Non-Gaussian statistics in soft & bio-matter

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THE

PHILOSOPHICAL MAGAZINE

AND

ANNALS OF PHILOSOPHY.

[NEW SERIES.]

SEPTEMBER 1828.

XXVII. *A brief Account of Microscopical Observations made in the Months of June, July, and August,* 1827, *on the Particles contained in the Pollen of Plants; and on the general Existence of active Molecules in Organic and Inorganic Bodies. By* ROBERT BROWN, *F.R.S., Hon. M.R.S.E. & R.I. Acad., V.P.L.S., Corresponding Member of the Royal Institutes of France and of the Netherlands, &c. &c.*

[We have been favoured by the Author with permission to insert the following paper, which has just been printed for private distribution.—ED.]

My inquiry on this point was commenced in June 1827, and the first plant examined proved in some respects remarkably well adapted to the object in view.

This plant was *Clarckia pulchella*, of which the grains of pollen, taken from antheræ full grown, but before bursting, were filled with particles or granules of unusually large size, varying from nearly $\frac{1}{4000}$th to about $\frac{1}{5000}$th of an inch in length, and of a figure between cylindrical and oblong, perhaps slightly flattened, and having rounded and equal extremities. While examining the form of these particles immersed in water, I observed many of them very evidently in motion; their motion consisting not only of a change of place in the fluid, manifested by alterations in their relative positions, but also not unfrequently of a change of form in the particle itself; a contraction or curvature taking place repeatedly about the middle of one side, accompanied by a corresponding swelling or convexity on the opposite side of the particle. In a few instances the particle was seen to turn on its longer axis. These motions were such as to satisfy me, after frequently repeated observation, that they arose neither from currents in the fluid, nor from its gradual evaporation, but belonged to the particle itself.

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 minerals of granite, a fragment of the Sphinx being one of the specimens examined.

Fluxes, random walks, & fluctuating forces . . .

Paul Langevin (1872-1946)
Albert Einstein (1879-1955)

Marian Smoluchowski
(1872-1917)

William Sutherland
(1859-1911)

Einstein's conditions on Brownian motion

Paul Lévy [Processus stochastiques & mouvement brownien (1965)]: $\ll$The stochastic process, that we will call linear Brownian motion, is a schematisation that well represents the properties of real Brownian motion, observable on a sufficiently small but not infinitely small scale, and which assumes that the same properties exist across the scales.$\gg$

Einstein's postulate: a stochastic process describes normal diffusion if

(i) $\exists$ finite correlation time beyond which displacements are independent

(ii) displacements are identically distributed

(iii) displacements have a finite second moment

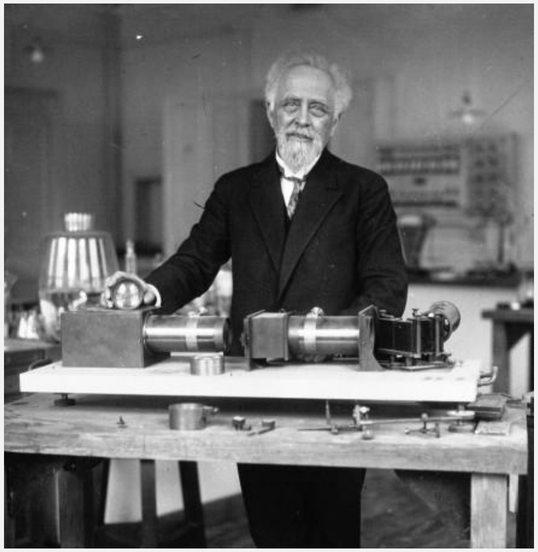
Main characteristics: linear mean squared displacement & Gaussian probability density

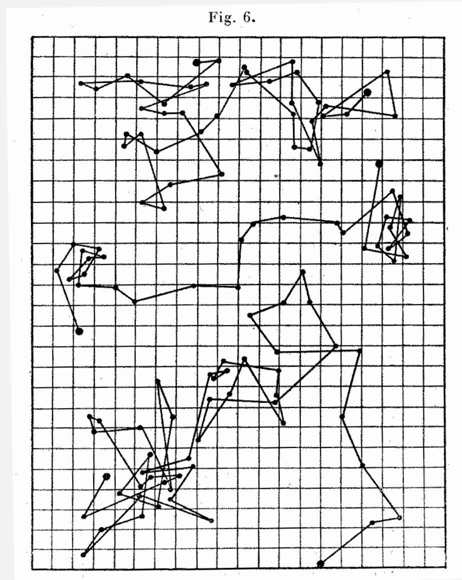
$$\langle \mathbf{r}^2(t)\rangle = 2dK_1 t, \quad P(\mathbf{r},t) = (4\pi K_1 t)^{-d/2} \exp\left(-\frac{\mathbf{r}^2}{4K_1 t}\right)$$

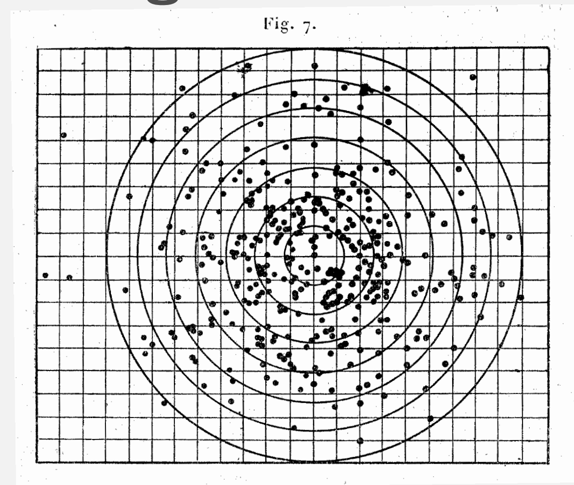
Violation of these conditions leads to anomalous diffusion with MSD $\langle \mathbf{r}^2(t)\rangle \simeq K_\alpha t^\alpha$ and/or non-Gaussian PDF

N van Kampen, Stochastic processes in physics & chemistry

Les atomes: Brownian motion and Avogadro's number

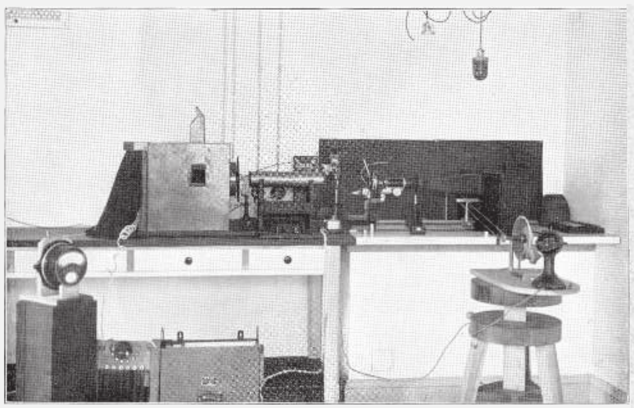


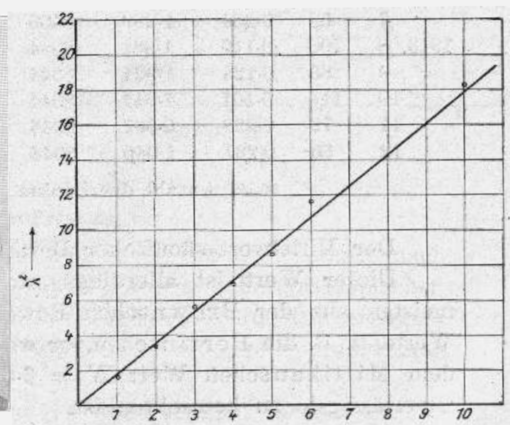


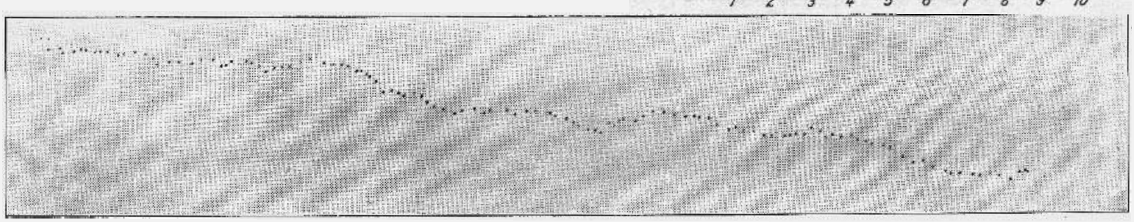


Δt=30 sec

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

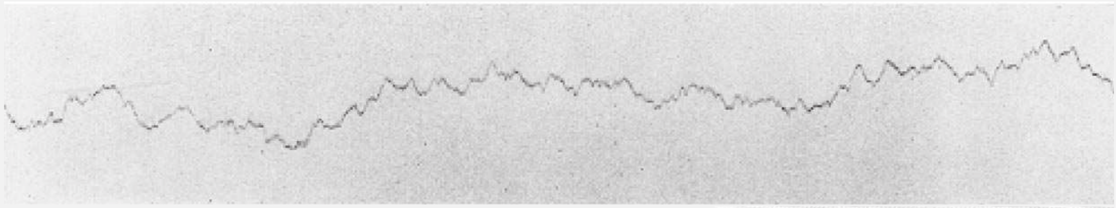


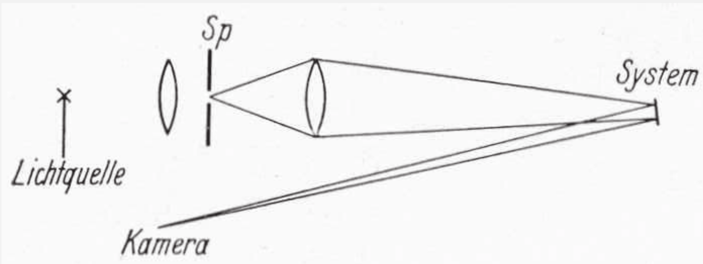




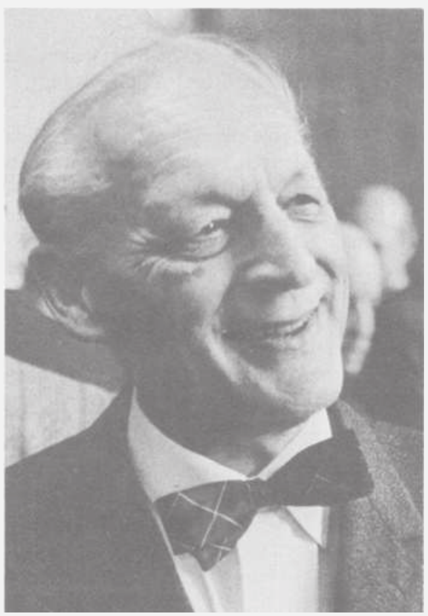
J Perrin, Comptes Rendus (Paris) 146 (1908) 967: $N_A = 70.5 \times 10^{22}$; I Nordlund, Z Physik (1914): $N_A = 5.91 \times 10^{23}$

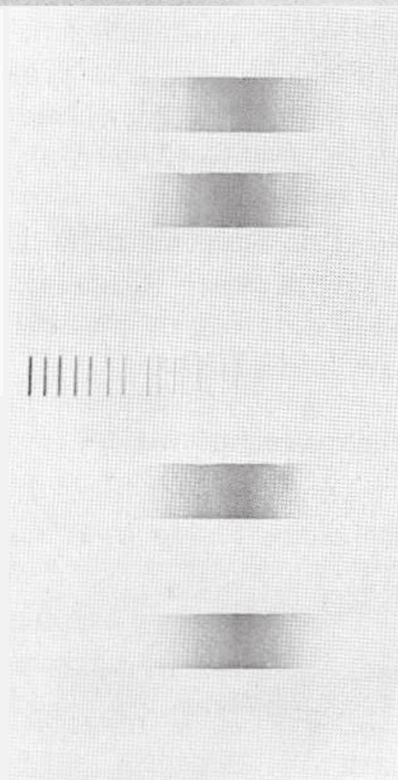
Kappler's diffusion measurements: mapping Boltzmann

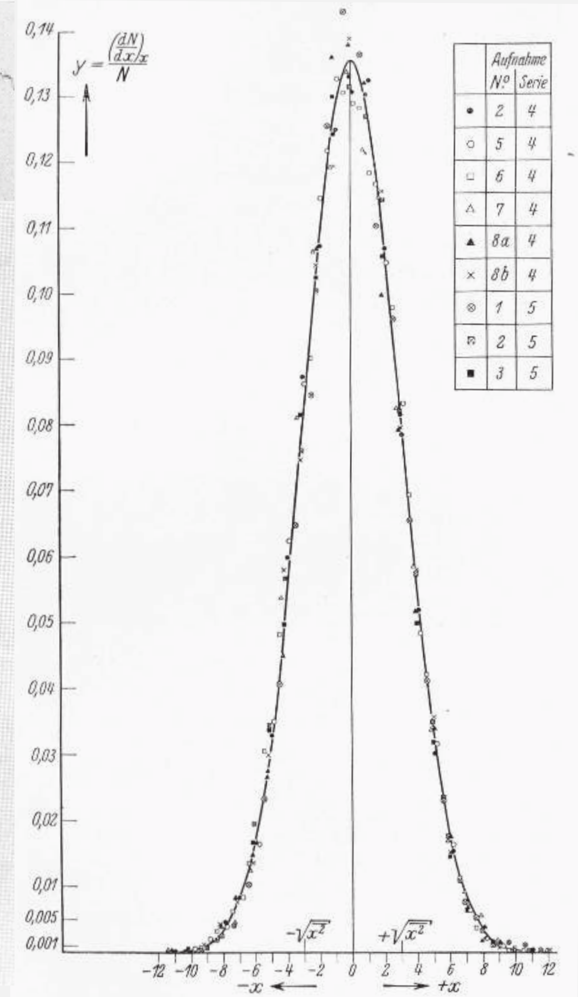




Schema der Meßanordnung
Fig. 1



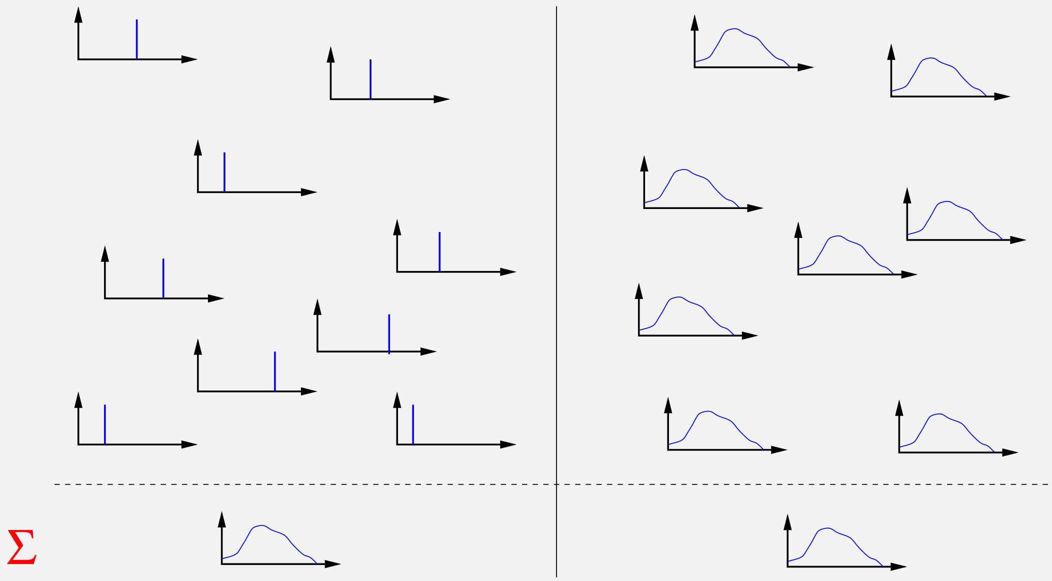


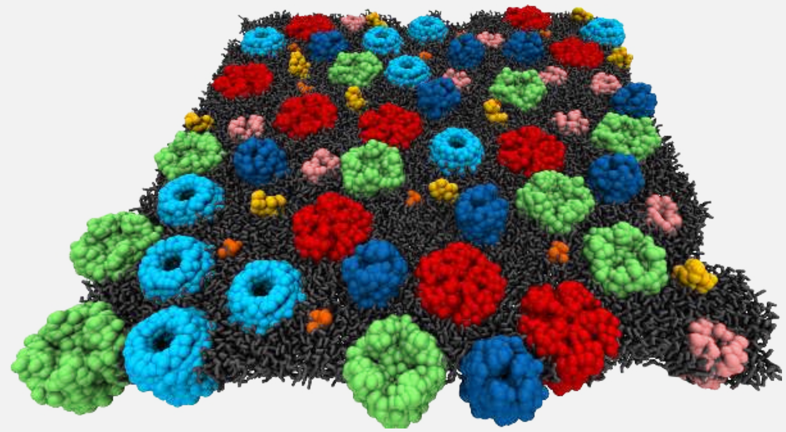


$$P_{\text{eq}}(x) = \mathscr{N} \exp\left(-\frac{\theta x^2}{k_B T}\right)$$

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

Single molecular insight & information from fluctuations



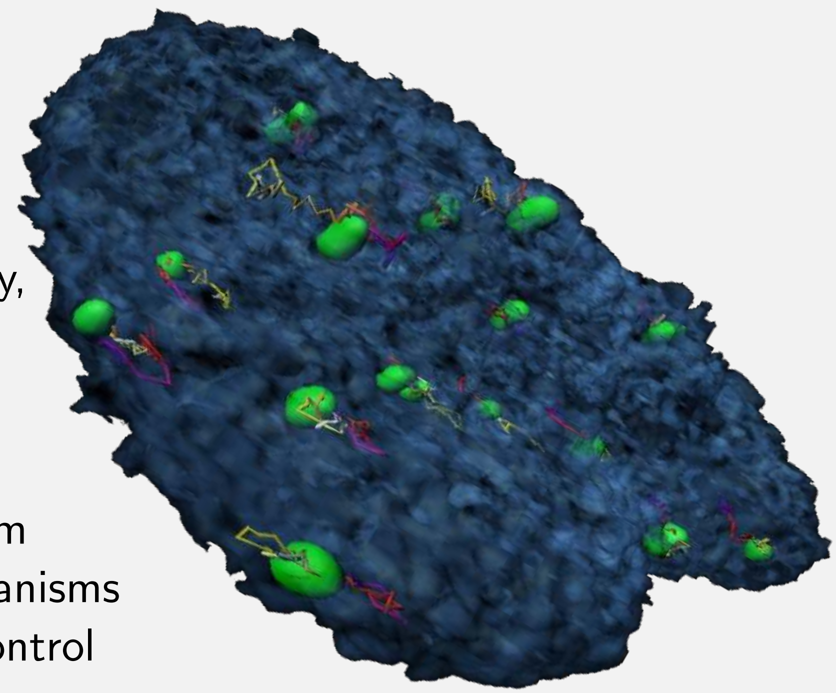


Courtesy Matti Javanainen

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

↷ New physics: anomalous diffusion, (non)ergodicity, ageing, quenched & annealed disorder & c.

