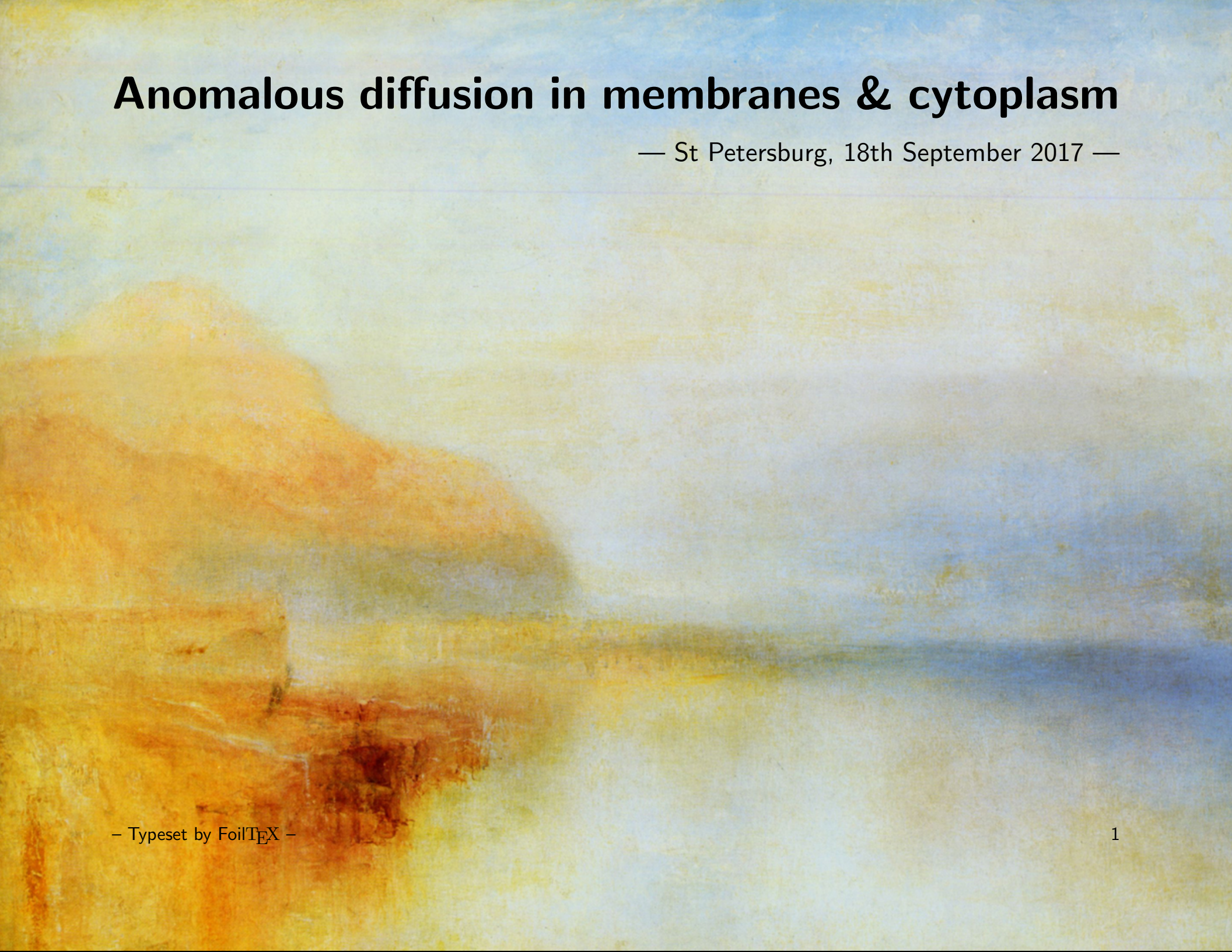
Anomalous diffusion in membranes & cytoplasm

— St Petersburg, 18th September 2017 —



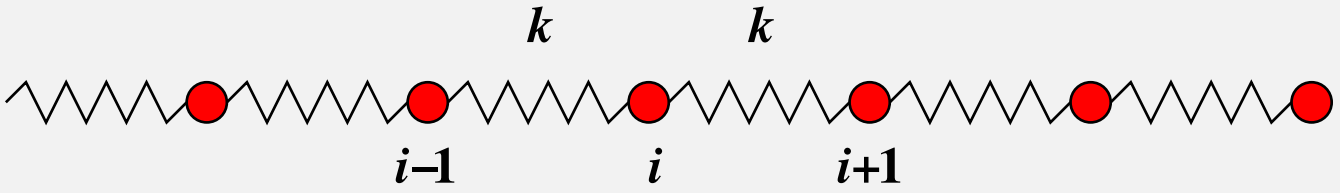
Fractional Langevin equations in viscoelastic systems

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):

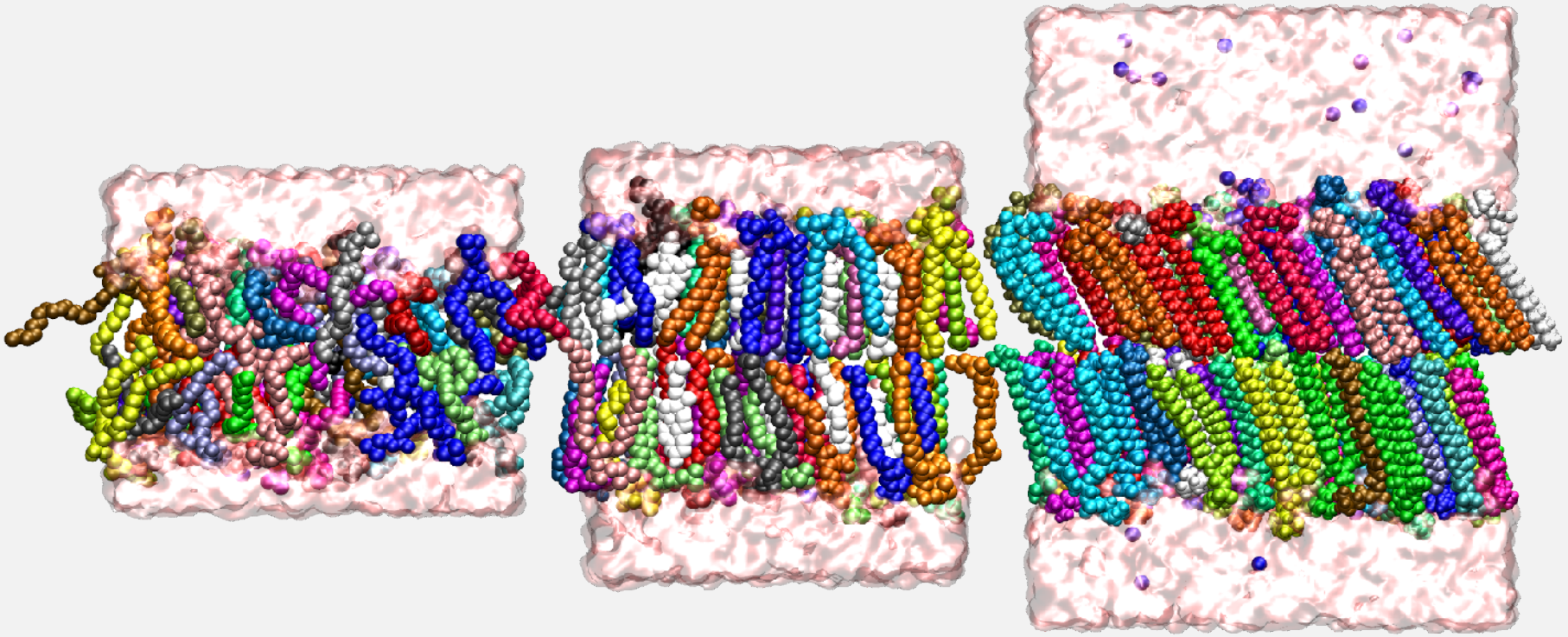
$$\langle \zeta_i(t)\zeta_j(t')\rangle = \delta_{ij}k_B T\eta(|t-t'|)$$

$\curvearrowright$ 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

Single lipid motion in bilayer membrane MD simulations

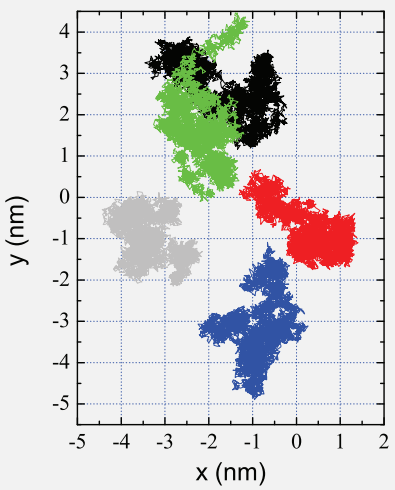


Liquid disordered Liquid ordered Gel phase

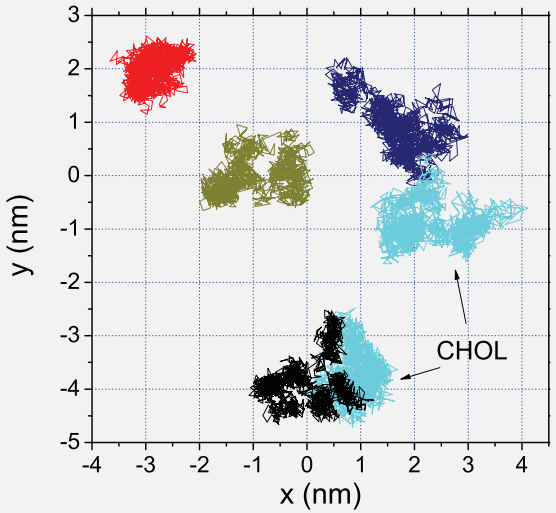
J-H Jeon, H Martinez-Seara Monne, M Javanainen & RM, PRL (2012)

Sample trajectories for the lipid & cholesterol motion

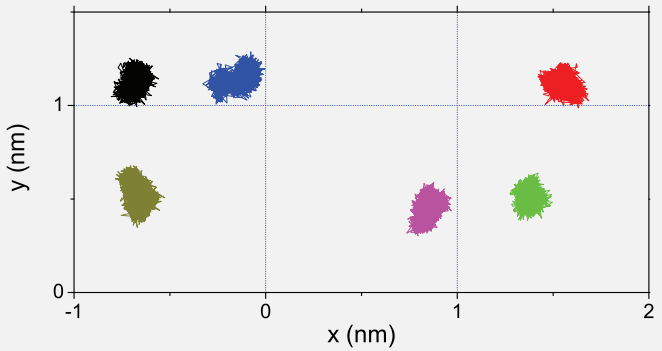
Liquid disordered



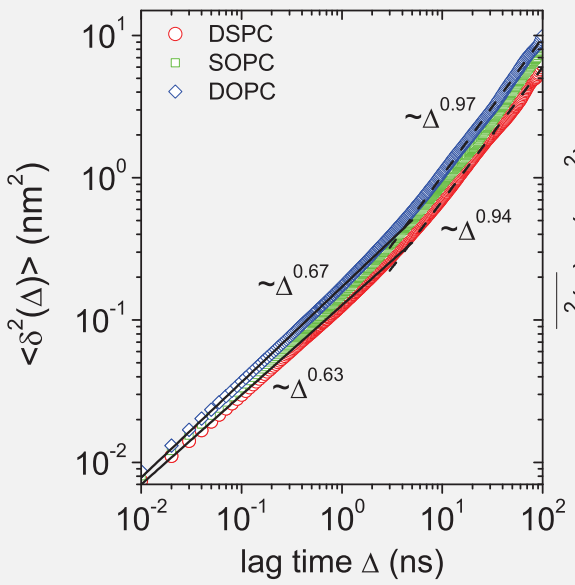
Liquid ordered

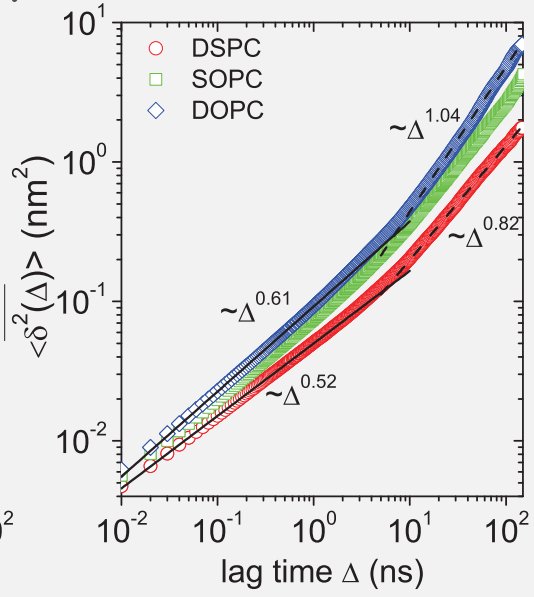


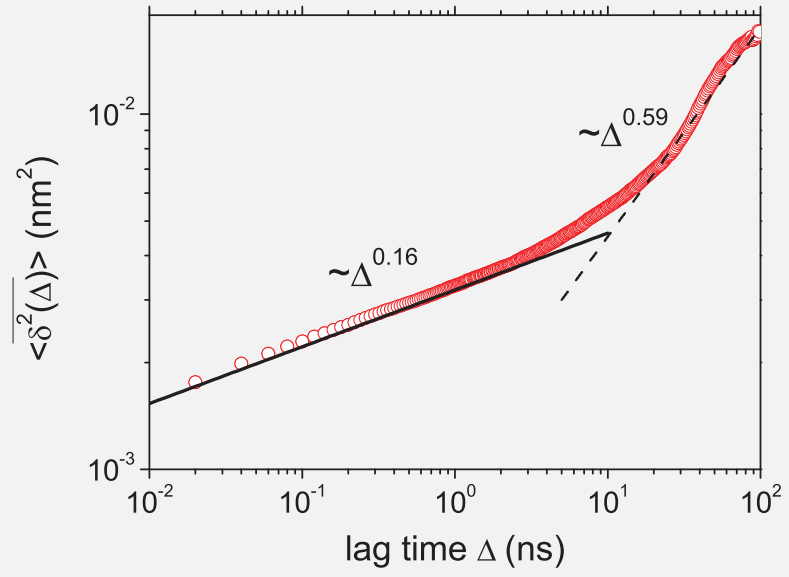
Gel phase



Liquid ordered/gel phases: extended anomalous diffusion

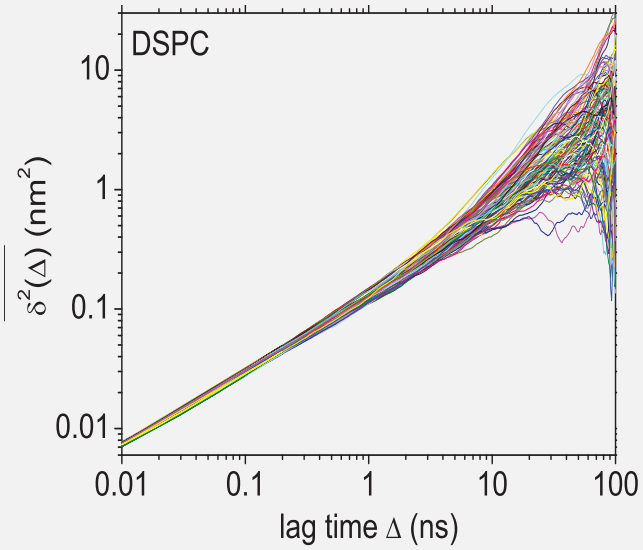


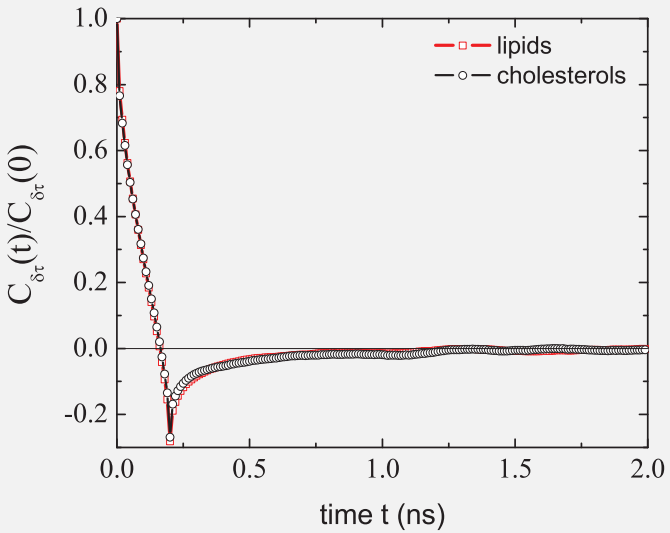


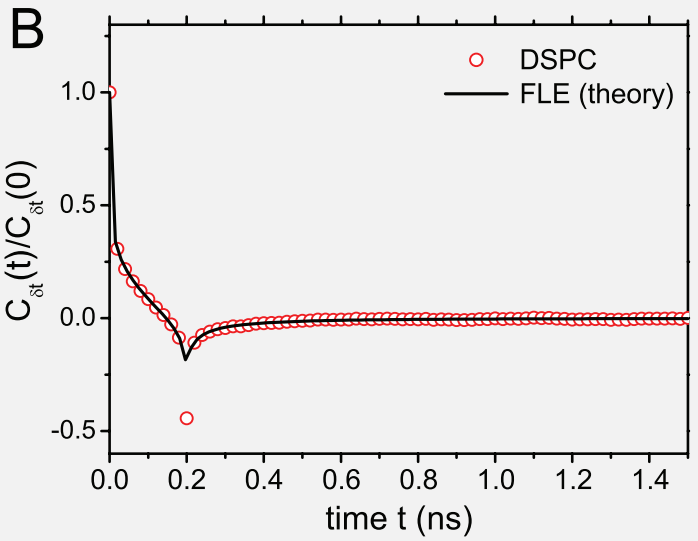


J-H Jeon, H Martinez-Seara Monne, M Javanainen & RM, PRL (2012)

