

Brownian motion & beyond

— Austin, 3rd December 2019 —



190+ years after Brown: Microscopical observations

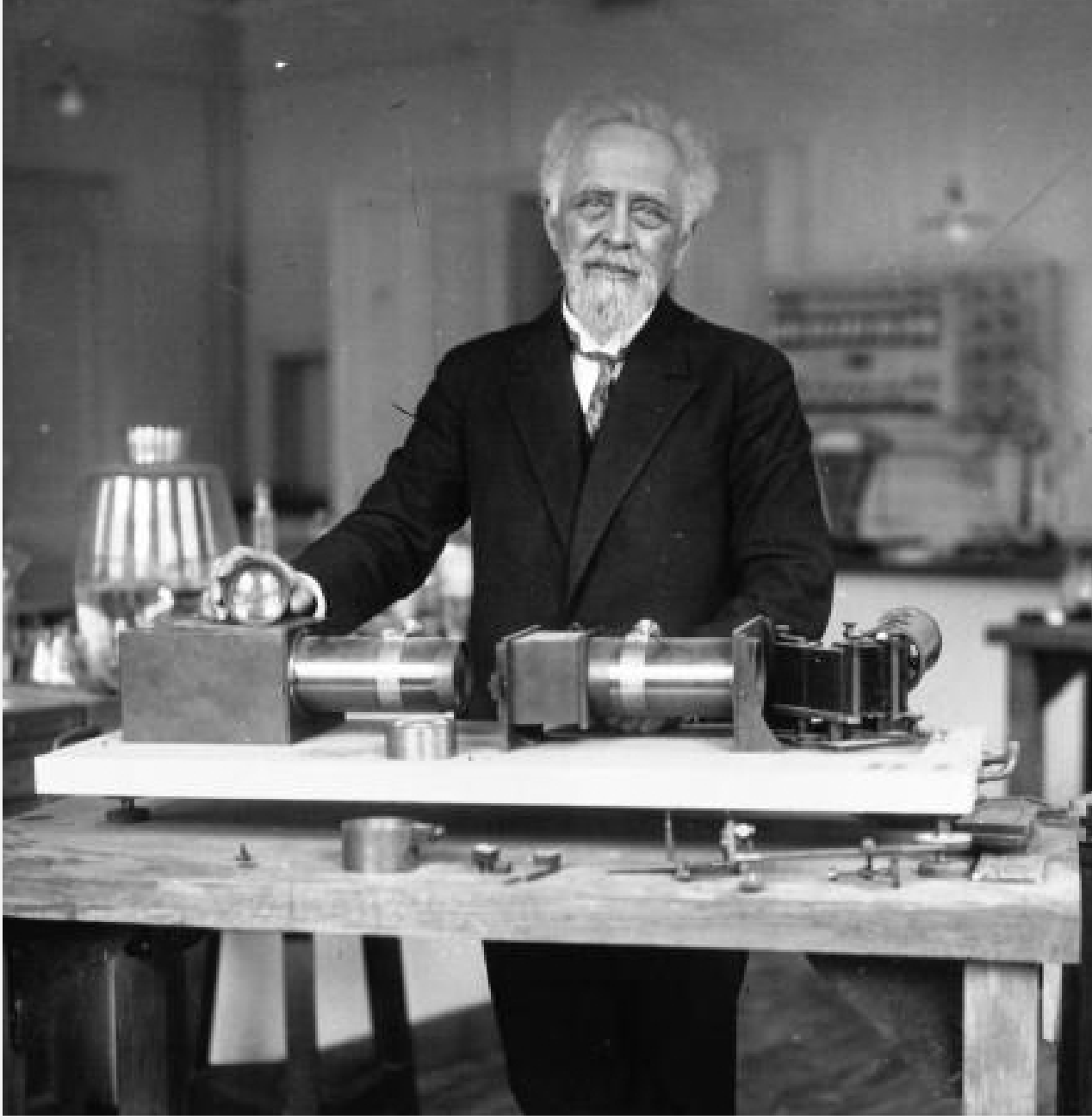
on the particles contained in the pollen of plants; and on the general existence of *active molecules* in organic and inorganic bodies

Grains of pollen, taken from *Clarkia pulchella* antherae fully grown but before bursting, were filled with particles or granules of unusually large size, varying from nearly 1/4000th to 1/5000th of an inch in length . . .

Rocks of all ages, including those in which organic remains have never been found, yielded the molecules in abundance. Their existence was ascertained in each of the constituent molecules of granite, a fragment of the Sphinx being one of the specimens examined.

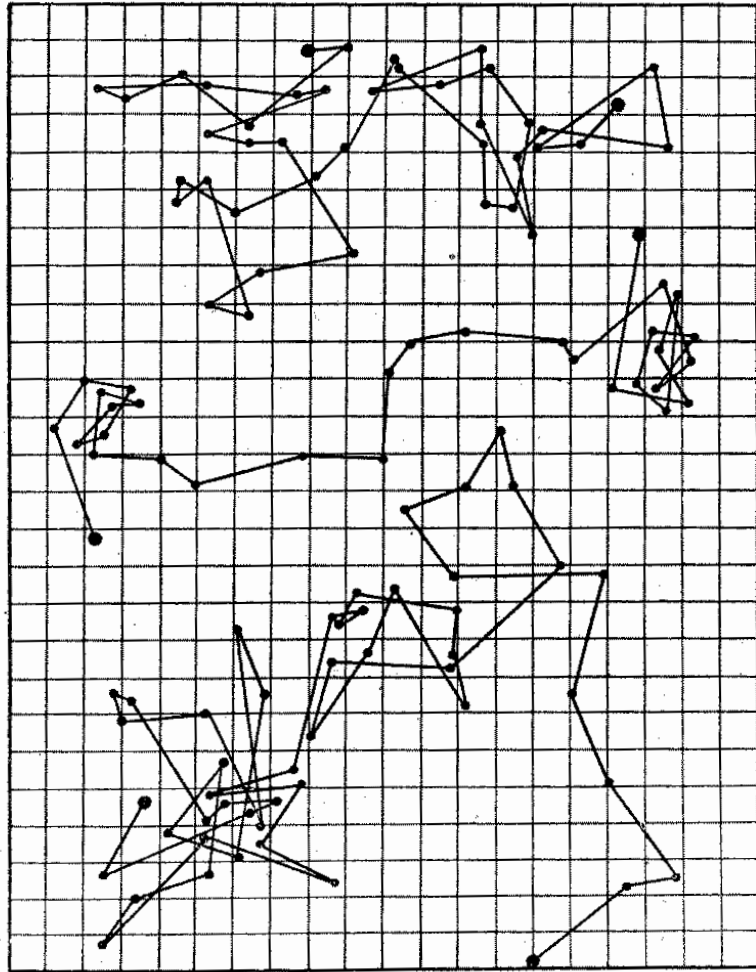


110+ years after Jean Perrin



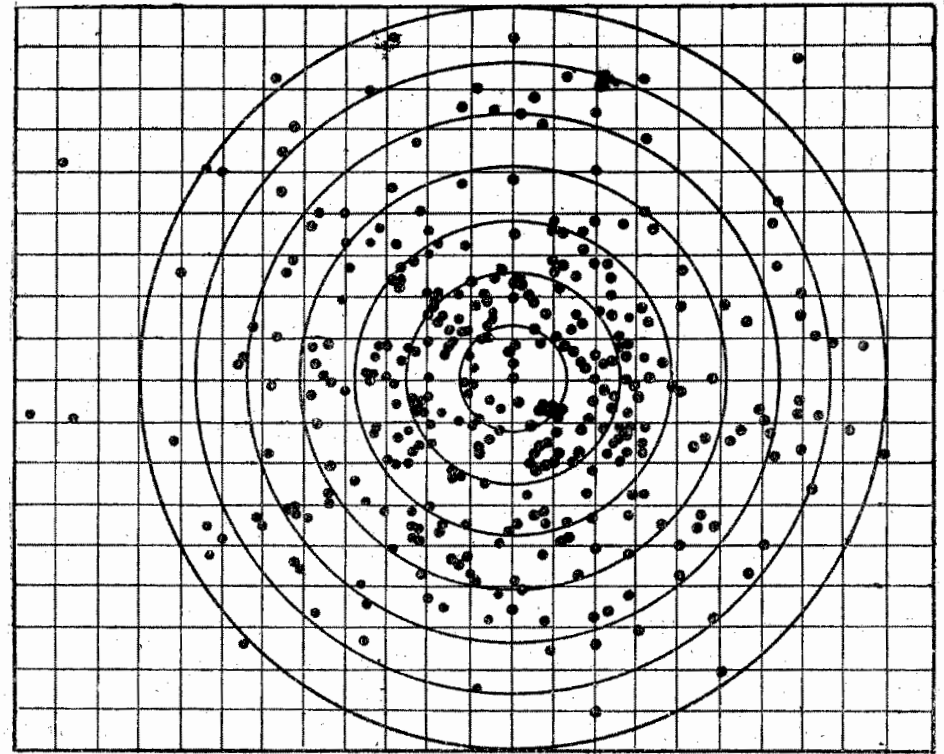
Brownian motion

Fig. 6.



$\Delta t = 30 \text{ sec}$

Fig. 7.



$$P(\mathbf{r}, \Delta t) = \frac{1}{(4\pi K \Delta t)^{d/2}} \exp\left(-\frac{r^2}{4K \Delta t}\right)$$

Einstein-Smoluchowski relation ($\langle r^2(t) \rangle = 2dKt$):

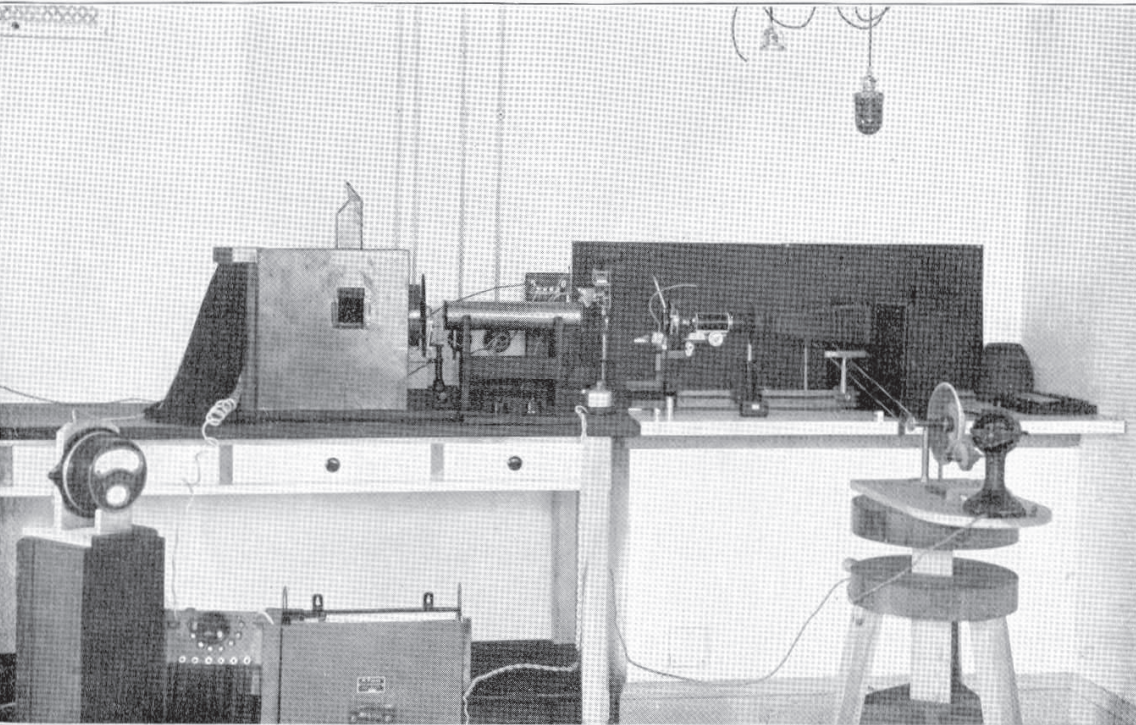
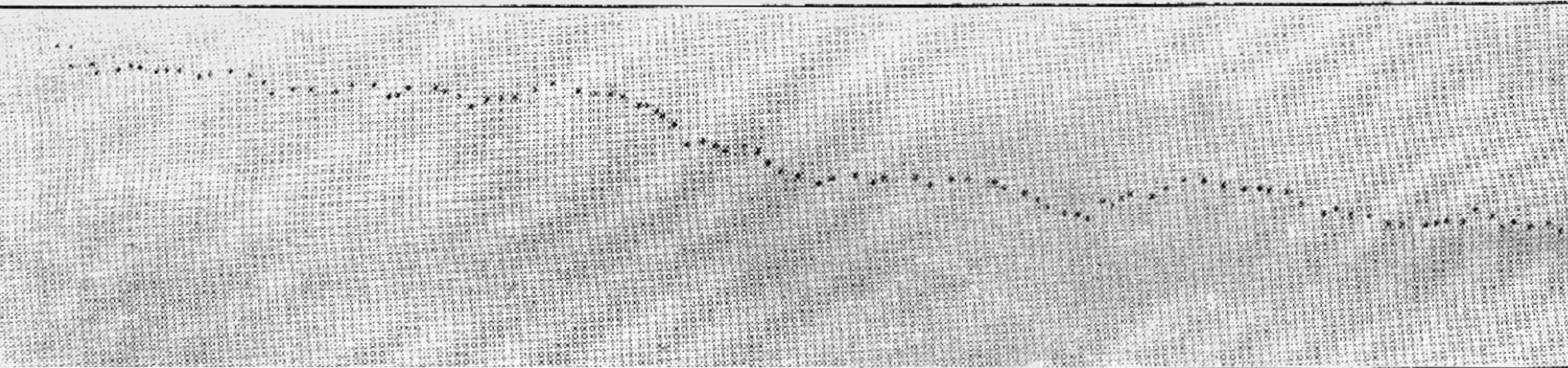
$$K = \frac{k_B T}{m\eta} = \frac{(R/N_A)T}{m\eta}$$

Ivar Nordlund (1887-1918)



Verksam ved fysikalisk-kemiska institutionen vid Uppsala universitet. Arbetade även som amatörfotograf. Svåger till A Hamberg 5

Ivar Nordlund: 100+ years of SPT with time series analysis



I Nordlund, Z Physik (1914): $N_A = 5.91 \times 10^{23}$

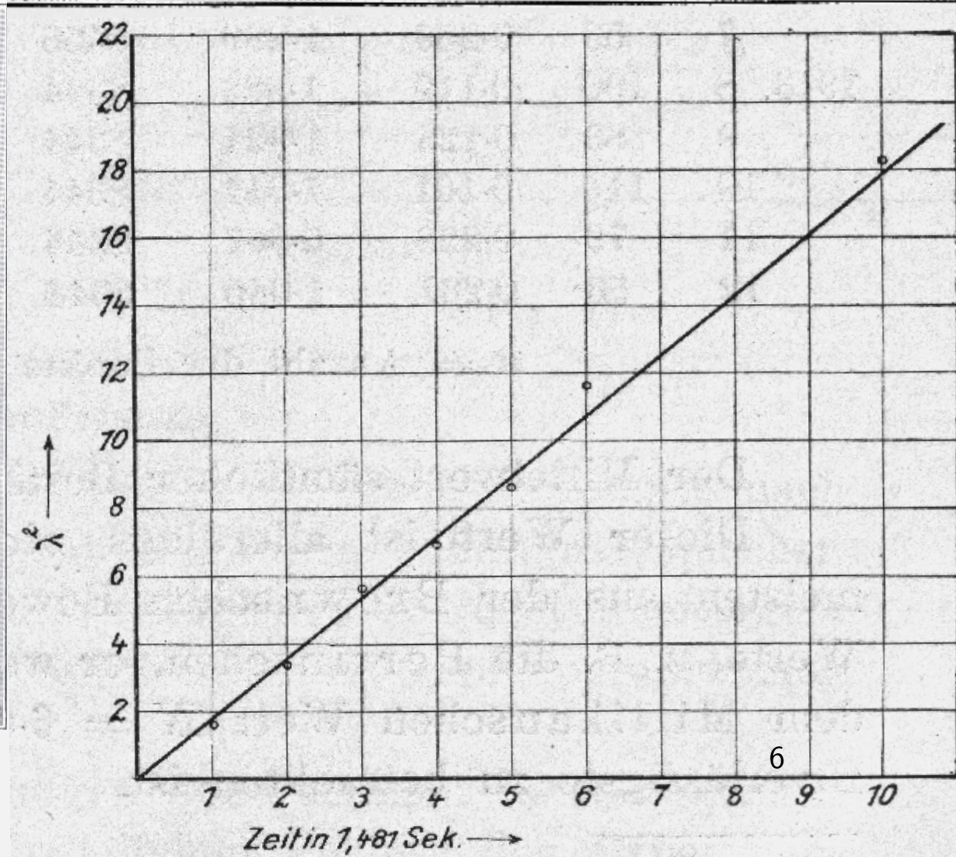


Fig. 11.

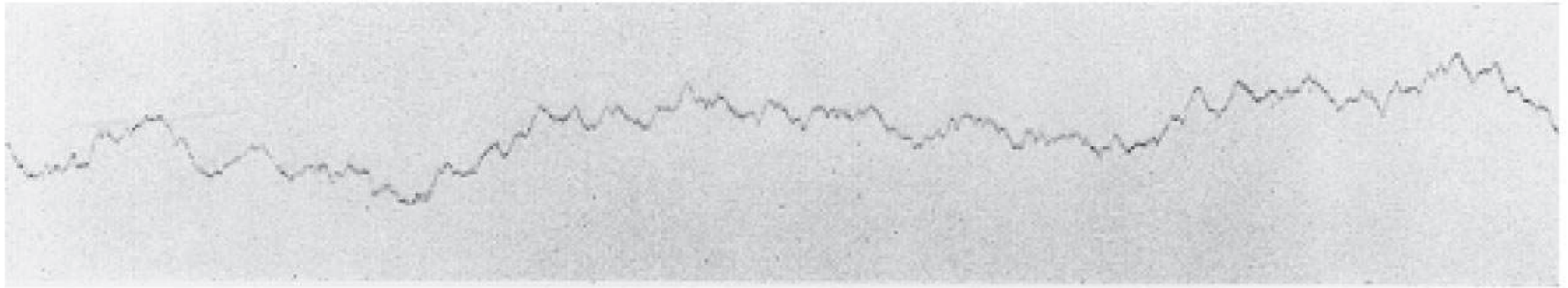
Eugen Kappler (1905-1977)



Obituary by L Reimer, Physikalische Blätter Feb 1978 pp 86

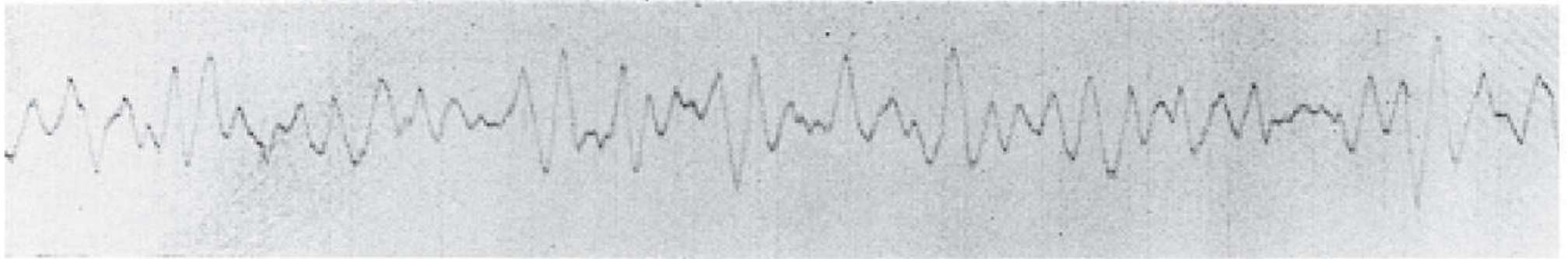


Eugen Kappler: ultimate diffusion measurements



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

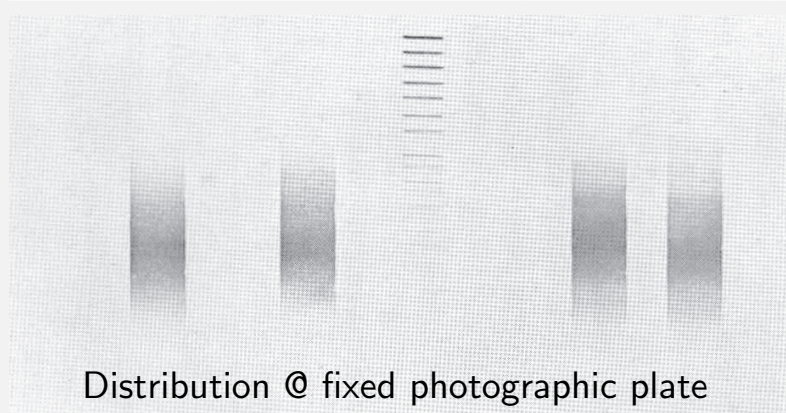
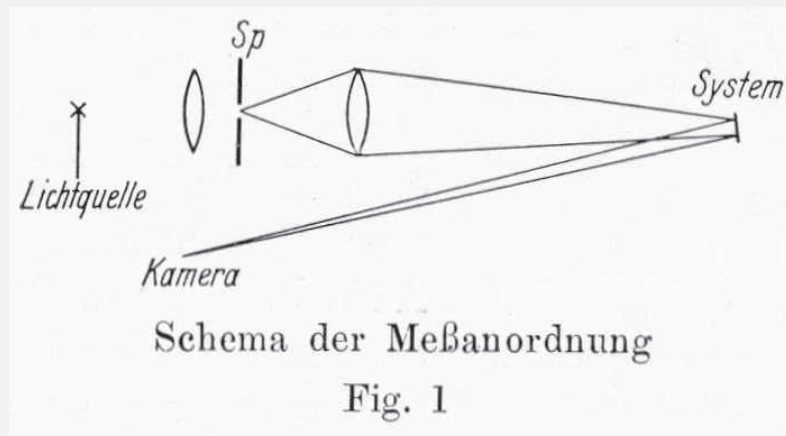
Fig. 5 a



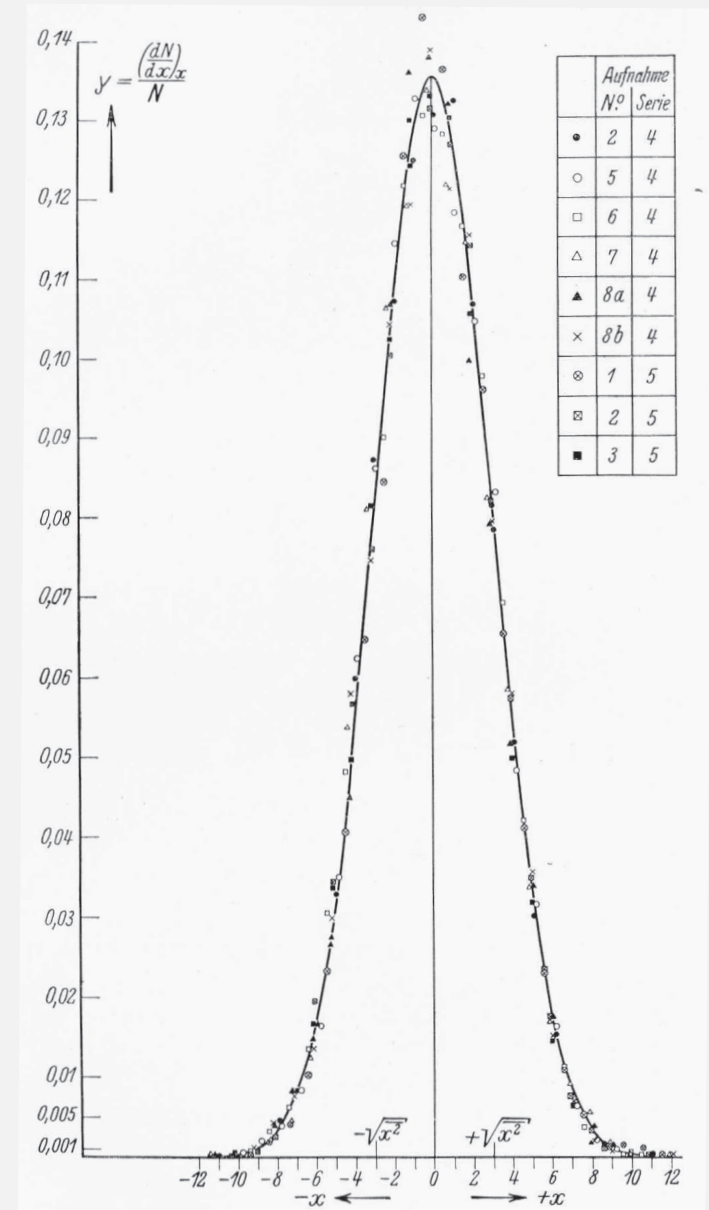
Registrieraufnahme der Brownschen Bewegung (natürliche Größe).
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Zeitmarke: 30 sec $dx = 1$ mm. b) $1 \cdot 10^{-3}$ mm Hg. Temperatur 13° C

Fig. 5 b

Kappler's diffusion measurements: mapping Boltzmann



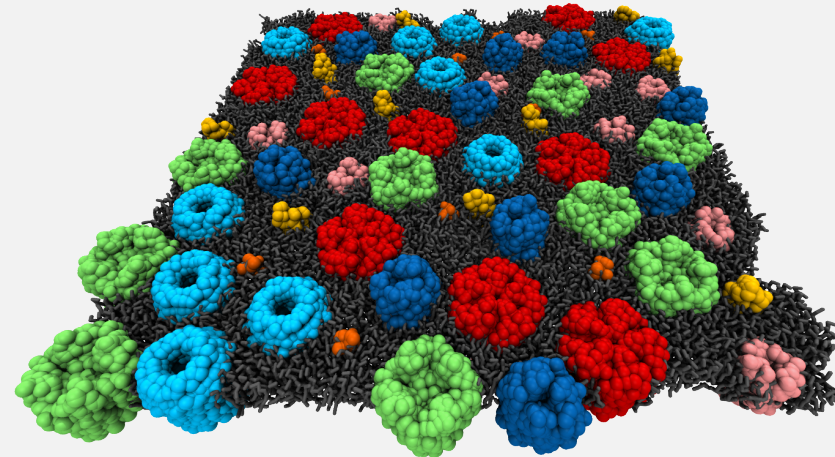
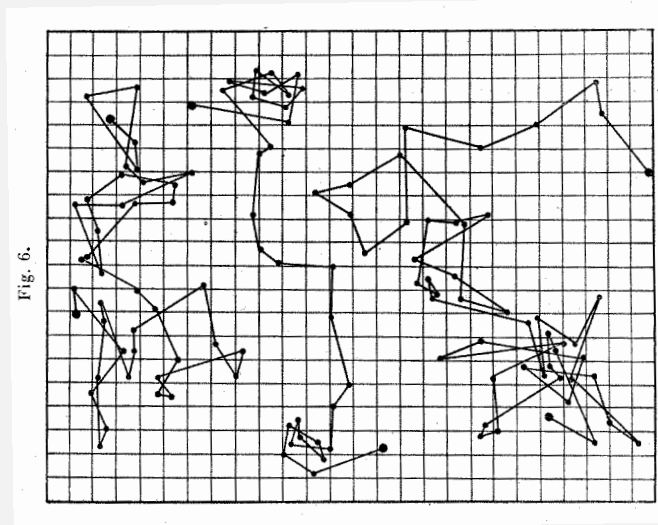
$$P_{\text{eq}}(x) = \mathcal{N} \exp\left(-\frac{\theta x^2}{k_B T}\right)$$



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

Stochastic processes in 2019: why should we care?