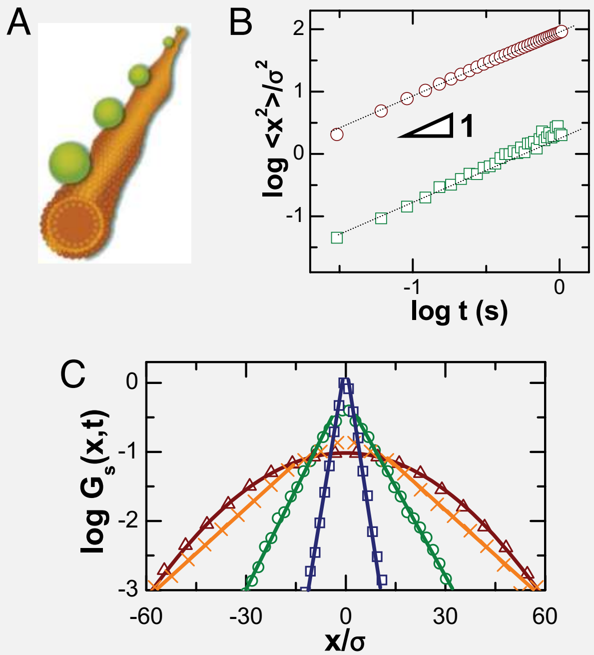
↷ Fluctuations & their distributions often provide important information on the system:
– fluctuating parameters reflect disorder in the system
– fluctuating single-particle observables reflect mechanisms
– fluctuating reaction times: geometry & reaction control



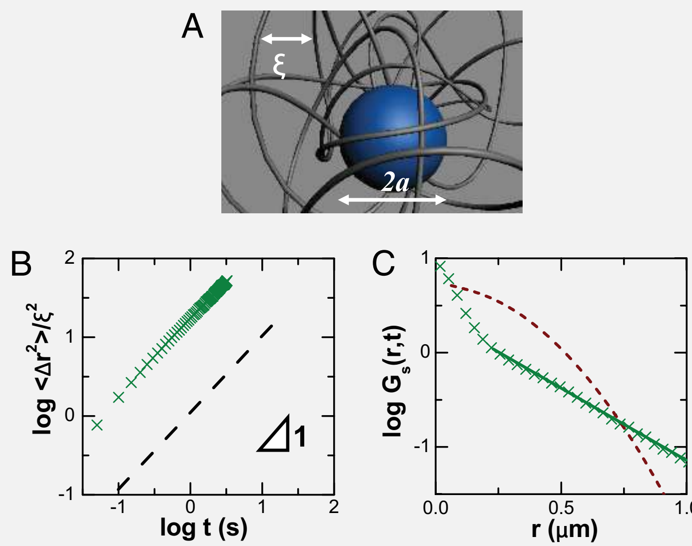
Courtesy Yuval Garini

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

Brownian yet non-Gaussian diffusion in soft & bio-matter

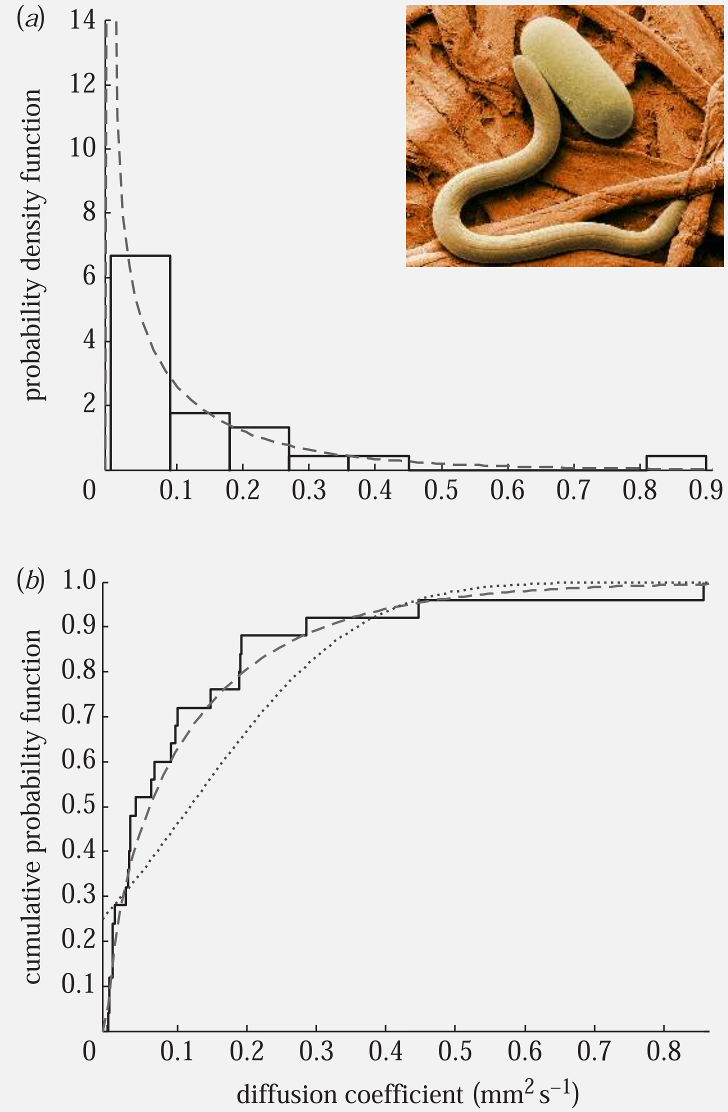


Colloidal beads on nanotubes



Nanospheres in entangled actin

Motion of *Phasmarhabditis* nematodes

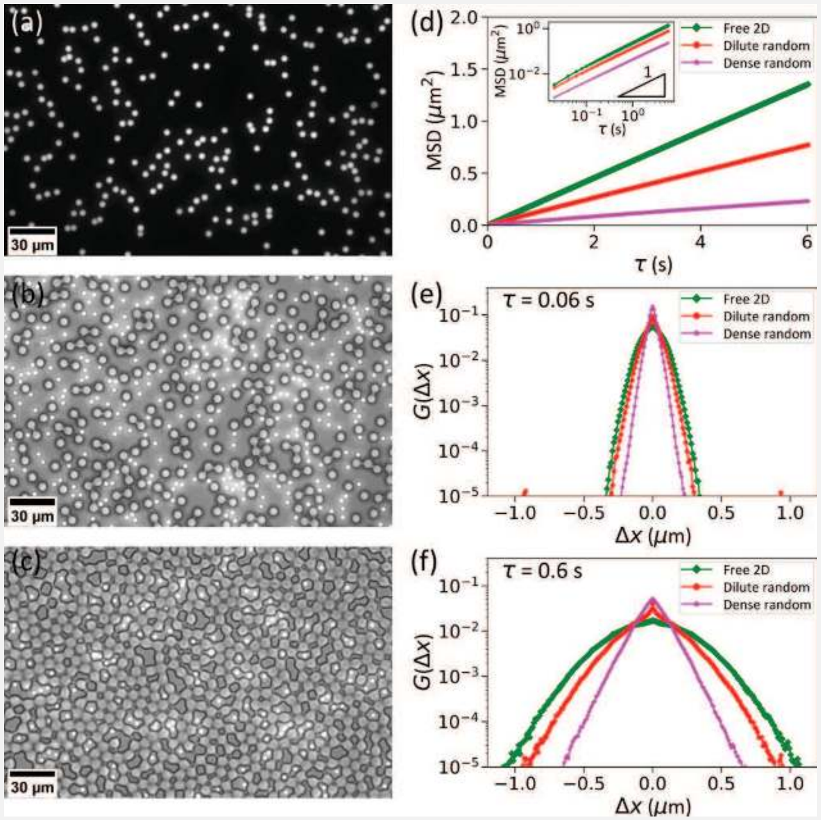


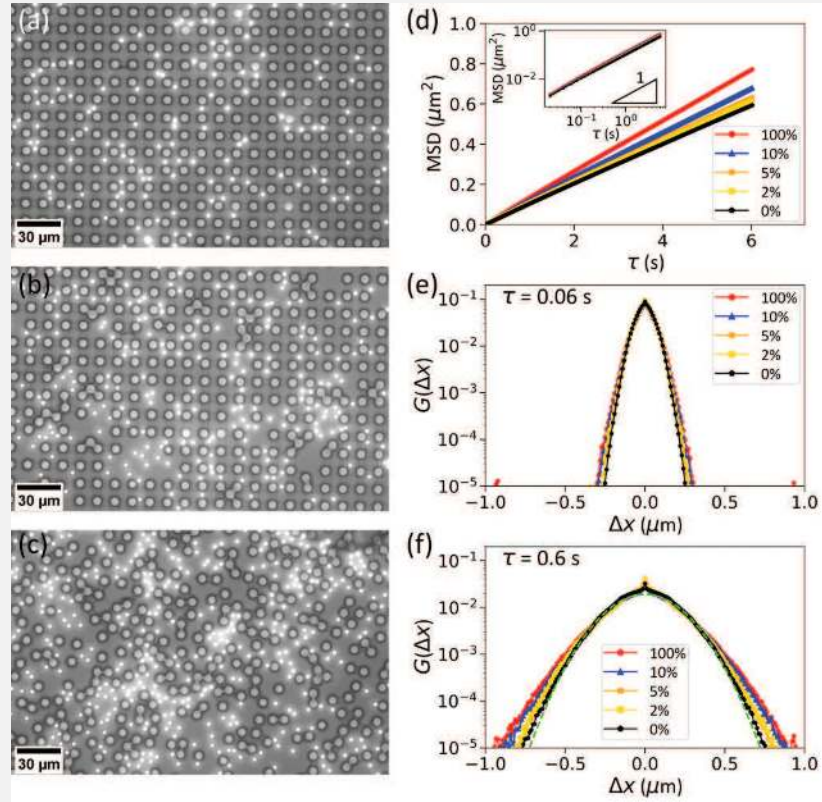
Wang et al, PNAS (2009); Nature Mat (2012)

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

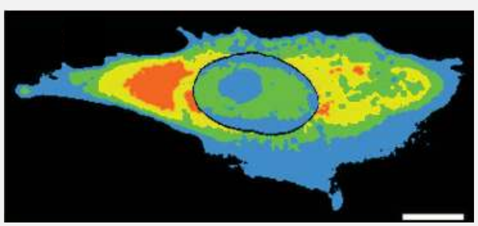
Fickian yet non-Gaussian diffusion in micropillar matrix

Increasing density ⟶





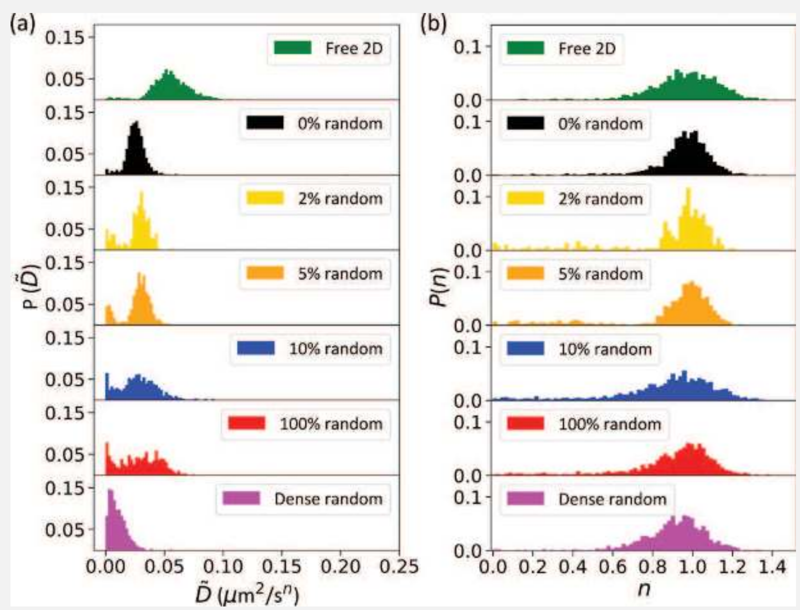
Increasing disorder ⟶



[Kühn et al, PLoS ONE (2011)]

I Chakraborty & Y Roichman, PRR (2020)

Apparent diffusivity

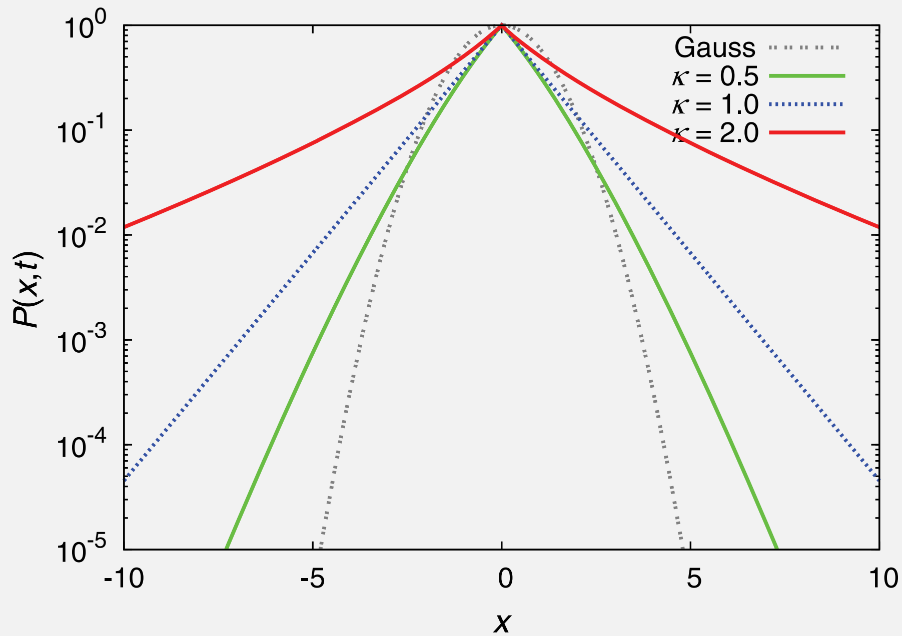


Anomalous diffusion exponent

Superstatistics for non-Gaussian probability densities

Superstatistical approach: patches of different diffusivities/mobilities or particles with different diffusivities (sizes/shapes) [$G(x,t|D)$ Gaussian Green's function for given D]:

$$P(x,t)=\int_0^\infty G(x,t|D)p(D)dD$$



- $p(D)\propto\exp(-D/D^\star)\rightsquigarrow$

$$P(x,t)=(4D^\star t)^{-1/2}\exp\left(-\frac{|x|}{[D^\star t]^{1/2}}\right)$$

- $p(D)\propto\exp(-[D/D^\star]^\kappa)\rightsquigarrow$

$$P(x,t)\simeq\frac{|x|^{(1-\kappa)/(1+\kappa)}}{(D^\star t)^{1/(1+\kappa)}}\times\exp\left(-a(\kappa)\left[\frac{x^2}{4D^\star t}\right]^{\kappa/(1+\kappa)}\right)$$

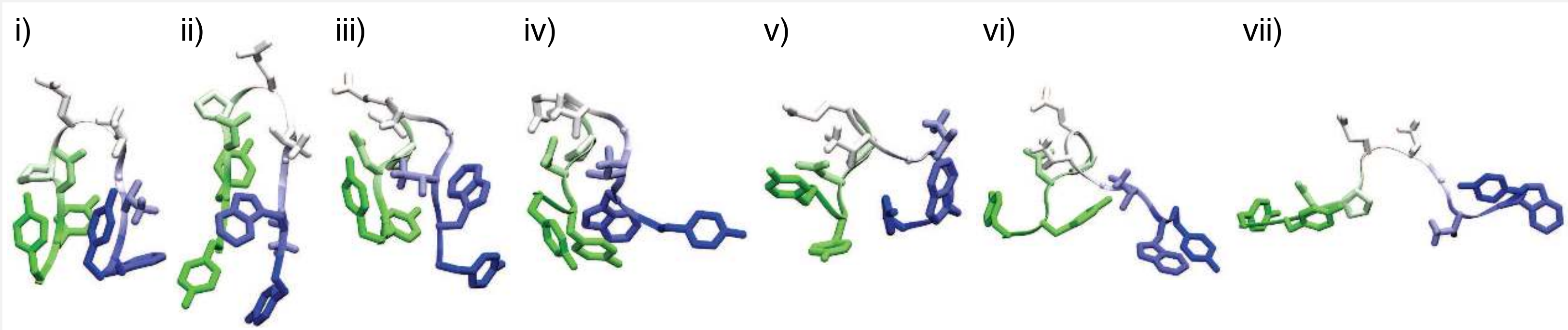
NB1: Superstatistics is closely related to (generalised) grey Brownian motion

[E.g., A Mura, MS Taqqu & F Mainardi, Physica (2008)]

NB2: $p(D)$ is static $\rightsquigarrow$ $P(x,t)$ has fixed shape ↯ observed cross-over