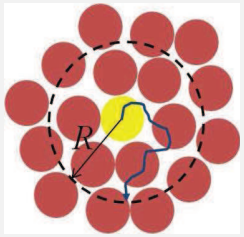
Reproducible TA MSD & antipersistent correlations

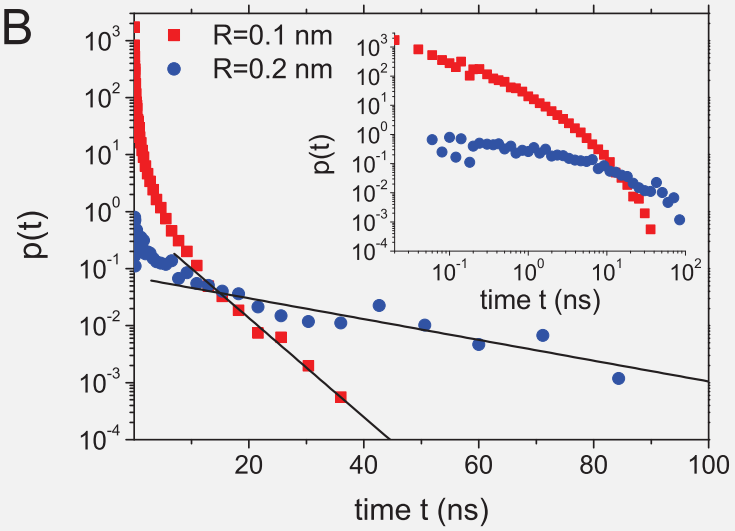


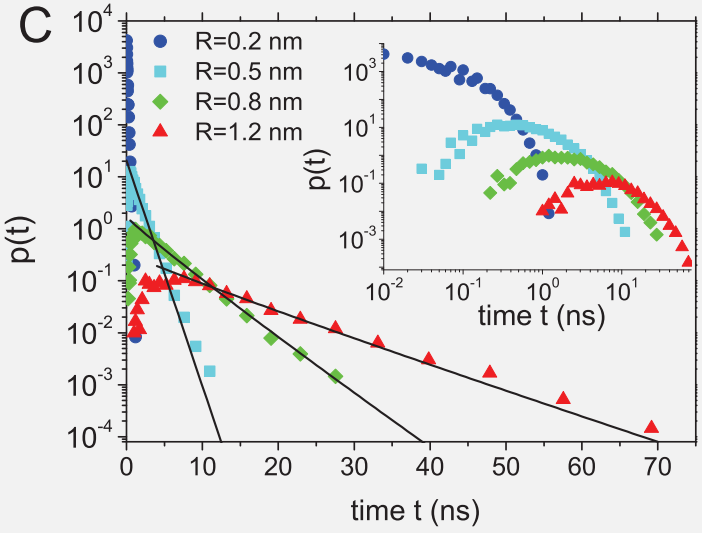




Rattling dynamics: exptl first passage PDF ↷ FLE motion







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

Membranes strongly & heterogeneously crowded by proteins

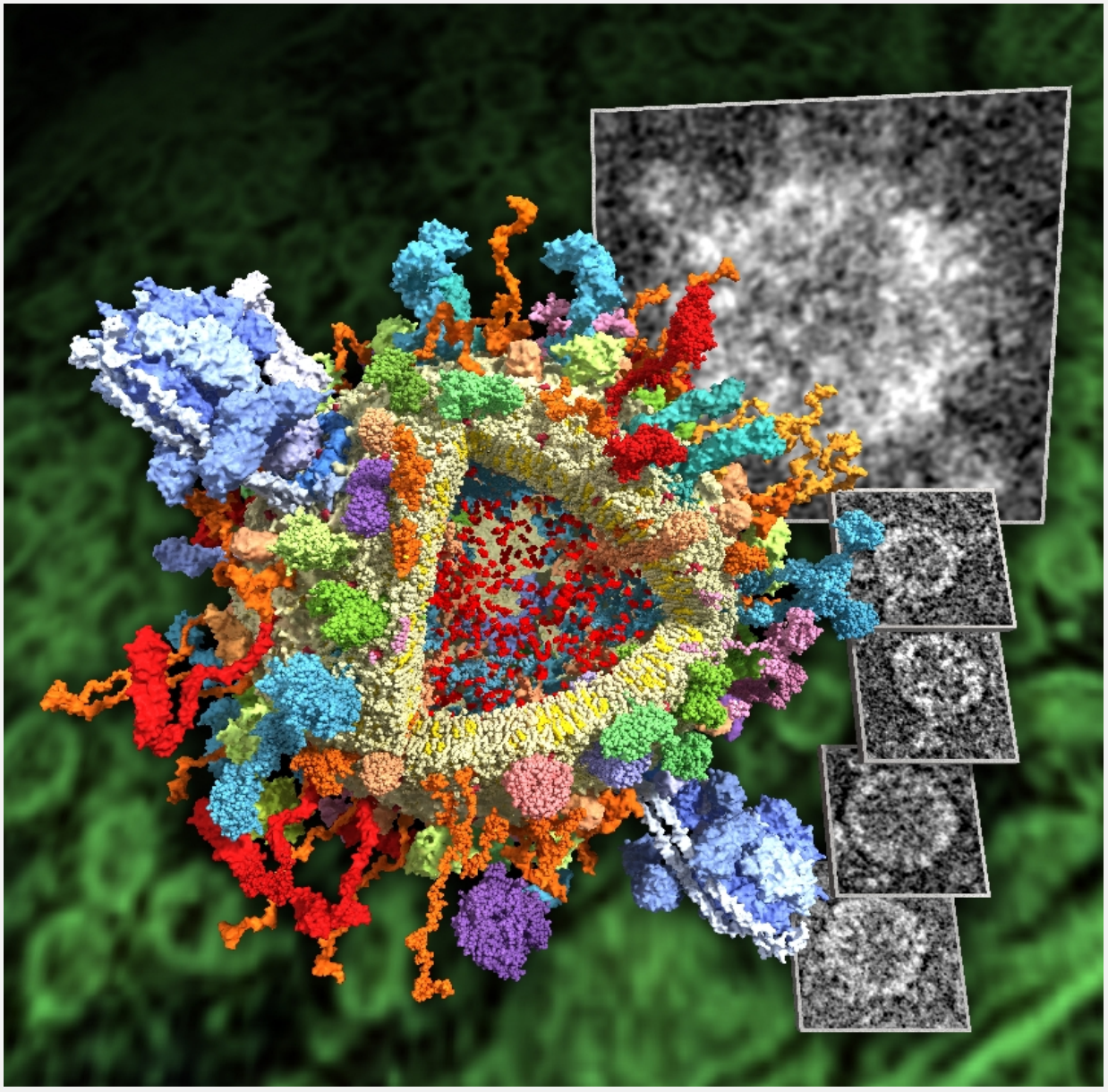
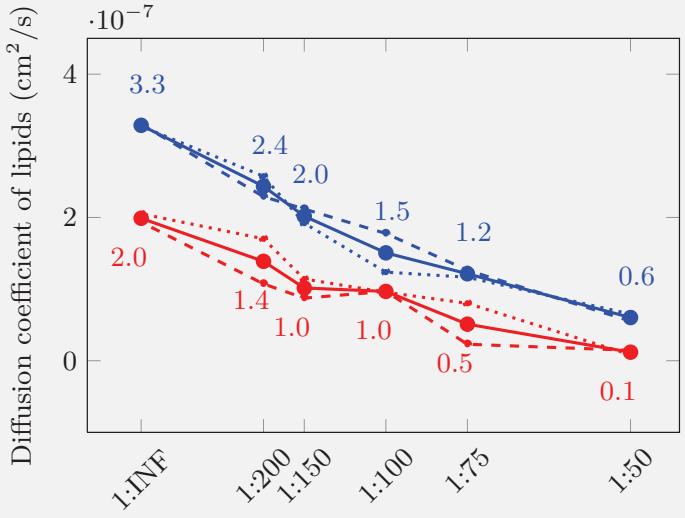
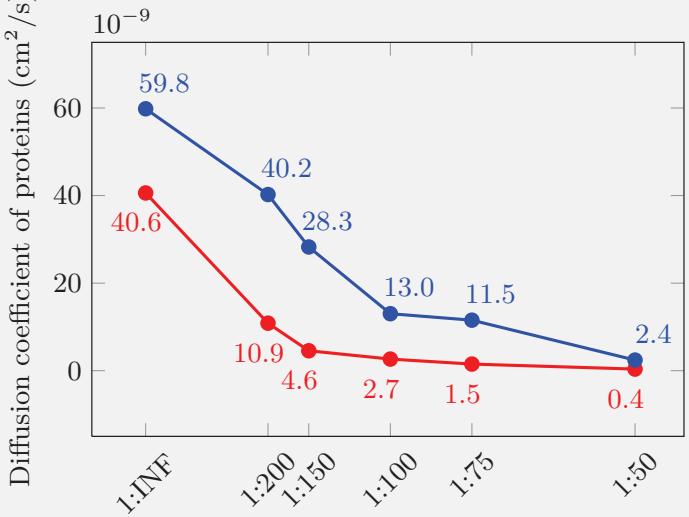


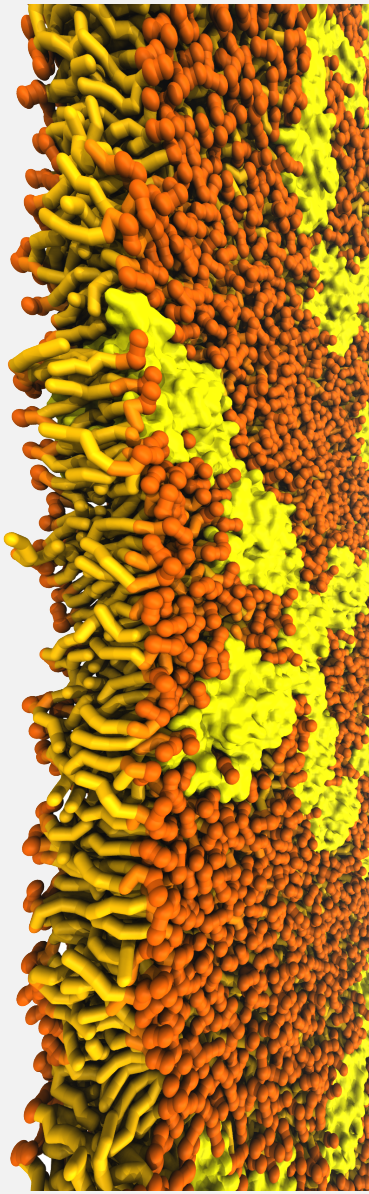
Figure courtesy Helmut Grubmüller

Protein crowded membranes reduce effective mobility

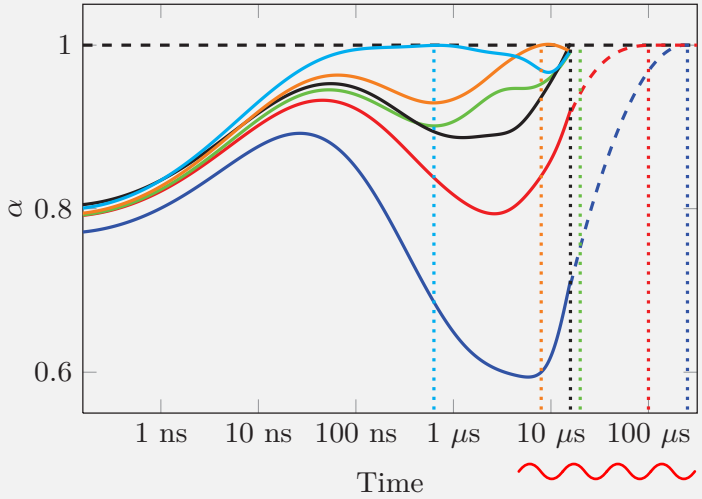


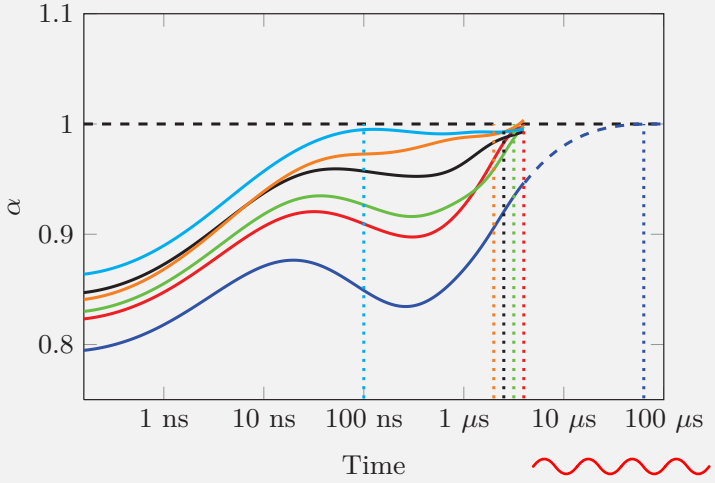


Blue: DLPC. Red: DPPC



Protein crowding effects anomalous lipid diffusion

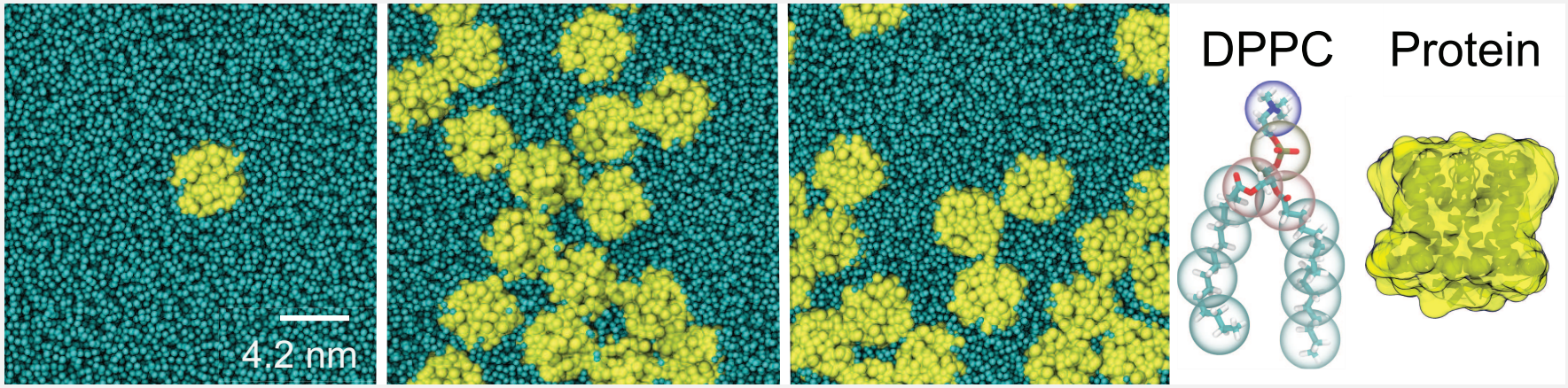


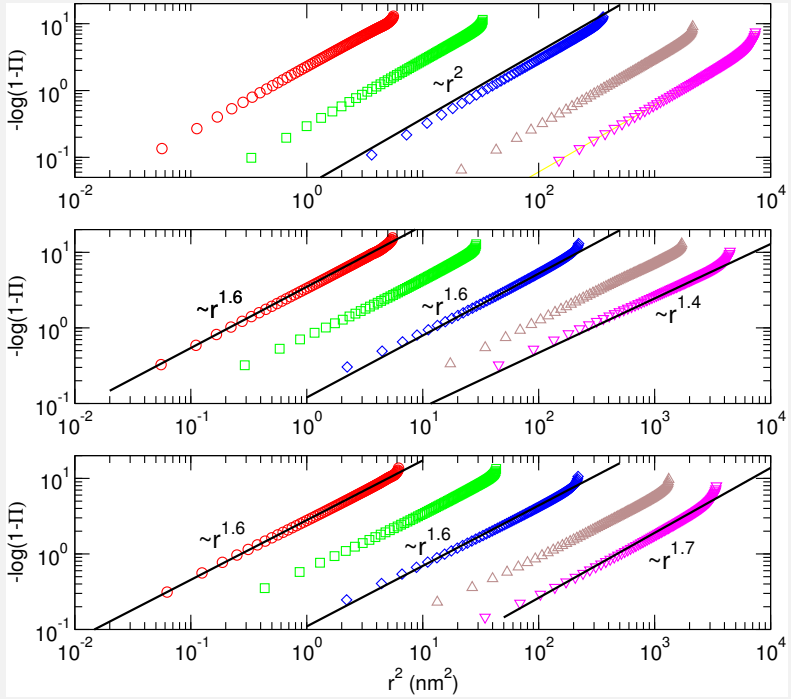


Left: DPPC (protein-aggregating) case. Right: DLPC protein non-aggregating case.