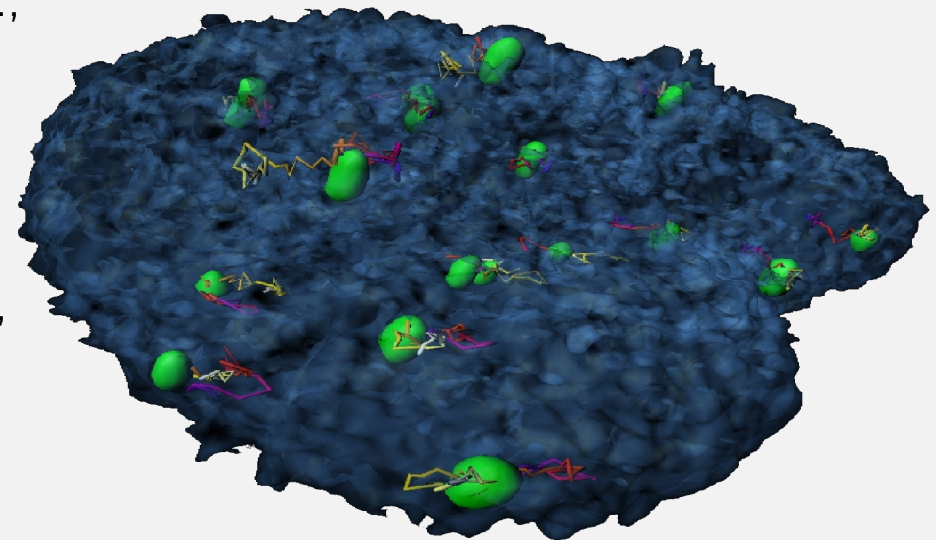
Jean Perrin (1908)



Courtesy Matti Javanainen

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

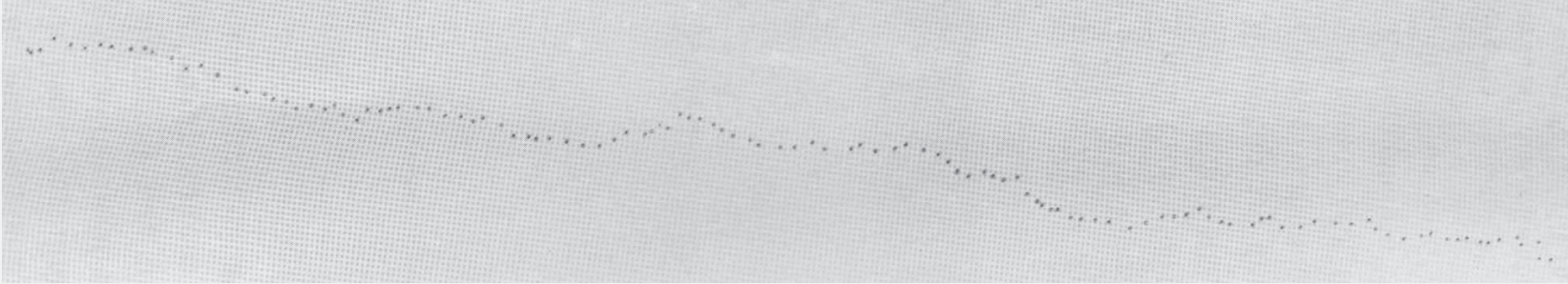
- ↪ Normal diffusion /w random parameters
- ↪ Anomalous diffusion of all sorts
- ↪ New physics: time averages, (non)ergodicity, ageing, non-Gaussianity
- ↪ Information from fluctuations
- ↪ Data analysis strategies



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

Courtesy Yuval Garini

Extracting information from single Brownian trajectories



Ensemble averaged MSD for normal diffusion (on average # jumps \sim elapsed time t):

$$\langle \mathbf{r}^2(t) \rangle = \int \mathbf{r}^2 P(\mathbf{r}, t) d\mathbf{r} = 2dK_1 t \quad \left(= \langle \delta \mathbf{r}^2 \rangle \frac{t}{\tau}, \quad K_1 = \frac{\langle \delta \mathbf{r}^2 \rangle}{2d\tau} \right)$$

Single particle trajectory $\mathbf{r}(t)$, $t \in [0, T]$:

$$\overline{\delta^2(t)} = \frac{1}{T-t} \int_0^{T-t} [\mathbf{r}(t'+t) - \mathbf{r}(t')]^2 dt' = \frac{1}{T-t} \int_0^{T-t} \langle \delta \mathbf{r}^2 \rangle \frac{t}{\tau} dt'$$

Single trajectory information equals ensemble information (*Boltzmann-Khinchin*):

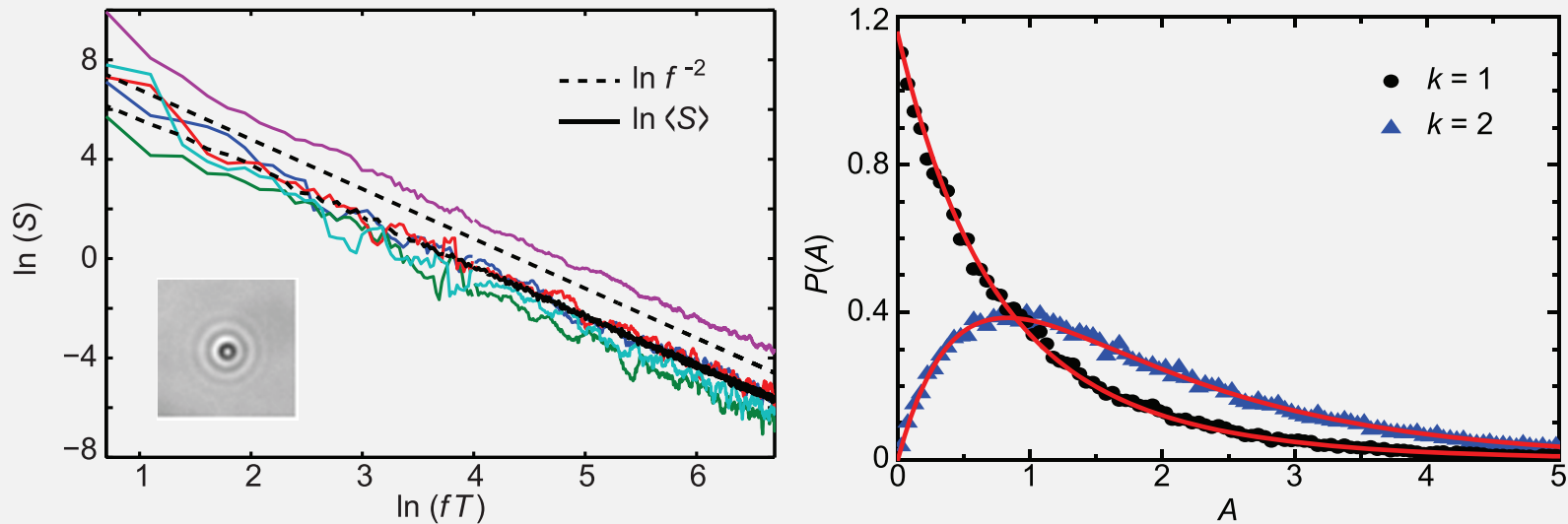
$$\lim_{T \rightarrow \infty} \overline{\delta^2(t)} = 2dK_1 t = \langle \mathbf{r}^2(t) \rangle$$

Anomalous diffusion is not always ergodic (weak or strong violation):

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

WEB: signature of non-stationarity of process. SEB: discontinuity of phase space

Power spectral density of a single Brownian trajectory



Standard ensemble-averaged power spectrum à la textbook definition:

$$\mu_S(f) = \lim_{T \rightarrow \infty} \langle S(f, T) \rangle$$

Single trajectory power spectrum suitable for finite-length & few trajectories:

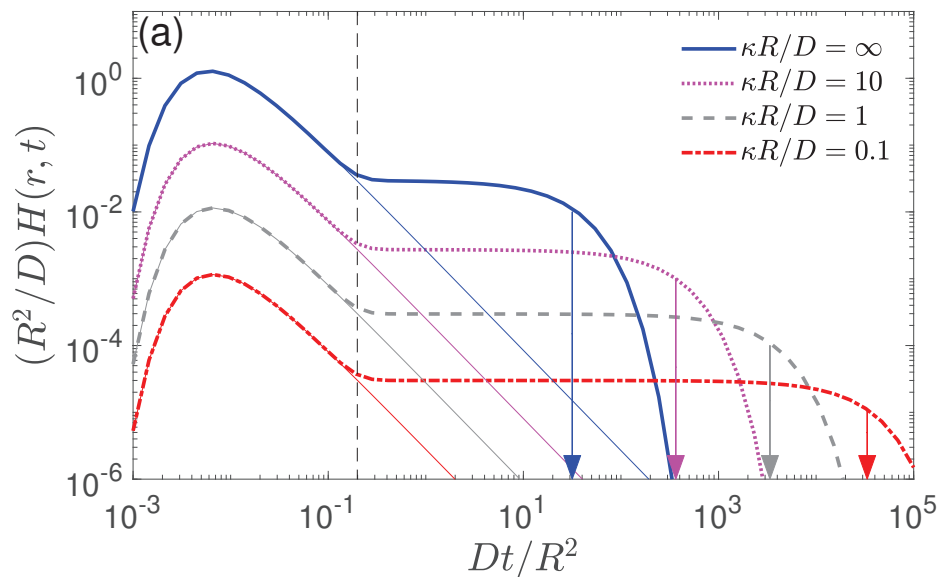
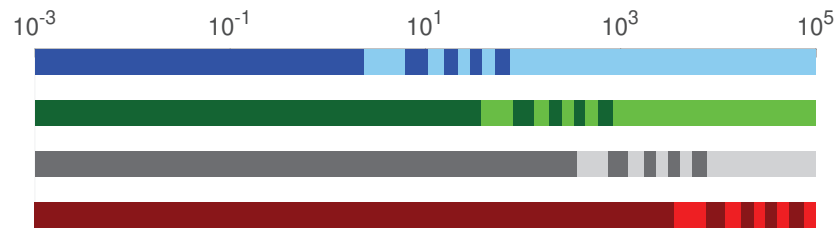
$$S(f, T) = \frac{1}{T} \left| \int_0^T \exp(i f t) X_t dt \right|^2$$

Strongly defocused reaction times: geometry/reaction control

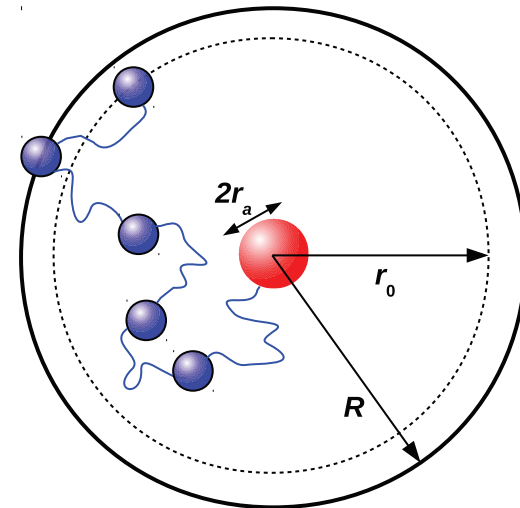
Mean/global mean first passage & cover times: O Bénichou, R Voituriez et al.: Nature (2007), Nature Phys (2008), Nature Chem (2010), Nature Phys (2015)

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

Full first passage time density:

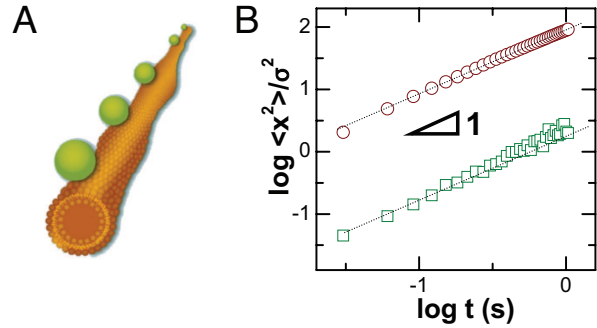


Direct vs indirect trajectories:

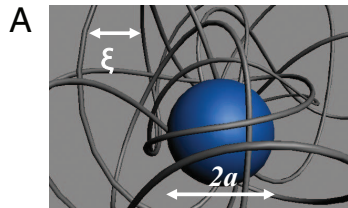
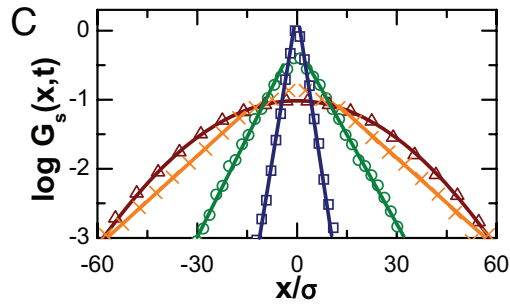


$$\langle t \rangle = \frac{(r_0 - r_a)(2R^3 - r_0 r_a [r_0 + r_a])}{6D r_0 r_a} + \frac{R^3 - r_a^3}{3\kappa r_a}$$

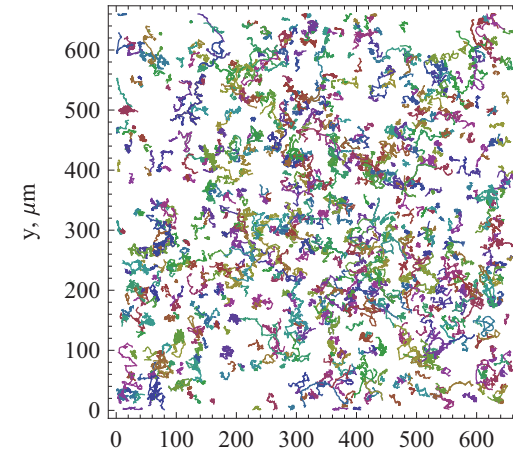
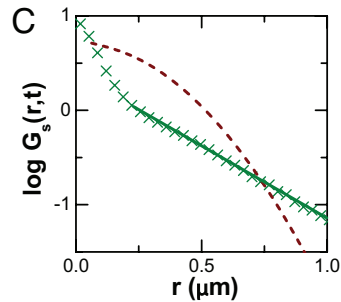
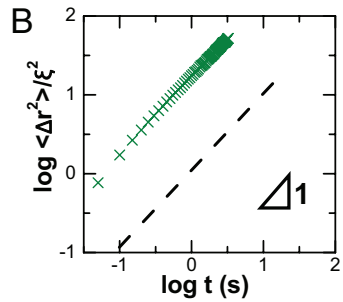
When Brownian diffusion is not Gaussian



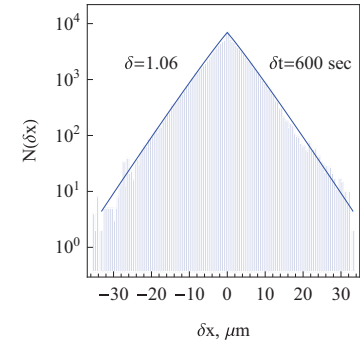
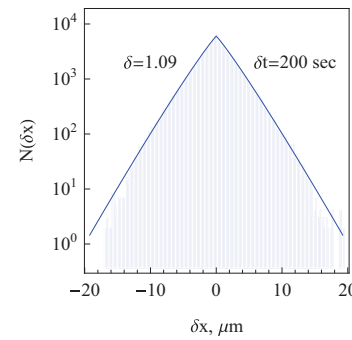
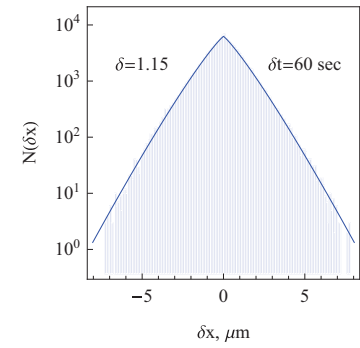
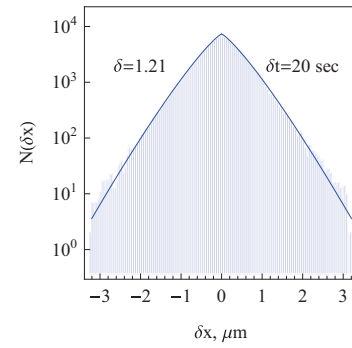
Colloidal beads on nanotubes



Nanospheres in entangled actin



Motion of dictyostelium cells



Fickian, non-Gaussian diffusion with diffusing diffusivity

B Wang, J Kuo, SC Bae & S Granick, Nat Mat (2012): $\langle x^2(t) \rangle = 2K_1t$, 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)]

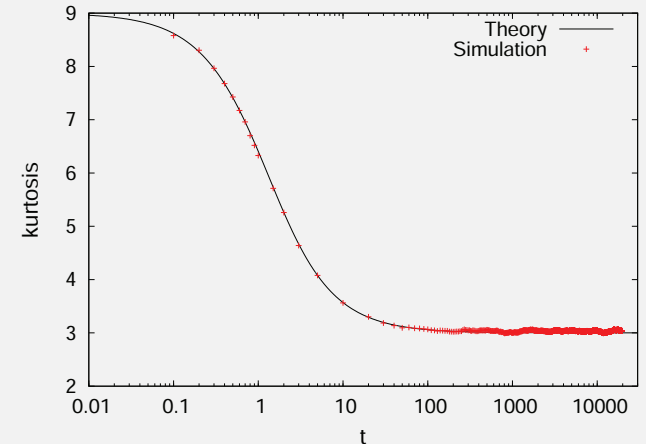
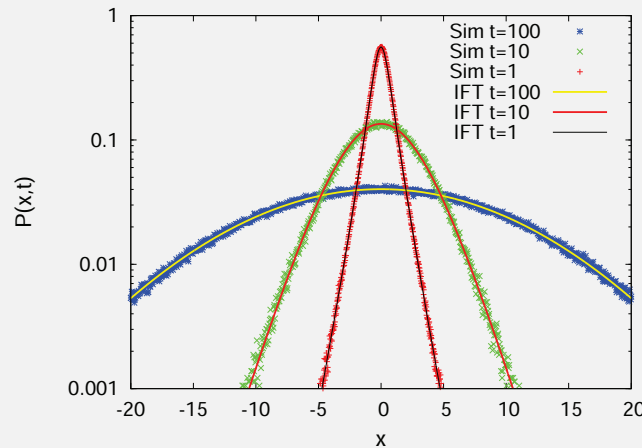
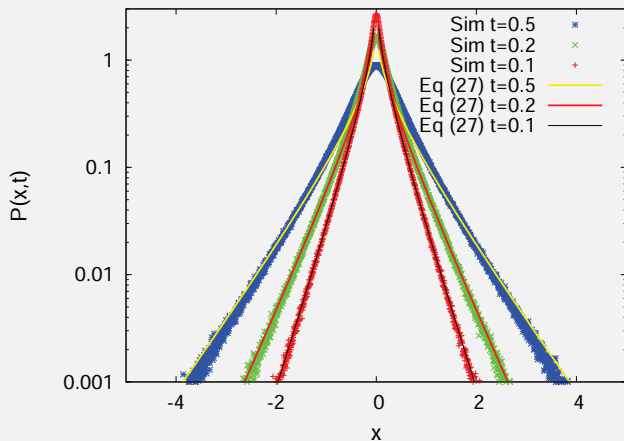
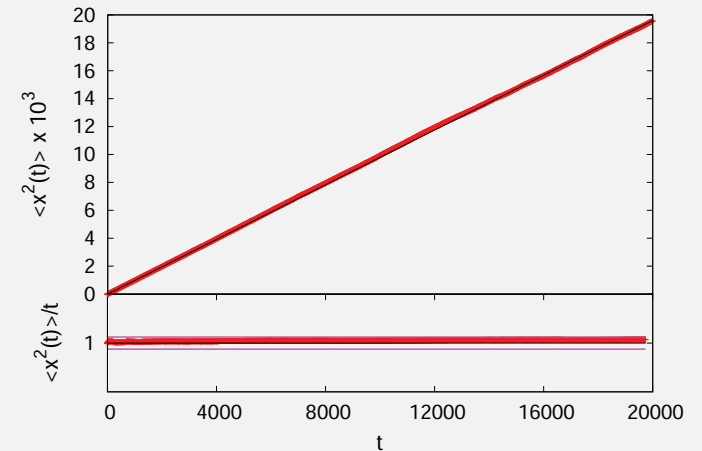
MV Chubinsky & G Slater, PRL (2014): diffusing diffusivity
 [see also R Jain & KL Sebastian, JPC B (2016)]

