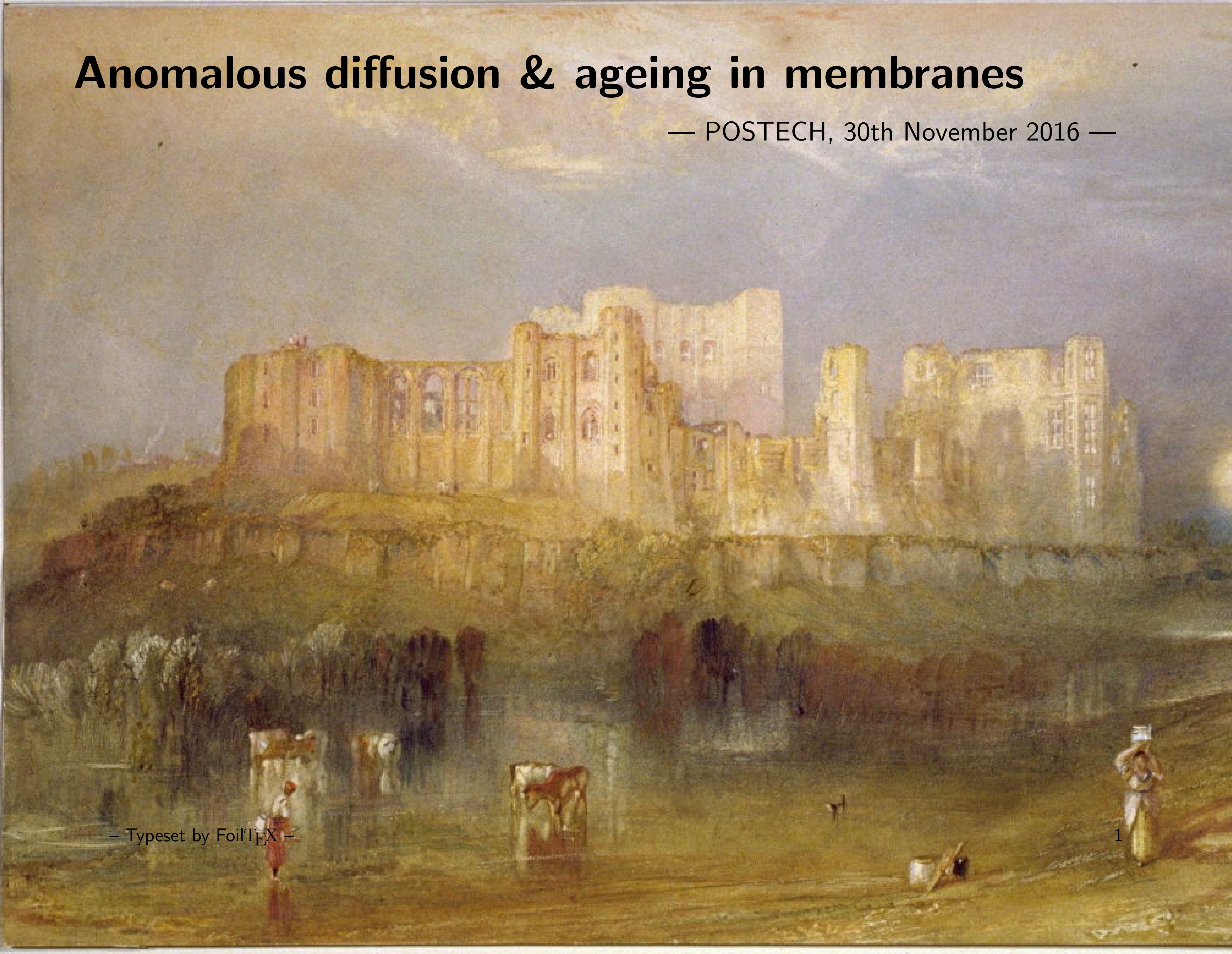
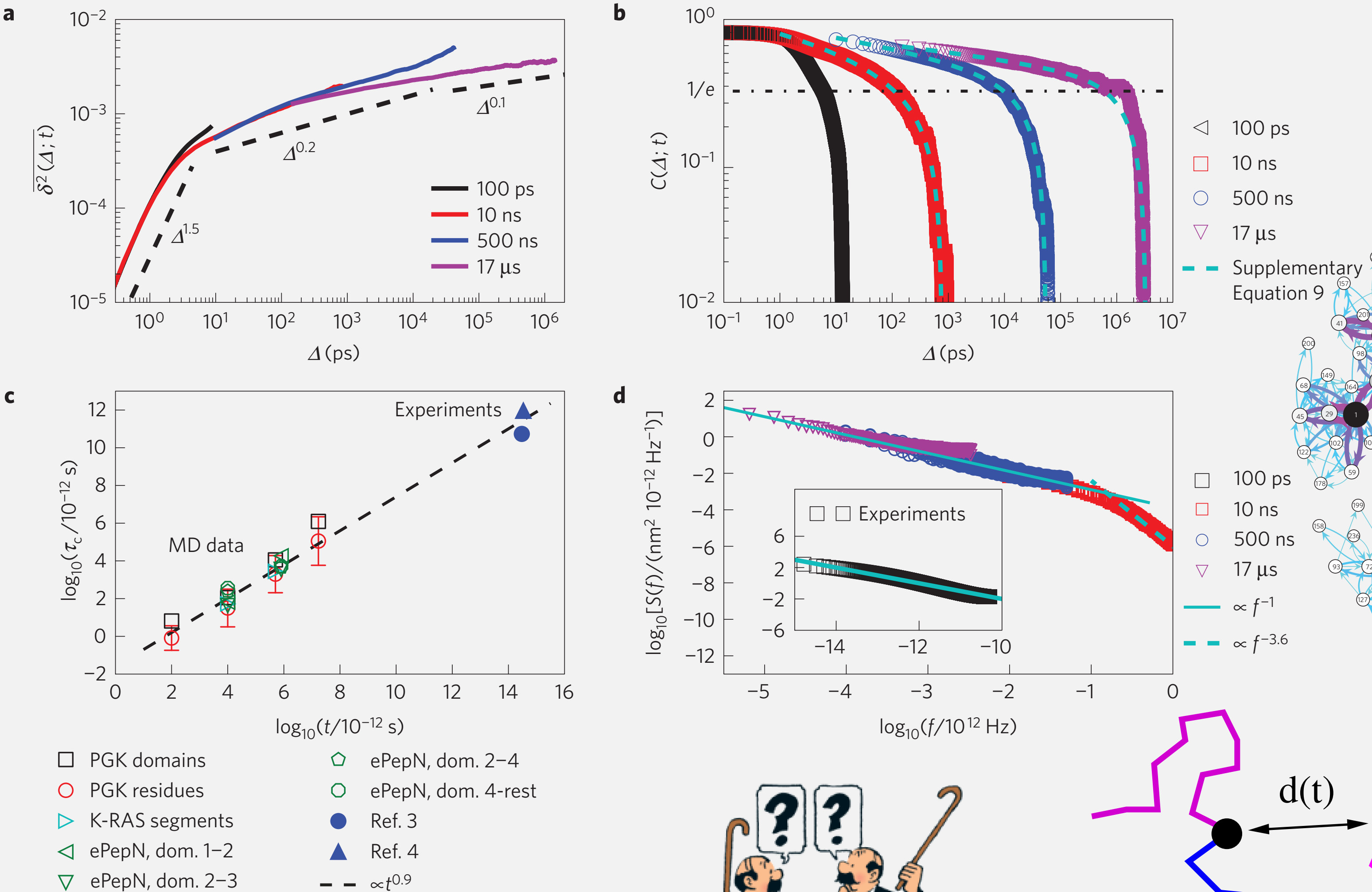
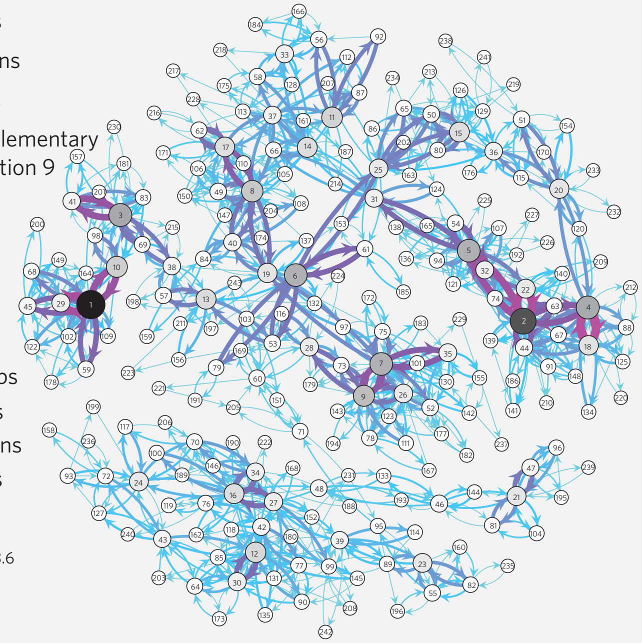
Anomalous diffusion & ageing in membranes

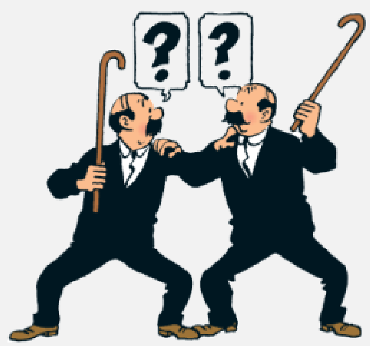
— POSTECH, 30th November 2016 —

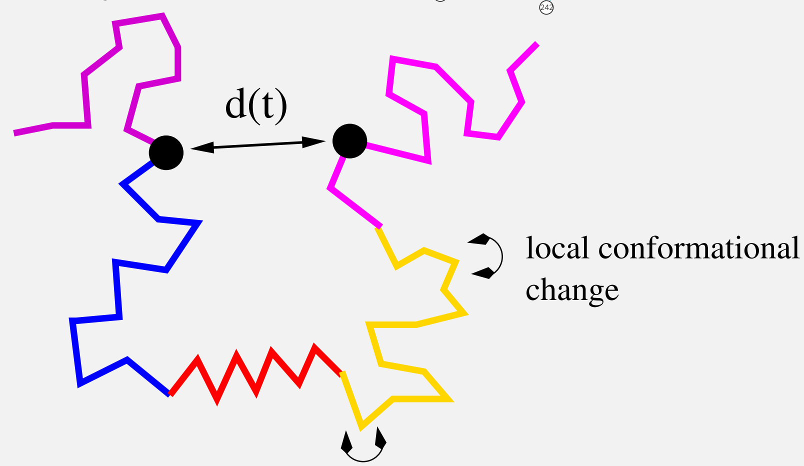


Self-similar internal dynamics: ageing over 13 decades



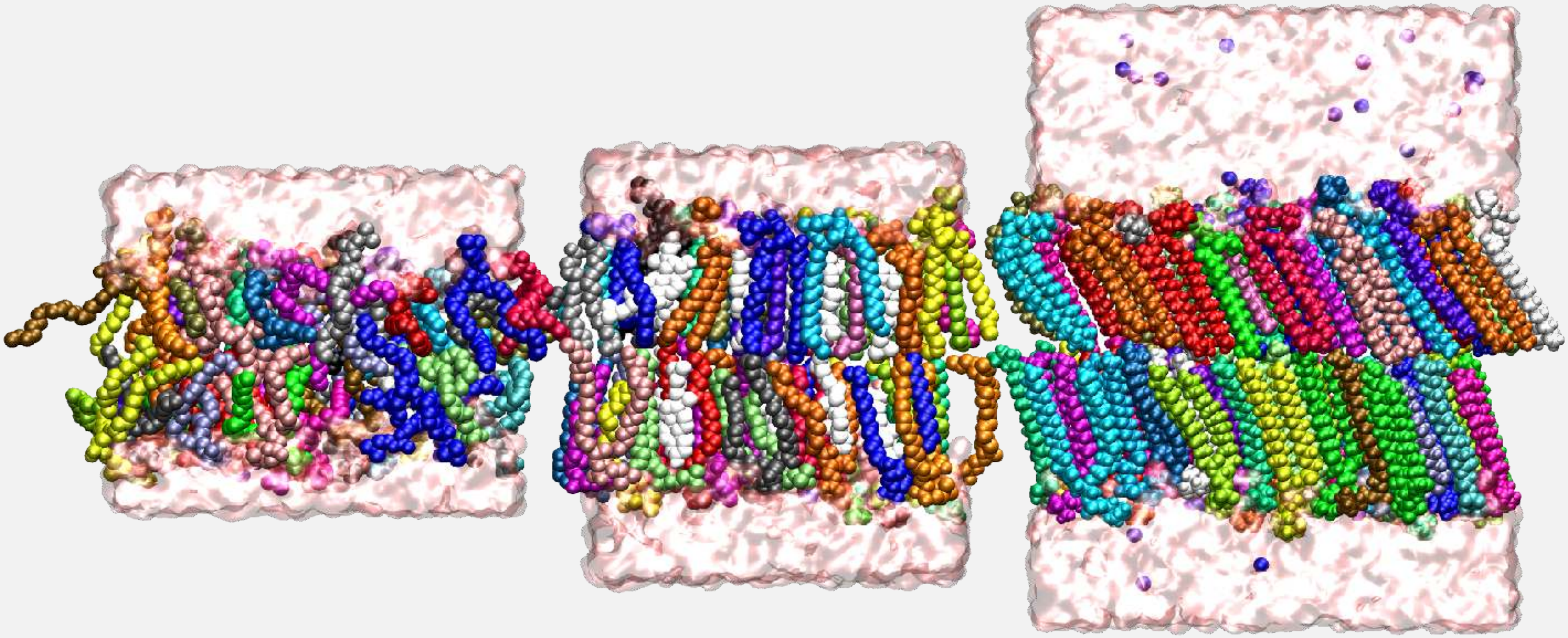






X Hu, L Hong, MD Smith, T Neusius, X Cheng & JC Smith, Nature Phys (2016); N&V RM Nature Phys (2016)

