

Random motion: from molecules to animals

—UP Plant Ecology & Conservation Biology, 14th January 2022—

Fluxes, random walks, & fluctuating forces . . .



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

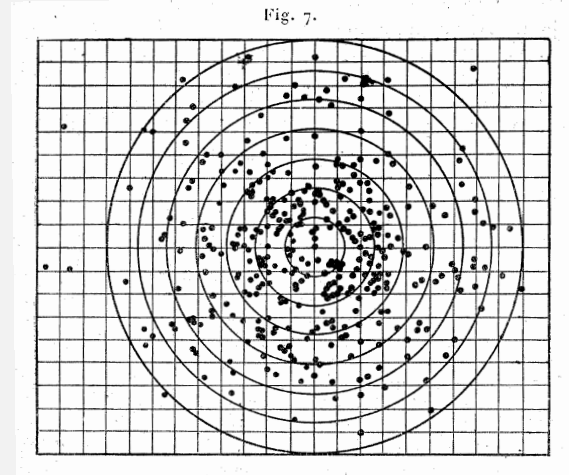
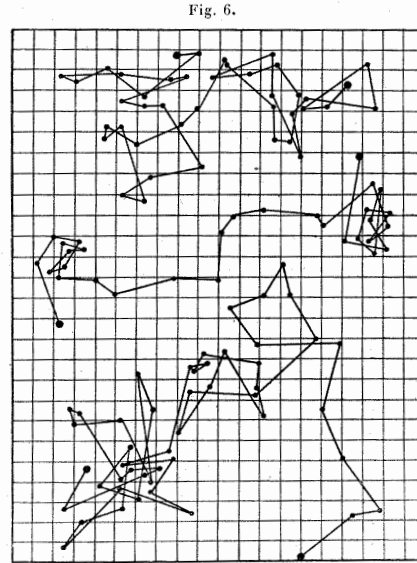
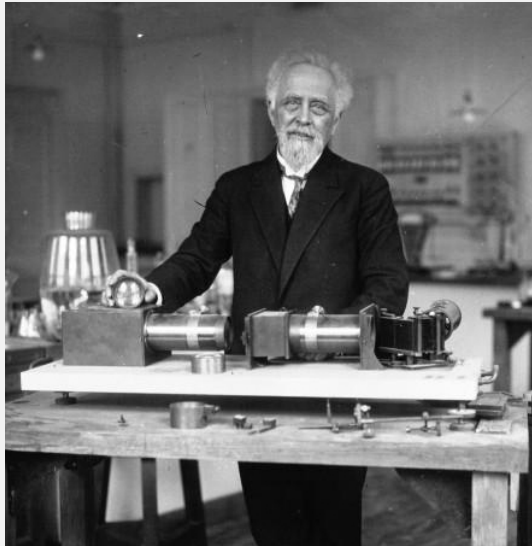


Marian Smoluchowski
(1872-1917)

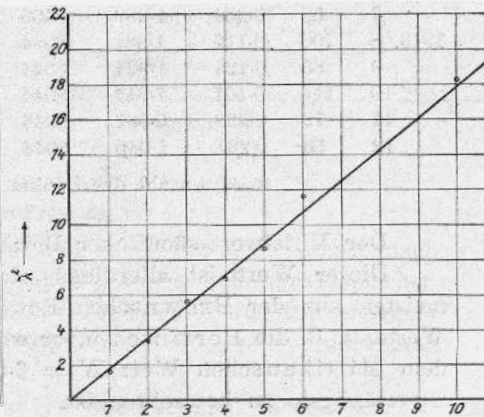
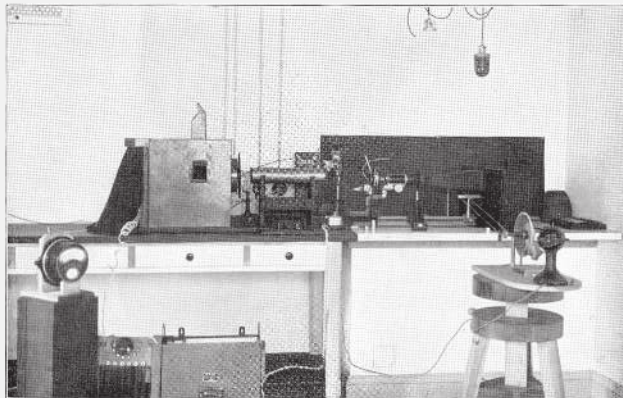


William Sutherland
(1859-1911)

Les atomes: Brownian motion and Avogadro's number



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

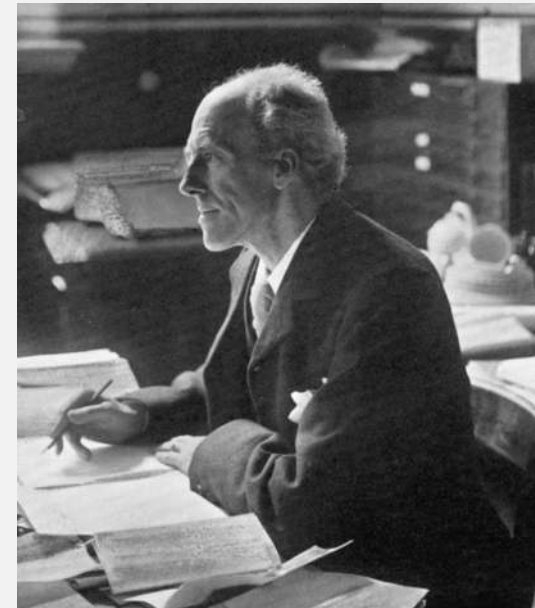


J Perrin, Comptes Rendus (Paris) 146 (1908) 967: $N_A = 70.5 \times 10^{22}$; I Nordlund, Z Physik (1914): $N_A = 5.91 \times 10^{23}$ 3

Brownian motion & random walks applied . . .



Louis Bachelier, 1900:
Brownian motion of
financial markets



Karl Pearson, 1905:
Spreading of mosquitoes
in rain forests

Marian v Smoluchowski, 1916:
Molecular reaction kinetics



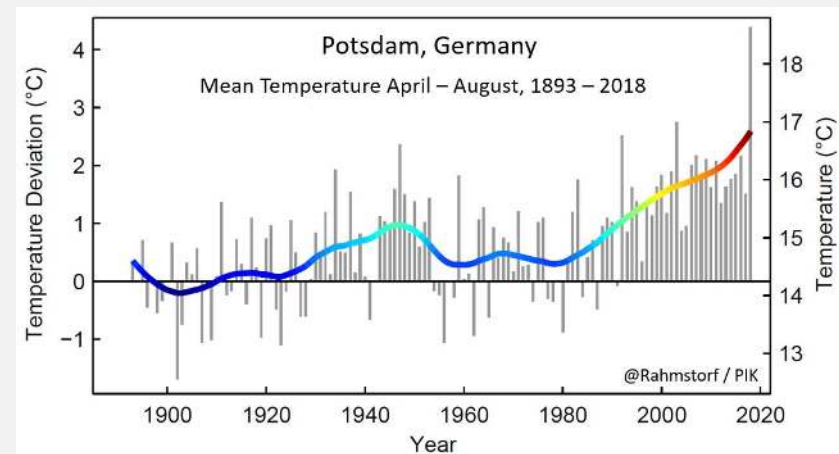
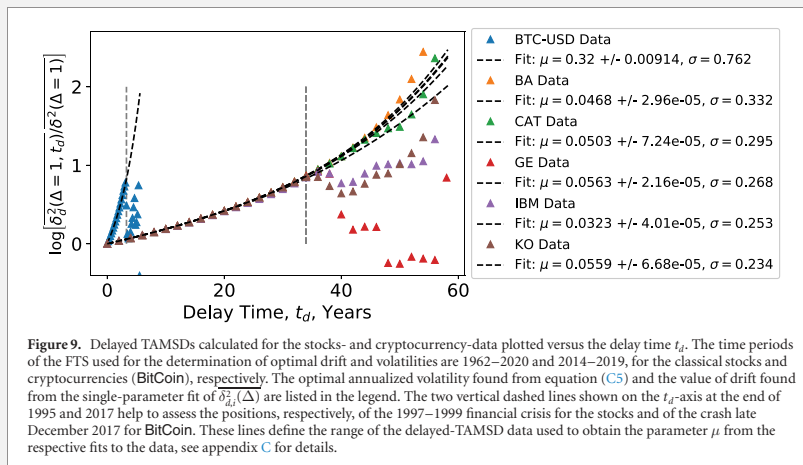
Elliott Montroll, 1943:
Manhattan project,
chain reaction of
neutrons



Ensemble versus single particle statistics



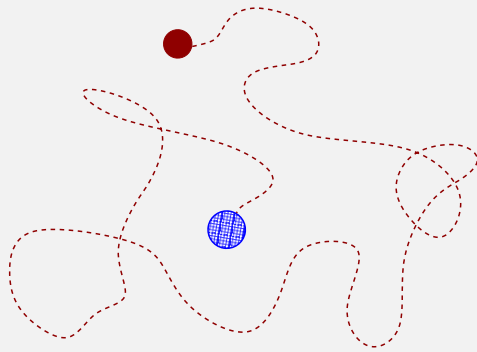
- Not all systems are ergodic: $\langle \cdot \rangle \neq \overline{\cdot}$ [RM et al, PCCP (2014)]
- Single particle statistics show useful fluctuations
- Some systems can only provide single time series:



Molecular reaction times: macro vs micro

Search rate for particle with diffusivity D_{3d} to find an immobile target of radius a (assuming immediate binding):

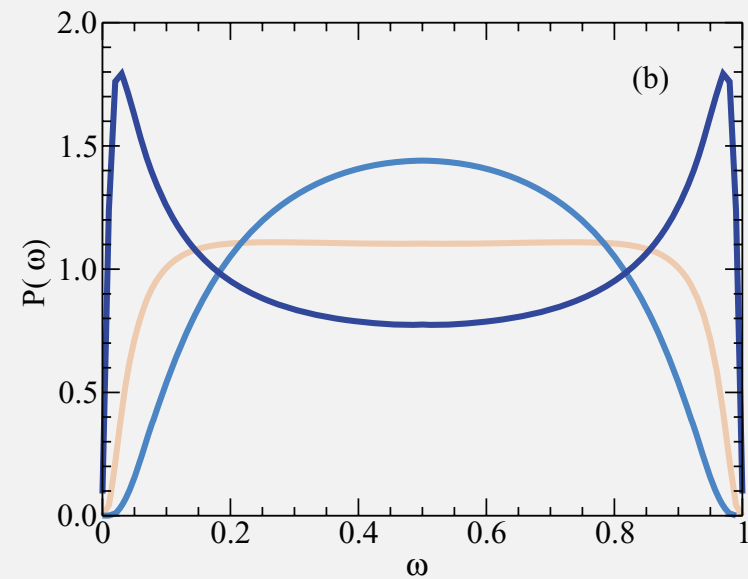
$$k_{\text{on}} = 4\pi D_{3d}a$$



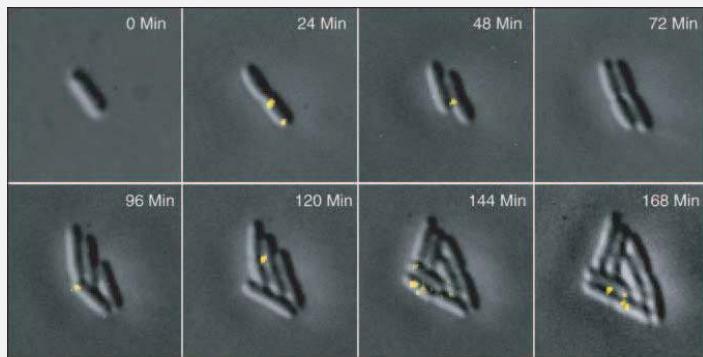
Uniformity index for two independent first-passage times τ_1, τ_2 :

$$\omega = \frac{\tau_1}{\tau_1 + \tau_2}$$

$\leadsto \omega = 1/2$ means good reproducibility $\blackleftarrow$ many processes



Yu et al, Science (2006)



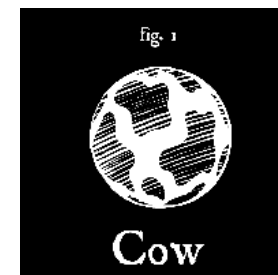
M v Smoluchowski, Physikal Zeitschr (1916)