Our minimal model for diffusing diffusivity:

$$\dot{x}(t) = \sqrt{2D(t)}\xi(t)$$

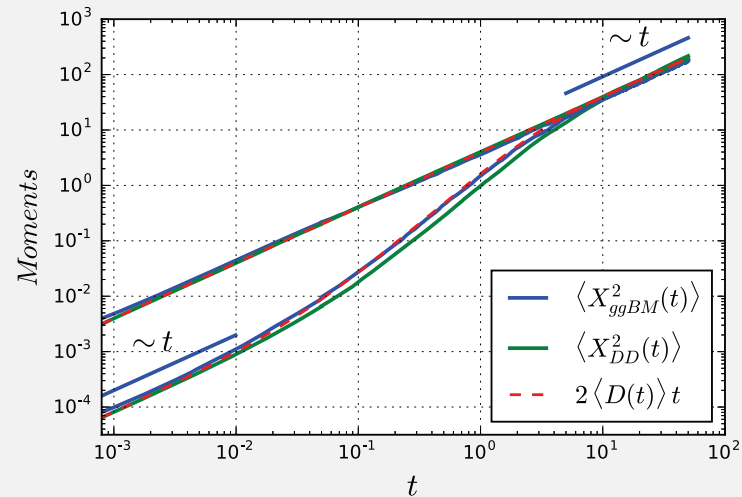
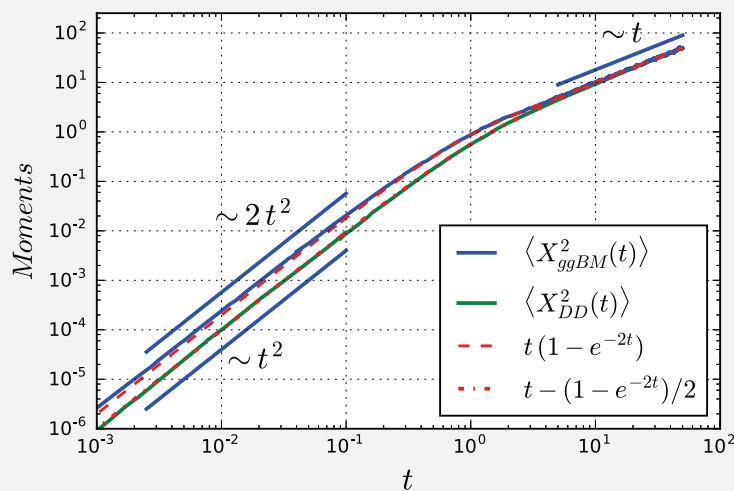
$$D(t) = y^2(t)$$

$$\dot{y}(t) = -\tau^{-1}y + \sigma\eta(t)$$

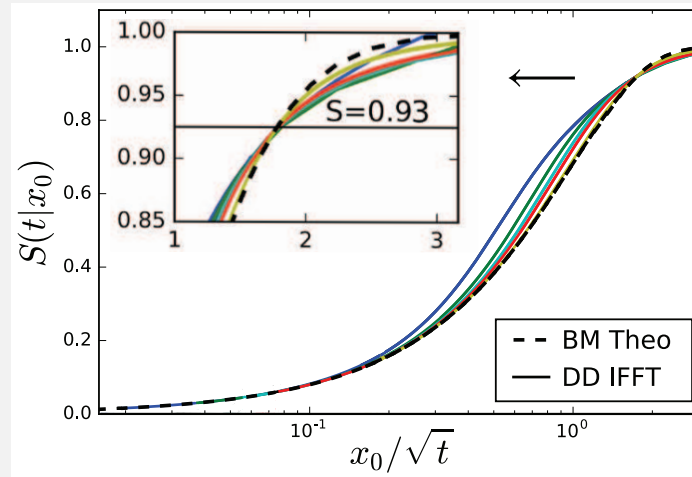
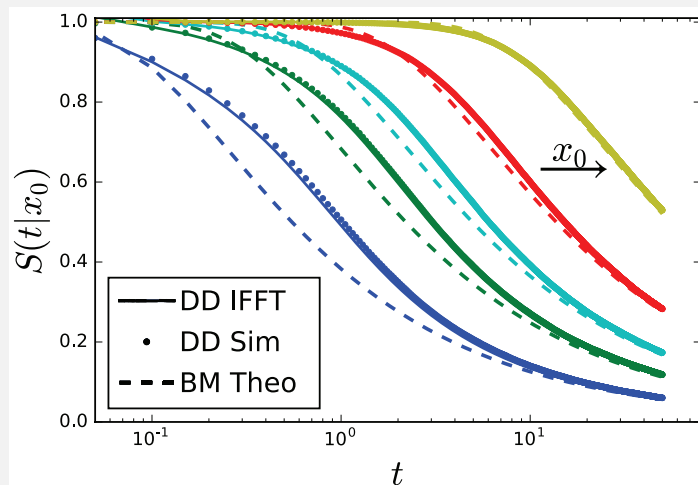


AV Chechkin, F Seno, RM & IM Sokolov, PRX (2017); generalised $\gamma(D)$: V Sposini, AV Chechkin, G Pagnini, F Seno & RM, NJP (2018)

Non-equilibrium initial conditions for $D(t)$ dynamics



First passage statistics for diffusing diffusivity



[See also Y Lanoiselée, N Moutal & D Grebenkov, Nat Comm (2019)]

V Sposini, AV Chechkin, G Pagnini, F Seno & RM, NJP (2018); V Sposini, AV Chechkin & RM, JPA (2019)

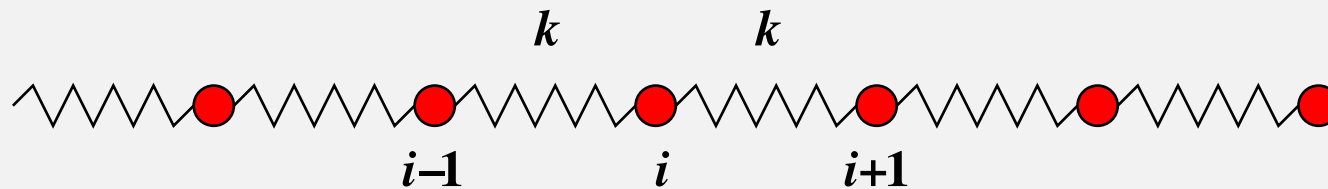
Fractional Langevin equations in viscoelastic systems

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

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

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

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



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

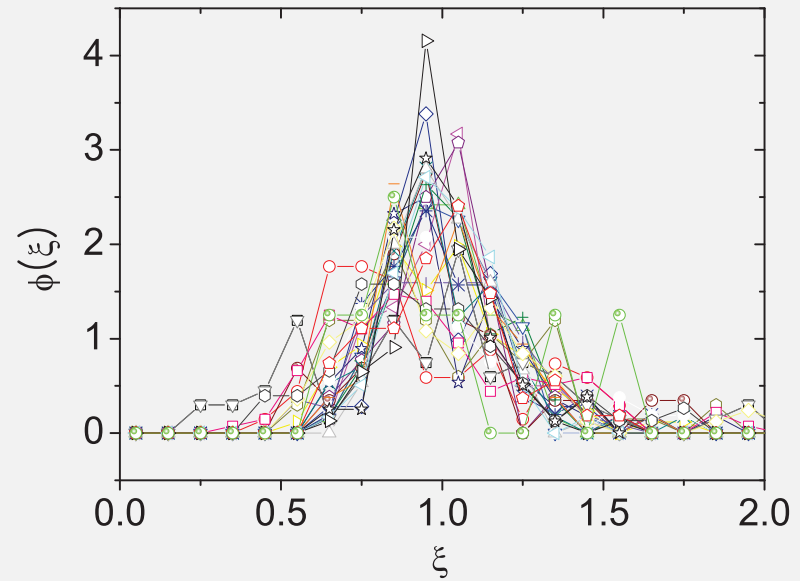
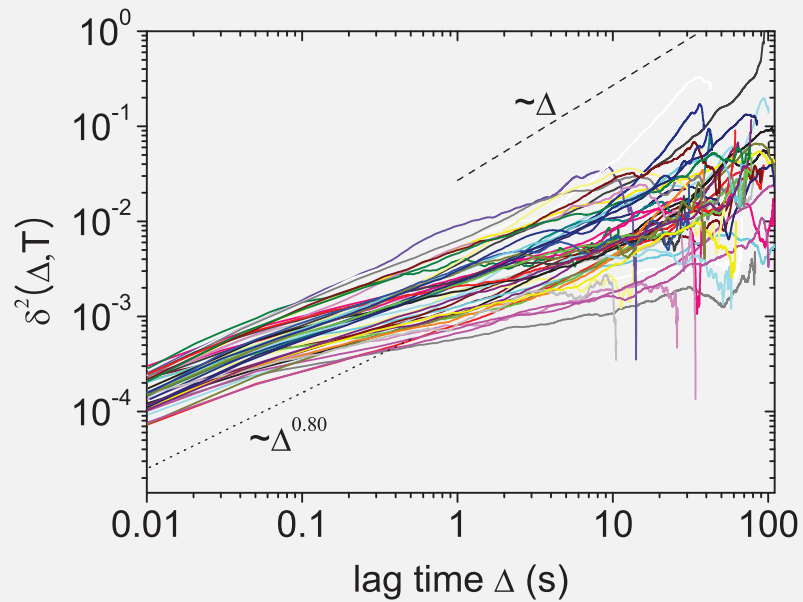
$$\langle \zeta_i(t) \zeta_j(t') \rangle = \delta_{ij} k_B T \eta(|t - t'|), \quad p(\eta) \text{ Gauss}$$

\leadsto fractional Langevin equation & anomalous diffusion: $\langle \mathbf{r}^2(t) \rangle \simeq t^2 \dots t^\alpha$

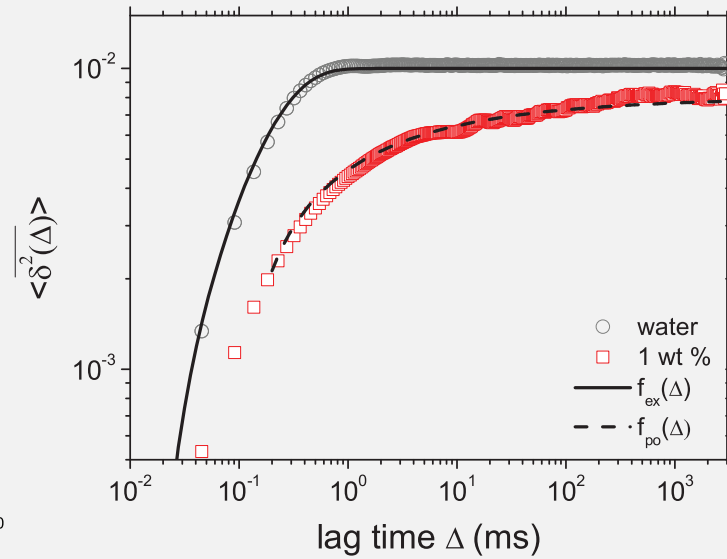
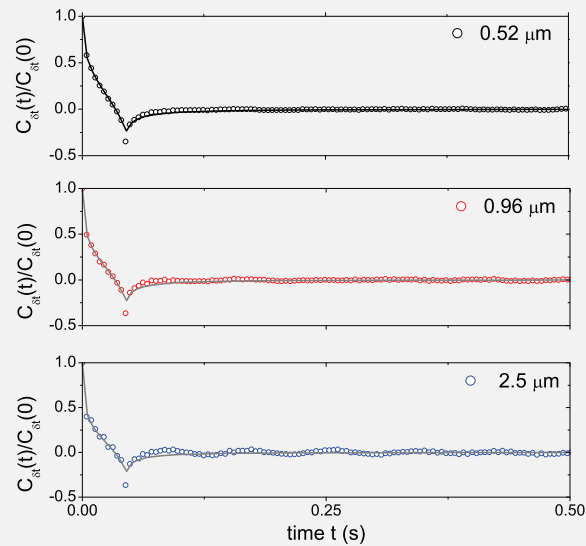
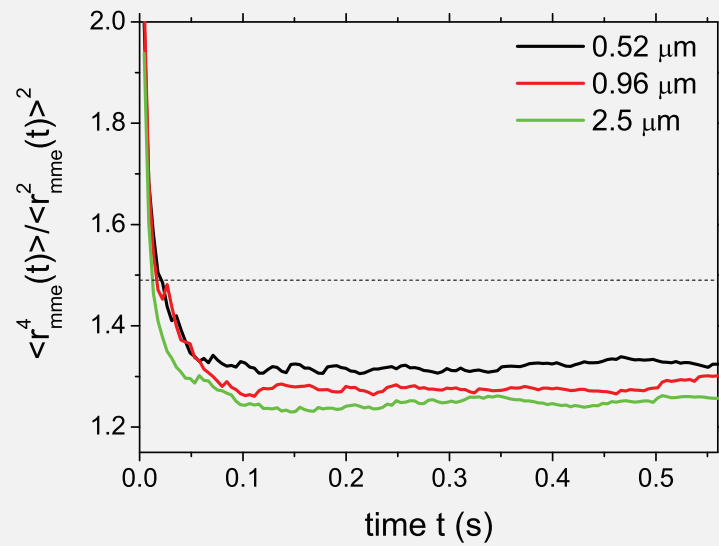
Quantum mechanics: Nakajima-Zwanzig equation using projection operators

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

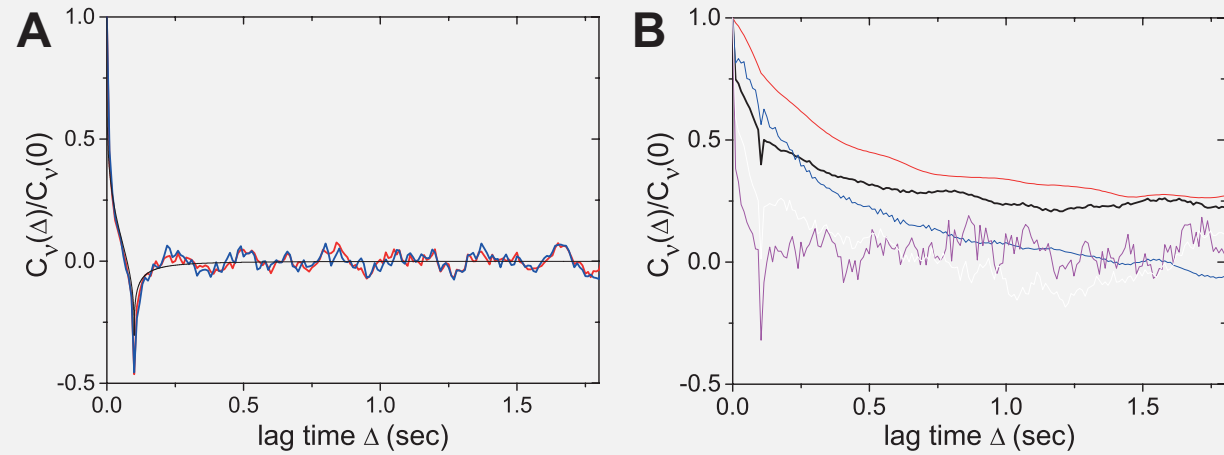
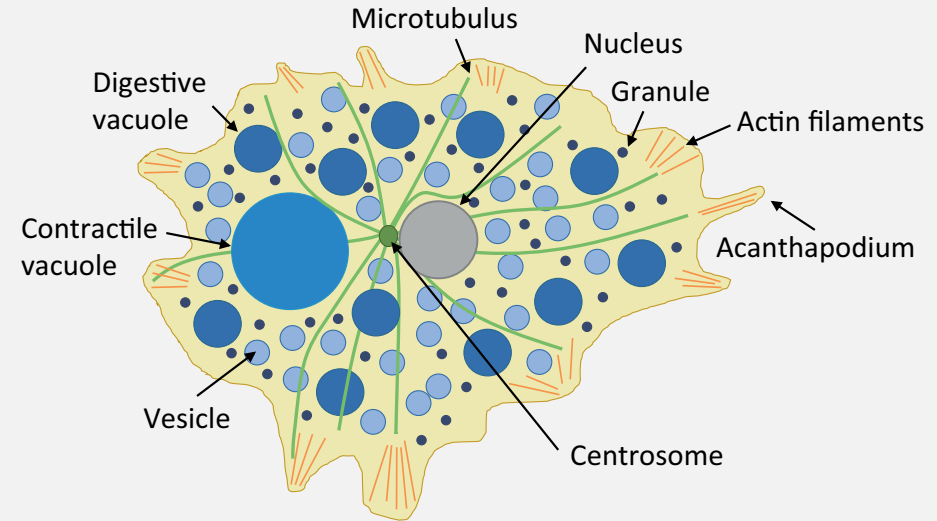
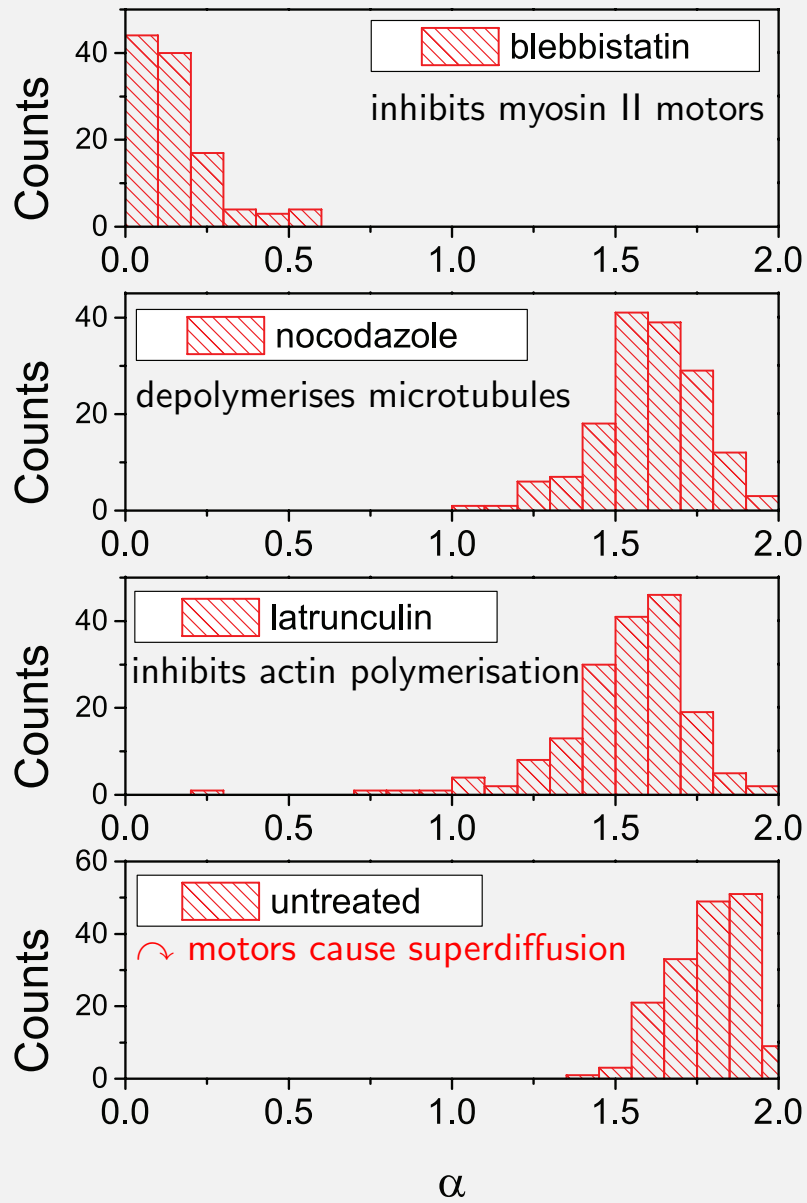
Passive motion of submicron tracers in cells is viscoelastic



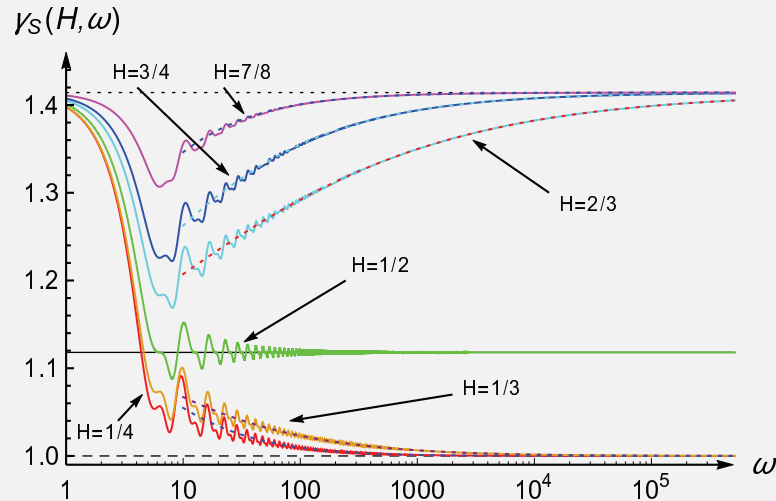
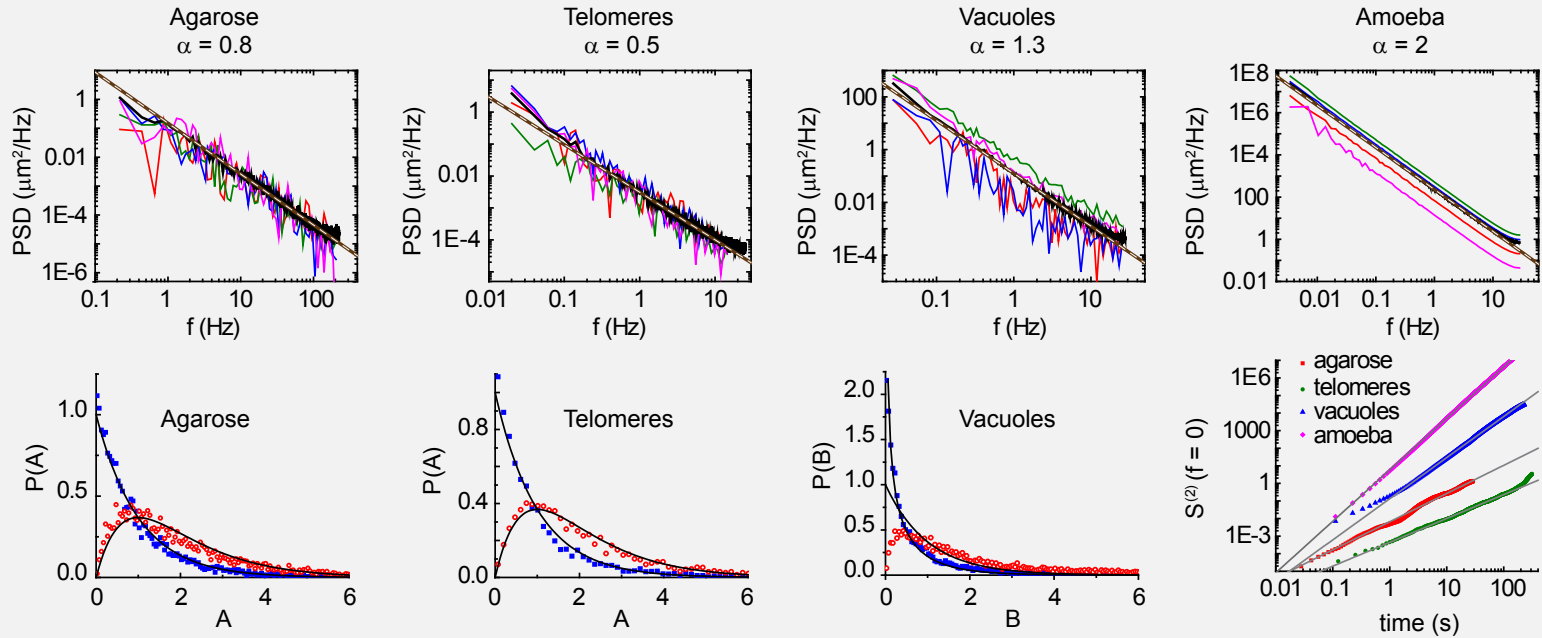
Lipid granules in living yeast cells ↓
 Tracer beads in wormlike micellar solution ↓