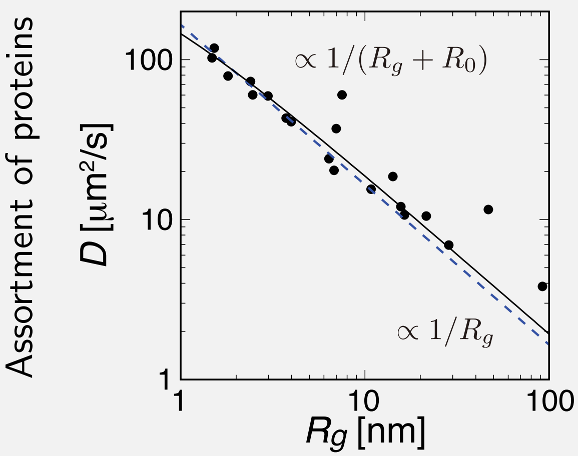
C Beck & EDB Cohen, Physica A (2003); AV Chechkin, F Seno, RM & IM Sokolov, PRX (2017)

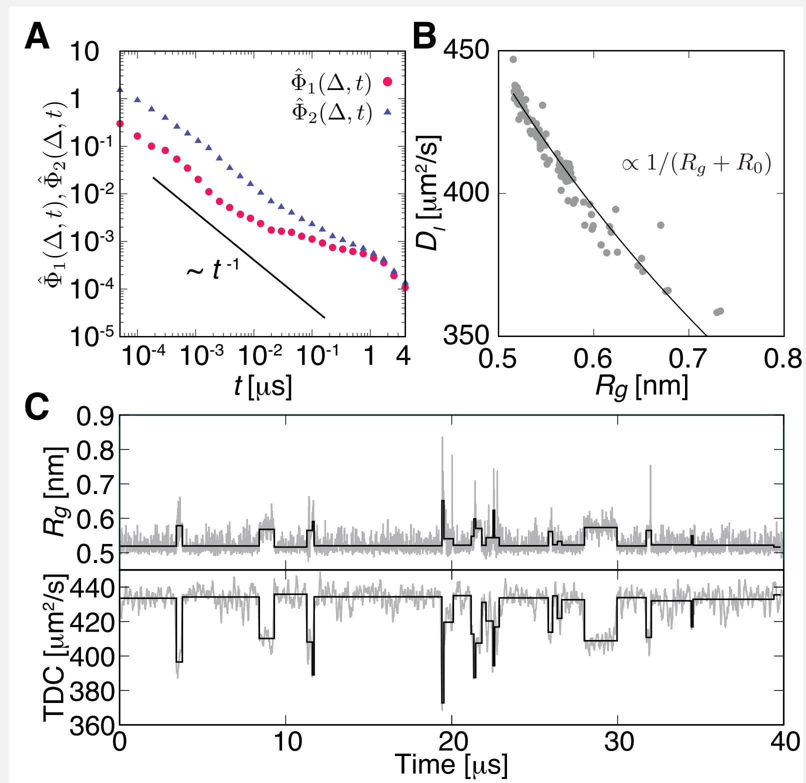
Instantaneous diffusivity of shape-fluctuating proteins



Instantaneous Einstein-Stokes-type relation (for different pressure & temperature):

$$D \propto \frac{1}{R_g + R_0}, \quad R_0 \approx 0.3\text{nm}$$





E Yamamoto, T Akimoto, A Mitsutake & RM, PRL (2021)

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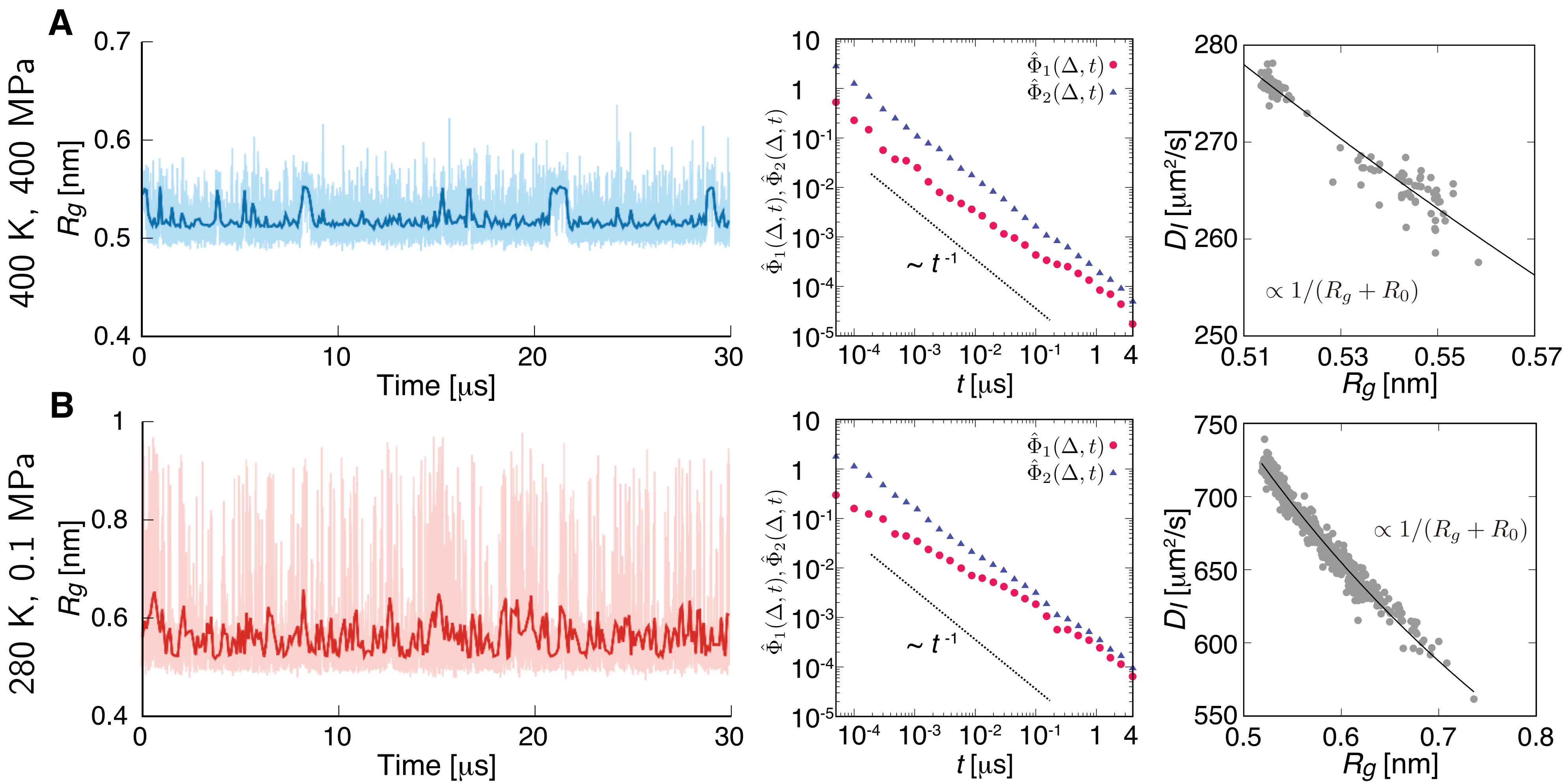

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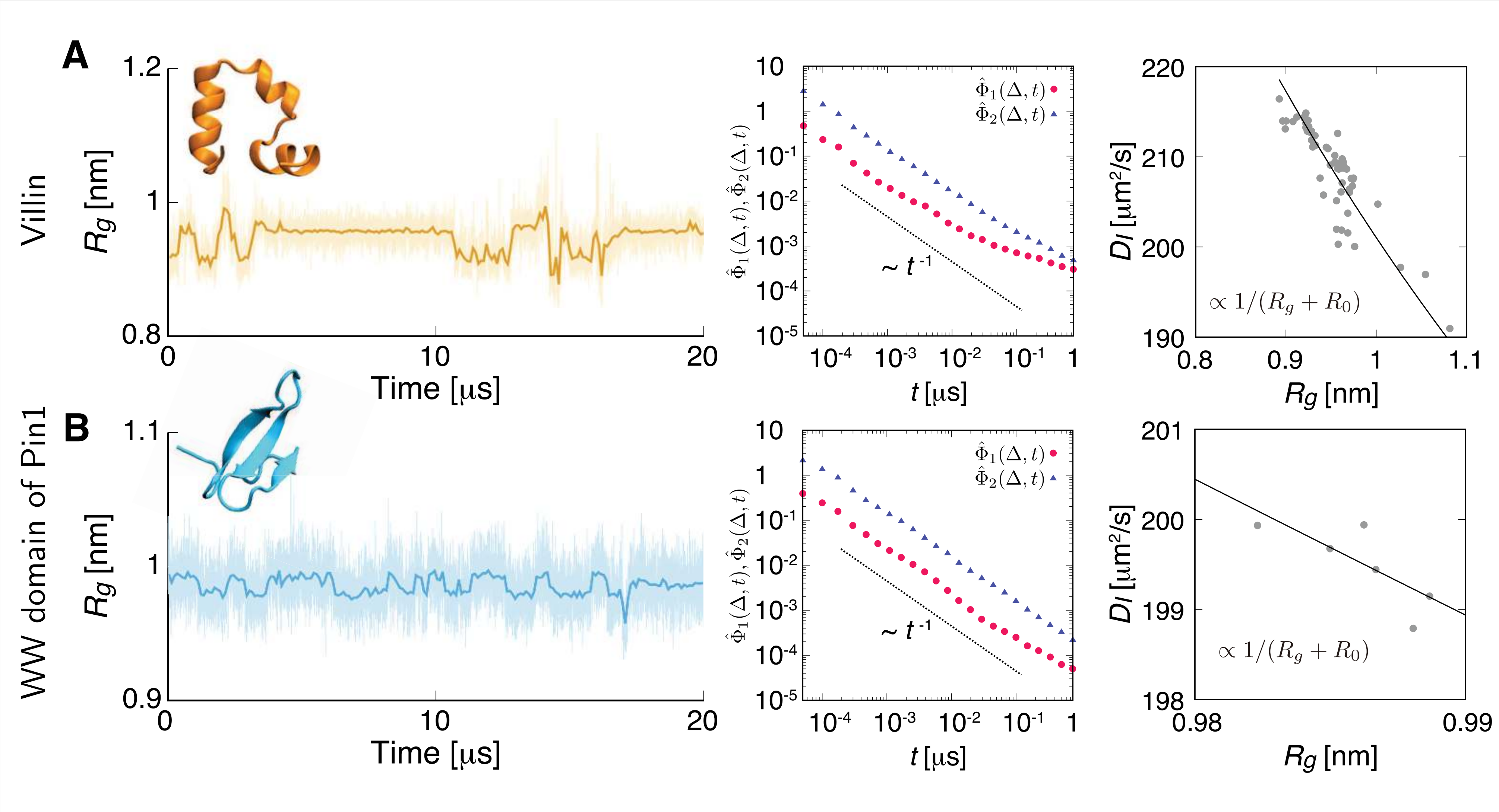


E Yamamoto, T Akimoto, A Mitsutake & RM, PRL (2021)

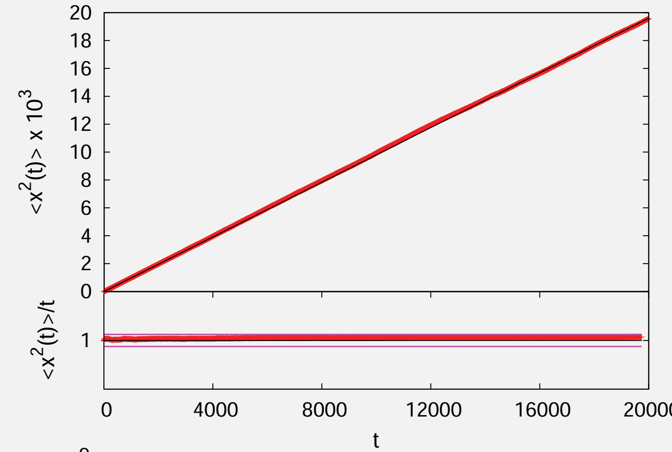
Fickian, non-Gaussian diffusion with diffusing diffusivity

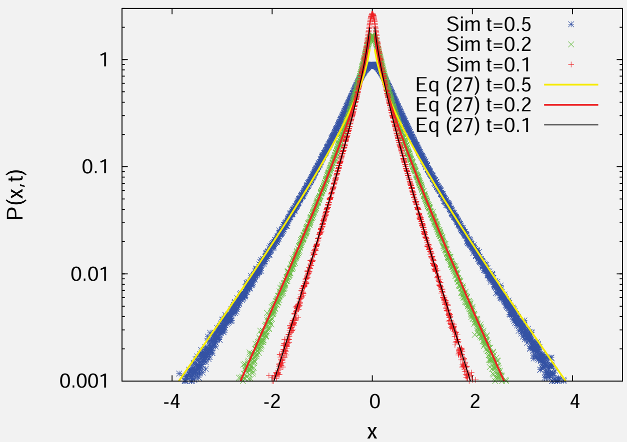
MV Chubinsky & G Slater, PRL (2014): diffusing diffusivity

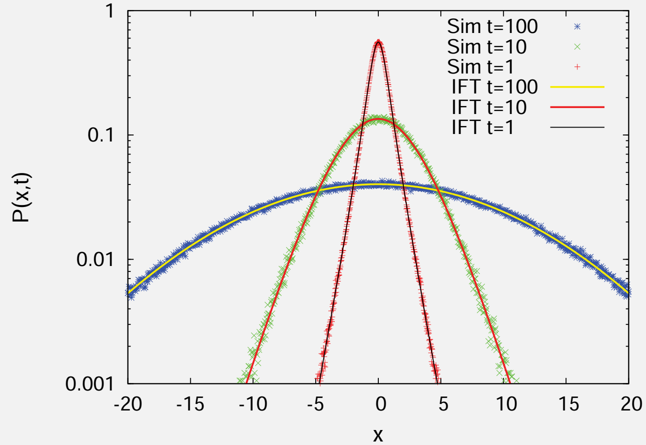
[see also R Jain & KL Sebastian, JPC B (2016)]

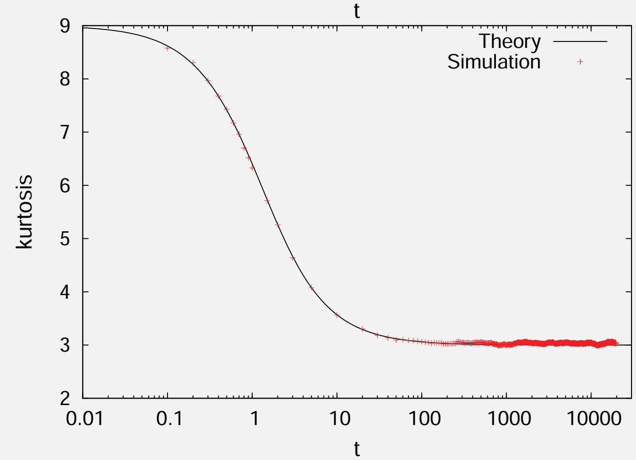
Our minimal model for diffusing diffusivity:

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





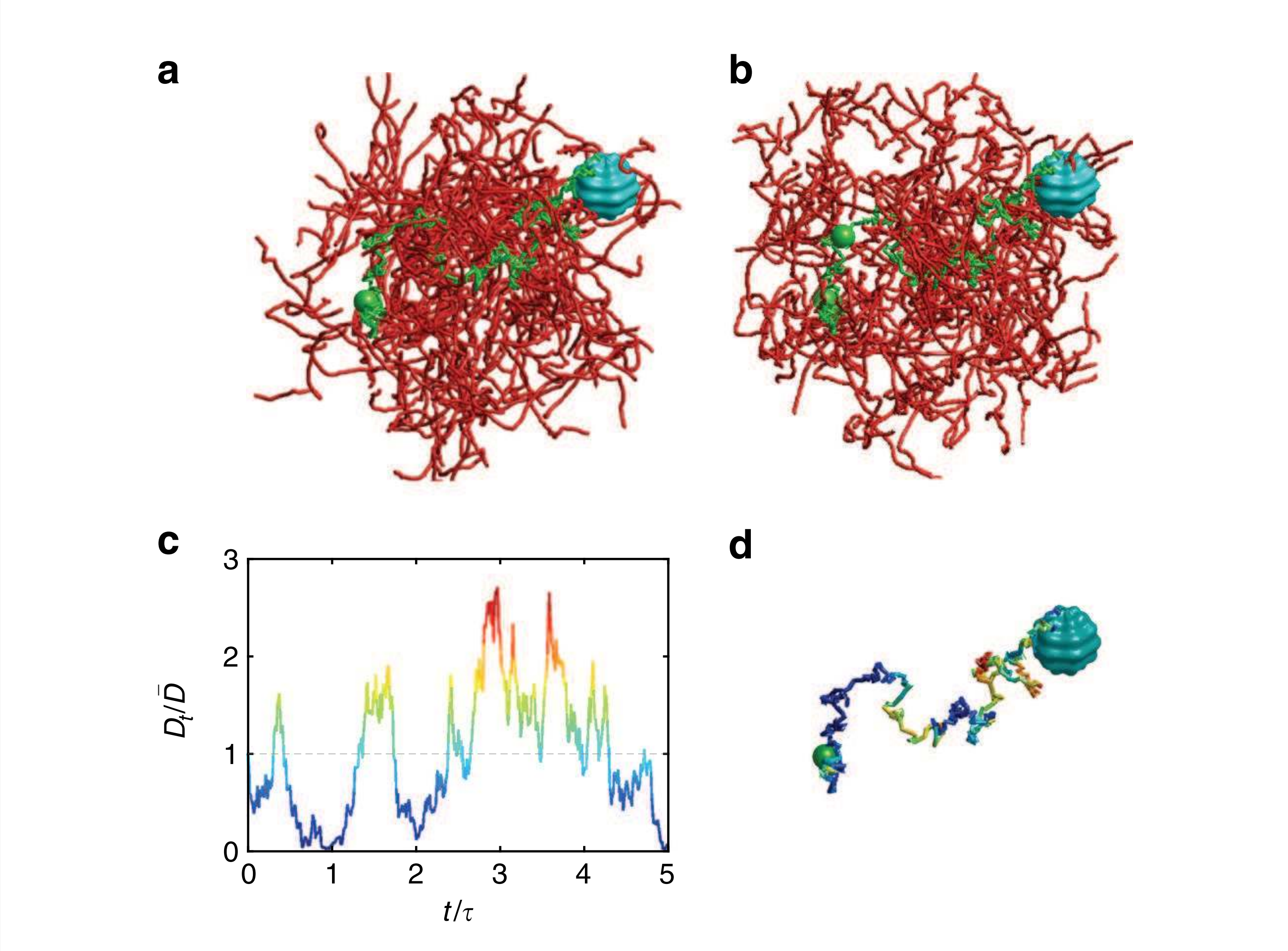




Generalised γ distribution & non-equilibrium diffusivity initial conditions: V Sposini, AV Chechkin, G Pagnini, F Seno & RM, NJP (2018)

