

Beyond Brownian motion: from data to models

—Pohang, 25th November 2022—



Fluxes, random walks, & fluctuating forces: $\langle r^2(t) \rangle \propto Kt$



Paul Langevin (1872-1946)

Albert Einstein (1879-1955)



Marian Smoluchowski
(1872-1917)

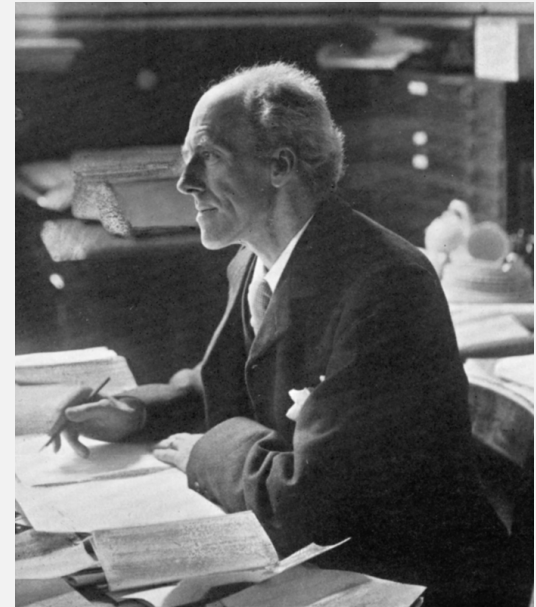


William Sutherland
(1859-1911)

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





Confinement in physical systems

I Harmonic oscillators are prototype physical system

II Harmonic potential as first-order in symmetric potentials: $V(x) = V_0 + \frac{k}{2}x^2 + o(x^4)$ S

II Hookean force from optical tweezers, anchoring by flexible polymer

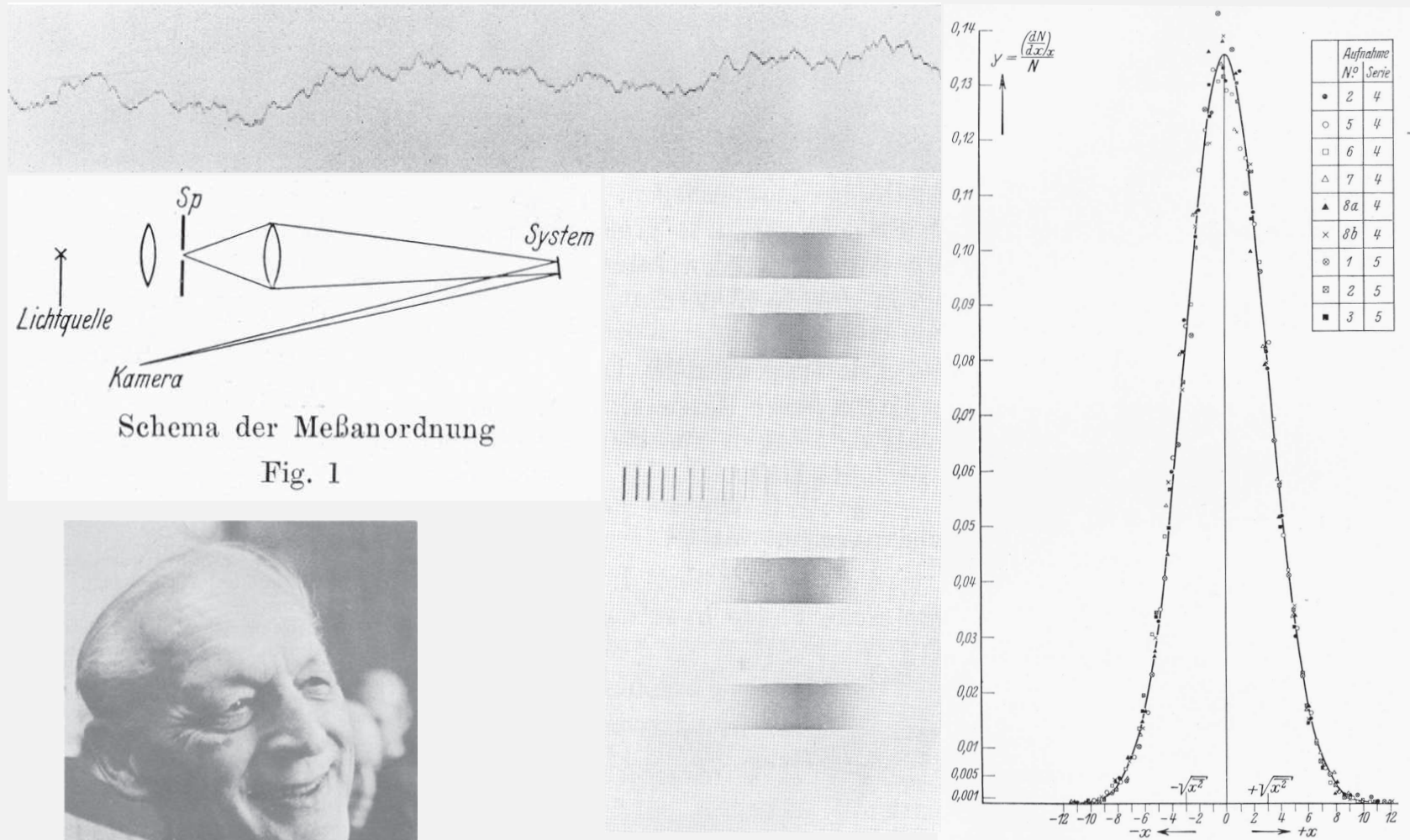
III Steeper potentials as higher order terms in confinement or ever better approximation to box potential

III Shallower potentials for entropic forcing in confining channels, symmetric linear potential as prototype, realisable in holographic optical systems; logarithmic potential in laser systems

III Potentials of different forms as models for home-ranging in habitat, representing different degrees of lockdowns in models for disease spreading, in complex free energy landscapes . . .

$$V(x) \simeq |x|^c, \quad c > 0$$

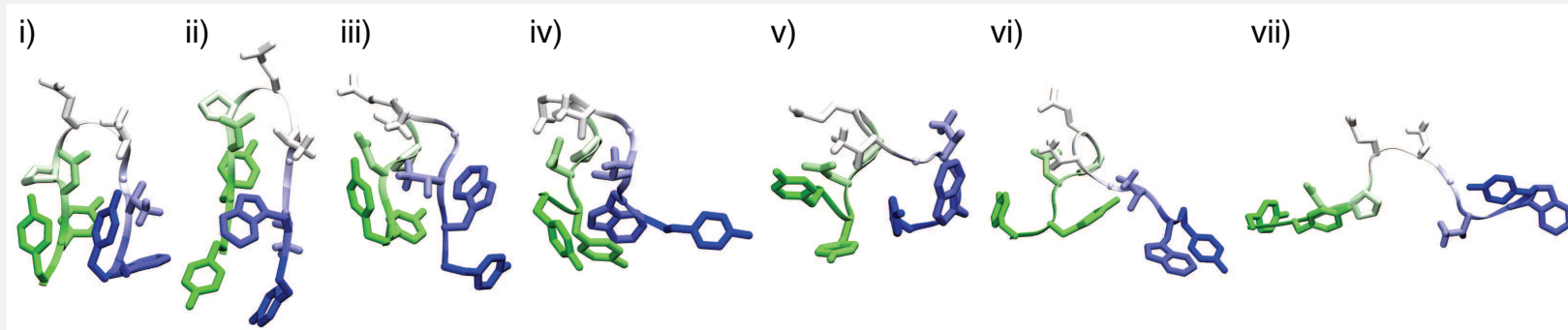
Kappler's torsional balance: mapping Boltzmann