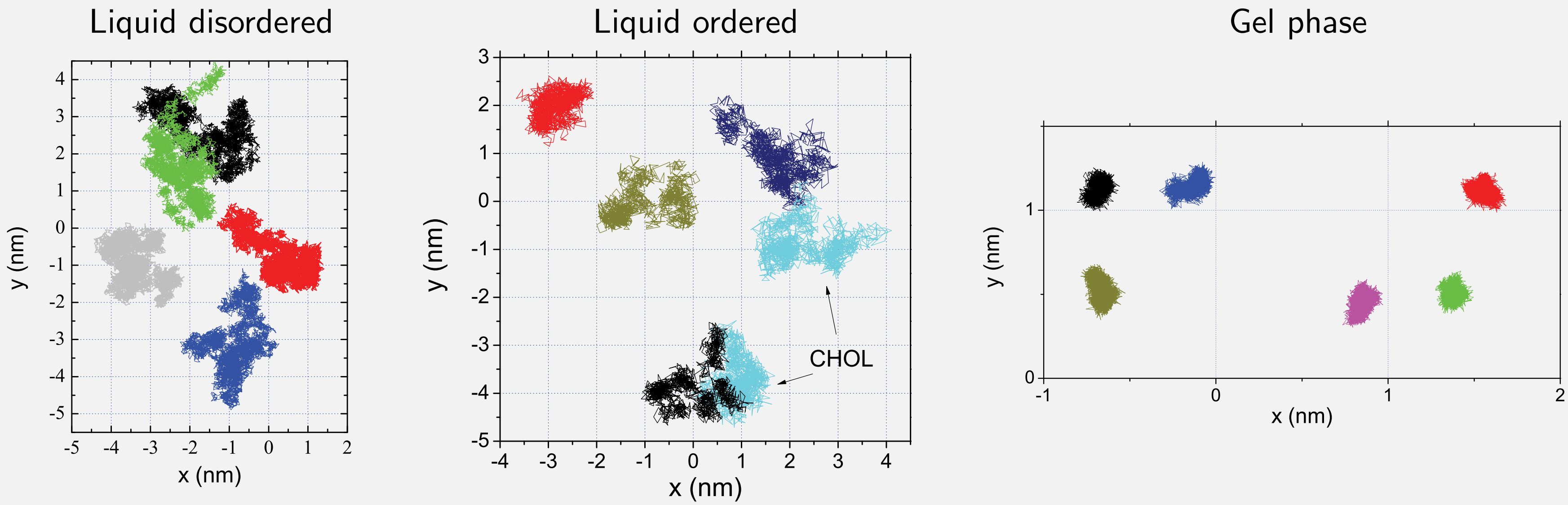
Single lipid motion in bilayer membrane MD simulations



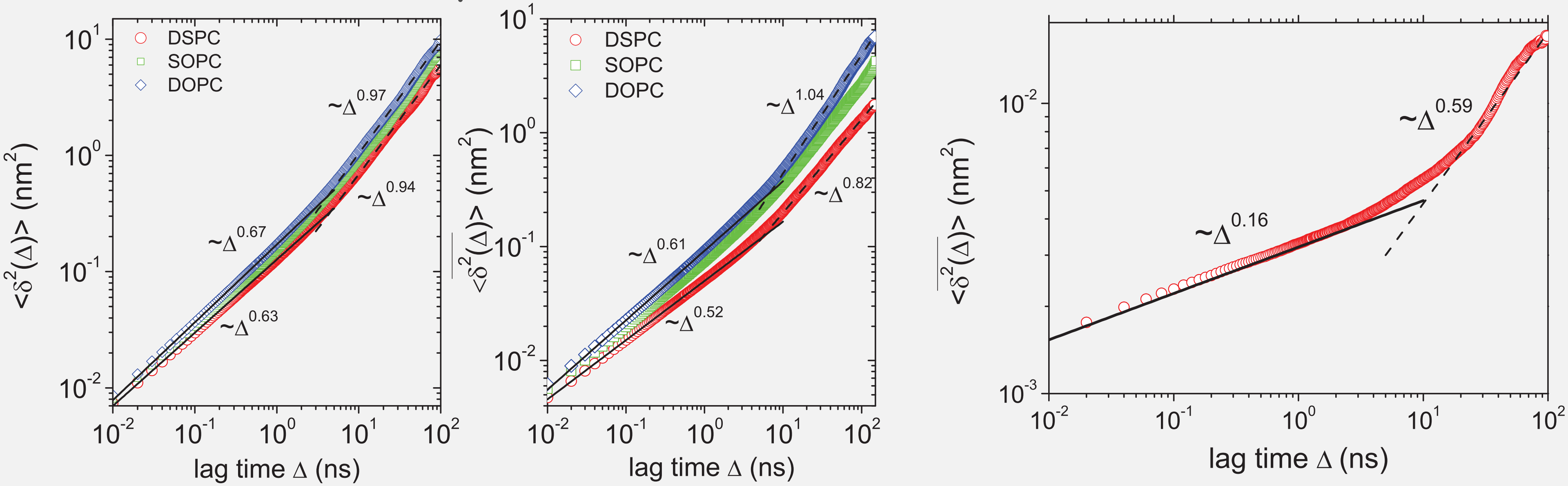
Liquid disordered   Liquid ordered   Gel phase

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

Sample trajectories for the lipid & cholesterol motion

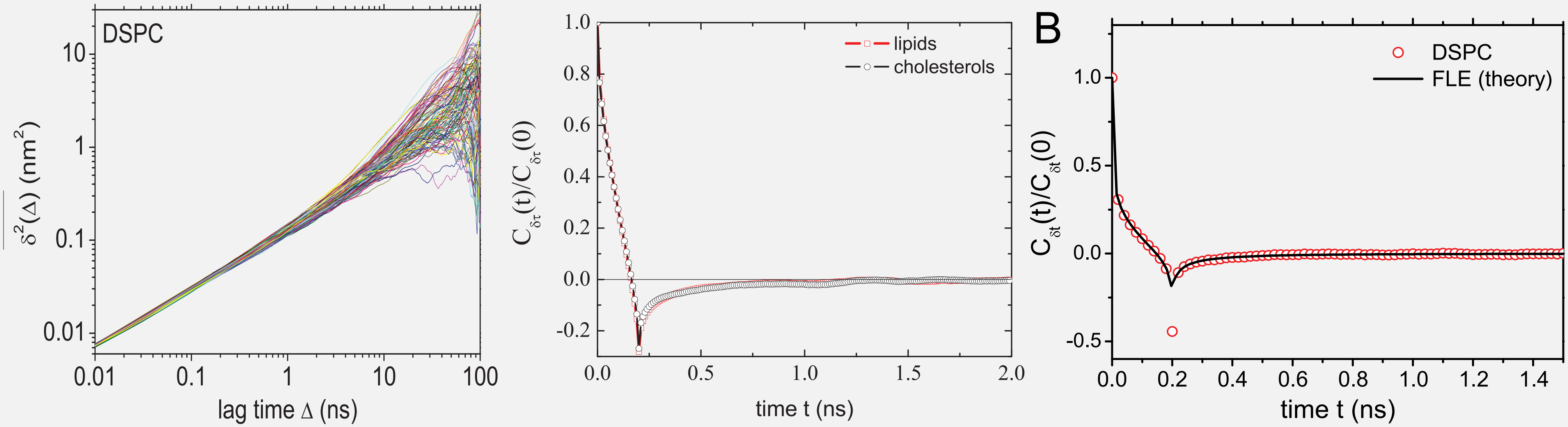


Liquid ordered/gel phases: extended anomalous diffusion

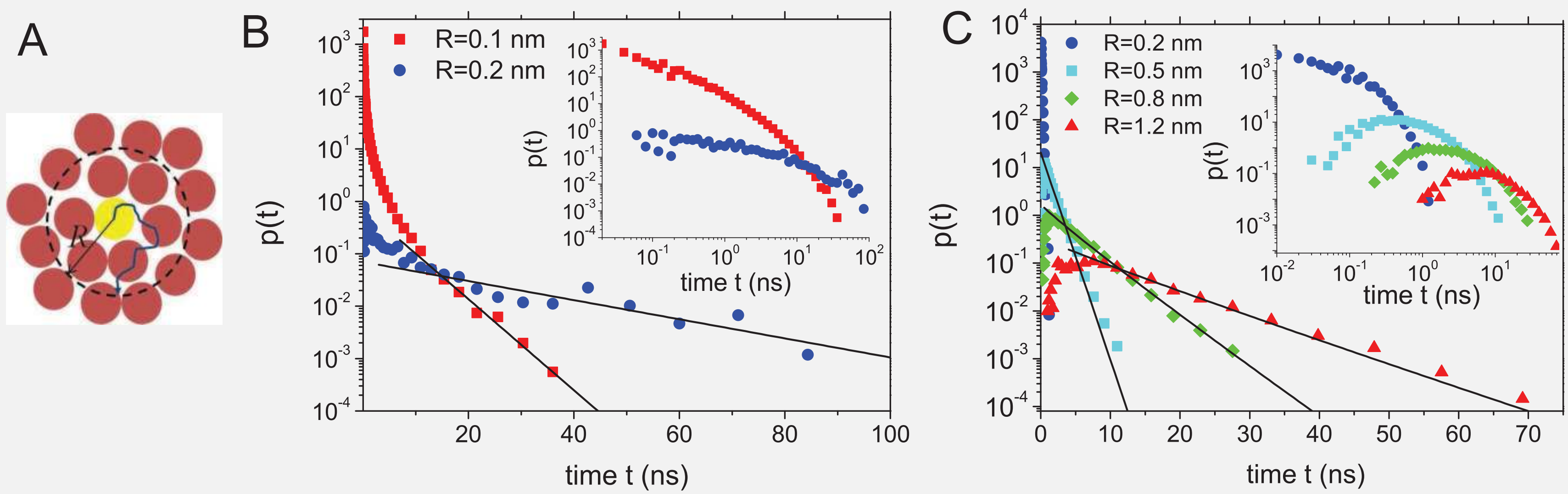


J-H Jeon, H Martinez-Seara Monne, M Javanainen & RM, PRL (2012)

Reproducible TA MSD & antipersistent correlations



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



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

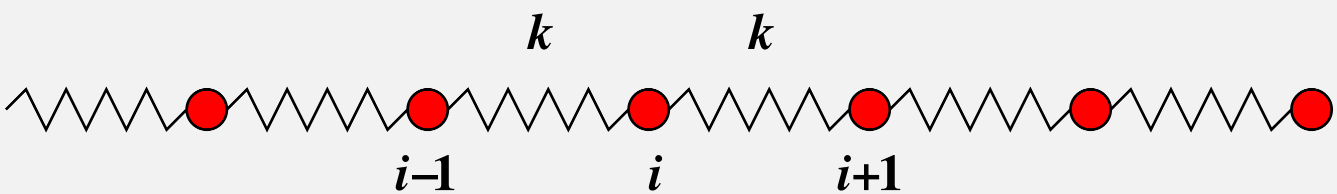
Generalised Langevin equations in viscoelastic systems

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):