T Mattos, C Mejía-Monasterio, RM & G Oshanin, PRE (2012) 6

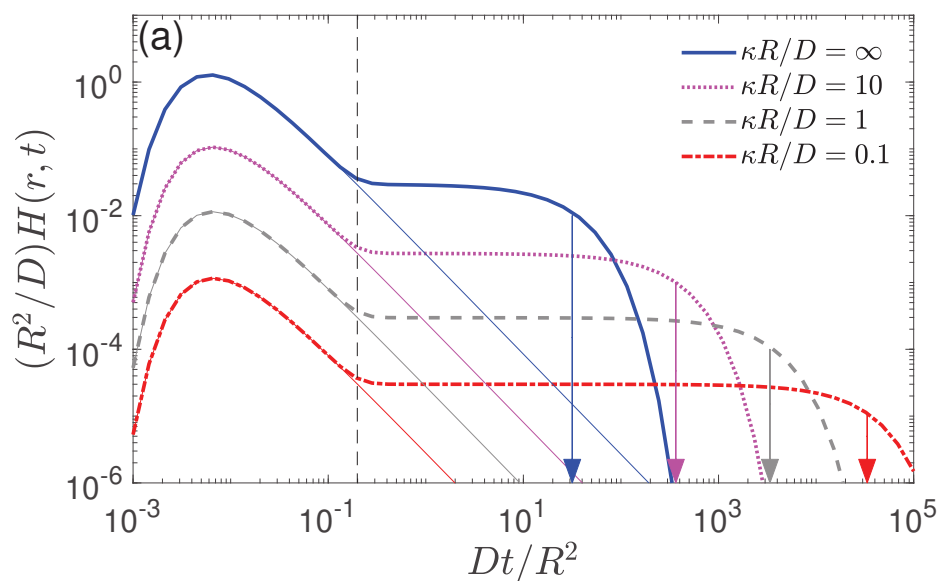
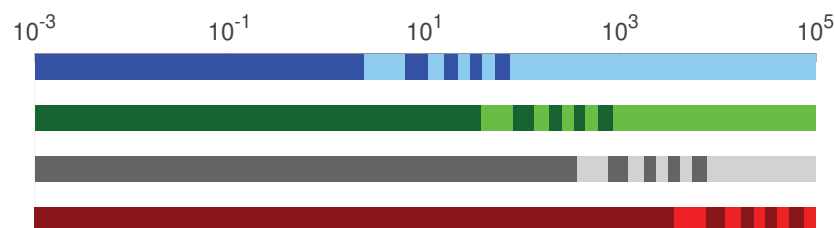
Strongly defocused (fluctuating) reaction times

Geometry control: direct trajectories independent of outer boundary

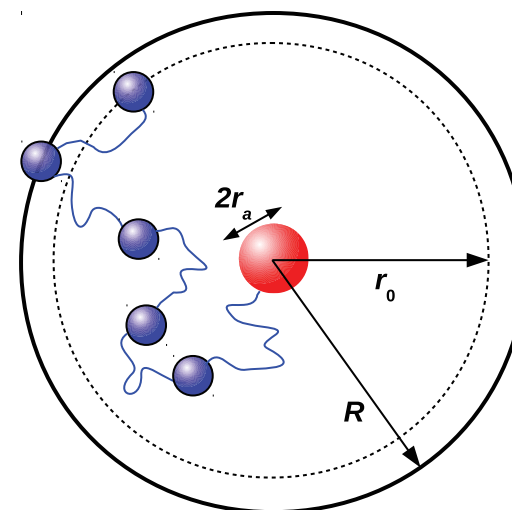
Reaction control: finite reactivity requires multiple collisions



Full first passage time density:



Direct vs indirect trajectories:

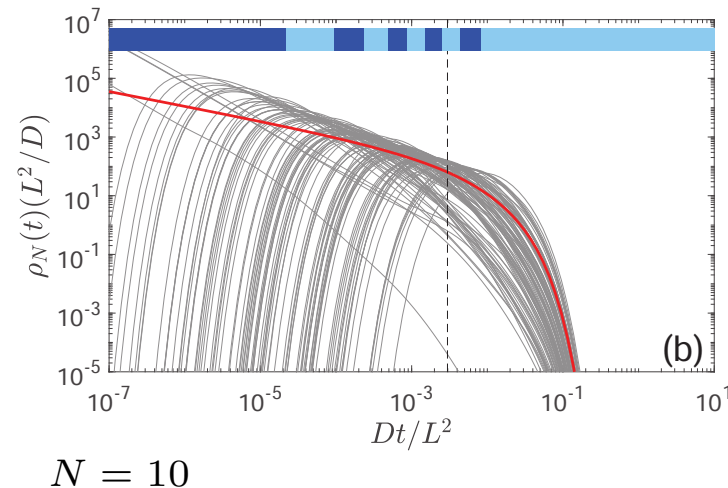
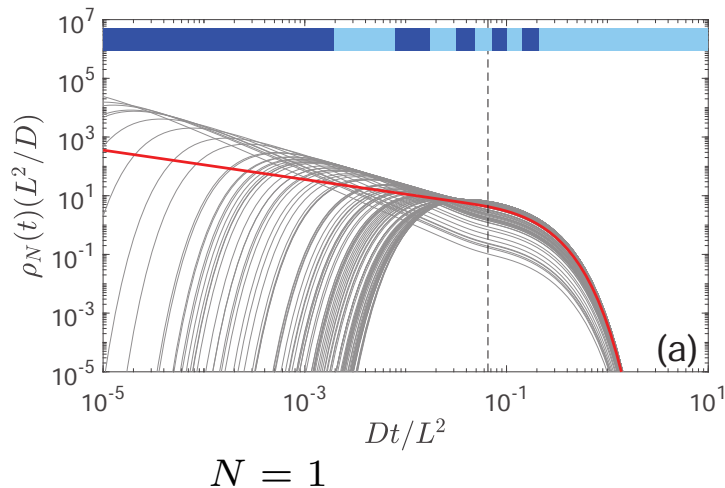


$$\langle t \rangle = \frac{(r_0 - r_a)(2R^3 - r_0 r_a [r_0 + r_a])}{6D r_0 r_a} + \frac{R^3 - r_a^3}{3\kappa r_a}$$

Reaction/search speedup for N "molecules" in parallel

Fixed starting point: fastest FPT $\langle t \rangle \simeq 1/\ln N$

Uniformly distributed initial conditions: $\langle t \rangle \simeq \begin{cases} 1/N^2, & \text{perfect reactivity} \\ 1/N, & \text{partial reactivity} \end{cases}$

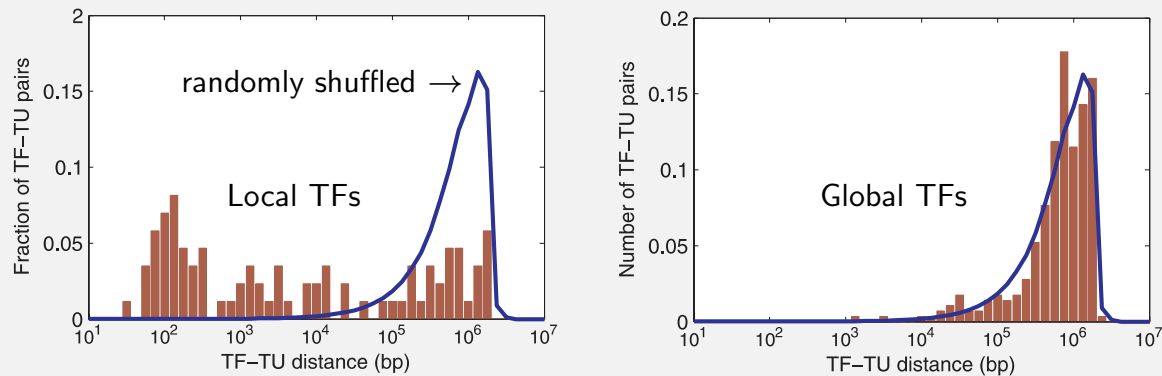
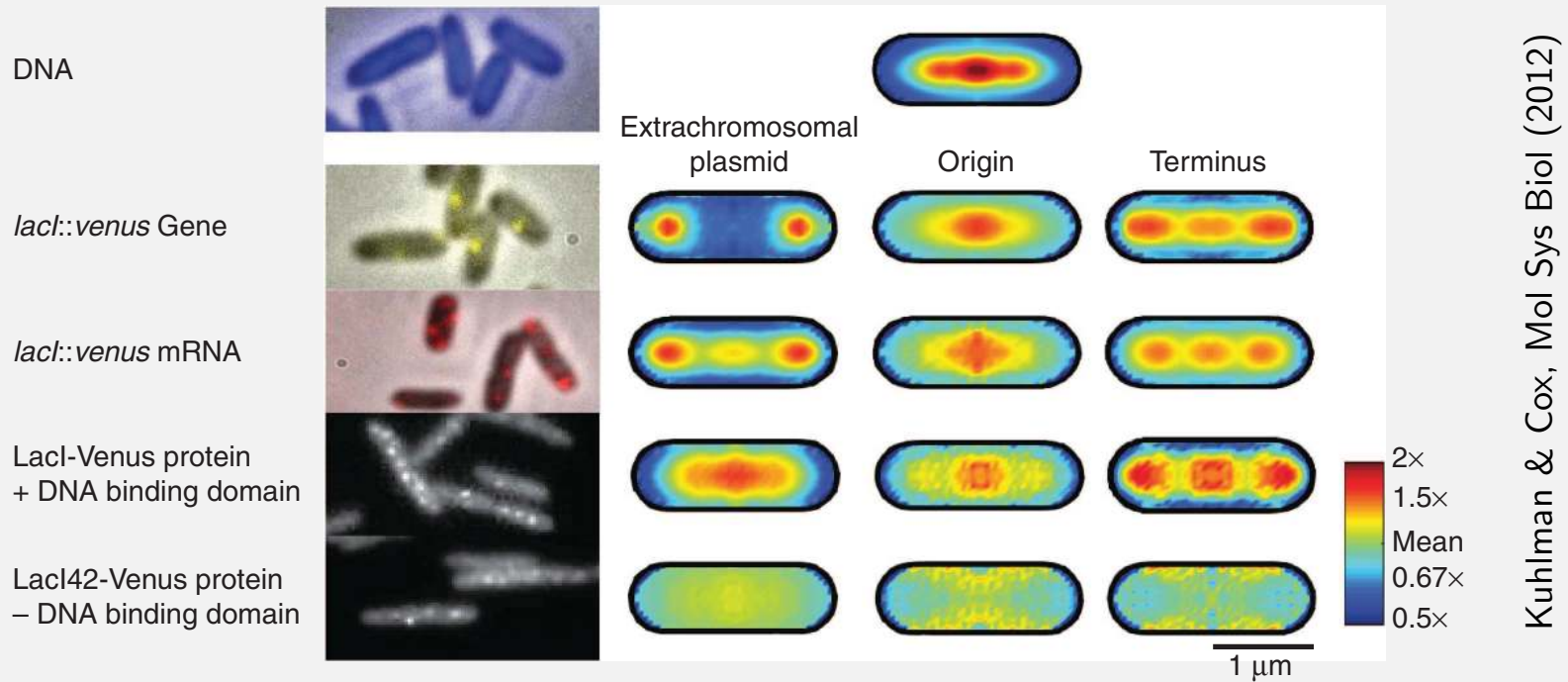


Grey lines: 100 random
initial configurations

~> Particles initially located close to target are purely reaction controlled

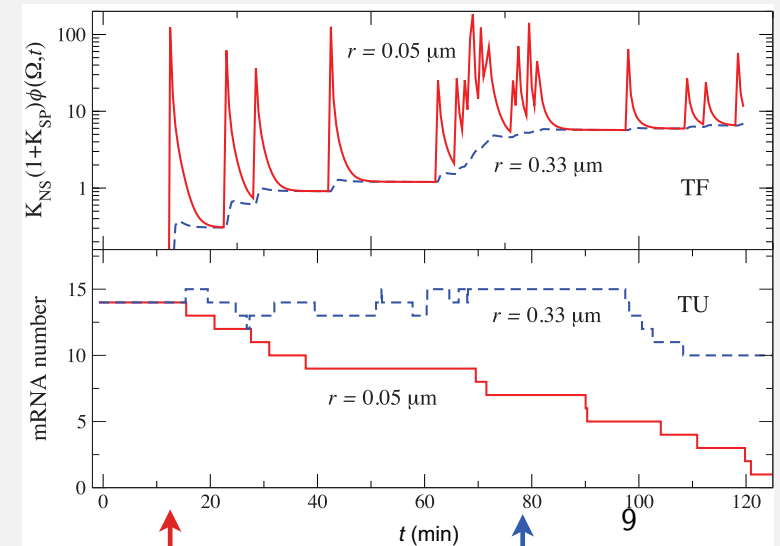
~> Initial conditions matter significantly & chemical rate approach requires sufficiently high concentrations