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

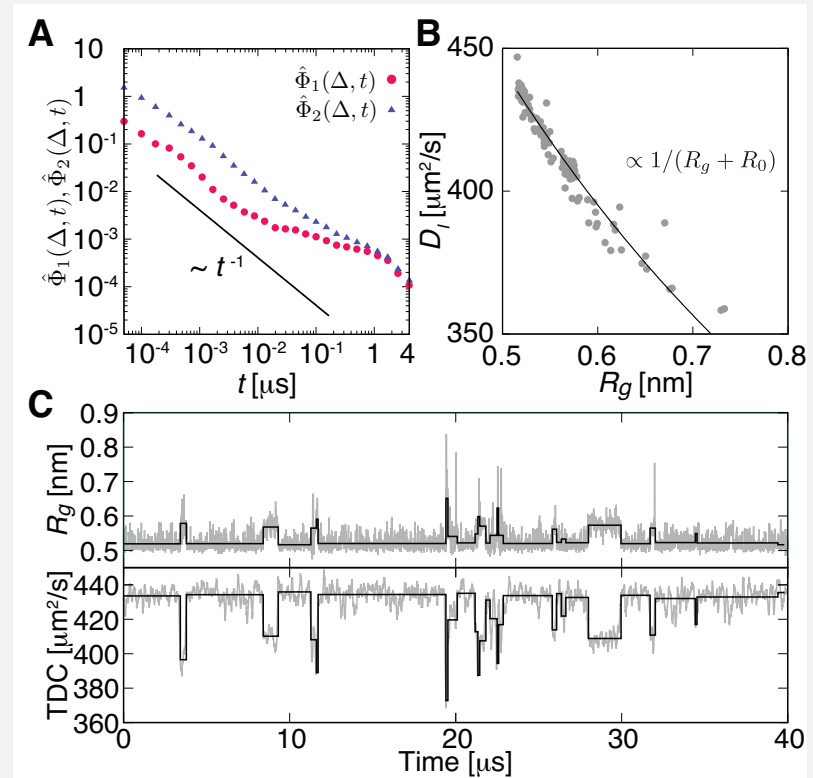
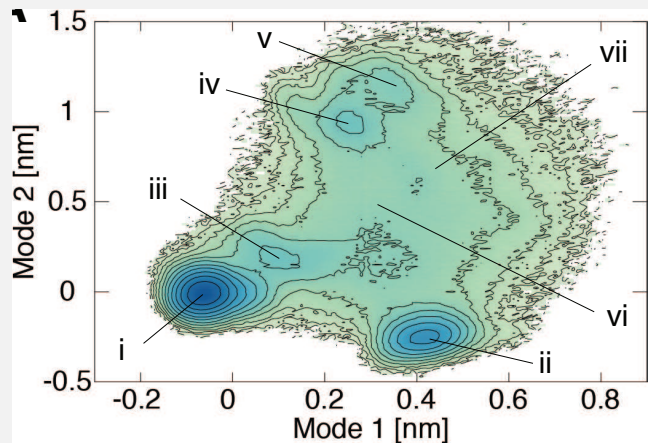
E Kappler, Ann d Physik (1931): $N_A = 60.59 \times 10^{22} \pm 1\%$

Instantaneous diffusivity of shape-fluctuating proteins

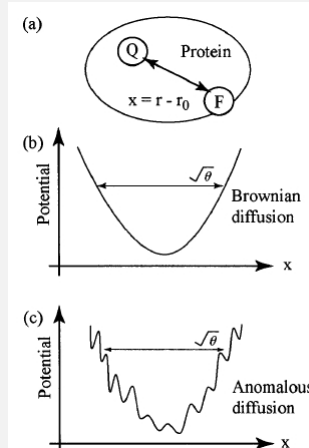
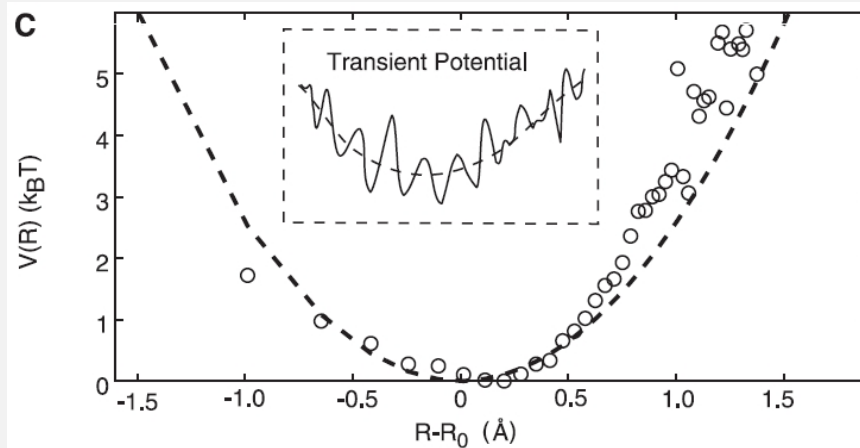
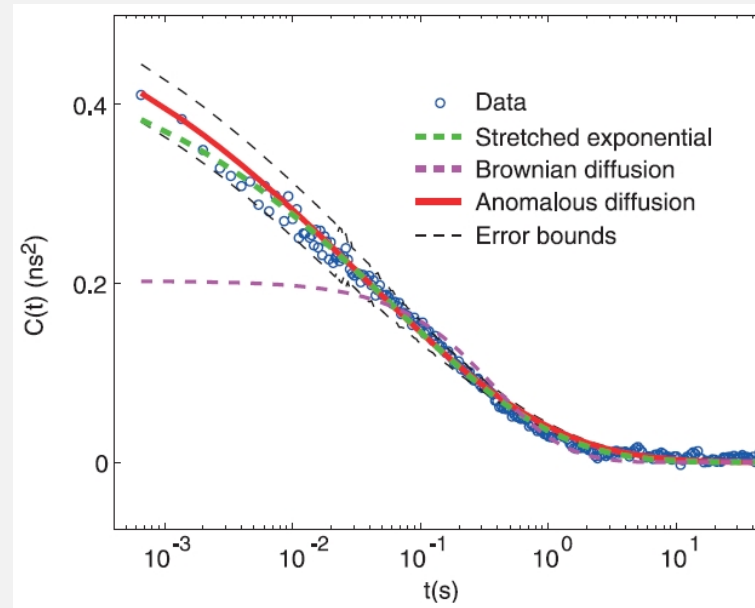
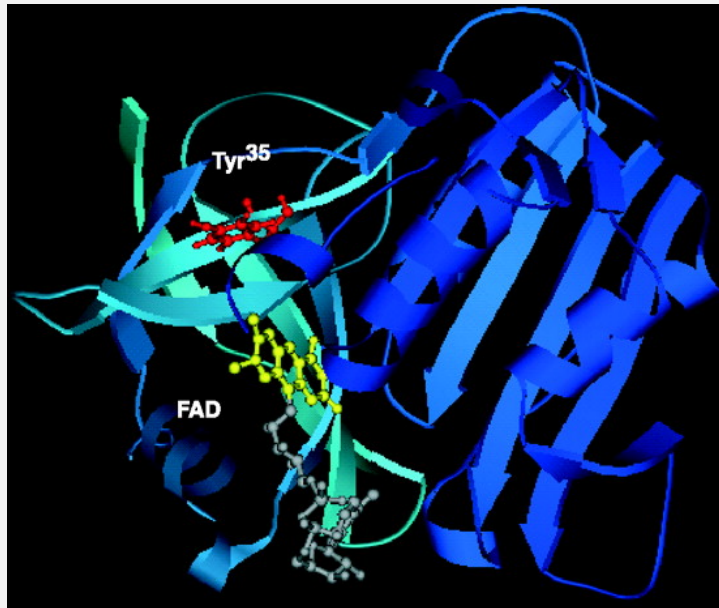


Instantaneous Einstein-Stokes-type relation (for different pressure & temperature):

