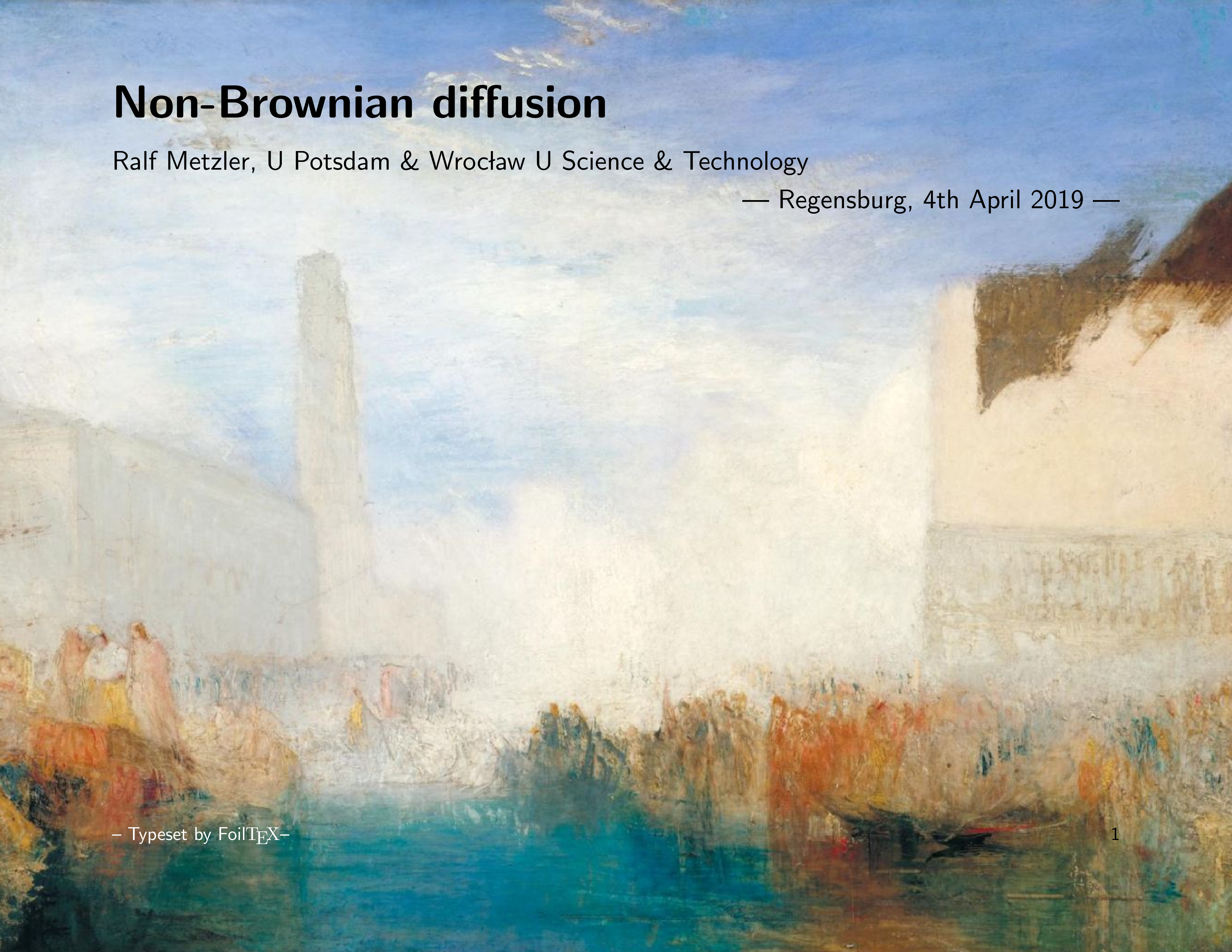
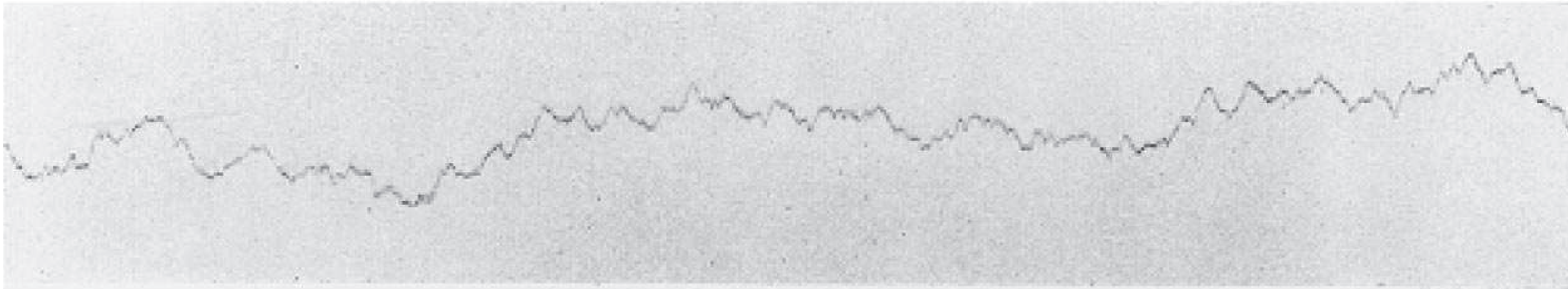


Non-Brownian diffusion

Ralf Metzler, U Potsdam & Wrocław U Science & Technology

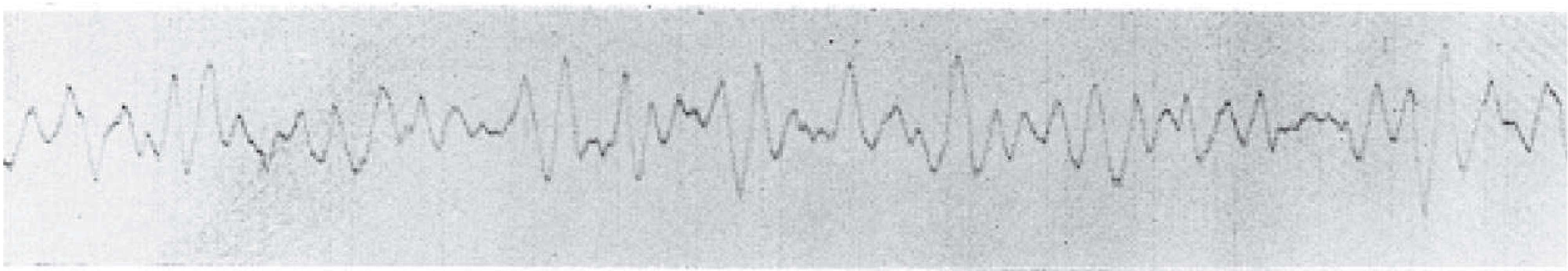
— Regensburg, 4th April 2019 —

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

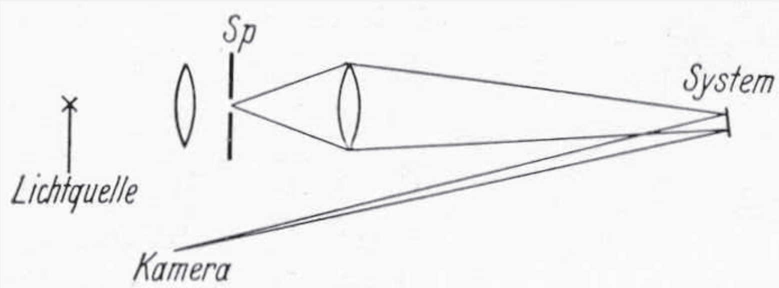


Registrieraufnahme der Brownschen Bewegung (natürliche Größe).
Direktionskraft $9{,}428 \cdot 10^{-9}$ abs. Einh. Trägheitsmoment $1 \cdot 10^{-7}$ abs. Einh. Abstand Spiegel–Kamera: 72,1 cm.
Zeitmarke: 30 sec $dx = 1$ mm. b) $1 \cdot 10^{-3}$ mm Hg. Temperatur 13° C

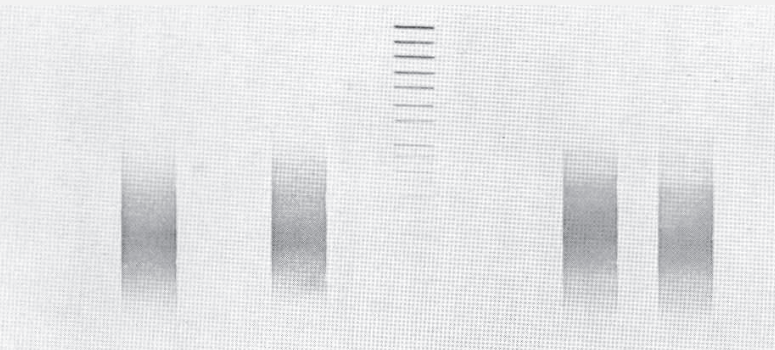
Fig. 5b

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

Kappler's diffusion measurements: mapping Boltzmann

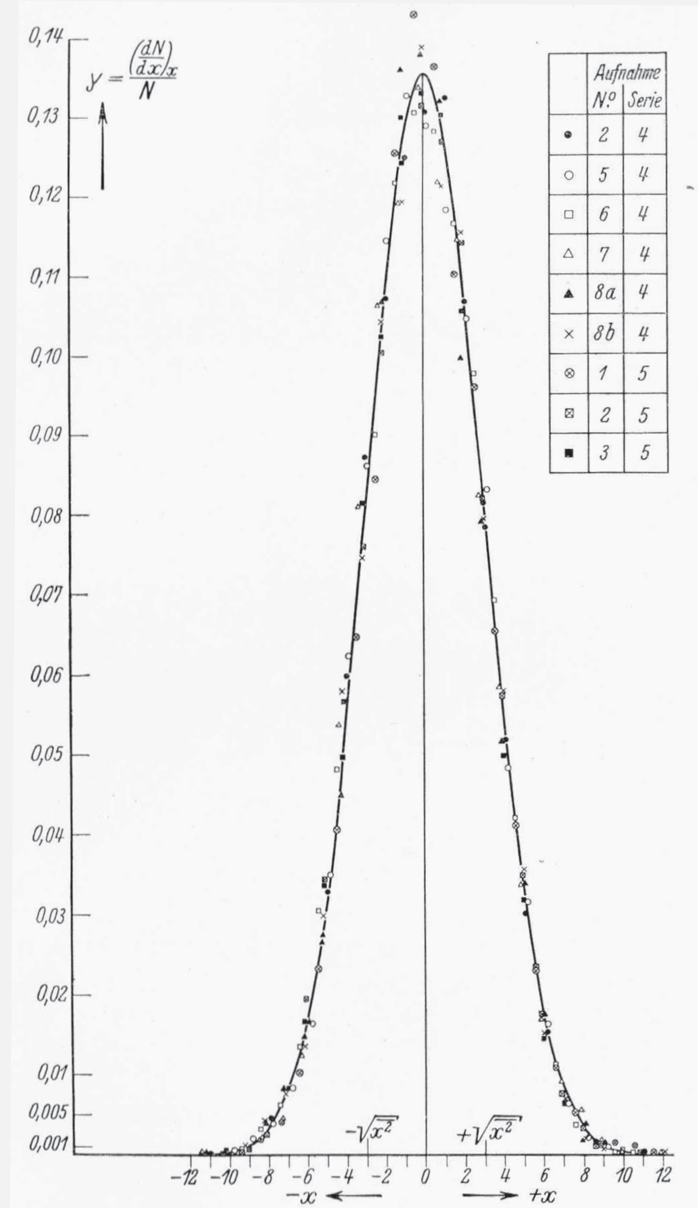


Schema der Meßanordnung
Fig. 1



Distribution @ fixed photographic plate

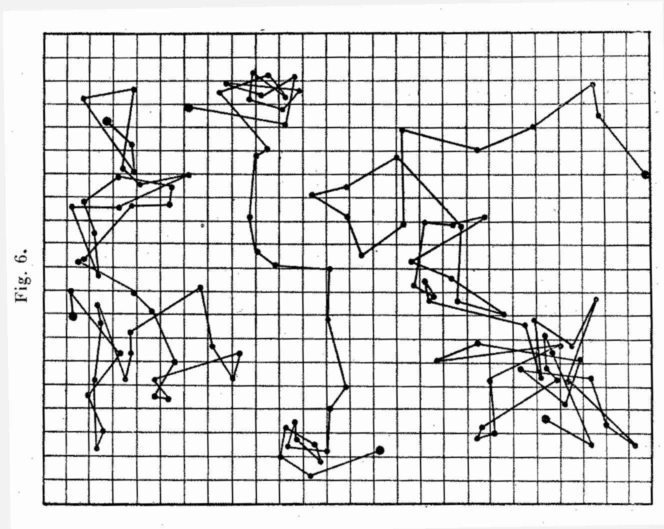
$$P_{\mathrm{eq}}(x) = \mathscr{N} \exp\left(-\frac{\theta x^2}{k_B T}\right)$$

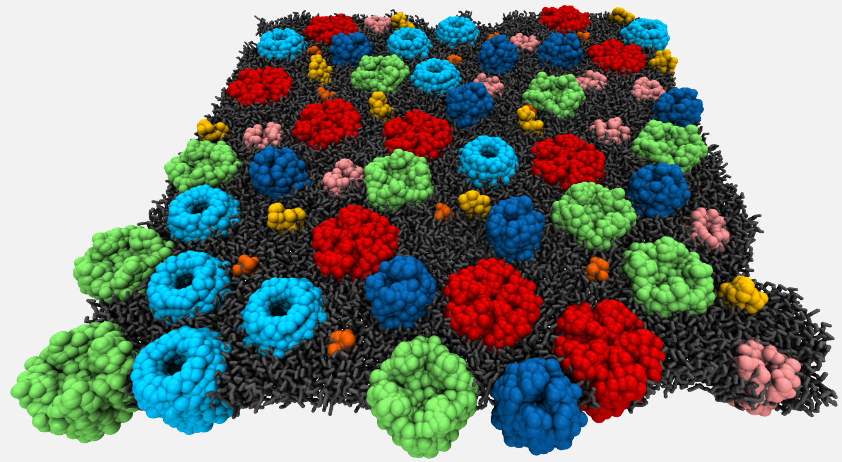


E Kappler, Ann d Physik (1931): $N_A = 60.59 \times 10^{22} \pm 1\%$

Stochastic processes in 2019: why should we care?