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



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

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

overdamped limit: FBM

Quantum mechanics: Nakajima-Zwanzig equation using projection operators

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

Membranes can be supercrowded

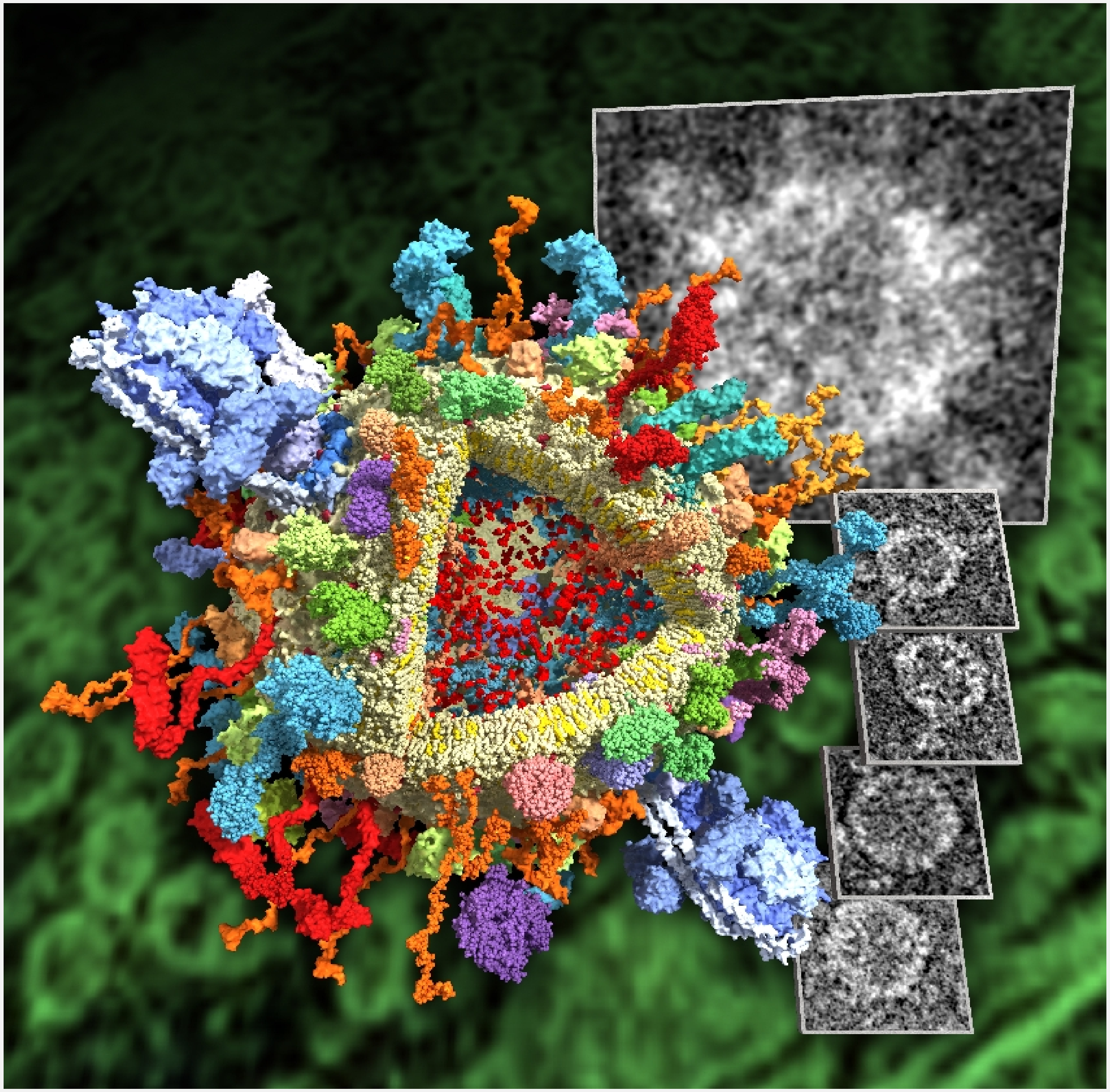
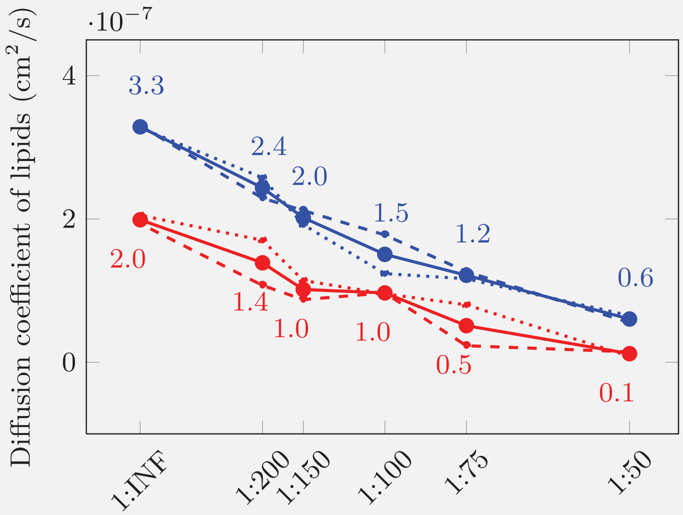
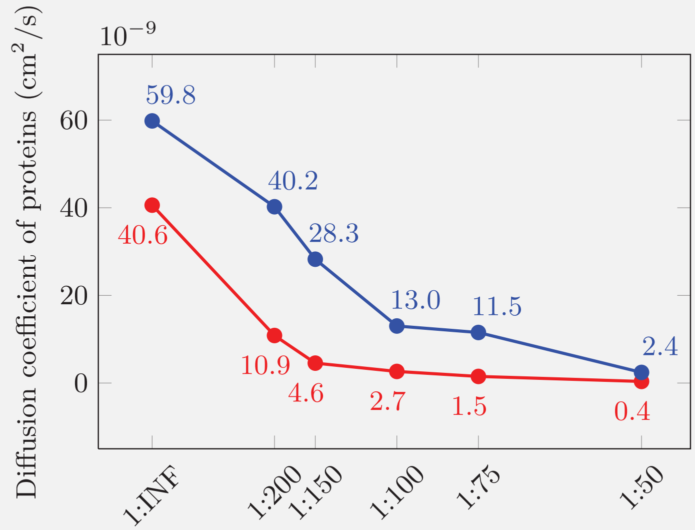


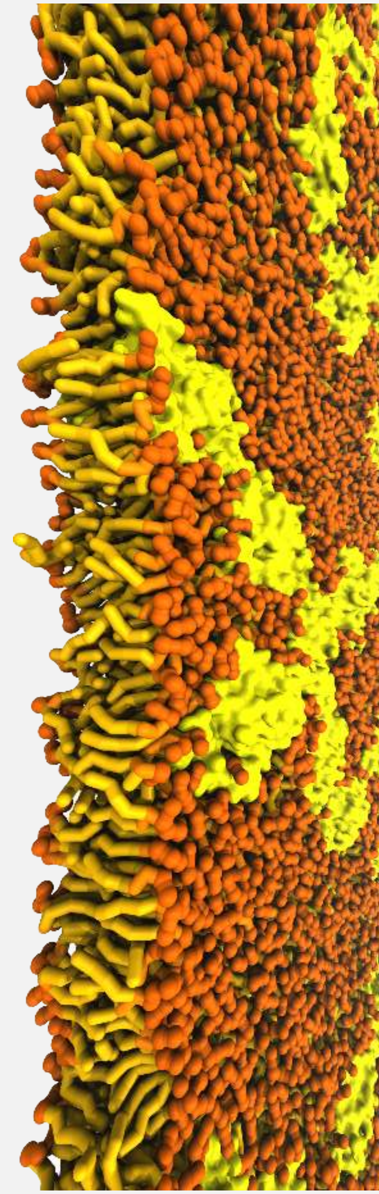
Figure courtesy Helmut Grubmüller

Protein crowded membranes reduce effective mobility

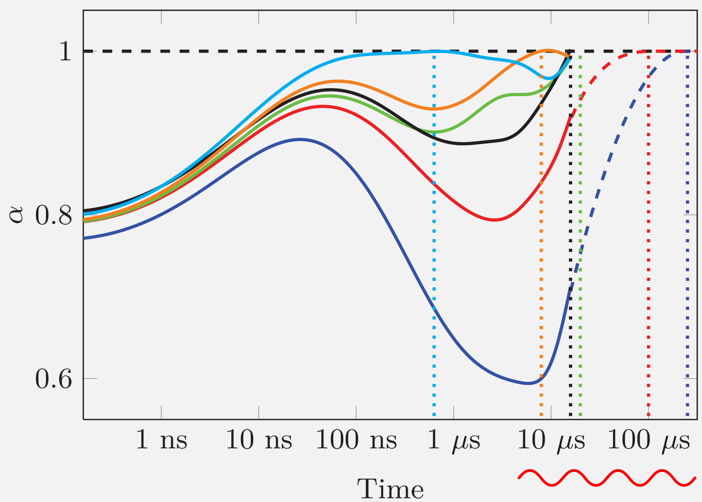


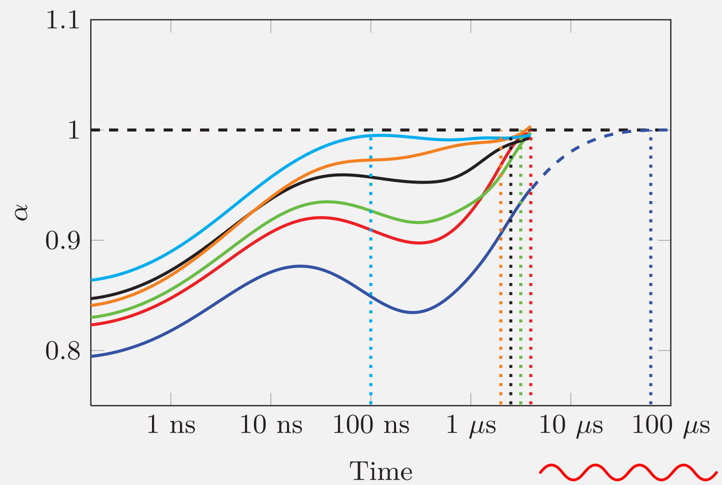


Blue: DLPC. Red: DPPC



Protein crowding effects anomalous lipid diffusion

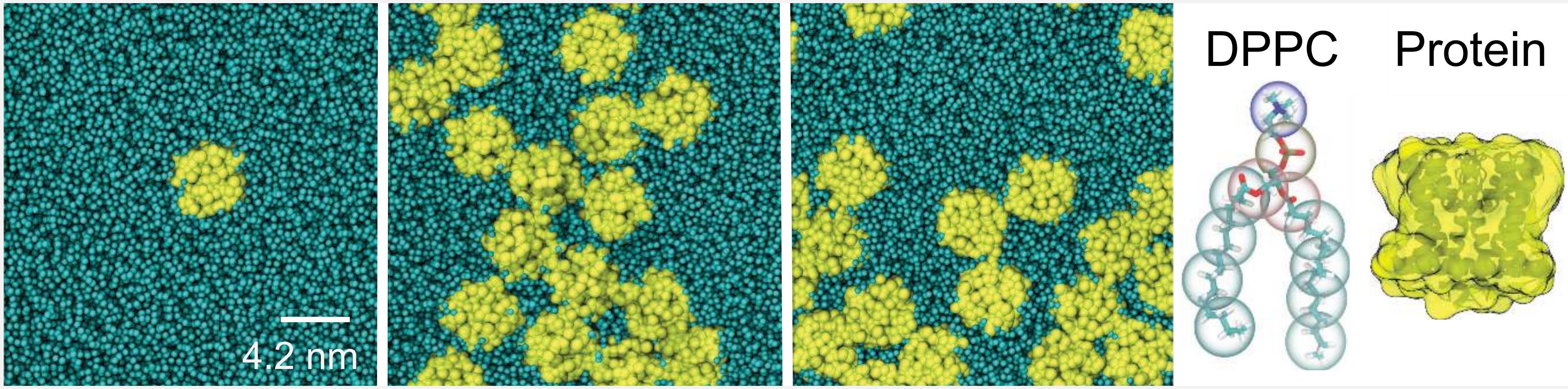


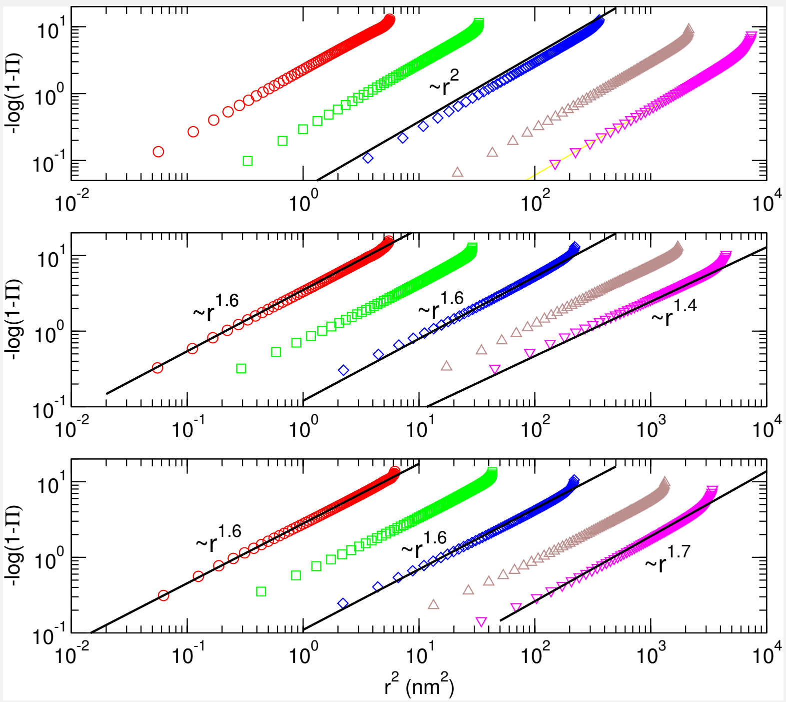


Left: DPPC (protein-aggregating) case. Right: DLPC protein non-aggregating case.