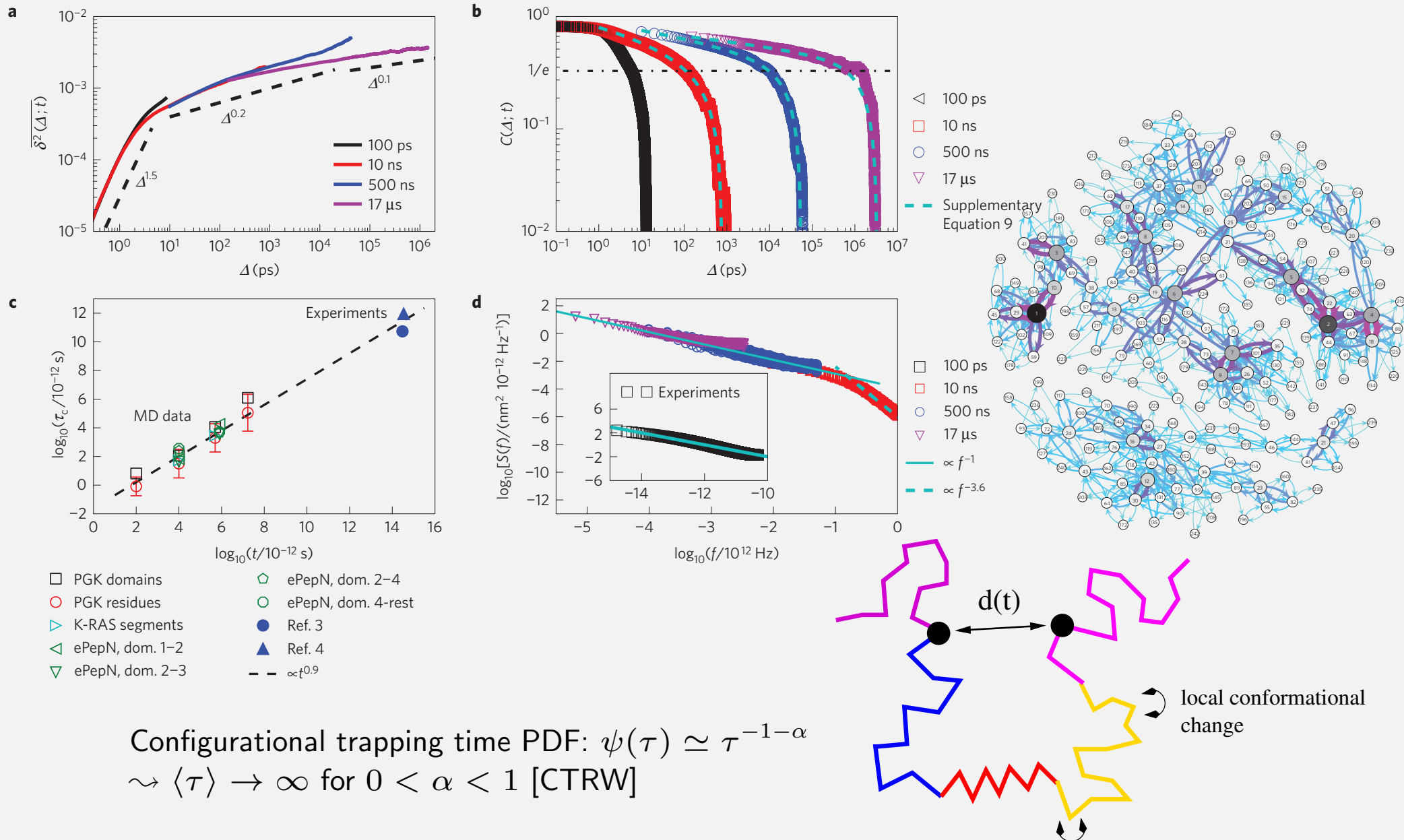
$$D \propto \frac{1}{R_g + R_0}, \quad R_0 \approx 0.3\text{nm}$$



Protein conformational dynamics



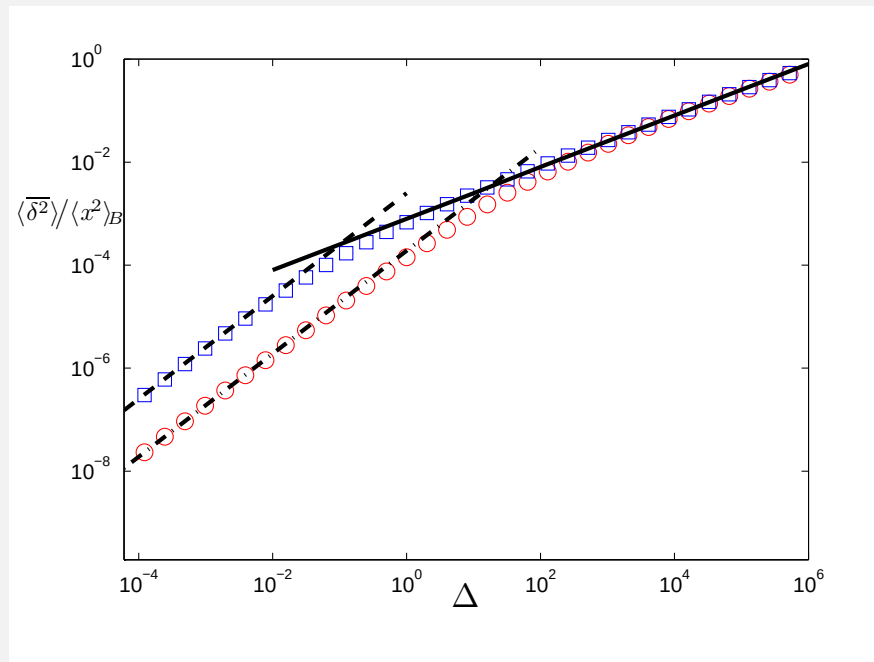
Self-similar internal protein dynamics: 13 decades of ageing



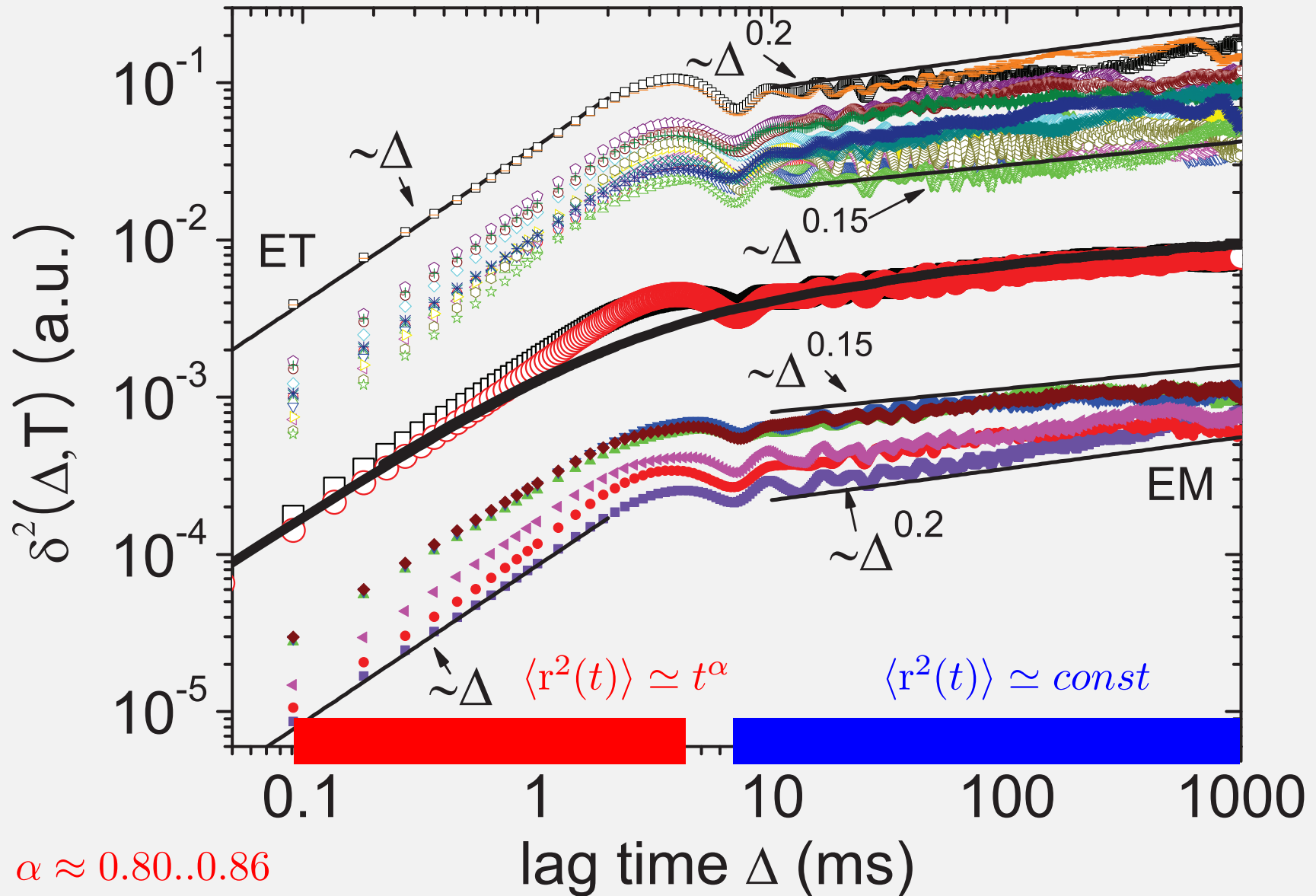
Universality dynamics in binding potential

$$\frac{\partial}{\partial t} P(x, t) = {}_0D_t^{1-\alpha} \left(\frac{\partial}{\partial x} \frac{V'(x)}{m\eta_\alpha} + K_\alpha \frac{\partial^2}{\partial x^2} \right) P(x, t)$$