Jean Perrin (1908)

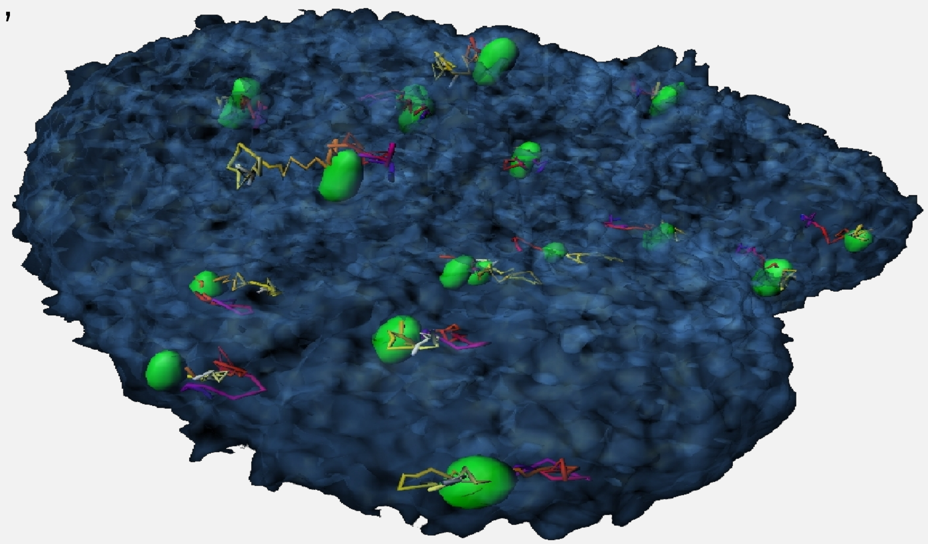




Courtesy Matti Javanainen

Novel insights from single particle tracking (e.g., superresolution microscopy, supercomputing)

- ↷ Normal diffusion /w random parameters
- ↷ Anomalous diffusion of all sorts
- ↷ New physics: time averages, (non)ergodicity, ageing, non-Gaussianity
- ↷ Information from fluctuations
- ↷ Data analysis strategies



Courtesy Yuval Garini

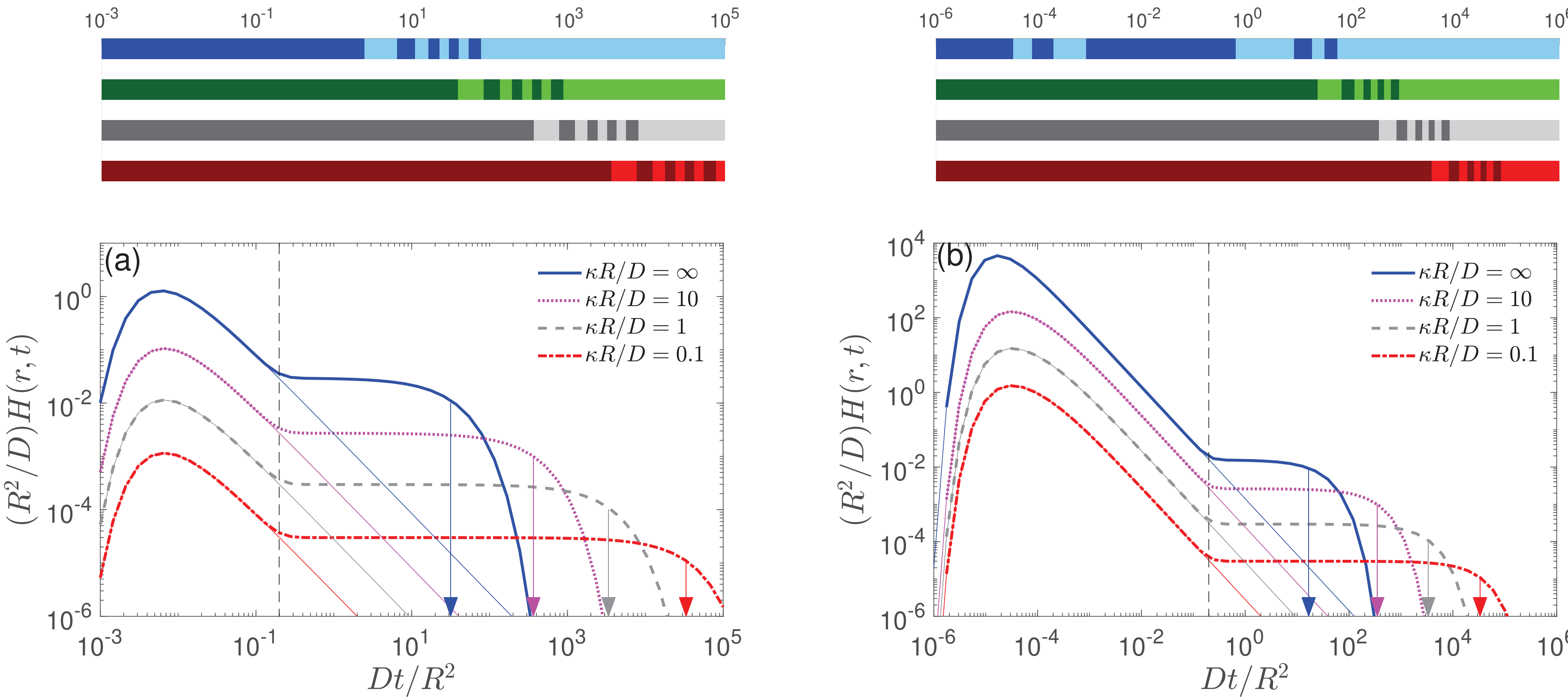
E Barkai, Y Garini & RM, Phys Today (2012)

Strongly defocused reaction times: geometry/reaction control

Mean/global mean first passage & cover times: O Bénichou, R Voituriez et al.: Nature (2007), Nature Phys (2008), Nature Chem (2010), Nature Phys (2015)

@ nM concentrations even on μm scale distance matters: O Pulkkinen & RM, PRL (2013)

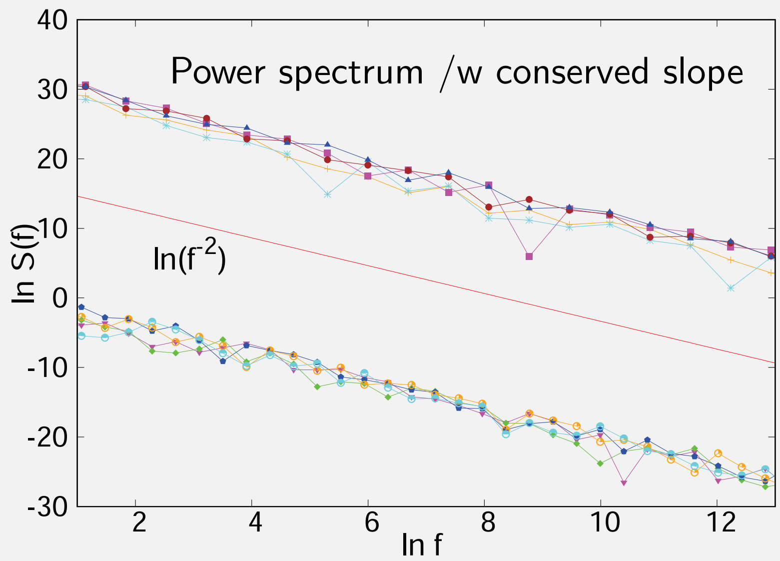
Full first passage time density:

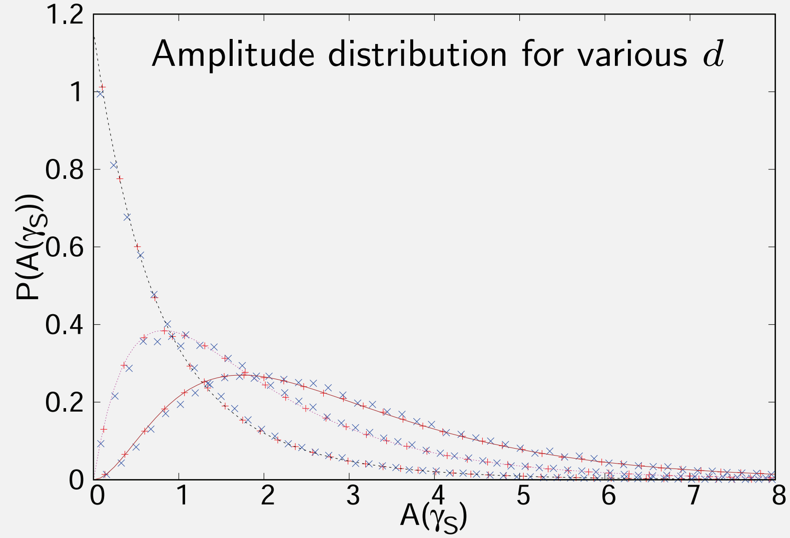


[Inner target radius $\rho/R = 0.01$ with starting point (a) $r/R = 0.2$ and (b) $r/R = 0.02$]

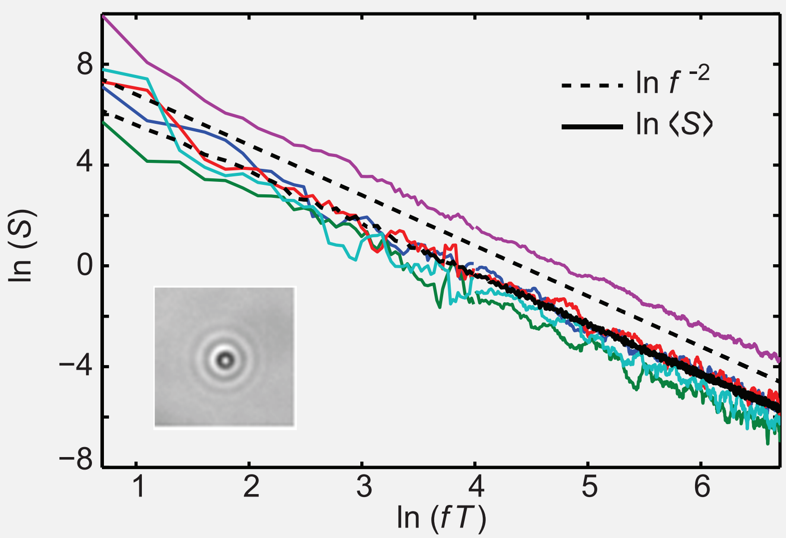
D Grebenkov, RM & G Oshanin, Comm Chem (2019), PCCP (2018); A Godec & RM, PRX (2016)

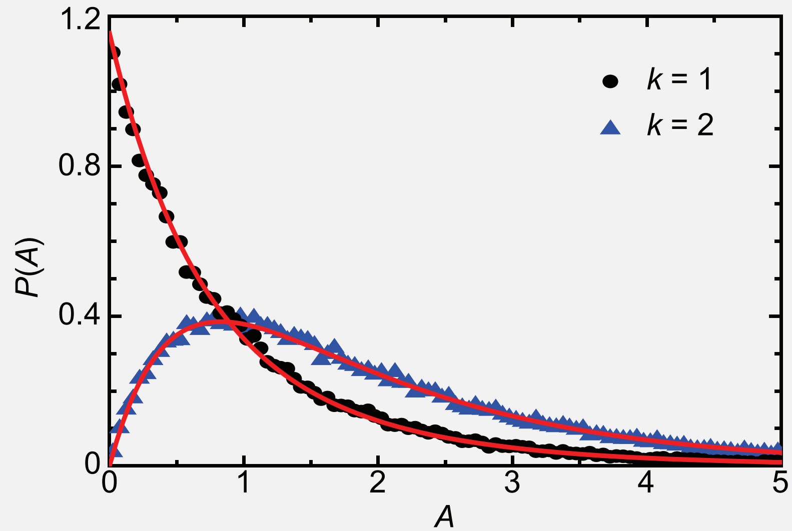
Power spectral density of a single Brownian trajectory