Superdiffusion in supercrowded *Acanthamoeba castellani*



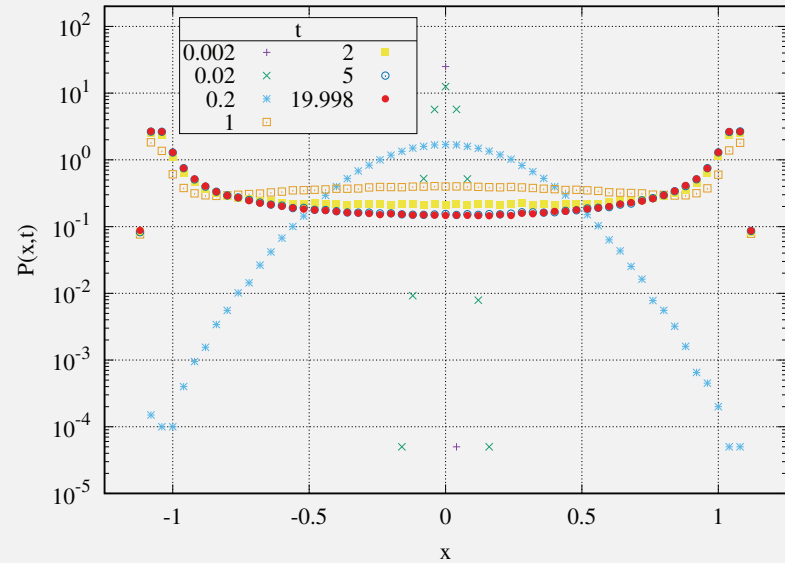
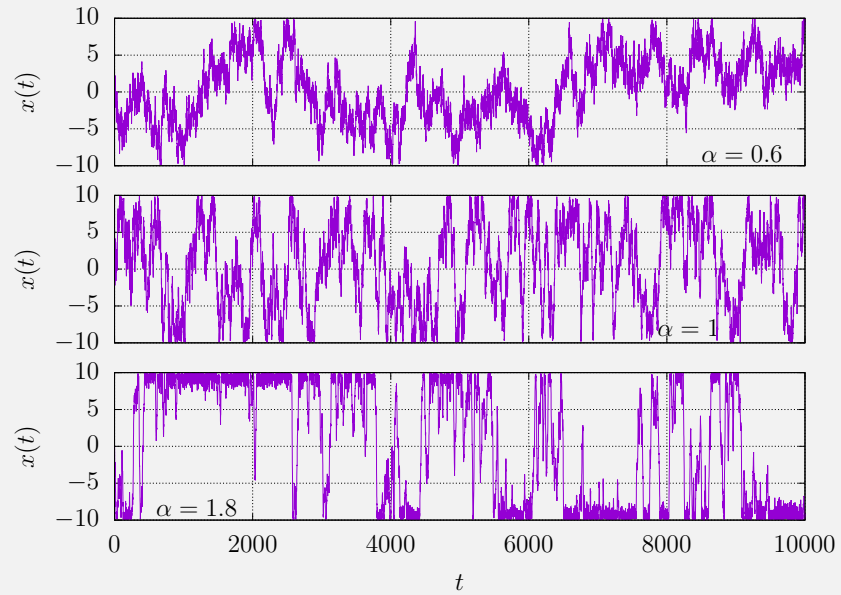
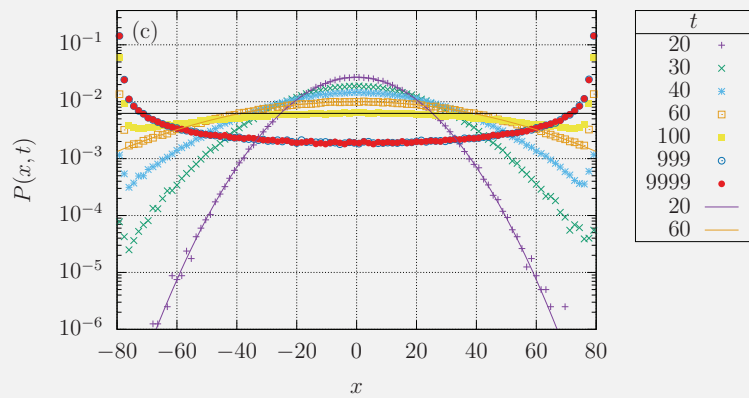
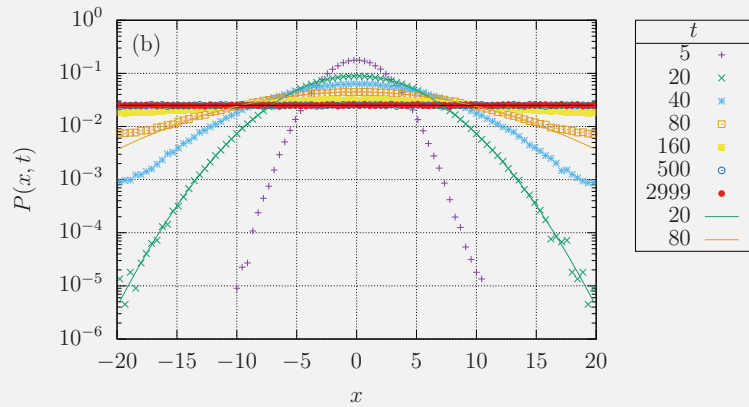
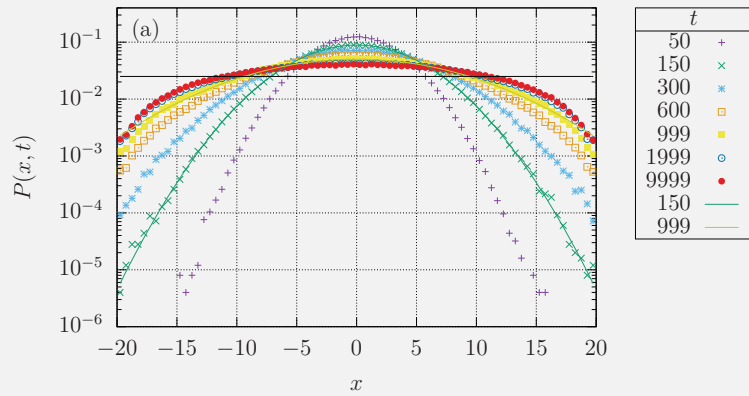
Power spectral density of a single FBM trajectory



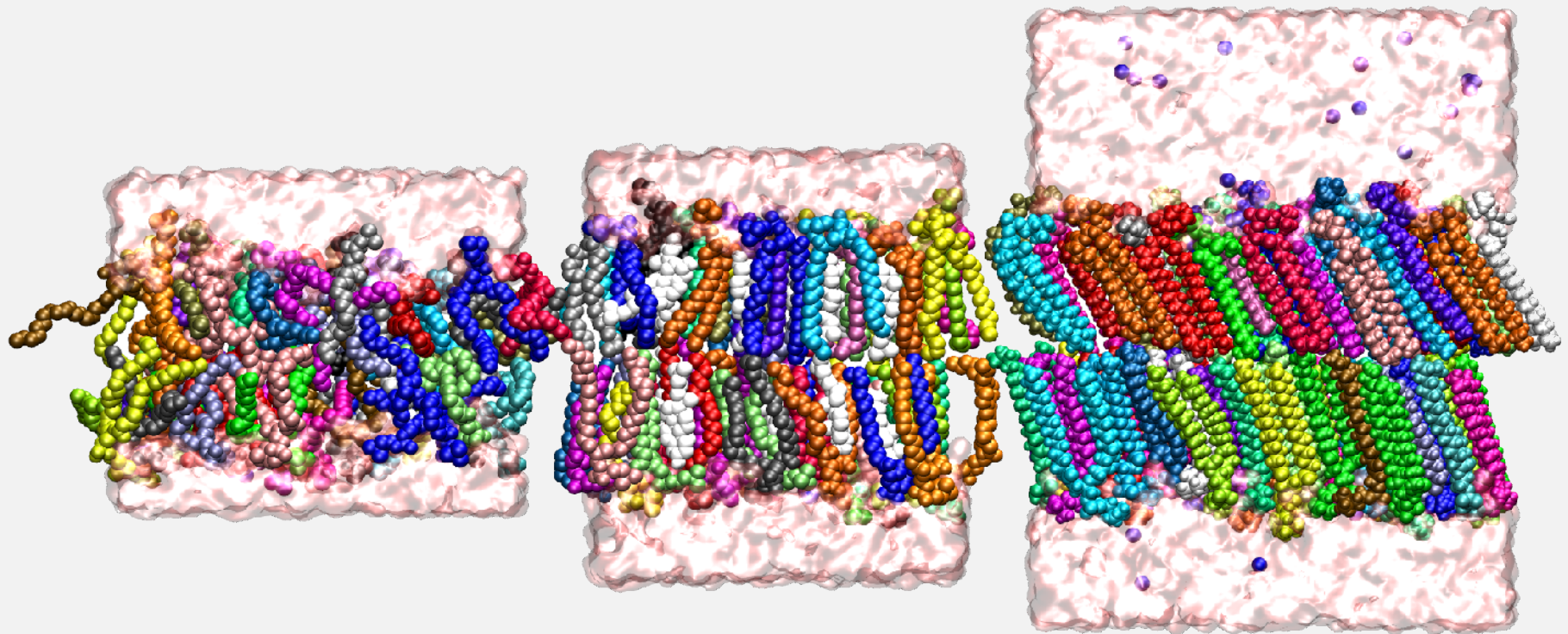
$$S(f, T) = \frac{1}{T} \left| \int_0^T \exp(ift) X_t dt \right|^2$$

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

FBM: accretion & depletion effects near boundaries



Single lipid motion in bilayer membrane MD simulations

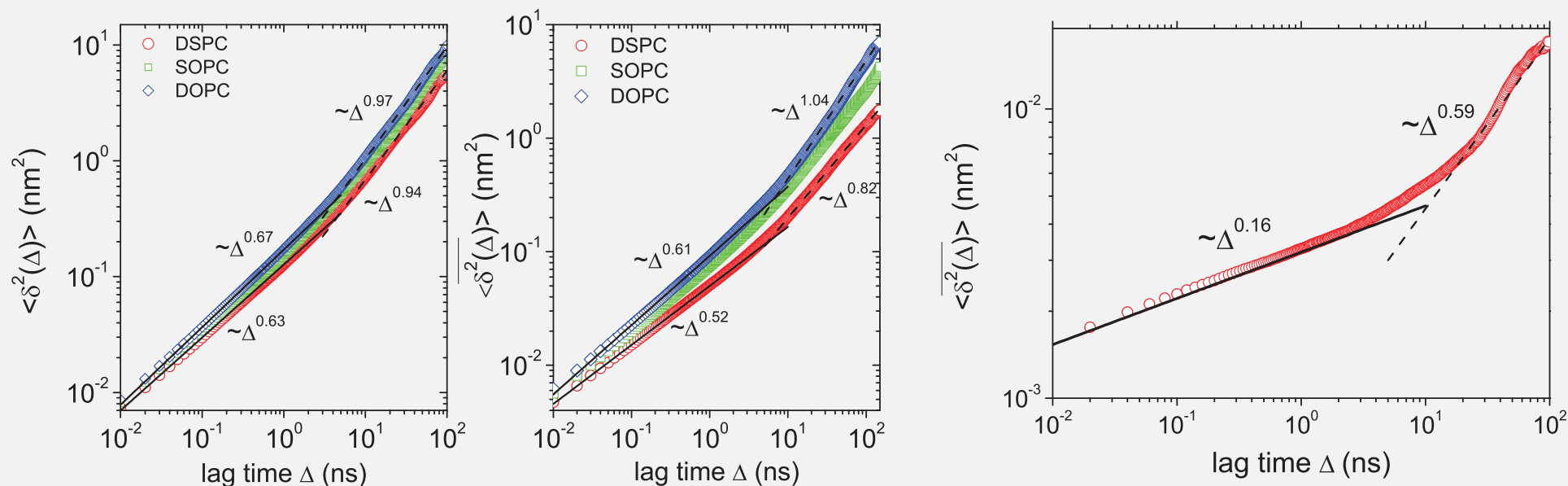


Liquid disordered

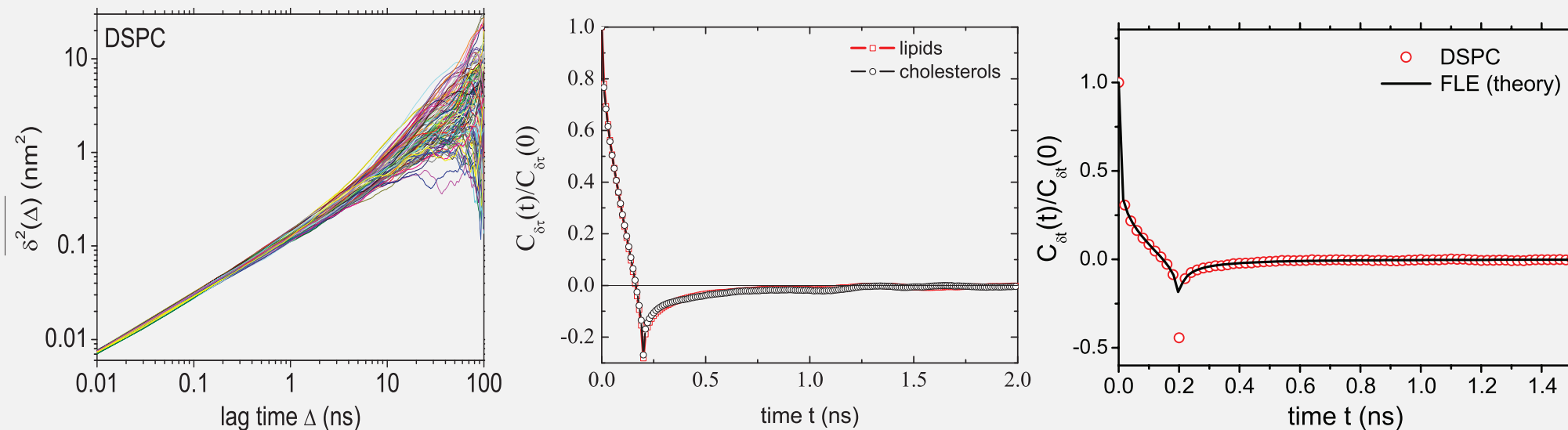
Liquid ordered

Gel phase

Liquid ordered/gel phases: extended anomalous diffusion



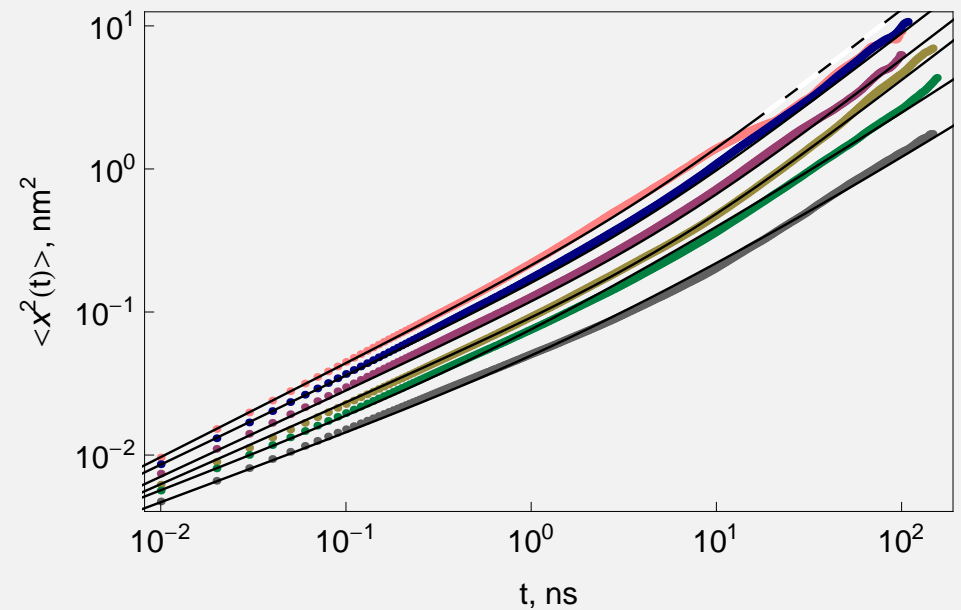
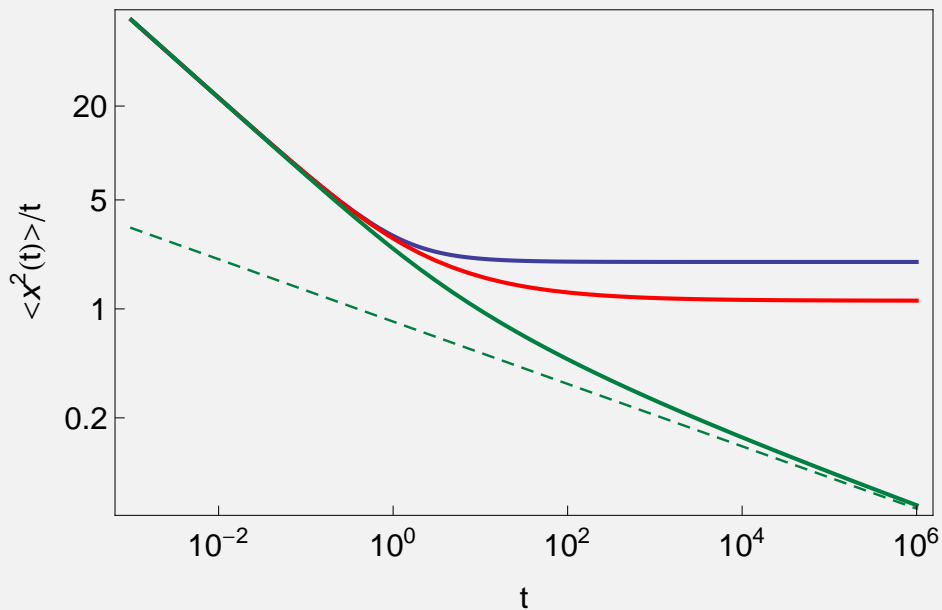
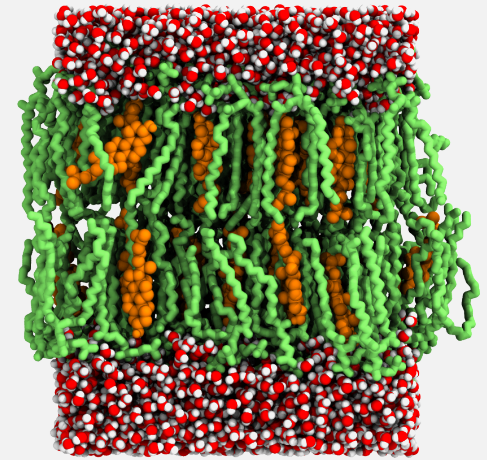
Reproducible TA MSD & antipersistent correlations



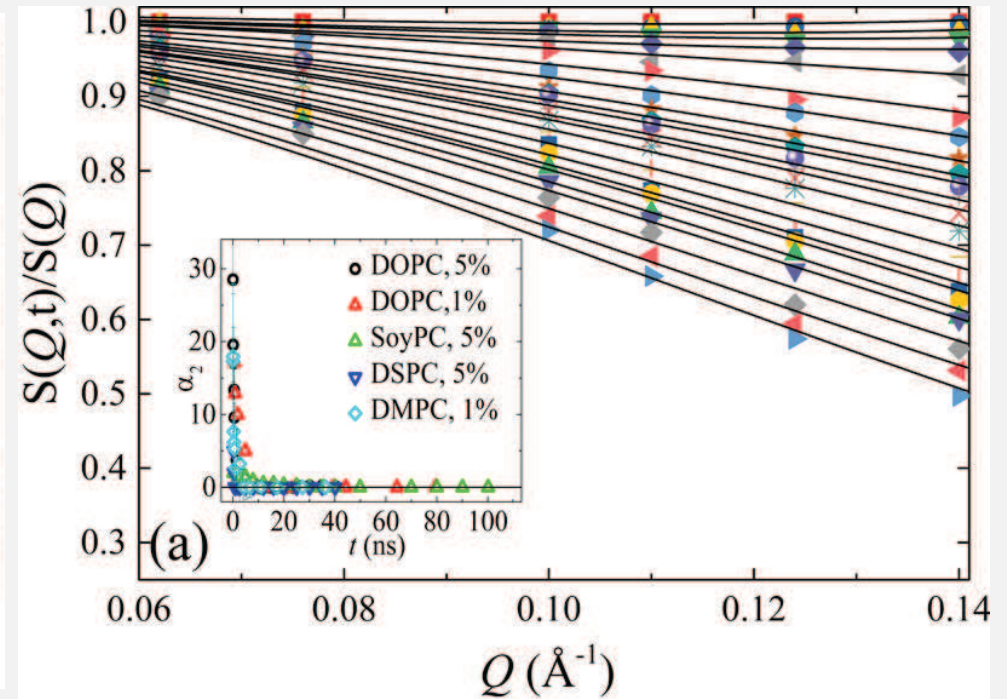
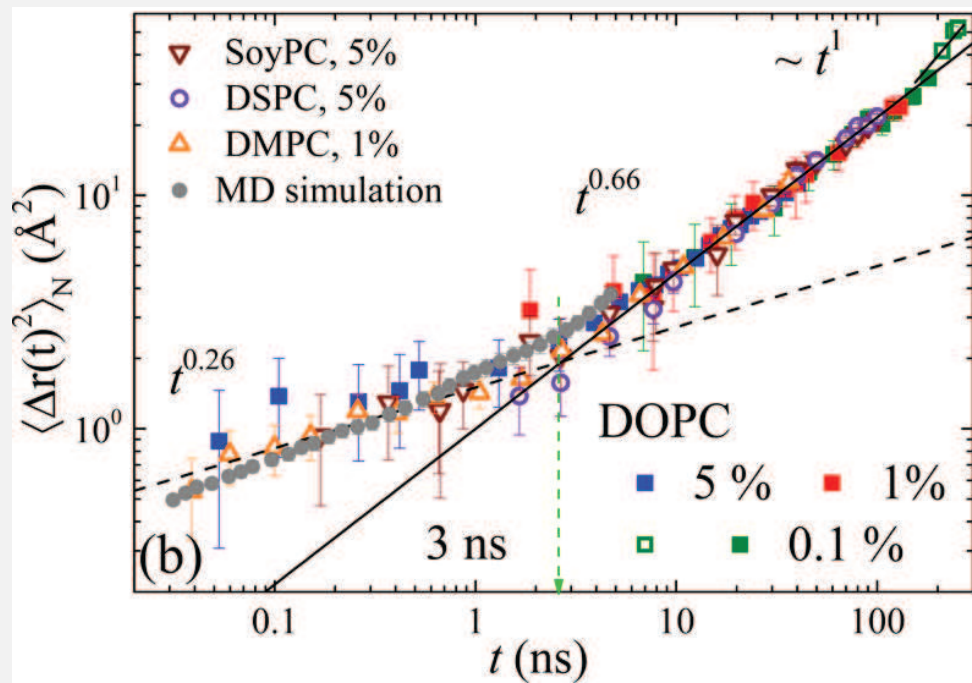
Tempered FLE motion: crossover to faster diffusion

Tempered fractional Gaussian noise:

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



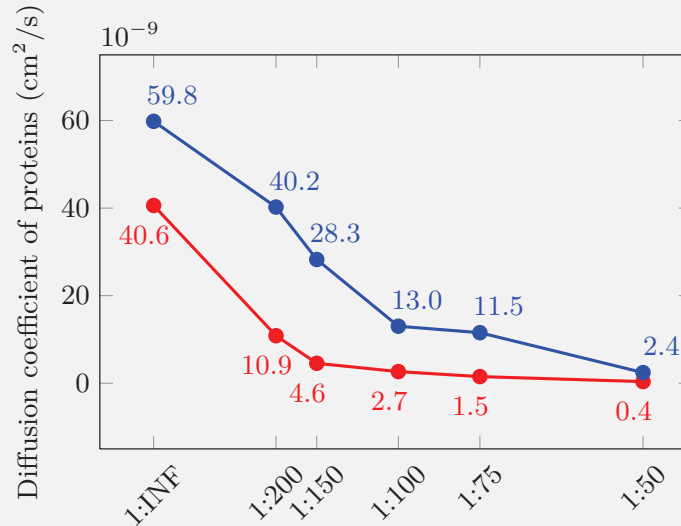
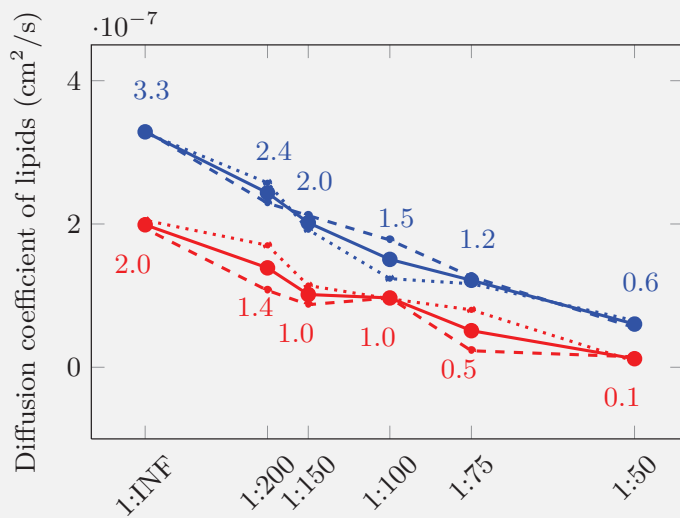
Extreme short time non-Gaussian subdiffusion