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

Crowding in membranes: non-Gaussian lipid/protein diffusion

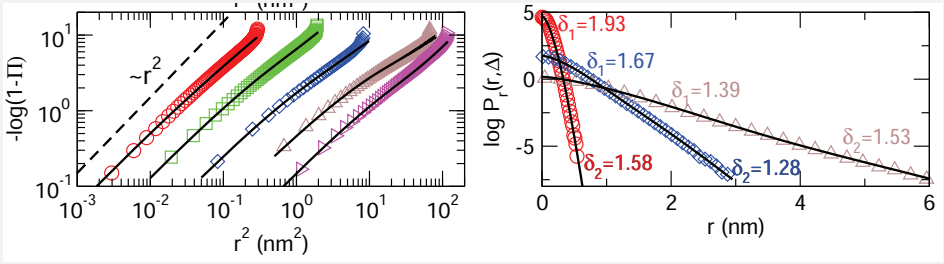




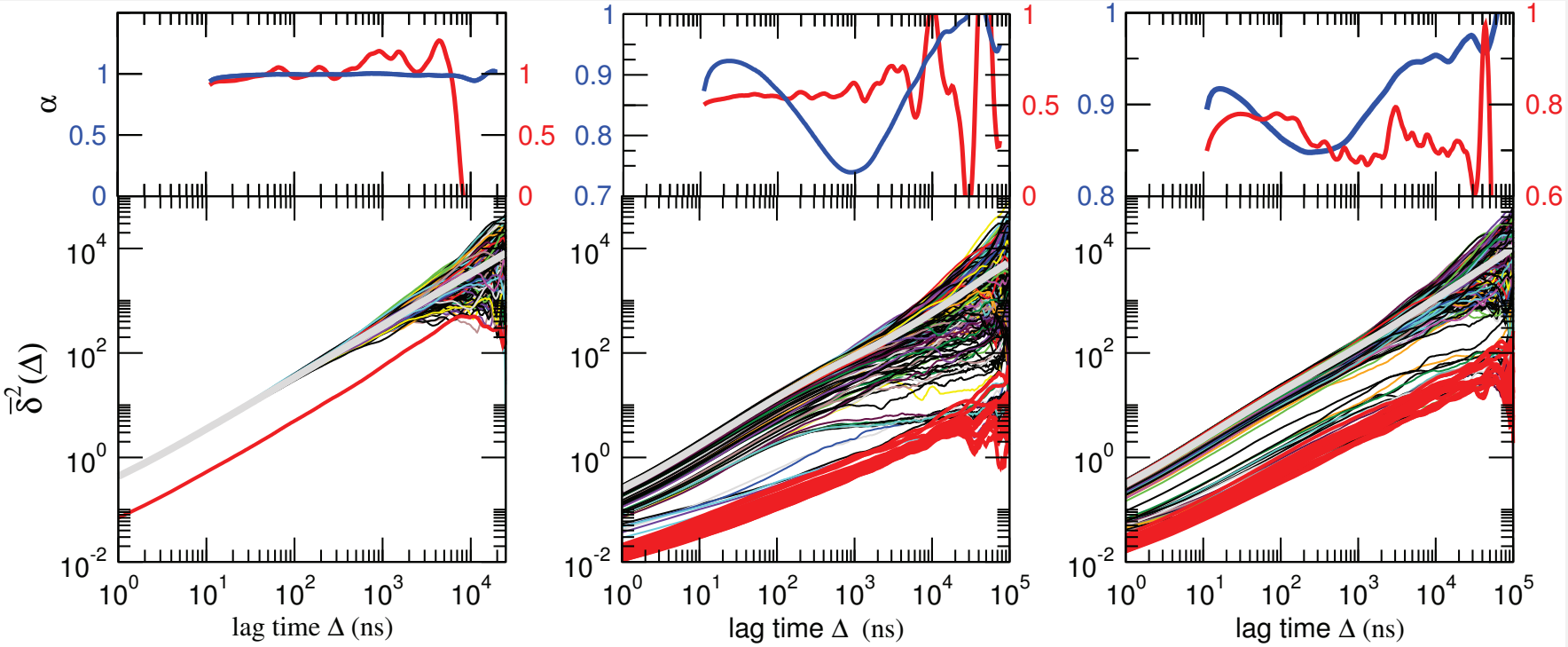
Dilute membrane: $P(r,t)$ Gauss

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

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



Crowding in membranes increases dynamic heterogeneity



↓ Blue: lipids. Red: protein(s)

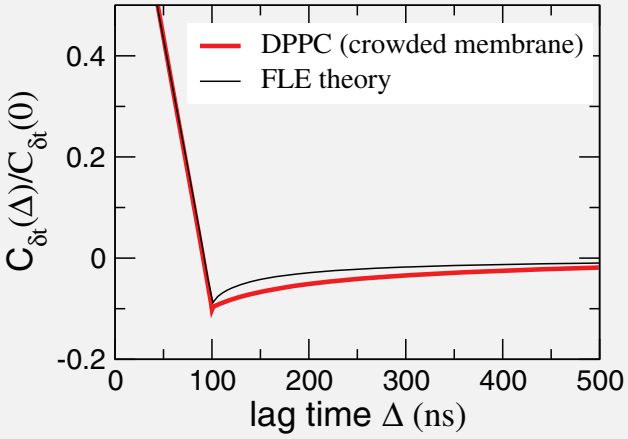
Single NaK channel

DLPC (non-aggregating)

DPPC (aggregating)

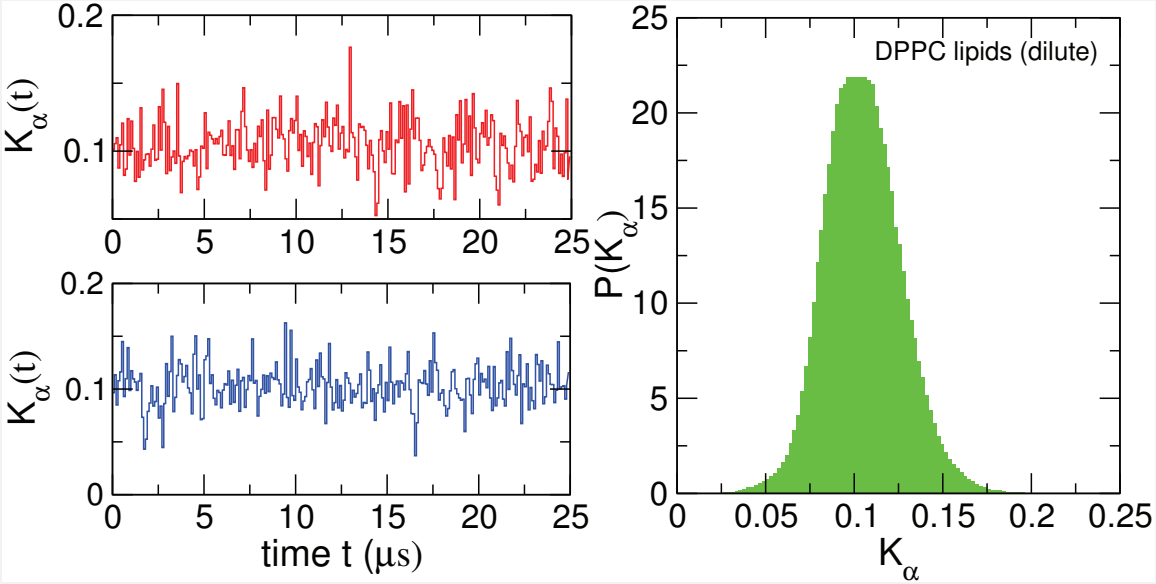
Lipids & proteins behave quite differently

Increment correlation no longer simple FBM ⟶



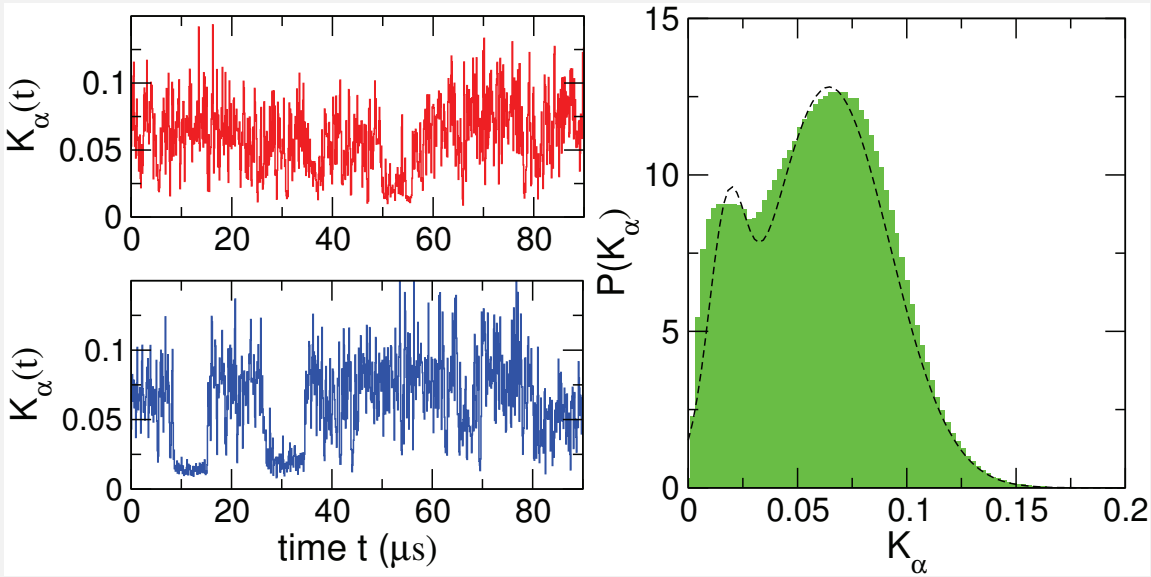
J-H Jeon, M Javanainen, H Martinez-Seara, RM & I Vattulainen, PRX (2016)

Crowding in membranes increases dynamic heterogeneity



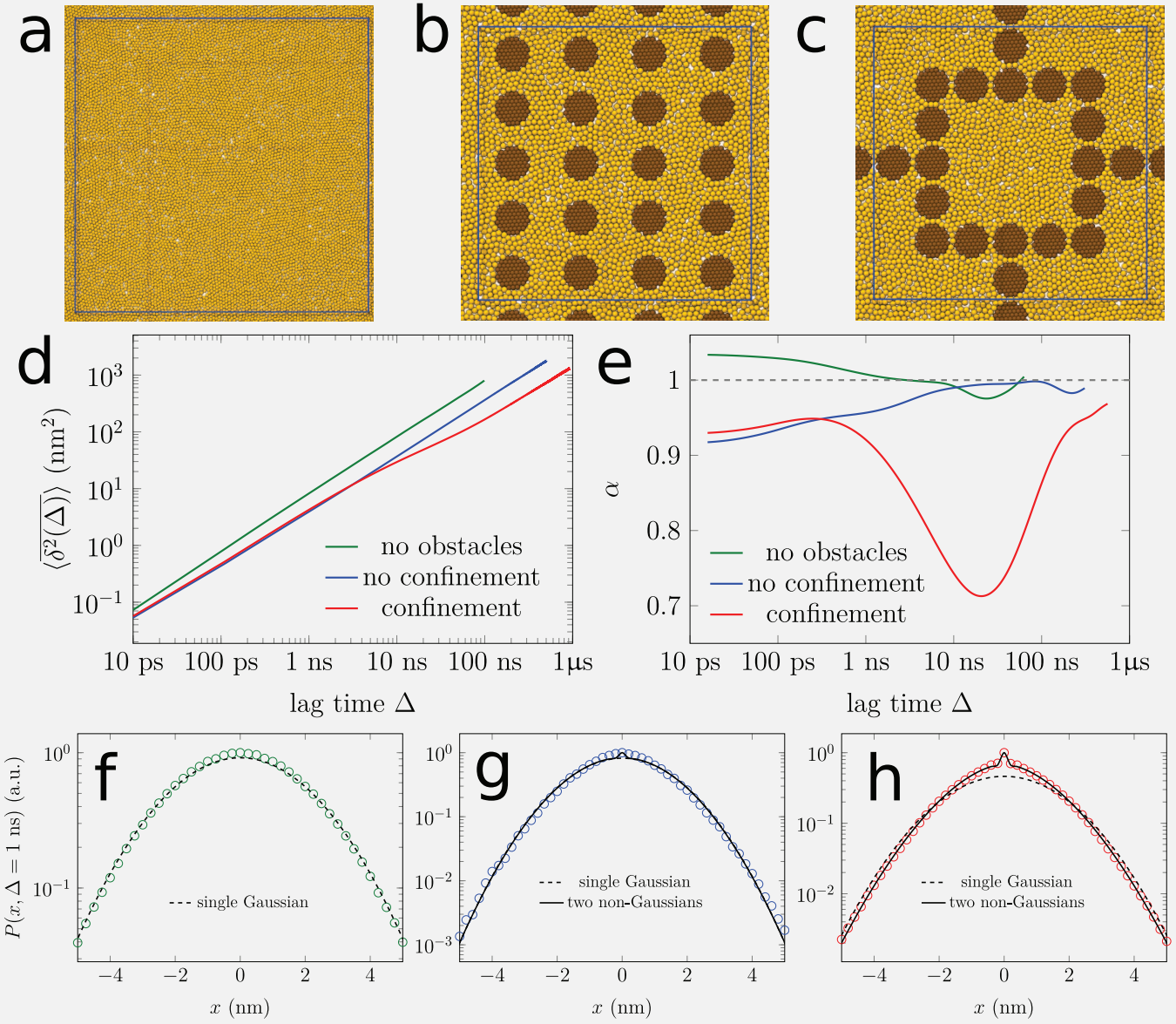
Diffusivity(t) for two lipids

Lipid diffusivity, dilute membrane



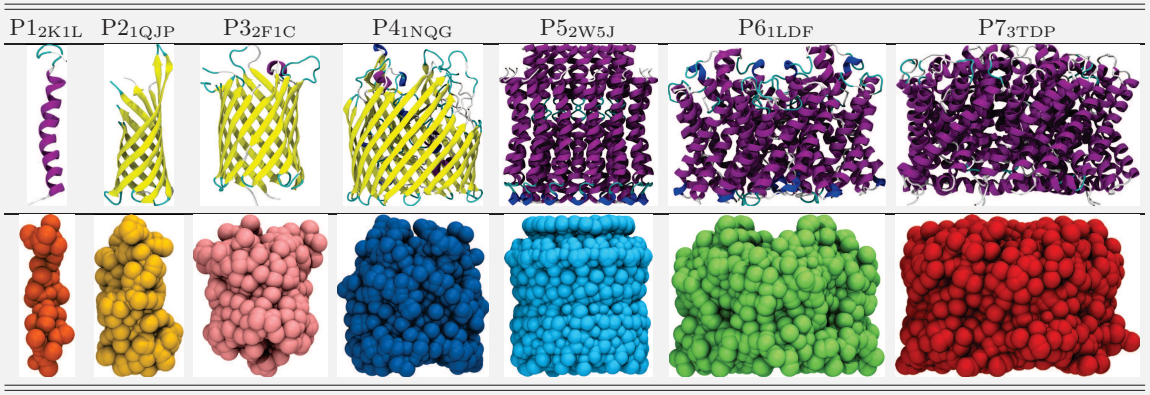
Lipid diffusivity, crowded membrane

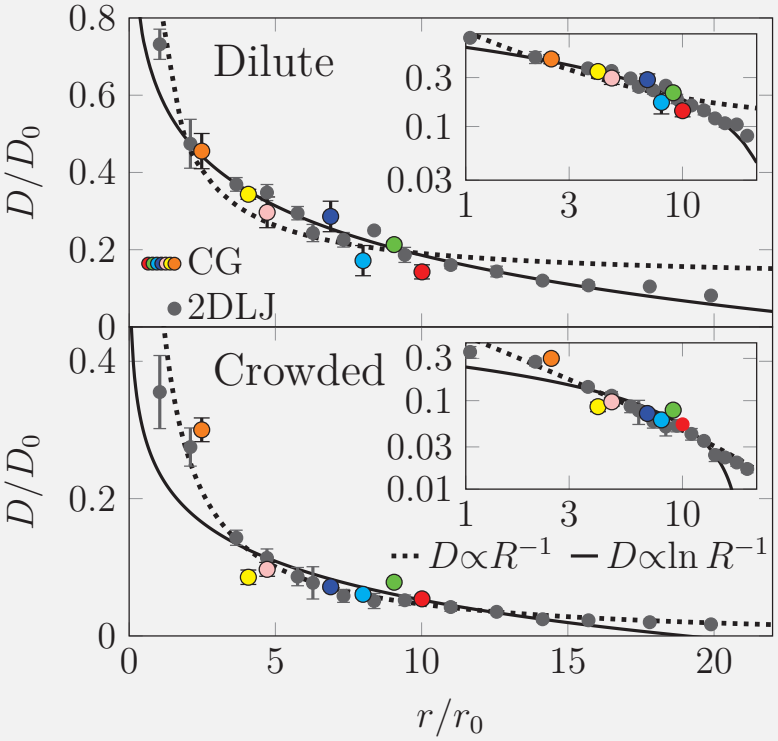
Confinement in argon system shows geometric origin