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

Crowding in membranes: non-Gaussian lipid/protein diffusion

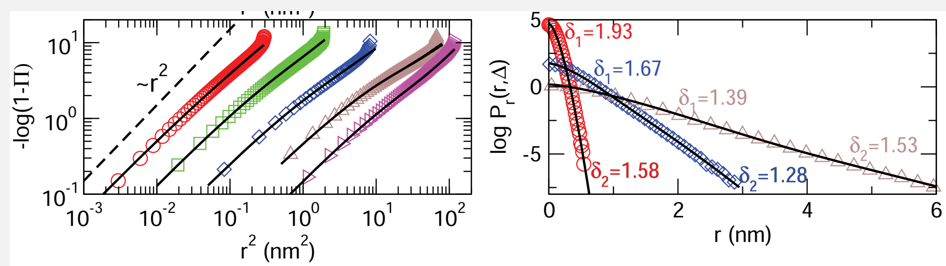




Dilute membrane: $P(r,t)$ Gauss

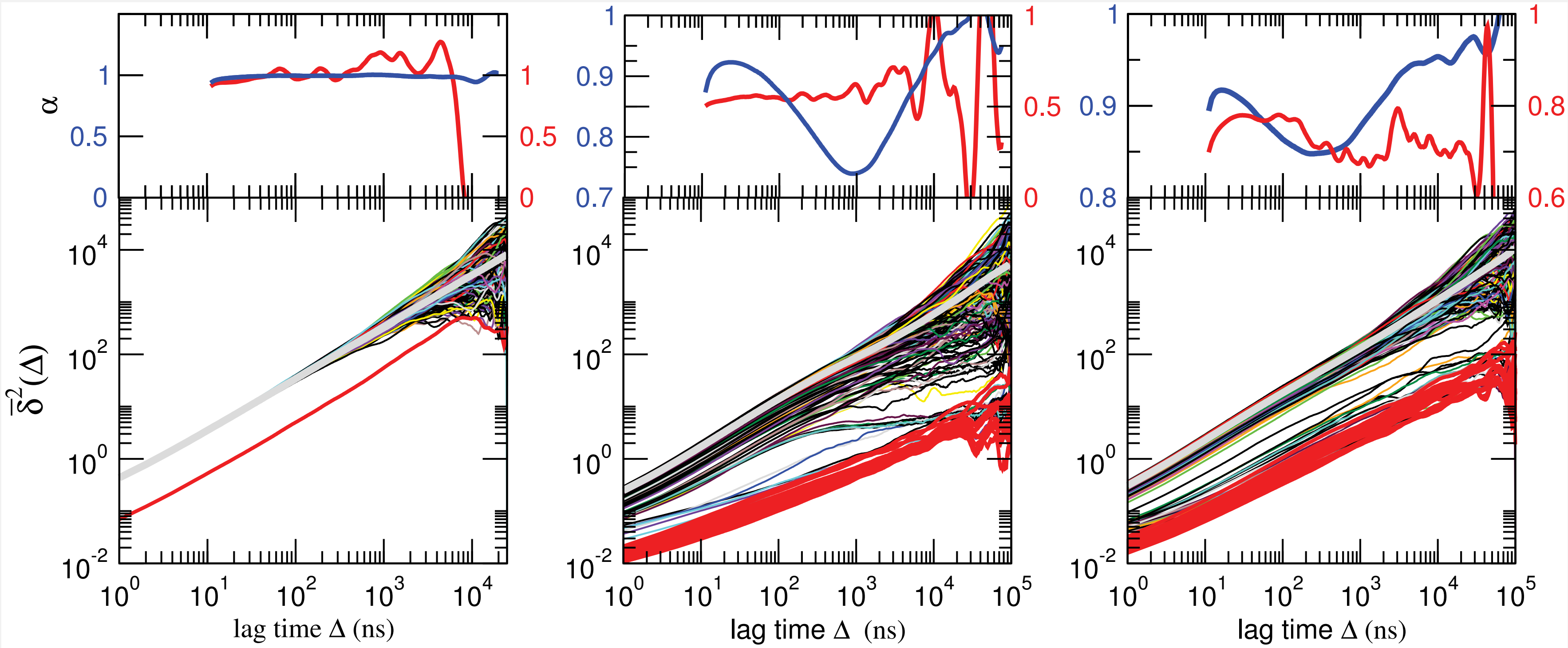
Crowded membrane ($\delta \approx 1.3 \ldots 1.7$):

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



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

Crowding in membranes increases dynamic heterogeneity

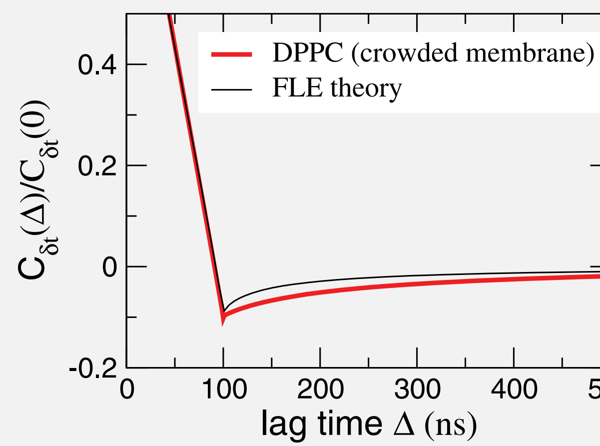


← Blue: lipids. Red: protein(s)

Single NaK channel DLPC (non-aggregating) DPPC (aggregating)

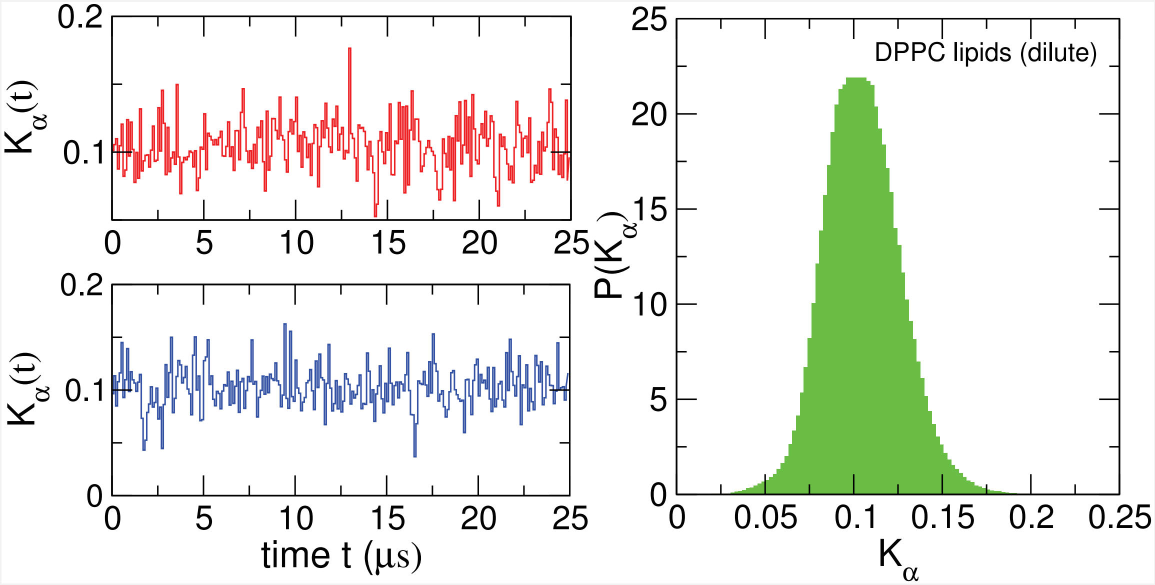
Lipids & proteins behave quite differently

Increment correlation no longer simple FBM ⟶



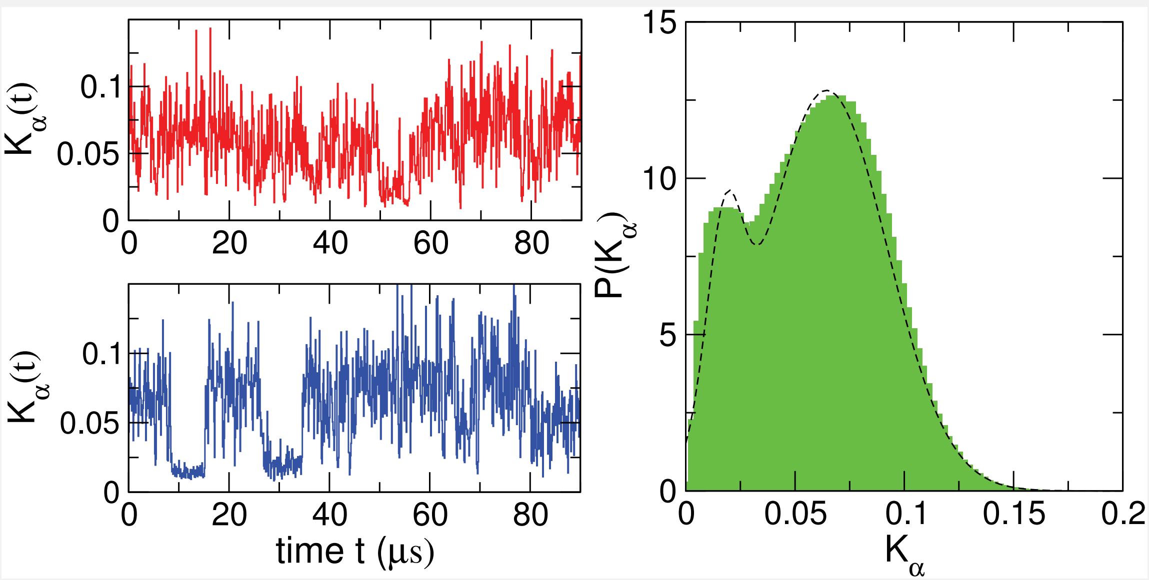
J-H Jeon, M Javanainen, H Martinez-Seara, RM & I Vattulainen, PRX (2016)

Crowding in membranes increases dynamic heterogeneity



Diffusivity(t) for two lipids

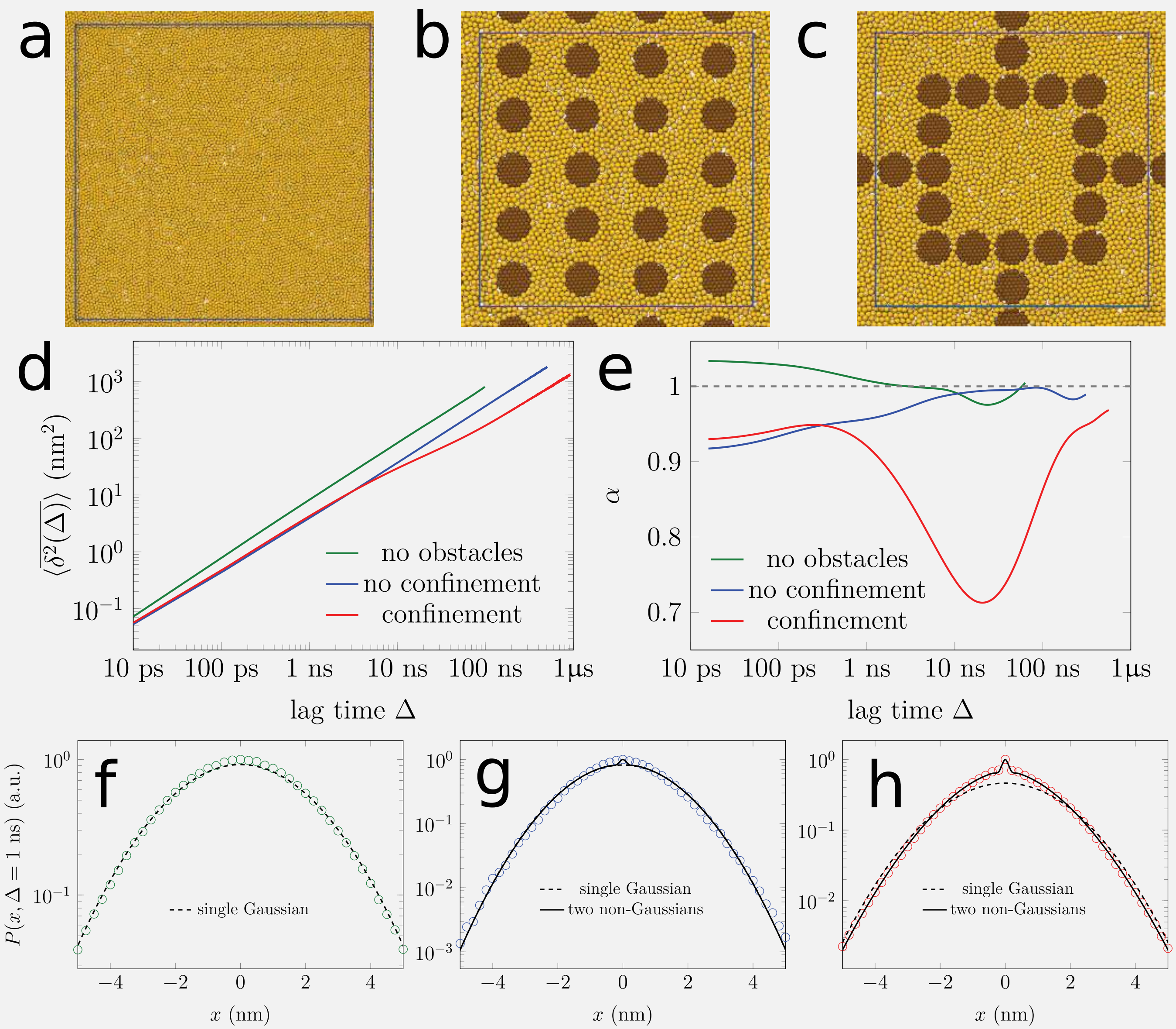
Lipid diffusivity, dilute membrane



Lipid diffusivity, crowded membrane

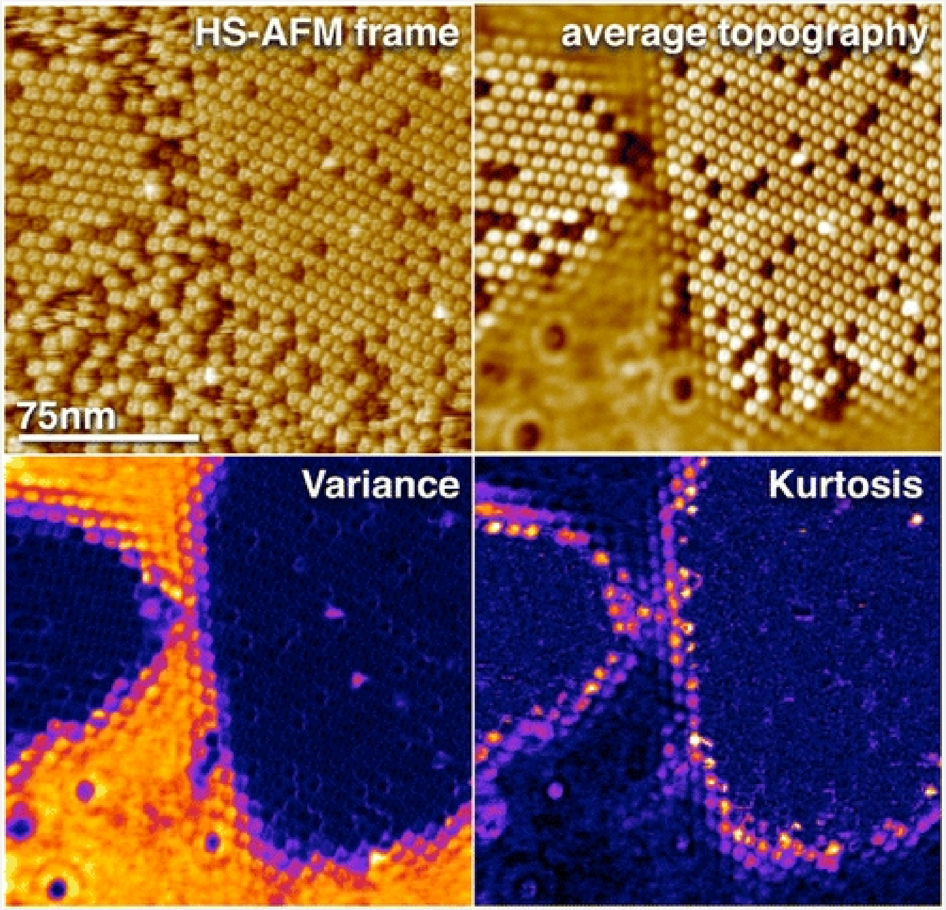
J-H Jeon, M Javanainen, H Martinez-Seara, RM & I Vattulainen, PRX (2016)

