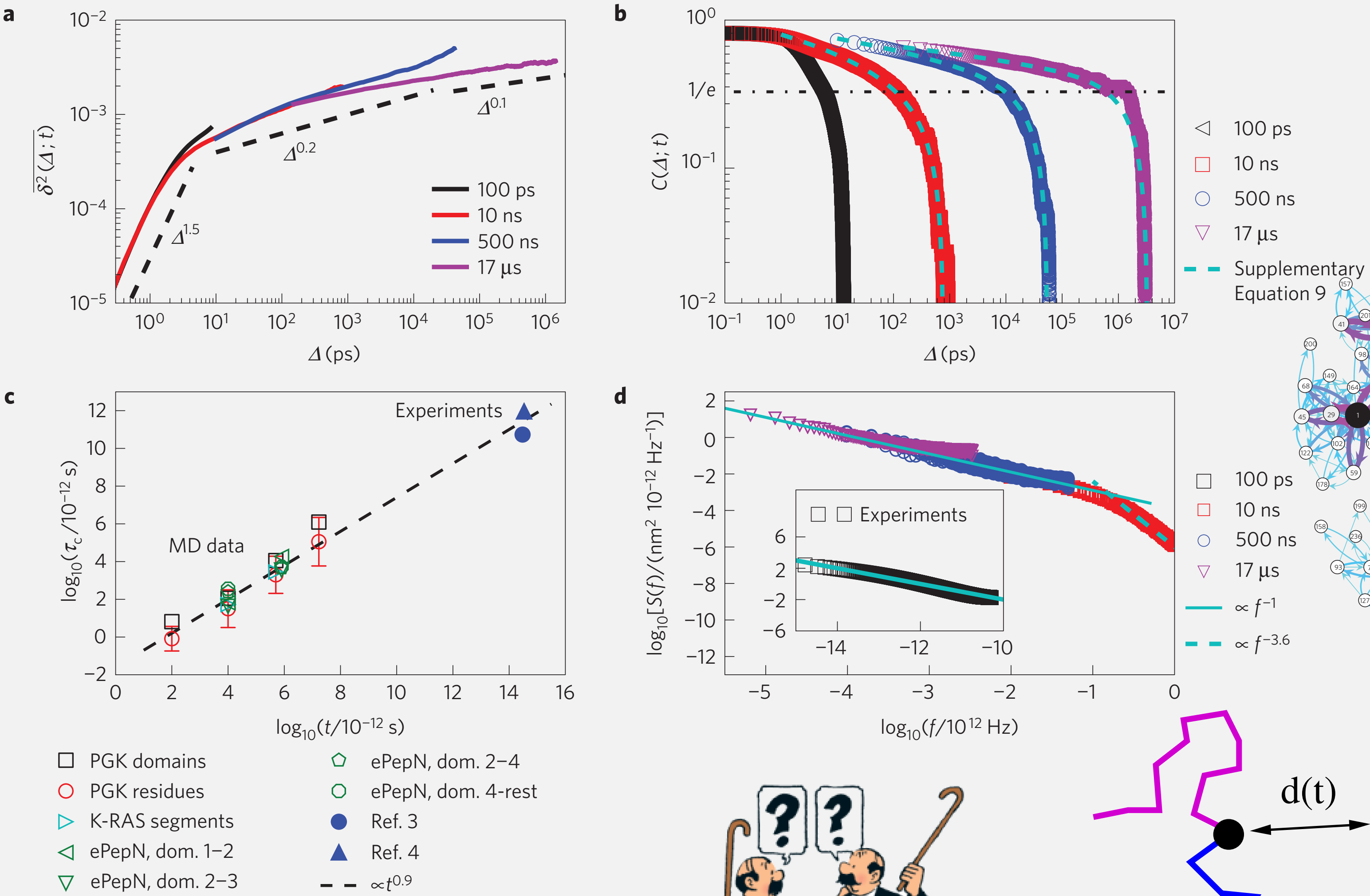
$$m_\alpha(T/t_a) \simeq (T/t_a)^{1-\alpha}, \quad T \ll t_a$$