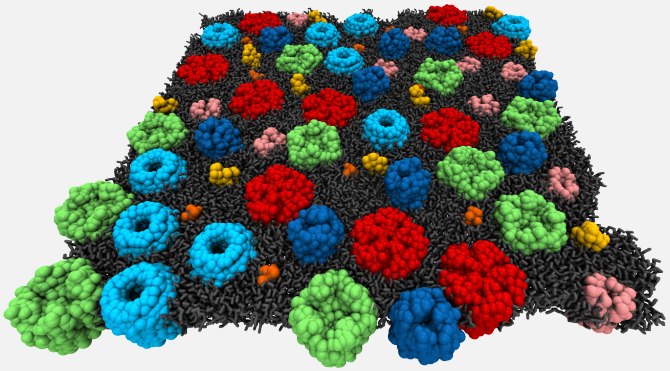


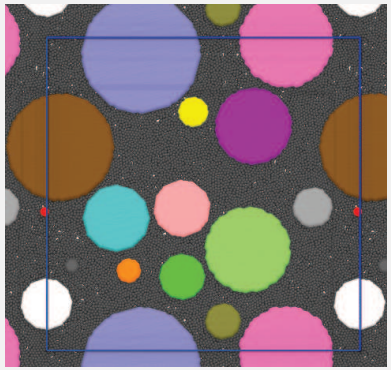
J-H Jeon, M Javanainen, H Seara Monne, RM & I Vattulainen, PRX (2016)

Geometry-induced violation of Saffman-Delbrück relation









Dilute system: Saffman-Delbrück law

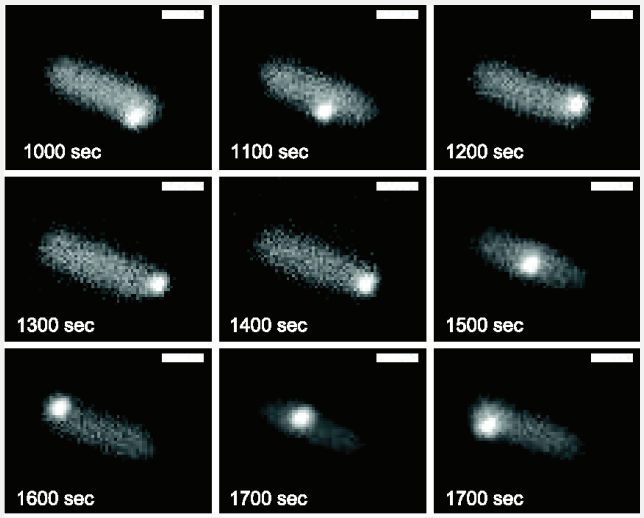
$$D(R) \simeq \log(1/R)$$

Crowded membrane & 2DLJ discs:

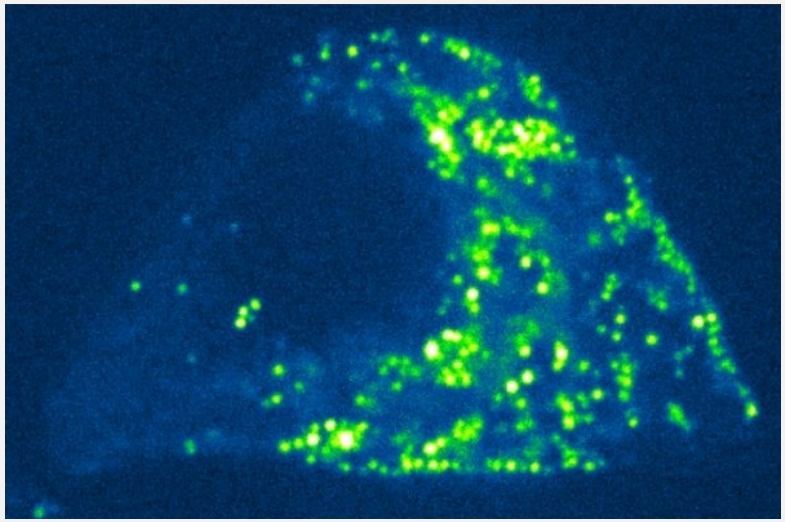
$$D(R) \simeq 1/R$$

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

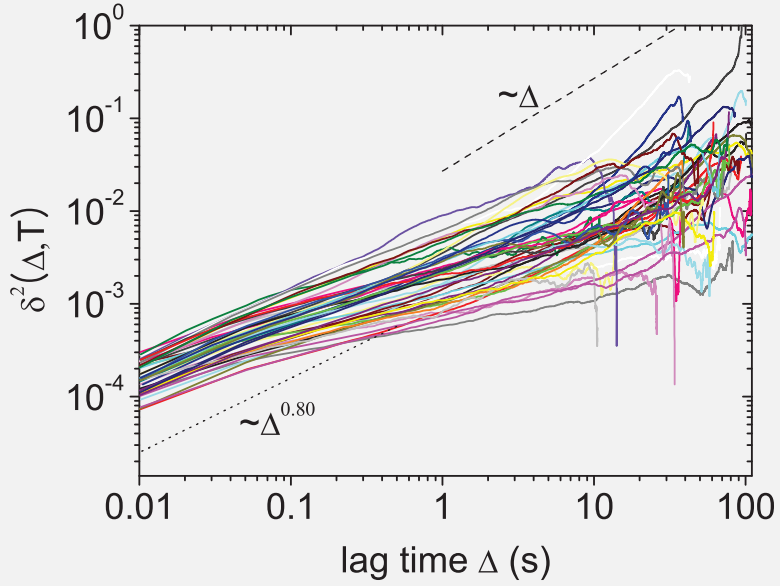
In vivo anomalous diffusion of submicron tracers: $\langle \mathbf{r}^2(t) \rangle \simeq t^{\alpha}$



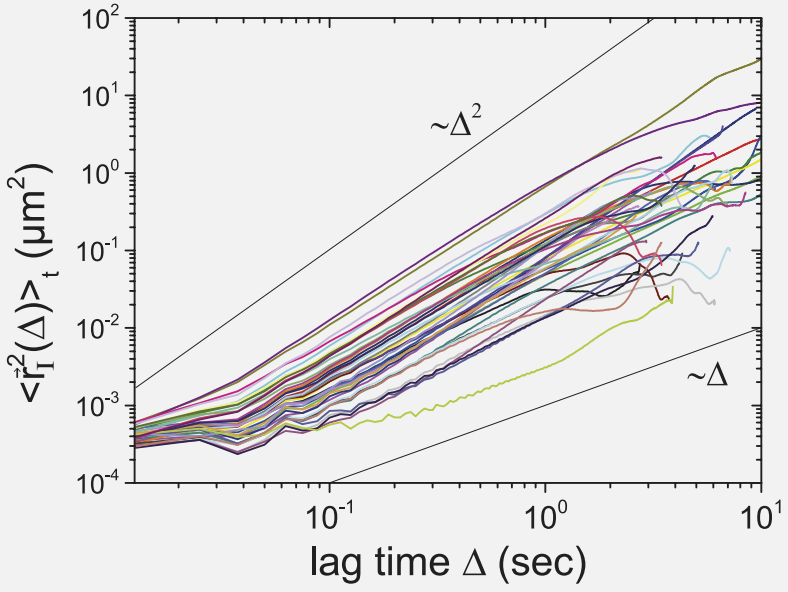
I Golding & EC Cox, PRL (2006)



SMA Tabei et al, PNAS (2013)

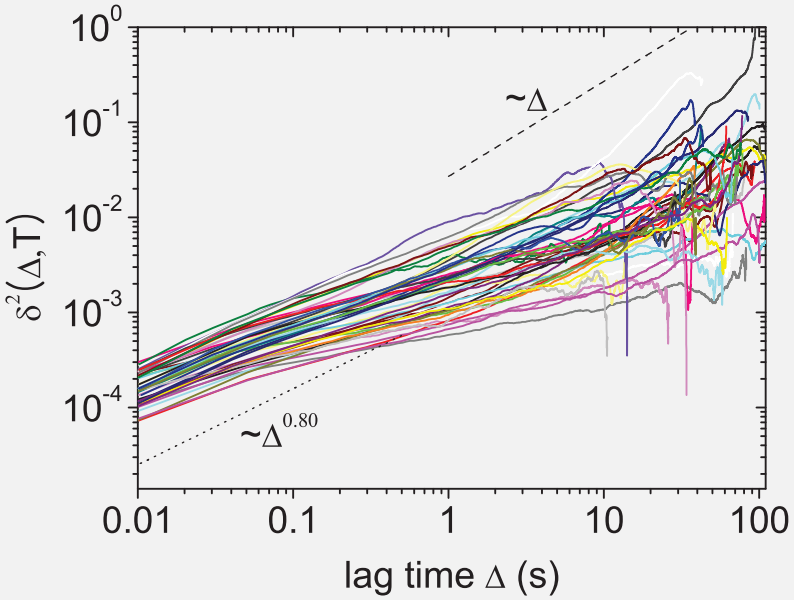


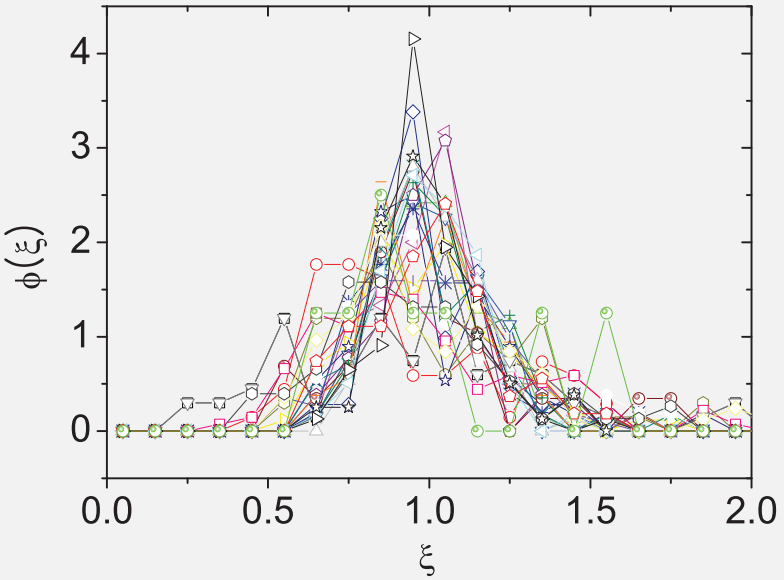
JH Jeon, . . . LB Oddershede & RM, PRL (2011)

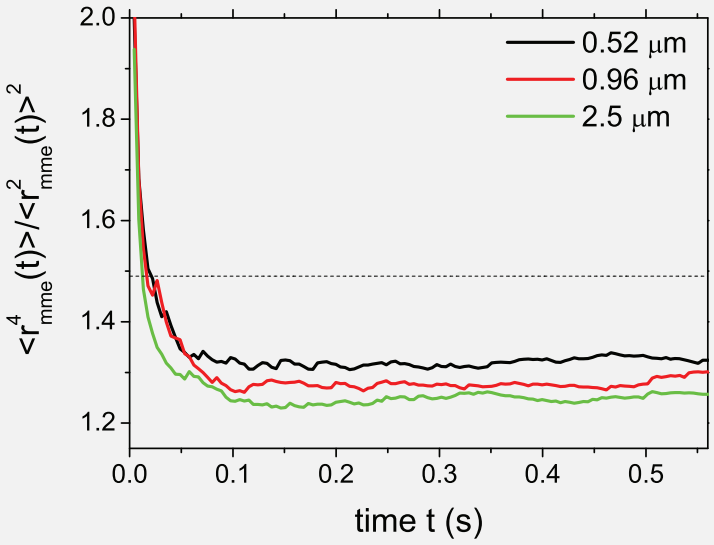


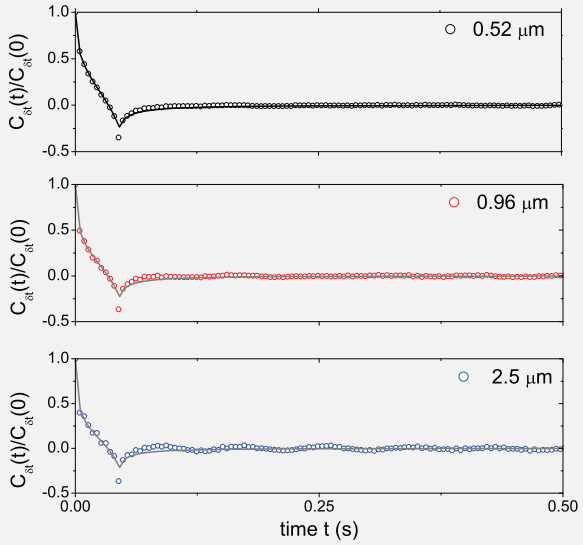
J Reverey, . . . RM & C Selhuber-Unkel, Sci Rep (2015)

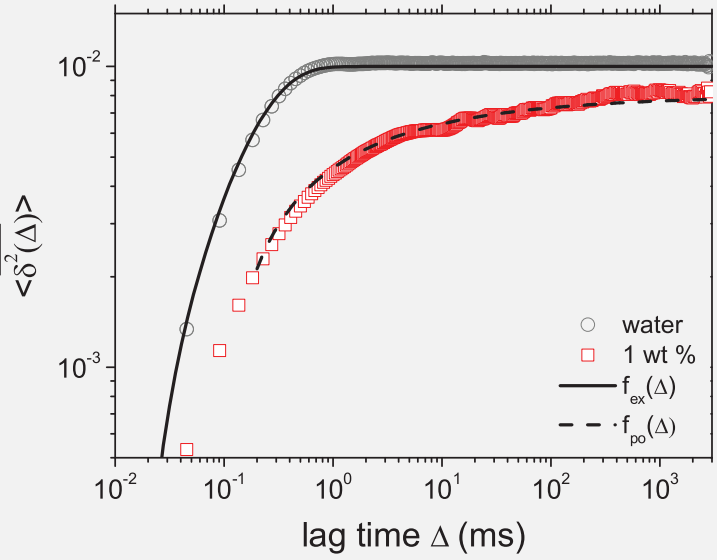
Passive motion of submicron tracers is viscoelastic