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



Granule subdiffusion in harmonic potential (@ short times)

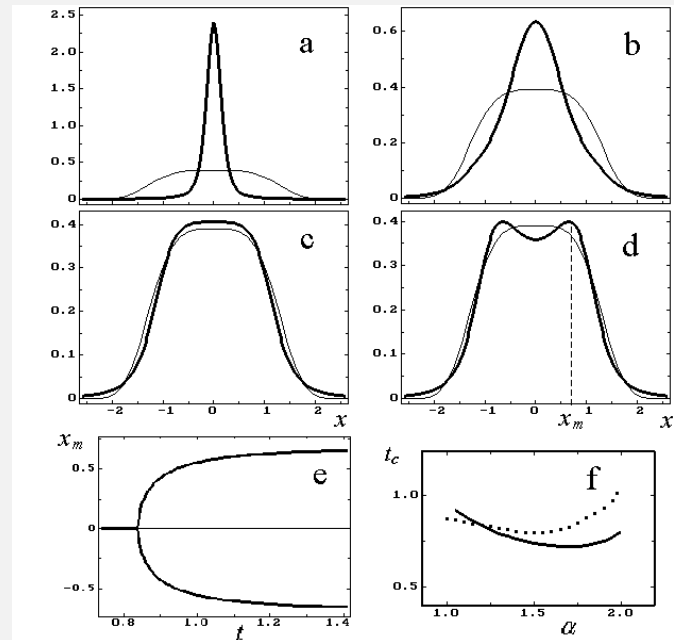
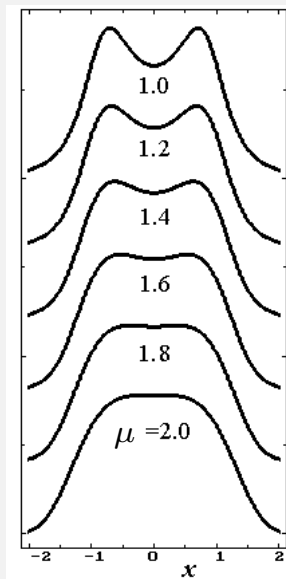


Lévy flights ($\lambda(x) \simeq |x|^{-1-\mu}$) in superharmonic potentials

$$\frac{\partial}{\partial t} P(x, t) = \frac{\partial}{\partial x} \frac{V'(x)}{m\eta} P(x, t) + K^\mu \frac{\partial^\mu}{\partial |x|^\mu} P(x, t), \quad V(x) \simeq |x|^c$$

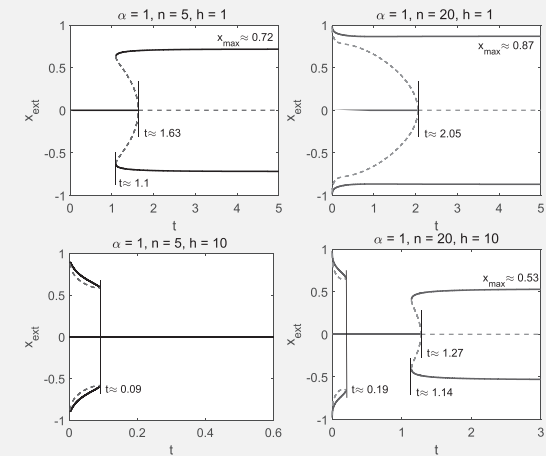
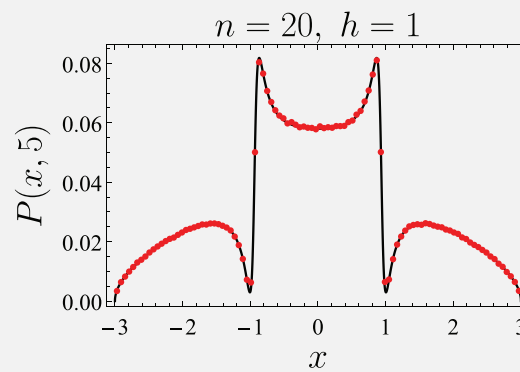
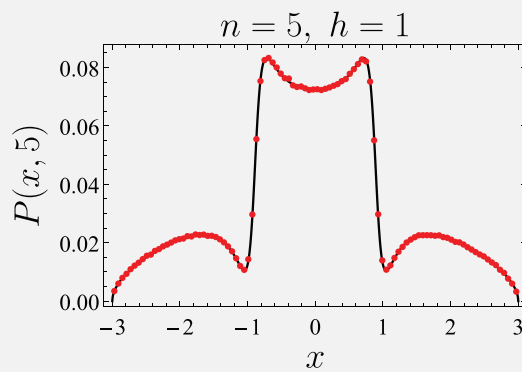
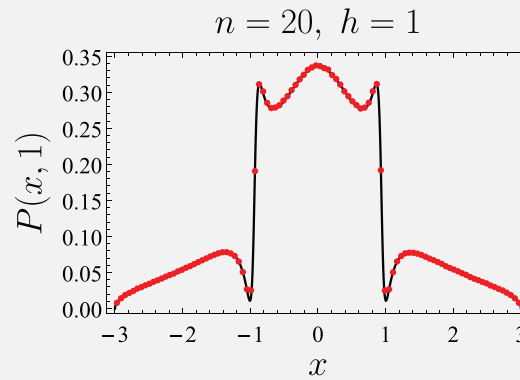
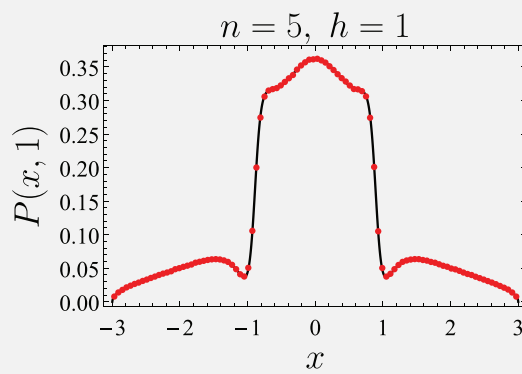
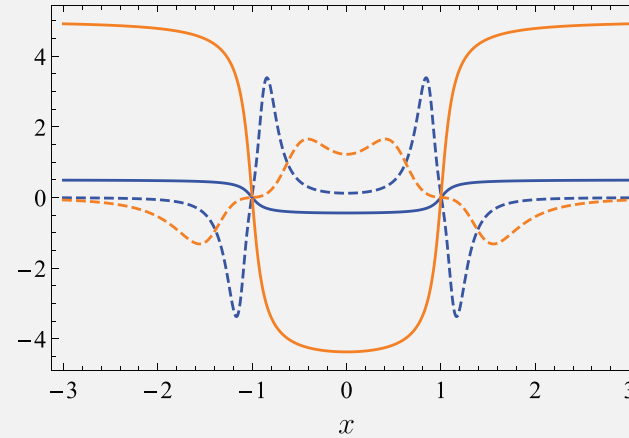
Harmonic potential: $P_{\text{st}}(x) = L_\mu(x)$ [S Jespersen, RM & HC Fogedby, PRE (1999)]