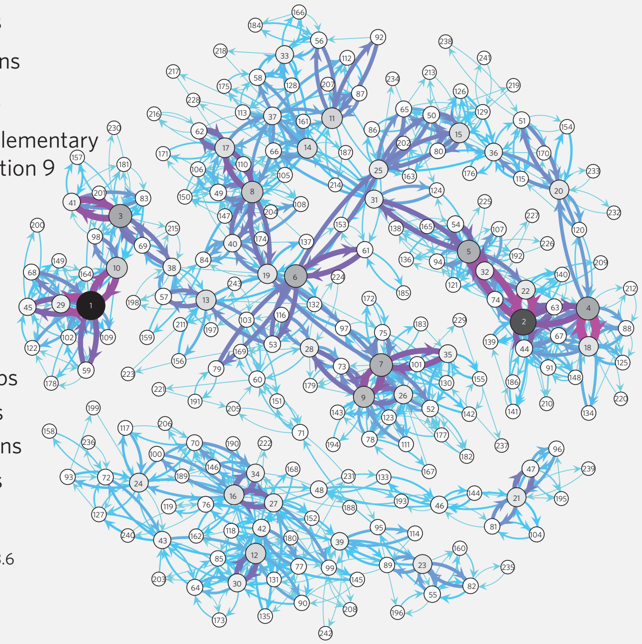


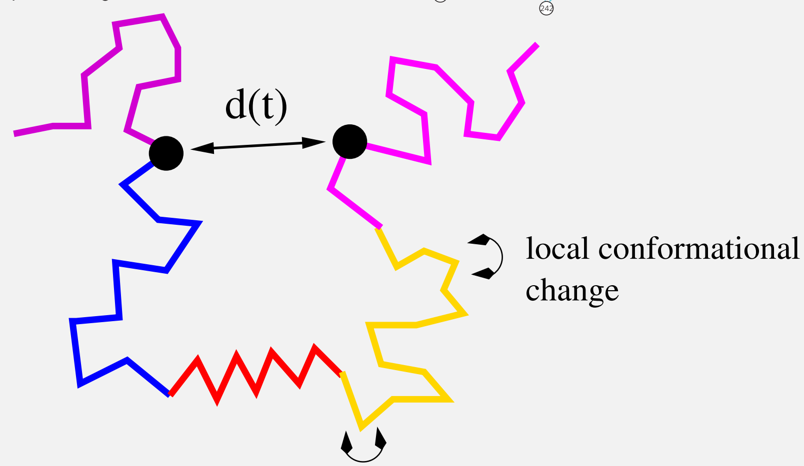




J Schulz, E Barkai & RM, PRL (2013), PRX (2014)