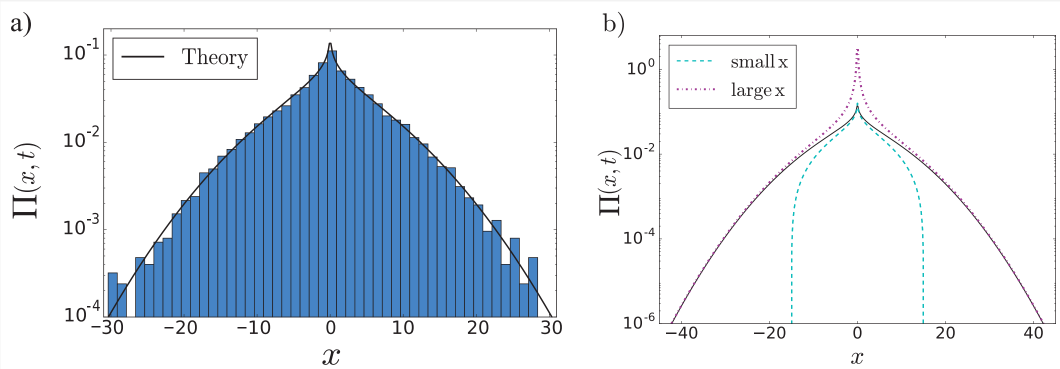
AV Chechkin, F Seno, RM & IM Sokolov, PRX (2017)

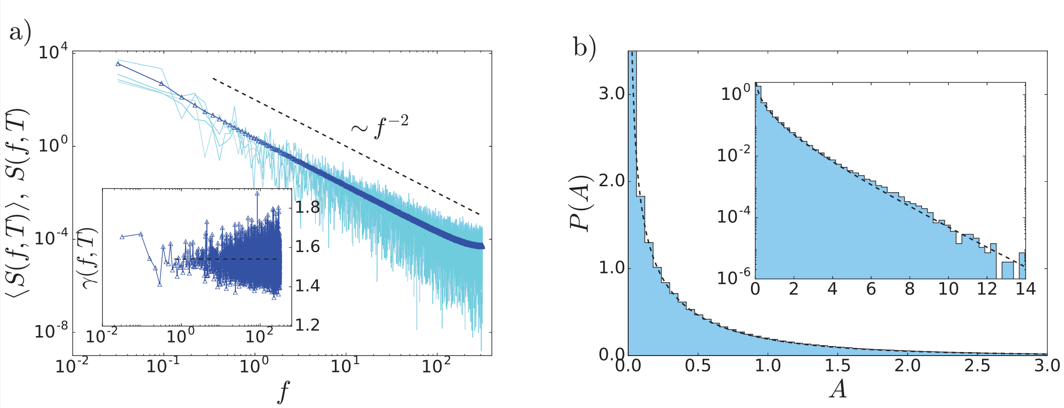
"Annealed" diffusing-diffusivity in rearranging heterogeneous enironment



Random-diffusivity models for non-Gaussian diffusion

1. Multimerisation of tracer [F Baldovin, F Seno & E Orlandini, Frontiers (2019); M Hidalgo-Soria & E Barkai, PRE (2020)]
2. Two-state model [A Sabri, X Xu, D Krapf & M Weiss, PRL (2020)]
3. Extreme value statistic of tails for small # jumps [E Barkai & S Burov, PRL (2020)]
4. Compartmenalisation model with partial reflectivity [J Ślęzak & S Burov, E-print (2020)]
5. Jump processes & functionals of Brownian motion [V Sposini, D Grebenkov, RM, G Oshanin & F Seno, NJP (2020)]



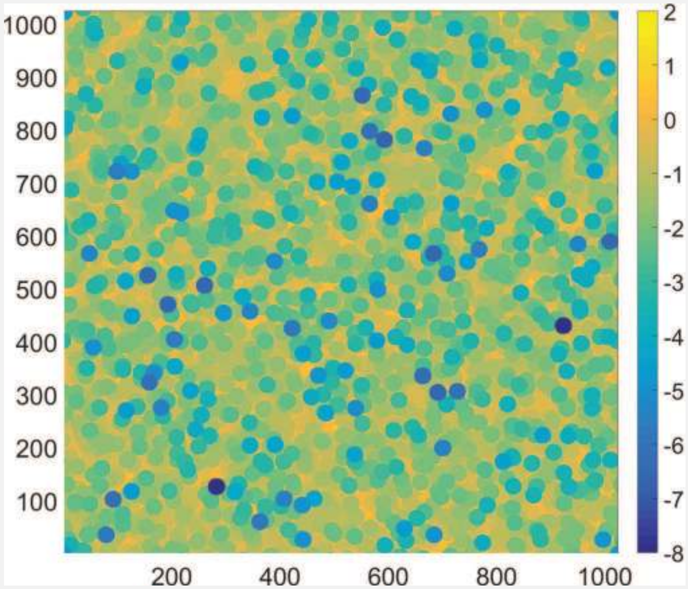


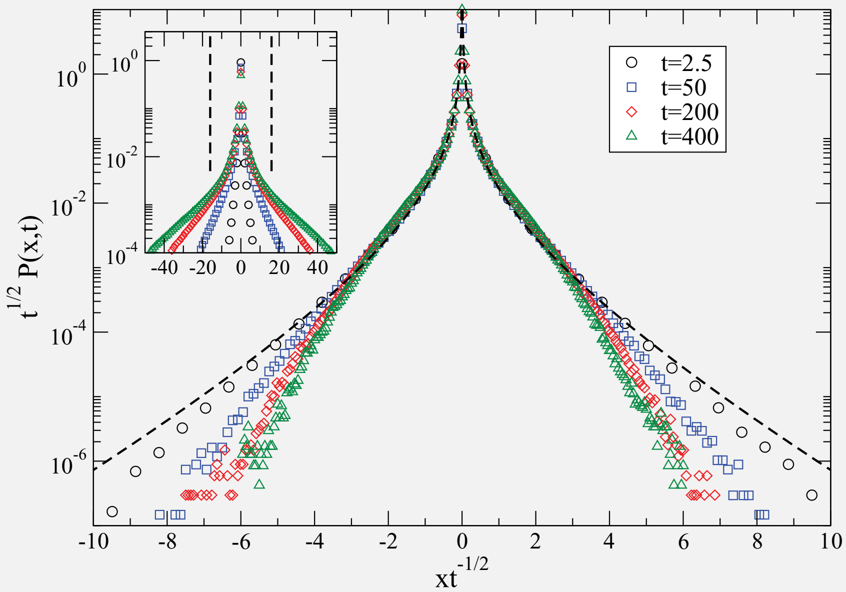
$$\dot{x}_t = \sqrt{2D_0\Psi_t}\xi_t \quad \therefore$$

Rectified BM: $\Psi_t \Theta(B_t)$:

$$P(x,t) = \frac{\exp(-x^2/[8D_0t])}{2\sqrt{\pi^3 D_0 t}} \times K_0\left(\frac{x^2}{8D_0t}\right)$$

Non-Gaussian diffusion in quenched landscape models



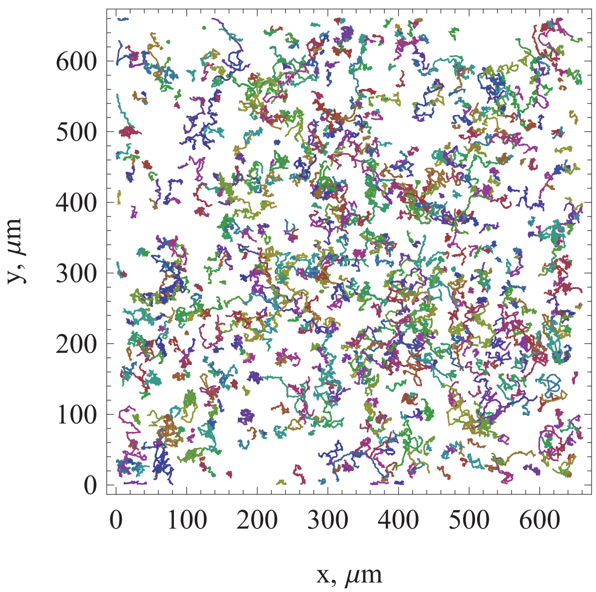


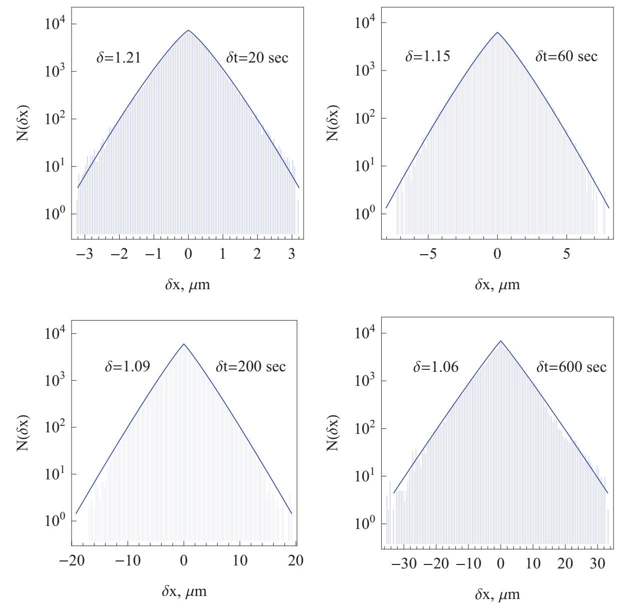
L Luo & M Yi, PRE (2018,2019)

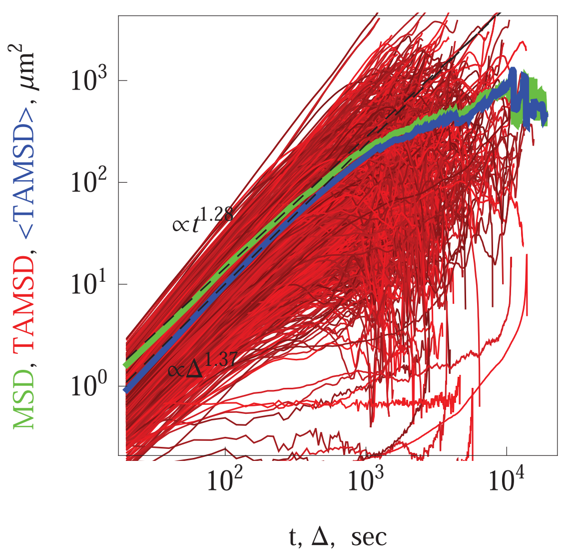
See also EB Postnikov, A Chechkin & IM Sokolov, NJP (2020)

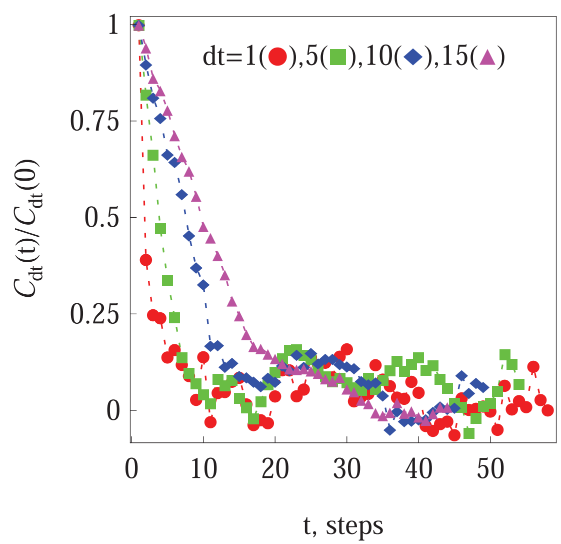
Quenched landscape theory: P Massignan, C Manzo, JA Torreno-Pina, MF García-Parajo, M Lewenstein & GJ Lapeyre Jr, PRL (2014)

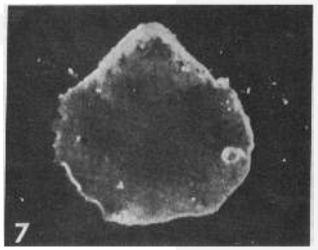
Increasing non-Gaussianity in moving amoeba cells





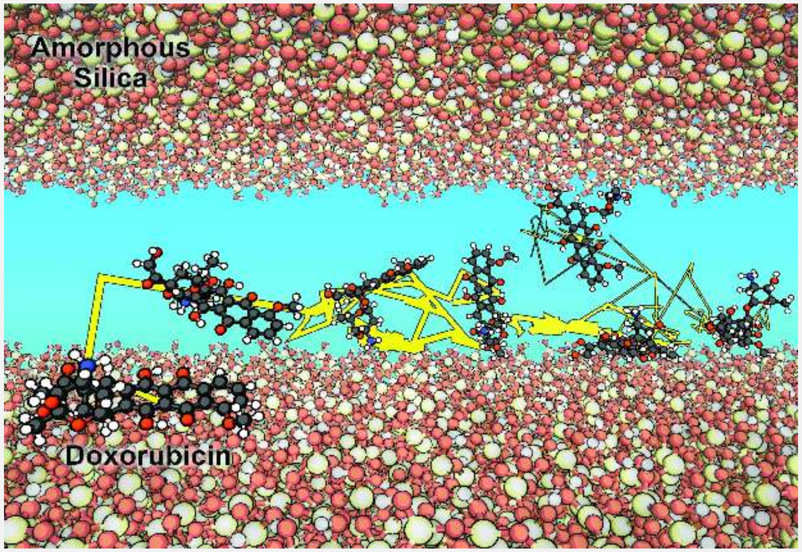


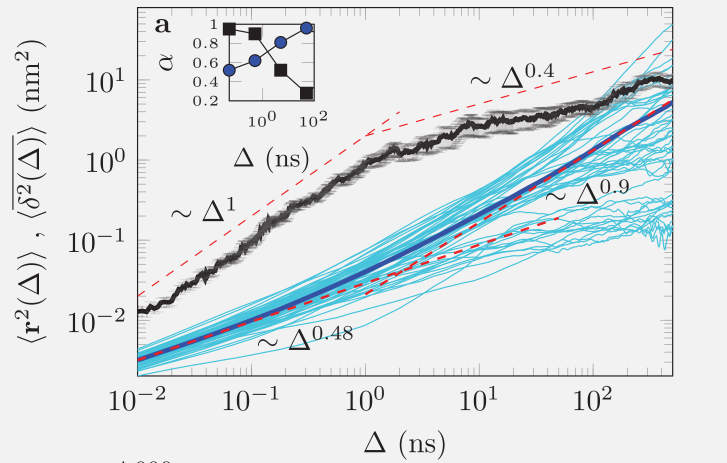


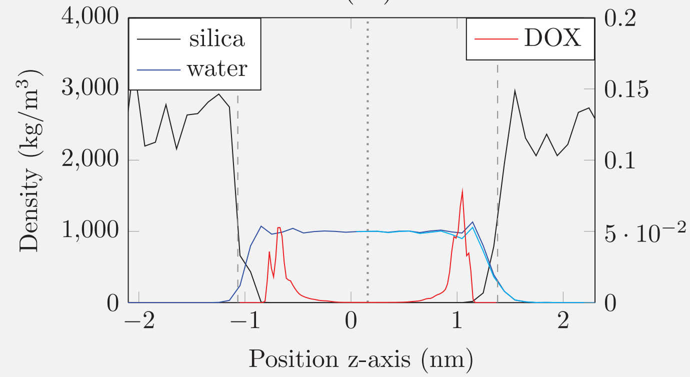


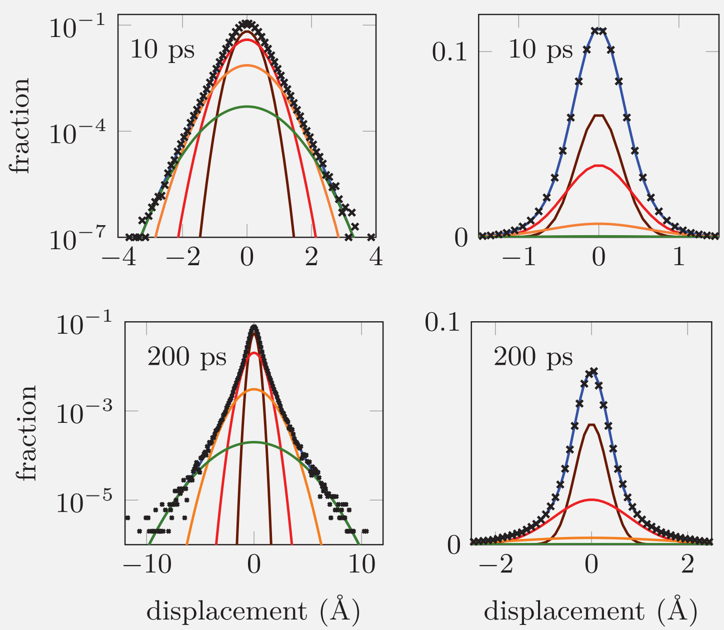
AG Cherstvy, O Nagel, C Beta & RM, PCCP (2018)