Inhomogeneous TF location, rapid search hypothesis

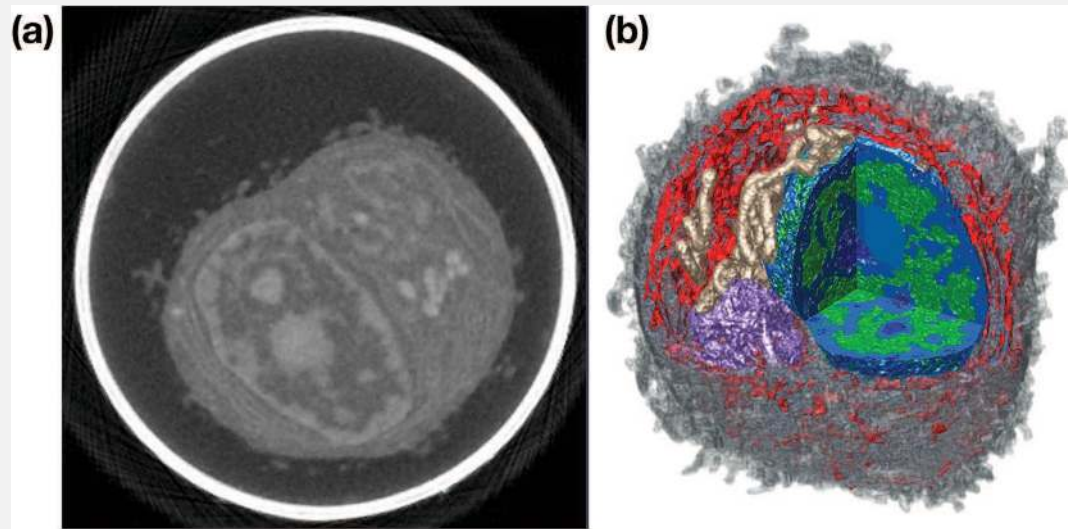


TF-TU gene-gene distance [G Kolesov . . . LA Mirny, PNAS (2007)]

O Pulkkinen & RM, PRL (2013): Distance TF-TU matters $\rightarrow$

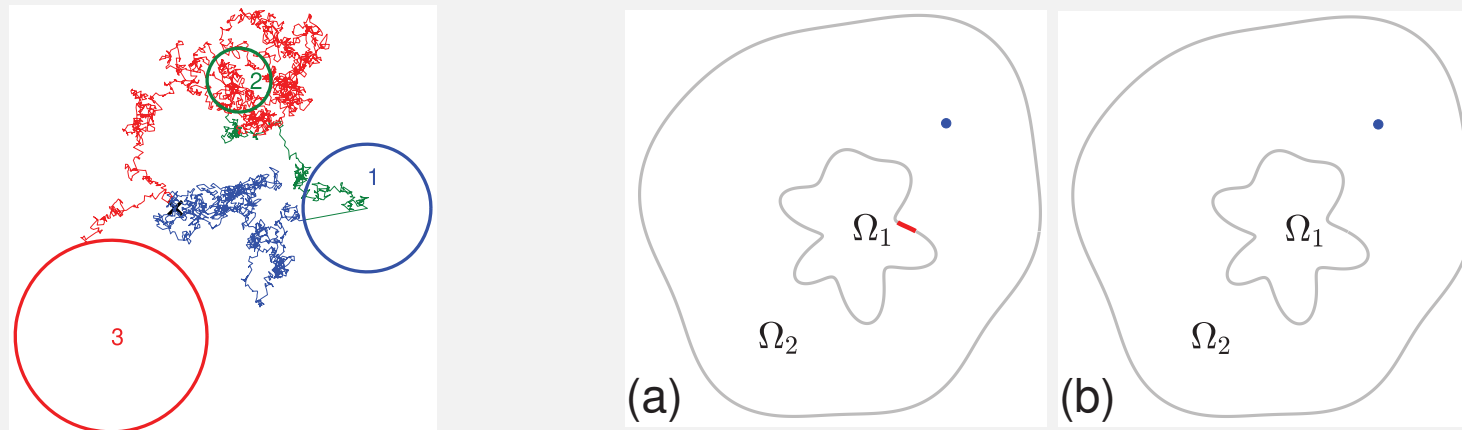


Computational models for intracellular signalling



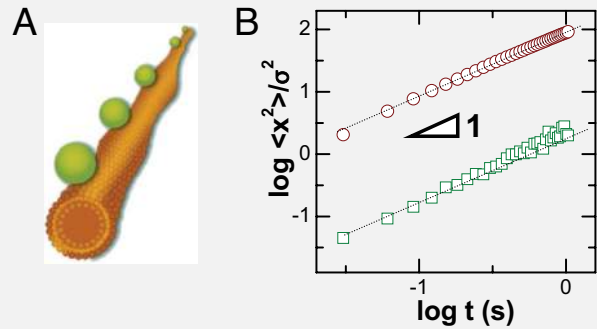
[J Ma . . . SA Isaacson, PLoS Comp Biol (2021)]

Reaction cascades & reaction in onion-like shell regions

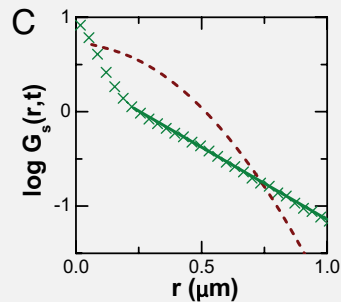
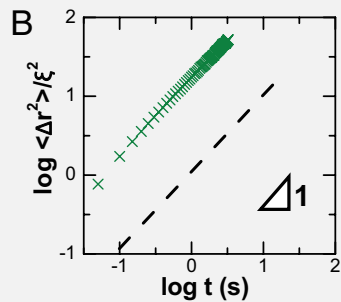
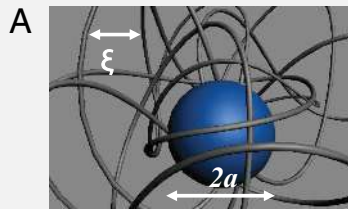
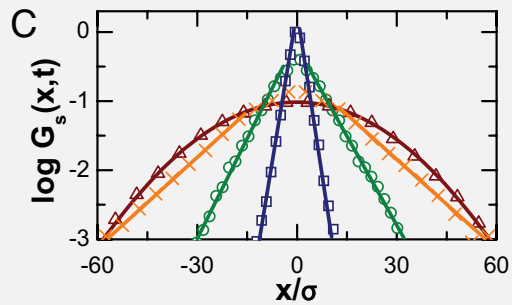


DS Grebenkov, RM & G Oshanin, NJP (2021); NJP (2021a)

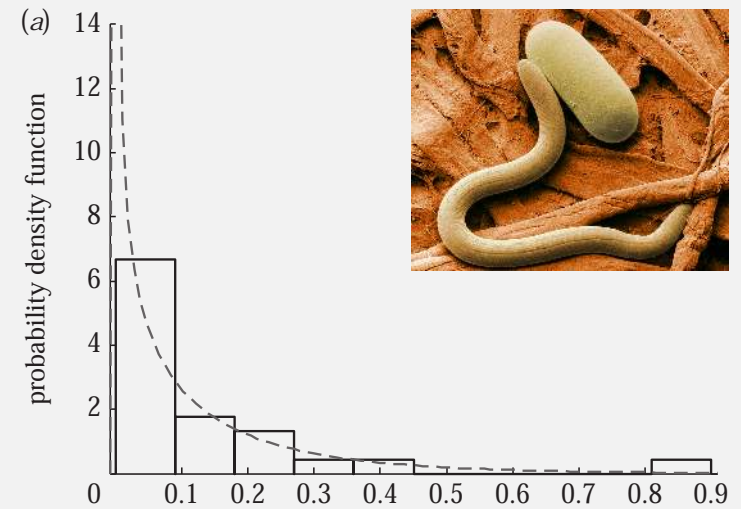
Brownian yet non-Gaussian diffusion in soft & bio-matter



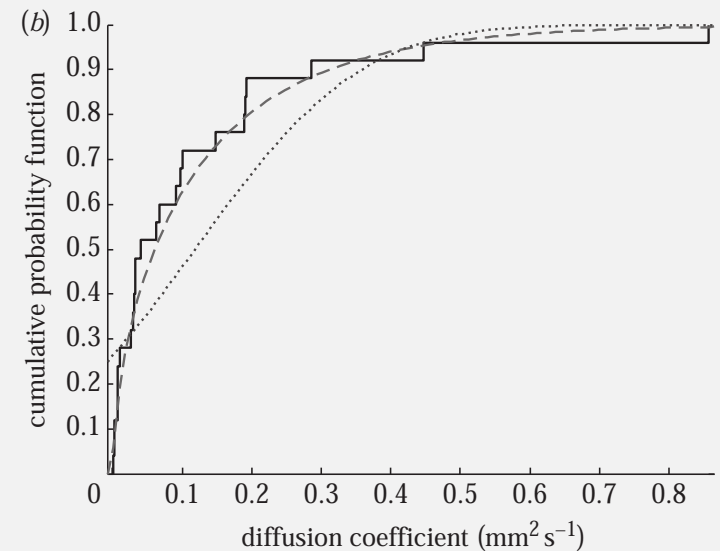
Colloidal beads on nanotubes



Nanospheres in entangled actin



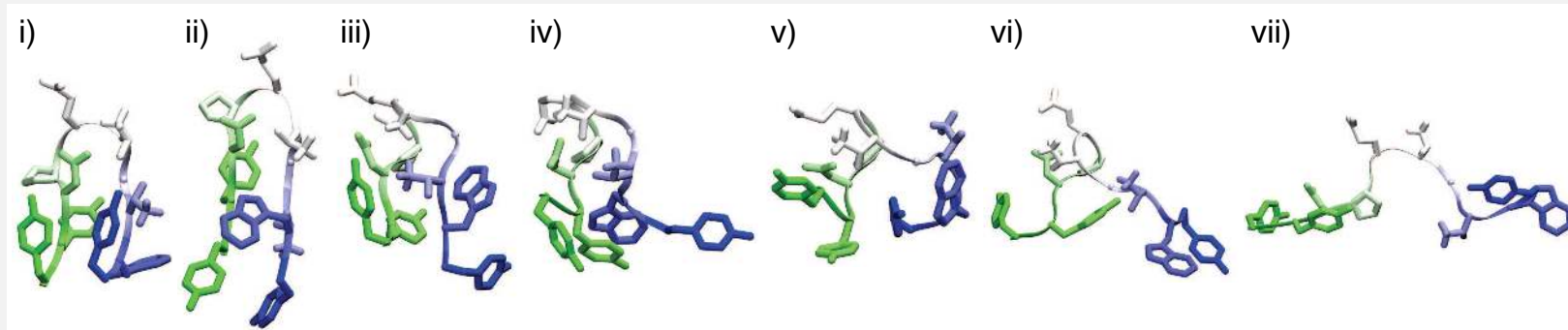
Motion of *Phasmarhabditis* nematodes



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

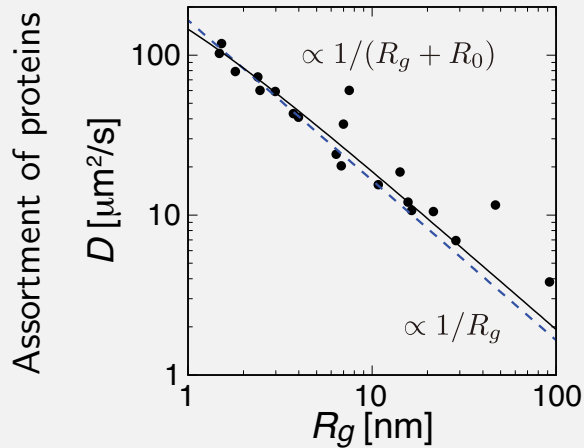
S Hapca, JW Crawford & IM Young, Interface (2009) 11