Quartic potential $V(x) = \frac{1}{4}x^4$



Lévy flights in confining box-like potentials

$$V(x) = \frac{h}{\pi} \arctan \left(nx^2 - n \right)$$



Lévy flights in subharmonic potentials

$$\frac{\partial}{\partial t} P(x, t) = \frac{\partial}{\partial x} \frac{V'(x)}{m\eta} P(x, t) + K^\mu \frac{\partial^\mu}{\partial |x|^\mu} P(x, t), \quad V(x) \simeq |x|^c$$

Convergence to stationary state only if:

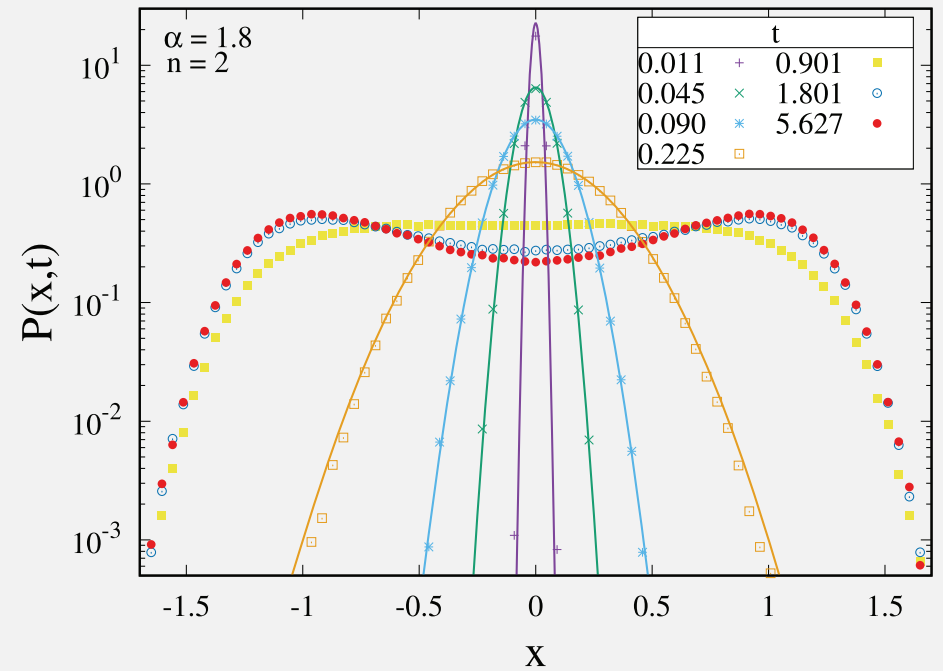
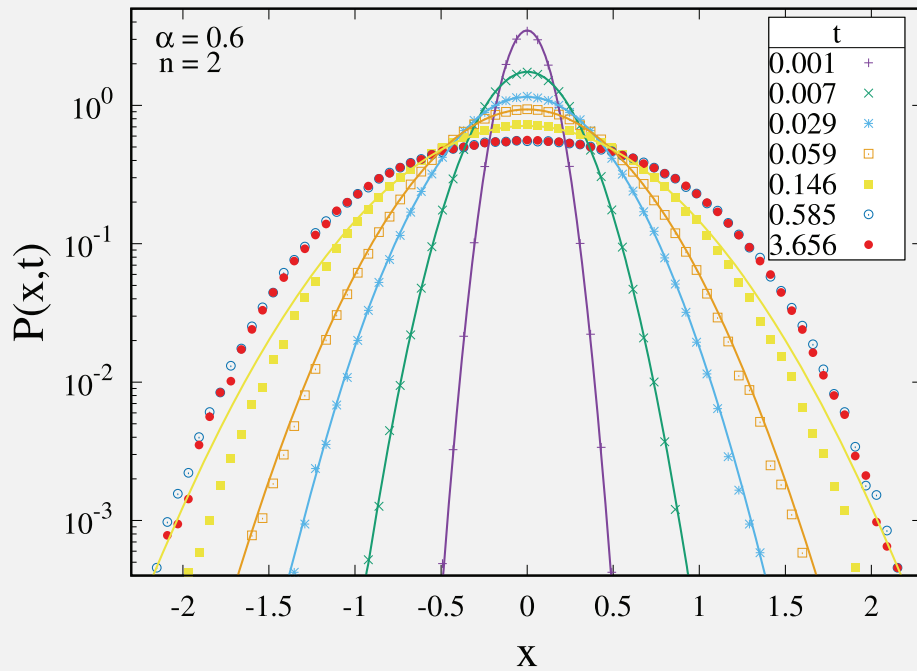
$$c > 2 - \mu, \quad 0 < \mu \leq 2$$

Otherwise motion is unconfined

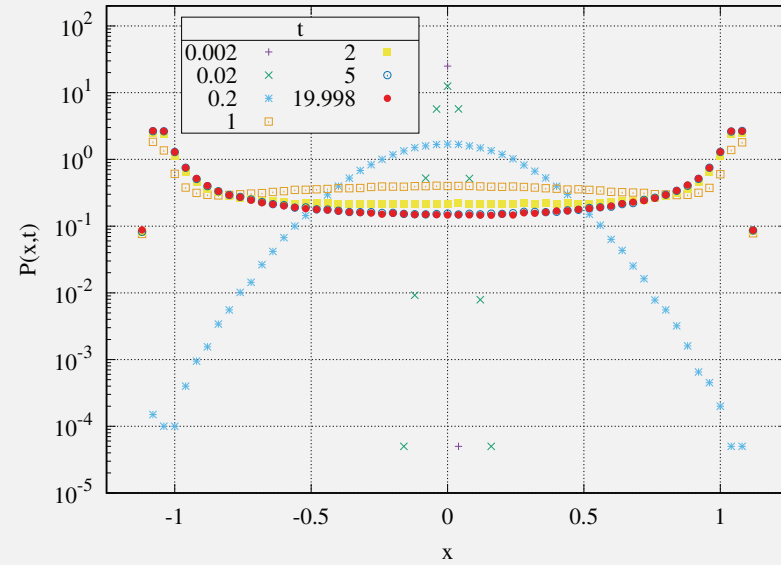
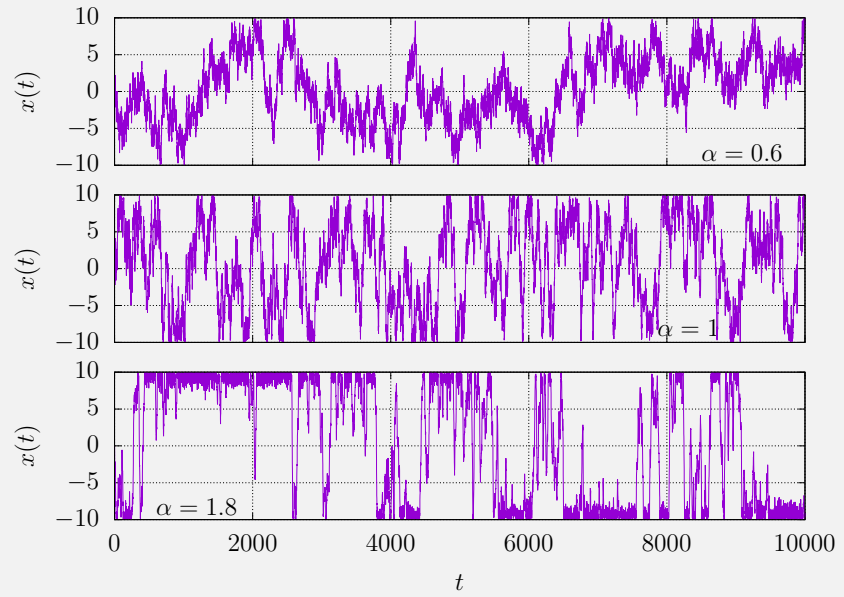
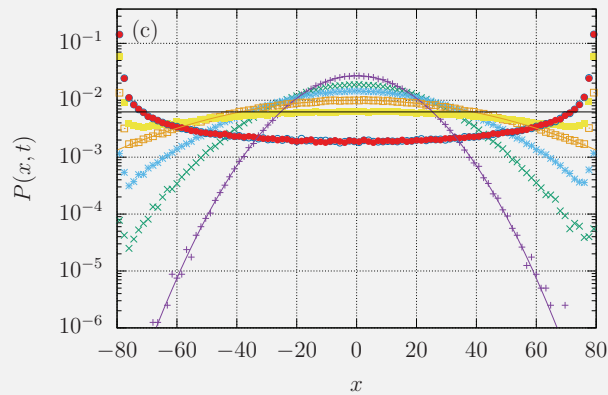
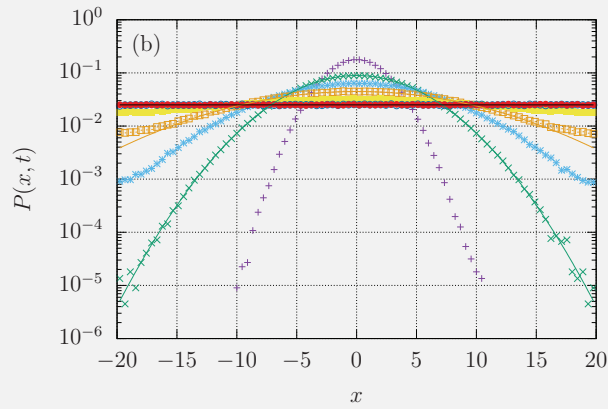
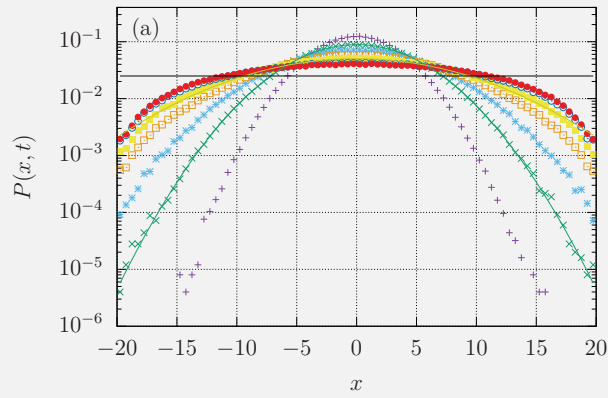
Here: competition of confining trend of external potential versus the tendency of extremely long jumps (NB: non-locality of FFPE)