# Self-similar internal protein dynamics: 13 decades of ageing

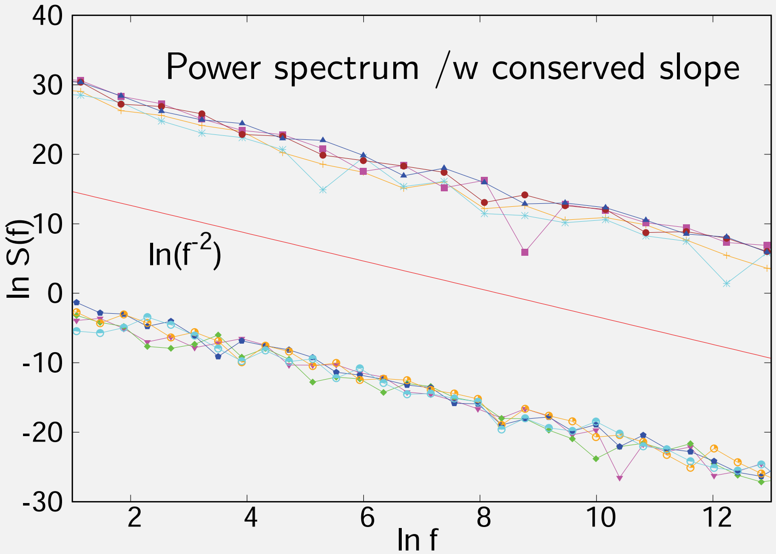


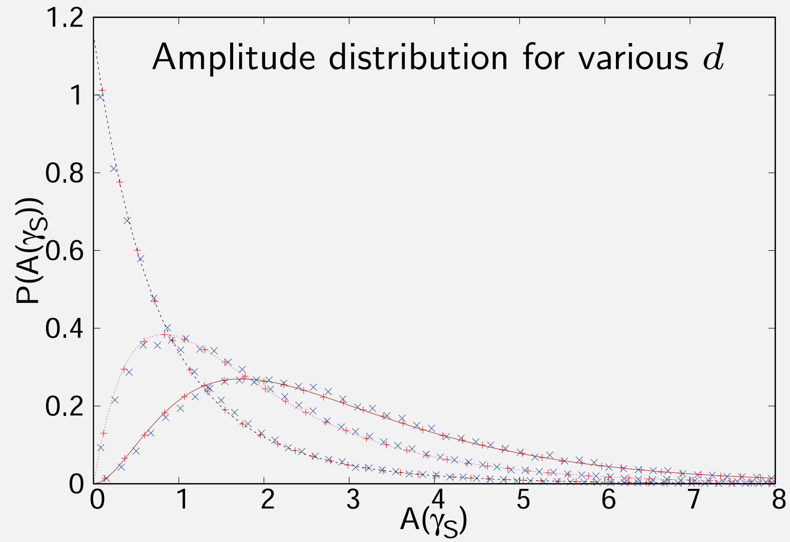





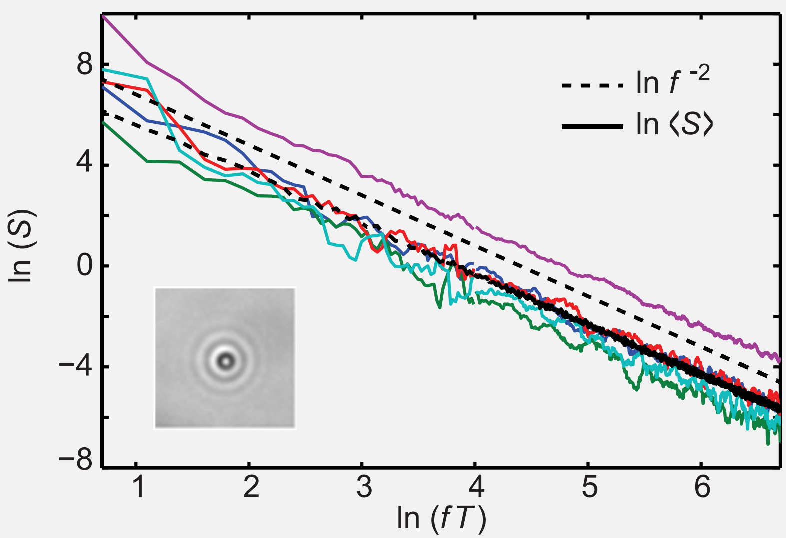

X Hu, L Hong, MD Smith, T Neusius, X Cheng & JC Smith, Nature Phys (2016); N&V RM Nature Phys (2016)

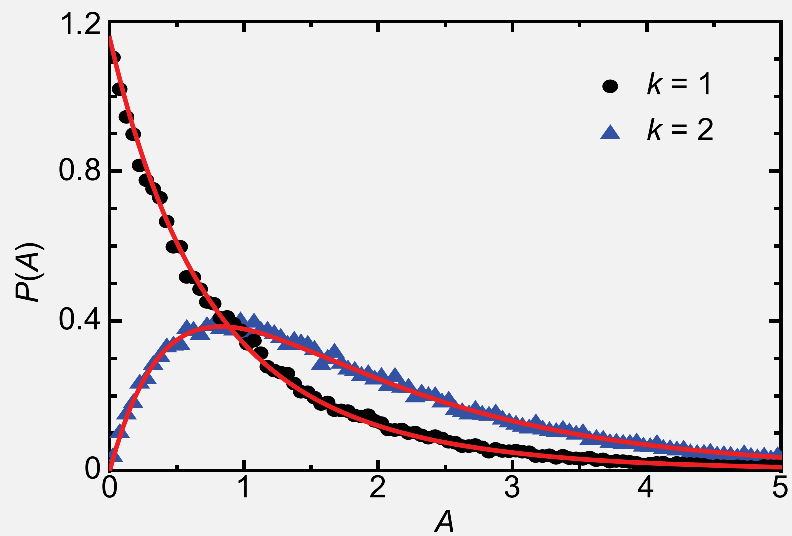
# Power spectral density of a single Brownian trajectory