Instantaneous diffusivity of shape-fluctuating proteins

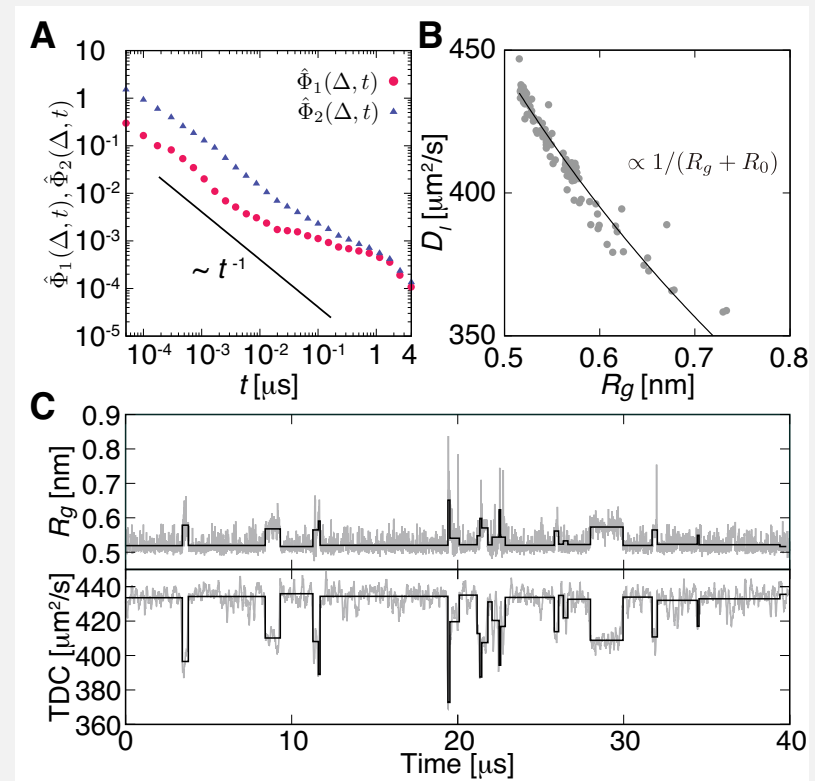


Instantaneous Einstein-Stokes-type relation (for different pressure & temperature):

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



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



Fickian, non-Gaussian diffusion with diffusing diffusivity

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

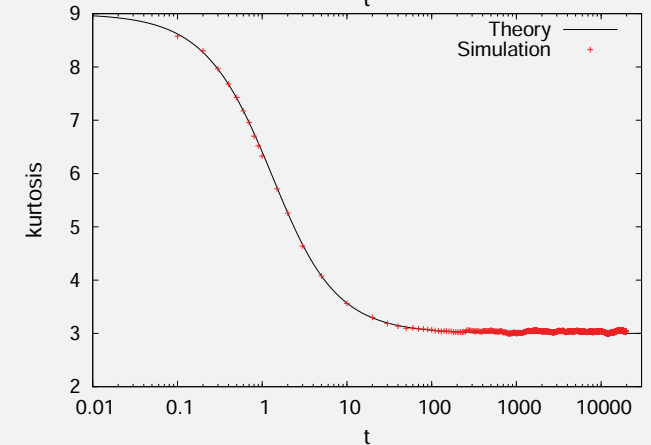
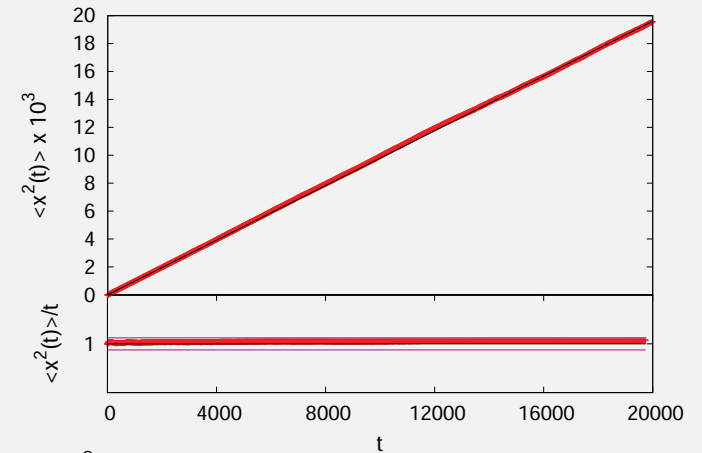
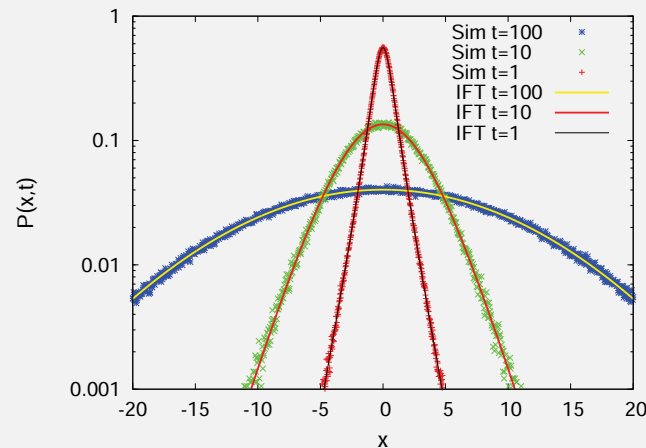
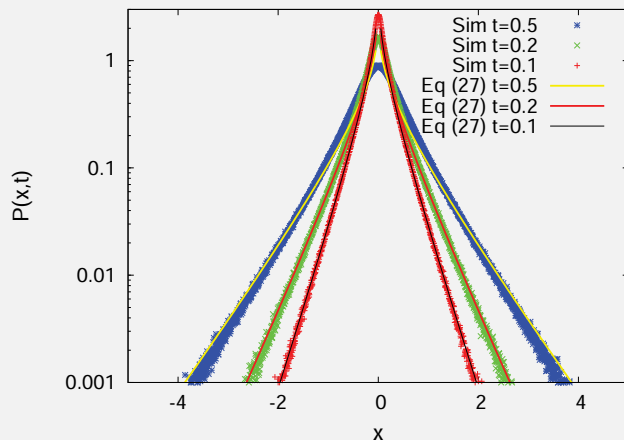
[see also R Jain & KL Sebastian, JPC B (2016)]

Our minimal model for diffusing diffusivity:

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

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

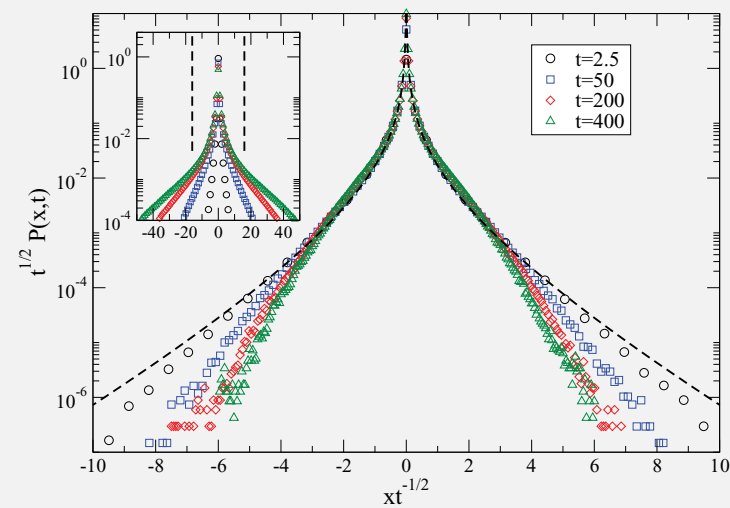
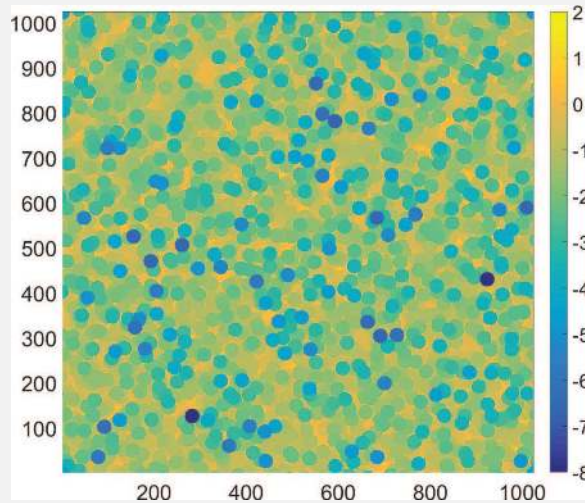
$$\dot{y}(t) = -\tau^{-1}y + \sigma\eta(t)$$



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

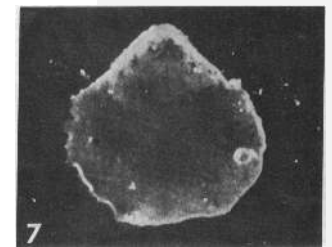
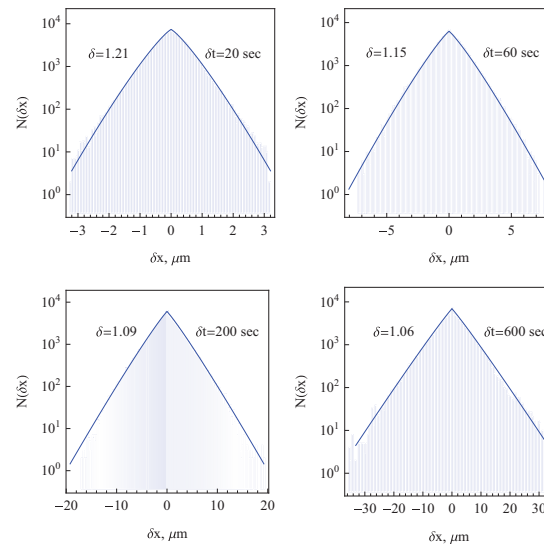
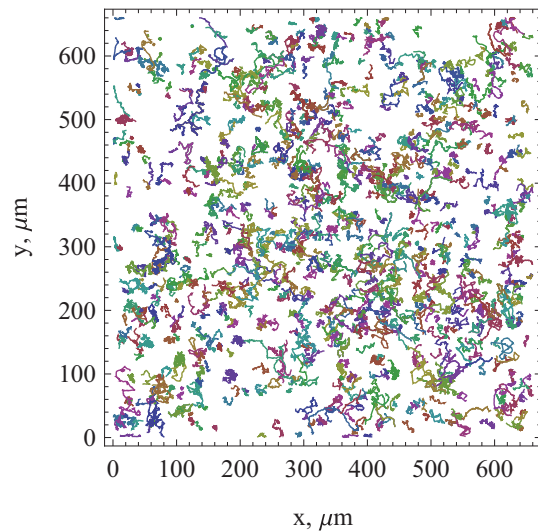
AV Chechkin, F Seno, RM & IM Sokolov, PRX (2017)