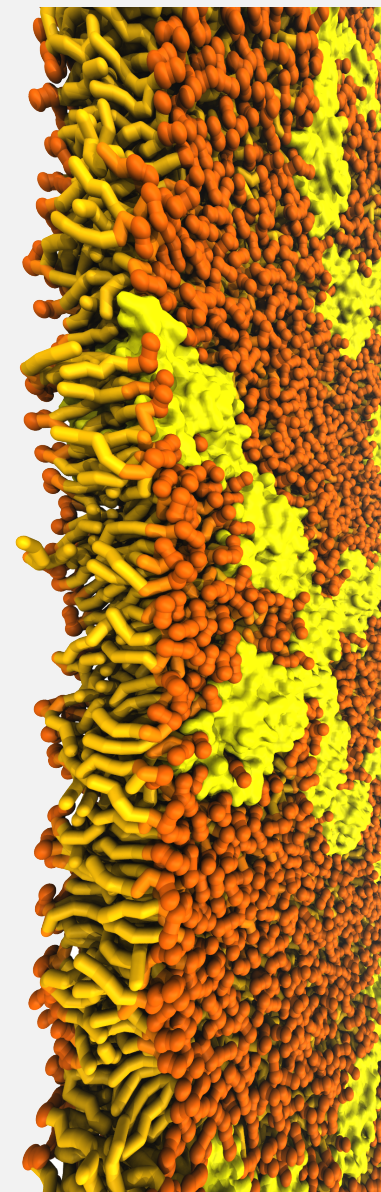
Authors suggest short time regime $\langle \mathbf{r}^2(t) \rangle \simeq t^{0.26}$
 & transient trapping of lipids leading to non-Gaussian displacement distribution

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

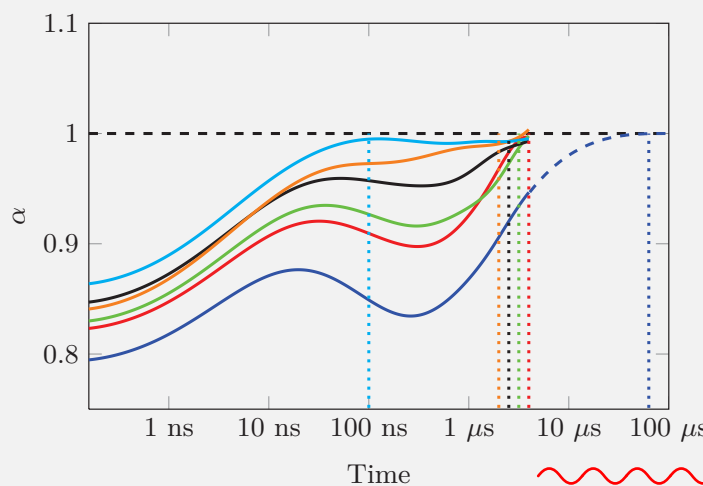
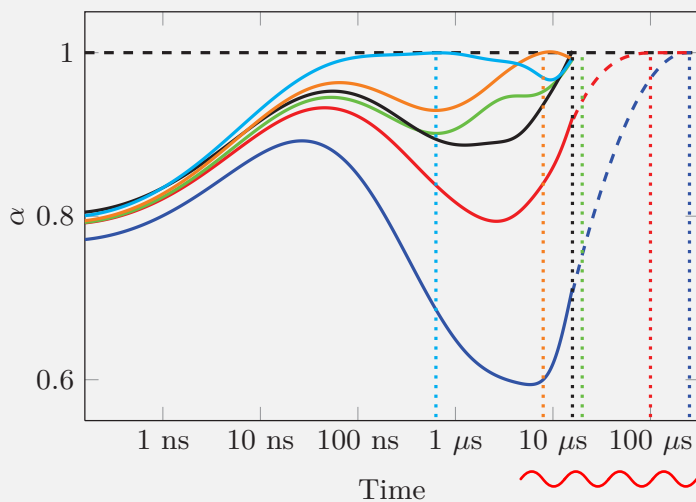
Protein crowded membranes reduce effective mobility



Blue: DLPC. Red: DPPC

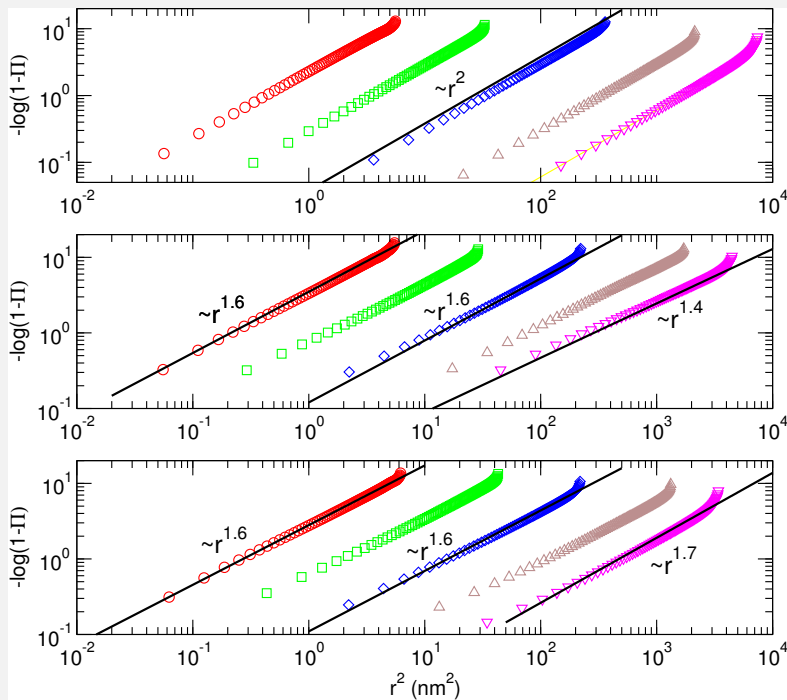
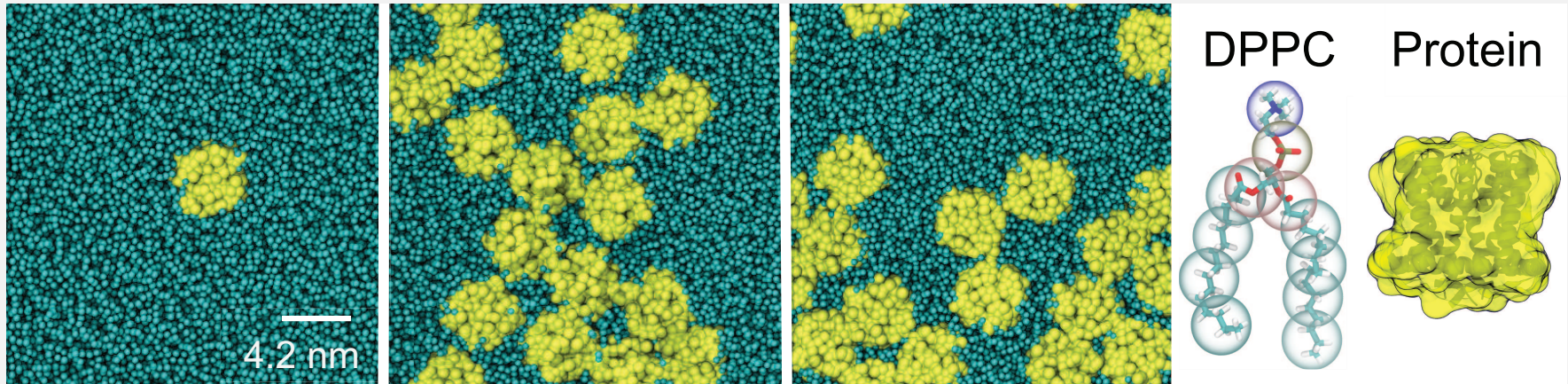


Protein crowding effects anomalous lipid diffusion



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

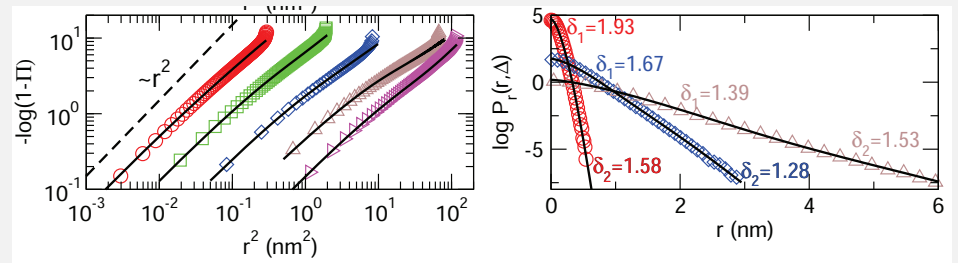
Crowding in membranes: non-Gaussian lipid/protein diffusion



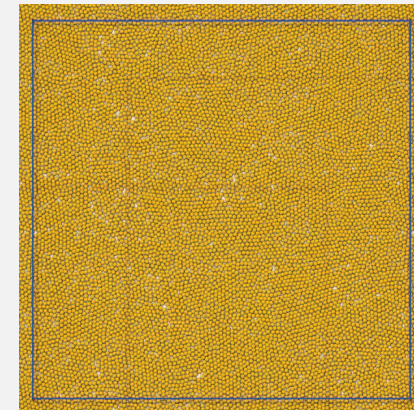
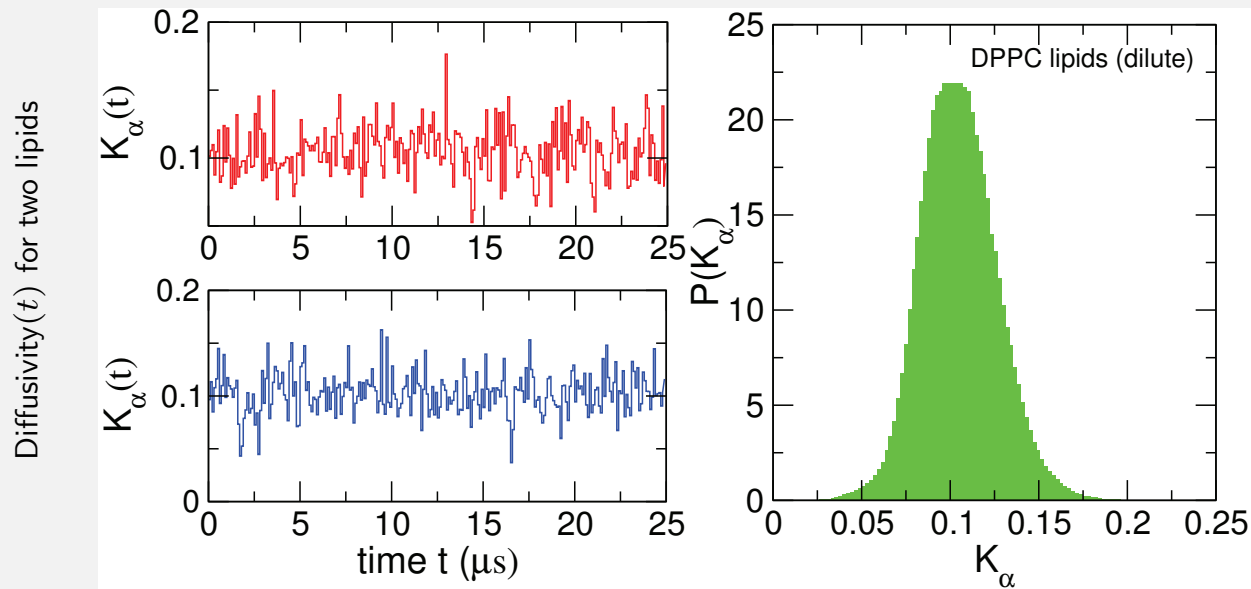
Dilute membrane: $P(r, t)$ Gauss

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

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

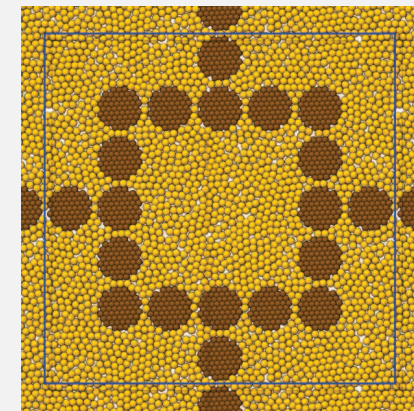
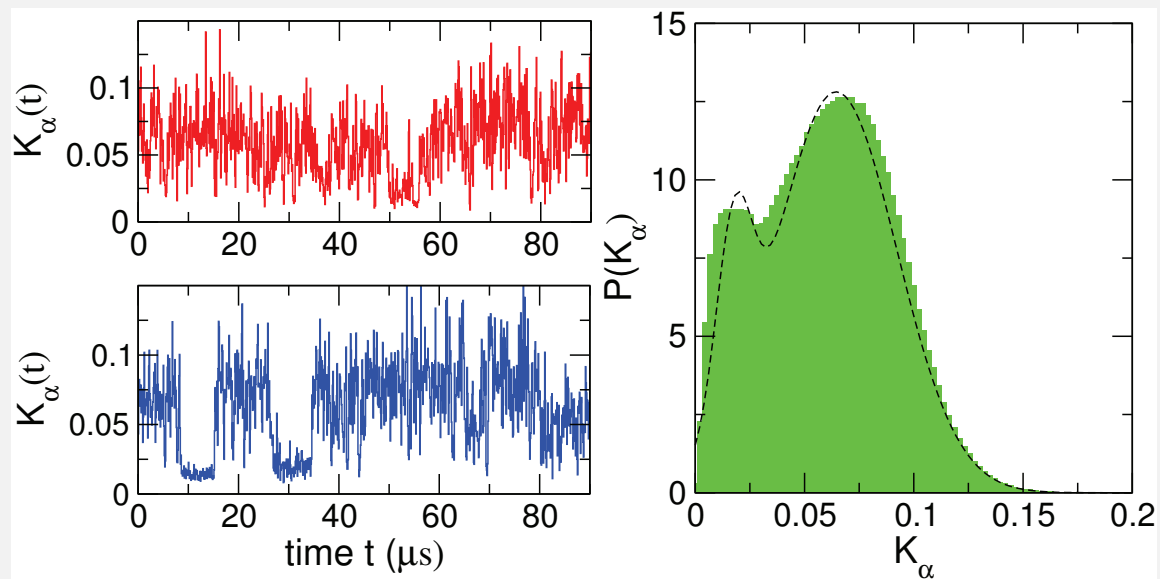


Crowding in membranes increases dynamic heterogeneity



2D argon liquid

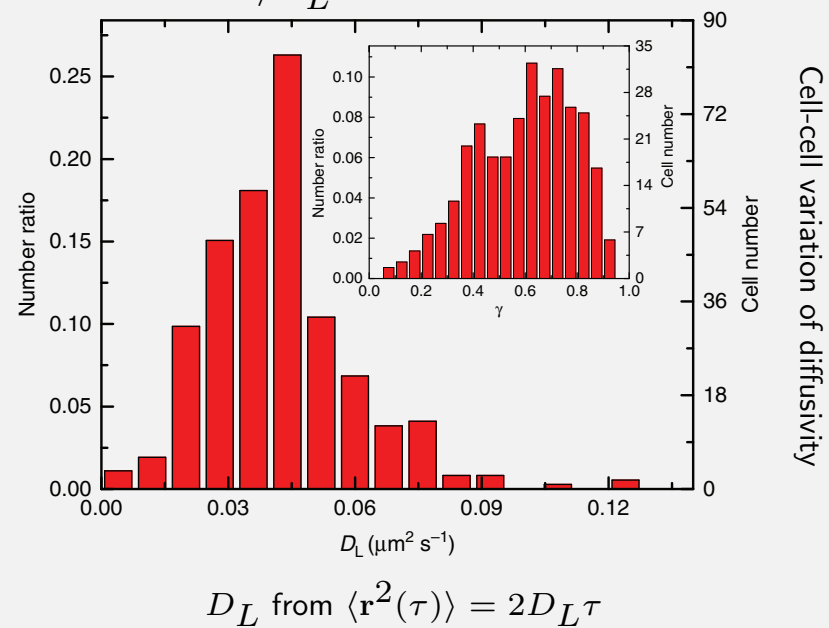
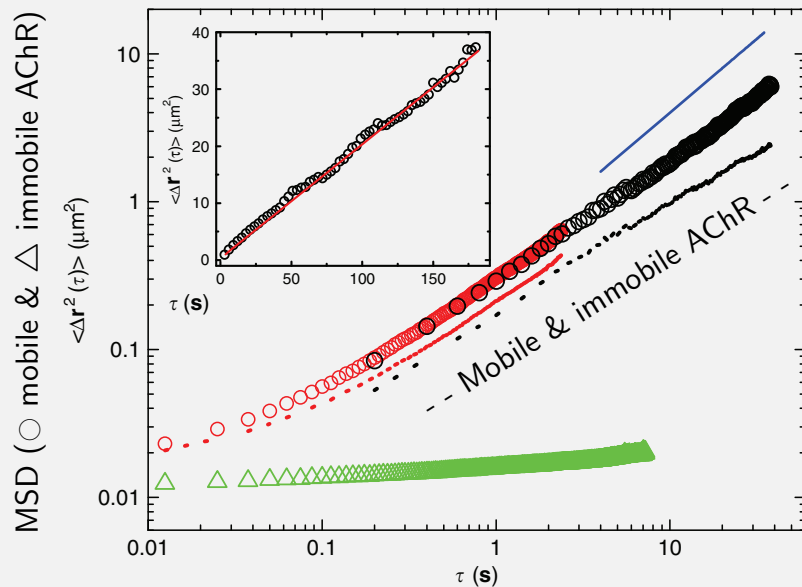
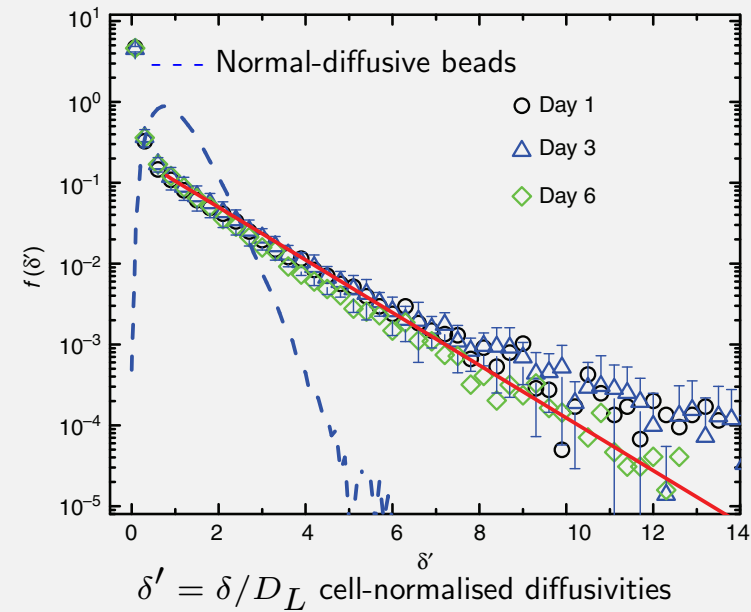
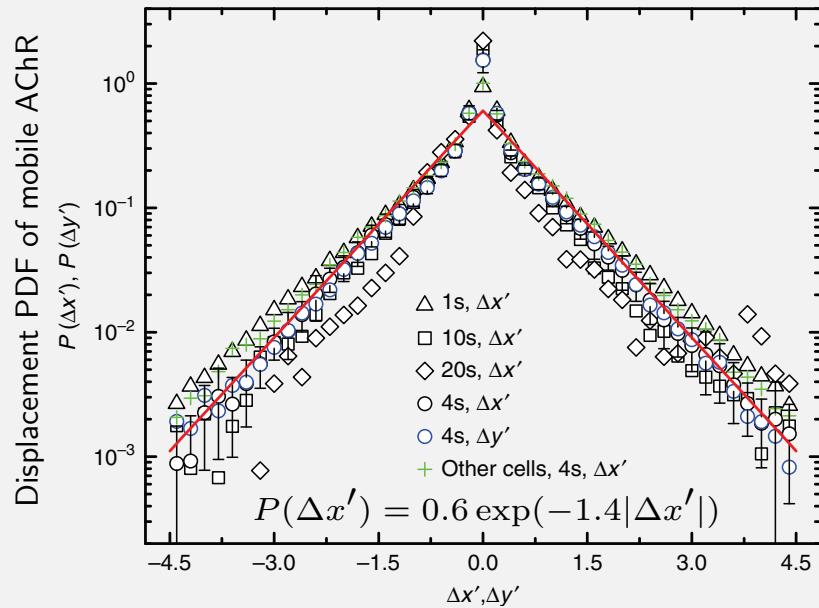
Lipid diffusivity, dilute membrane