Theory

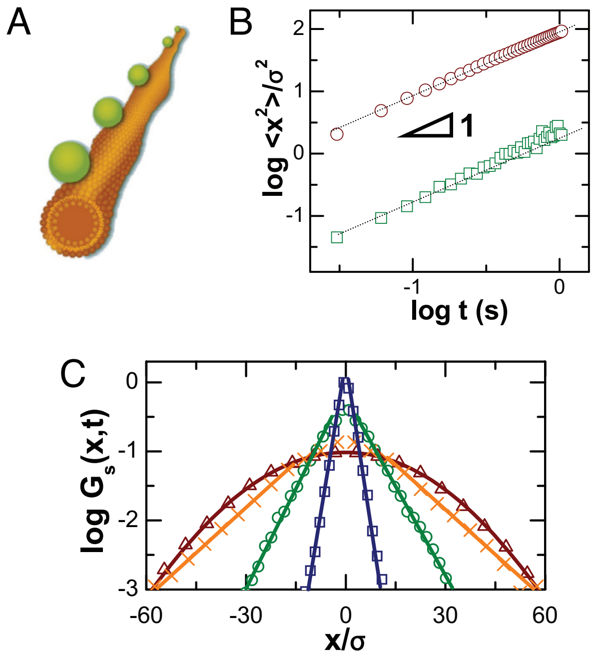




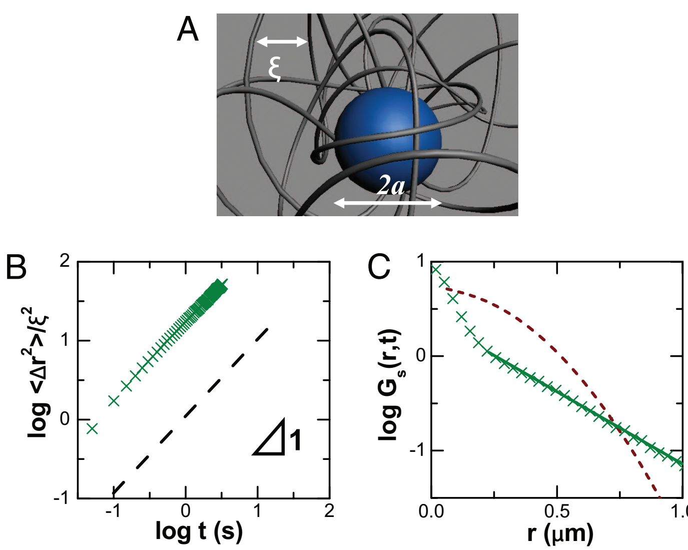
Experiment

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

When Brownian diffusion is not Gaussian

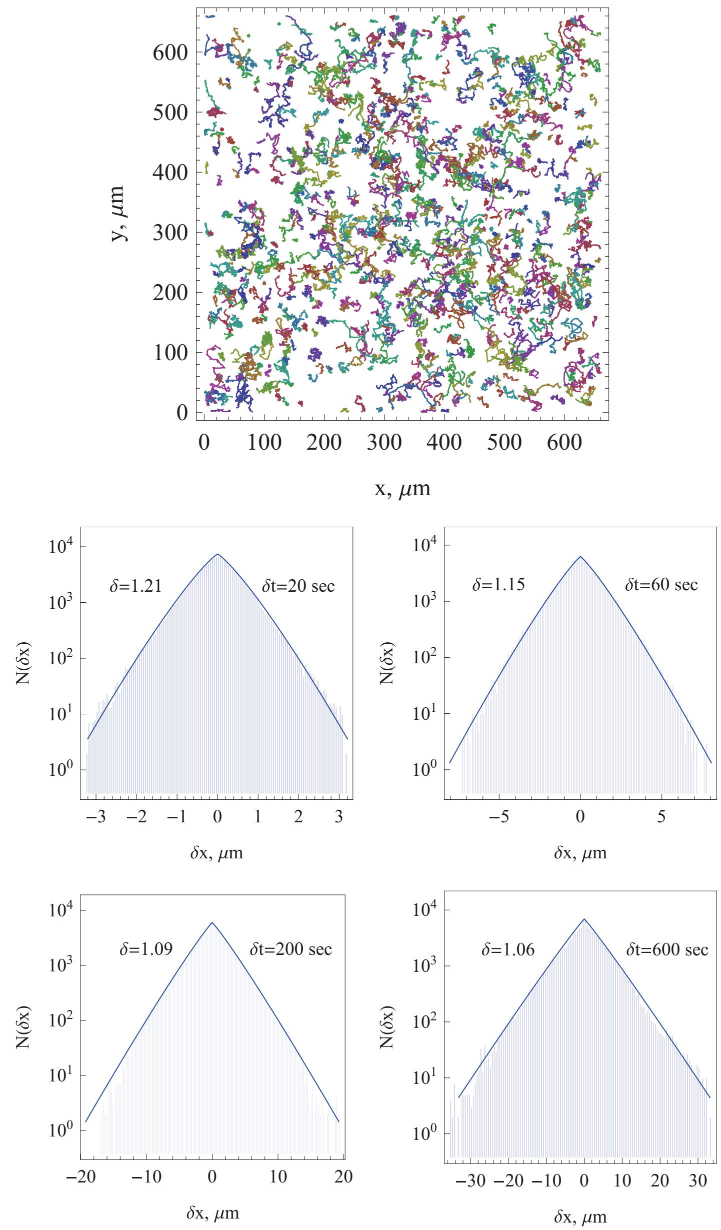


Colloidal beads on nanotubes



Nanospheres in entangled actin

Motion of dictyostelium cells



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

AG Cherstvy, O Nagel, C Beta & RM, PCCP (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 $P(x,t) = \int_0^\infty G(x,t|D)p(D)dD$

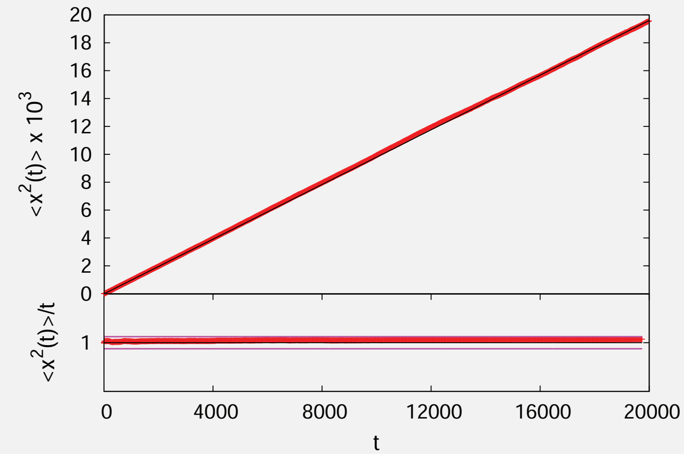
[C Beck & EDB Cohen, Physica A (2003); C Beck Prog Theor Phys Suppl (2006)]

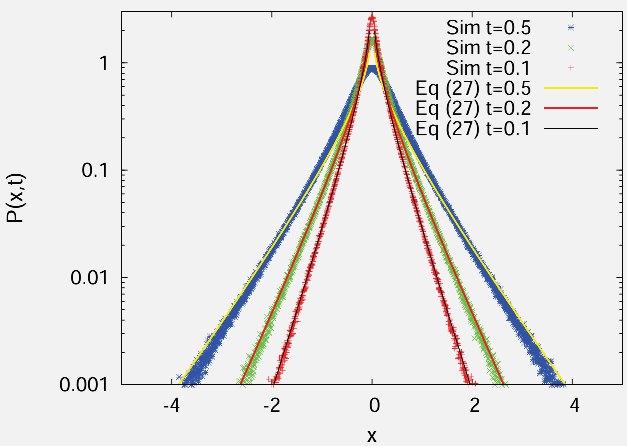
MV Chubinsky & G Slater, PRL (2014): diffusing diffusivity

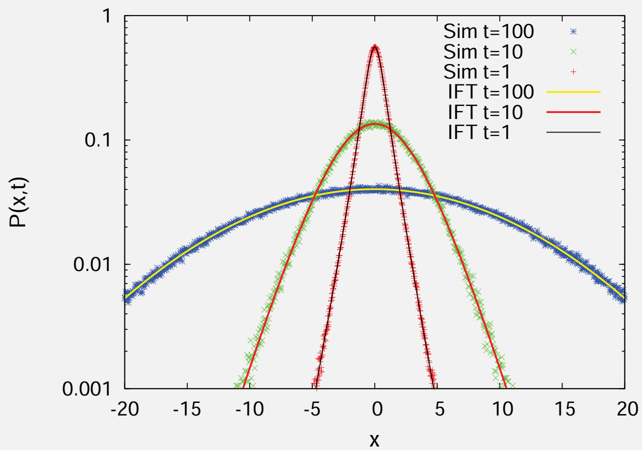
[see also R Jain & KL Sebastian, JPC B (2016)]

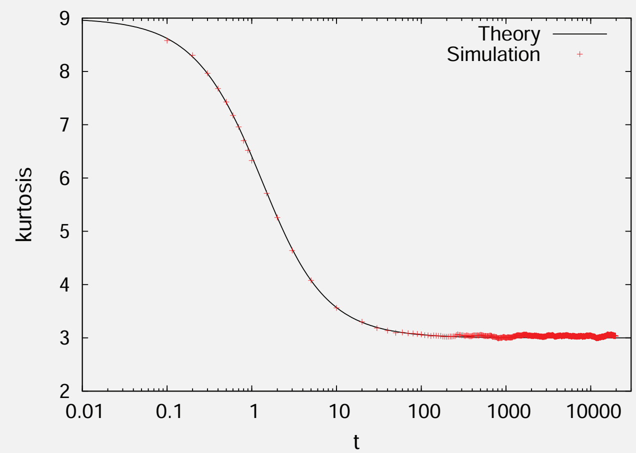
Our minimal model for diffusing diffusivity:

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









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

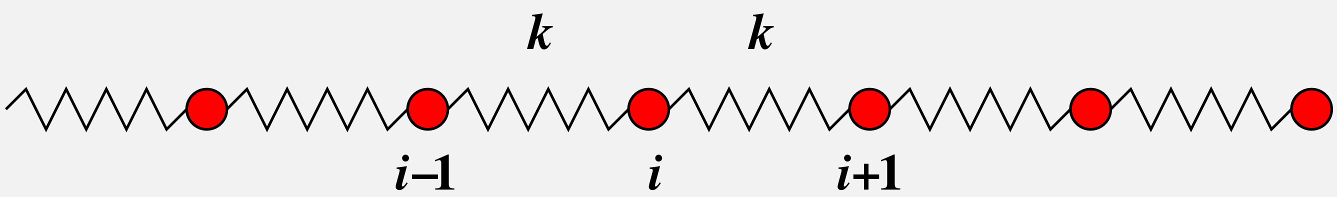
Fractional Langevin equations in viscoelastic systems

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):

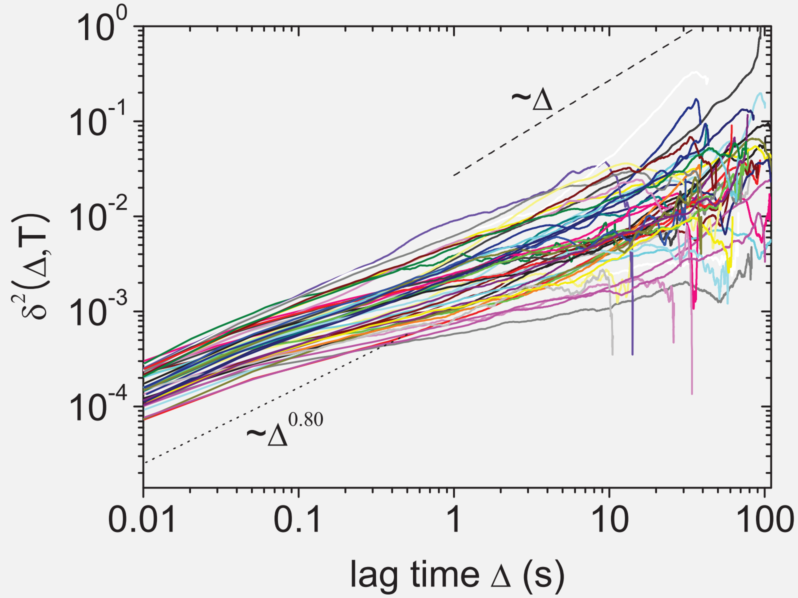
$$\langle\zeta_i(t)\zeta_j(t')\rangle = \delta_{ij}k_B T\eta(|t-t'|)$$

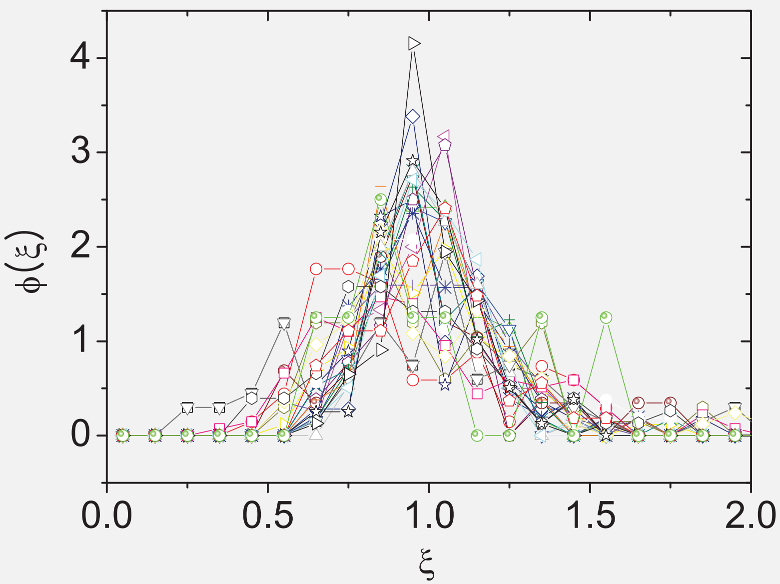
$\curvearrowright$ fractional Langevin equation. Overdamped limit: Mandelbrot's FBM

Quantum mechanics: Nakajima-Zwanzig equation using projection operators

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

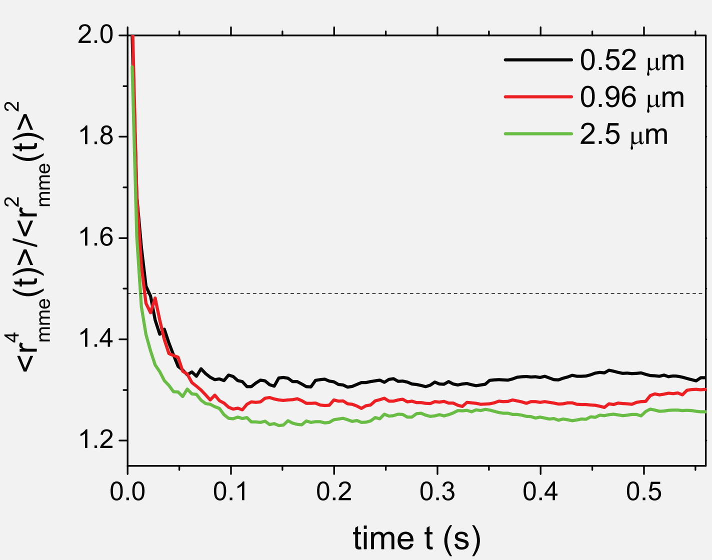
Passive motion of submicron tracers in cells is viscoelastic