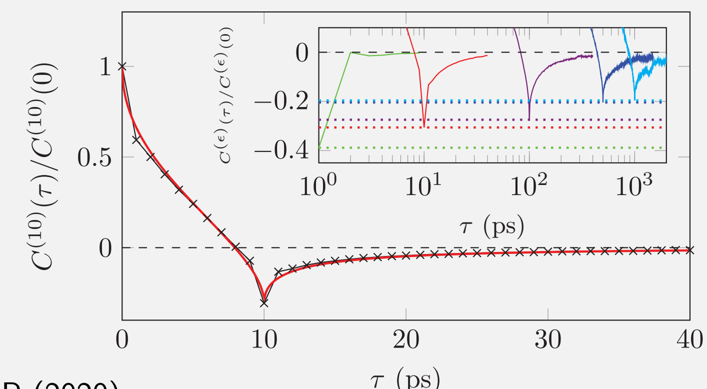
Doxorubicin drug molecule diffusion in silica nanochannels





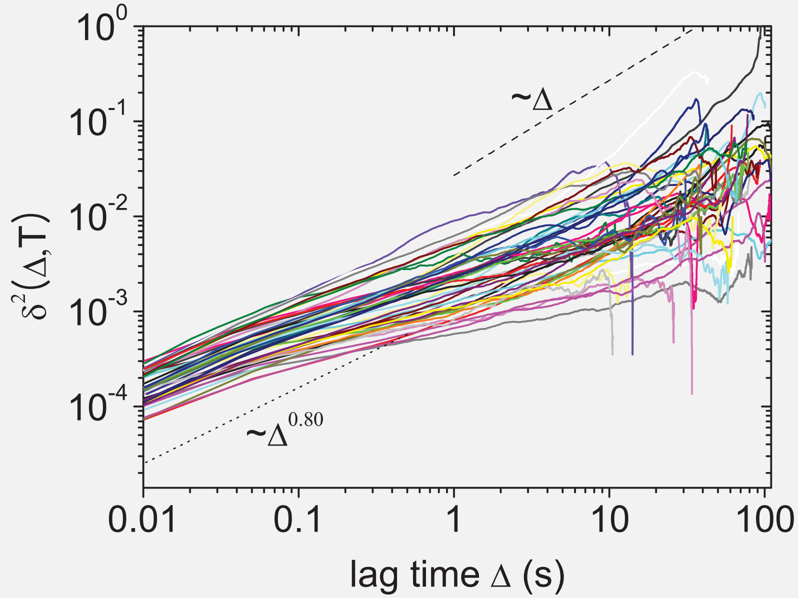


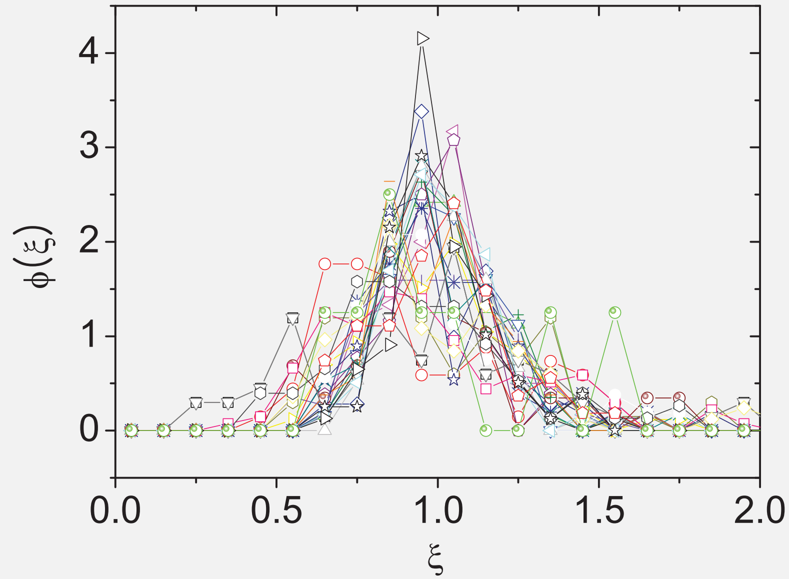




A Díez Fernández, P Charchar, AG Cherstvy, RM & MW Finnis, PCCP (2020)

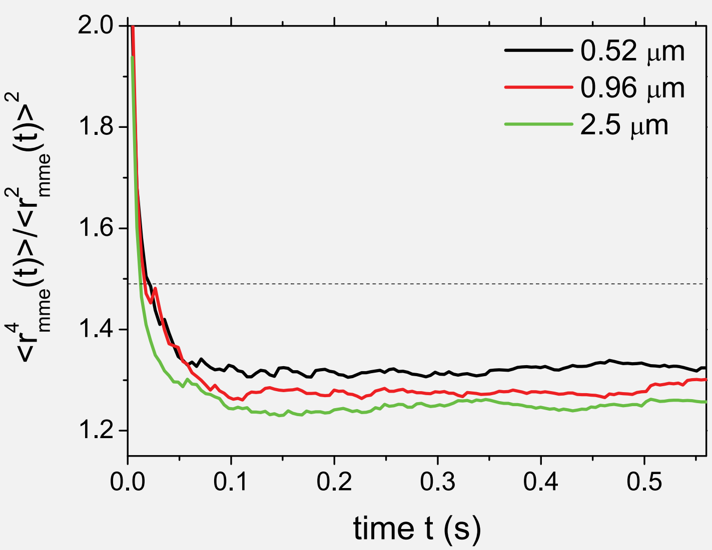
Passive motion of submicron tracers in cells is viscoelastic

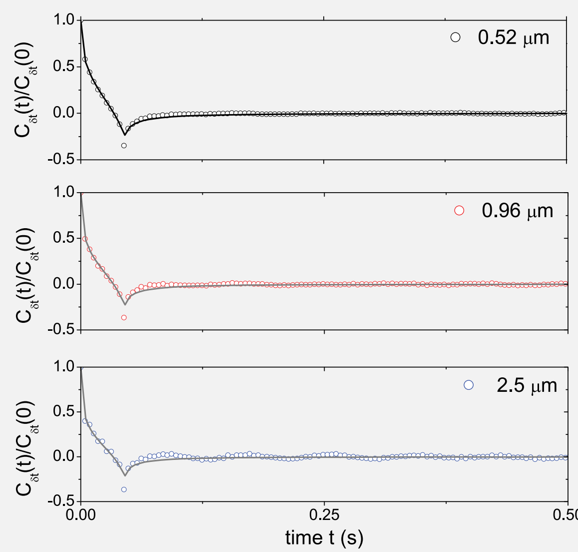


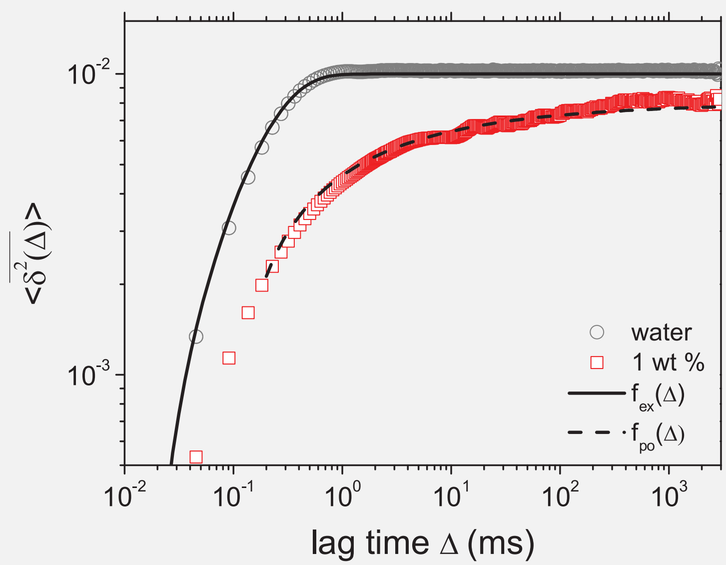


Lipid granules in living yeast cells ←

Tracer beads in wormlike micellar solution ⟶



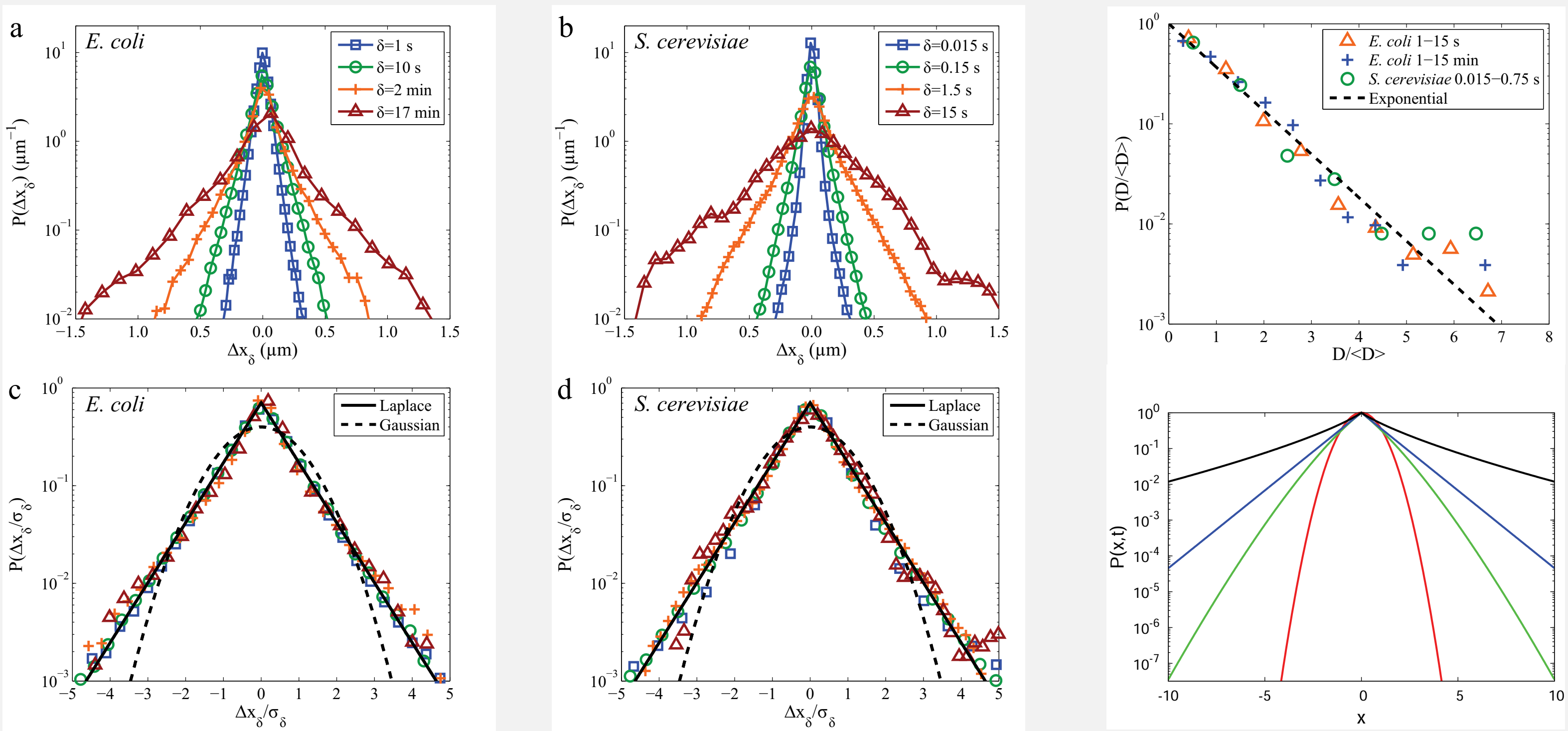




JH Jeon, . . . L Oddershede & RM, PRL (2011); JH Jeon, N Leijnse, L Oddershede & RM, NJP (2013)

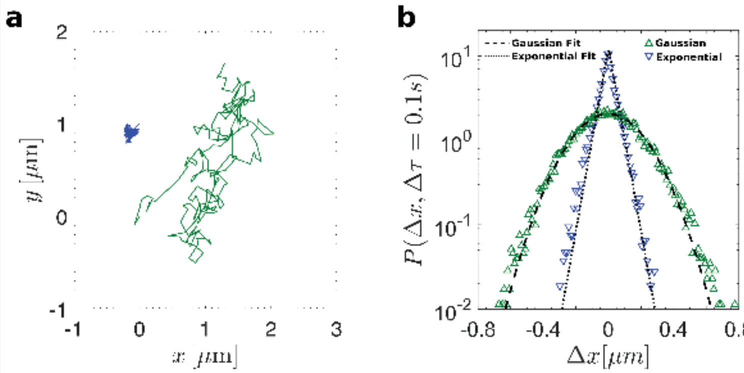
Non-Gaussian diffusion in viscoelastic systems

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:

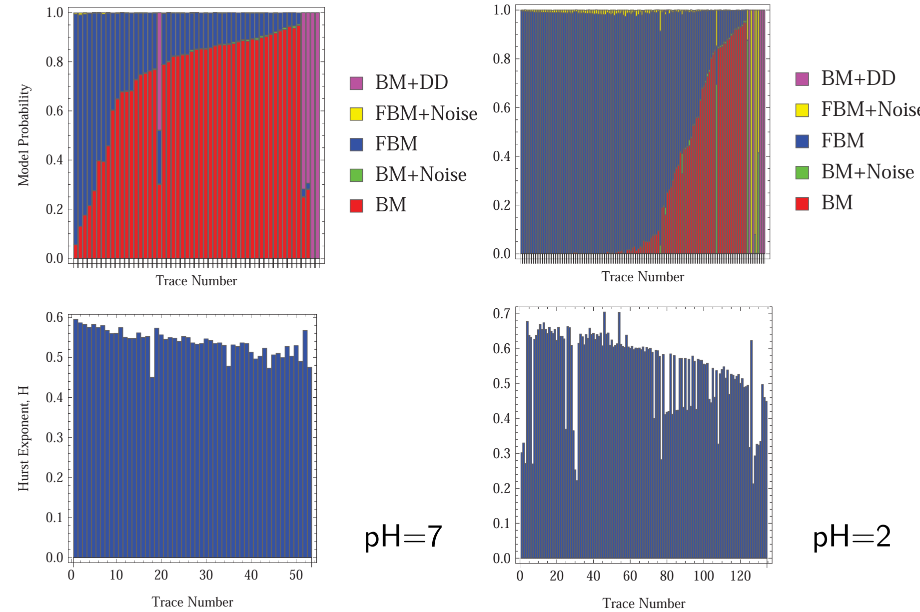


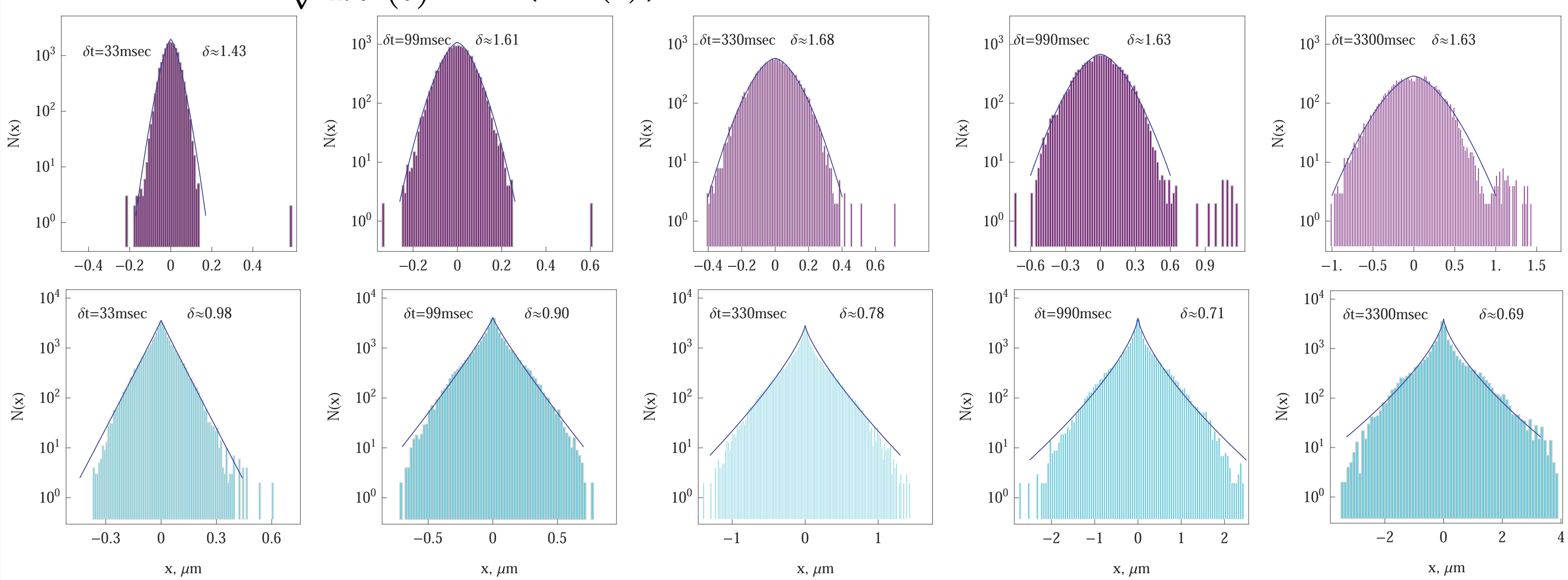
Non-Gaussian & non-Fickian diffusion in mucin hydrogels

CE Wagner et al, Biomacromol (2017)