2D "blocked" argon

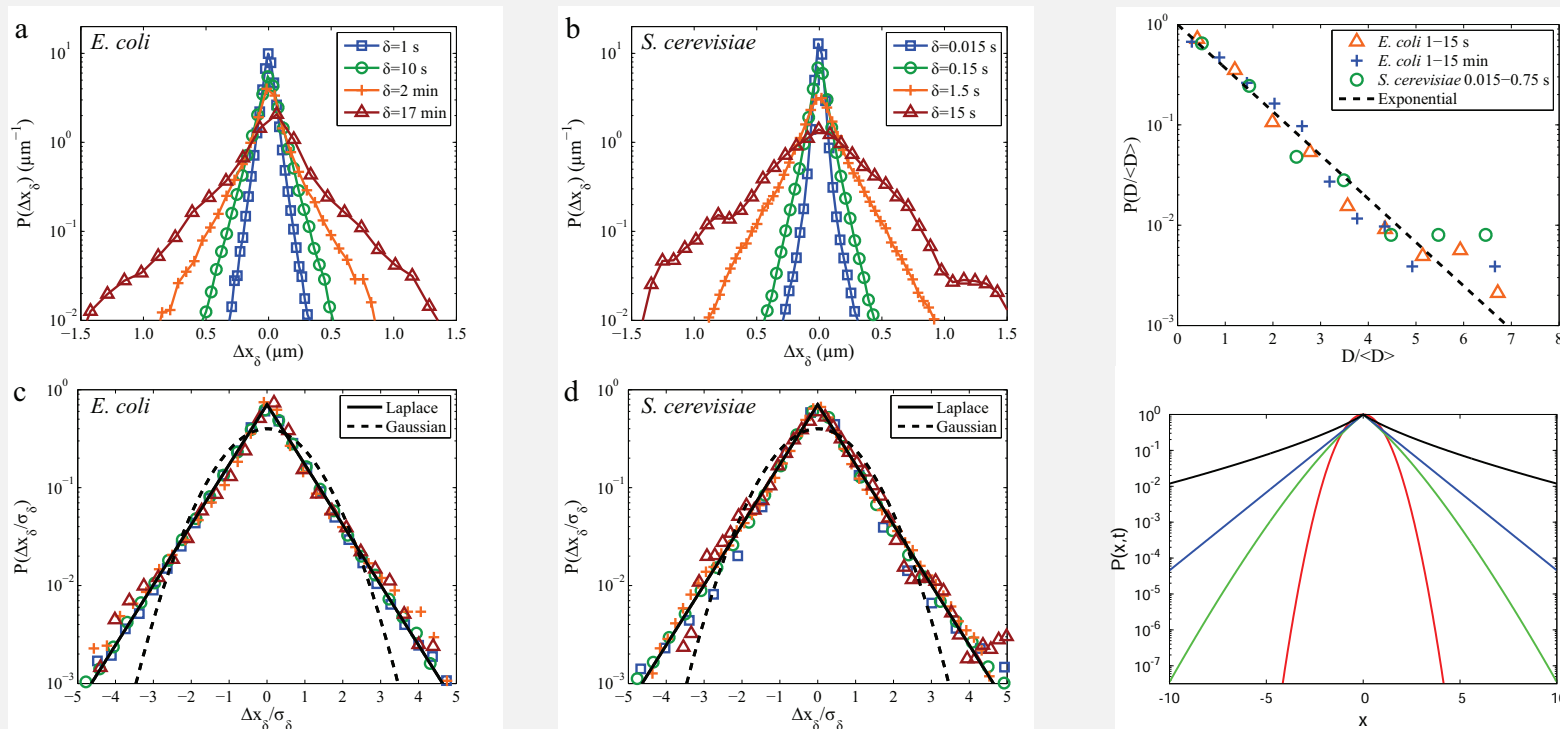
Lipid diffusivity, crowded membrane

Non-Gaussianity of acetylcholine receptors in *Xenopus* cells

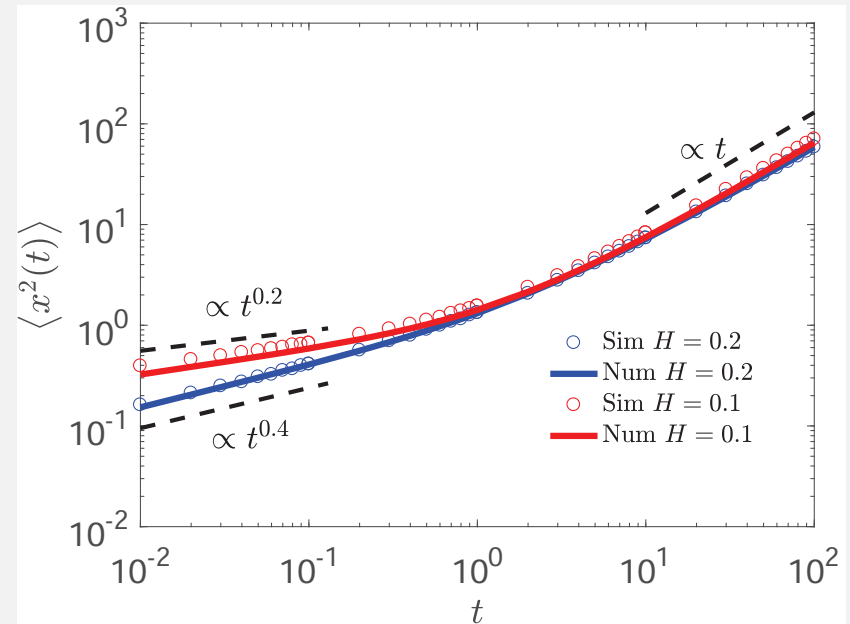
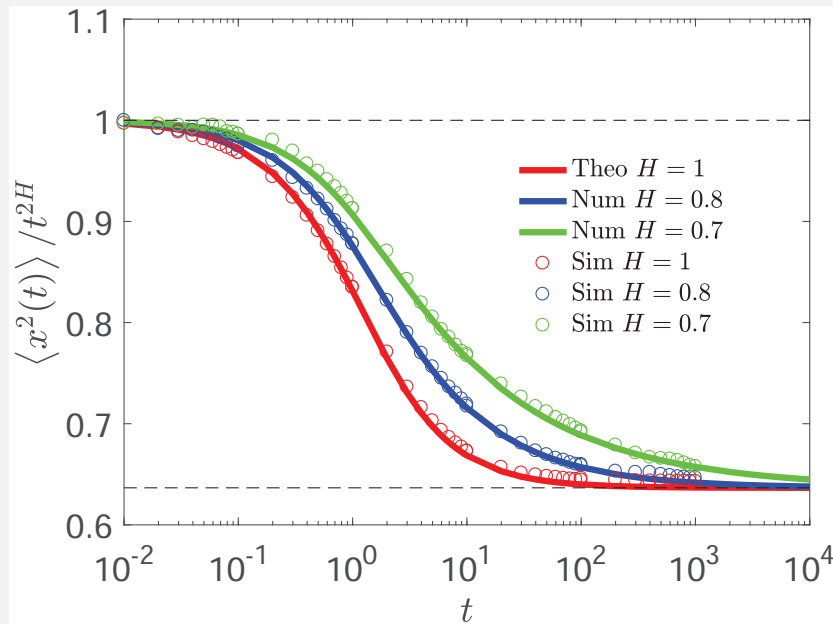


Non-Gaussian diffusion in viscoelastic systems

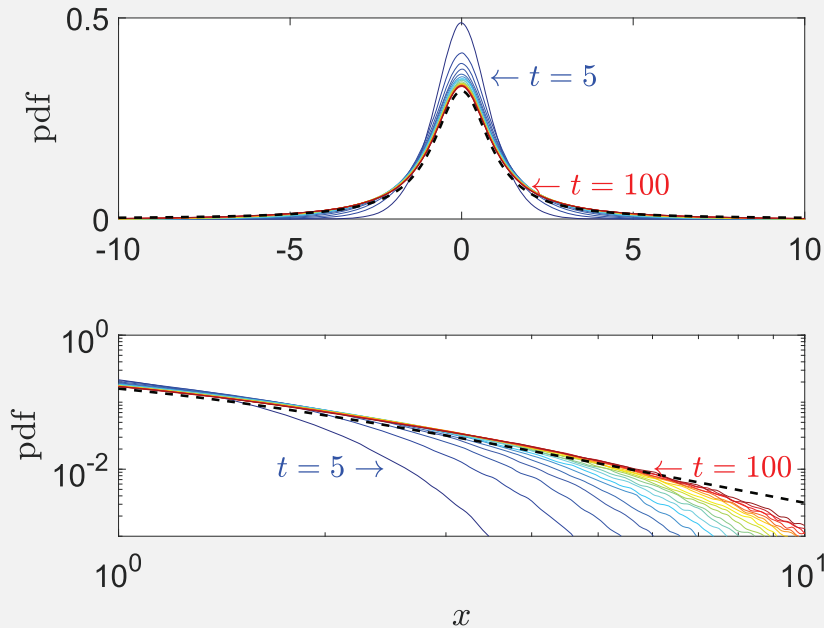
So far consensus: submicron tracer motion in cytoplasm is FBM-like, i.e., Gaussian RNA-protein particles in *E.coli* & *S.cerevisiae* perform exponential anomalous diffusion:



Diffusing-diffusivity driven by FBM

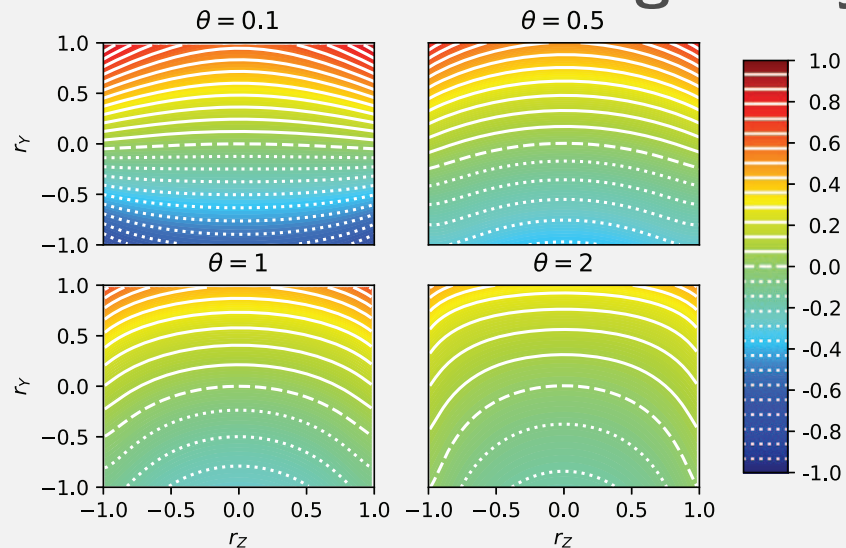


Superstatistical GLE: non-Gaussian viscoelastic diffusion

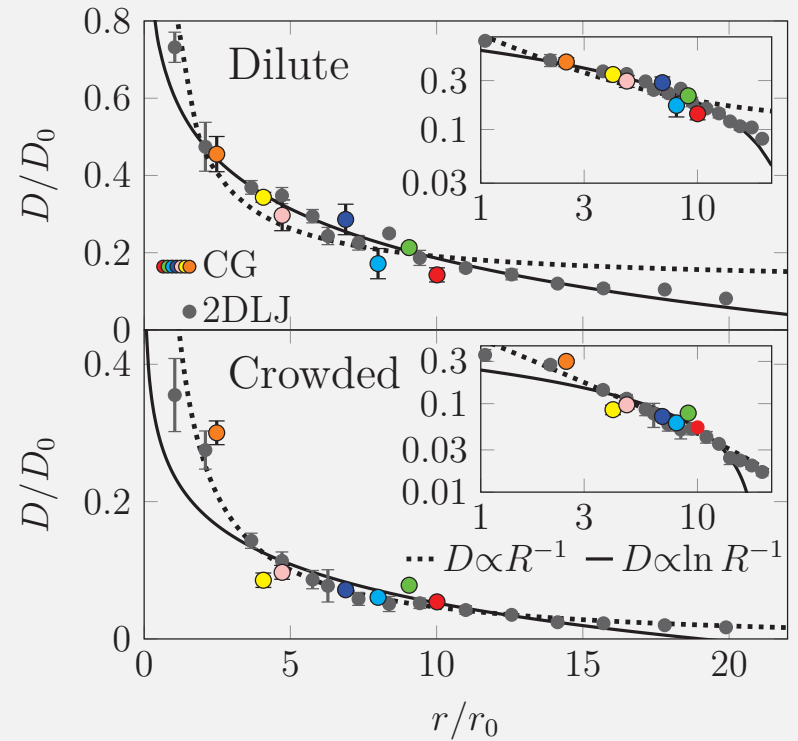
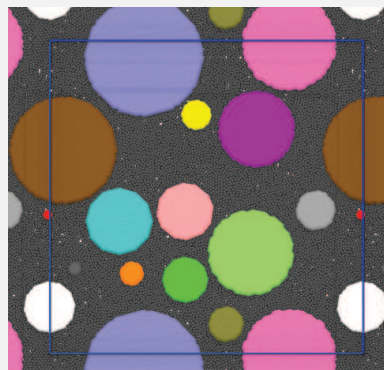
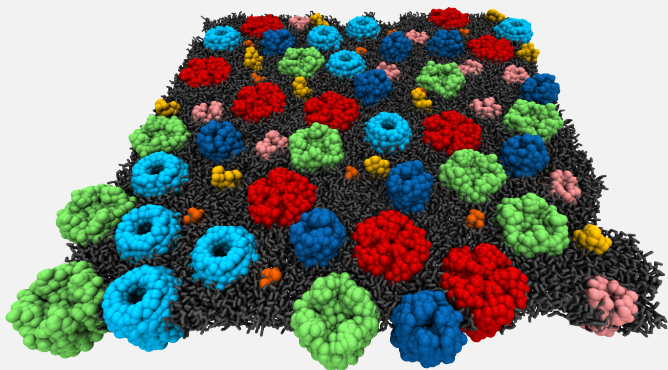
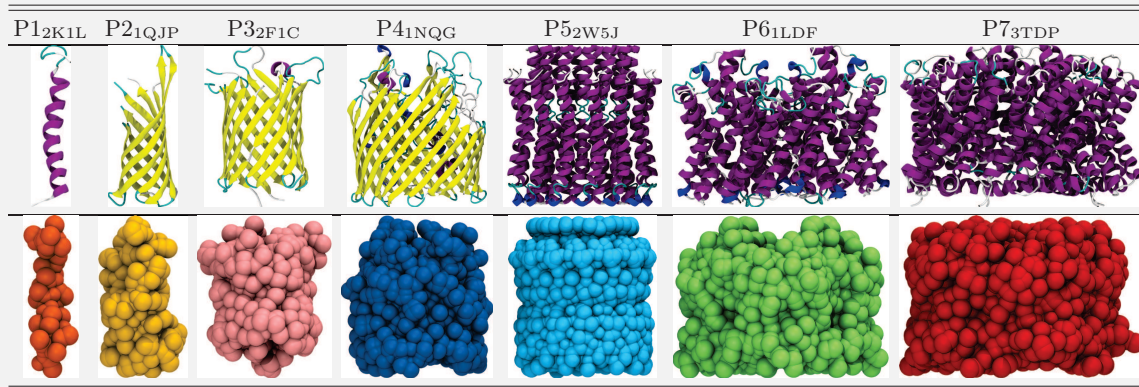


$$\langle \mathbf{r}^2(t) \rangle \simeq K_\alpha t^\alpha$$

Codifference detects non-ergodicity & non-Gaussianity



Geometry-induced violation of Saffman-Delbrück relation



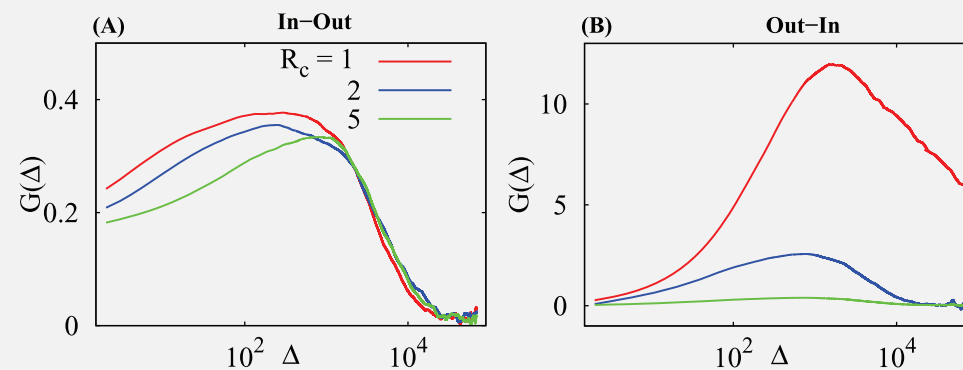
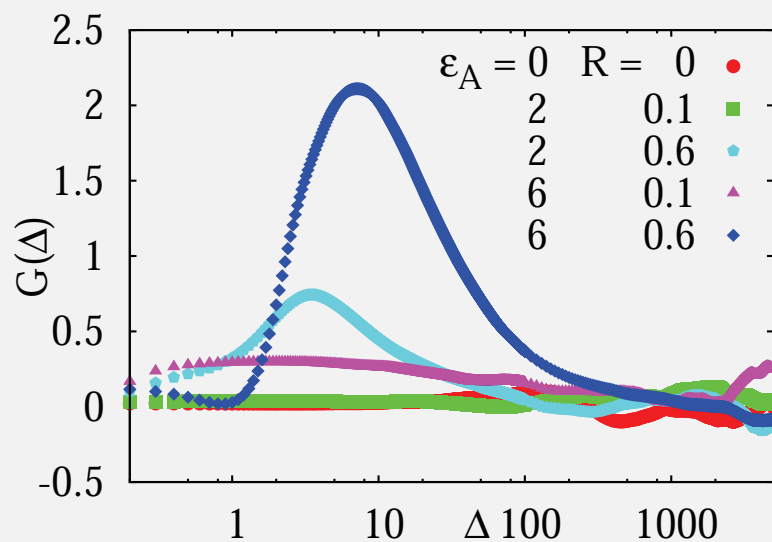
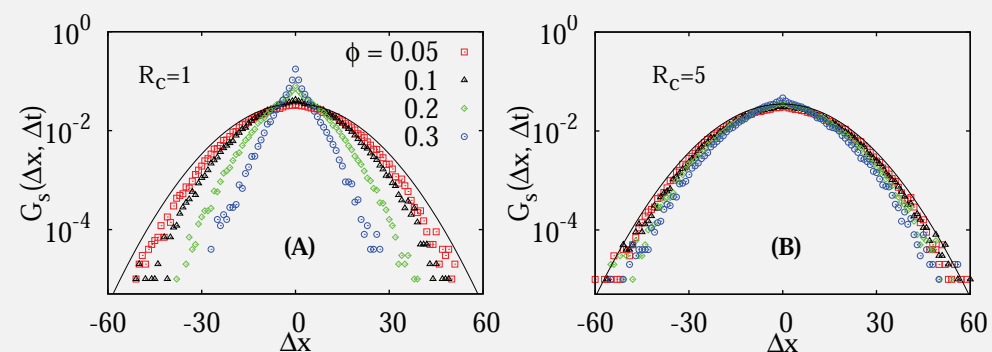
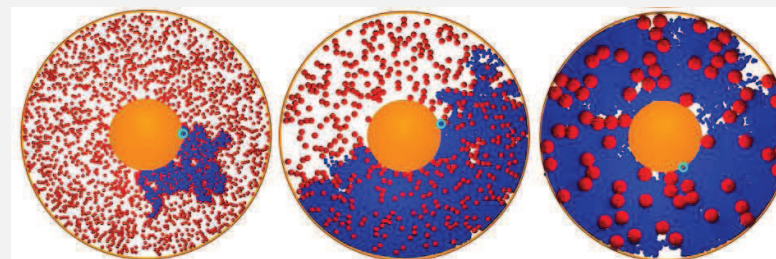
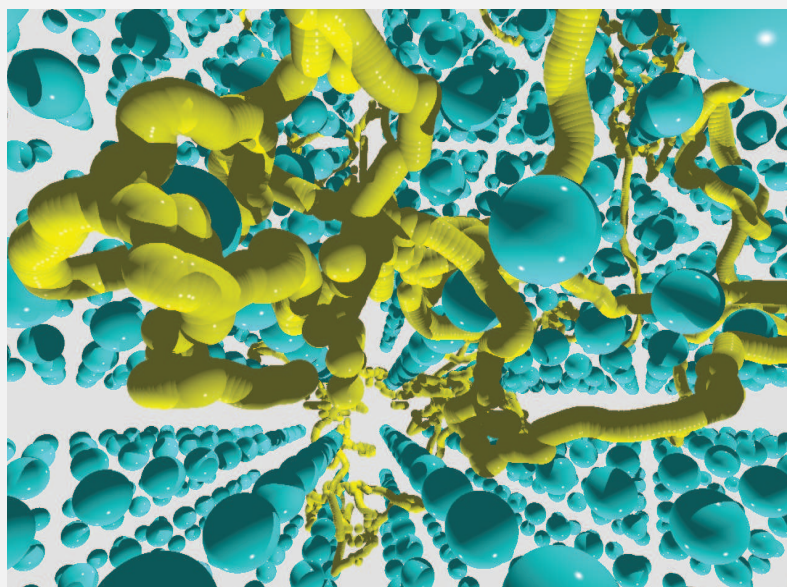
Dilute system: Saffman-Delbrück law

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

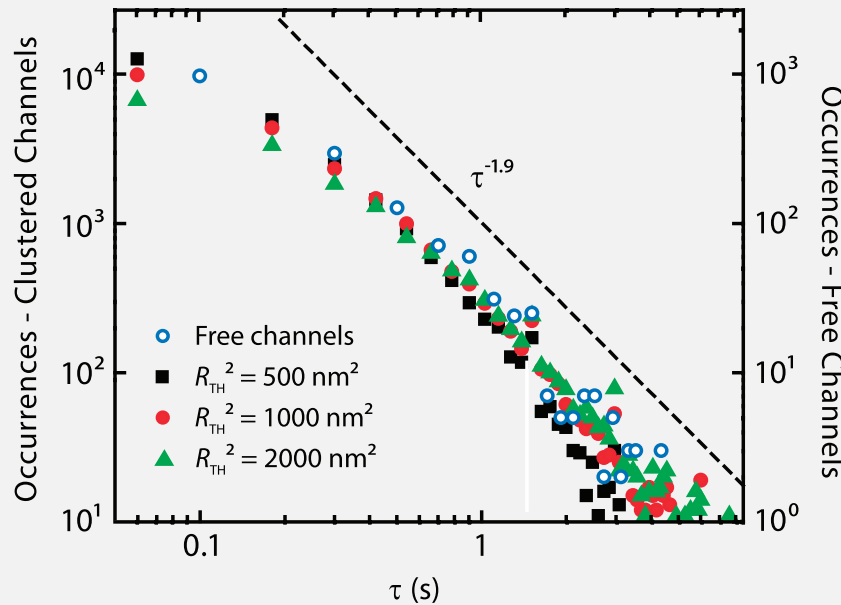
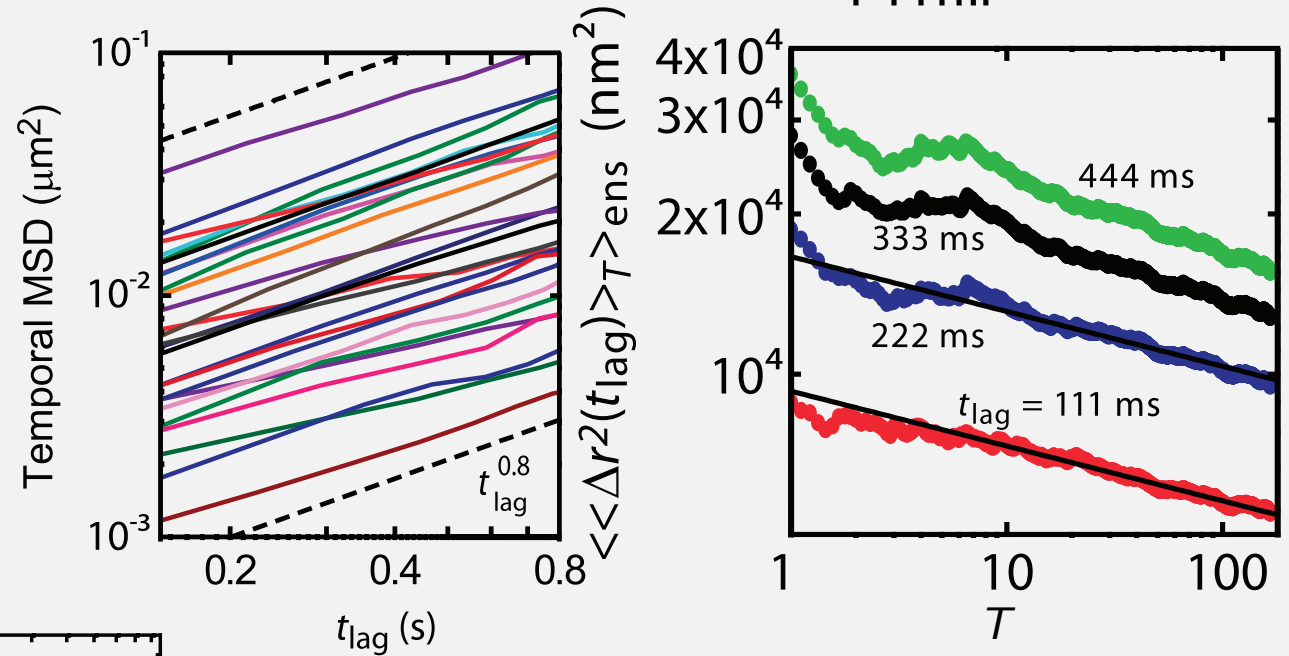
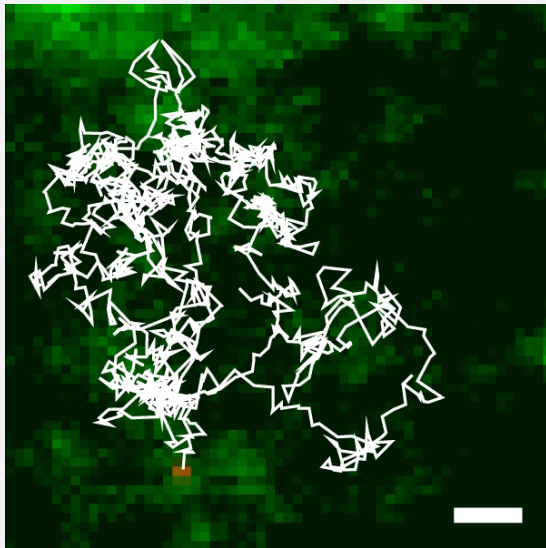
Crowded membrane & 2DLJ discs:

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

Transient non-Gaussianity in disordered systems



CTRW-like motion of Ka channels in plasma membrane



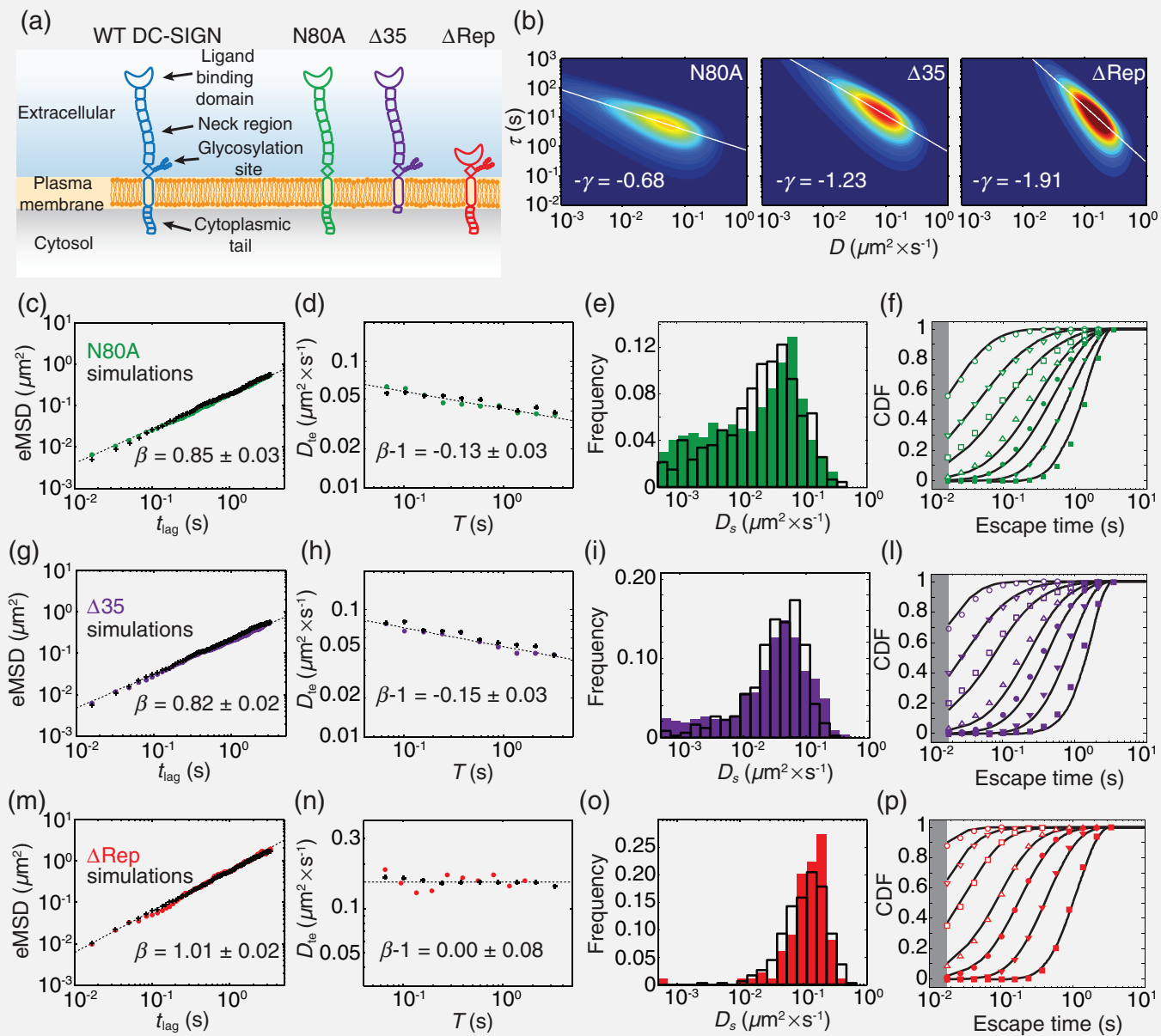
$$\psi(\tau) \simeq \tau^{-1-\alpha} \text{ scale free}$$

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

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

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

Ageing in the motion of membrane embedded proteins



Time averaged MSD & weak ergodicity breaking (WEB)

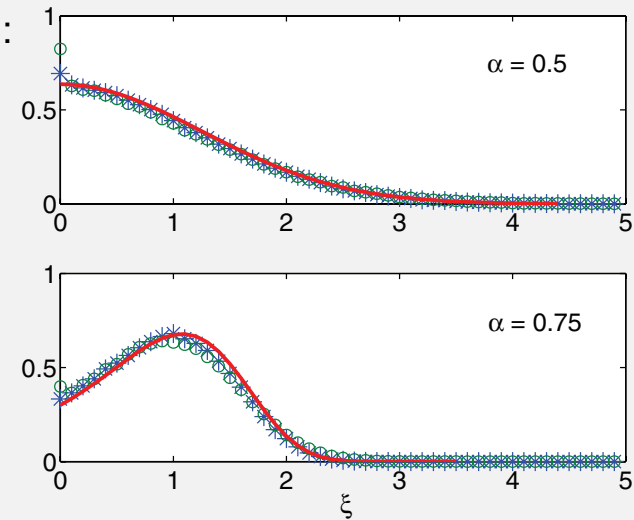
Time averaged MSD $\simeq \Delta$ is pseudo-Brownian and ageing ($\langle x^2(t) \rangle \simeq K_\alpha t^\alpha$):

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

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

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

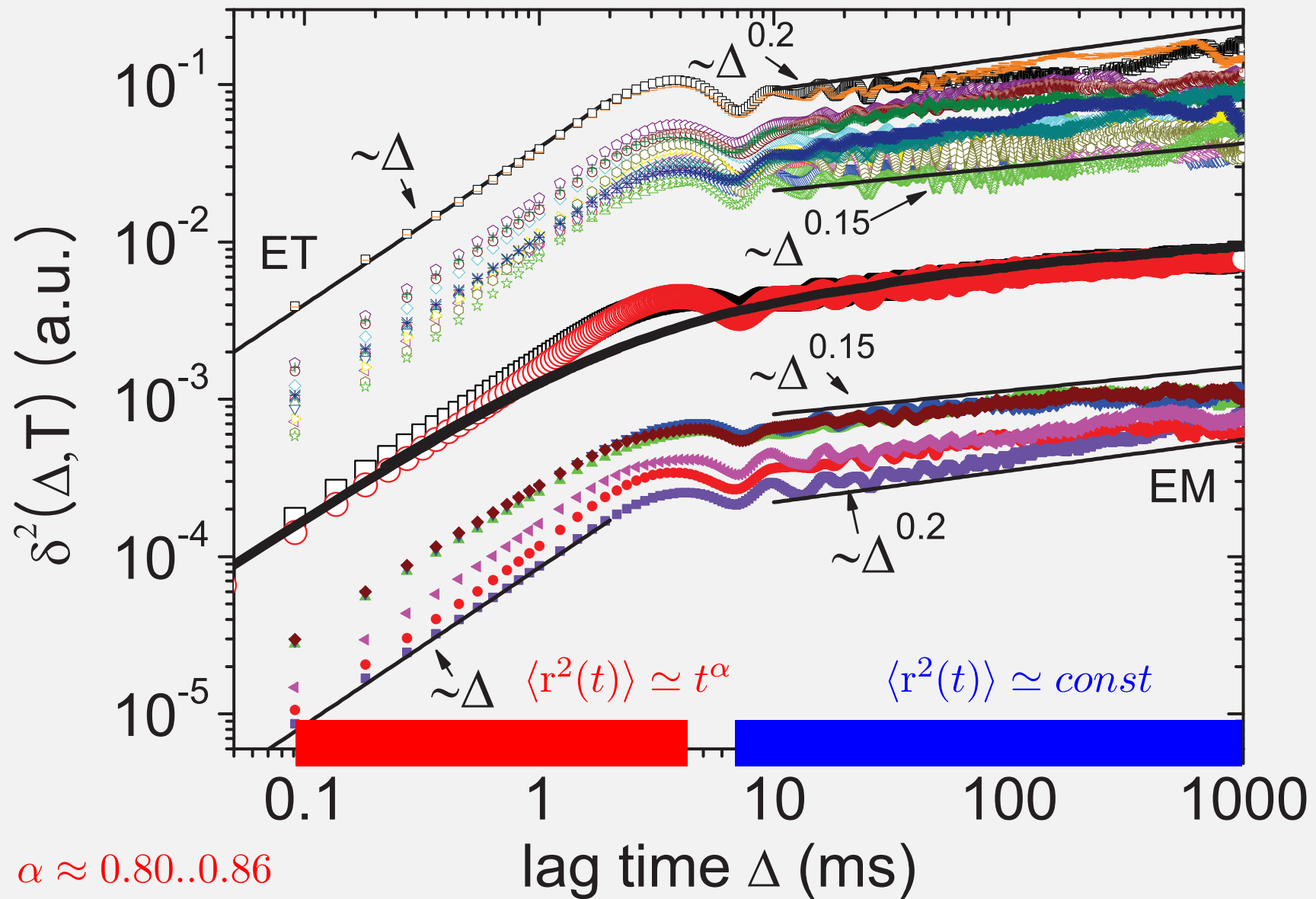
$$\phi_{1/2}(\xi) = \frac{2}{\pi} \exp\left(-\frac{\xi^2}{\pi}\right); \quad \phi_1(\xi) = \delta(\xi - 1)$$



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

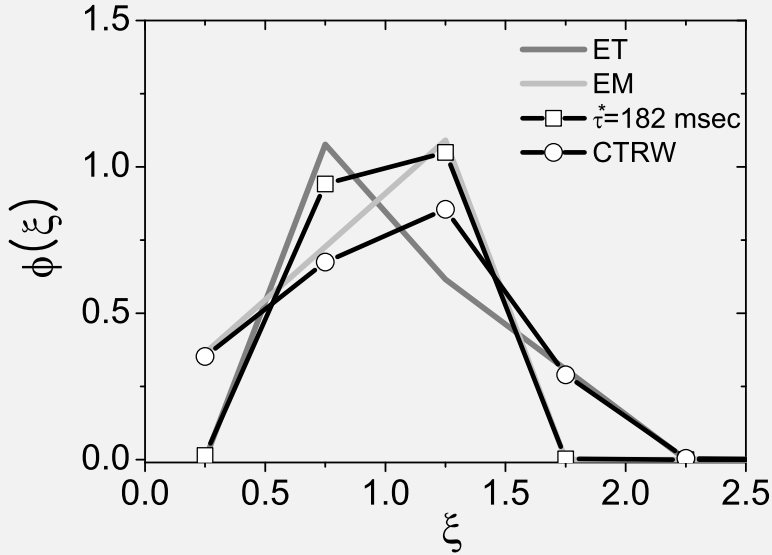
$$\langle \overline{\delta^2(\Delta)} \rangle \sim \left(\langle x^2 \rangle_B - \langle x \rangle_B^2 \right) \frac{2 \sin(\pi\alpha)}{(1-\alpha)\alpha\pi} \left(\frac{\Delta}{T} \right)^{1-\alpha}; \quad \frac{1}{(K_\alpha \lambda_1)^{1/\alpha}} \ll \Delta \ll T$$

Granule subdiffusion in harmonic optical tweezer potential

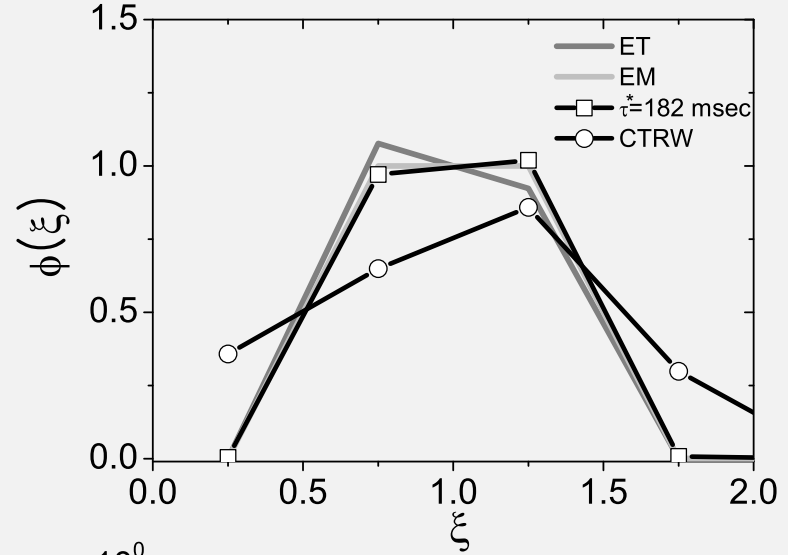


Further analysis of the lipid granule data

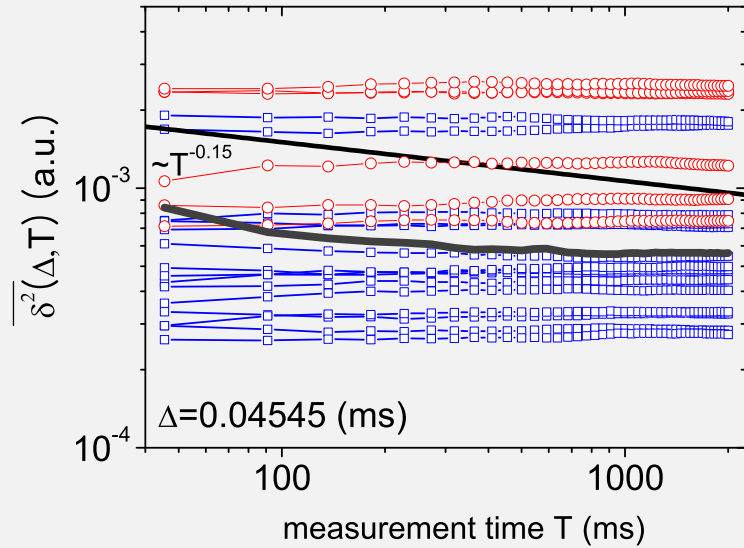
$\Delta = 0.04545$ msec:



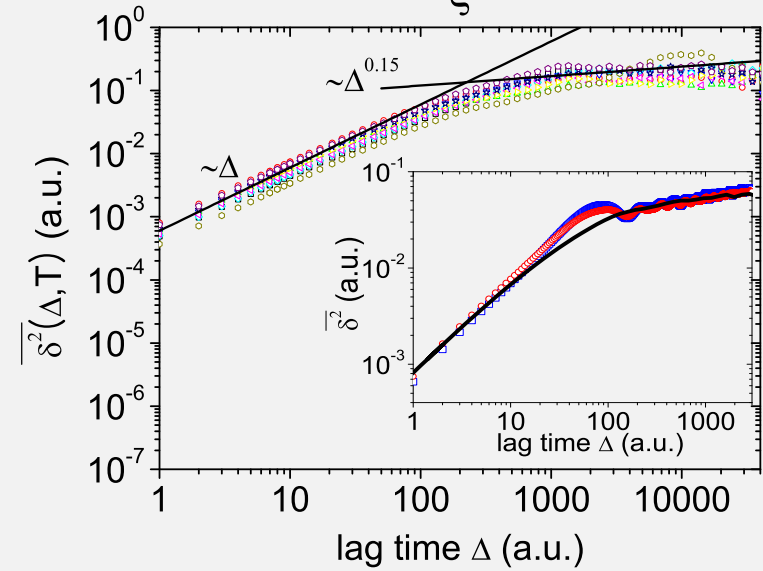
$\Delta = 4.545$ msec:



Ageing plot:



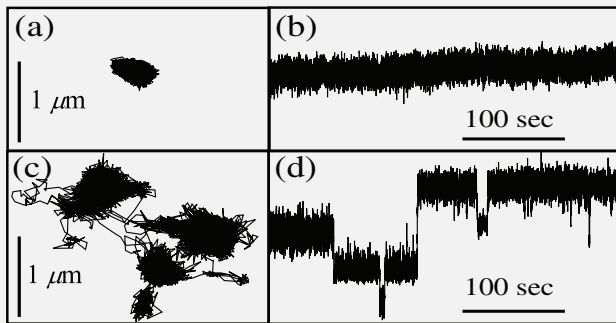
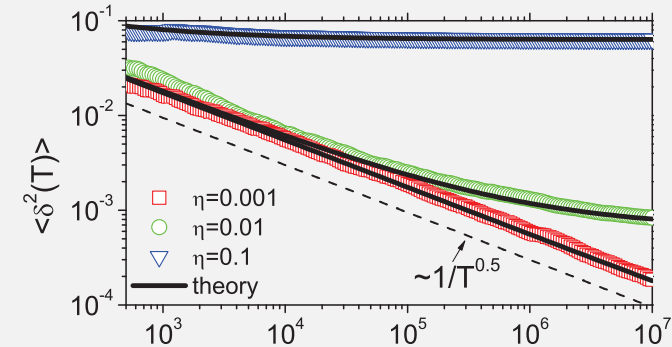
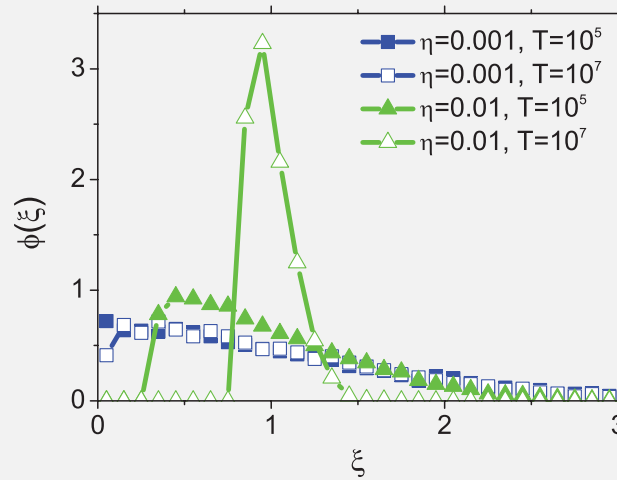
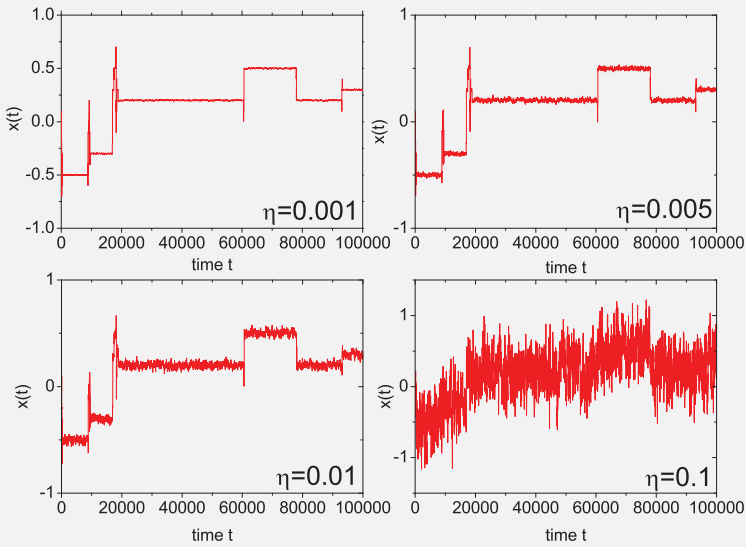
Time averaged MSD:



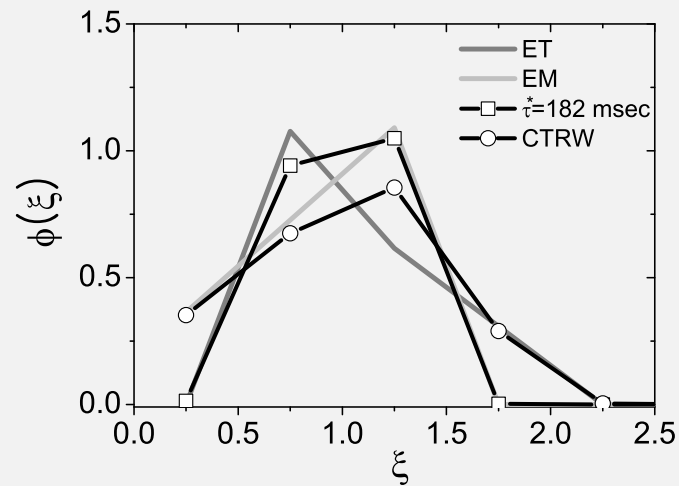
$$\psi(t) = \frac{d}{dt} \left[1 - \tau^\alpha (\tau + t)^{-\alpha} \exp\left(-\frac{t}{\tau^*}\right) \right] \therefore \tau^* \approx 182 \text{ msec}$$

Noisy CTRW processes /w Ornstein-Uhlenbeck-noise

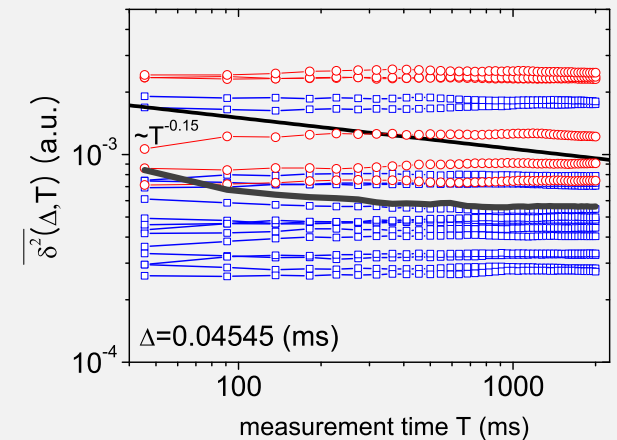
$$\langle x^2(t) \rangle = \frac{2K_\alpha}{\Gamma(1 + \alpha)} t^\alpha + \frac{\eta^2 D}{k} (1 - e^{-2kt})$$



IY Wong . . . DA Weitz, PRL (2004)

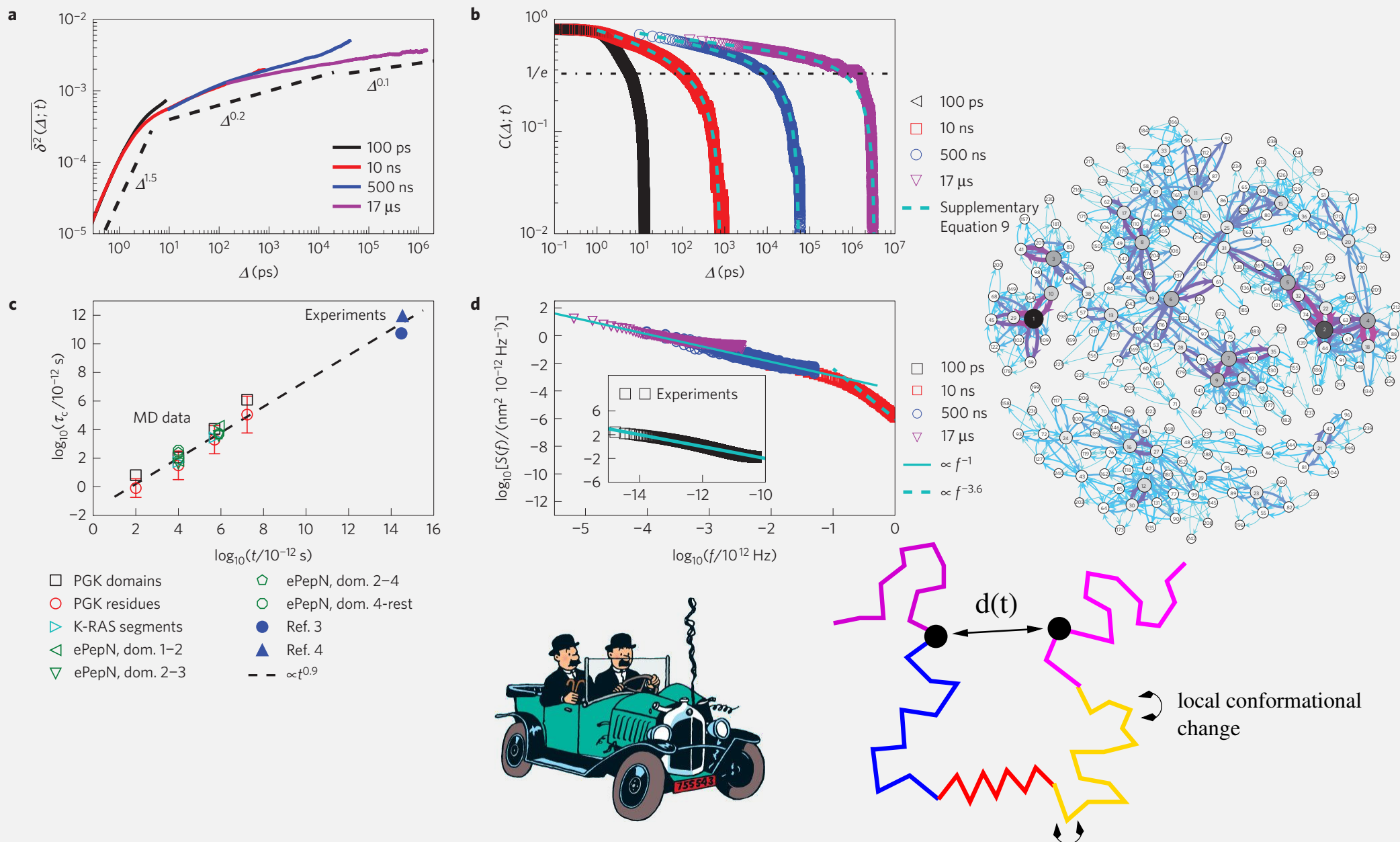


JH Jeon . . . K Berg-Sørensen, L Oddershede & RM, PRL (2011)