Theory

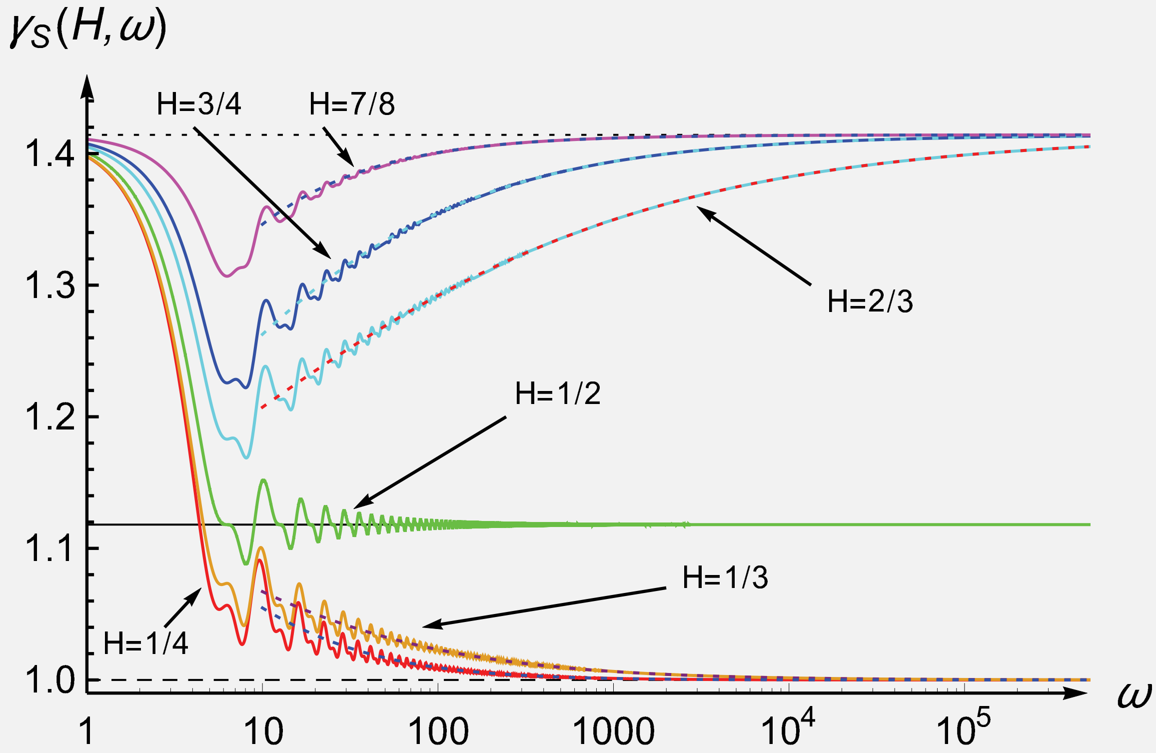



Experiment

D Krapf, E Marinari, RM, G Oshanin, A Squarcini & X Xu, NJP (2018); Perspective: ND Schnellbächer & US Schwarz, NJP (2018)