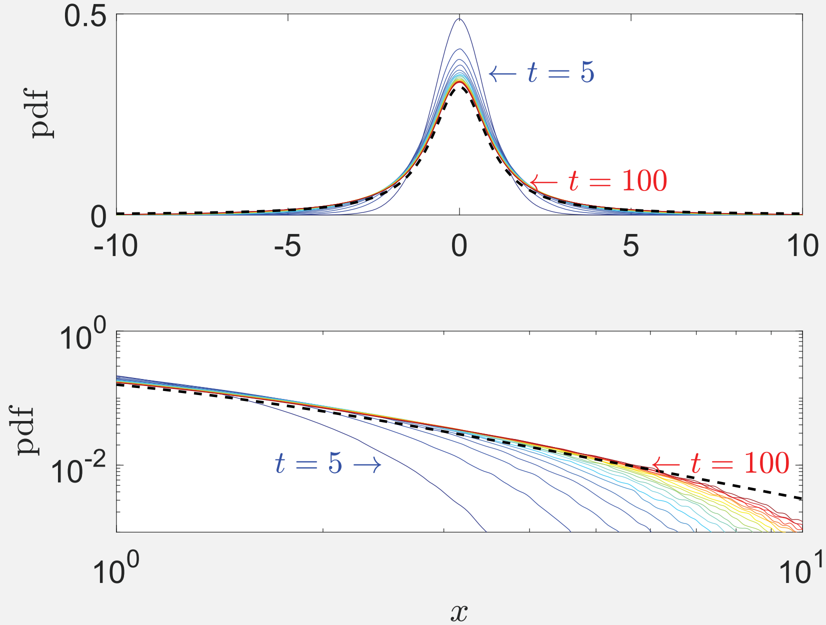
$$P(x,t) = \frac{A}{\sqrt{2\pi\sigma^2(t)}} \exp\left(-\frac{x^2}{2\sigma^2(t)}\right) + \frac{1-A}{\sqrt{4\lambda^2(t)}} \exp\left(-\frac{|x|}{\lambda(t)}\right)$$

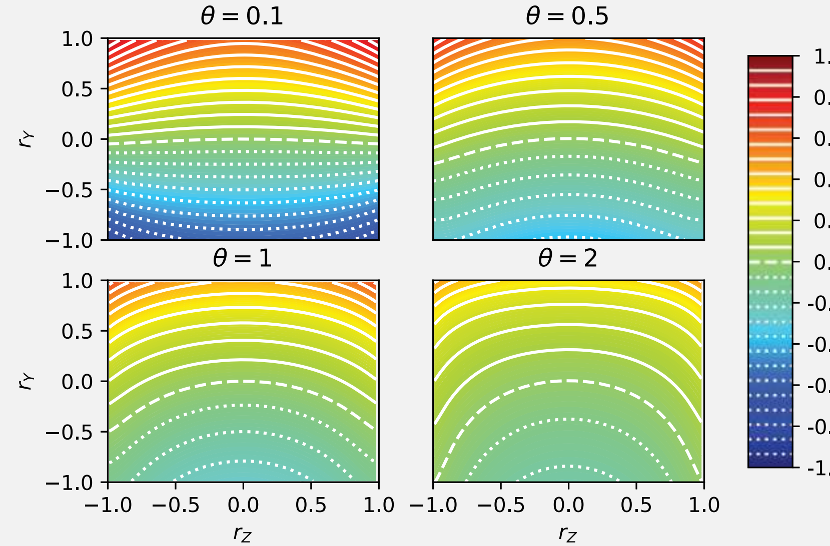




AG Cherstvy, S Thapa, CE Wagner & RM, Soft Matter (2019); Bayes: S Thapa, AG Cherstvy & RM, PCCP (2018)

Non-Gaussian dynamics in the presence of correlated noise

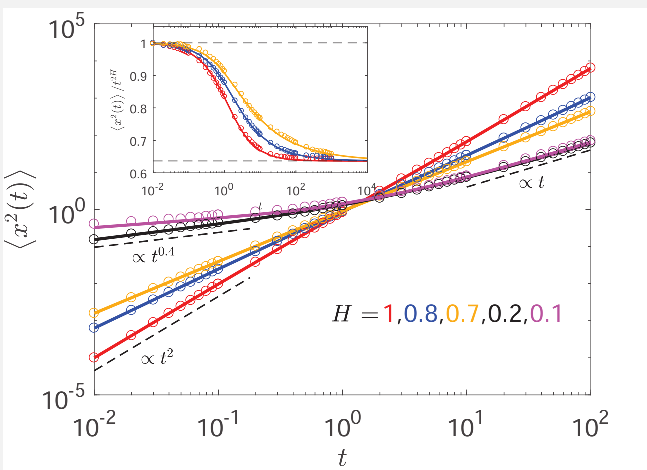


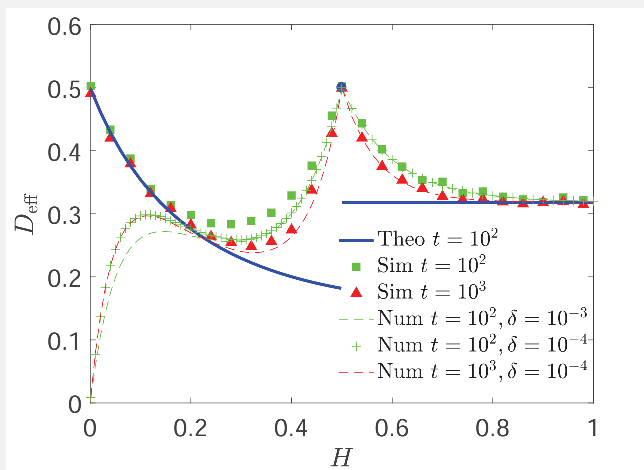


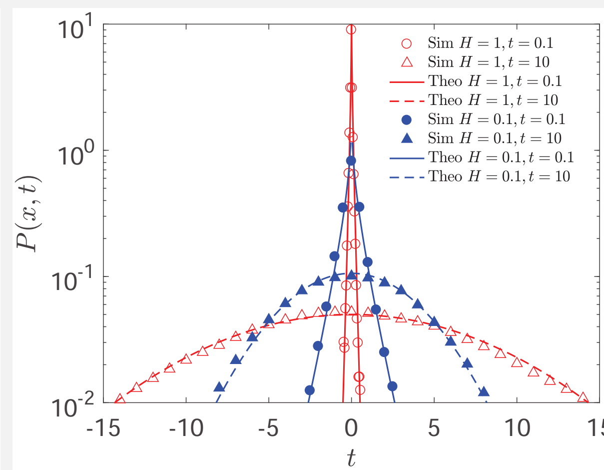
Codifference detects non-Gaussianity
& non-ergodicity

Viscoelastic diffusing-diffusivity model

Prosecco-DD



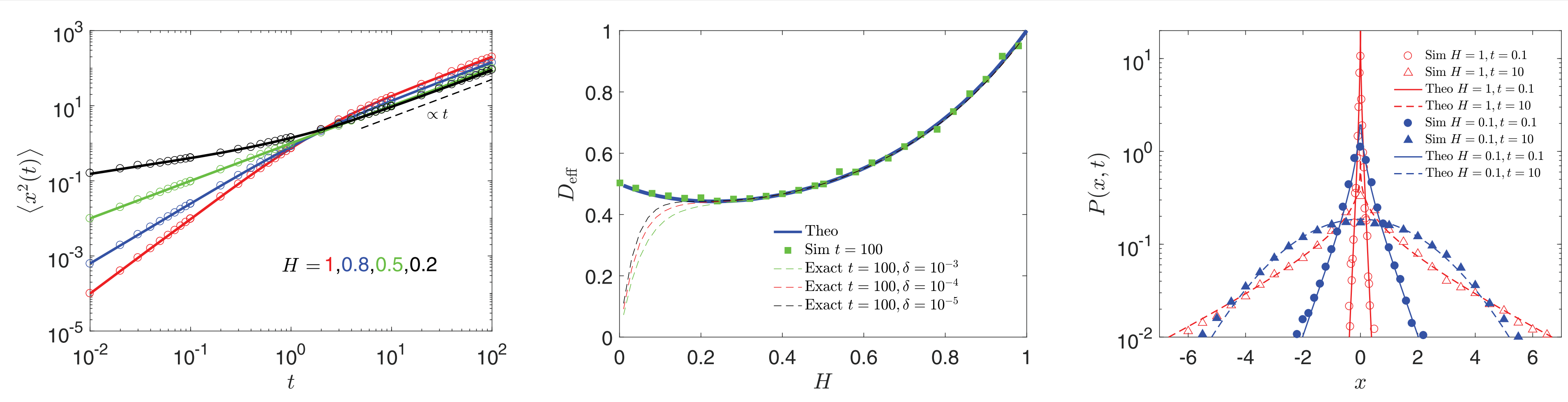




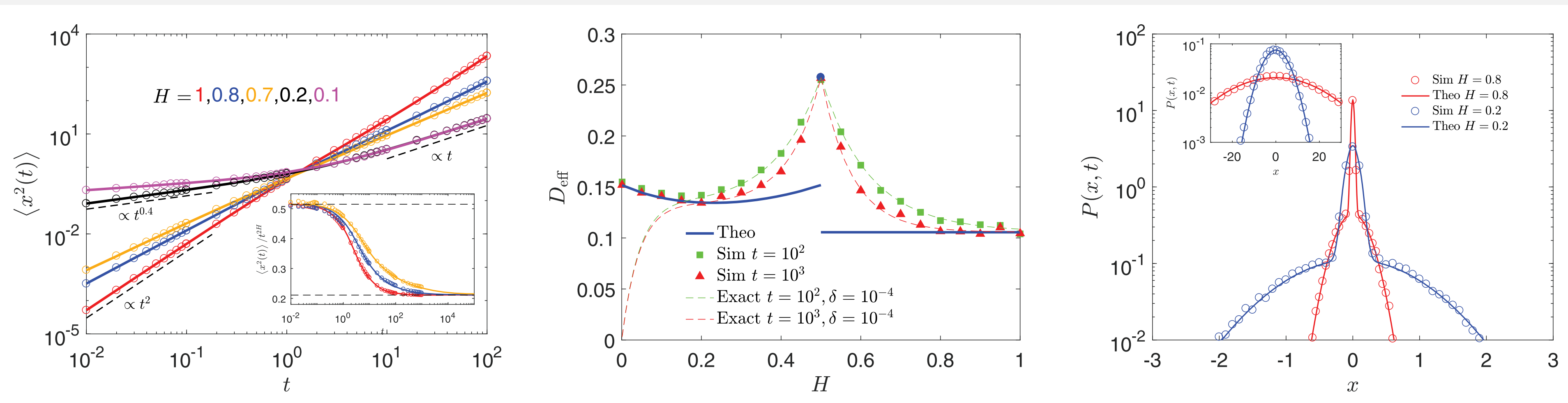
J Ślęzak, M Magdziarz & RM, NJP (2018), NJP (2019); W Wang, AV Chechkin, F Seno, IM Sokolov & RM, NJP (2020)

Viscoelastic diffusing-diffusivity model

Tyagi model

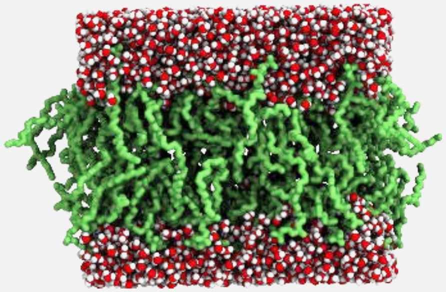


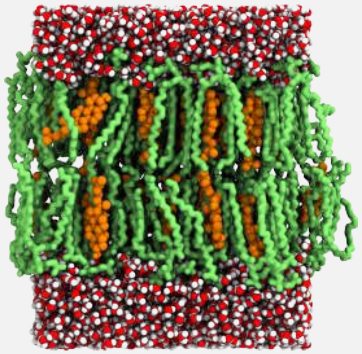
Switching model

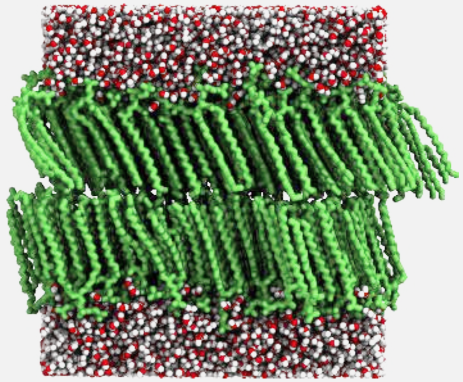


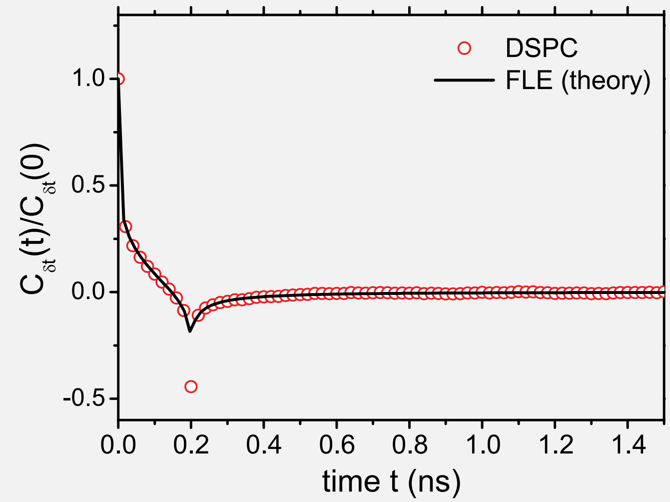
J Ślęzak, M Magdziarz & RM, NJP (2018), NJP (2019); W Wang, AV Chechkin, F Seno, IM Sokolov & RM, NJP (2020)

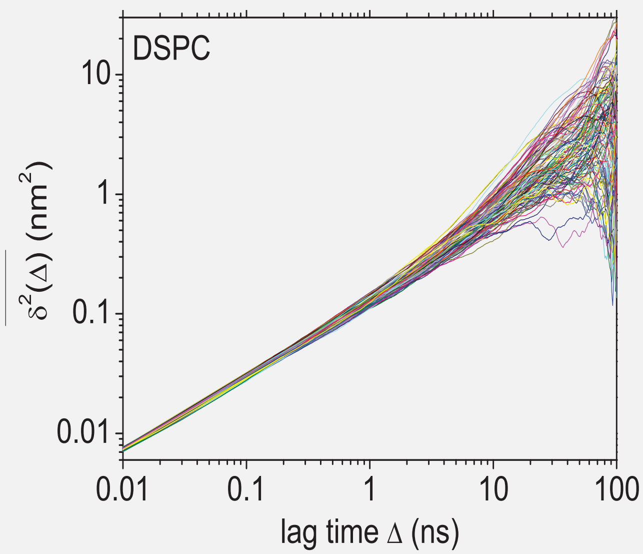
Single lipid motion in bilayer membranes

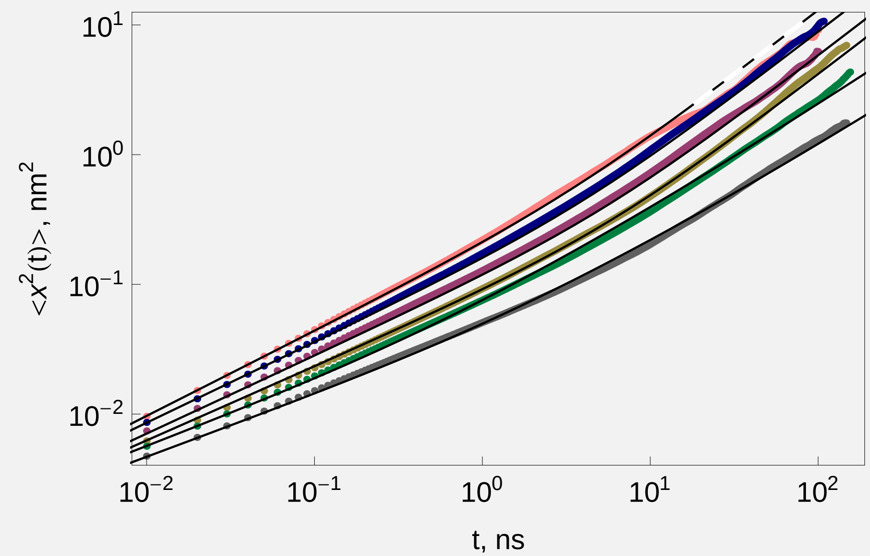












Pure bilayer:

$t^{2/3} \longrightarrow t^1$

/w cholesterol/gel:

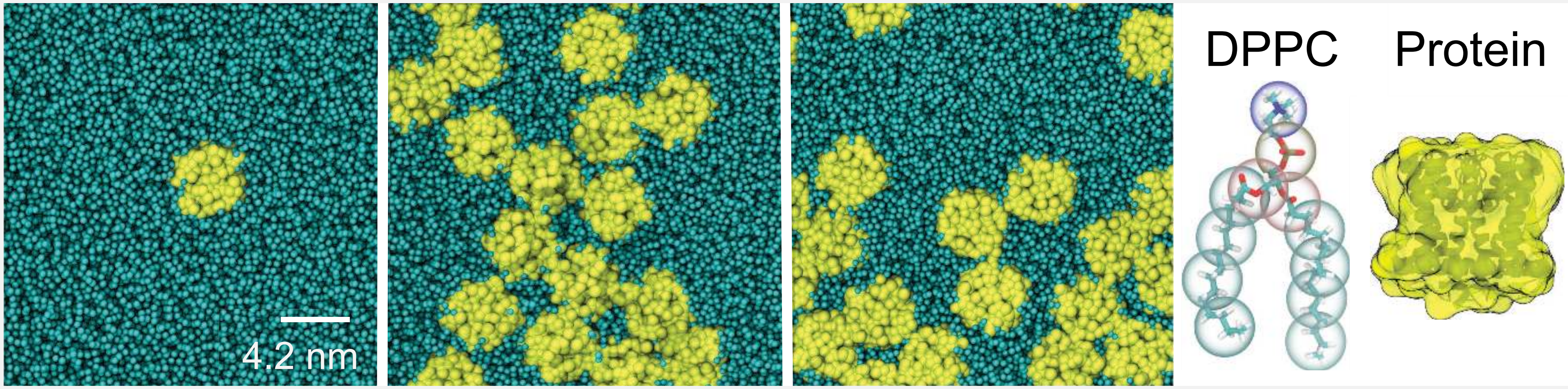
$t^{\alpha} \longrightarrow t^{\alpha' > \alpha}$