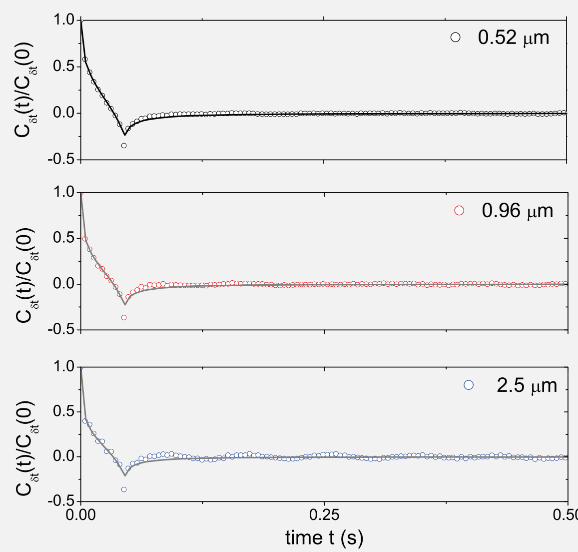


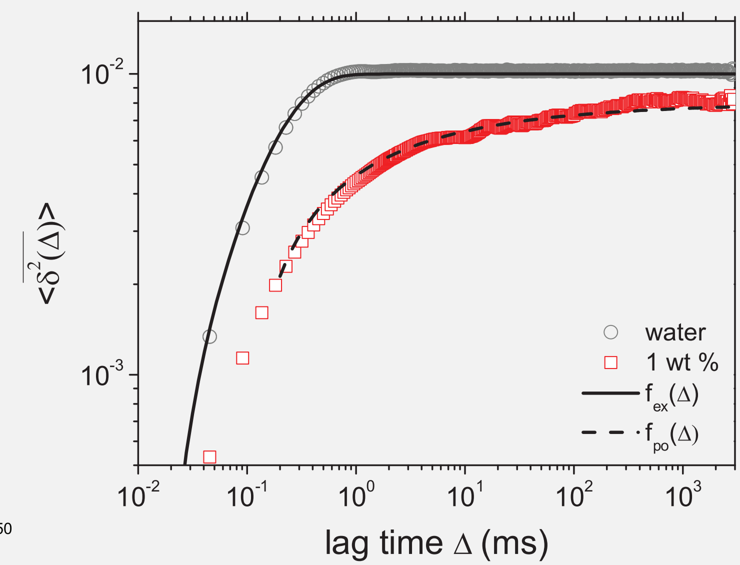


Lipid granules in living yeast cells ←

Tracer beads in wormlike micellar solution →

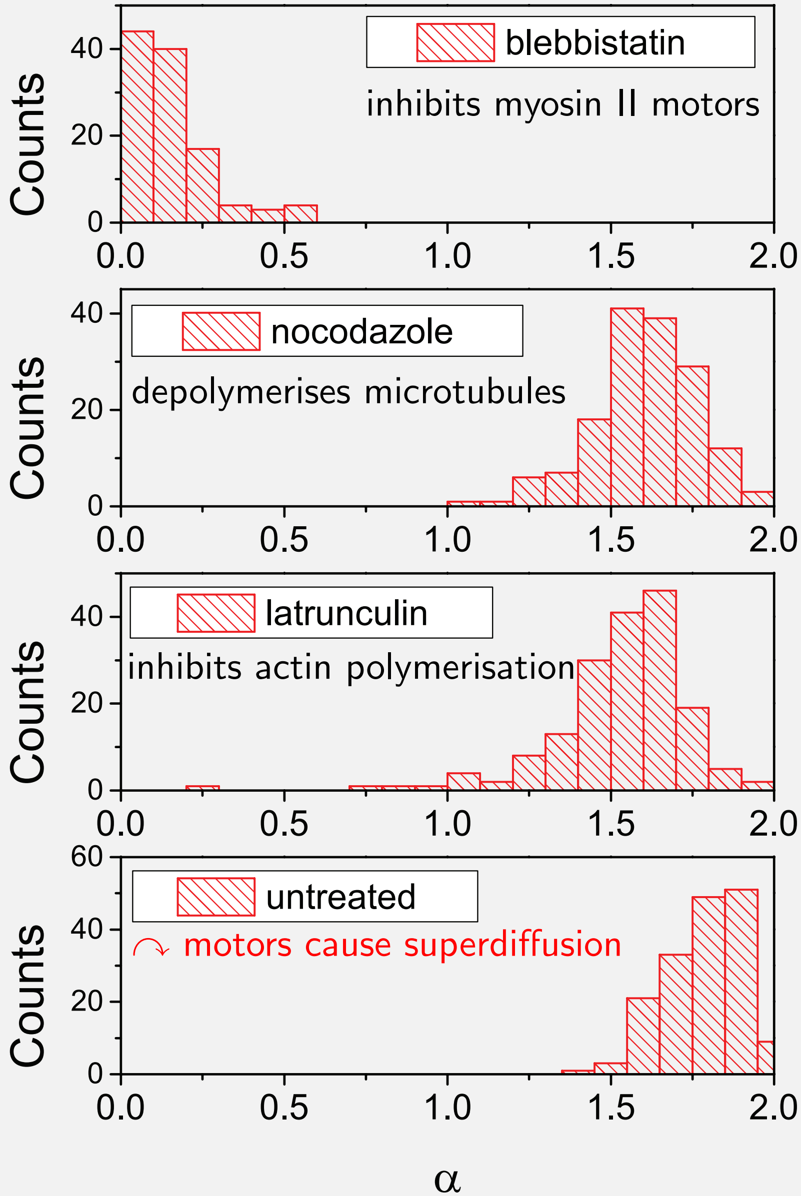


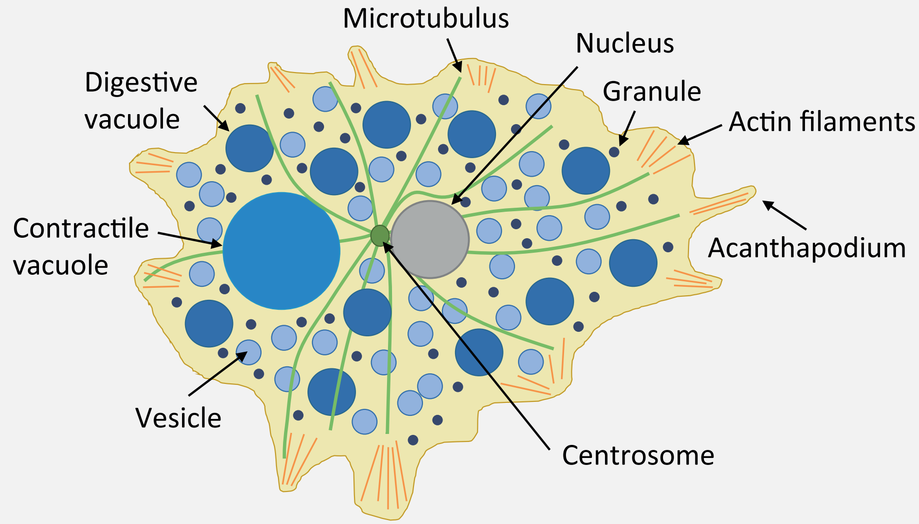


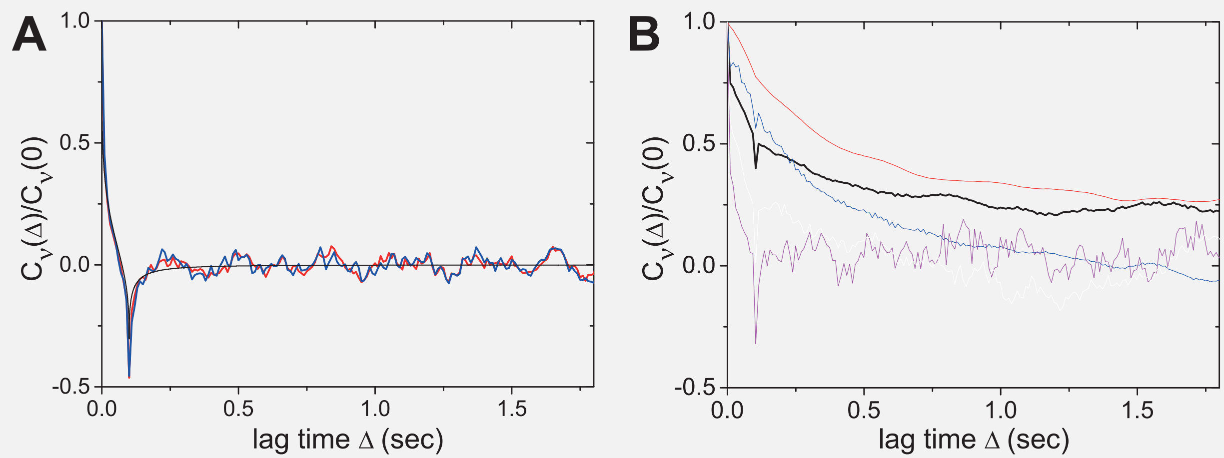


JH Jeon, . . . L Oddershede & RM, PRL (2011); JH Jeon, N Leijnse, L Oddershede & RM, NJP (2013)

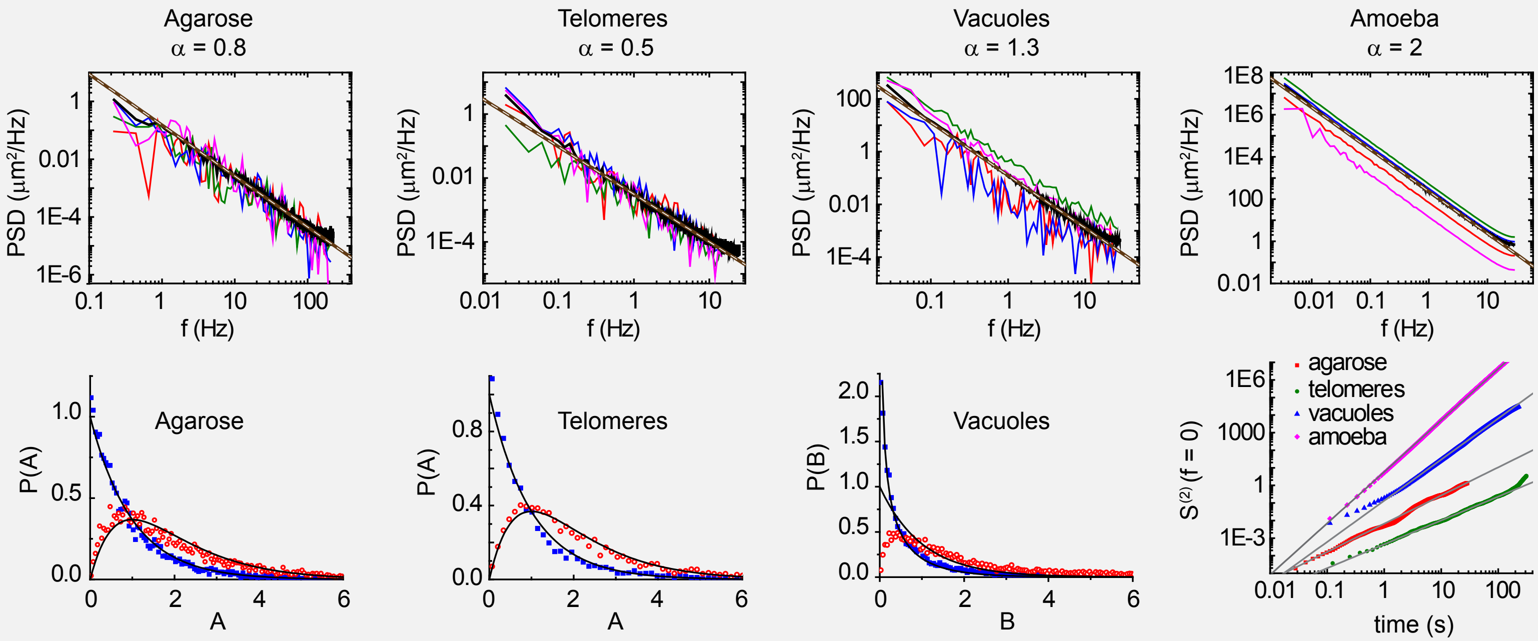
Superdiffusion in supercrowded Acanthamoeba castellani

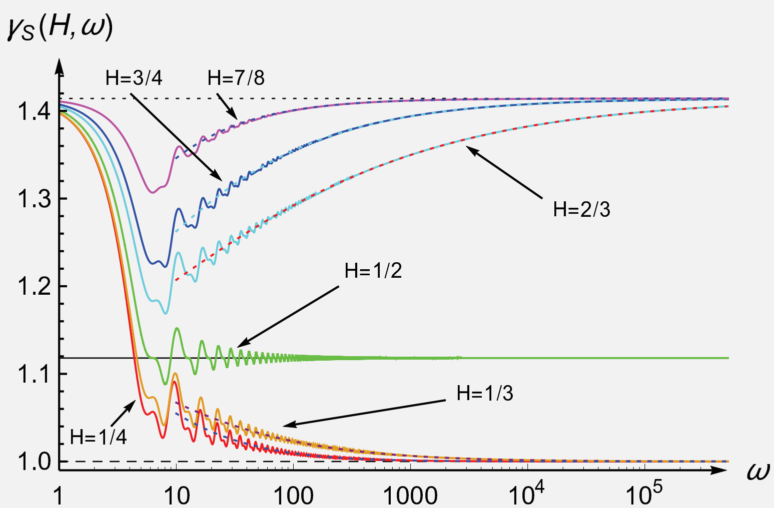






Power spectral density of a single FBM trajectory

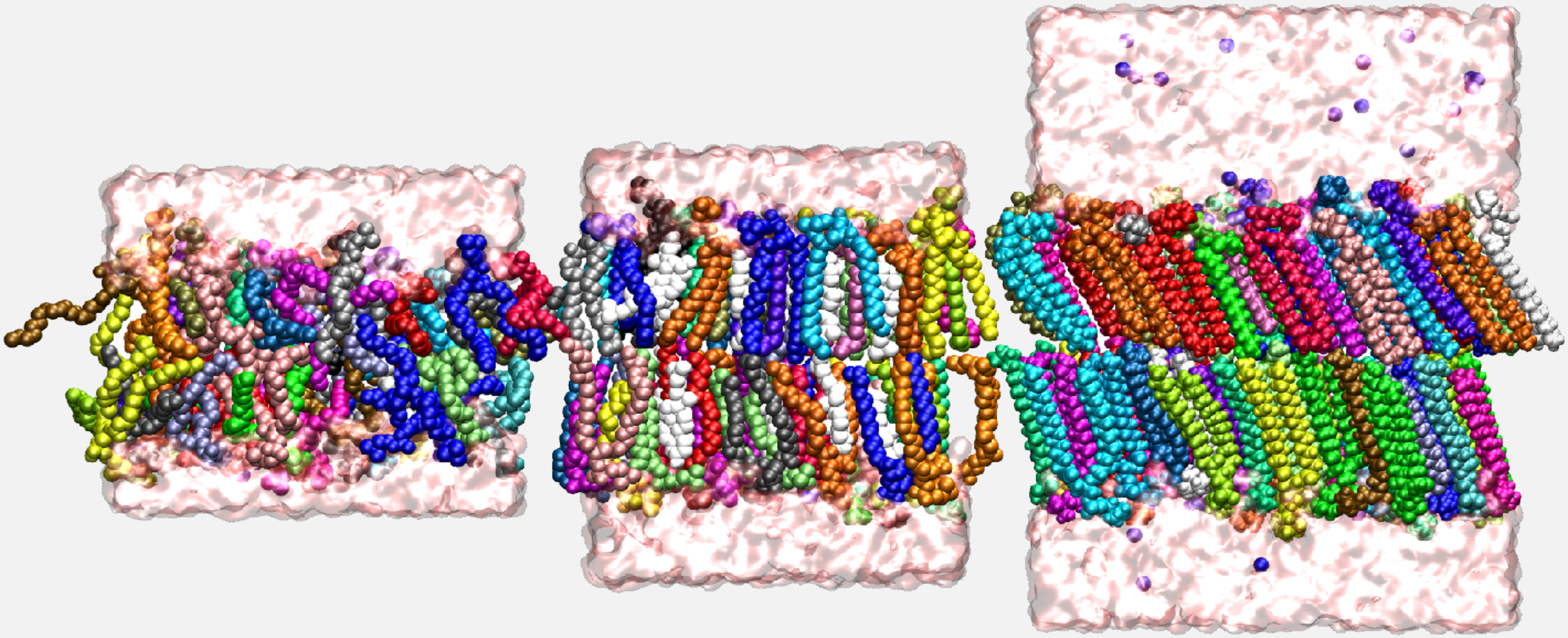




$$\gamma = \frac{\left(\langle S_T^2(f)\rangle - \langle S_T(f)\rangle^2\right)^{1/2}}{\langle S_T(f)\rangle}$$

D Krapf, N Lukat, E Marinari, RM, G Oshanin, C Selhuber-Unkel, A Squarcini, L Stadler, M Weiss & X Xu, PRX (2019)