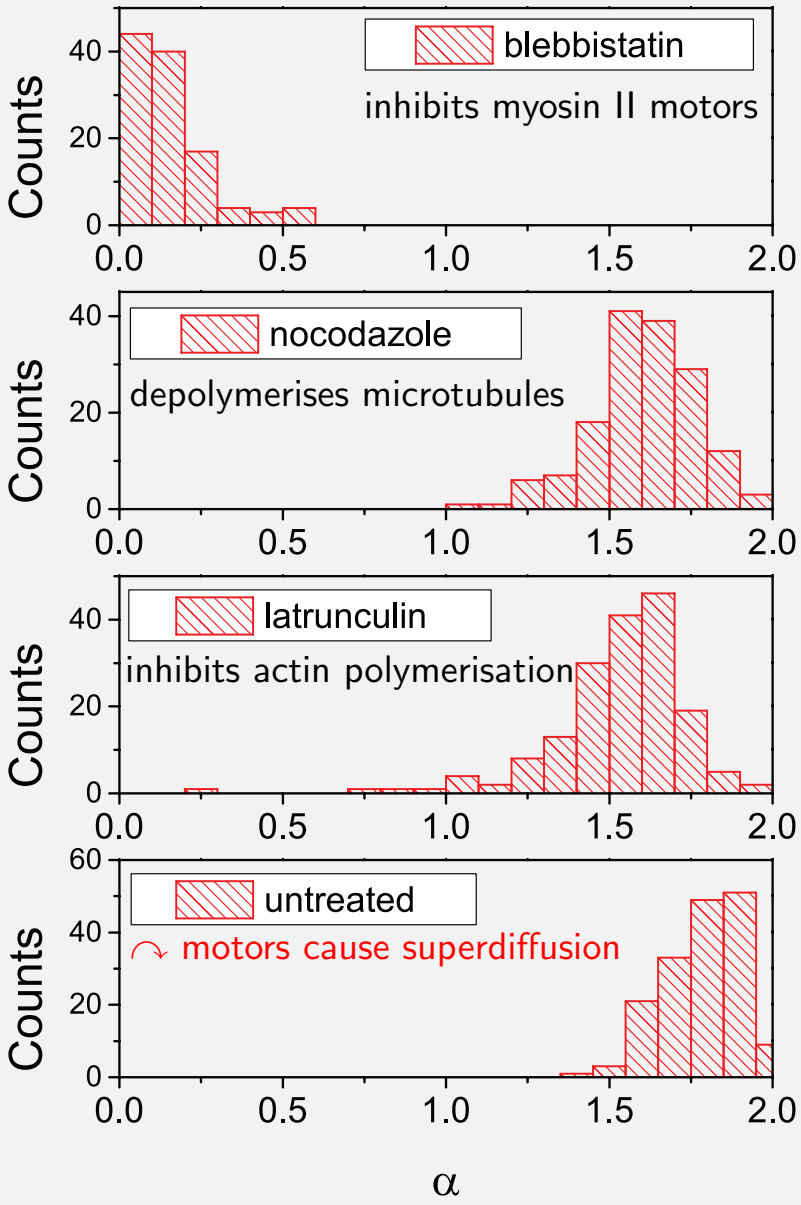


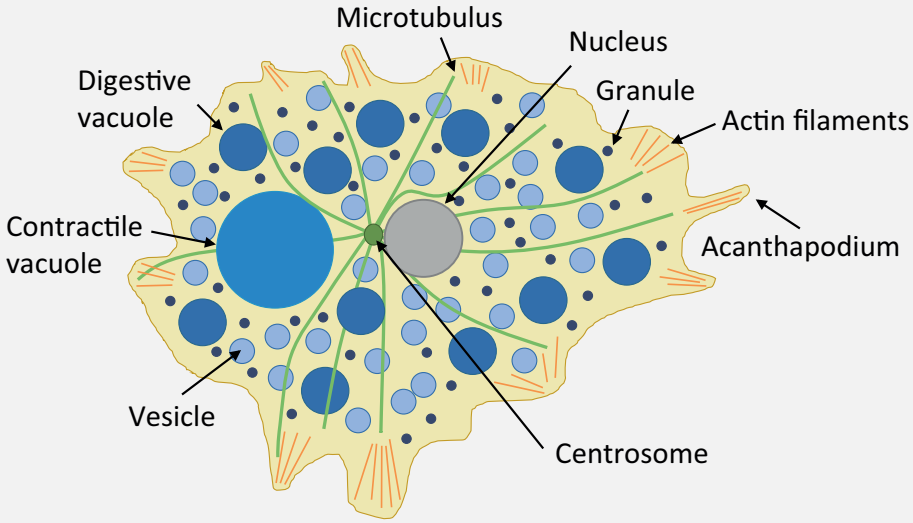


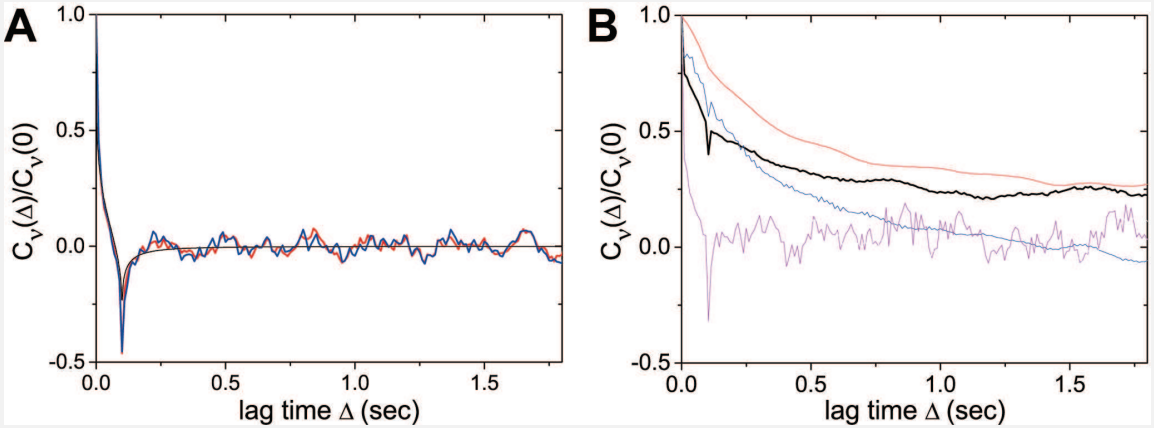


JH Jeon, . . . L Oddershede & RM, PRL (2011); JH Jeon, N Leijnse, L Oddershede & RM, NJP (2013)

Superdiffusion in living Acanthamoeba castellani



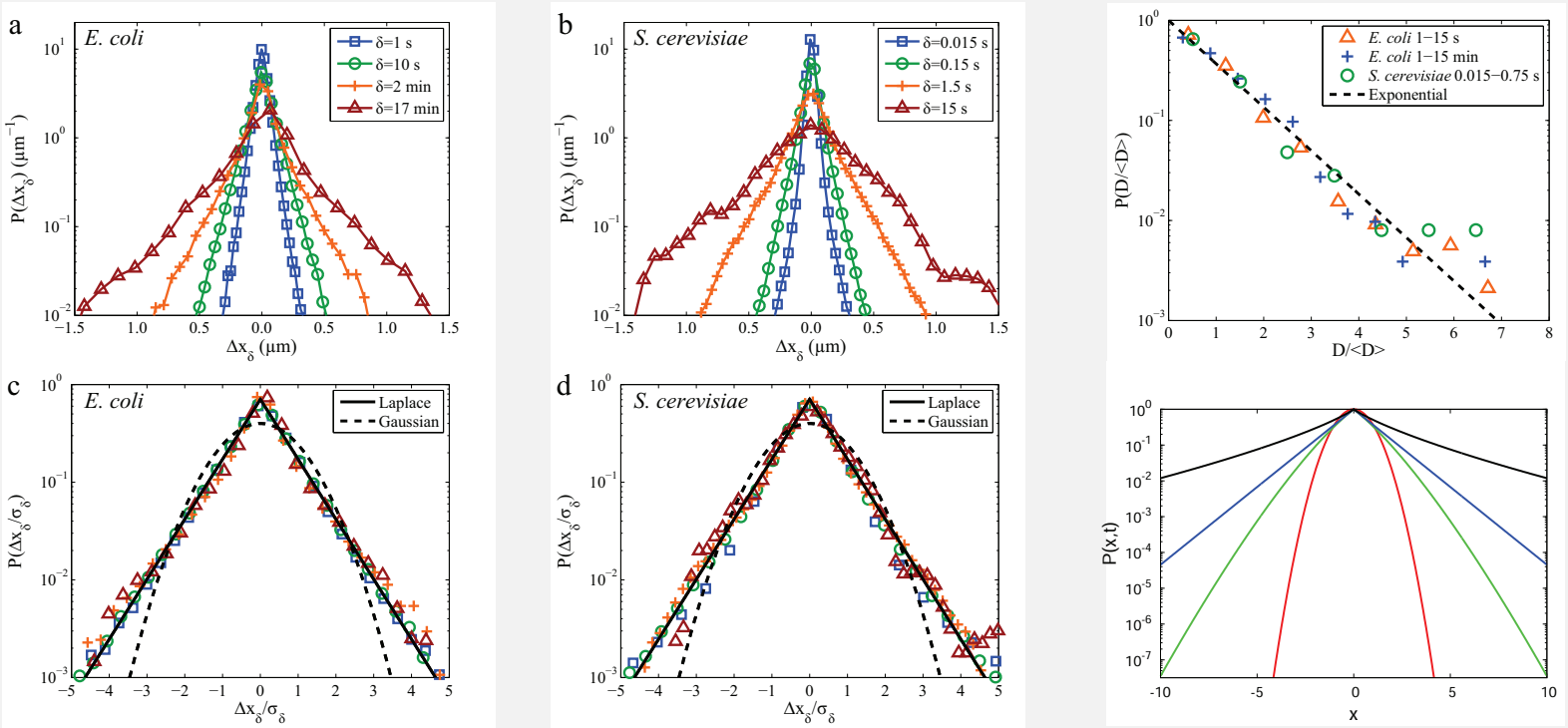




JF Reverey, J-H Jeon, H Bao, M Leippe, RM & C Selhuber-Unkel, Sci Rep (2015)

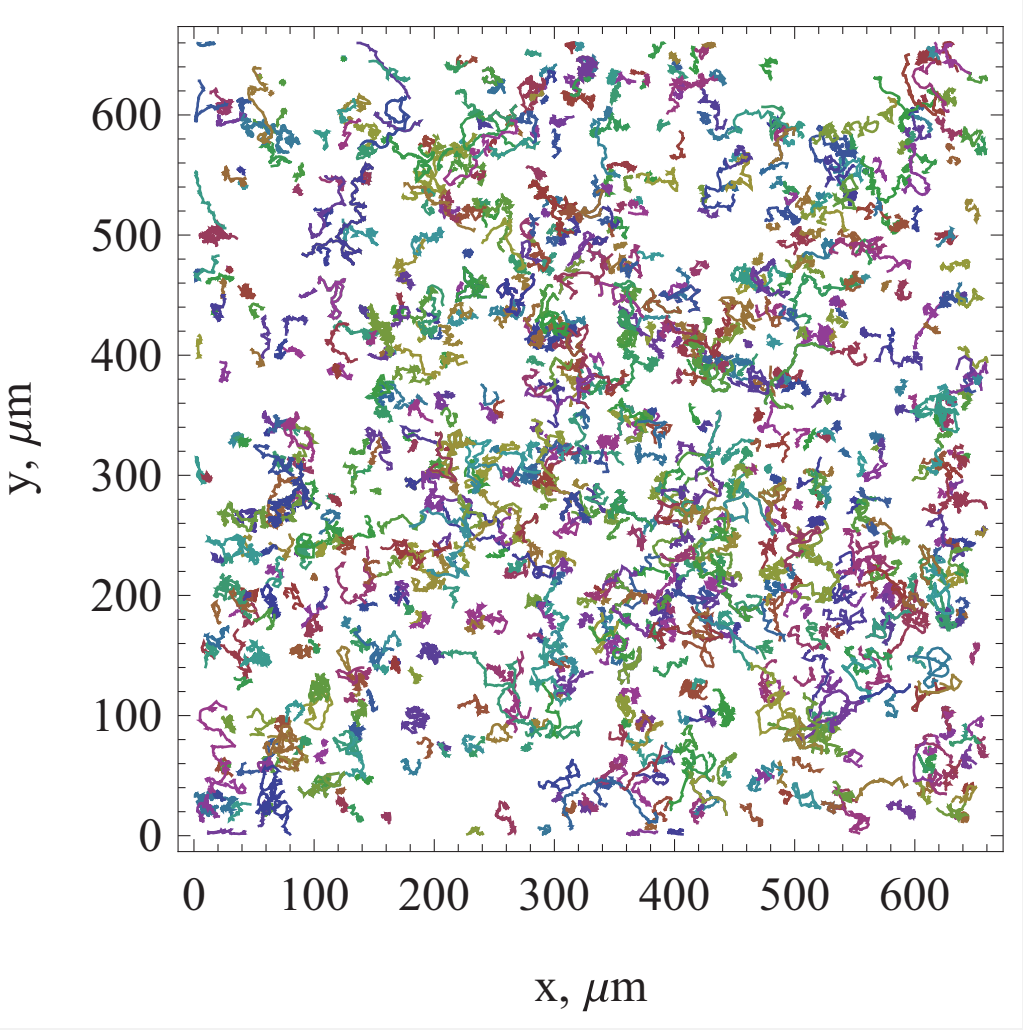
Non-Gaussian diffusion in viscoelastic systems

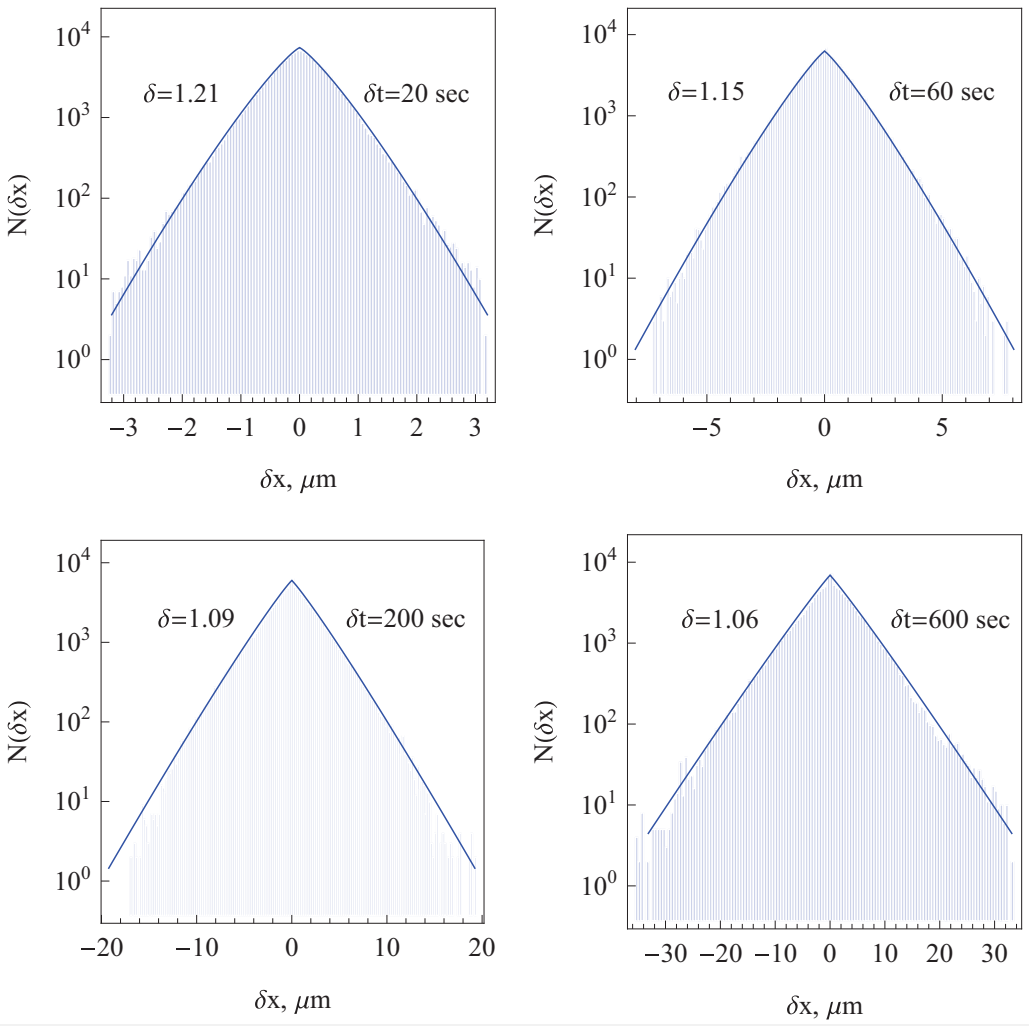
So far consensus: submicron tracer motion in cytoplasm is FBM-like, i.e., Gaussian
RNA-protein particles in E.coli & S.cerevisiae perform exponential anomalous diffusion:



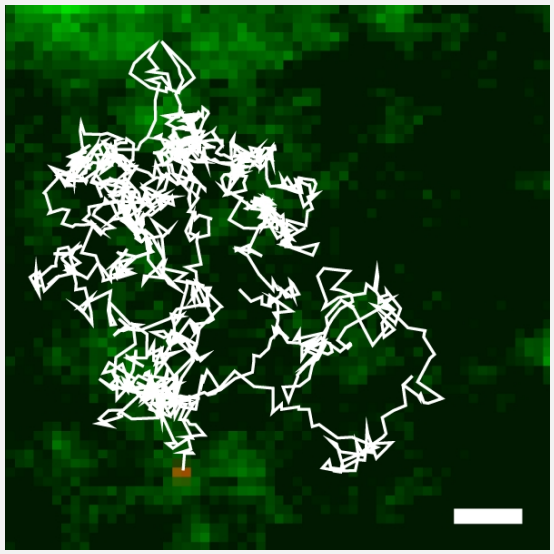
Diffusing diffusivity model: AV Chechkin, F Seno, RM & IM Sokolov, PRX (2017)

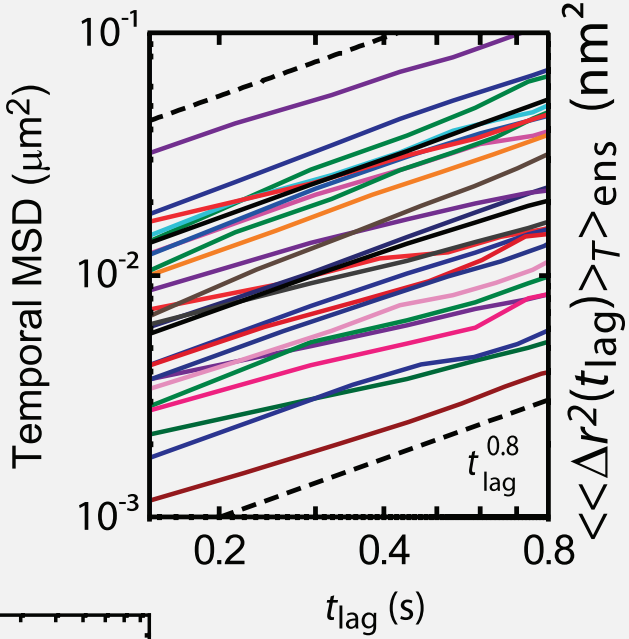
Non-Gaussian diffusion of Dictyostelium cells