Crowding in membranes: confinement in argon system



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

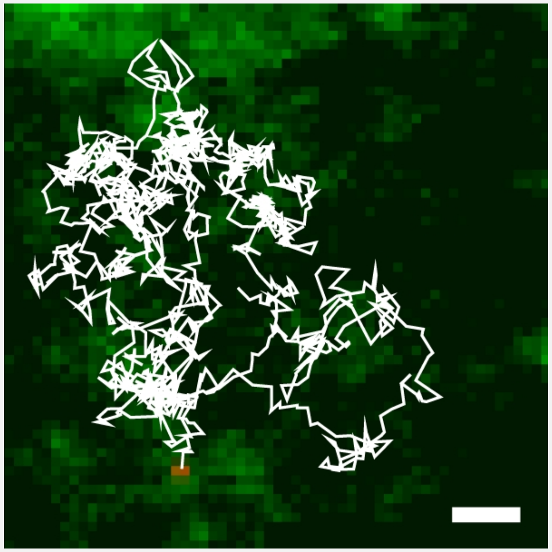
Glass-like protein diffusion in crowded membranes

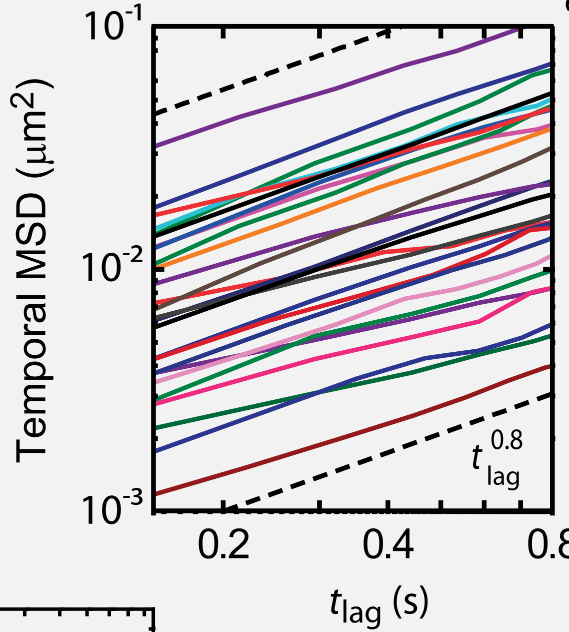


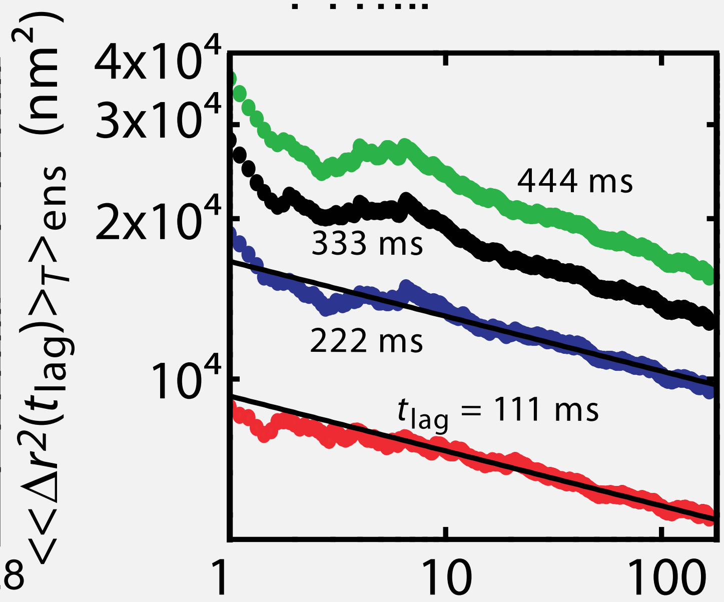
In vitro high speed AFM of supported lipid biliayers reveals trapped proteins in neighbour-formed cages for time scales up to **10 sec**. Clearly separated areas of different diffusive (in particular, non-Gaussian) diffusion.

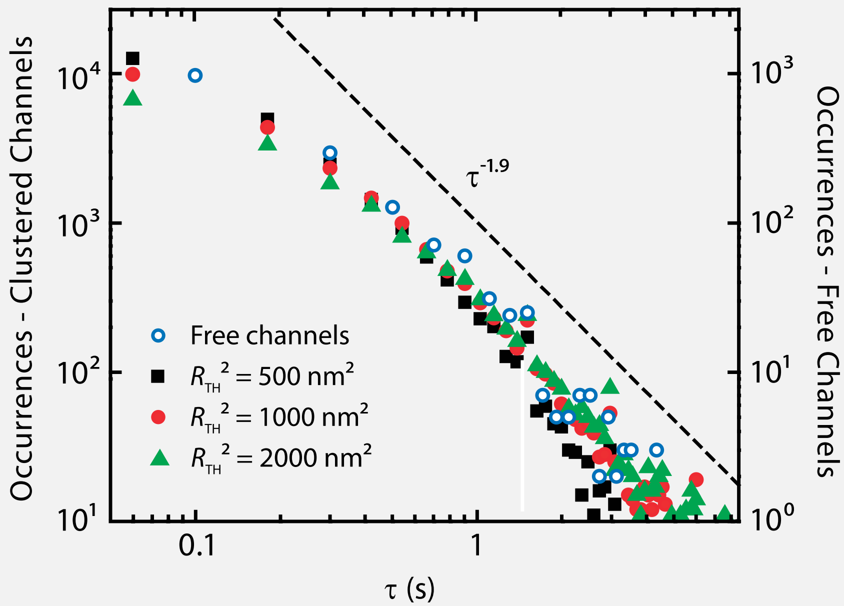
I Munguira et al, ACS Nano (2016)

CTRW-like motion of Ka channels in plasma membrane









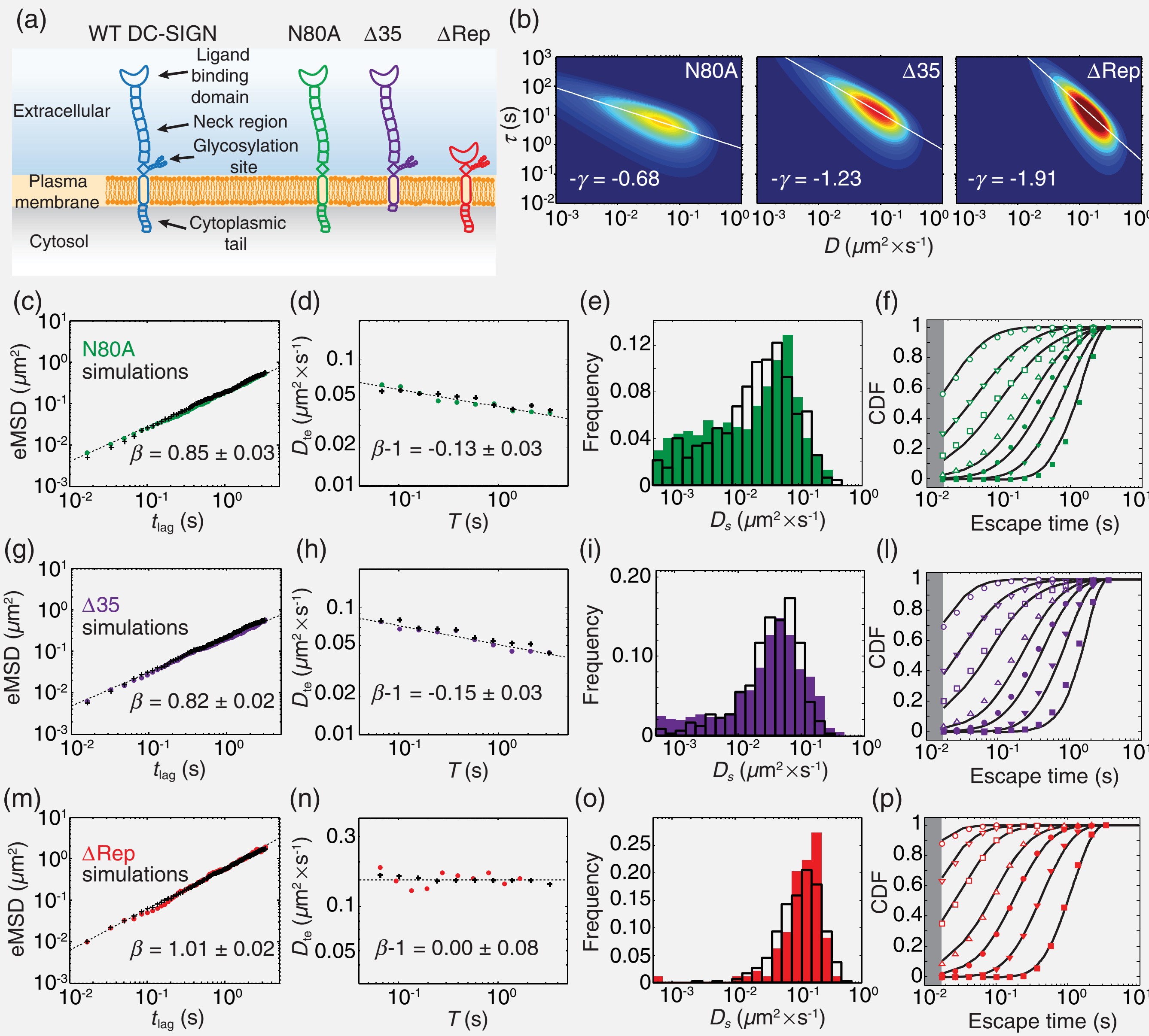
$$\psi(\tau) \simeq \tau^{-1-\alpha} \curvearrowright \langle \mathbf{r}^2(t) \rangle \simeq t^{\alpha}$$

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

$$\overline{\delta^2(\Delta)} \simeq K_\alpha \frac{\Delta}{T^{1-\alpha}}$$

AV Weigel, B Simon, MM Tamkun & D Krapf, PNAS (2011); RM, AG Cherstvy, JH Jeon & E Barkai, PCCP (2014)

Ageing in the motion of membrane embedded proteins



C Manzo et al, PRX (2015); RM, JH Jeon & AG Cherstvy, Biochim Biophys Acta (2016)

Time averaged MSD & weak ergodicity breaking (WEB)

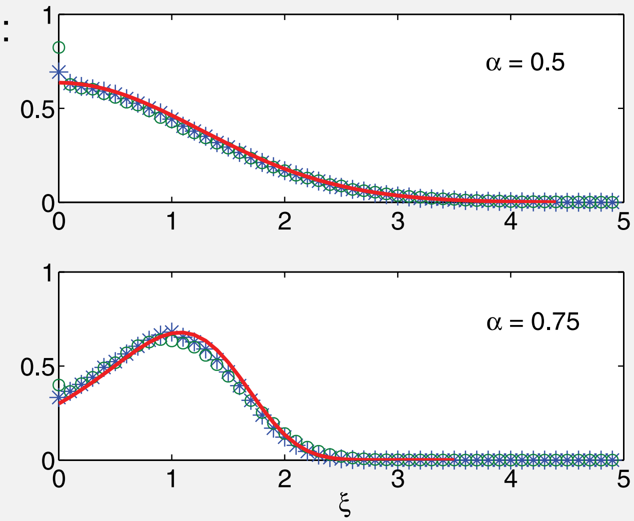
Time averaged MSD $\simeq \Delta$ is pseudo-Brownian and ageing ($\langle x^2(t)\rangle \simeq K_\alpha t^\alpha$):