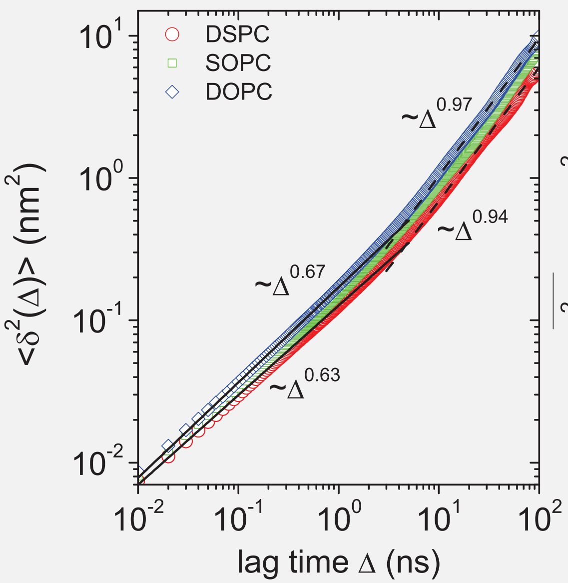
Single lipid motion in bilayer membrane MD simulations

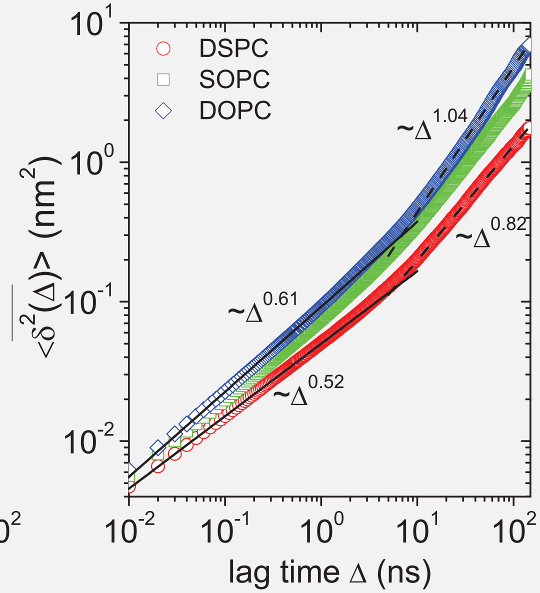


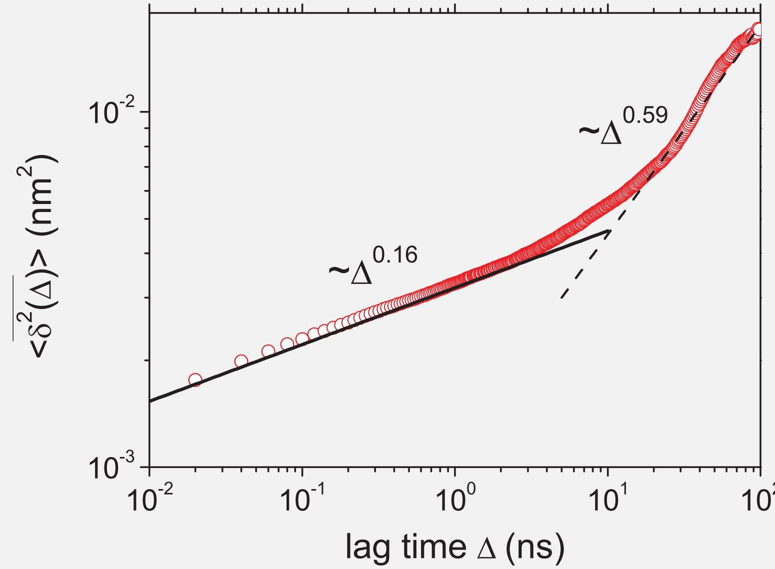
Liquid disordered | Liquid ordered | Gel phase

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

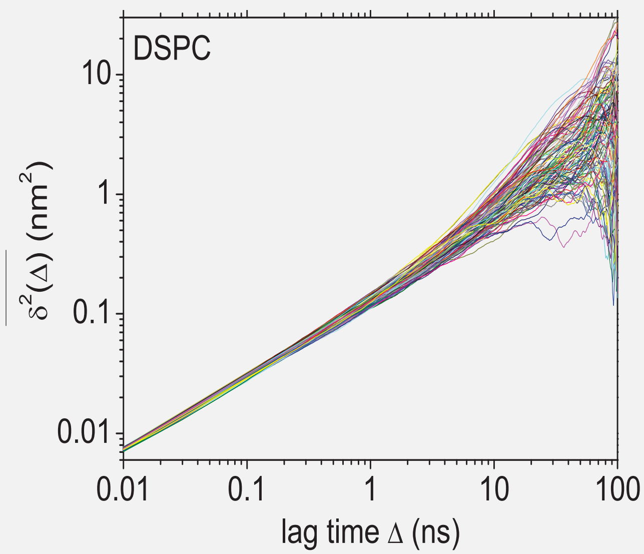
Liquid ordered/gel phases: extended anomalous diffusion

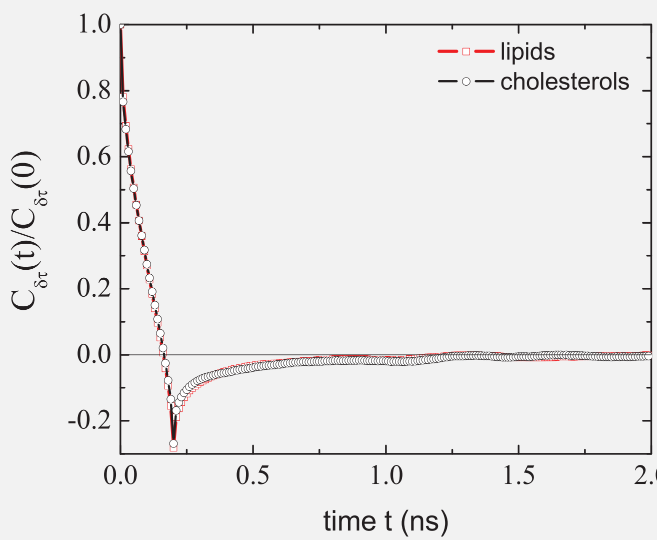


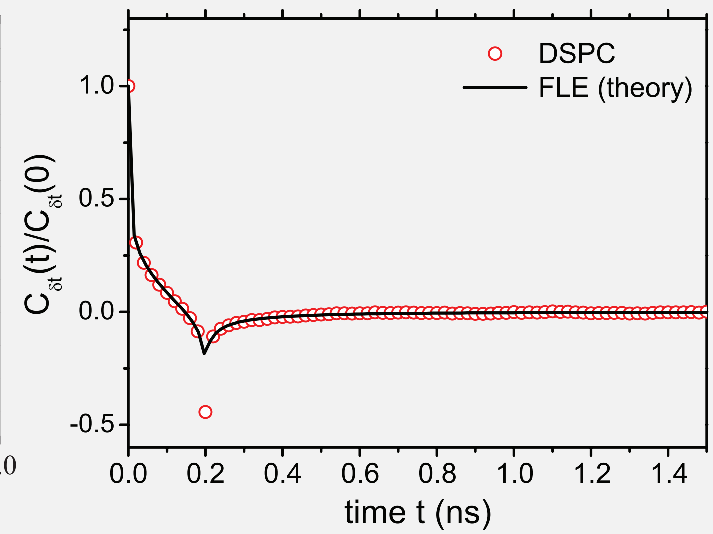




Reproducible TA MSD & antipersistent correlations





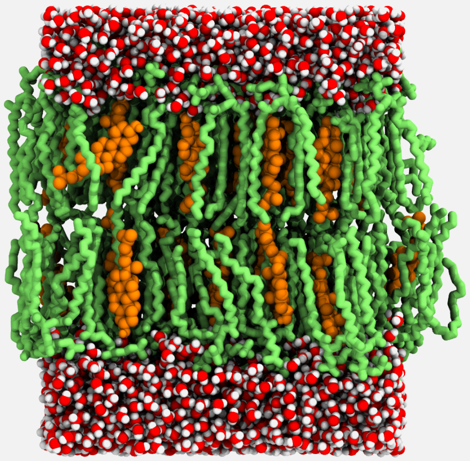


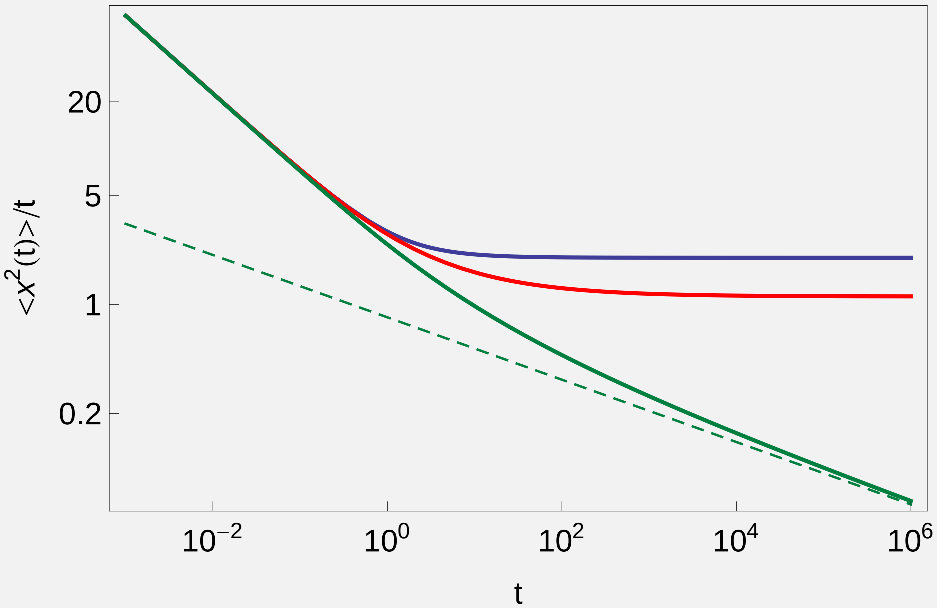
J-H Jeon, H Martinez-Seara Monne, M Javanainen & RM, PRL (2012)

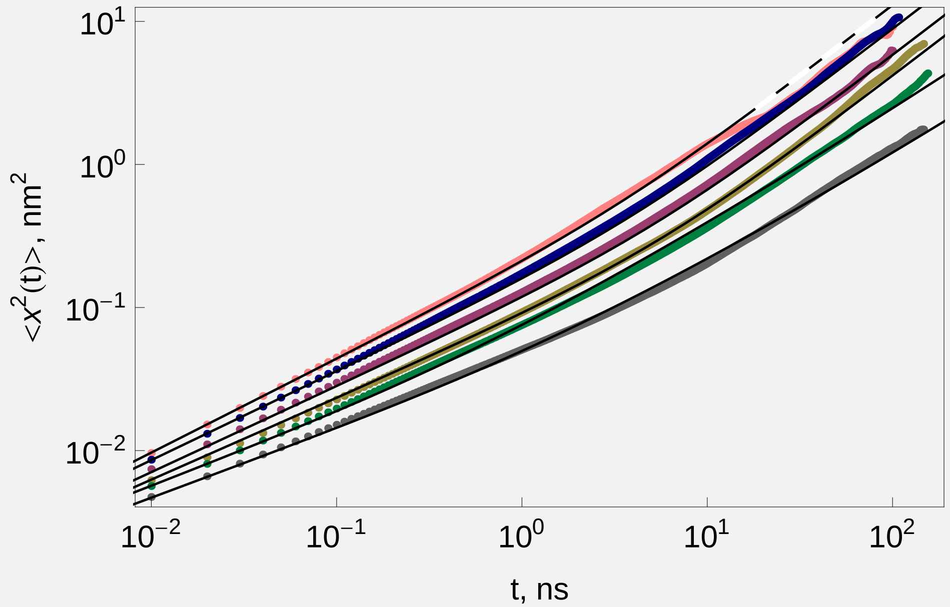
Tempered FLE motion: crossover to faster diffusion

Tempered fractional Gaussian noise:

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

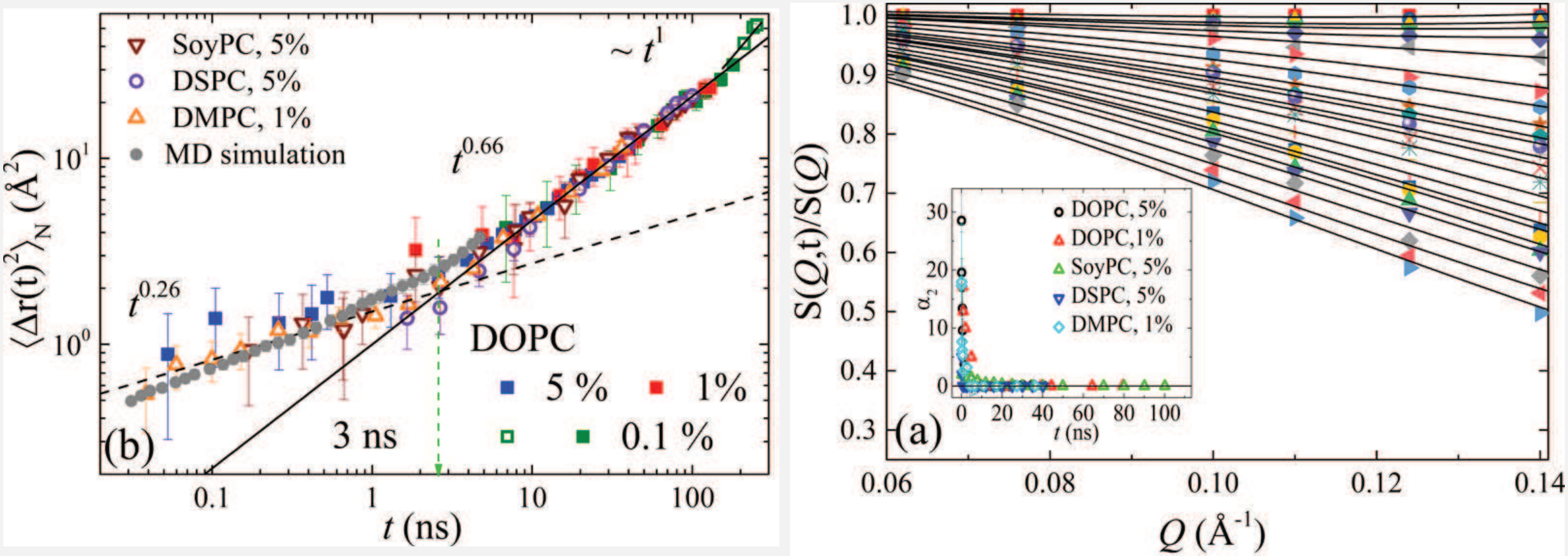






D Molina-Garcia, T Sandev, H Safdari, G Pagnini, AV Chechkin & RM, NJP (2018)