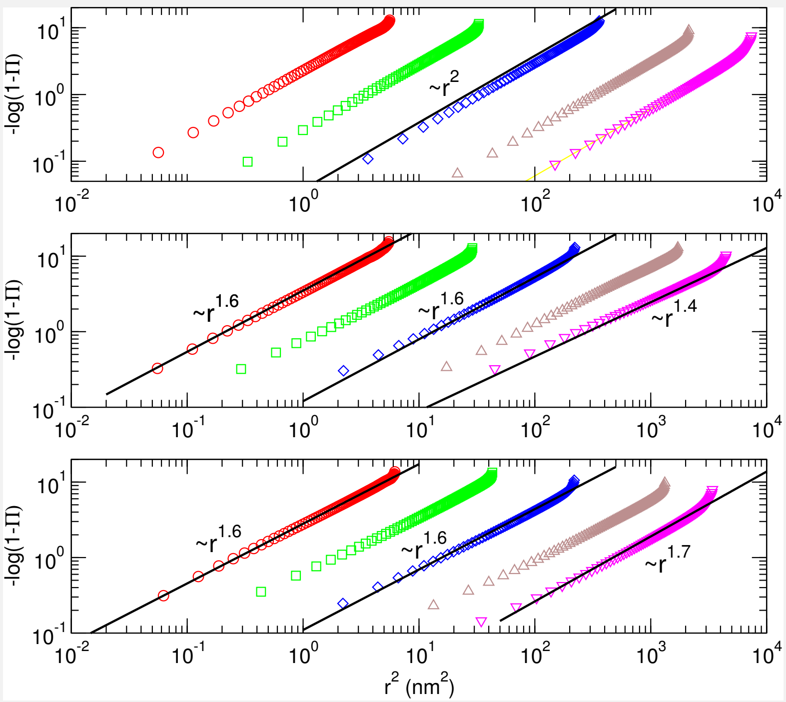
Tempered GLE

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

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

Crowding in membranes: non-Gaussian lipid/protein diffusion

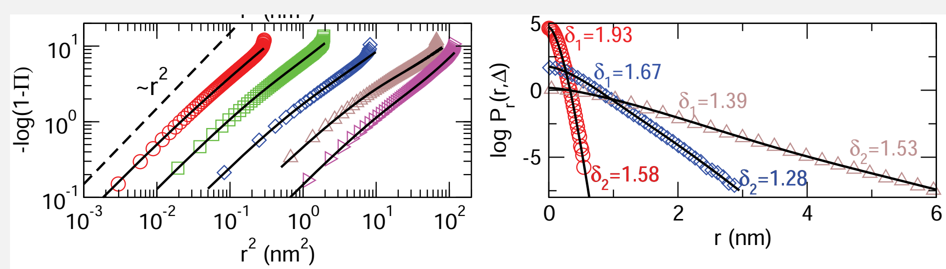




Dilute membrane: $P(r,t)$ Gauss

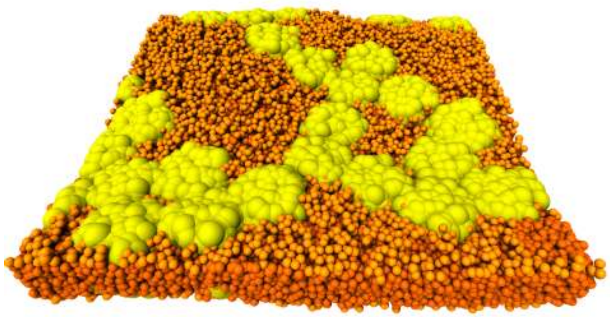
Crowded membrane ($\delta \approx 1.3 \ldots 1.7$):

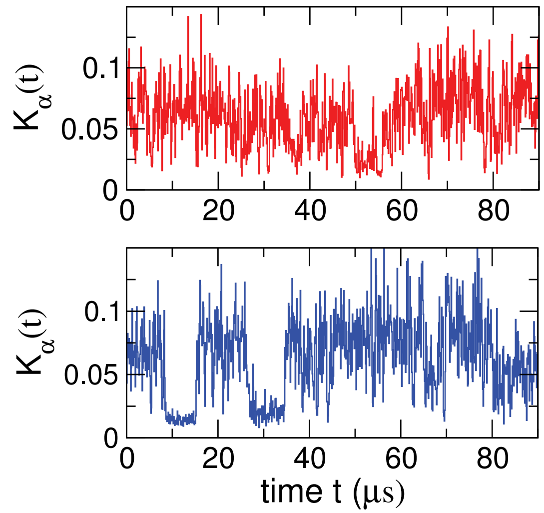
$$P(r,t) \propto \exp\left(-\left[\frac{r}{ct^{\alpha/2}}\right]^{\delta}\right)$$

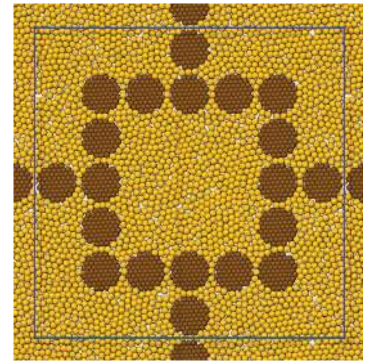


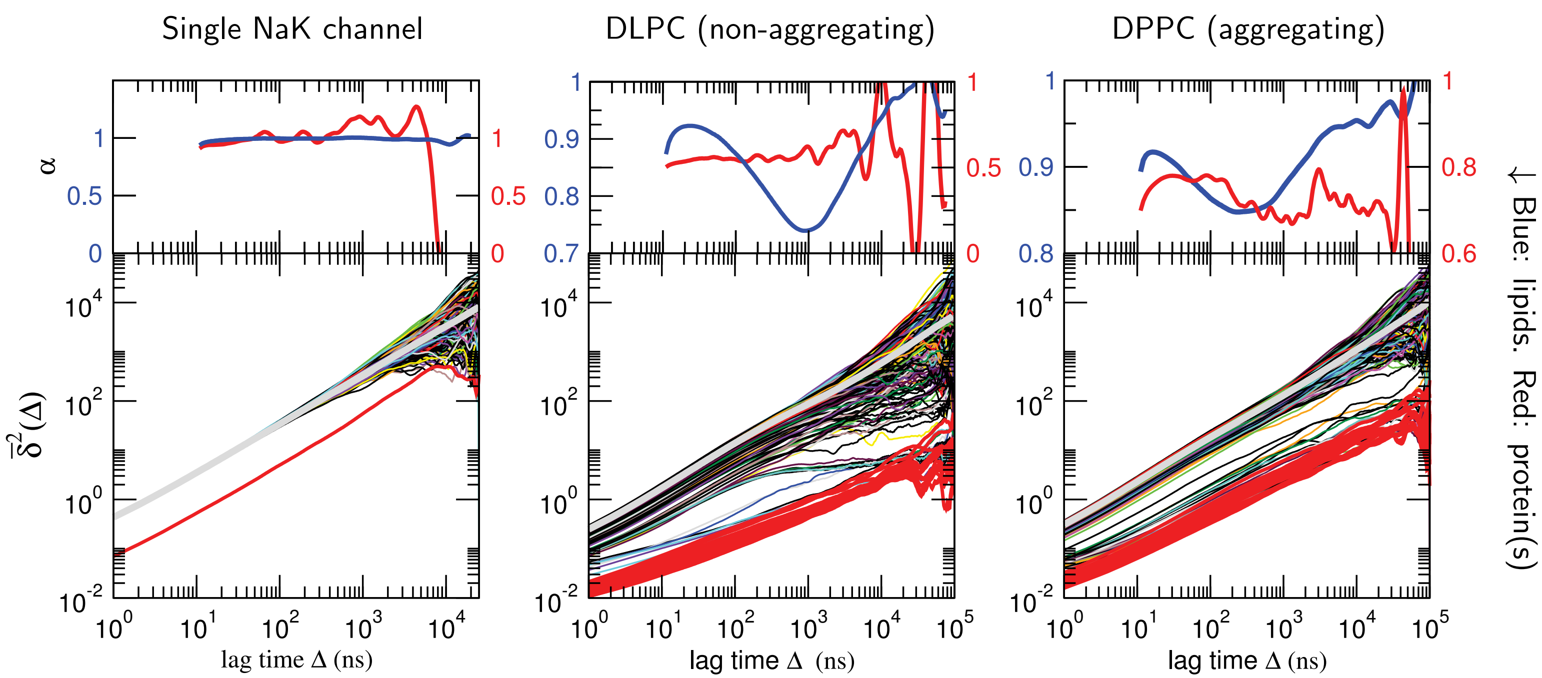
J-H Jeon, M Javanainen, H Martinez-Seara, RM & I Vattulainen, PRX (2016); compare Faraday Disc (2013)

Intermittent lipid diffusion in protein-crowded membranes



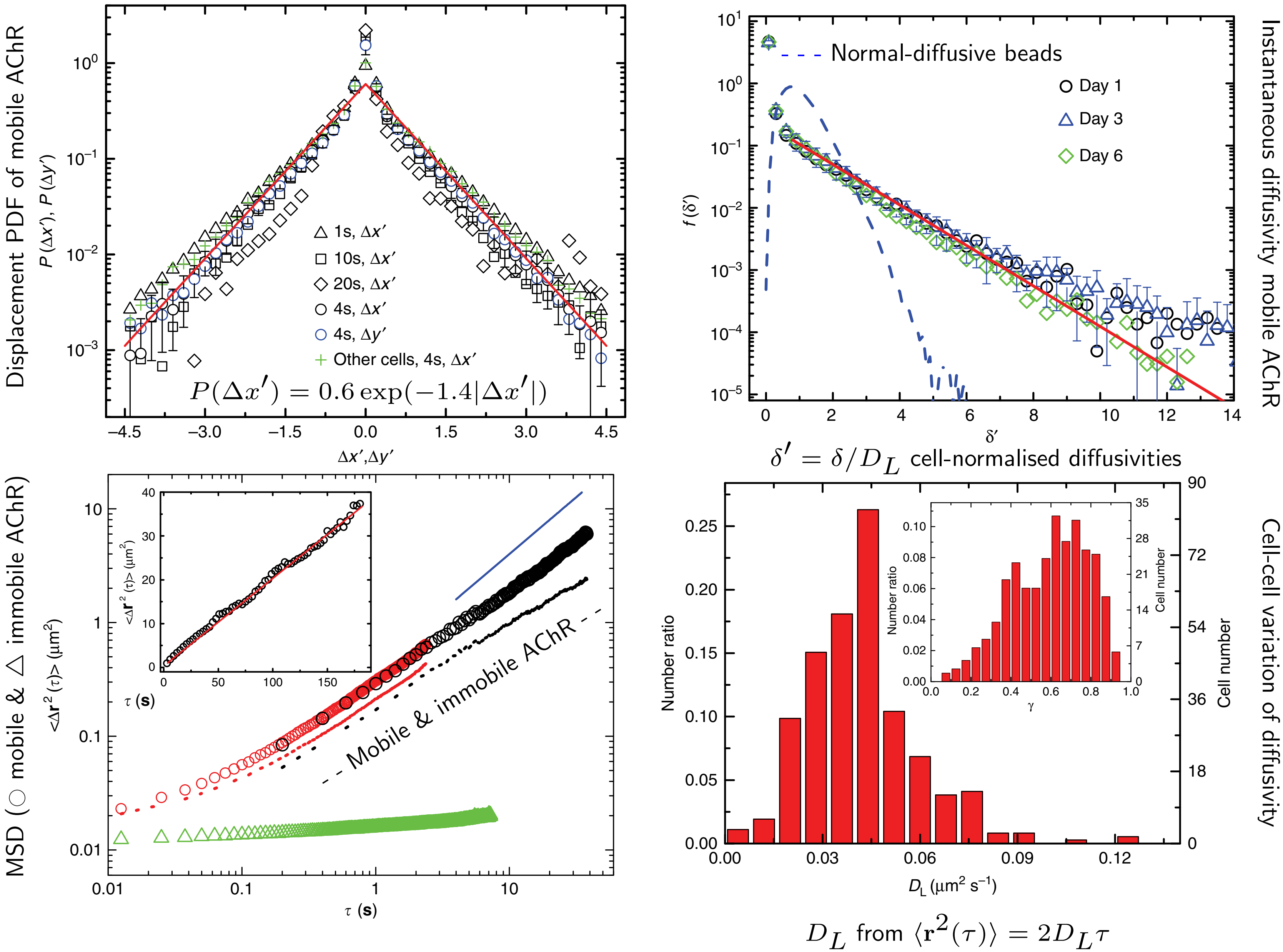




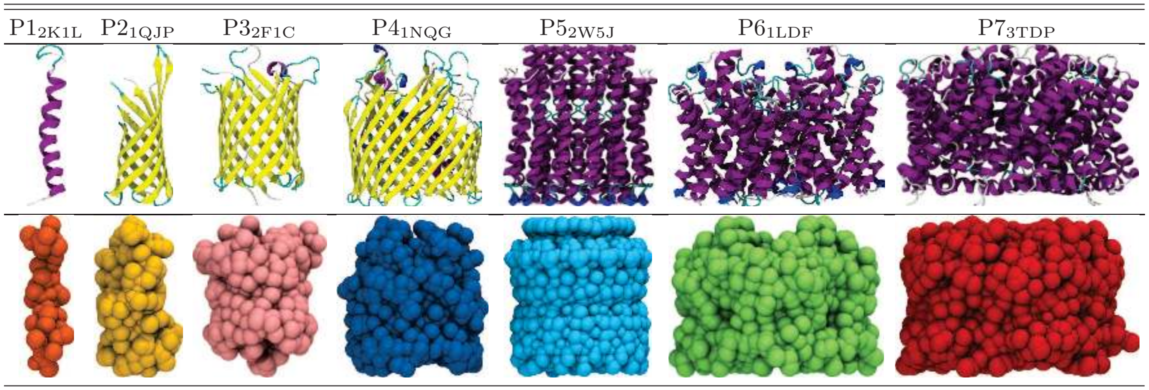


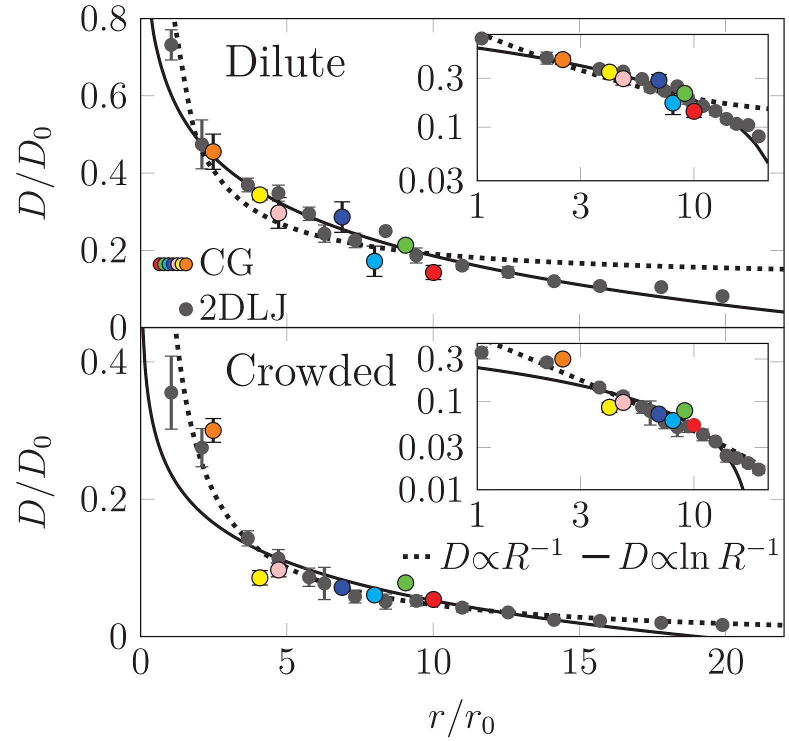
J-H Jeon, M Javanainen, H Martinez-Seara, RM & I Vattulainen, PRX (2016); compare Faraday Disc (2013)

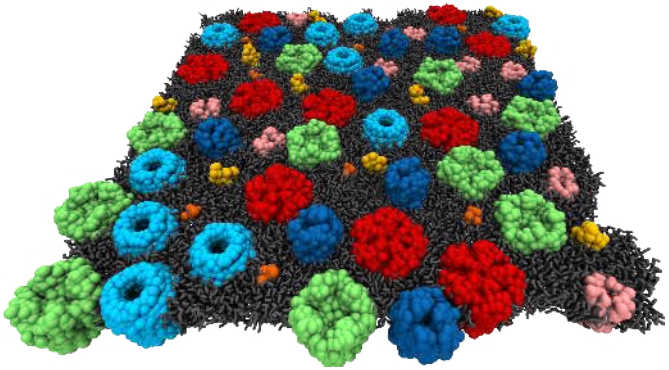
Non-Gaussianity of acetylcholine receptors in Xenopus cells