Non-Gaussian diffusion in quenched landscape models



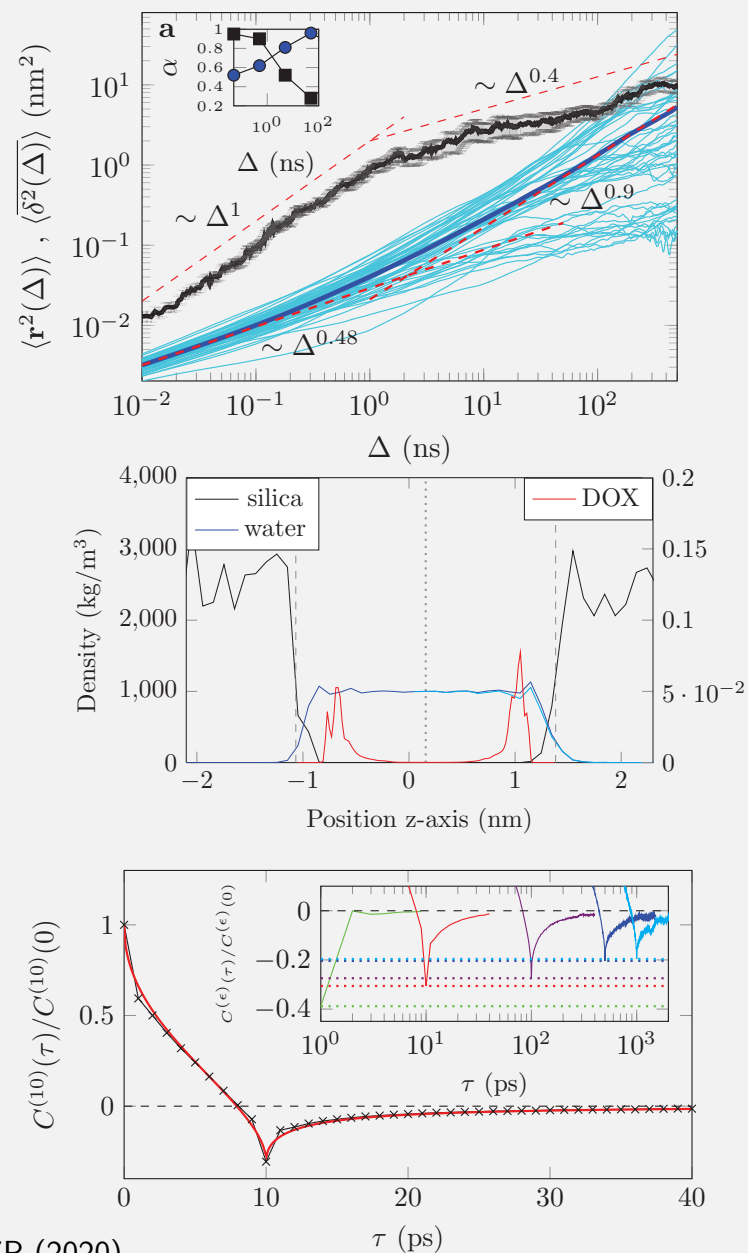
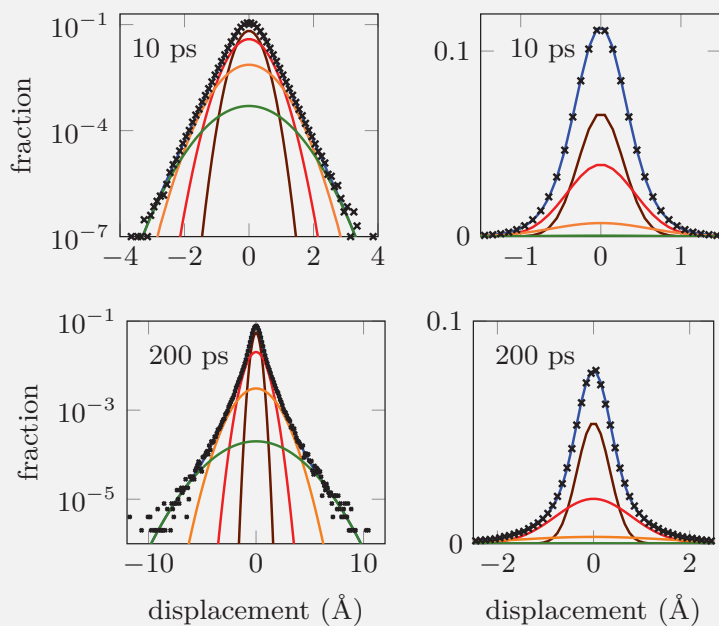
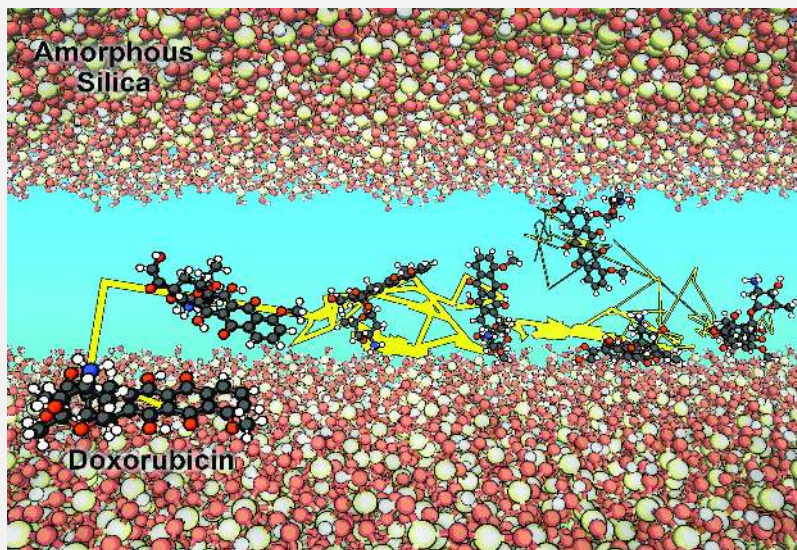
L Luo & M Yi, PRE (2018,2019); see also EB Postnikov, A Chechkin & IM Sokolov, NJP (2020)

Increasing non-Gaussianity in moving amoeba cells



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

Doxorubicin drug molecule diffusion in silica nanochannels



Lévy foraging hypothesis: to avoid oversampling

Shlesinger & Klafter (1986): Lévy flights as efficient search mechanism

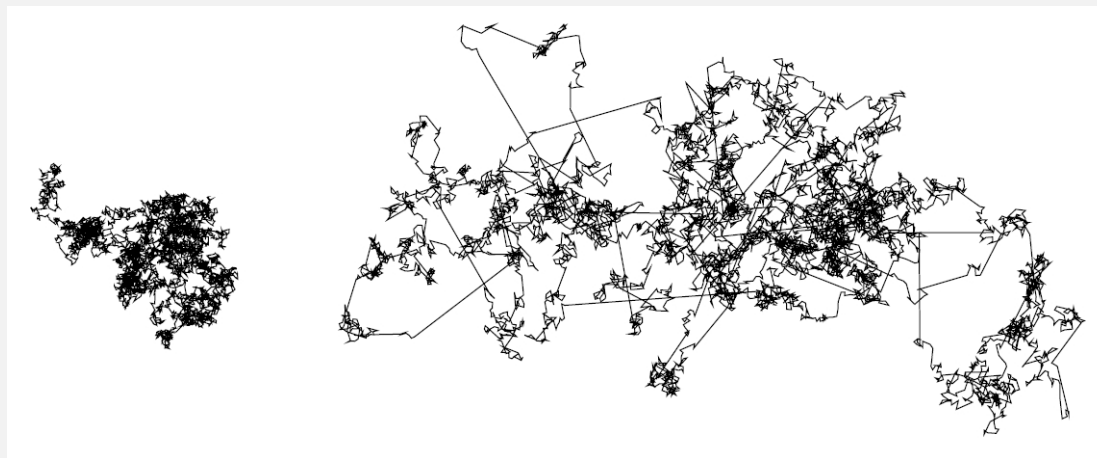
Lévy foraging hypothesis: *Superdiffusive motion governed by fat-tailed propagators optimise encounter rates under specific (but common) circumstances: hence some species must have evolved mechanisms that exploit these properties [...].*

Lévy flight (Mandelbrot): $\psi(t) = \tau^{-1} \exp(-t/\tau) \wedge$

$$\lambda(x) \simeq |x|^{-1-\mu}, \quad 0 < \mu < 2 \quad \curvearrowright \quad \langle x^2(t) \rangle \rightarrow \infty$$

Lévy walk (Shlesinger, Klafter & Wong, JSP, 1982): spatiotemporal coupling

$$\psi(x, t) = \lambda(x) \delta(|x| - vt) \quad \curvearrowright \quad \langle x^2(t) \rangle \simeq t^{3-\alpha}; \quad 1 < \alpha < 2$$



Lévy flight/walk as random search model

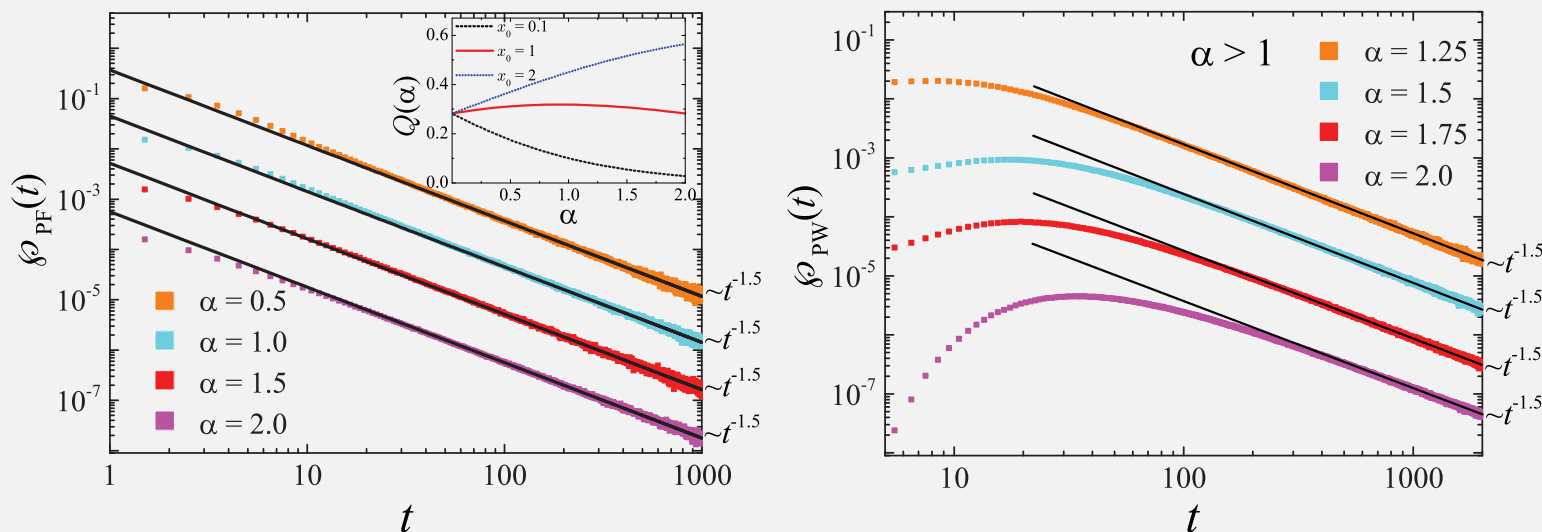
I First-passage & first-arrival (-hitting) are different; leapovers [AV Chechkin et al, JPA (2003); T Koren et al, Phys Rev Lett (2007)]

II Statistical model transcription factor search leads to Lévy flights [MA Lomholt et al, Phys Rev Lett (2005)]

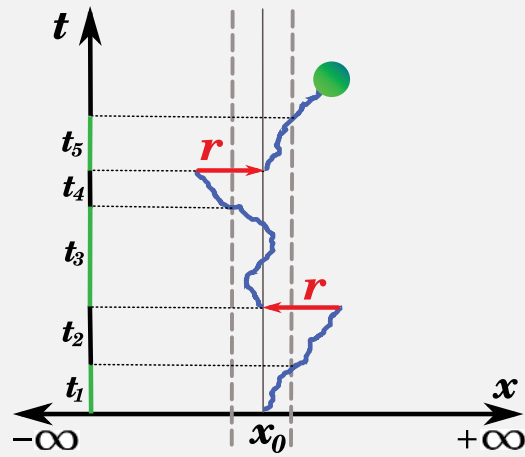
III Lévy flights do not always optimise random search for sparse targets [VV Palyulin et al, PNAS (2014)]

IIII First-passage statistics of asymmetric Lévy flights [A Padash et al, J Phys A (2019), (2020)]

IIIII First-passage & first-hitting time densities for Lévy flights & Lévy walks [VV Palyulin et al, New J Phys (2019)]



Soft resets of Lévy walk

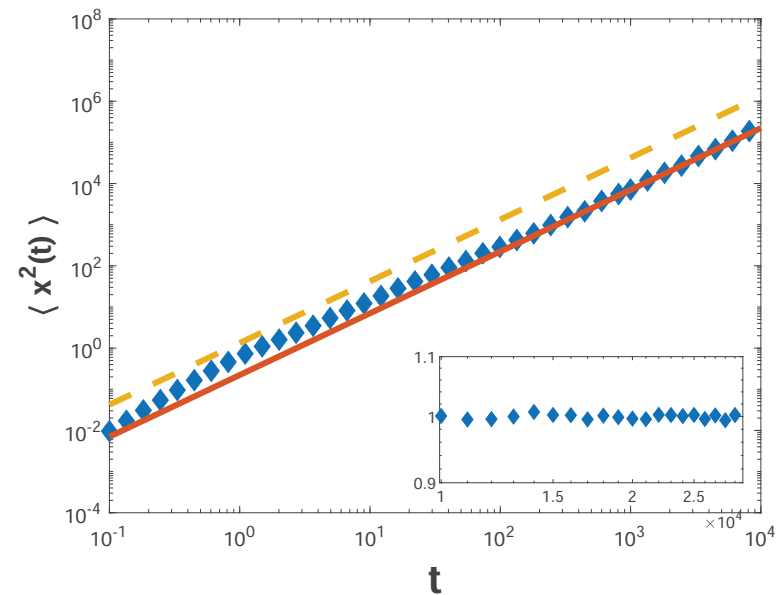
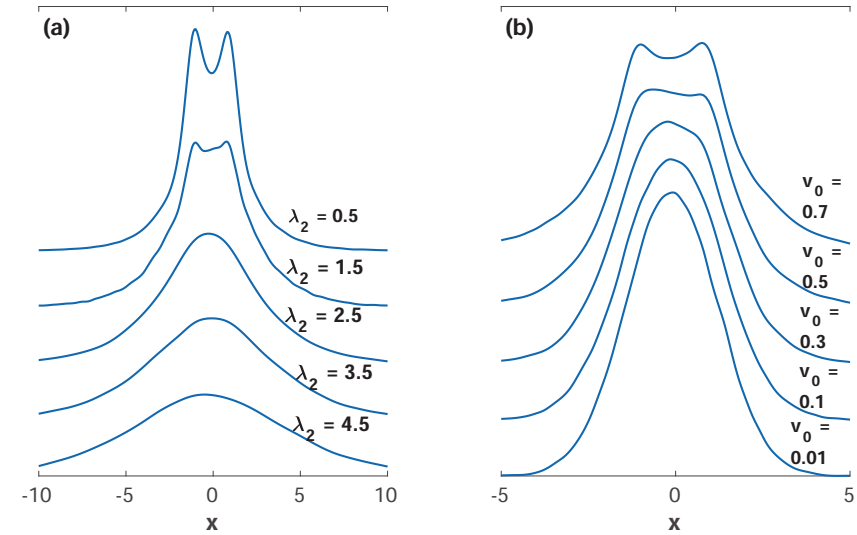