Extreme short time non-Gaussian subdiffusion

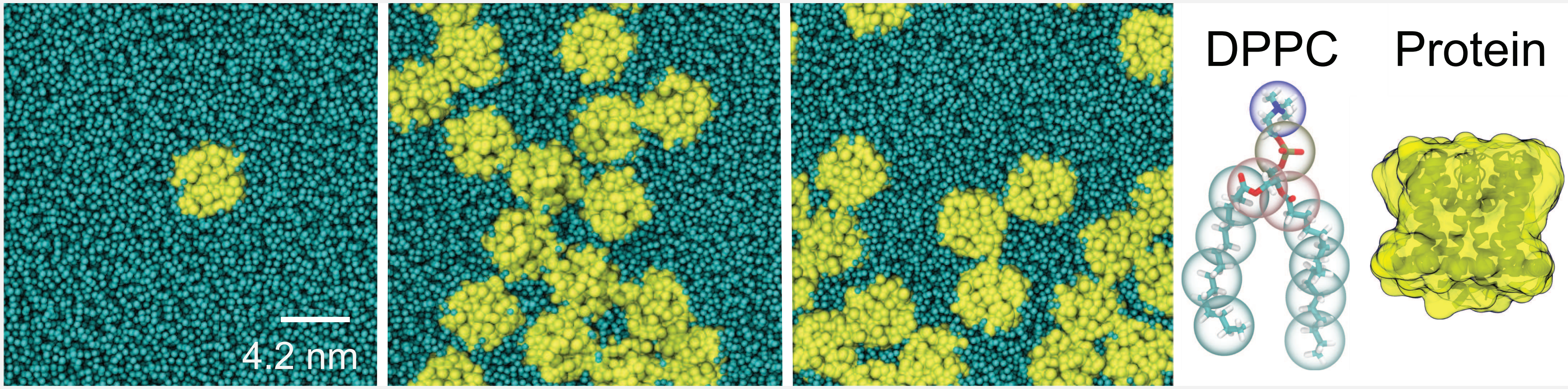


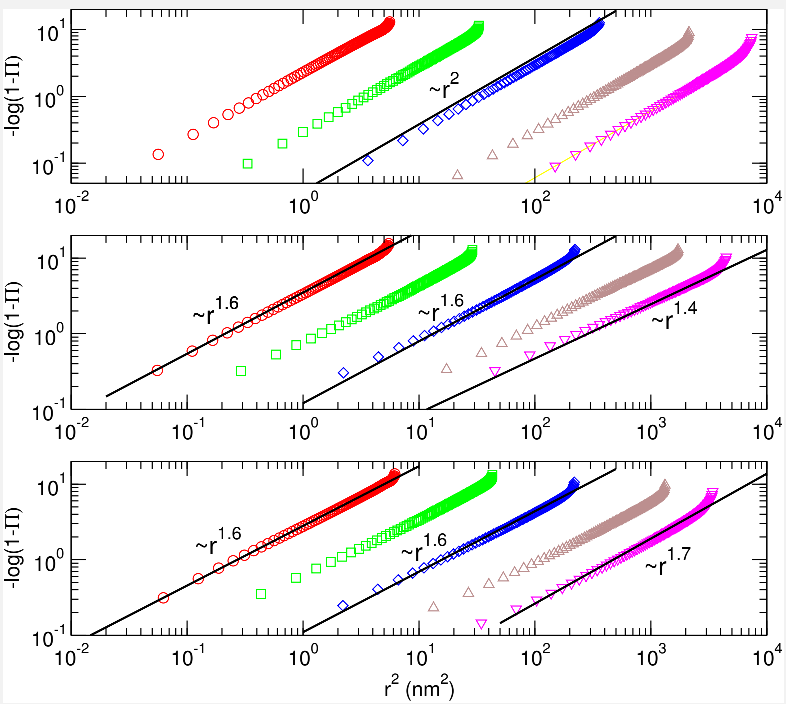
Authors suggest short time regime $\langle \mathbf{r}^2(t) \rangle \simeq t^{0.26}$
& transient trapping of lipids leading to non-Gaussian displacement distribution

[NB: Non-Gaussianity could also come from inhomogeneity]

S Gupta, JU de Mel, RM Perera, P Zolnierczuk, M Bleuel, A Faraone & GJ Schneider, JPC Lett (2018)

Crowding in membranes: non-Gaussian lipid/protein diffusion

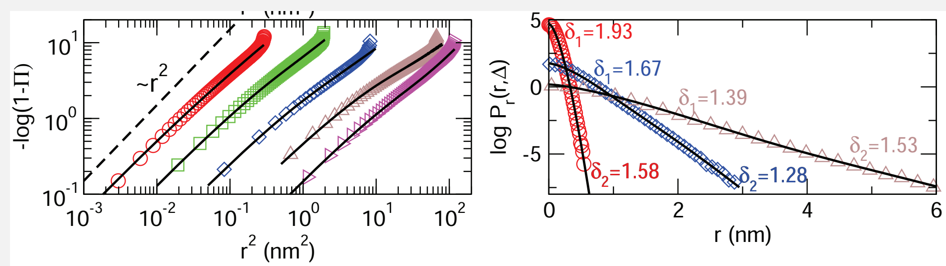




Dilute membrane: $P(r,t)$ Gauss

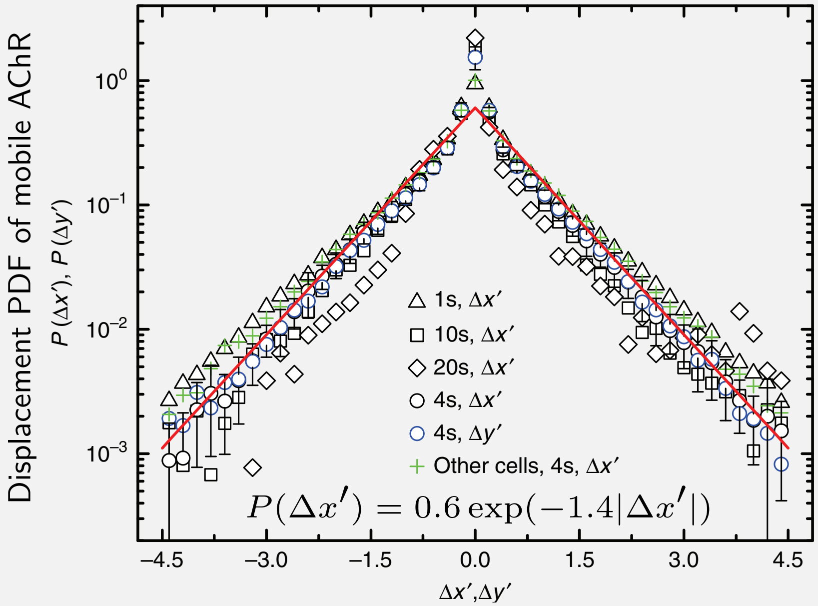
Crowded membrane ($\delta \approx 1.3 \ldots 1.7$):

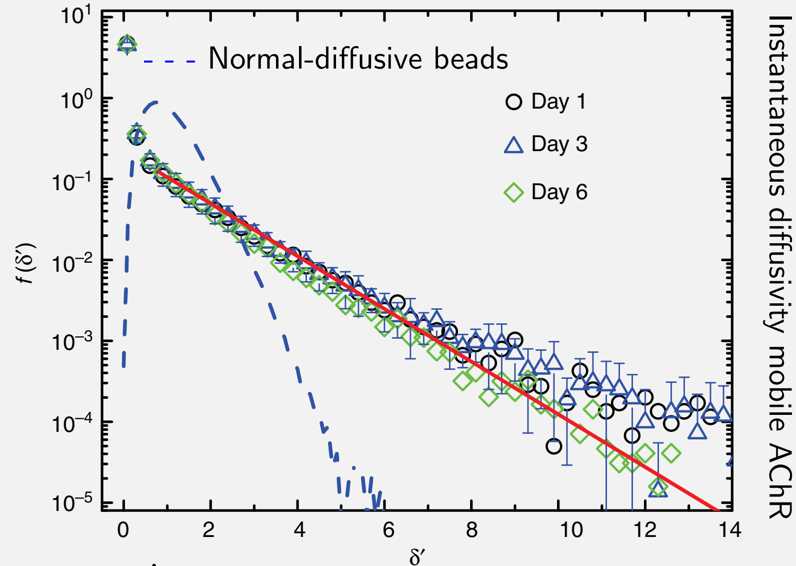
$$P(r,t) \propto \exp\left(-\left[\frac{r}{ct^{\alpha/2}}\right]^{\delta}\right)$$



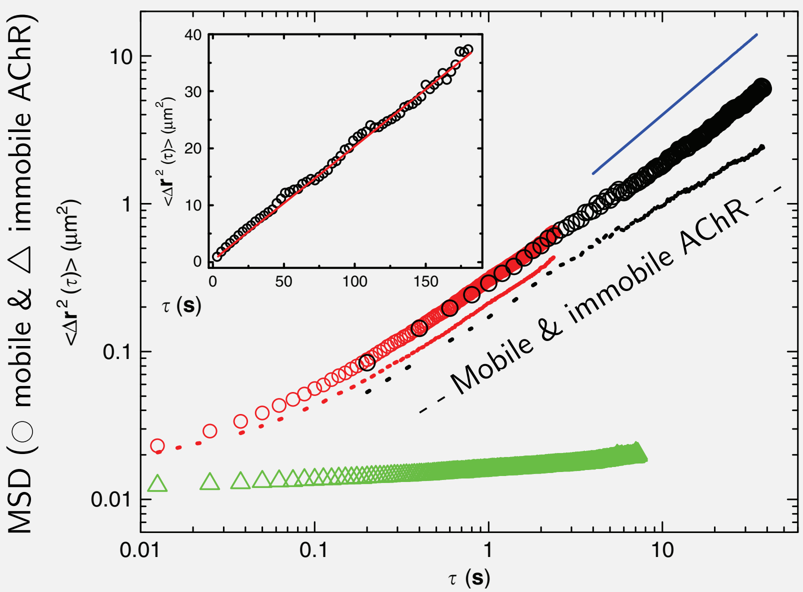
J-H Jeon, M Javanainen, H Martinez-Seara, RM & I Vattulainen, PRX (2016); see also Faraday Disc (2013)

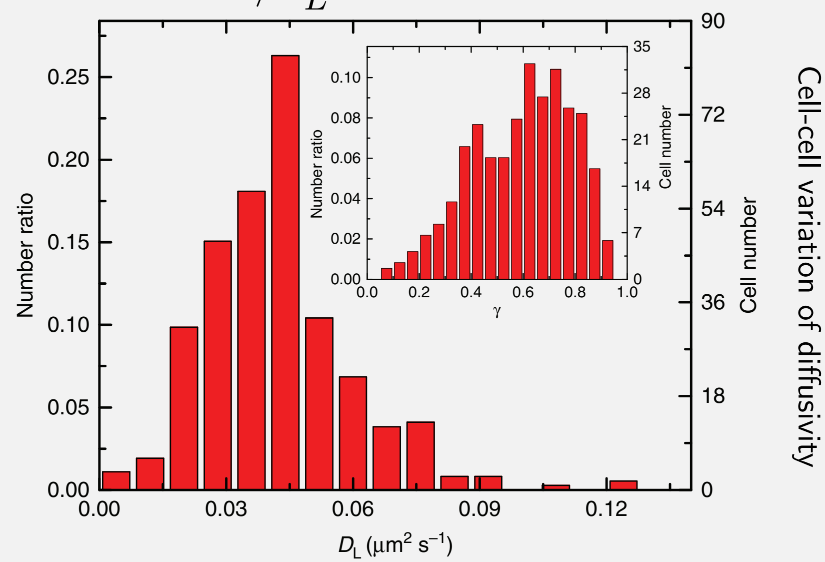
Non-Gaussianity of acetylcholine receptors in Xenopus cells





$\delta' = \delta/D_L$ cell-normalised diffusivities



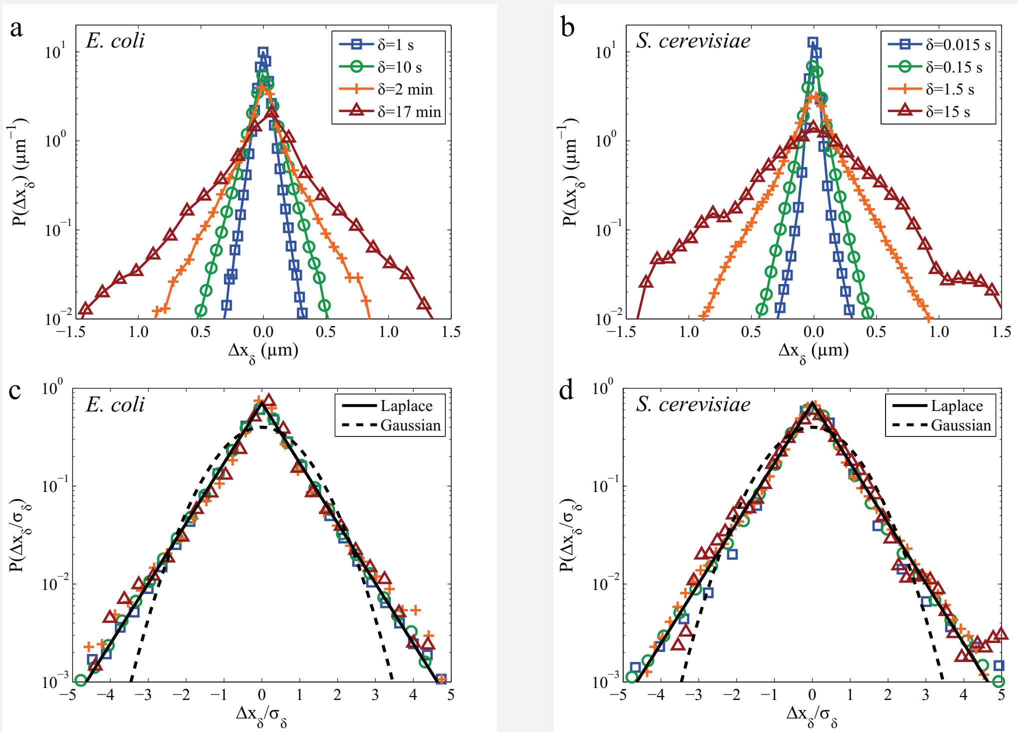


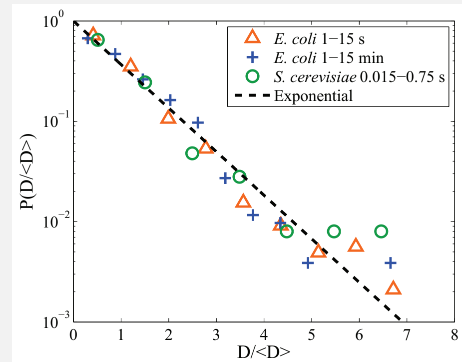
D_L from $\langle \mathbf{r}^2(\tau)\rangle = 2D_L\tau$