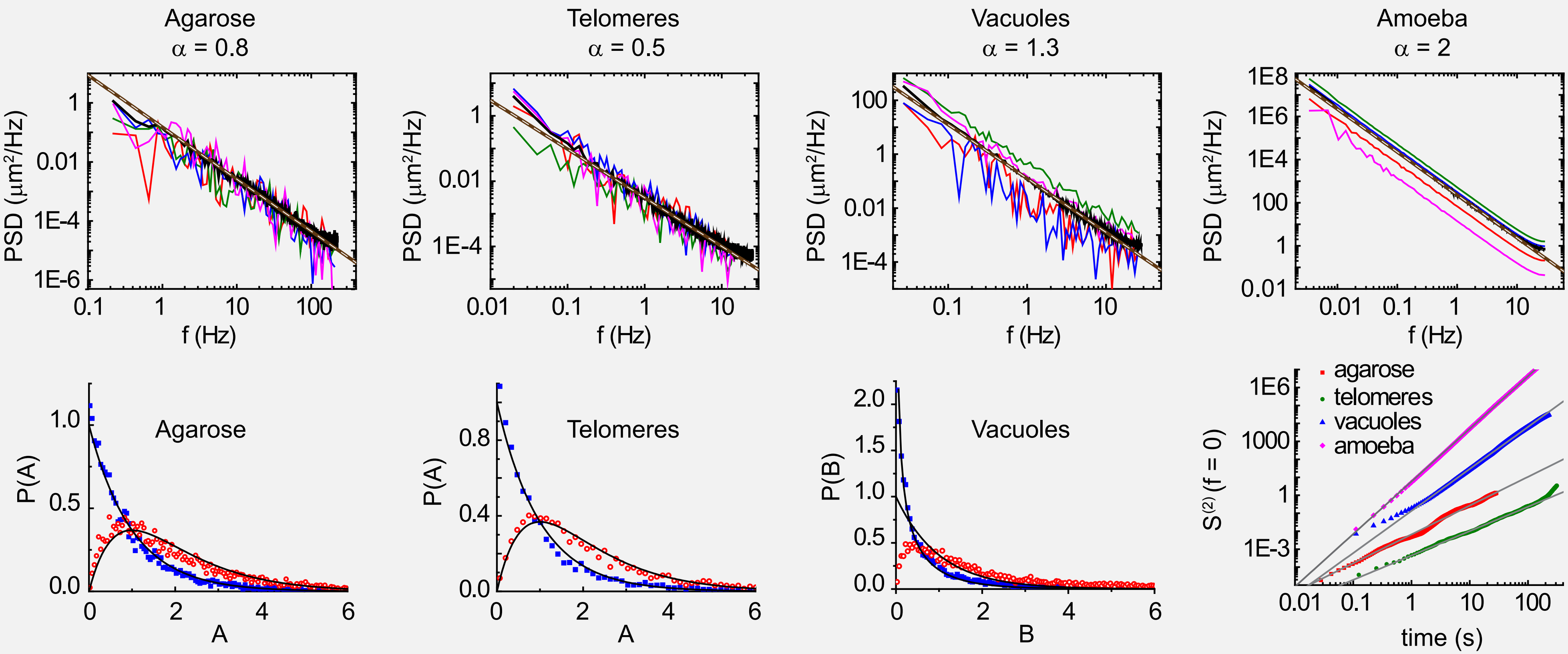
# Power spectral density of a single FBM trajectory




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

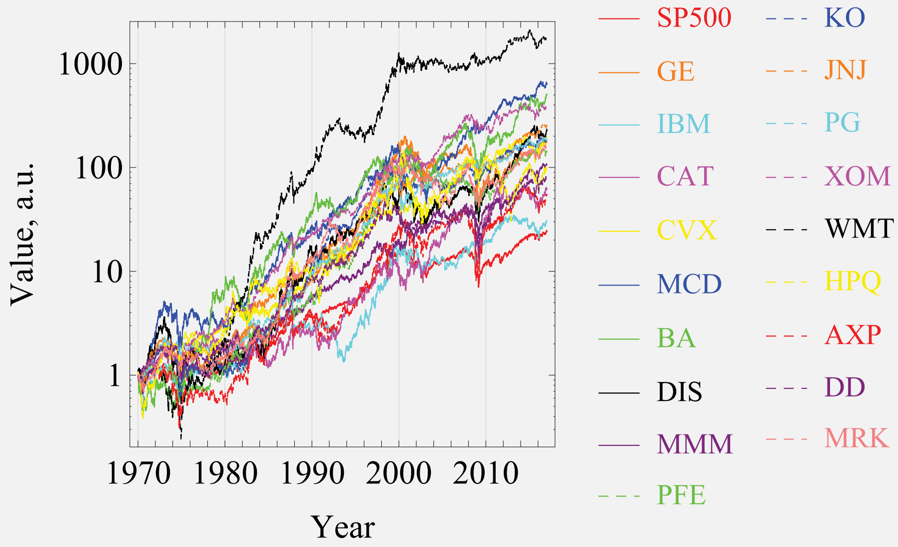
D Krapf, N Lukat, E Marinari, RM, G Oshanin, C Selhuber-Unkel, A Squarcini, L Stadler, M Weiss & X Xu (2018)