Soft reset phase: motion in harmonic potential with Hooke constant γ :

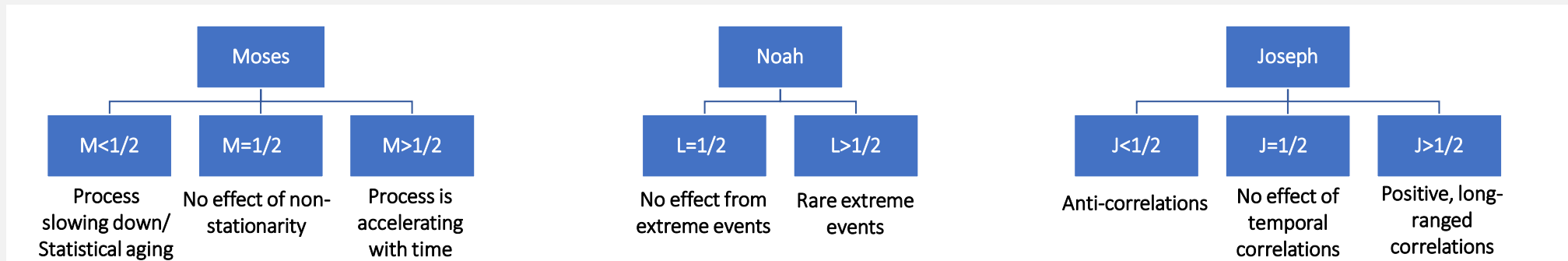
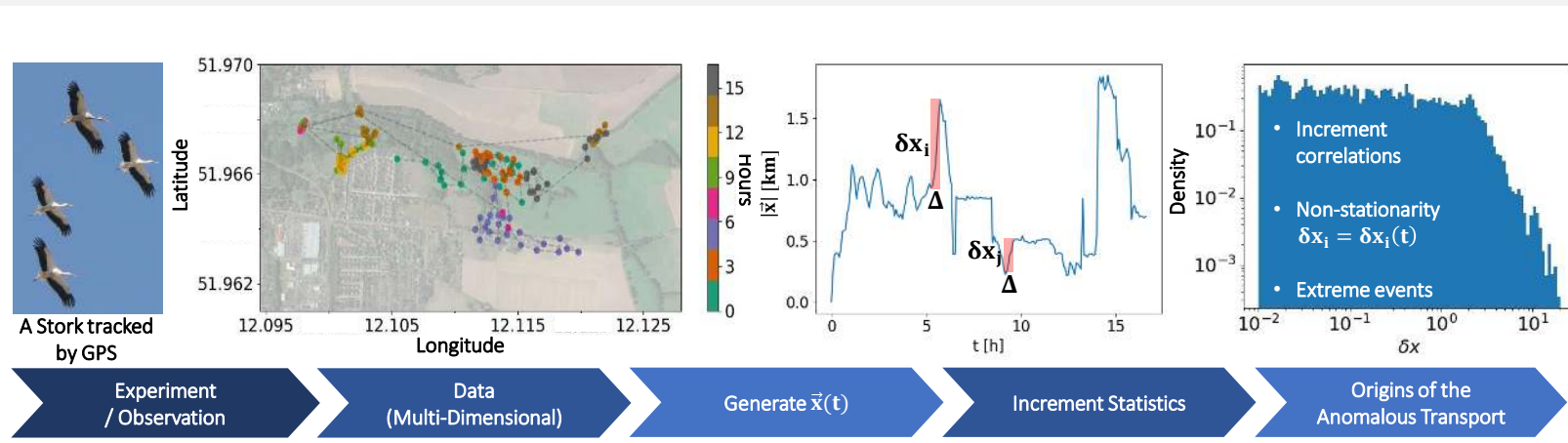
$$m \frac{d^2 x}{dt^2} = -\gamma x$$

Free Lévy walk phase:

$$\frac{dx}{dt} = \pm v_0$$

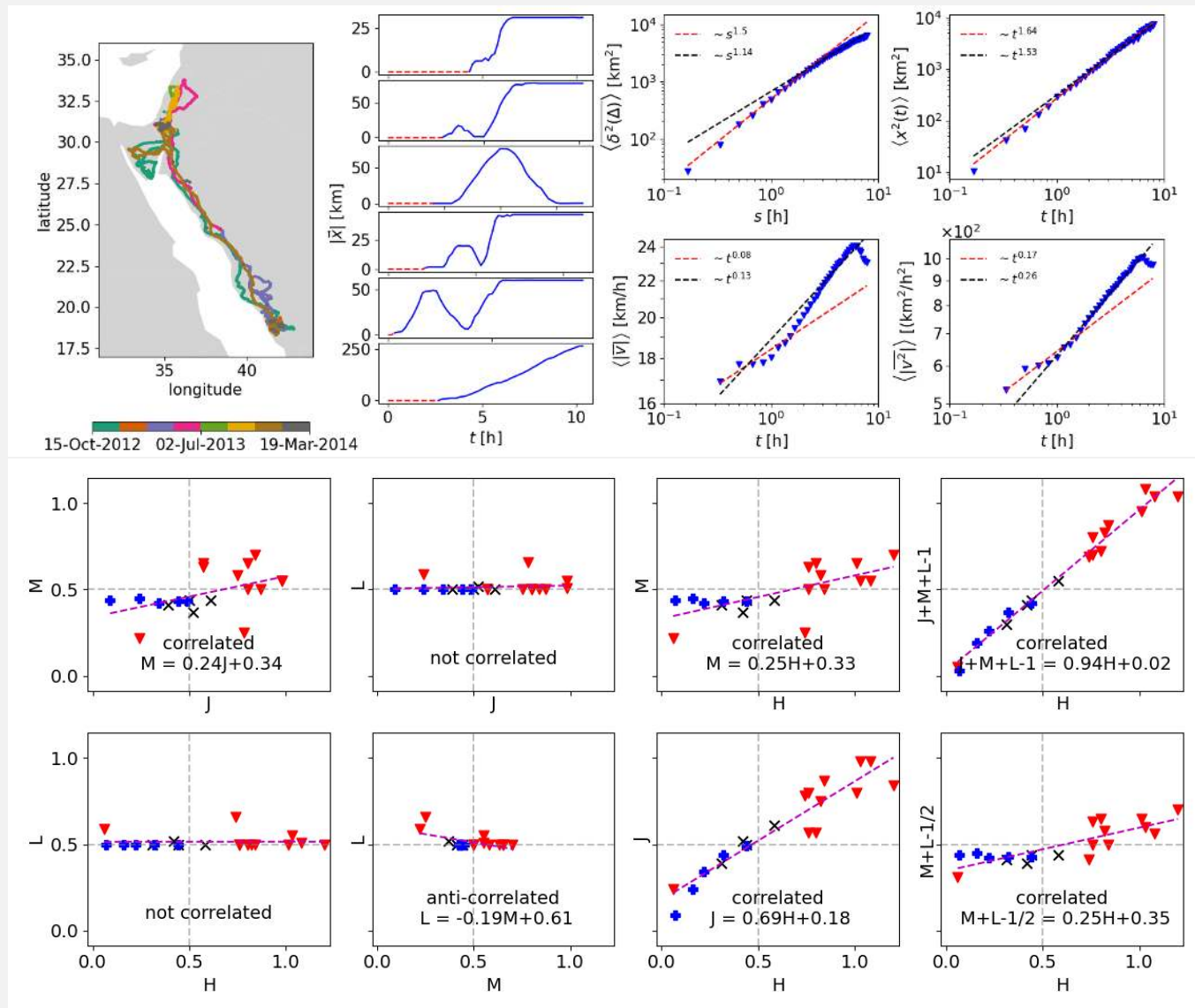


Scaling analysis of anomalous diffusion

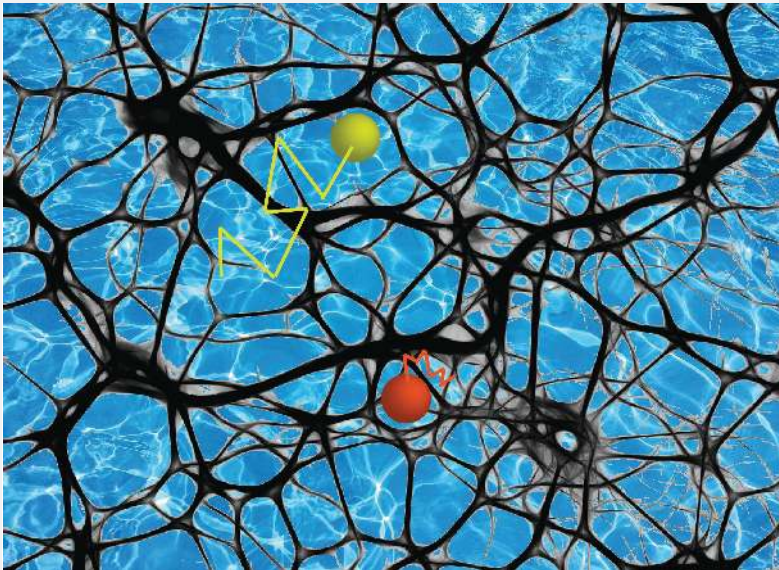
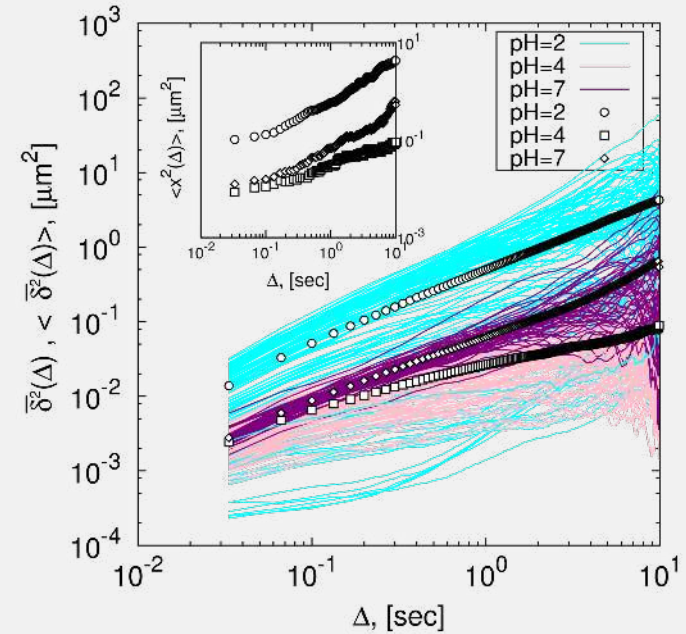
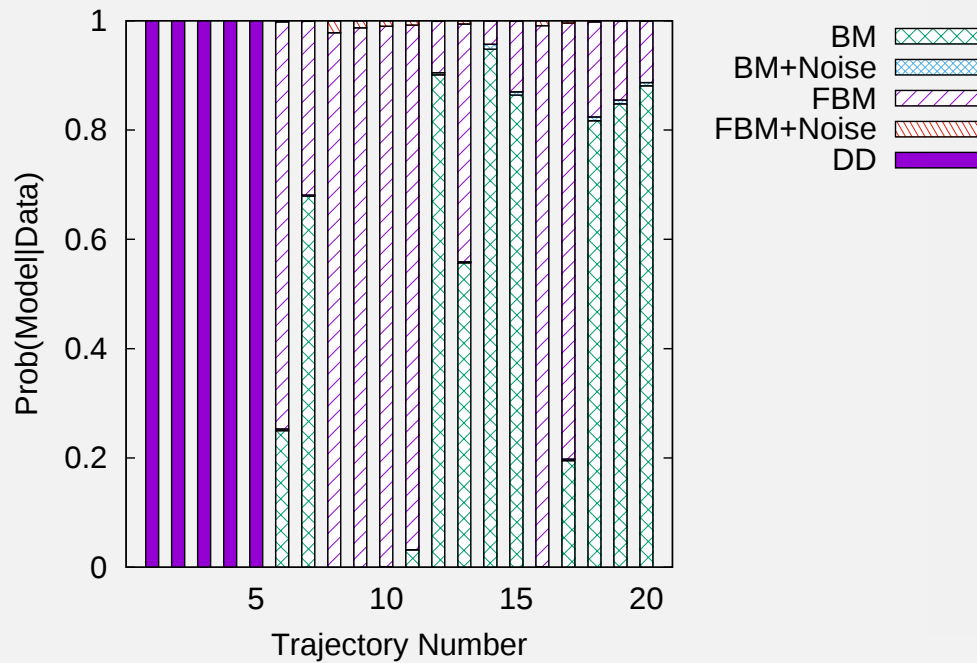