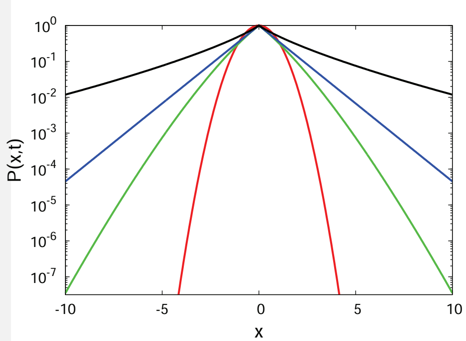
W He, H Song, Y Su, L Geng, BJ Ackerson, HB Peng & P Tong, Nat Comm (2016)

Non-Gaussian diffusion in viscoelastic systems

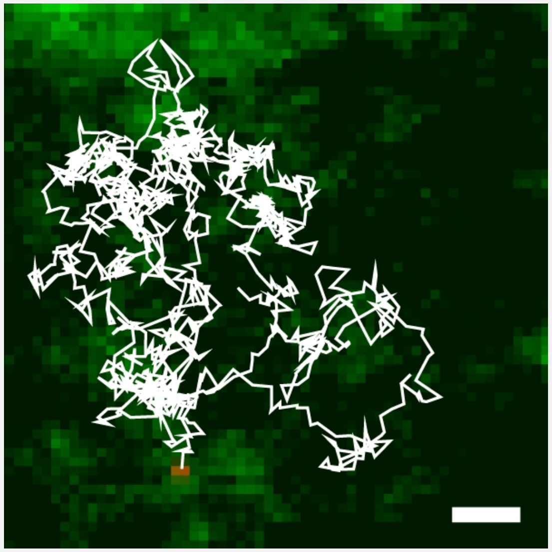
So far consensus: submicron tracer motion in cytoplasm is FBM-like, i.e., Gaussian
RNA-protein particles in E.coli & S.cerevisiae perform exponential anomalous diffusion:

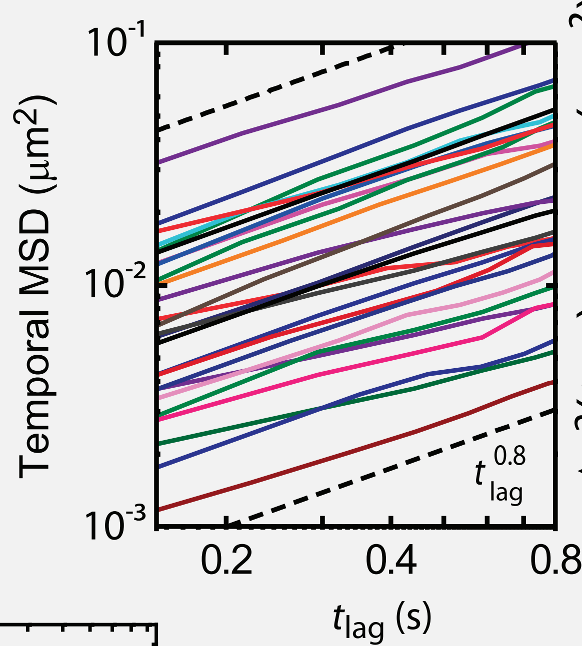


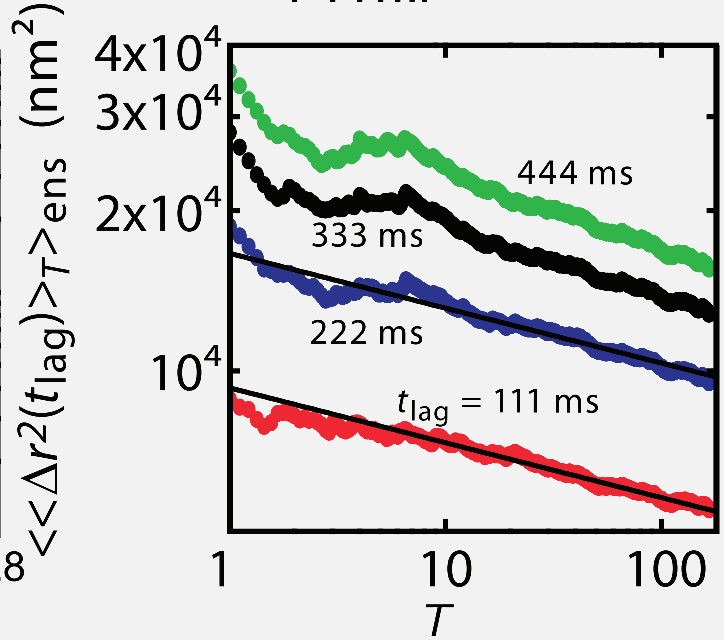


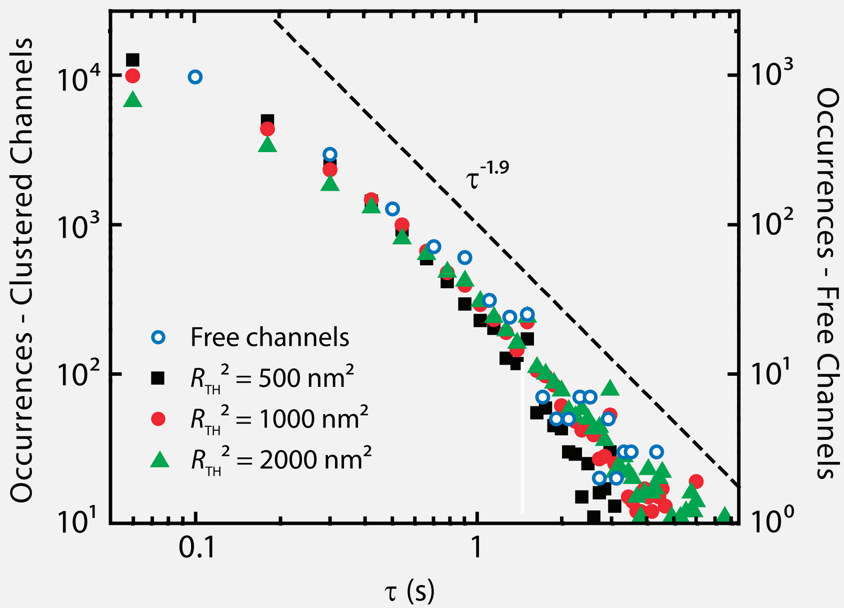


CTRW-like motion of Ka channels in plasma membrane









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

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

$\Delta/T^{1-\alpha} \simeq \overline{\delta^2(\Delta)} \neq \langle \mathbf{r}^2(\Delta)\rangle \simeq \Delta^\alpha$

$P(\mathbf{r},t) \simeq \exp\left(-\beta r^{1/[1-\alpha/2]}\right)$

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

Time averaged MSD & weak ergodicity breaking (WEB)

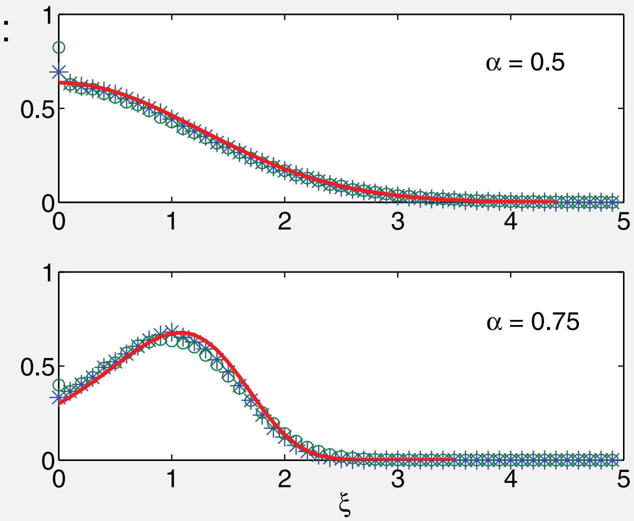
Time averaged MSD $\simeq \Delta$ is pseudo-Brownian and ageing ($\langle x^2(t)\rangle \simeq K_\alpha t^\alpha$):

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

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

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

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



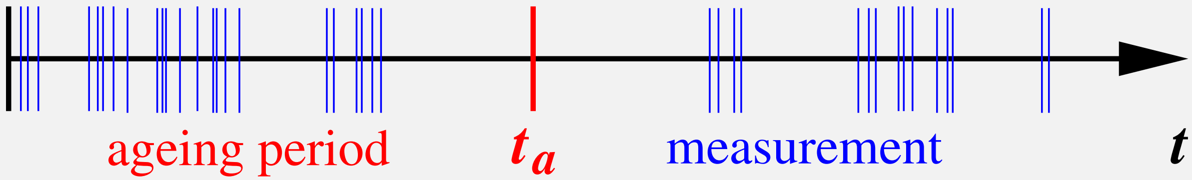
Confinement does not effect a plateau ($\langle x^2(t)\rangle \simeq \mathrm{const}(T)$):

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

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

Optical tweezers expt: J-H Jeon, . . . L Oddershede & RM, PRL (2011) ↓

Ageing effects in single trajectory time averages

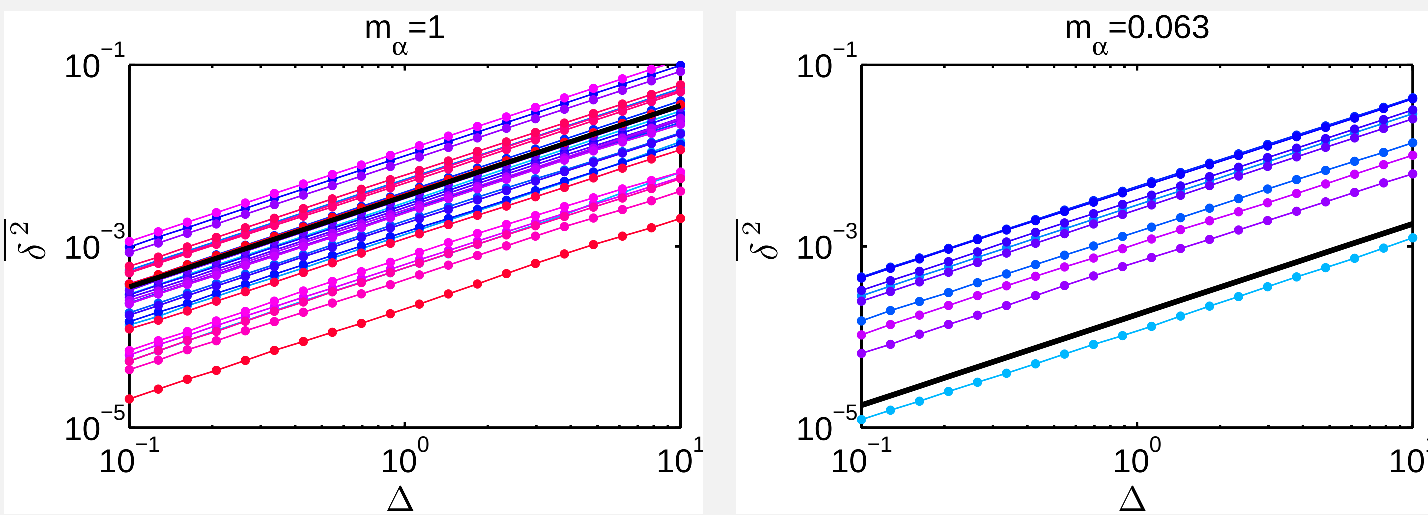


Ageing mean squared displacement ($\Lambda(z)=(1+z)^\alpha-z^\alpha$)

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

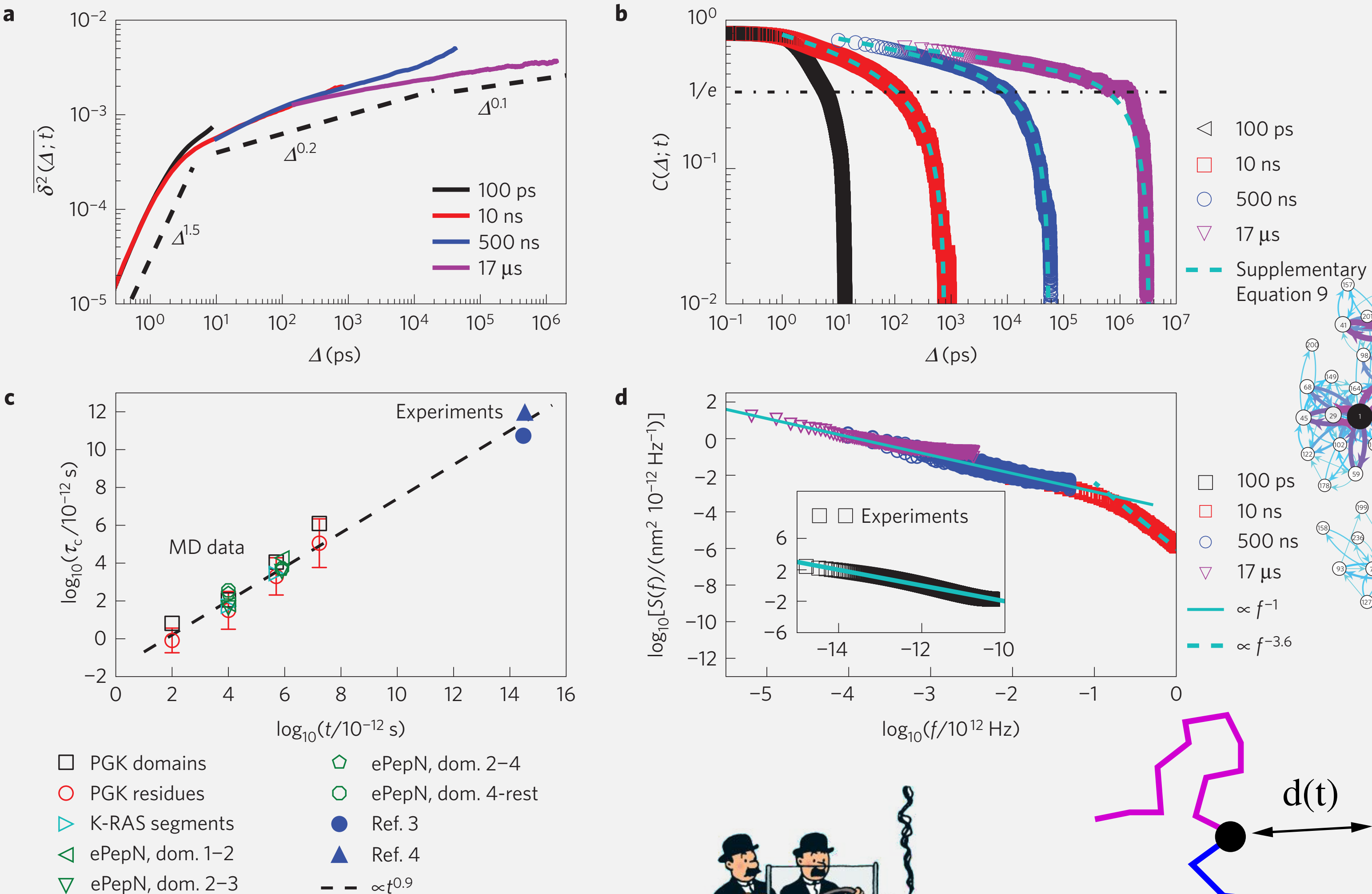
Probability to make at least one step during $[t_a,t_a+T]$: *population splitting*