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

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

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

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

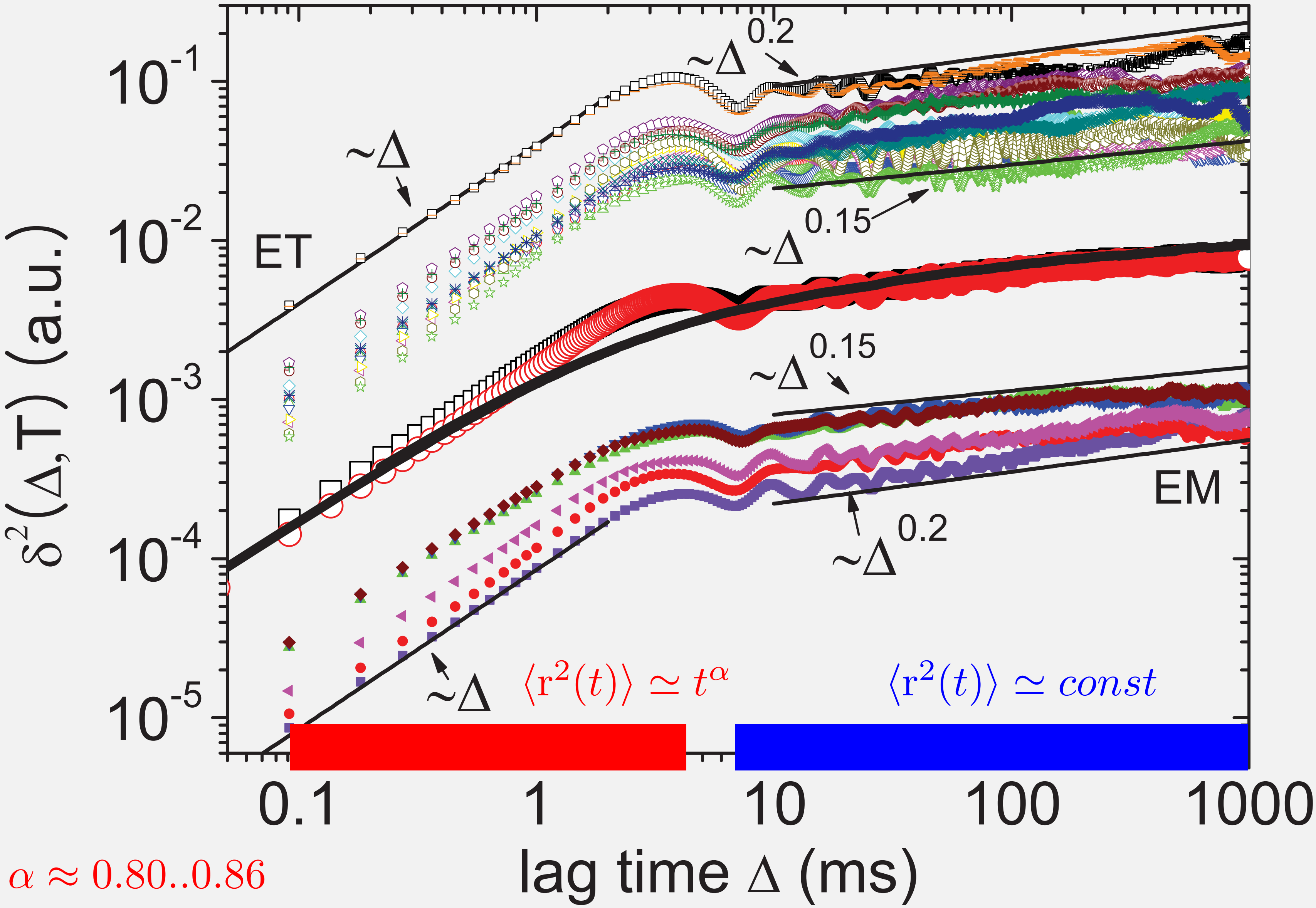


Confinement does not effect a plateau ($\langle x^2(t)\rangle \simeq \mathrm{const}(T)$):

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

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



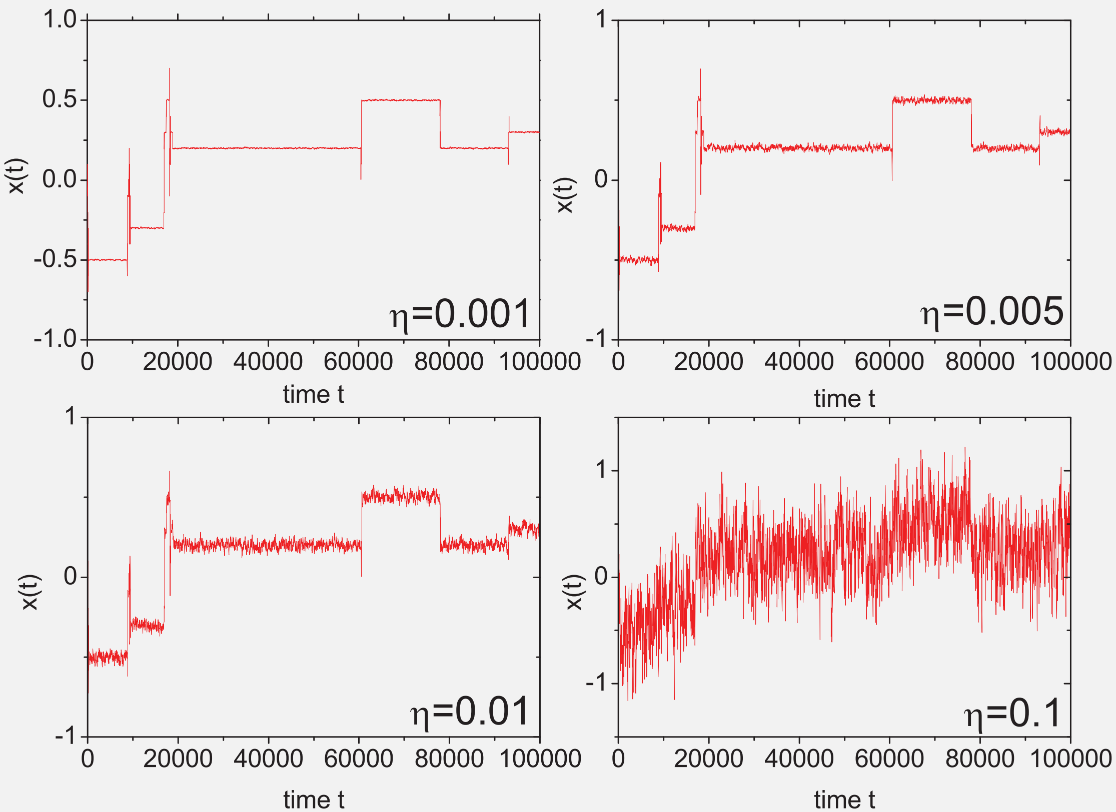
$\alpha \approx 0.80..0.86$

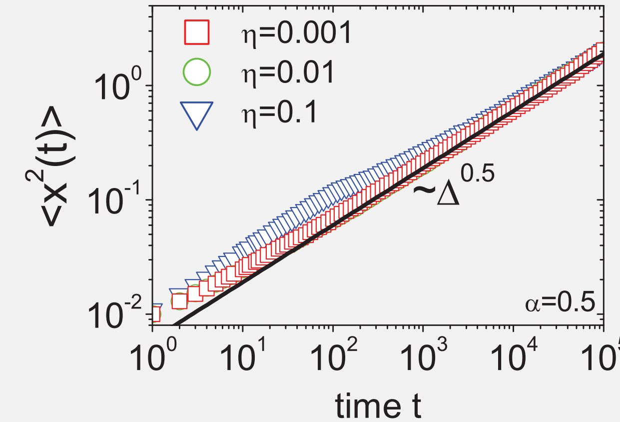
J-H Jeon, V Tejedor, S Burov, E Barkai, C Selhuber-Unkel, K Berg-Sørensen, L Oddershede & RM, PRL (2011)

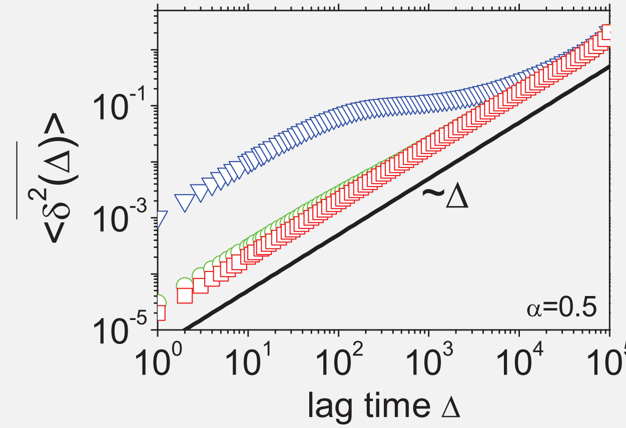
Noisy CTRW processes /w OU-noise

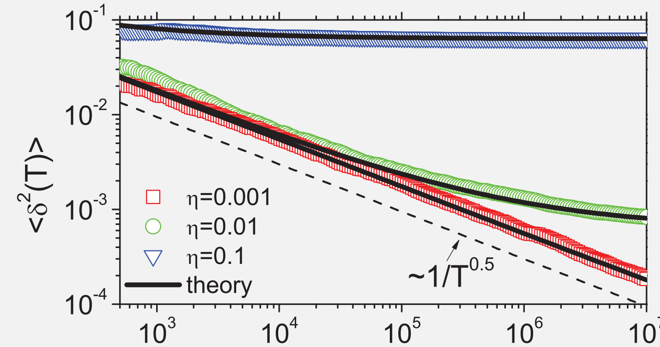
$$\langle x^2(t)\rangle = \frac{2K_\alpha}{\Gamma(1+\alpha)}t^\alpha + \frac{\eta^2 D}{k}\left(1-e^{-2kt}\right)$$

$$\left\langle\overline{\delta^2(\Delta)}\right\rangle \sim \frac{2K_\alpha}{\Gamma(1+\alpha)}\frac{\Delta}{T^{1-\alpha}} + \frac{2\eta^2 D}{k}\left(1-e^{-k\Delta}\right)$$



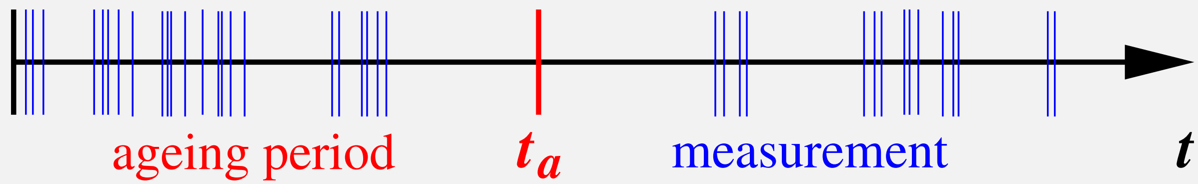






JH Jeon, E Barkai & RM, JCP (2013)

Ageing effects in single trajectory time averages

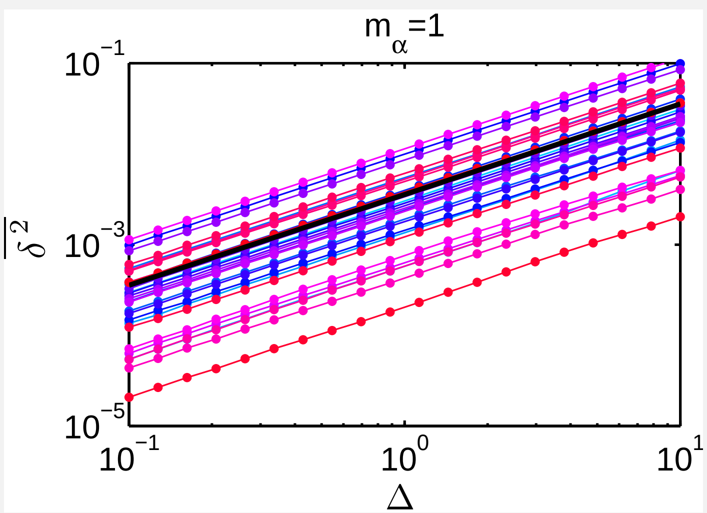


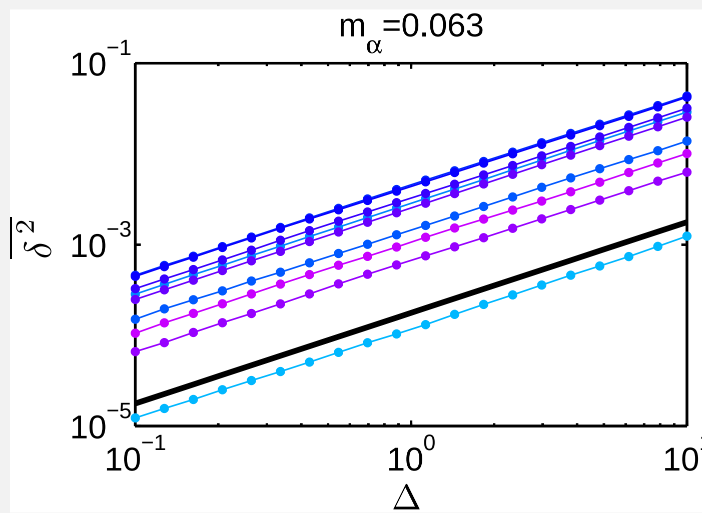
Ageing mean squared displacement ($\Lambda(z) = (1+z)^\alpha - z^\alpha$)