Fractional BM in superharmonic potentials

$$\frac{d}{dt}X(t) = -V'(x)X(t) + \xi_\alpha(t) \quad \therefore \quad \langle \xi_\alpha(t)\xi_\alpha(t+\tau) \rangle \sim \alpha(\alpha-1)K_\alpha\tau^{\alpha-2}$$



FBM: accretion & depletion effects near hard boundaries

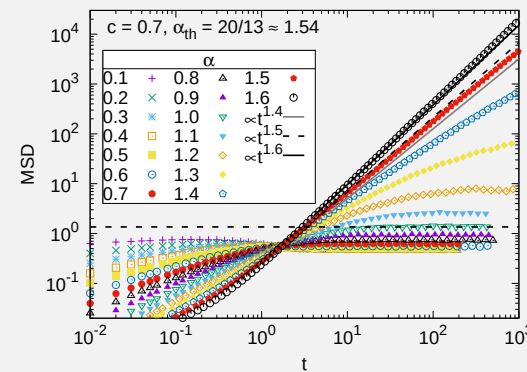
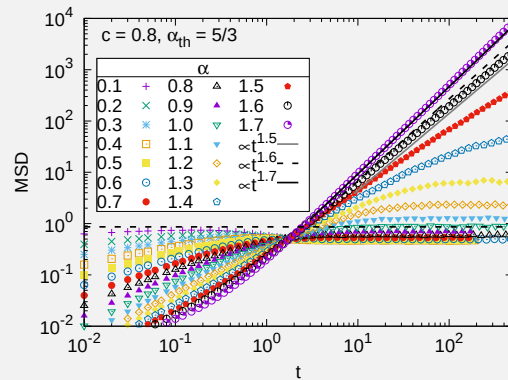
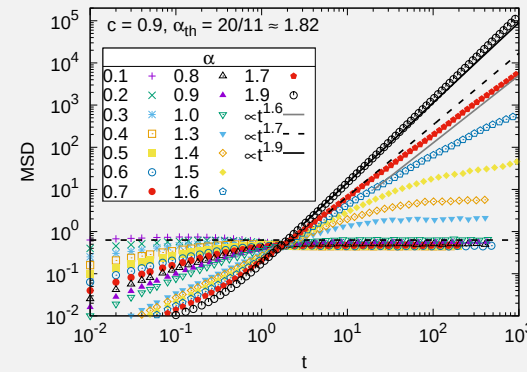
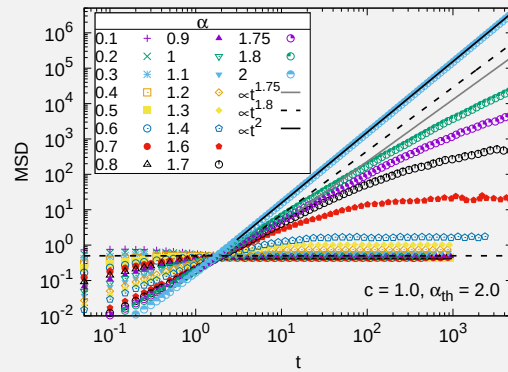


FBM in subharmonic potentials

Convergence to stationary state only if:

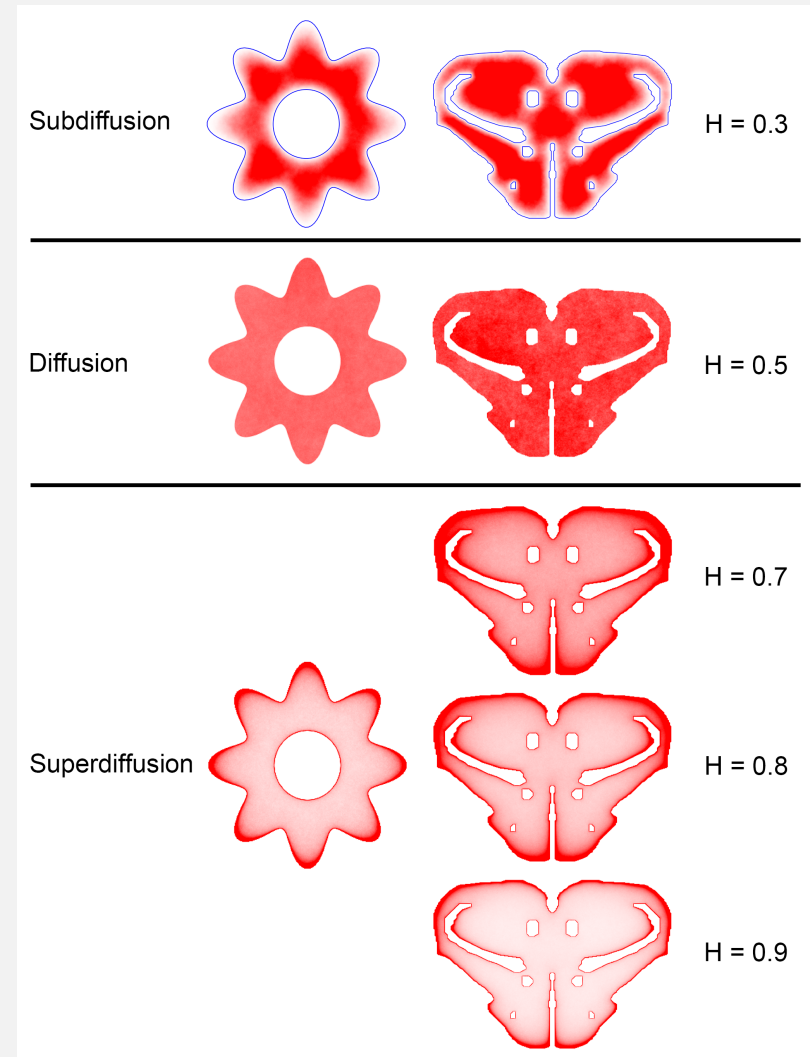
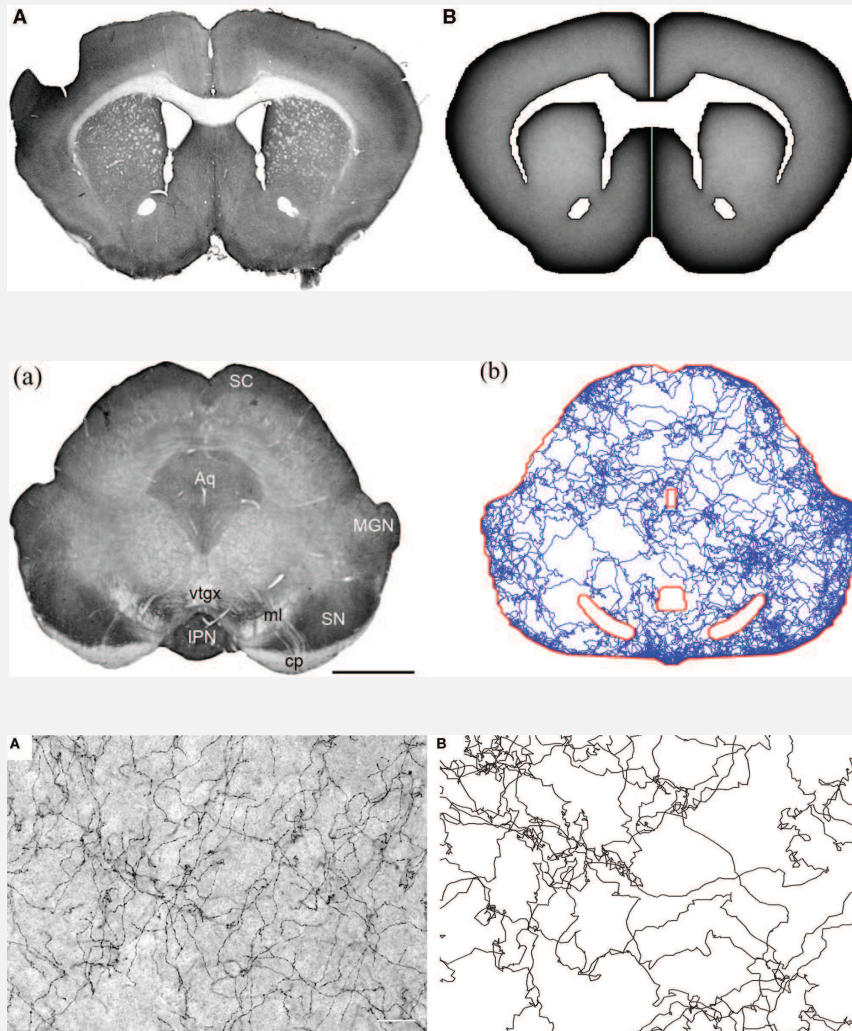
$$c > 2 - \frac{2}{\alpha} \text{ self-similarity index } H = \alpha/2 : \quad c > 2 - 1/H$$

For Lévy flight $H = 1/\mu \Rightarrow$ same criterion for existence for stationary states

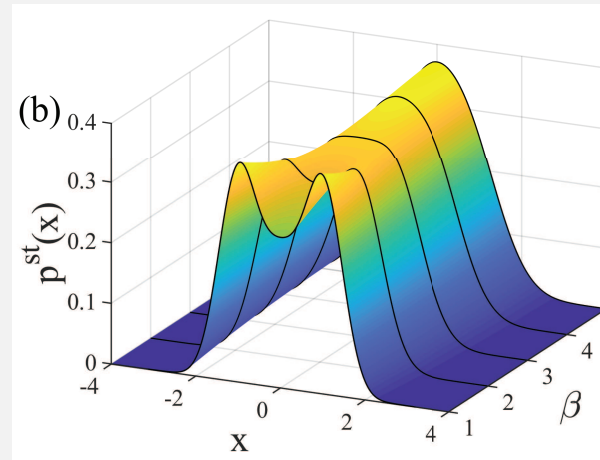
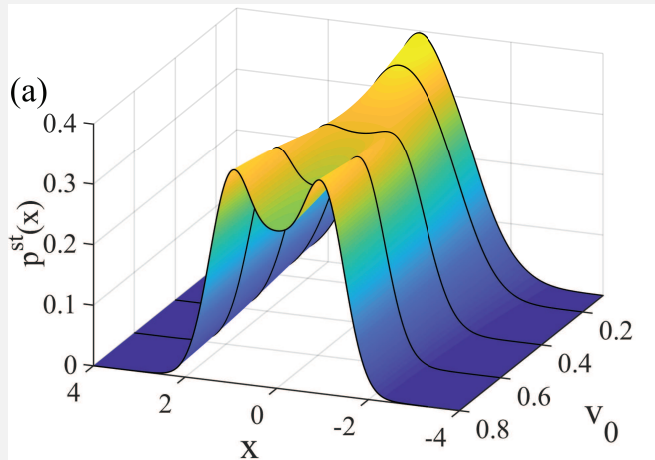


Brain serotonergic axons as FBM paths

Correlated fluctuations effect non-flat profile



Lévy walk in harmonic potential



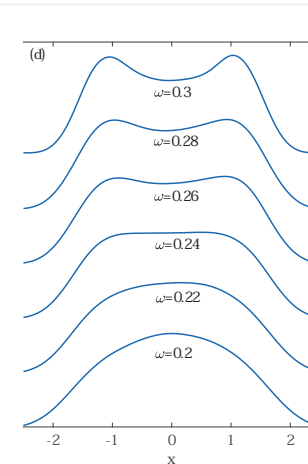
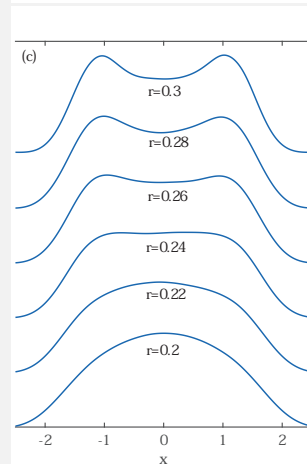
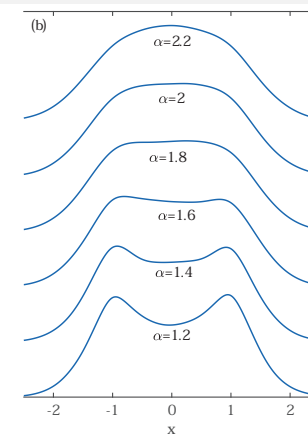
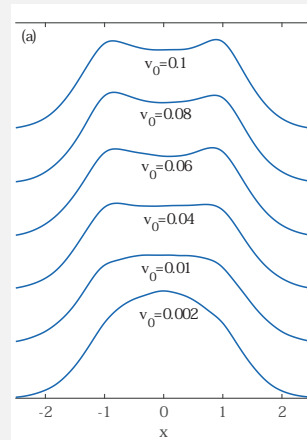
$\uparrow v_0$: LW speed

β : rate of walking time PDF $\psi(t)$

$\rightarrow$

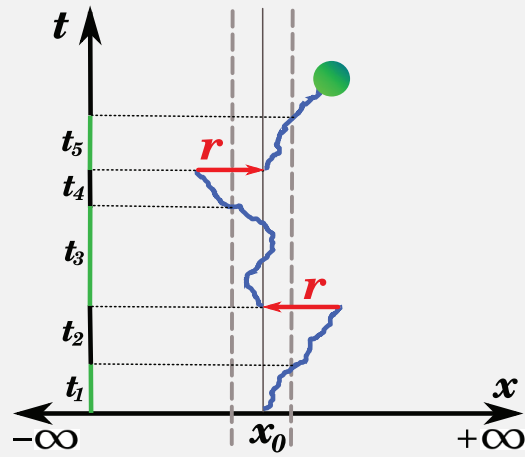
(a) & (b): power-law form of $\psi(t)$

(c) & (d): uniform $\psi(t)$



P Xu, T Zhou, RM & W Deng, PRE (2021)