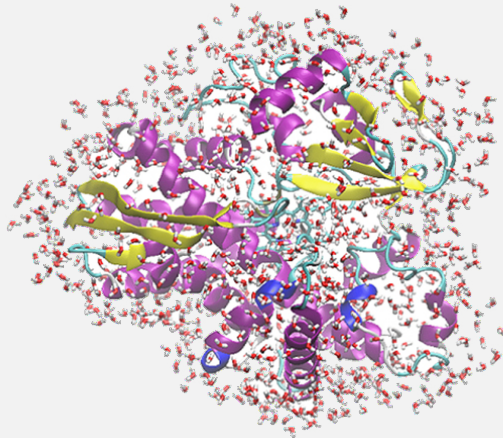
JH Jeon, E Barkai & RM, JCP (2013)

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)

Intermittent localisation of surface water on proteins

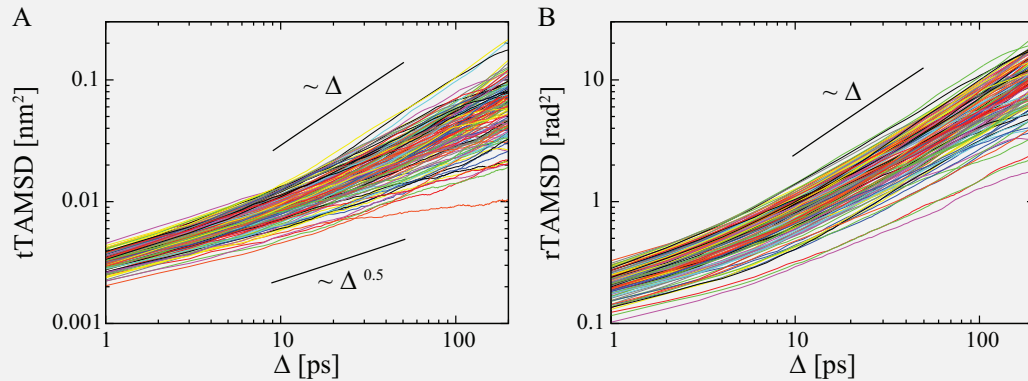


Uncorrelated jumps between cages

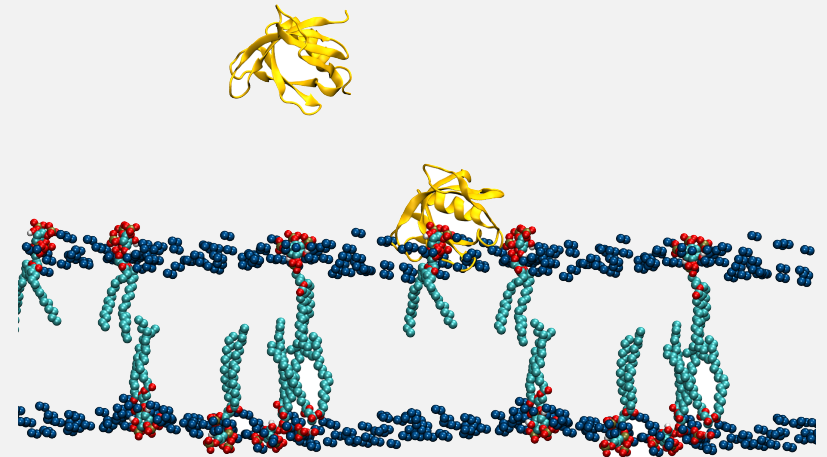


[P Tan, Y Liang, Q Xu, E Mamontov, J Li, X Xing & L Hong, Phys Rev Lett (2018); see also RM, Viewpoint Phys (2018)]

Intermittency of surface water & proteins on membranes



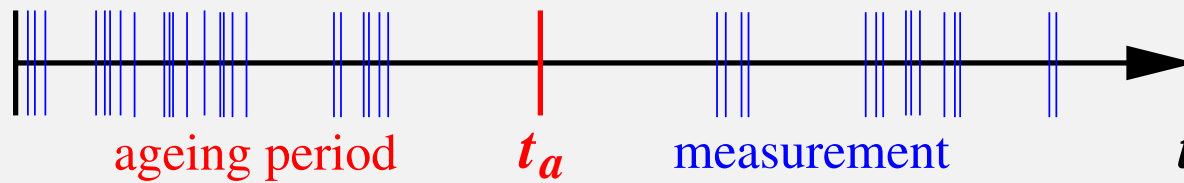
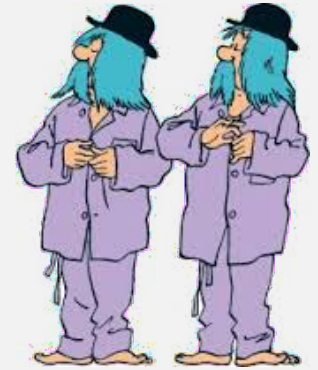
↑ Translational & rotational water surface diffusion



E Yamamoto, T Akimoto, M Yasui & K Yasuoka; E Yamamoto, AC Kalli, T Akimoto, K Yasuoka & MSP Sansom, Sci Rep (2014,2015) 43

Non-Gaussian ↗

Ageing effects in single trajectory time averages

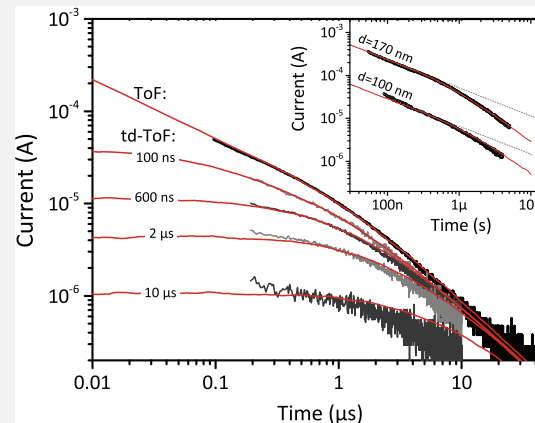
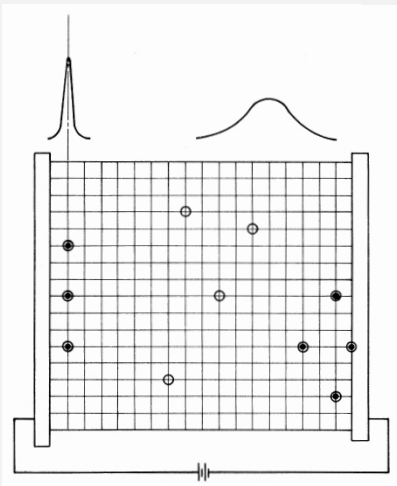


Ageing mean squared displacement ($\Lambda(z) = (1 + z)^\alpha - z^\alpha$)

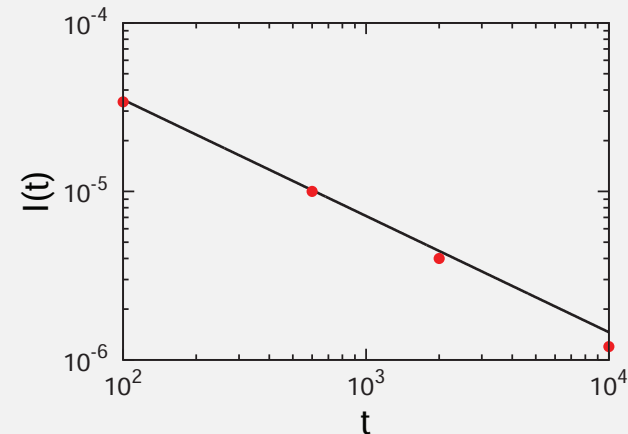
$$\langle \overline{\delta^2(\Delta)} \rangle_a = \frac{\Lambda_\alpha(t_a/T) g(\Delta)}{\Gamma(1 + \alpha) T^{1-\alpha}} \Leftrightarrow \langle x^2(t) \rangle_a \simeq \begin{cases} t^\alpha, & t_a \ll t \\ t_a^{\alpha-1} t, & t_a \gg t \end{cases}$$

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

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



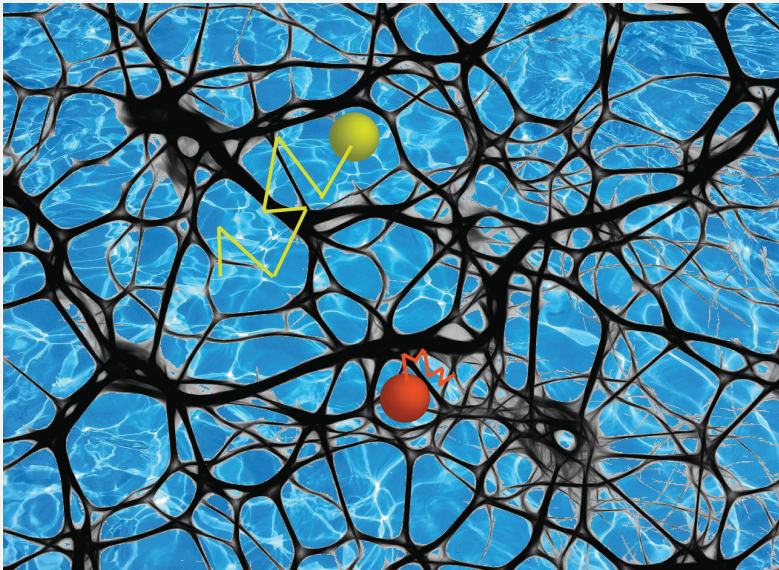
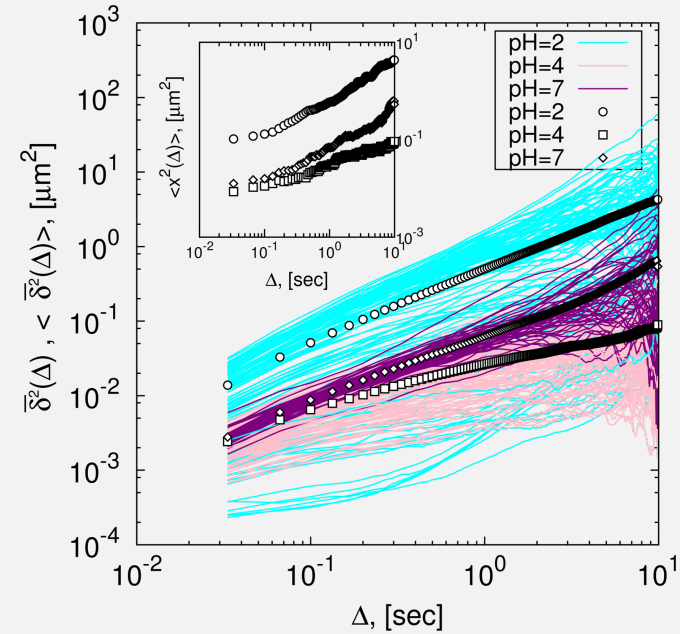
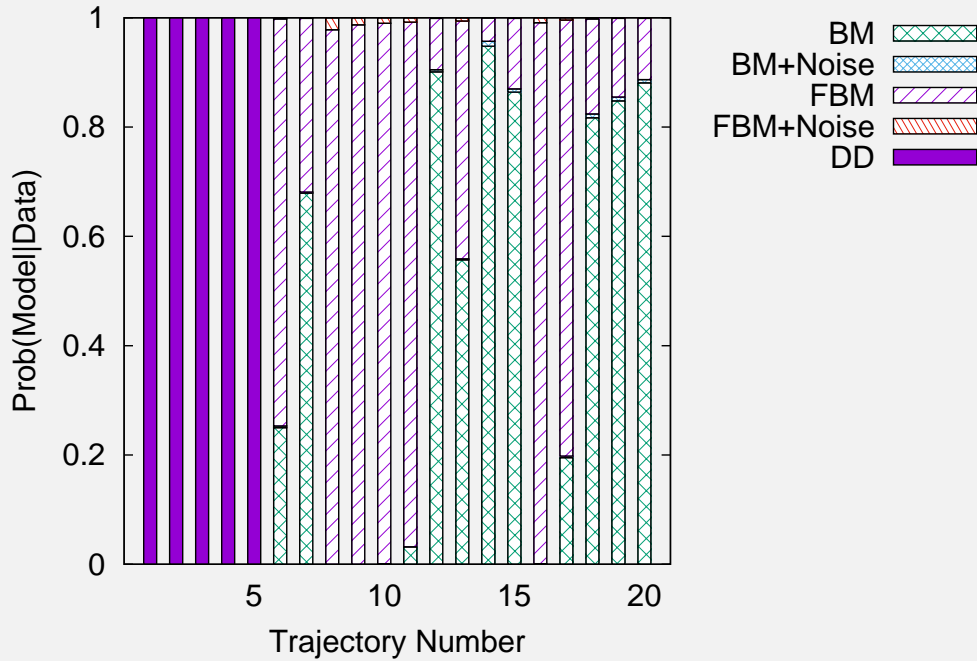
M Schubert, . . . & D Neher,
Phys Rev B (2013)



H Krüsemann, R Schwarzl & RM,
Transp Porous Media (2016), PRE (2015)

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

Maximum likelihood Bayesian data analyses



Nested sampling à la Skilling

Objective model selection

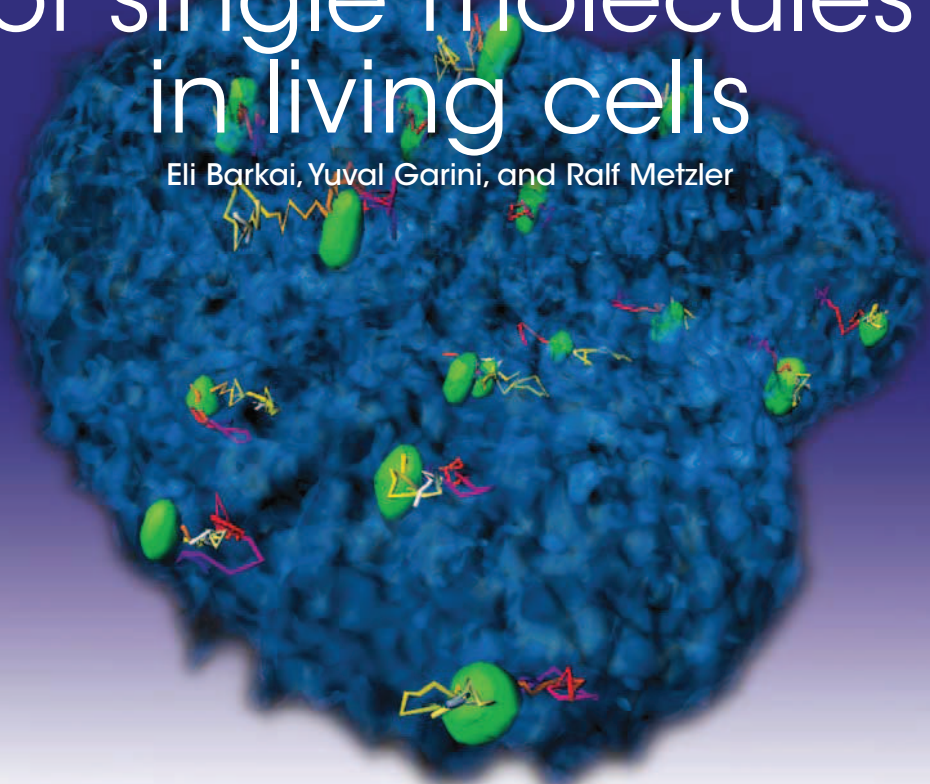
Parameter estimation



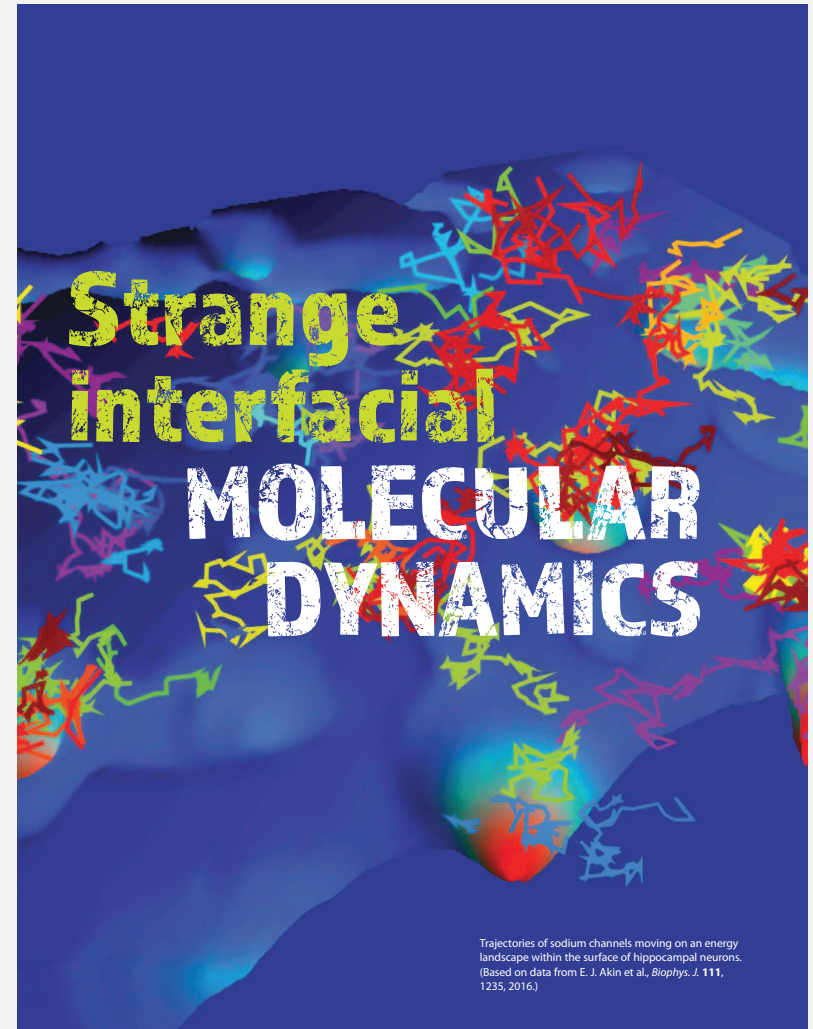
Popular articles

STRANGE KINETICS of single molecules in living cells

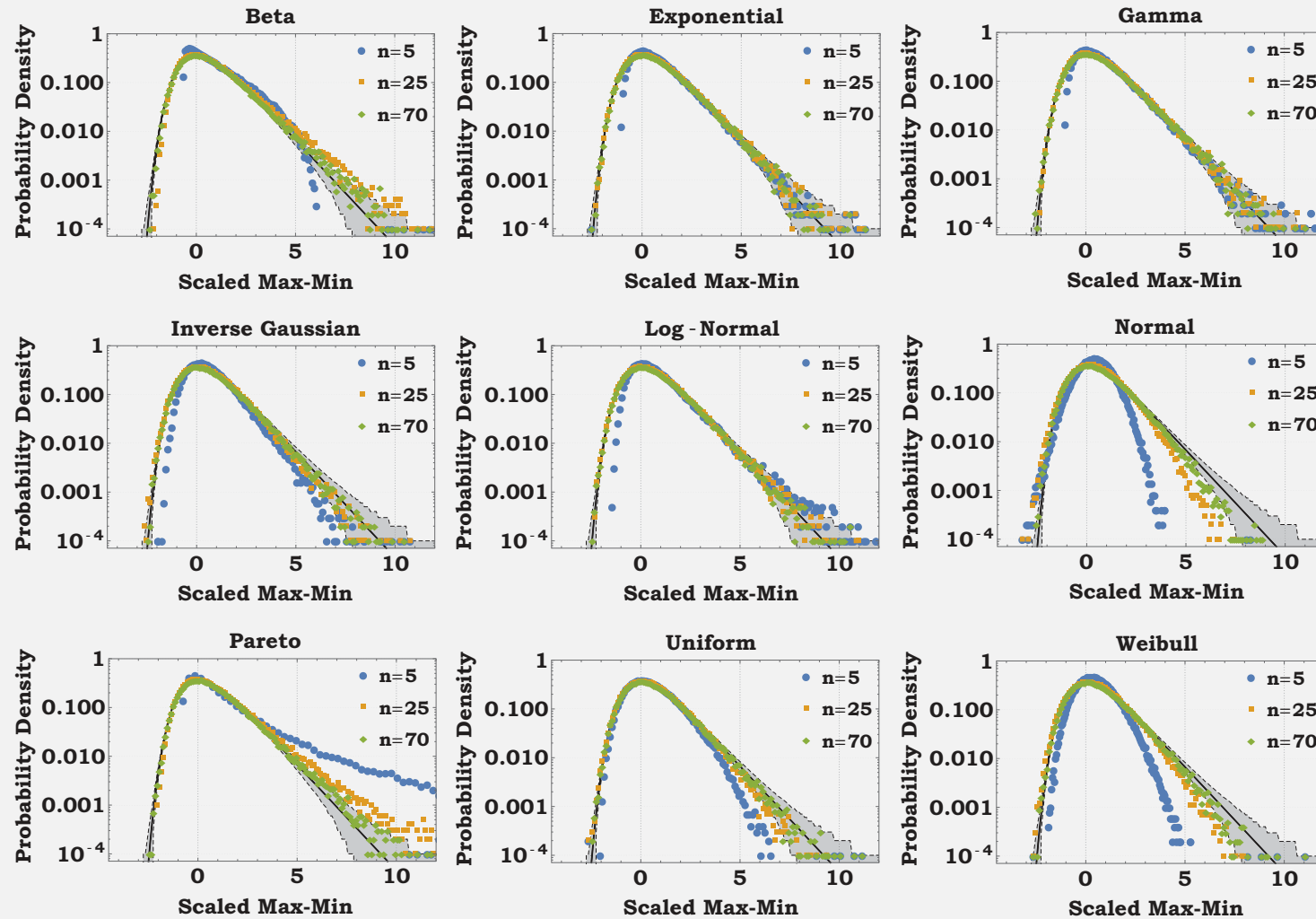
Eli Barkai, Yuval Garini, and Ralf Metzler



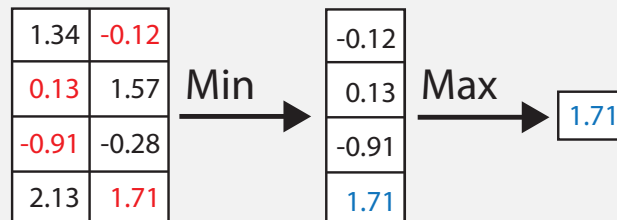
The irreproducibility of time-averaged observables in living cells poses fundamental questions for statistical mechanics and reshapes our views on cell biology.



Gumbel universal limit law for Min-Max/Max-Min reliability



I Eliazar, RM & S Reuveni, PRE² (2019)



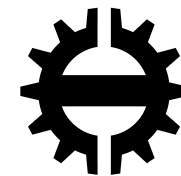
Σ Summary

- I Brownian yet non-Gaussian or non-Gaussian viscoelastic diffusion quite ubiquitously observed in heterogeneous media
- II Excluded volume effects can explain basic features in 2D membranes
- III Non-stationary processes such as CTRW are non-Gaussian by nature
- IIII Non-ergodic, ageing dynamics on molecular scale
- IIII Physics ↔ ARIMA time series analysis: J Ślęzak, RM, M Magdziarz, NJP (2019)
- IIII Bayes/max likelihood model determination: PCCP (2018), Soft Matter (2019)
- 🔗 Membrane dynamics: RM, JH Jeon & AG Cherstvy, Biochimica et Biophysica Acta - Biomembranes **1858**, 2451 (2016)
- 🔗 Single molecule experiments: C Nørregaard, RM, CM Ritter, K Berg-Sørensen & LB Oddershede, Chem Rev **117**, 4342 (2017)
- 🔗 Anomalous diffusion models: RM, JH Jeon, AG Cherstvy & E Barkai, Phys Chem Chem Phys **16**, 24128 (2014)

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Matthias Weiss (U Bayreuth)
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