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

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

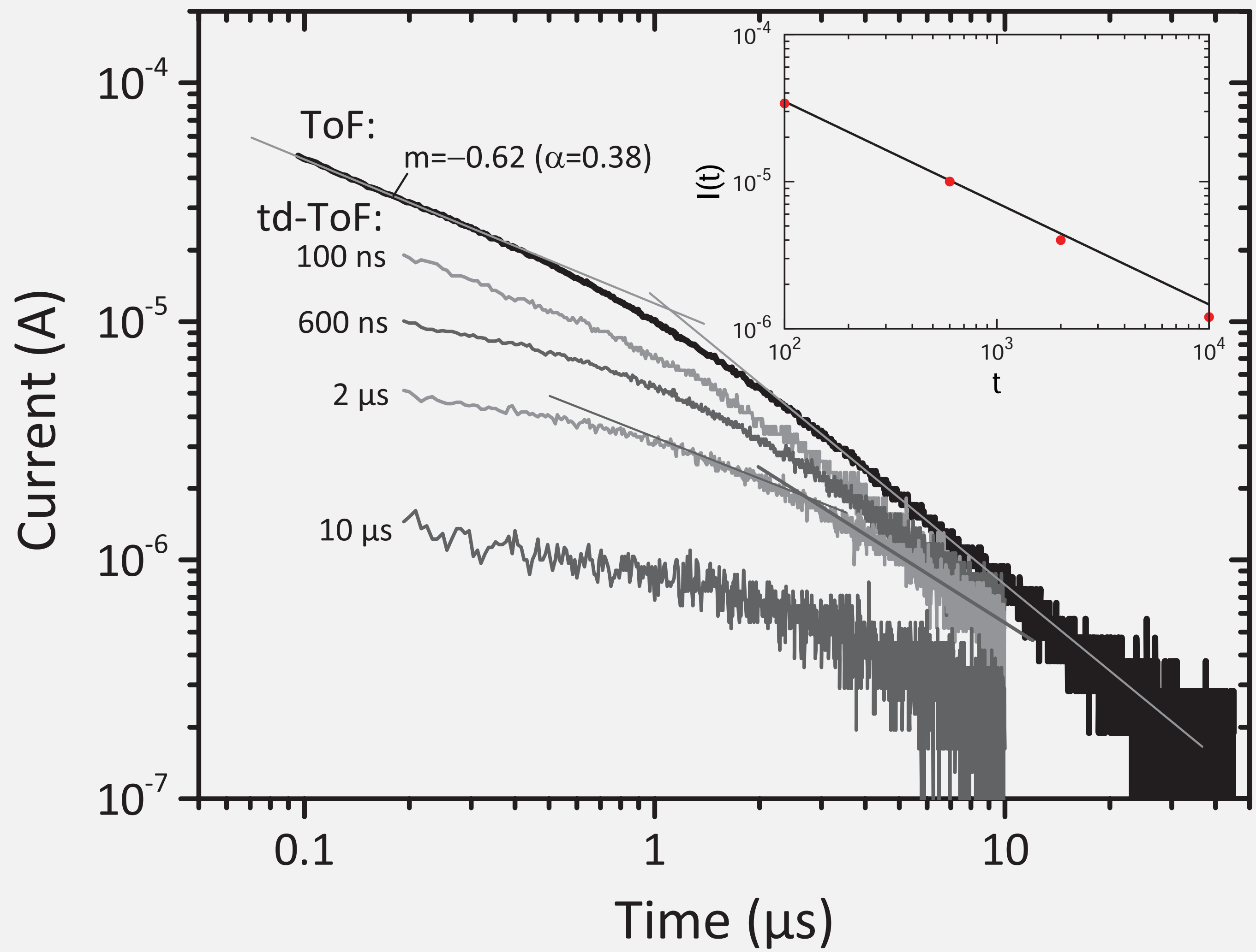
$$m_\alpha(T/t_a) \simeq (T/t_a)^{1-\alpha}, \quad T \ll t_a$$





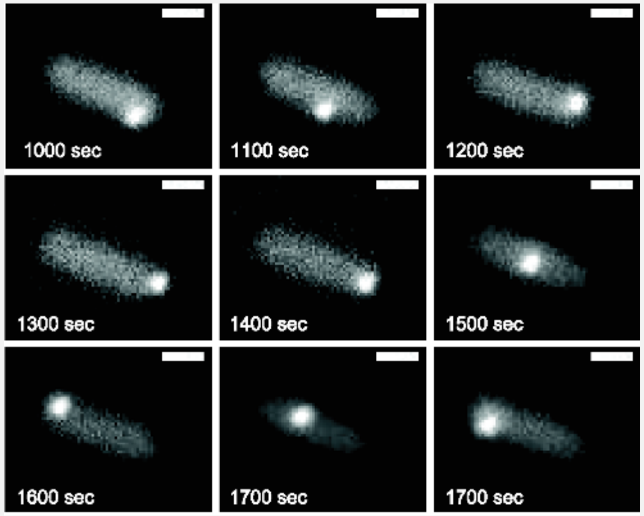
J Schulz, E Barkai & RM, PRL (2013), PRX (2014)

Ageing charge carrier motion in polymeric semiconductors

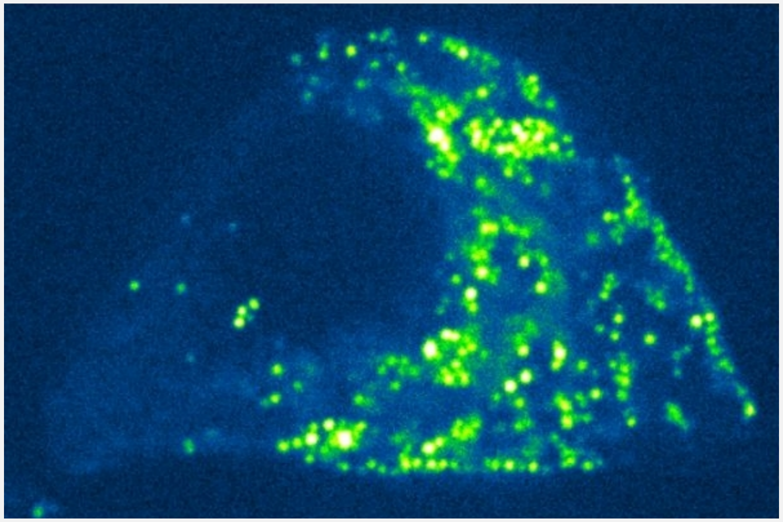


M Schubert, . . . & D Neher, Phys Rev B (2013); H Krüsemann, A Godec & RM, PRE (2014), JPA (2015), TiPM (2016)

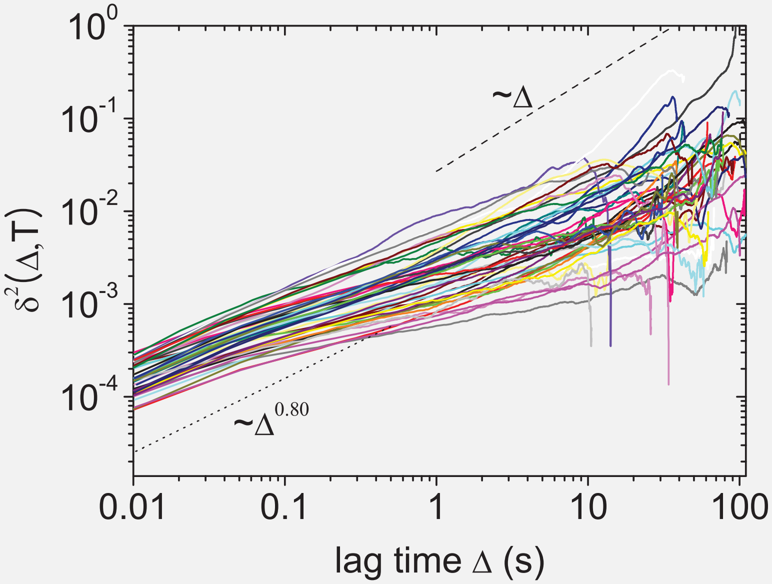
In vivo anomalous diffusion of submicron tracers



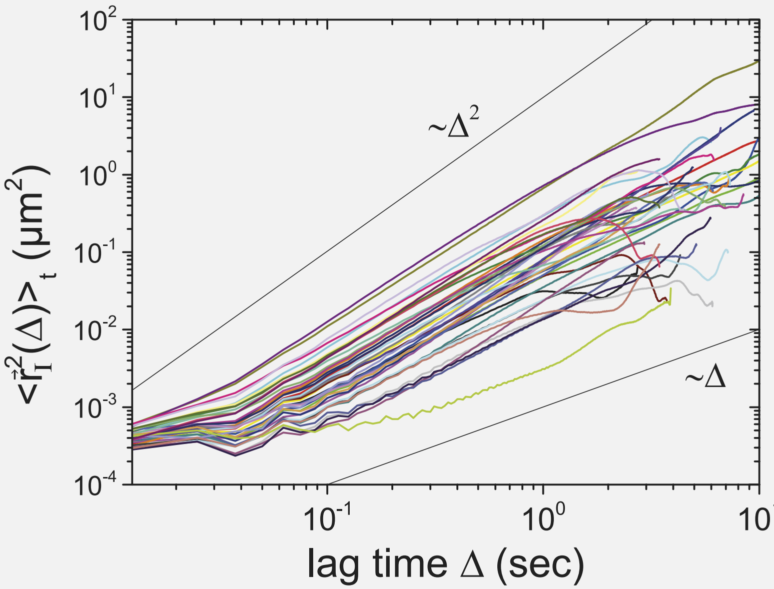
I Golding & EC Cox, PRL (2006)



SMA Tabei et al, PNAS (2013)

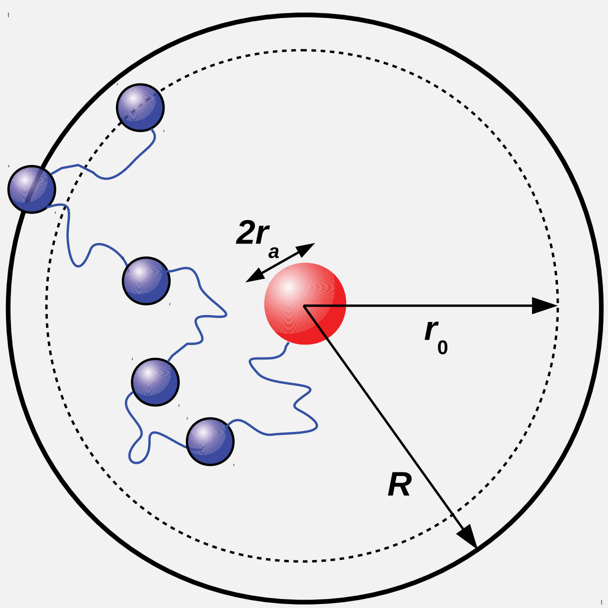


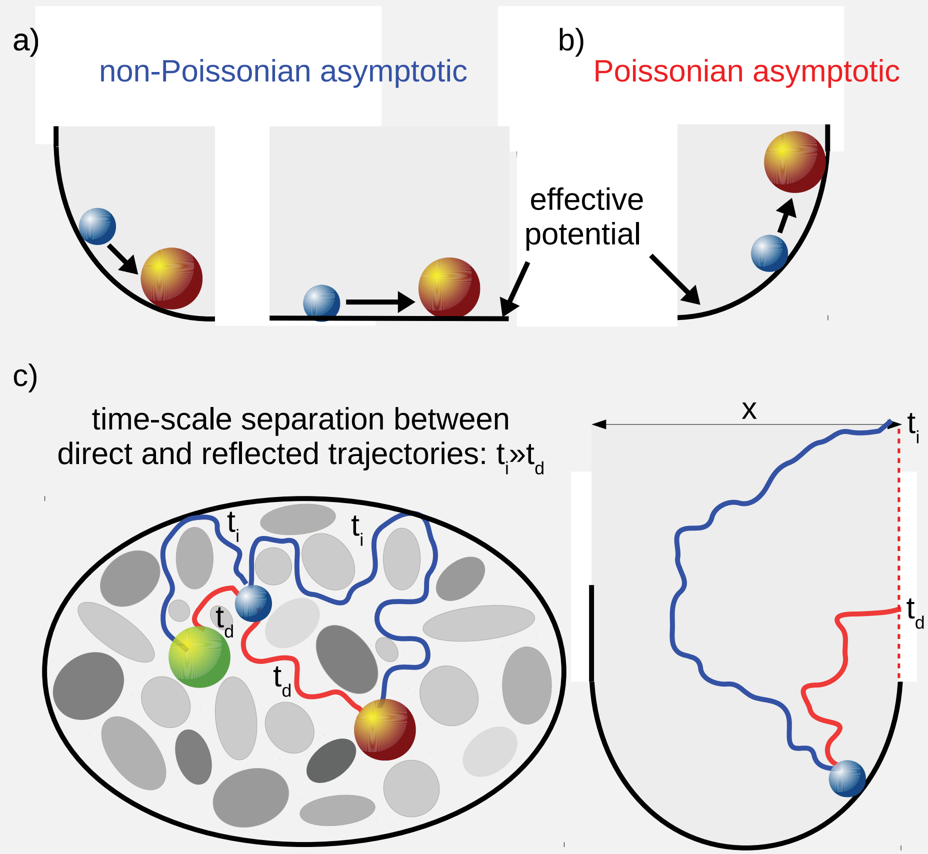
JH Jeon, . . . LB Oddershede & RM, PRL (2011)