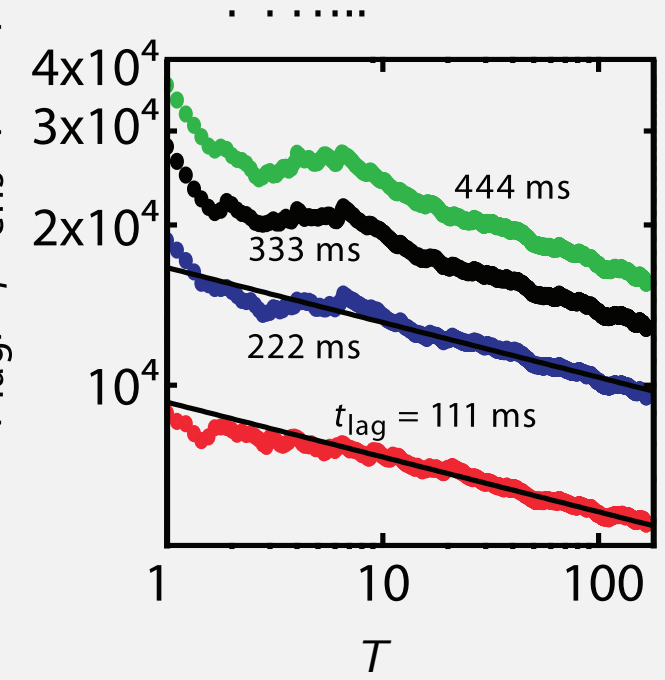


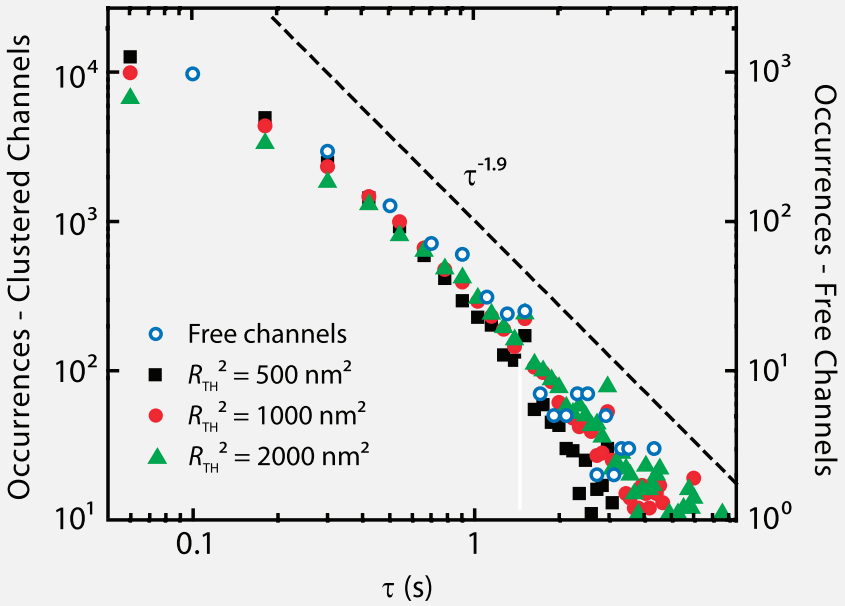


CTRW-like motion of Ka channels in plasma membrane









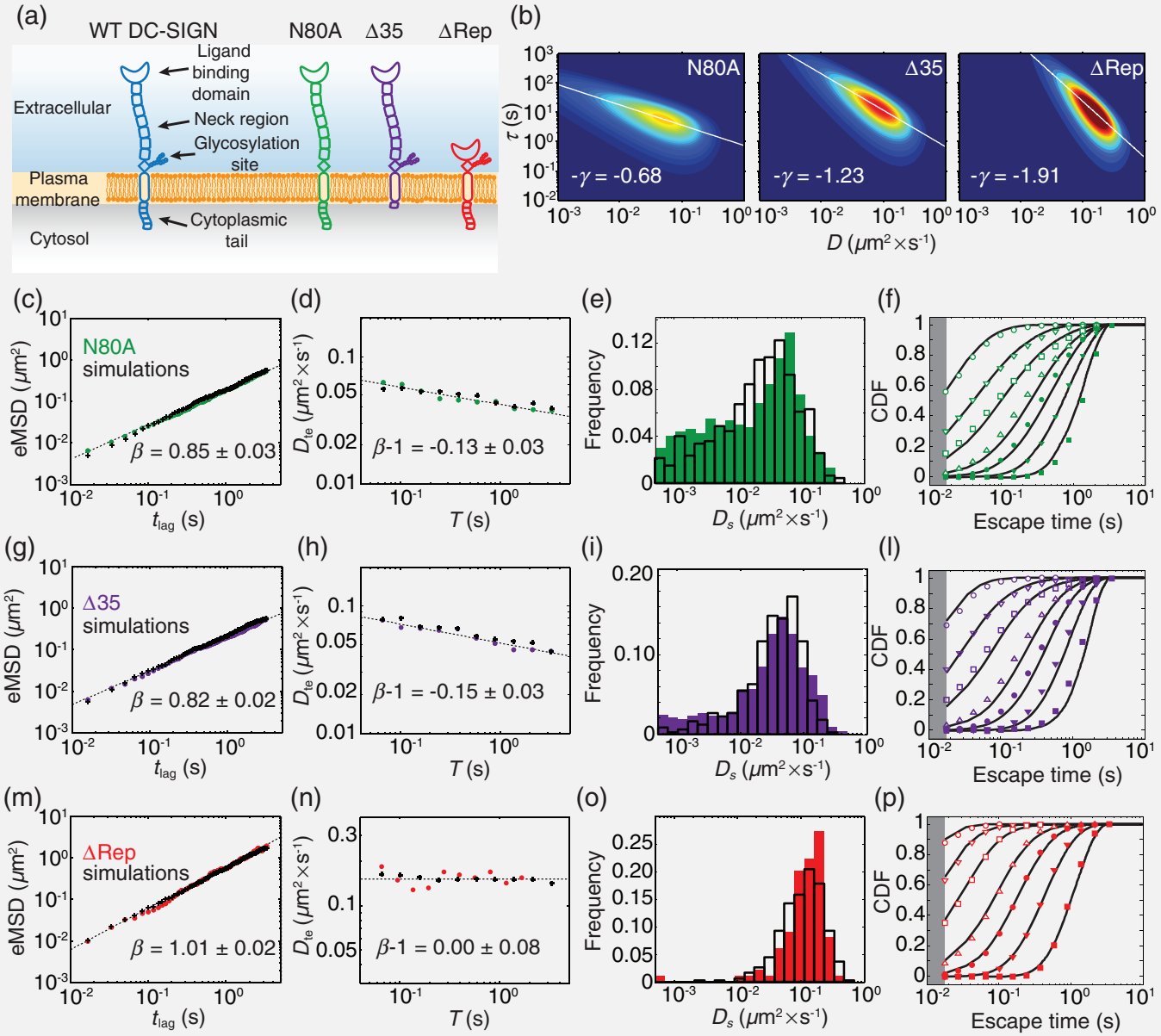
$\psi(\tau) \simeq \tau^{-1-\alpha}$ scale free

$\overline{\delta^2(\Delta)}$ 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 in the motion of membrane embedded proteins



C Manzo . . . M Garcia Parajo, PRX (2015)

Time averaged MSD & weak ergodicity breaking (WEB)

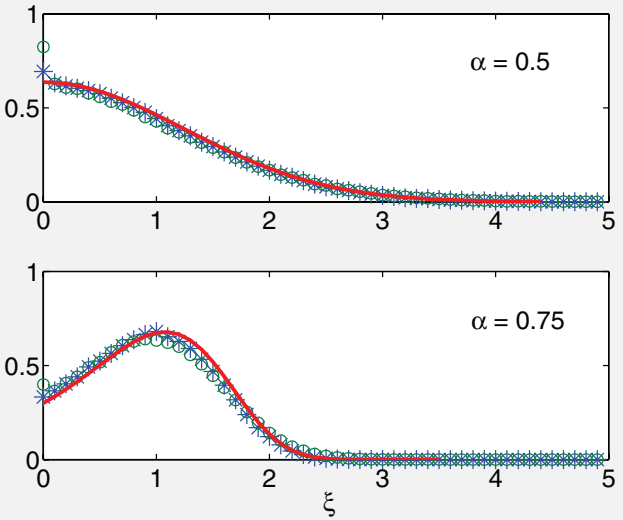
Time averaged MSD $\simeq \Delta$ is pseudo-Brownian and ageing ($\langle x^2(t)\rangle \simeq K_\alpha t^\alpha$):

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

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

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

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

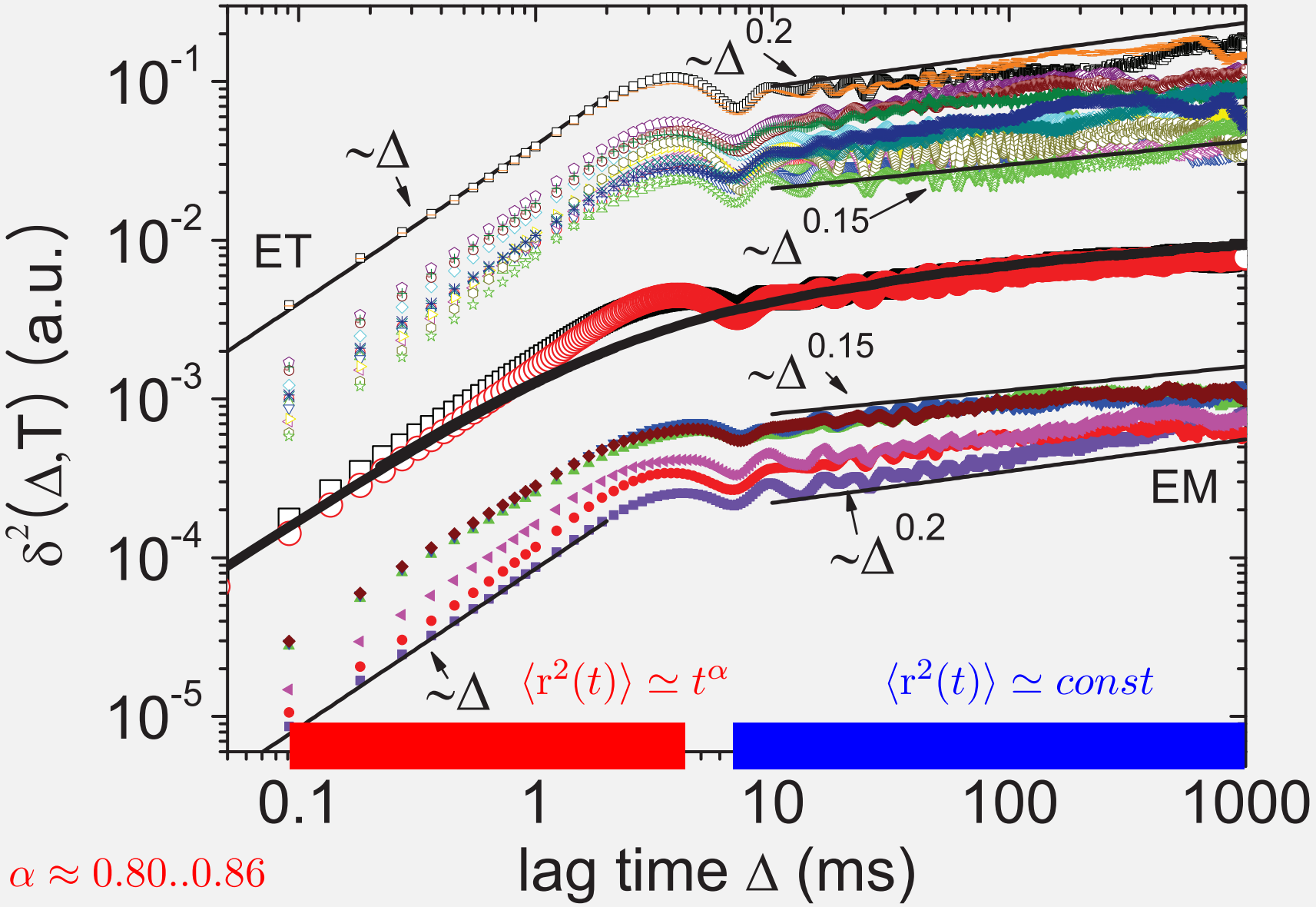


Confinement does not effect a plateau ($\langle x^2(t)\rangle \simeq \mathrm{const}(T)$):

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

Y He, S Burov, RM & E Barkai, PRL (2008); Generalised Khinchin theorem: S Burov, RM, & E Barkai, PNAS (2010)

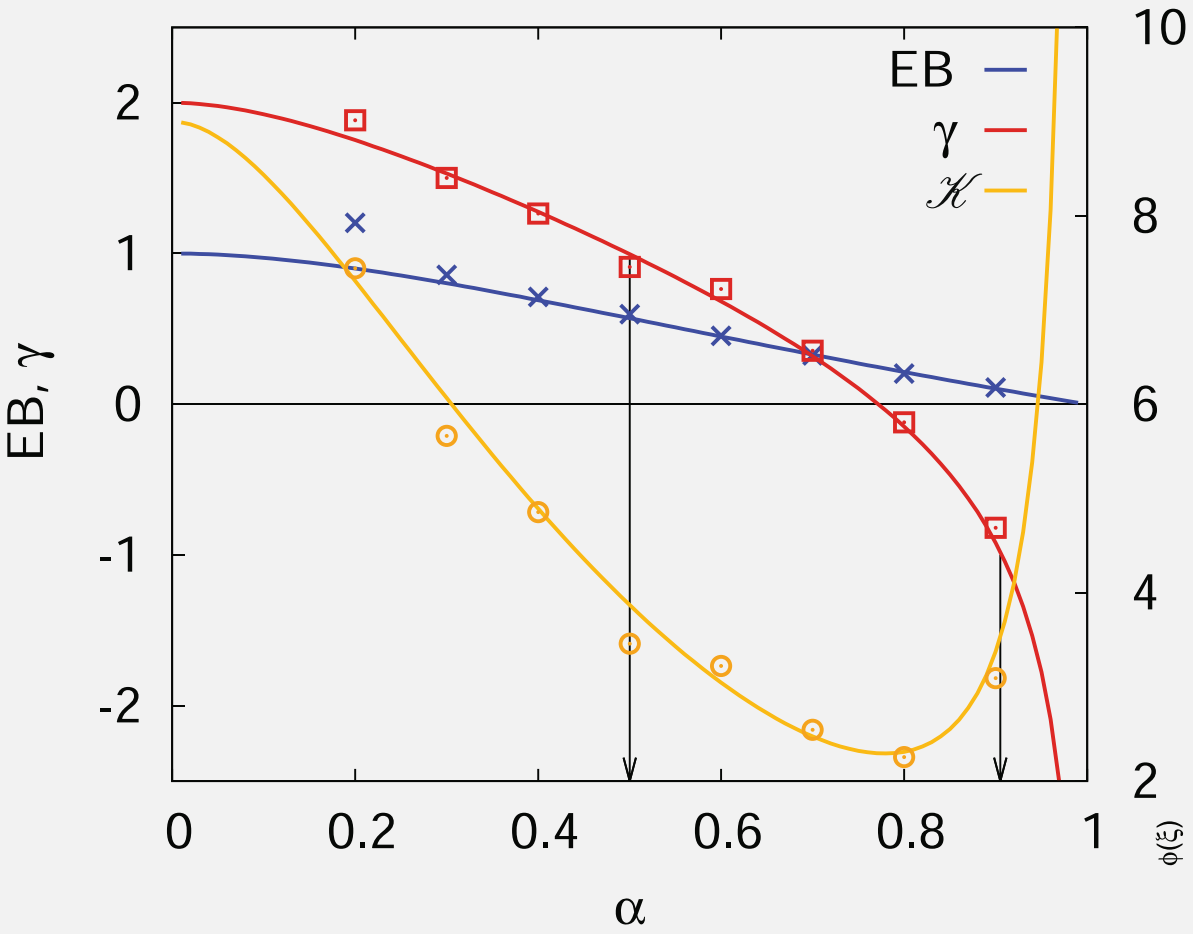
Granule subdiffusion in harmonic optical tweezer potential

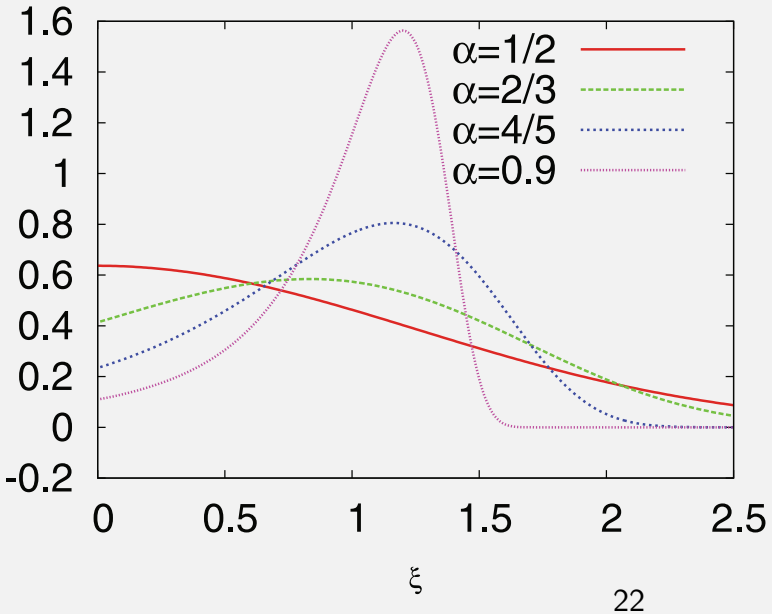


$\alpha \approx 0.80..0.86$

J-H Jeon, V Tejedor, S Burov, E Barkai, C Selhuber-Unkel, K Berg-Sørensen, L Oddershede & RM, PRL (2011)