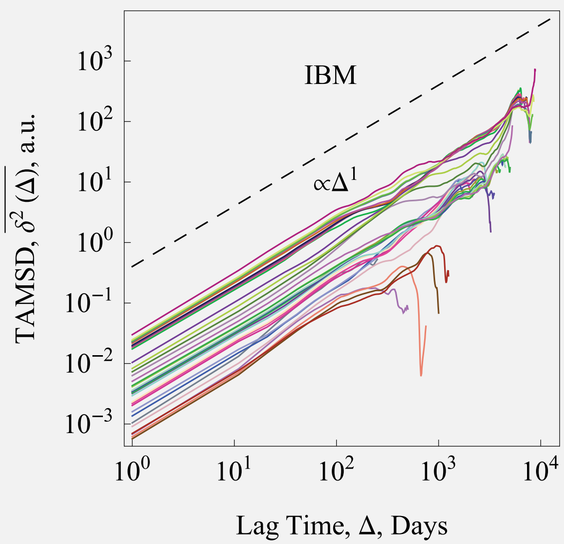
# Power spectral density of a single FBM trajectory

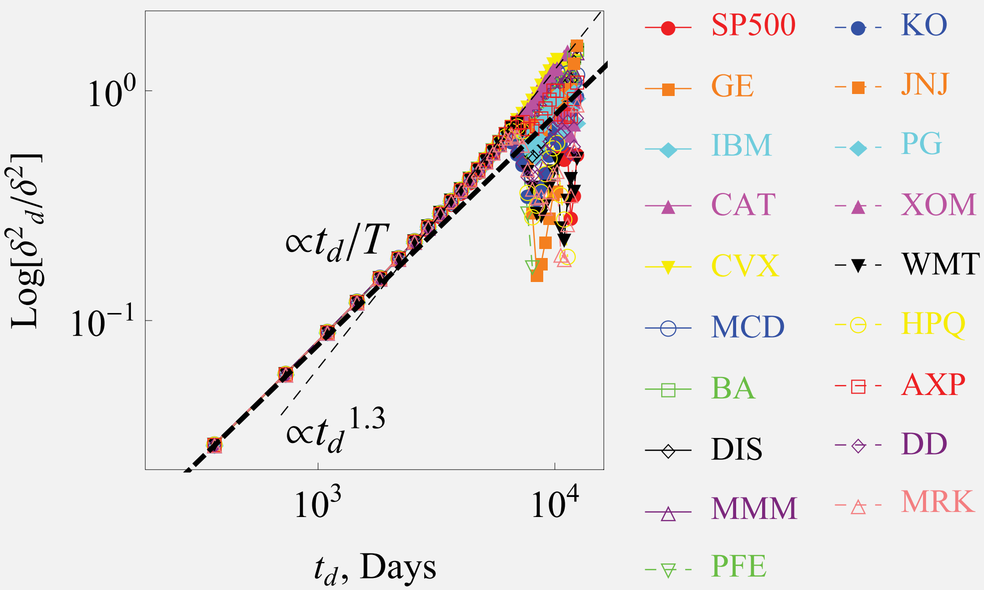



D Krapf, N Lukat, E Marinari, RM, G Oshanin, C Selhuber-Unkel, A Squarcini, L Stadler, M Weiss & X Xu (2018) 