data set	ensemble size	regime	J	L	M	H measured	H prediction	$\frac{ H_p - H }{H}$
Rhodamine 100%	174	$50 < t < 1500$ ms	0.50	0.50	0.41	0.38 ± 0.02	0.42 ± 0.04	10%
Rhodamine 90%	298	$50 < t < 1500$ ms	0.38	0.50	0.42	0.28 ± 0.02	0.30 ± 0.03	7%
Rhodamine 85%	239	$50 < t < 1500$ ms	0.34	0.50	0.40	0.22 ± 0.02	0.24 ± 0.05	9%
Rhodamine 75%	258	$50 < t < 1500$ ms	0.22	0.51	0.44	0.18 ± 0.02	0.18 ± 0.01	>1%
Rhodamine 30%	436	$50 < t < 1500$ ms	0.09	0.50	0.44	0.07 ± 0.02	0.04 ± 0.03	**
Tracers in	200	$0.1 < t < 5$ s	0.39	0.50	0.41	0.31 ± 0.01	0.30 ± 0.02	3%
treated cells		$5 < t < 50$ s	0.50	0.50	0.44	0.44 ± 0.01	0.44 ± 0.01	<1%
Tracers in	1000	$0.1 < t < 2$ s	0.39	0.50	0.44	0.31 ± 0.01	0.33 ± 0.02	6%
untreated cells		$2 < t < 8$ s	0.60	0.50	0.47	0.55 ± 0.01	0.57 ± 0.01	4%
Amoeba	1142	$1 < t < 6$ min	0.61	0.50	0.44	0.58 ± 0.01	0.55 ± 0.03	5%
		$10 < t < 100$ min	0.52	0.52	0.37	0.42 ± 0.02	0.40 ± 0.02	5%
Harvester ants	67	$10 < t < 100$ s	0.88	0.50	0.57	0.92 ± 0.12	0.95 ± 0.08	3%
		$100 < t < 400$ s	0.59	0.51	0.35	0.47 ± 0.03	0.45 ± 0.03	4%
Commuting kite	107	$0.1 < t < 3$ min	0.87	0.50	0.49	0.84 ± 0.02	0.86 ± 0.02	2%
		$3 < t < 12$ min	0.80	0.50	0.50	0.76 ± 0.01	0.80 ± 0.02	5%
Searching kite	587	$0.5 < t < 20$ min	0.24	0.59	0.22	0.06 ± 0.02	0.06 ± 0.01	<1%
Stork (Jun-Jul)	455	$0.2 < t < 2$ h	0.46	0.88	-0.24	*	0.10 ± 0.03	–
		$2 < t < 10$ h	0.18	0.50	0.48	*	0.16 ± 0.08	–
Stork (Aug-Sep)	394	$0.2 < t < 2$ h	0.98	0.55	0.55	1.20 ± 0.03	1.08 ± 0.02	10%
		$2 < t < 10$ h	0.84	0.50	0.70	1.03 ± 0.01	1.04 ± 0.06	1%
Stork (Oct-Jan)	854	$0.2 < t < 2$ h	0.78	0.66	0.25	0.74 ± 0.02	0.68 ± 0.03	8%
		$2 < t < 10$ h	0.57	0.50	0.65	0.80 ± 0.02	0.73 ± 0.10	9%
Stork (Mar-Apr)	391	$0.2 < t < 2$ h	0.98	0.51	0.55	1.08 ± 0.02	1.04 ± 0.02	4%
		$2 < t < 10$ h	0.80	0.50	0.65	1.01 ± 0.01	0.95 ± 0.07	6%
Vulture	444	$0.1 < t < 2$ h	0.75	0.50	0.58	0.82 ± 0.02	0.84 ± 0.02	1%
		$2 < t < 5.5$ h	0.57	0.50	0.63	0.76 ± 0.02	0.70 ± 0.04	9%

Scaling analysis of anomalous diffusion



Maximum likelihood Bayesian data analyses

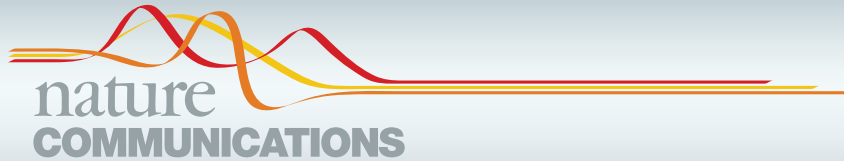


Nested sampling à la Skilling

Objective model selection

Parameter estimation

The ANomalous Diffusion challenge



ARTICLE



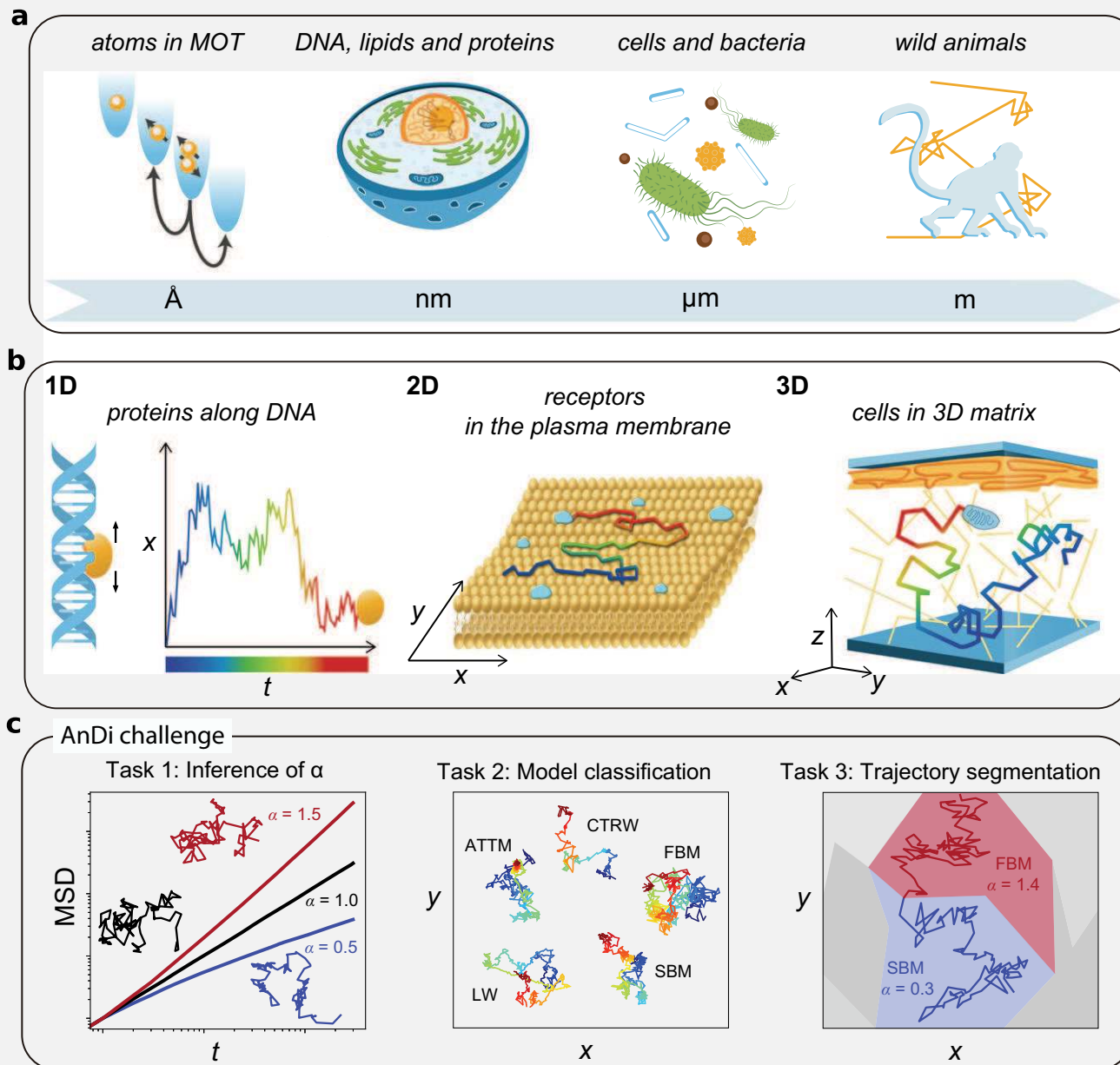
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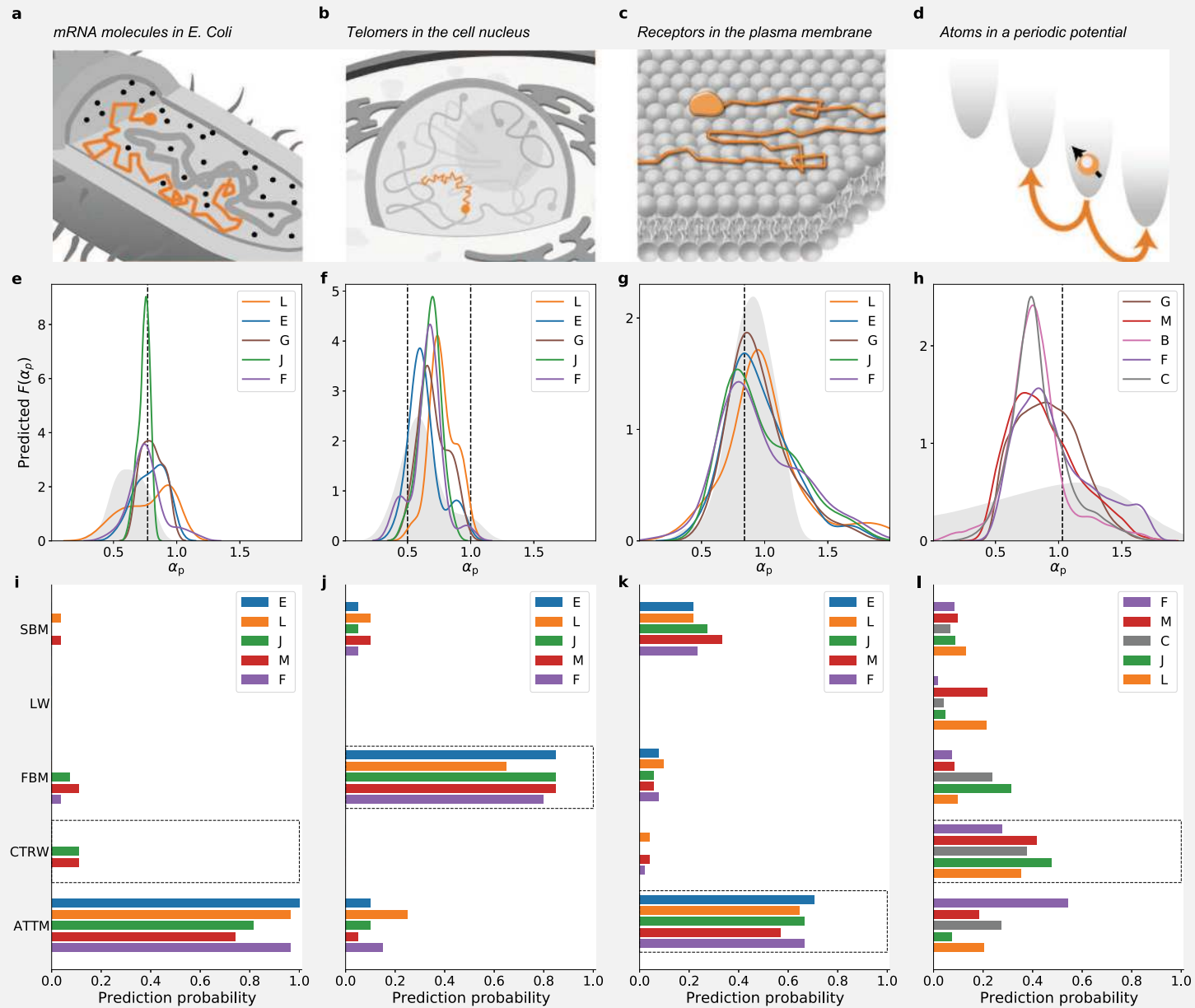
Objective comparison of methods to decode anomalous diffusion