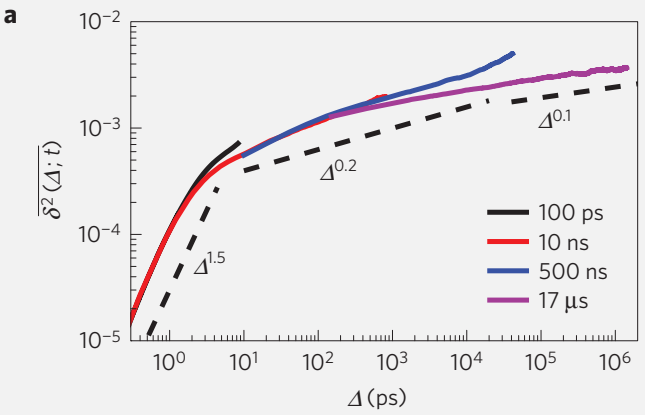
Higher order moments of the scatter: skewness & kurtosis

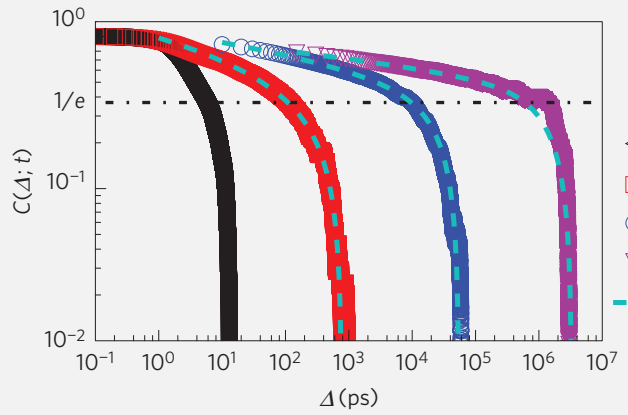


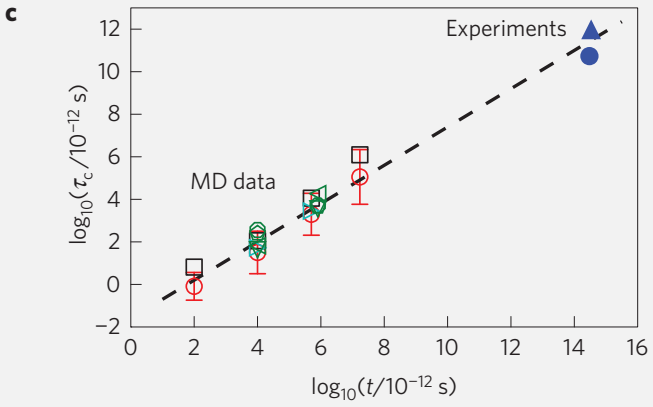


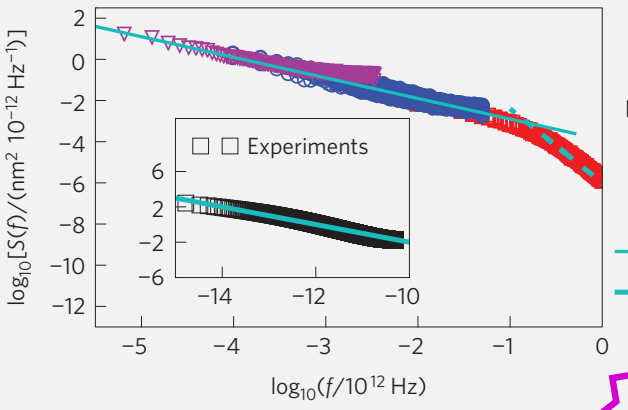
M Schwarzl, A Godec & RM, Sci Rep (2017)

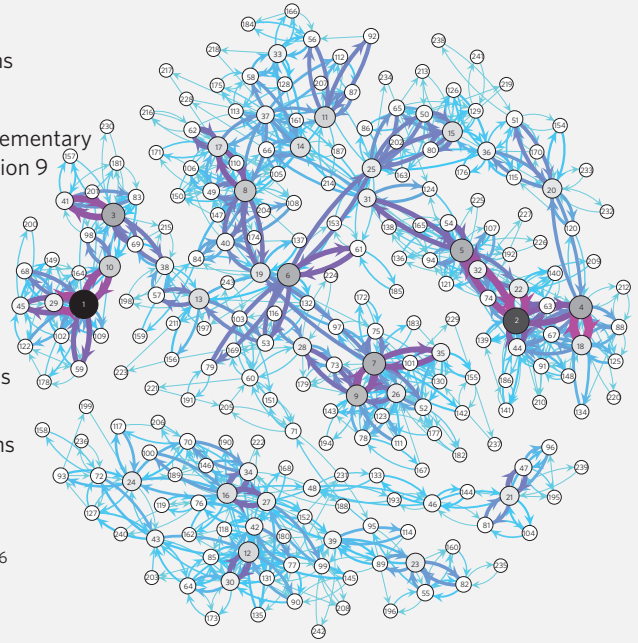
Self-similar internal protein dynamics: 13 decades of ageing



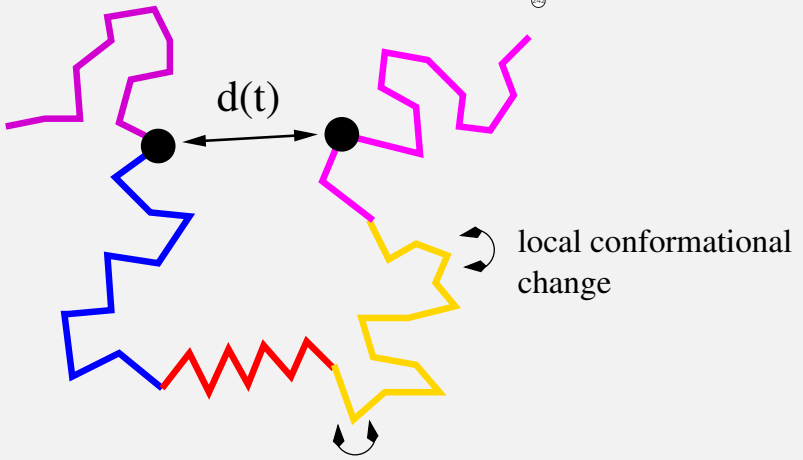






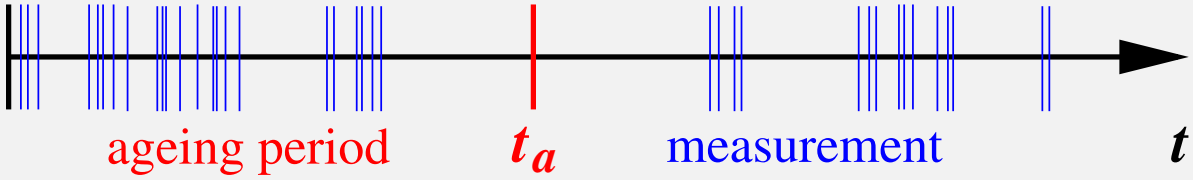


PGK domains
PGK residues
K-RAS segments
ePepN, dom. 1–2
ePepN, dom. 2–3
ePepN, dom. 2–4
ePepN, dom. 4-rest
Ref. 3
Ref. 4
$\propto t^{0.9}$



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

Ageing effects in single trajectory time averages

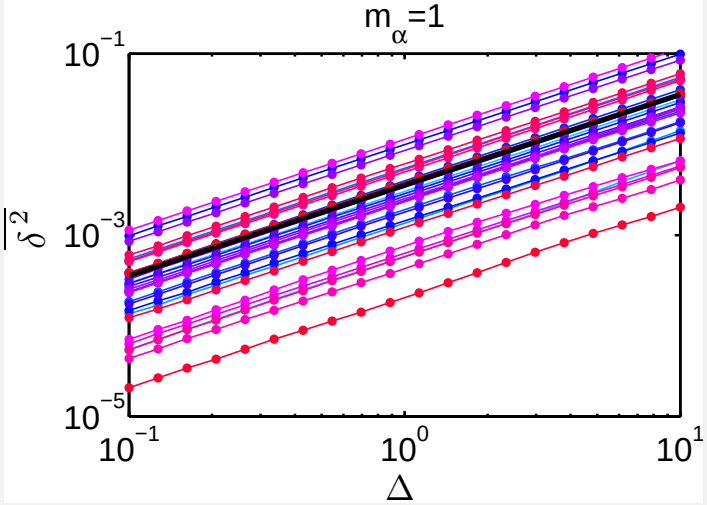


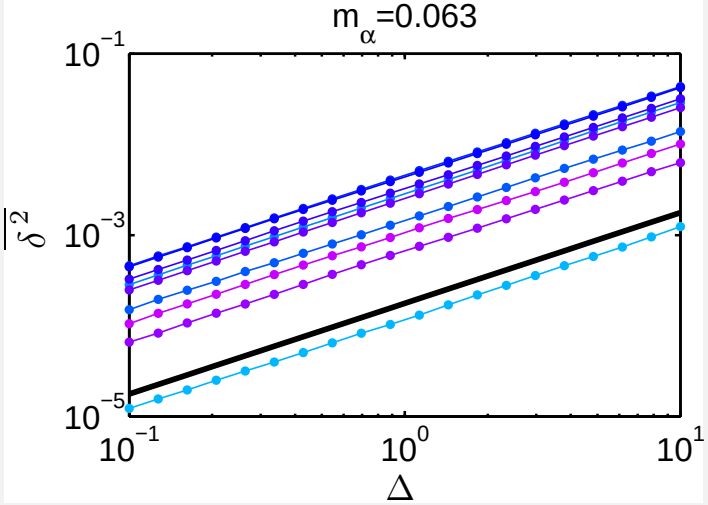
Ageing mean squared displacement $(\Lambda(z) = (1+z)^\alpha - z^\alpha)$

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

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

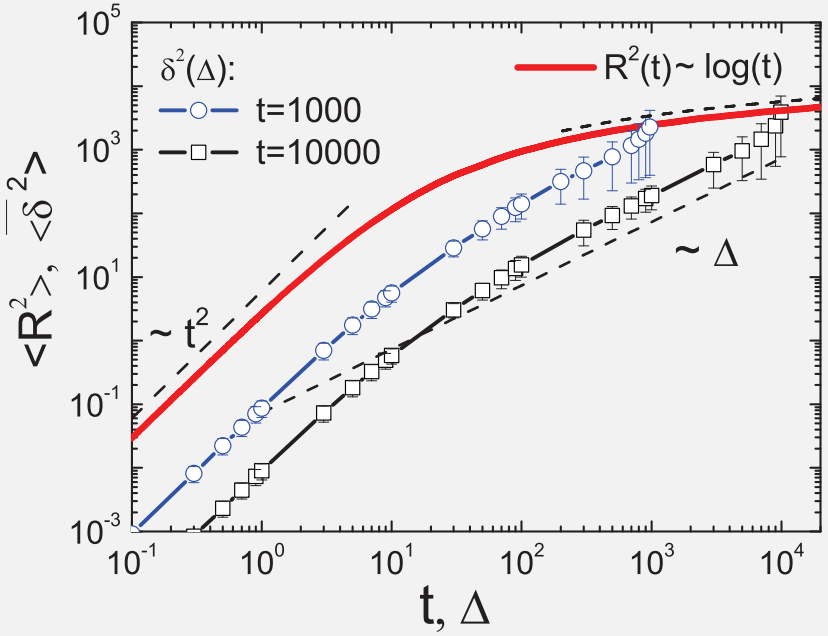
$$m_\alpha(T/t_a) \simeq (T/t_a)^{1-\alpha}, \quad T \ll t_a$$

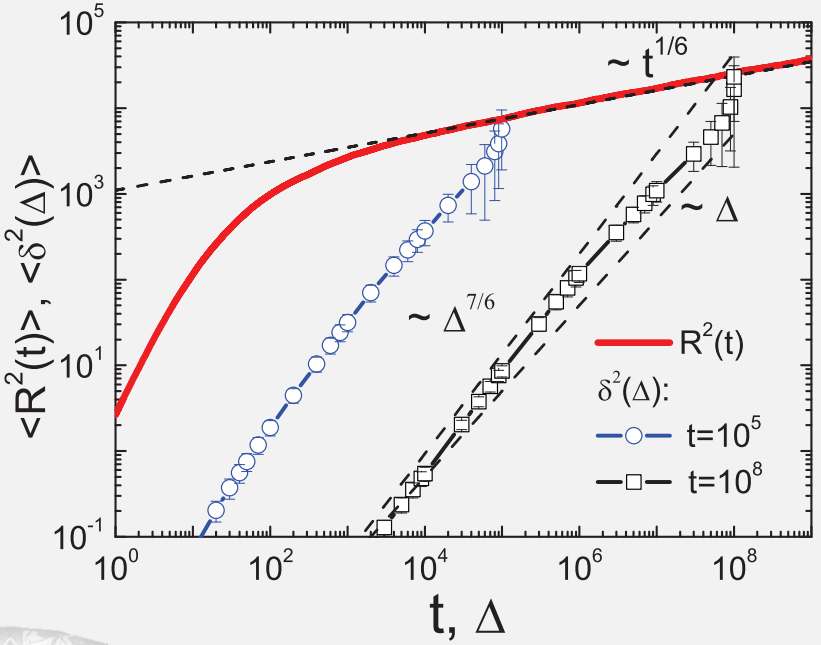




J Schulz, E Barkai & RM, PRL (2013), PRX (2014)

WEB in granular gas & SBM as mean field theory

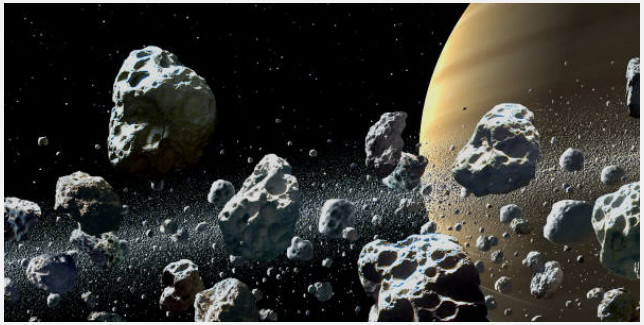




Haff's law: $\mathscr{T}(t) = \mathscr{T}_0/(1 + t/\tau_0)^2$

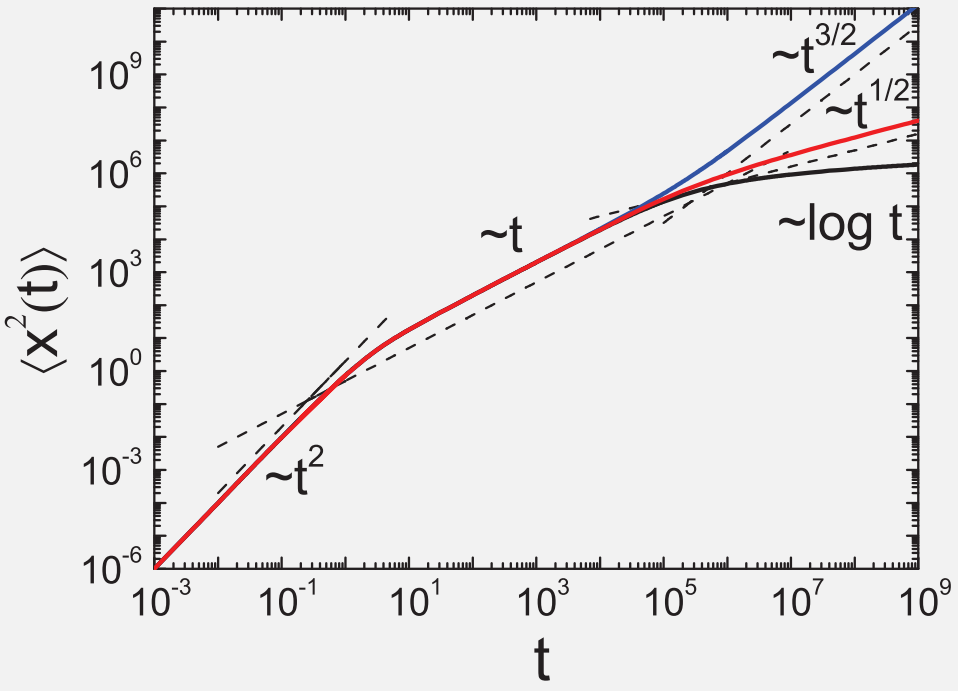
$$\langle \mathbf{r}^2(t) \rangle \sim 6 D_0 \tau_0 \log(1 + t/\tau_0)$$