# Time averages & ageing in financial market time series



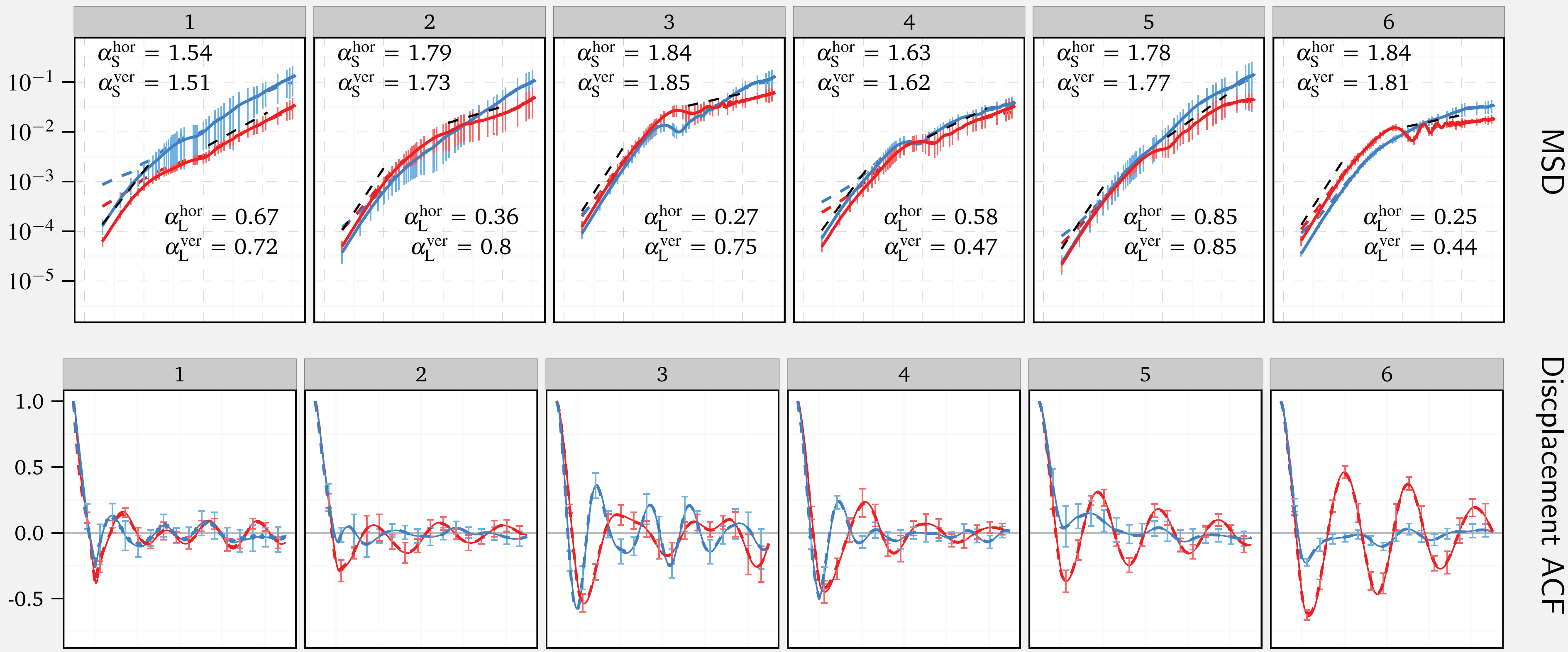

$$dX(t) = \mu X(t)dt + \sigma X(t)dW(t)$$

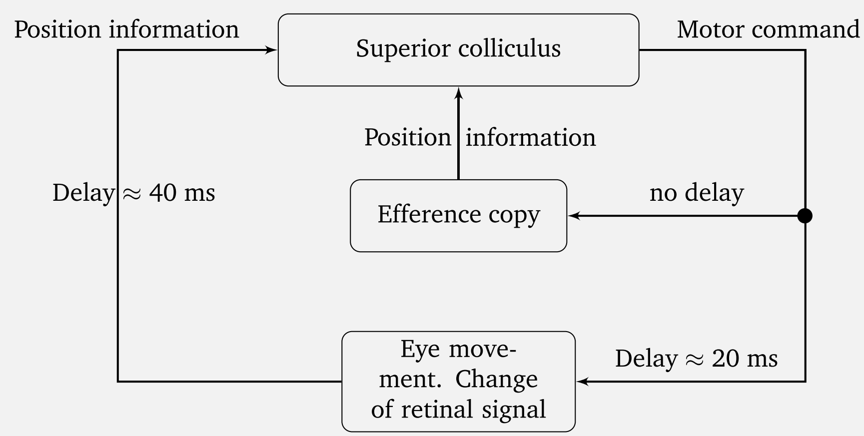
$$\overline{\delta_d^2(\Delta)} = \frac{\int_{t_d}^{T-\Delta} [X(t+\Delta) - X(t)]^2\, dt}{T - t_d - \Delta} \sim \frac{\Delta}{T - t_d} X_0^2 \left(e^{\sigma^2 T} - e^{\sigma^2 t_d}\right)$$

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

AG Cherstvy, D Vinod, E Aghion, AV Chechkin & RM, NJP (2017)

# Stochasticity of fixational eye movements




CJJ Herrmann, RM & R Engbert, Sci Rep (2017)

# 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)