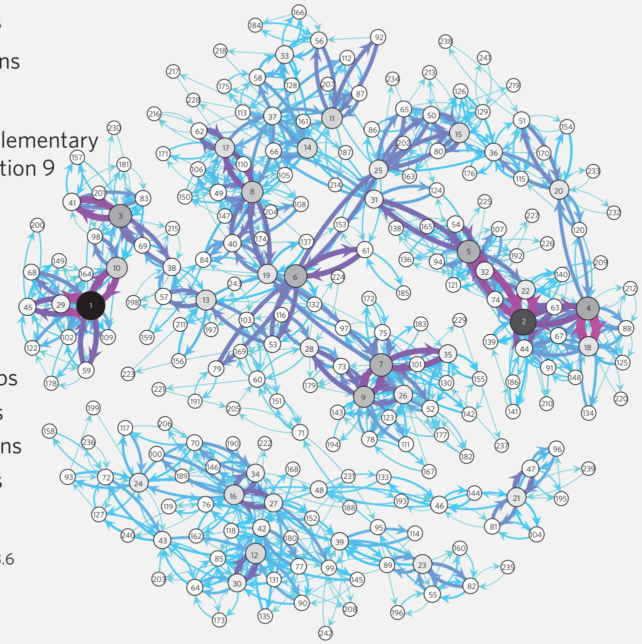
$$m_\alpha(T/t_a)\simeq(T/t_a)^{1-\alpha},\quad T\ll t_a$$

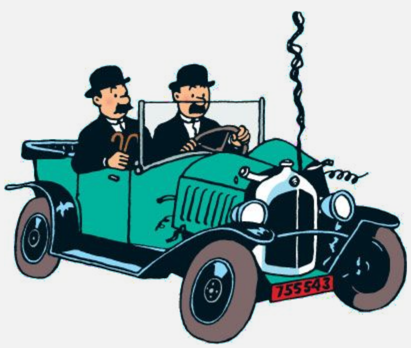


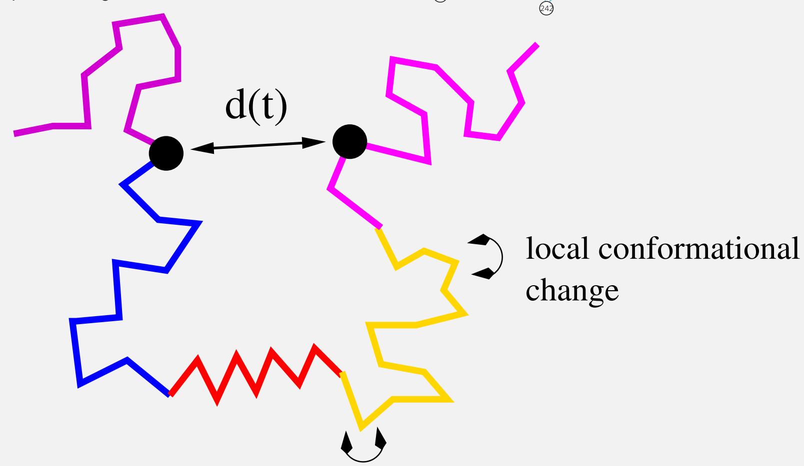
J Schulz, E Barkai & RM, PRL (2013), PRX (2014)

Self-similar internal protein dynamics: 13 decades of ageing





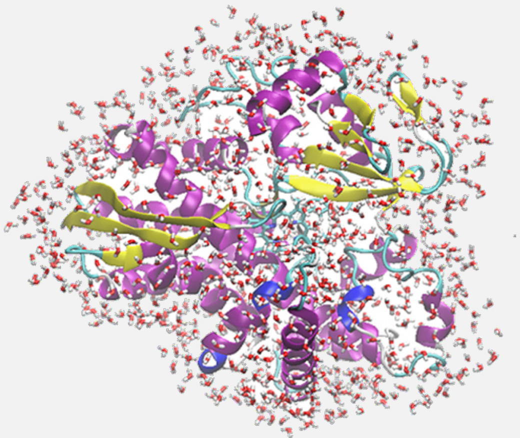




X Hu, L Hong, MD Smith, T Neusius, X Cheng & JC Smith, Nature Phys (2016); N&V RM Nature Phys (2016)

↙ Non-Gaussian ↗

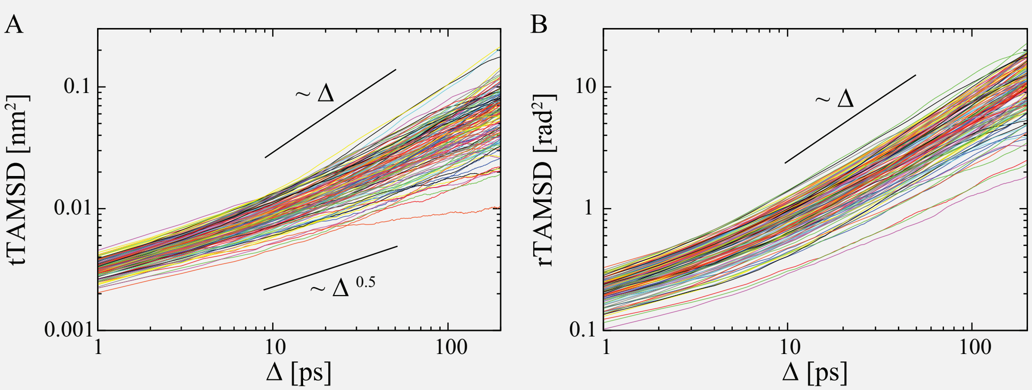
Intermittent localisation of surface water on proteins

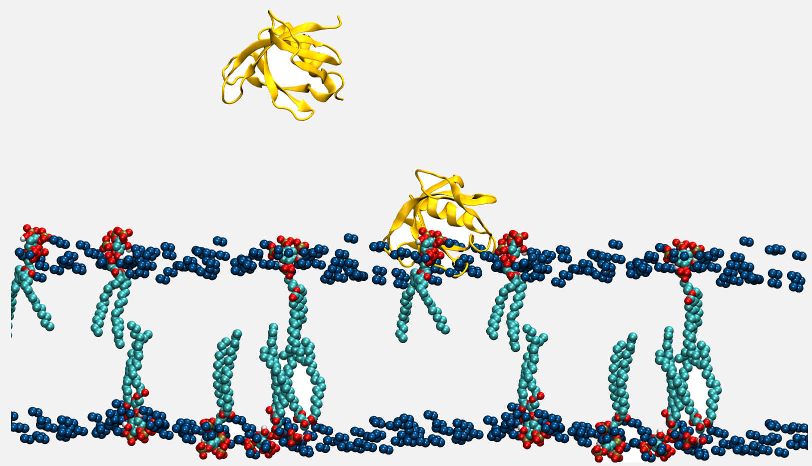


Uncorrelated jumps between cages

[P Tan, Y Liang, Q Xu, E Mamontov, J Li, X Xing & L Hong, Phys Rev Lett (2018); see also RM, Viewpoint Phys (2018)]

Intermittency of surface water & proteins on membranes

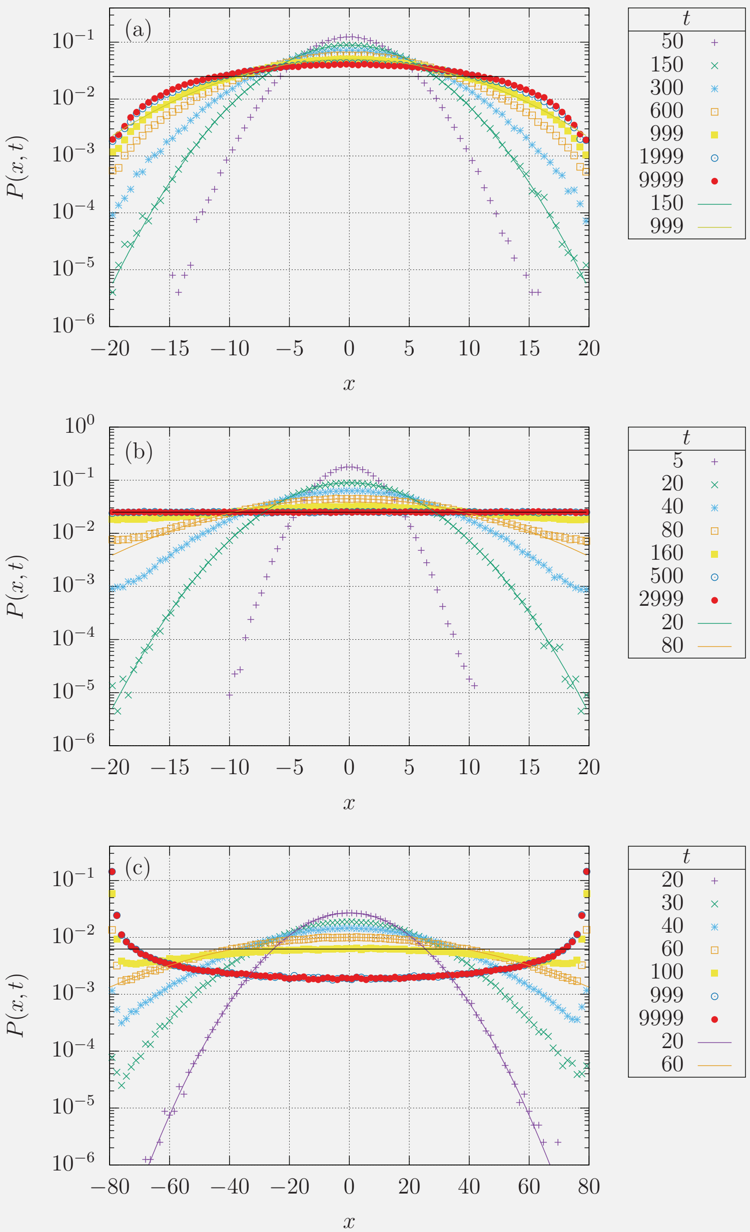


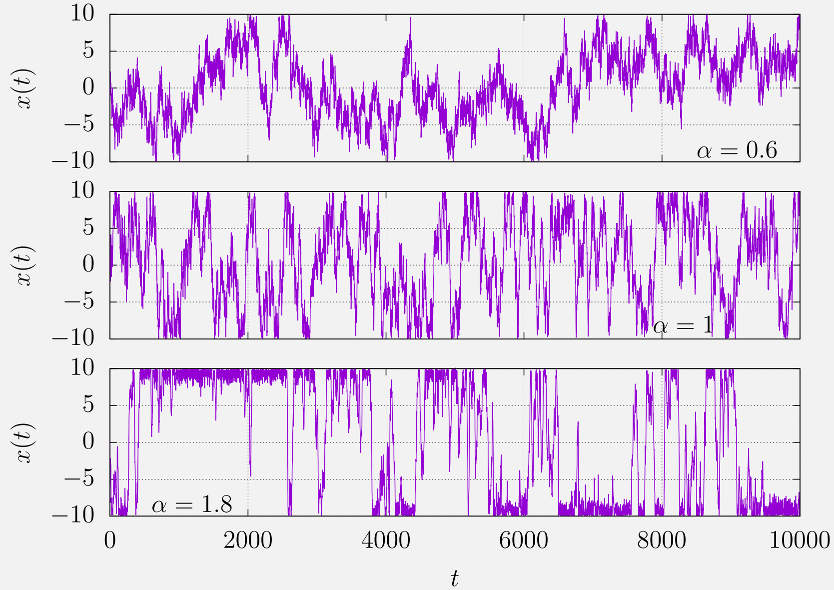


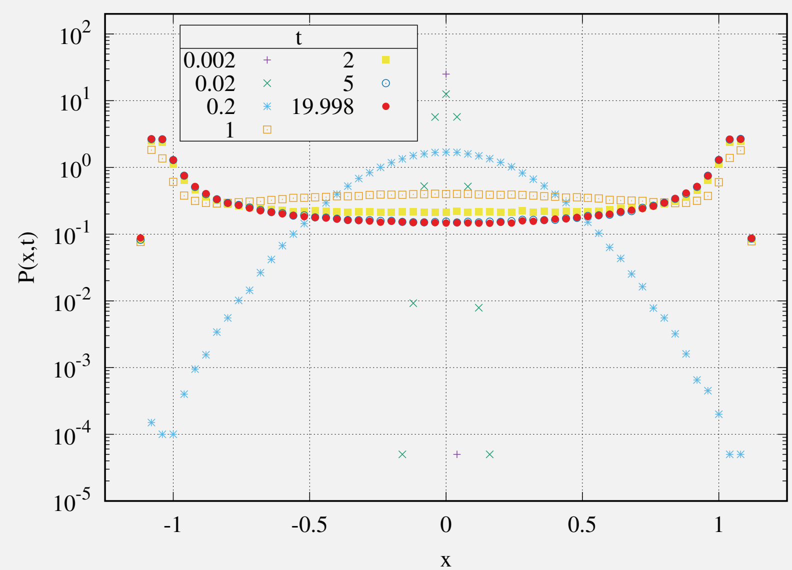
↑ Translational & rotational water surface diffusion

E Yamamoto, T Akimoto, M Yasui & K Yasuoka; E Yamamoto, AC Kalli, T Akimoto, K Yasuoka & MSP Sansom, Sci Rep (2014,2015)

FBM: accretion & depletion effects near boundaries







T Guggenberger, G Pagnini, T Vojta & RM, NJP (2019); see also AHO Wada & T Vojta, PRE (2018)

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)

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FNP Fundacja na rzecz Nauki Polskiej
DFG Deutsche Forschungsgemeinschaft
FIDIPRO Finland Distinguished Professor Programme