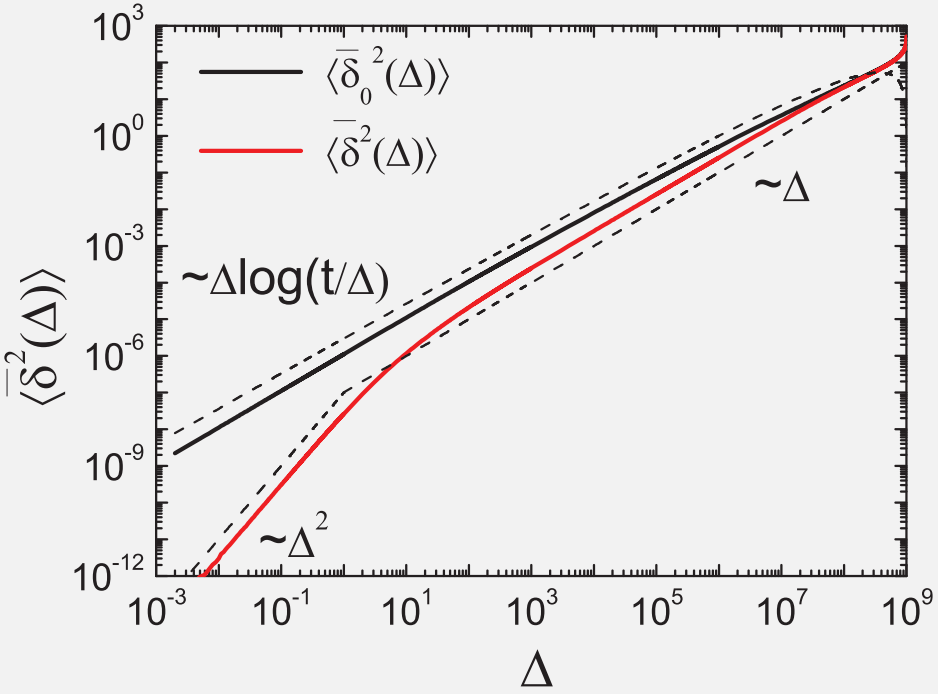
$$\left\langle \overline{\delta^2(\Delta)} \right\rangle \sim 6 D_0 \tau_0 \Delta / T$$



A Bodrova, AV Chechkin, AG Cherstvy & RM, NJP (2015); PCCP (2015); suppressed overdaming transition: Sci Rep (2016)

Non-existence of the overdamped limit in slow SBM

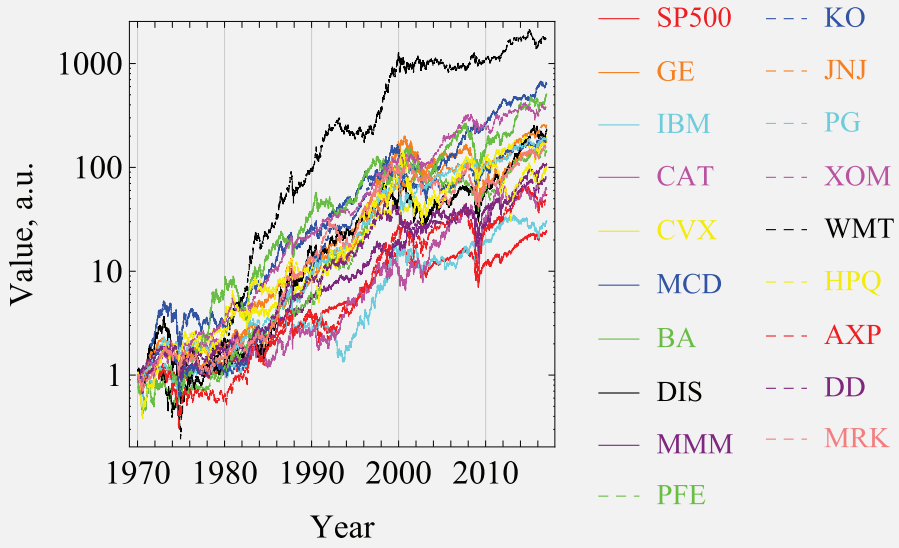


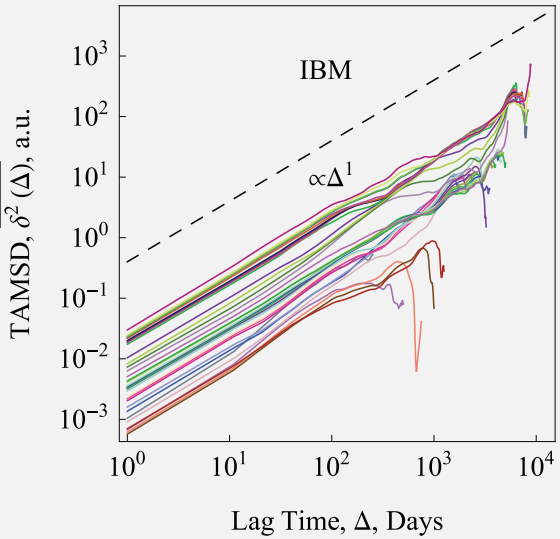


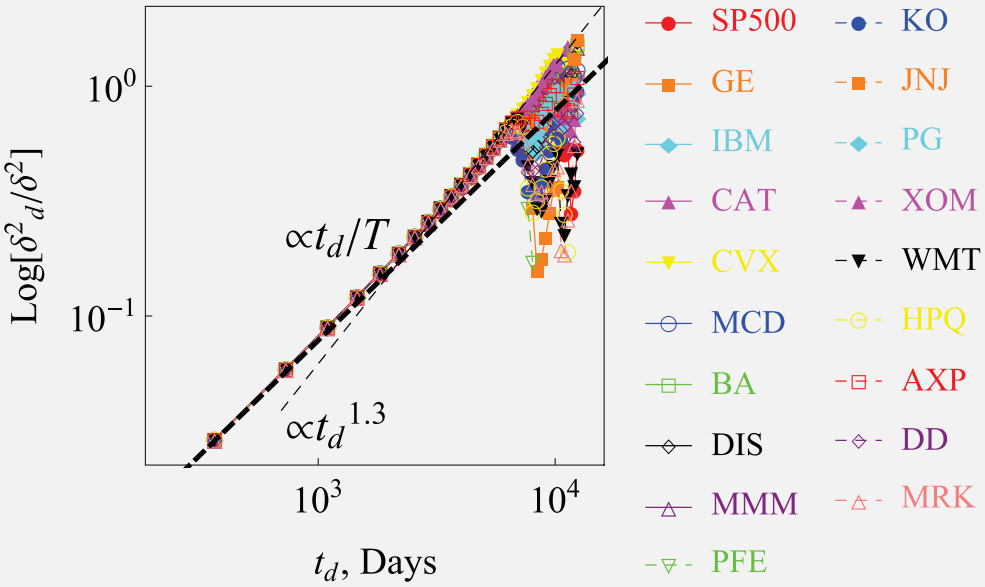
Crossover from ballistic to overdamped motion no longer defined by time scale of inverse friction. For small α & ultraslow the SBM overdamped limit is never fulfilled

Ageing case: [H Safdari, A Bodrova, AV Chechkin, AG Cherstvy & RM, PRE (2017)]

Time averages & ageing in financial market time series







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

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

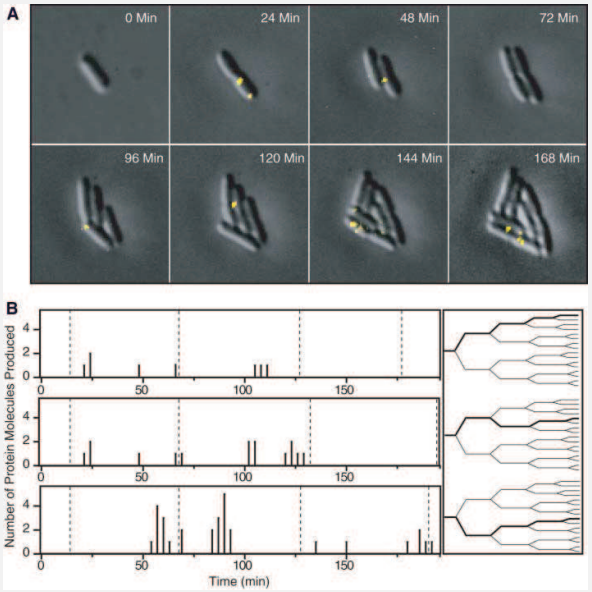
$$\sim \frac{\Delta}{T - t_d} X_0^2 \left(e^{\sigma^2 T} - e^{\sigma^2 t_d} \right)$$

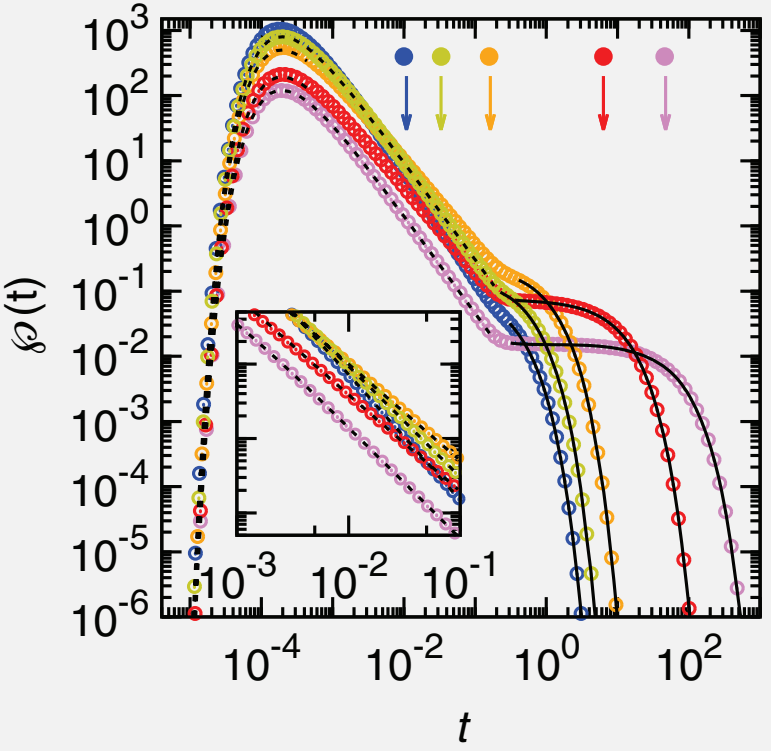
$$\log \left[\left\langle \overline{\delta^2_d(\Delta, t_d)} \right\rangle \Big/ \left\langle \overline{\delta^2(\Delta)} \right\rangle \right] \sim t_d/T$$

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

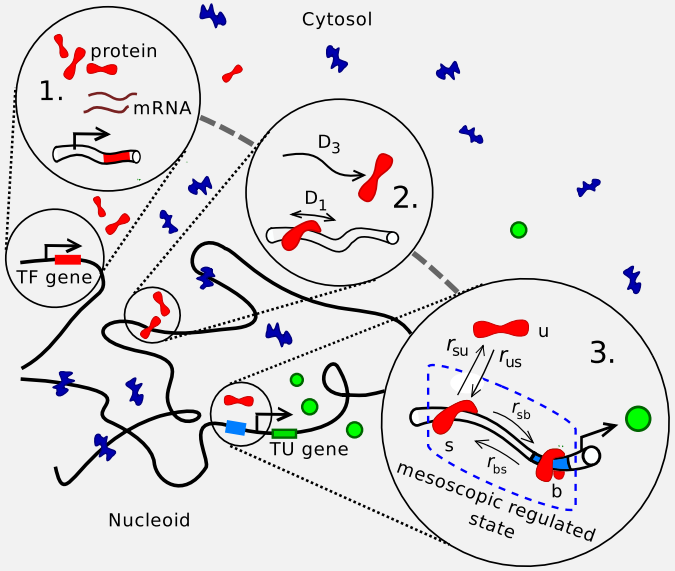
First-past-the-post: few-encounter limit in cell signalling

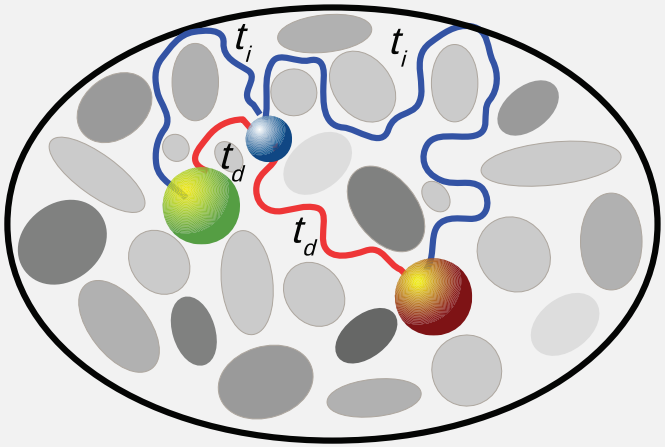
Yu et al, Science (2006)





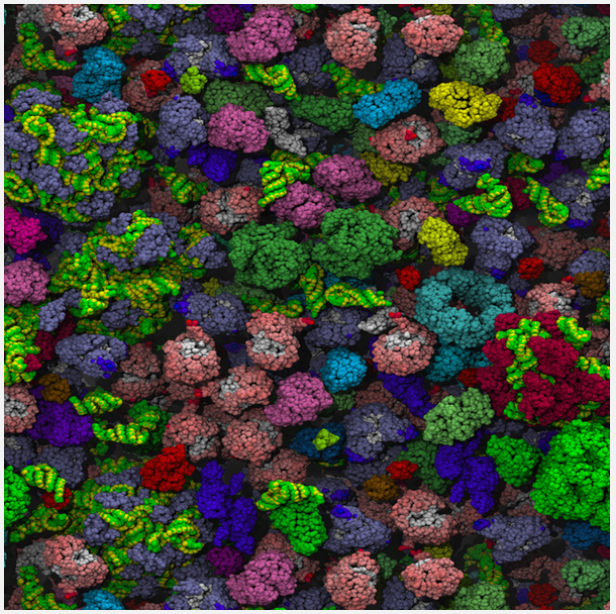
O Pulkkinen & RM, PRL (2013)



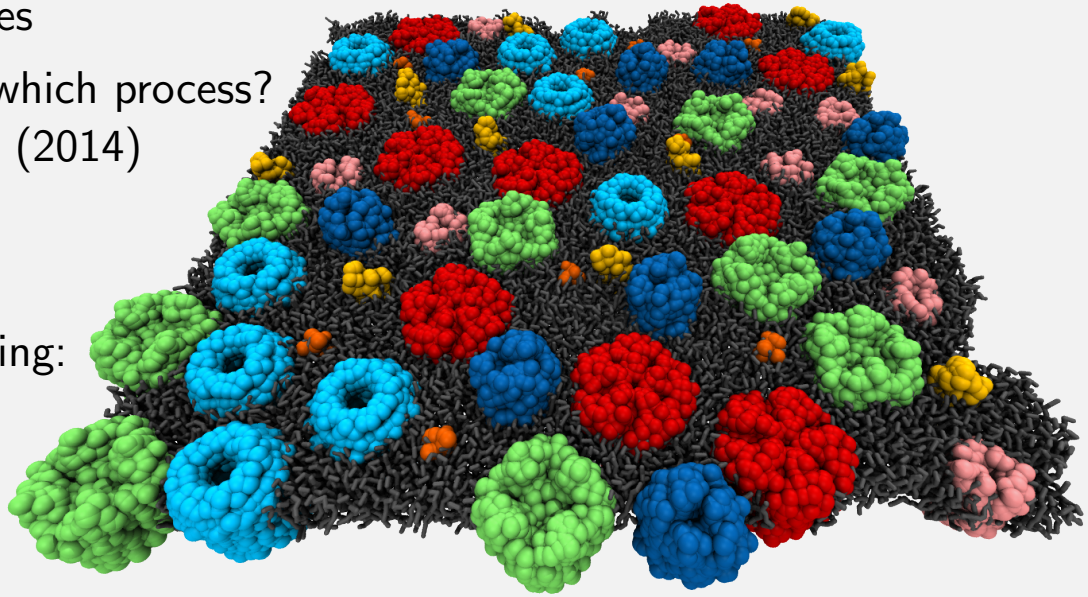


A Godec & RM, PRX (2016); Sci Rep (2016)

Summary



- Antipersistent & persistent FBM-like motion
- Transient anomalous diffusion in lipid bilayers:
  Disorder increases anomalies
- Non-Gaussian, heterogeneous diffusion in crowded bilayers
  Features qualitatively reproduced in confined argon
- 13 decades of ageing in single proteins
- CTRW-like, ageing & weakly non-ergodic diffusion
  of protein channels in plasma membranes
- Anomalous diffusion non-universal ↷ which process?
  ↷ Inference methods: RM & al, PCCP (2014)
- Anomalous diffusion in membranes:
  RM & al, BBA Biomembranes (2016)
- Single molecule manipulation & tracking:
  C Nørregaard et al, Chem Rev (2017)



E Barkai, Y Garini & RM, Phys Today (2012)

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