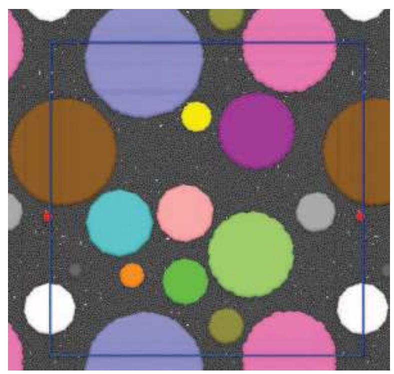


Geometry-induced violation of Saffman-Delbrück relation









Dilute system: Saffman-Delbrück law

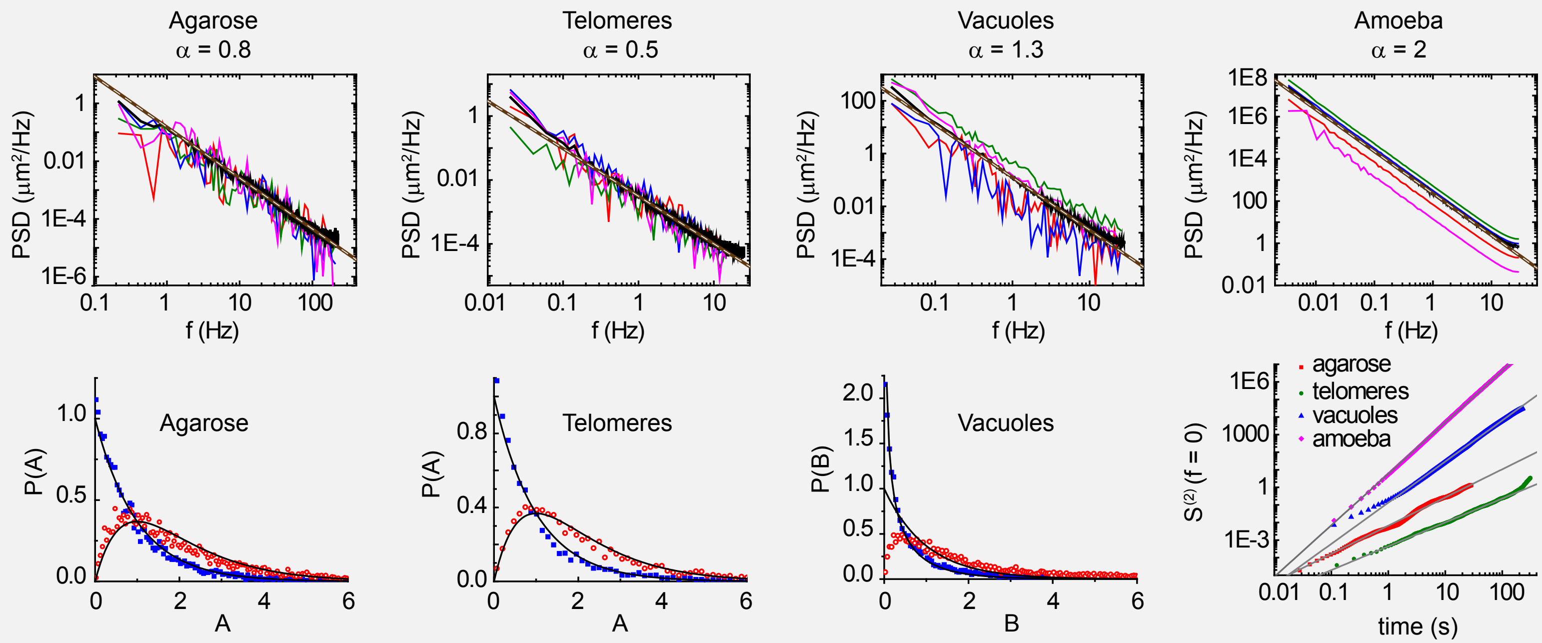
$$D(R) \simeq \log(1/R)$$

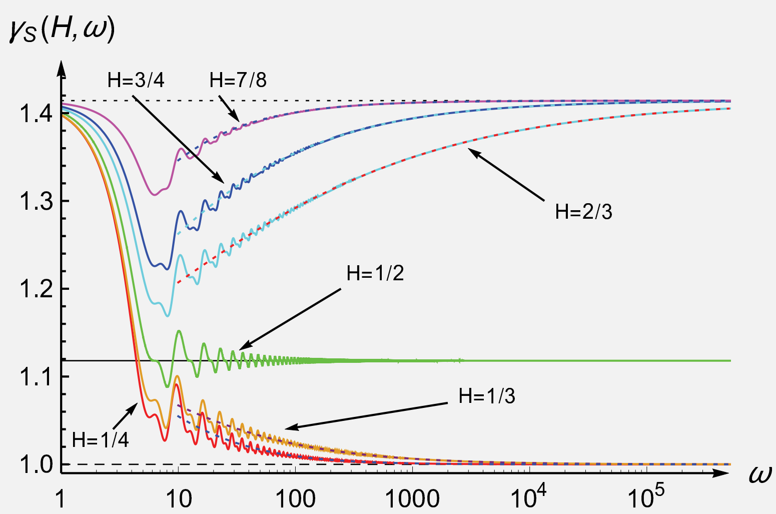
Crowded membrane & 2DLJ discs:

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

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

Power spectral density of a single FBM trajectory





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

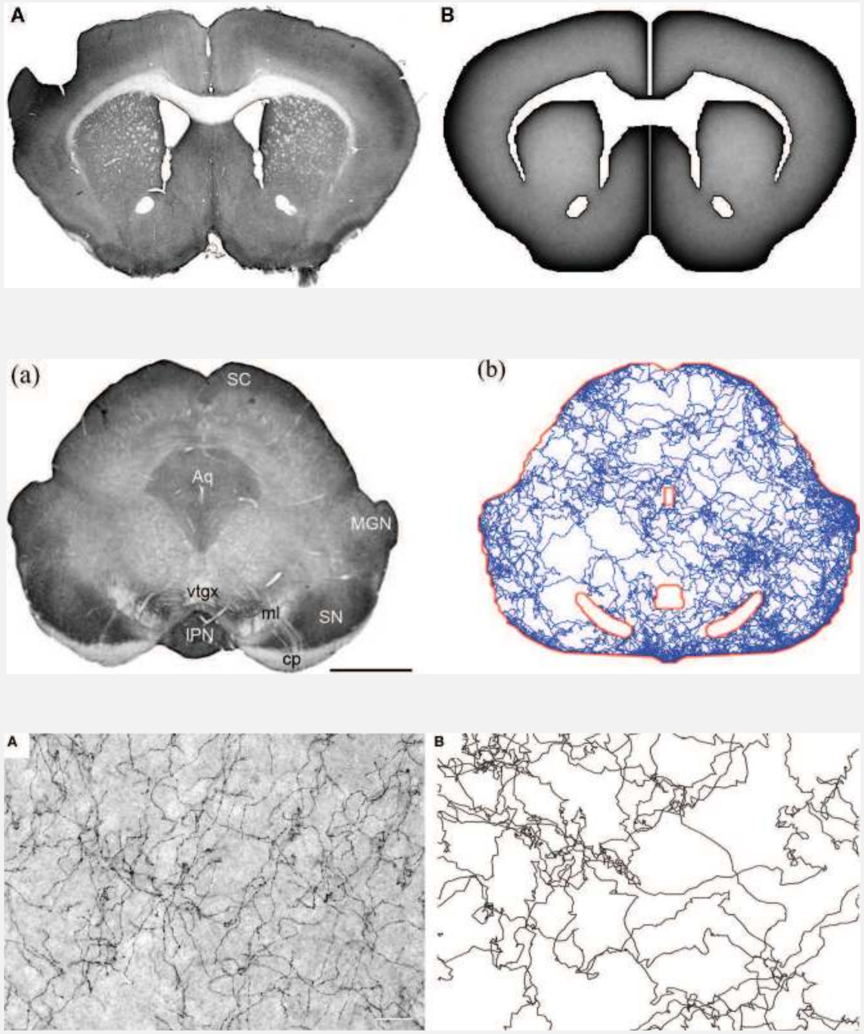
$$\gamma = \frac{\left(\langle S_T^2(f)\rangle - \langle S_T(f)\rangle^2\right)^{1/2}}{\langle S_T(f)\rangle}$$

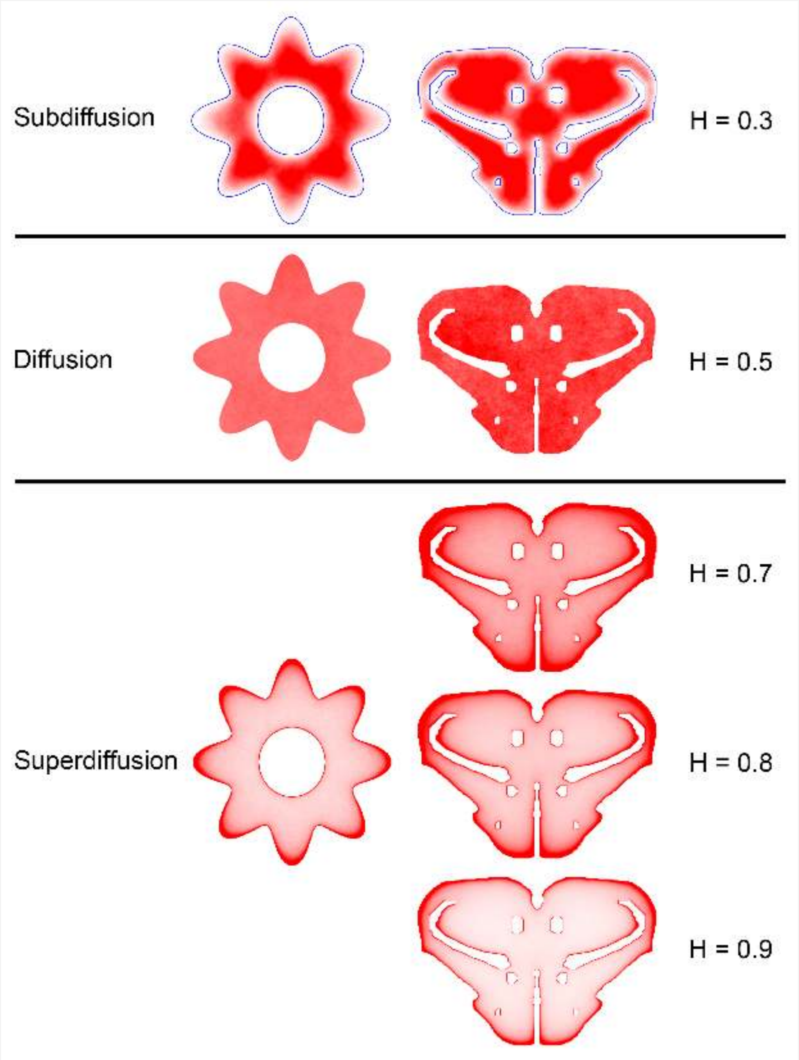
D Krapf, N Lukat, E Marinari, RM, G Oshanin, C Selhuber-Unkel, A Squarcini, L Stadler, M Weiss & X Xu, PRX (2019)

Brain serotonergic axons as FBM paths

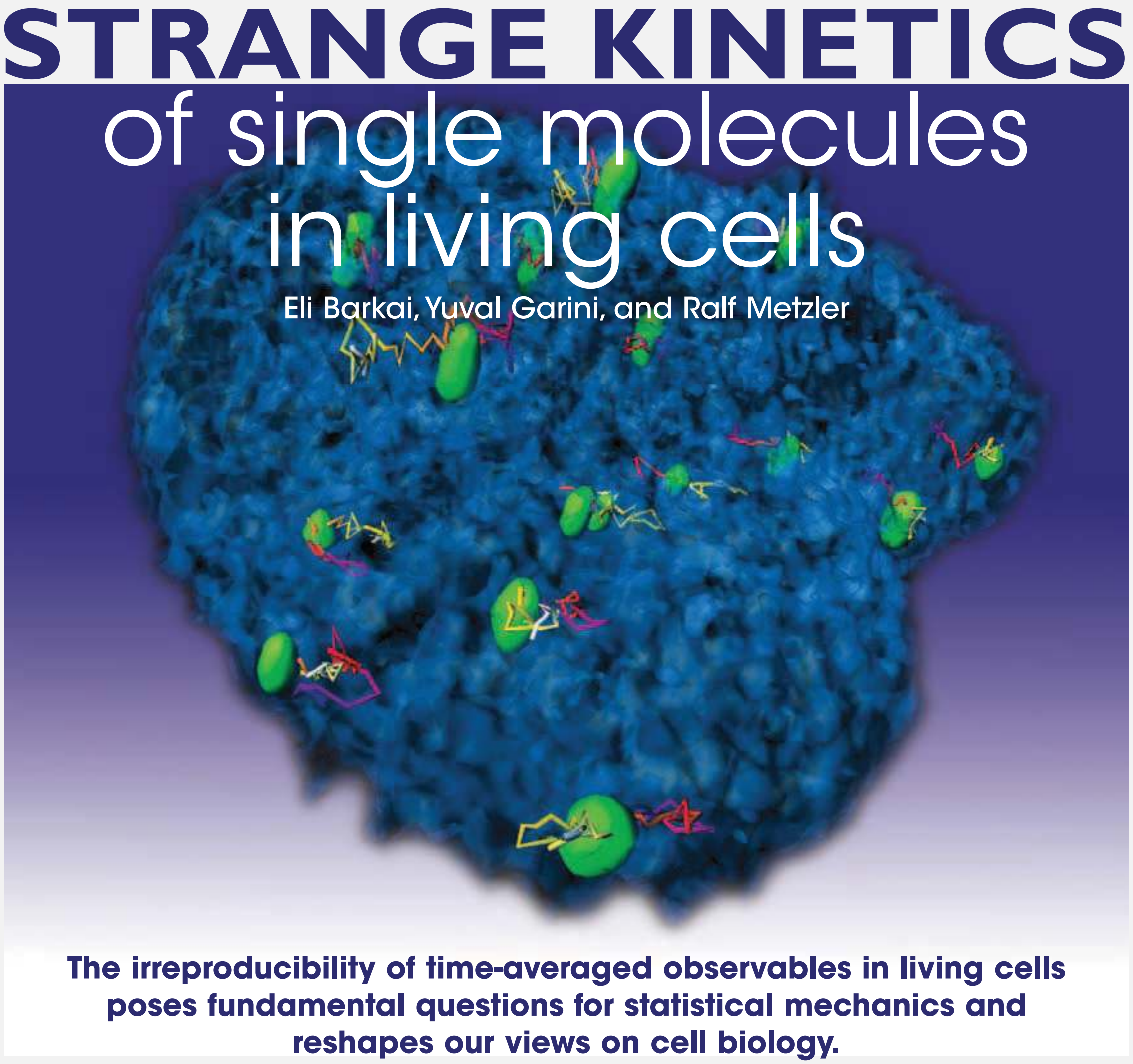
DIVERSION AHEAD

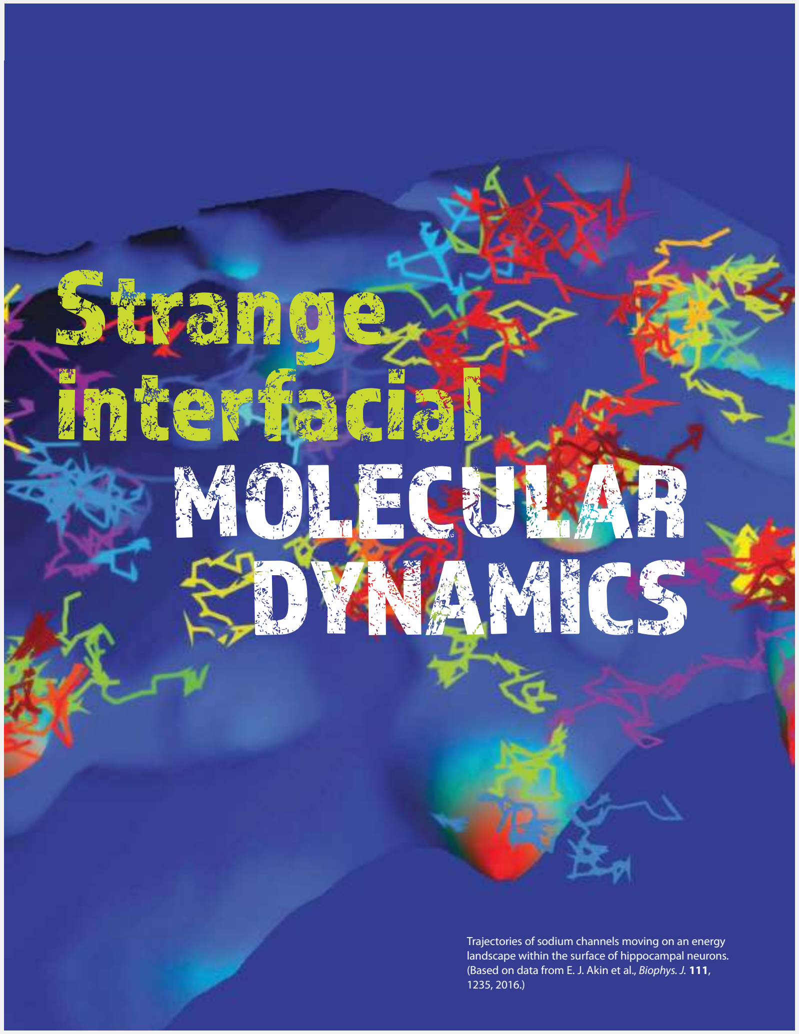
Correlated fluctuations effect non-flat profile





S Janušonis, N Detering, RM & T Vojta, Front Comp Neurosc (2020); T Guggenberger, T Vojta & RM, NJP (2019)





E Barkai, Y Garini & RM, Phys Today (2012); D Krapf & RM, Phys Today (2019)

$\sum$ummary

1. Non-Gaussianity is a ubiquitous phenomenon
2. Likely associated with numerous systems (not studied)
3. Fluctuations of diffusivities: Brownian yet non-Gaussian fluctuations
4. Shape-changing induces fluctuating diffusivity $D \propto D_0/(R_0 + R_g)$
5. Disorder-induced non-Gaussianity & annealed limit
6. Detection of non-Gaussianity by codifference [J Ślęzak, RM & M Magdziarz, NJP (2018)] & large deviation TAMSD statistic [S Thapa & al, NJP (2021)]
7. Physics$\leftrightarrow$ARIMA time series analysis [J Ślęzak, K Burnecki & RM, NJP (2019)]
8. Bayes/max likelihood model determination

- 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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