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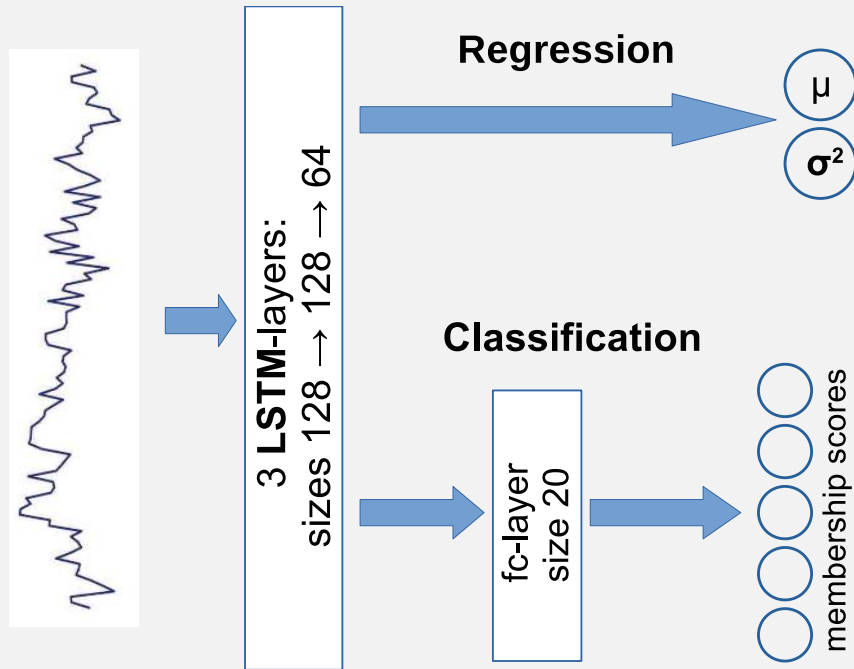


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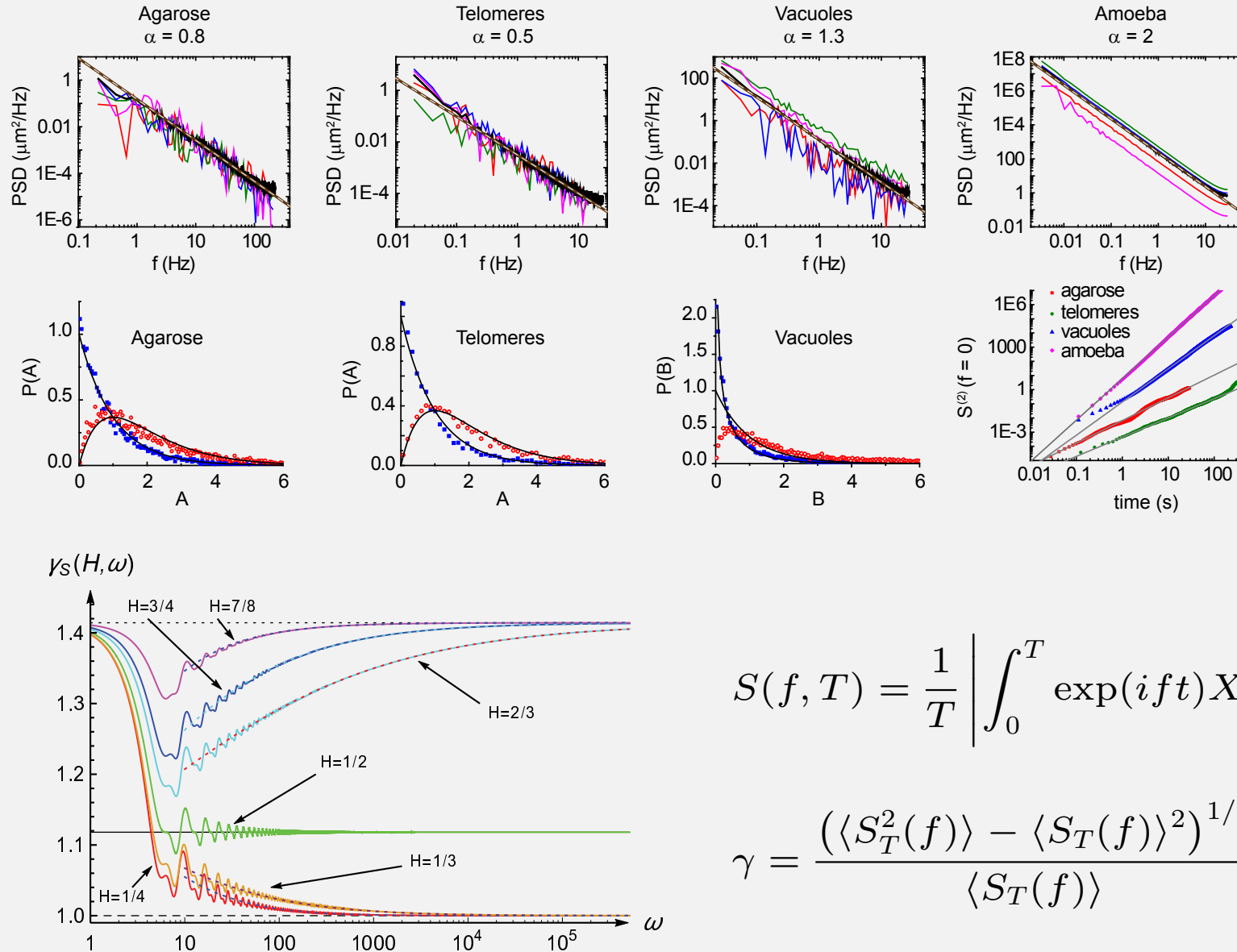
Bayesian-weighted deep learning model selection

Long Short-Term Memory approach (recurrent neural network architecture)



Predicted model	attn	0.54	0.048	0.065	0.0013	0.099
	ctrw	0.1	0.93	0.033	0	0.0025
	fbm	0.13	0.014	0.73	0.01	0.14
	lw	0.0061	0	0.015	0.98	0.01
	sbm	0.22	0.0071	0.16	0.0082	0.75
		attn	ctrw	fbm	lw	sbm
True model						

Power spectral density of a single FBM trajectory



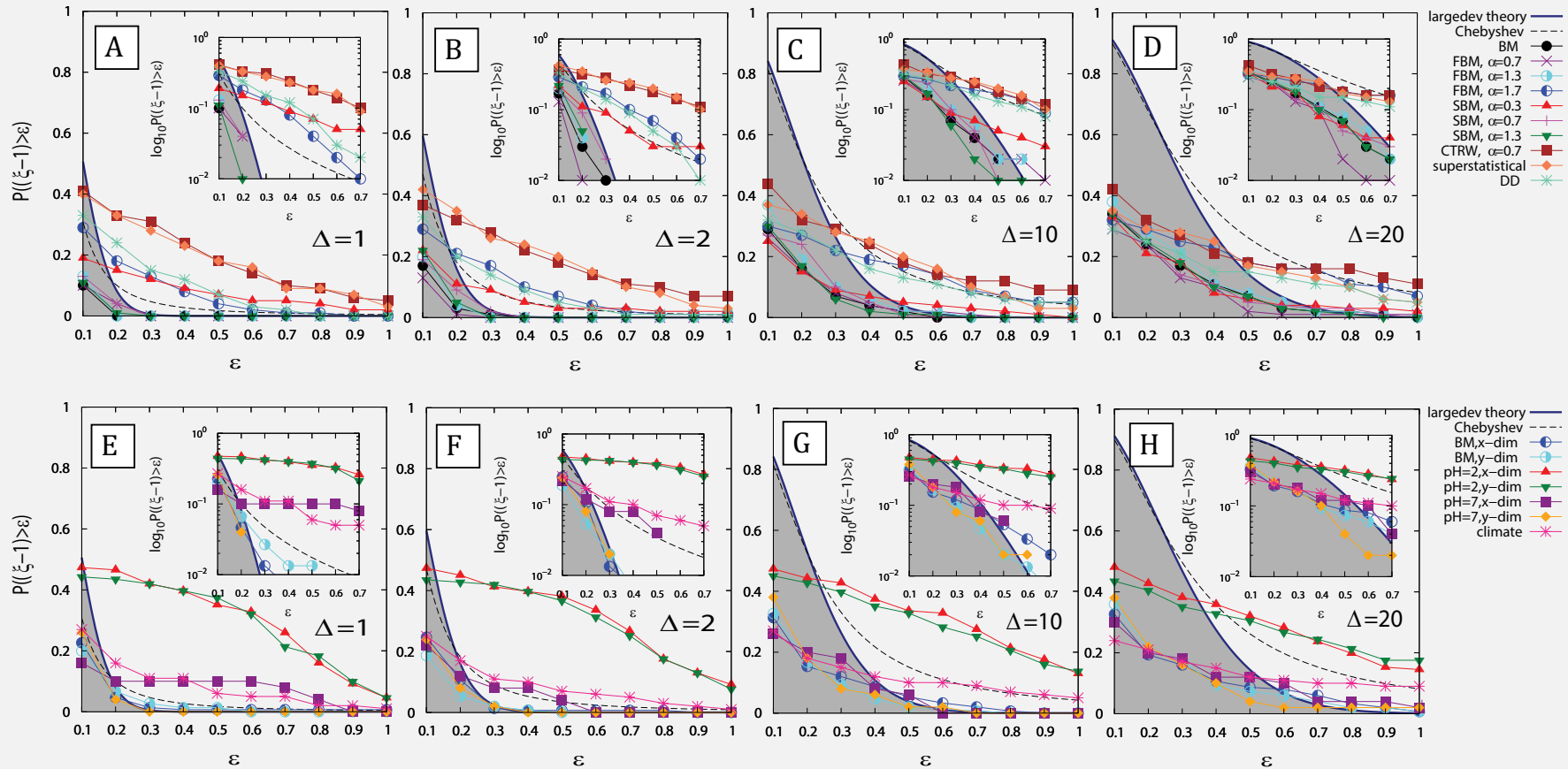
Large-deviation statistics for TAMSD

Chebyshev's inequality for Brownian motion $X(1), X(2), \dots, X(N)$, given deviation ε :

$$P((\xi - 1) \geq \varepsilon) \leq \frac{4\Delta}{4\Delta + 3N\varepsilon^2}, \quad \xi = \frac{\overline{\delta^2(\Delta)}}{\langle \delta^2(\Delta) \rangle}, \quad \langle \xi \rangle = 1$$

Large-deviation result:

$$P((\xi - 1) \geq \varepsilon) \leq \exp(-a\mathcal{H}(b)), \quad \mathcal{H}(b) = 1 + b - \sqrt{1 + 2b}; \quad a, b = f(\Delta, \dots)$$



Σ ummary

- I Random search processes have characteristic search/reaction times that may differ by orders of magnitude $\leadsto$ chemical rates or (global) mean search times inappropriate for quantitative description
- II Lévy walk search processes can be adequately quantified by stochastic observables, including the first-passage & first-hitting time statistics
- III Instead of Lévy walks persistent fractional Brownian motion may be relevant for the search dynamics of larger animals
- IIII Random-parameter models may adequately describe ensembles of animals, or different trajectories of the same animal
- IIII Objective data analysis methods aid in identification of models & parameters: Bayesian-maximum likelihood, deep learning, & their combinations

For slides or questions: write to rmetzler@uni-potsdam.de

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