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

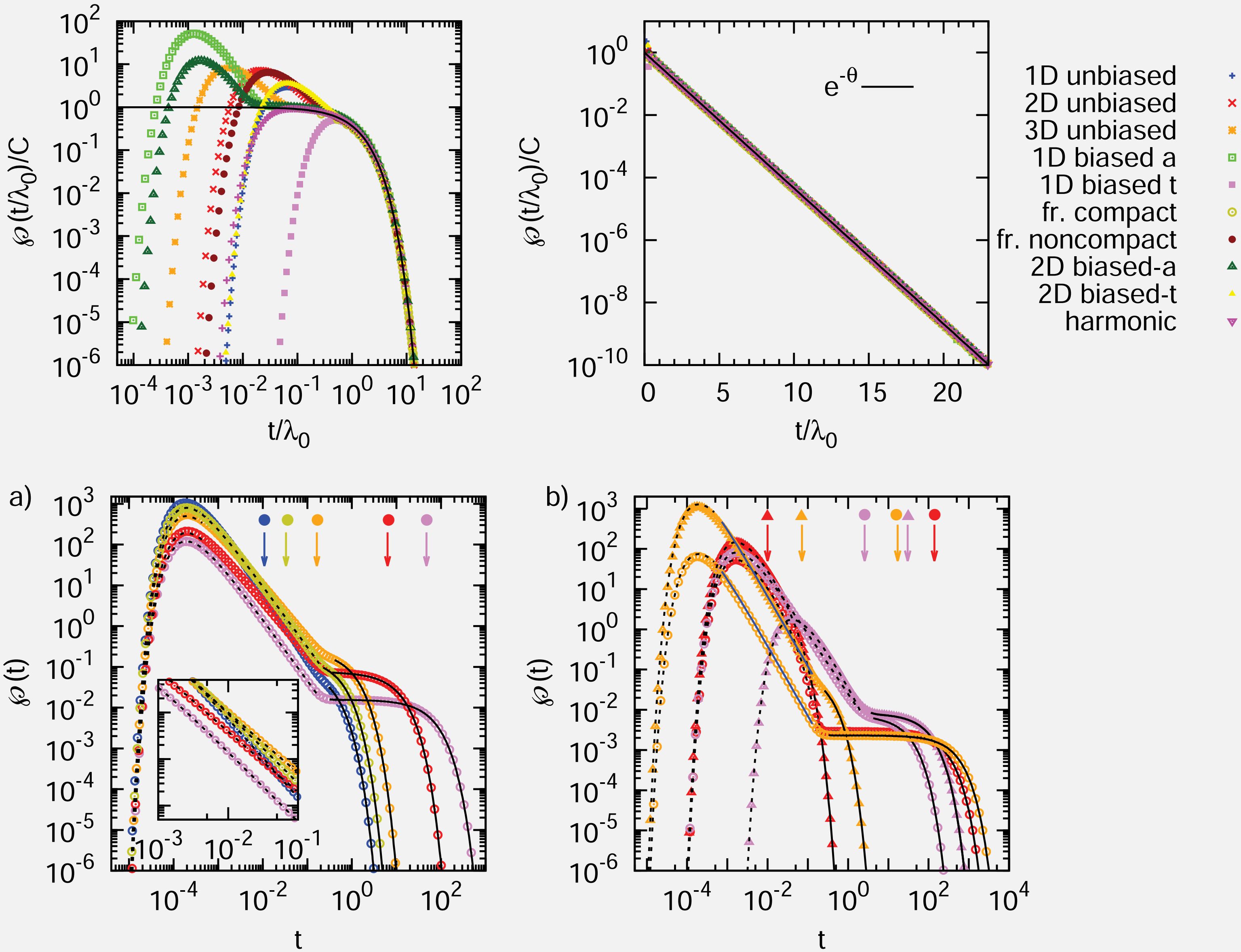
Universal proximity effect in few encounter limit





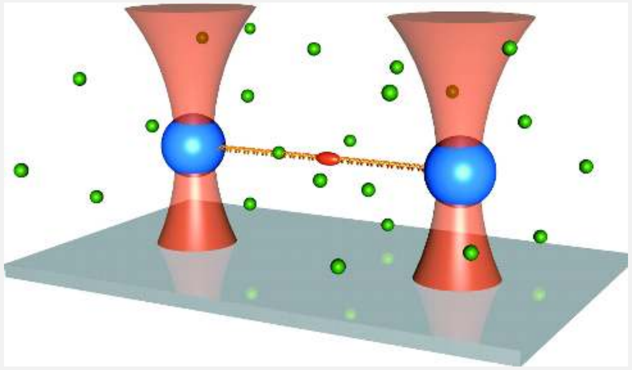
direct trajectories are typical, indirect ones are strongly dissimilar

Universal proximity effect in few encounter limit



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

Spatiotemporal gene regulation by diffusing regulatory proteins

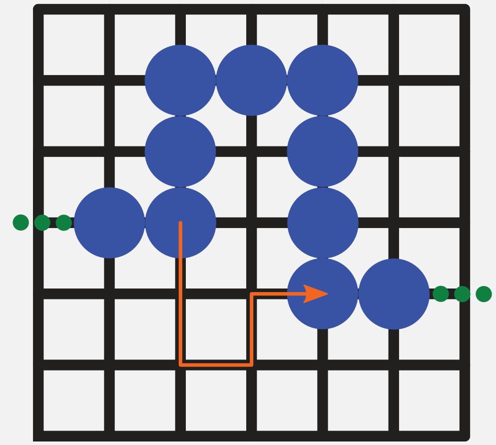


⟵ **DNA conformations**

B van den Broek, S-M Kalisch, MA Lomholt, RM & GJL Wuite, PNAS (2008)

MA Lomholt, B van den Broek, S-M Kalisch, GJL Wuite & RM, PNAS (2009)

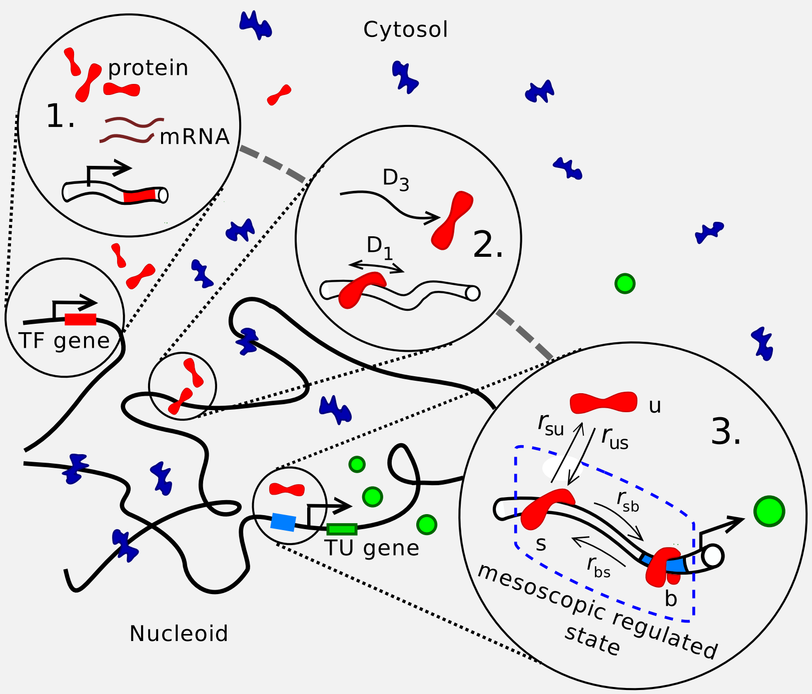
In vivo facilitated diffusion ⟶



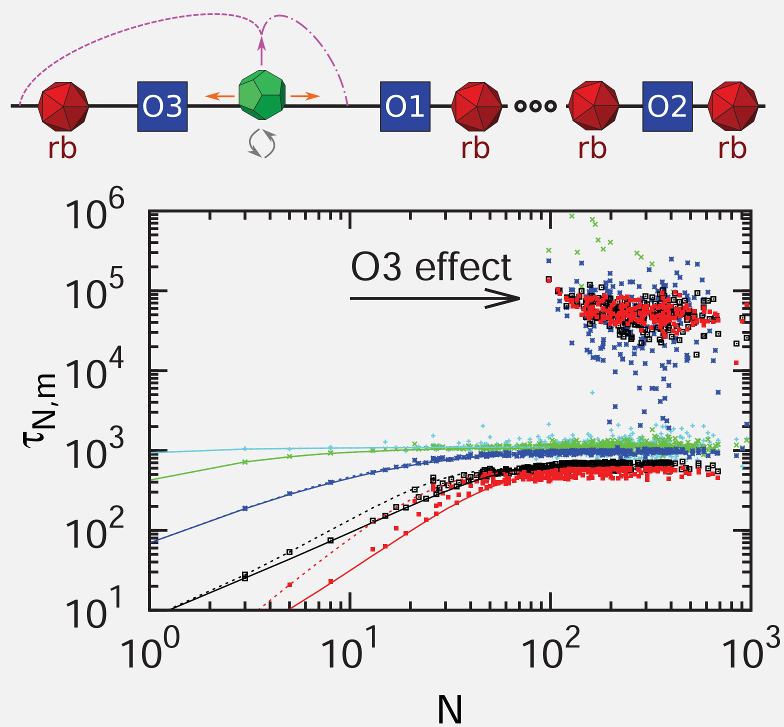
M Bauer & RM, PLoS ONE (2013)

Gene-gene talk: distance matters

O Pulkkinen & RM, PRL (2013)



Real sequence effects



M Bauer & RM, Sci Rep (2015)

$\sum$ummary

I Transient anomalous diffusion in lipid bilayers:
FBM-type motion

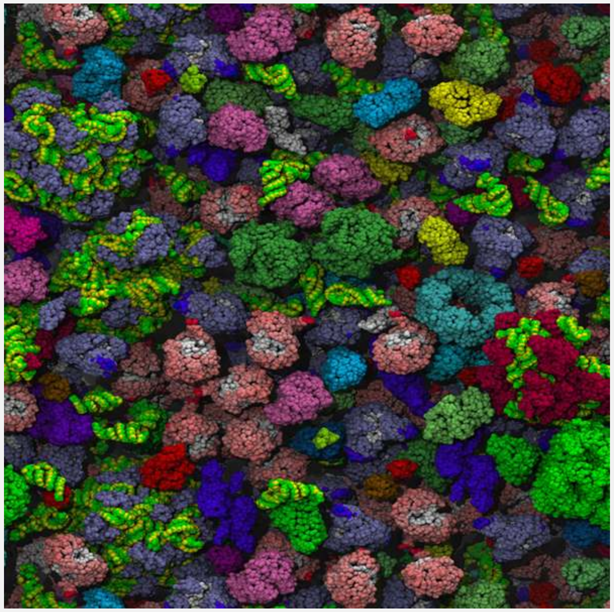
II Disorder increases anomalies: cholesterol
Also anomaly persistence in gel phase

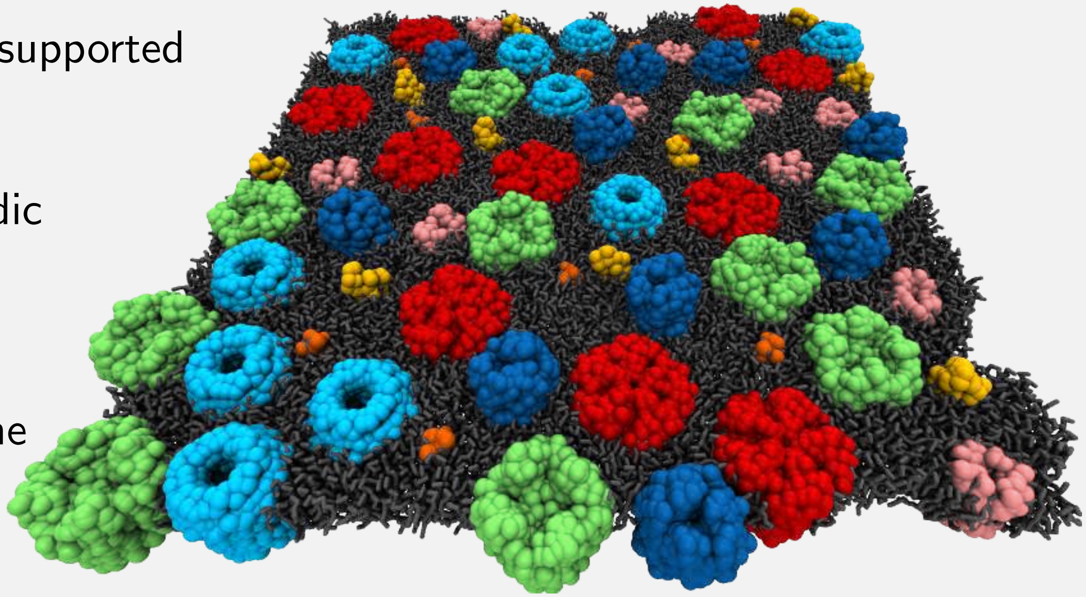
III Non-Gaussian, heterogeneous diffusion in crowded bilayers
Features qualitatively reproduced in confined argon

IIII Glass-like dynamics in crowded in vitro supported
lipid bilayers

卌 CTRW-like, ageing & weakly non-ergodic
diffusion of protein channels in
plasma membranes

卌I To analyse data you need to know some
of the tricks: RM & al, PCCP (2014)





E Barkai, Y Garini & RM, Phys Today (2012); RM, JH Jeon & AG Cherstvy, BBA Biomembranes (2016)

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