Soft resets of Lévy walk

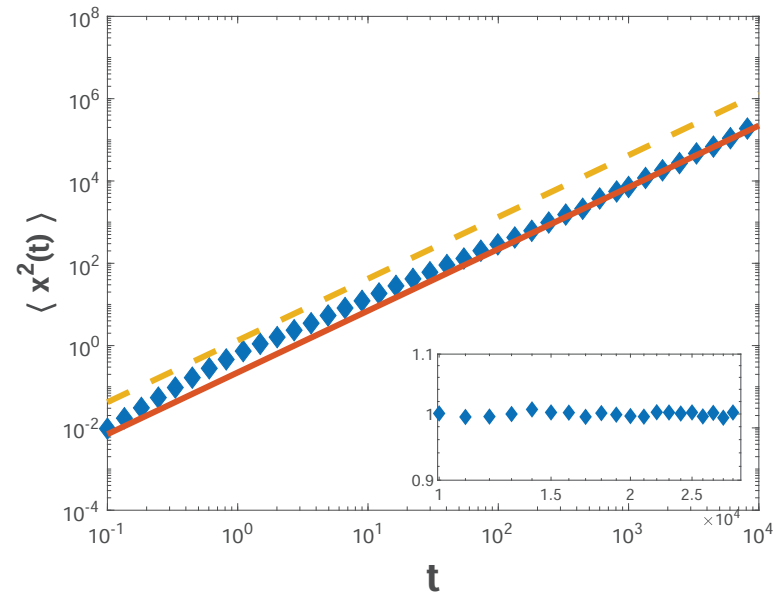
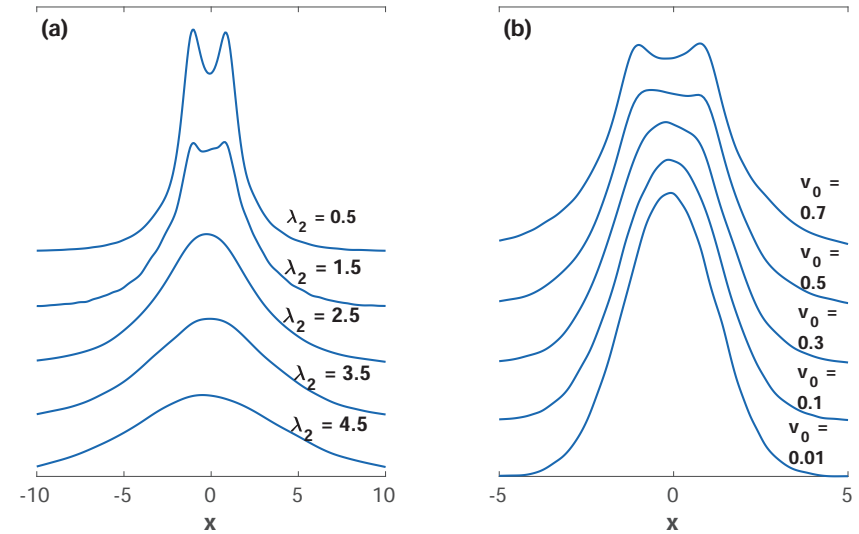


Soft reset phase: motion in harmonic potential with Hooke constant γ :

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

Free Lévy walk phase:

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



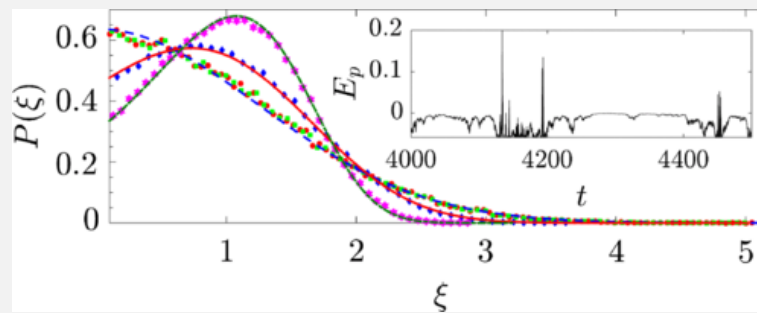
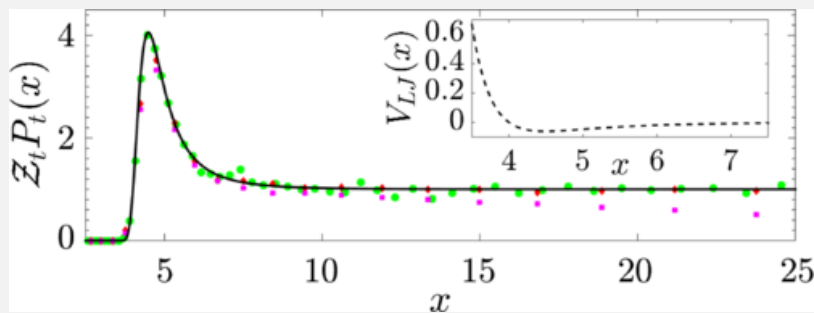
Asymptotically flat external potentials

Lennard-Jones potential:

$$V_{\text{LJ}}(x) = \begin{cases} \infty, & x \leq 0 \\ V_0(a^{12}/x^{12} - b^6/x^6), & x > 0 \end{cases}$$

Uniform approximation:

$$P_t(x) \approx \frac{1}{\sqrt{\pi Dt}} \exp \left(-\frac{V(x)}{k_B T} - \frac{x^2}{4Dt} \right), \quad x \geq 0$$



$$\xi = \frac{\overline{V_{\text{LJ}}[x(t)]}}{\langle V_{\text{LJ}}[x(t)] \rangle}$$

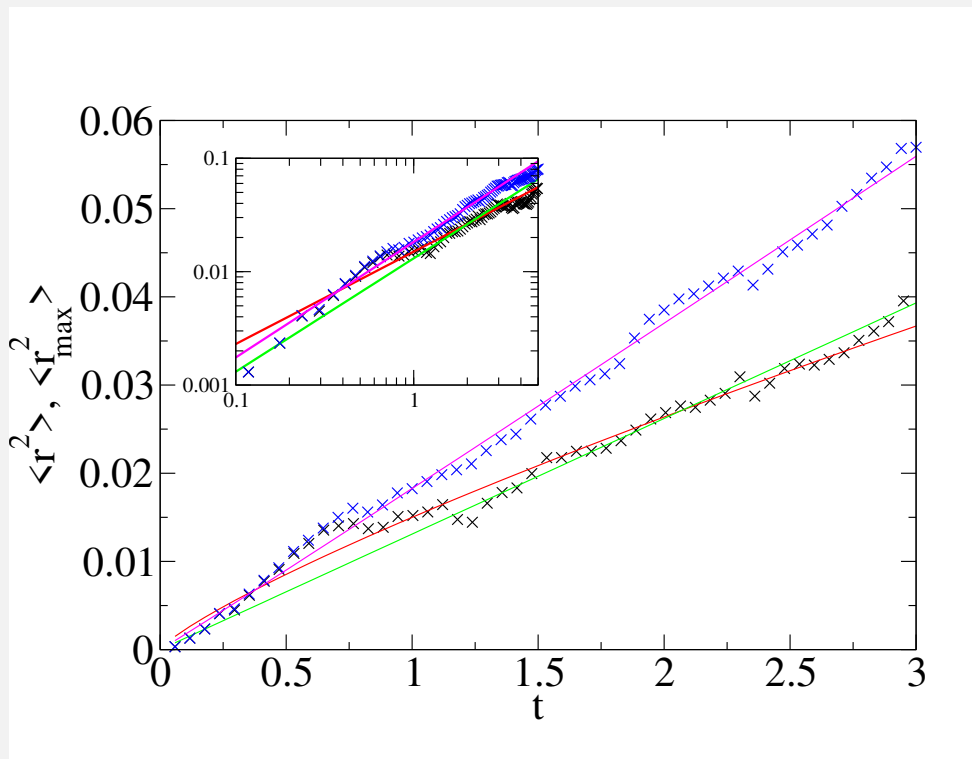
& now it's time for something completely different



Fitting power-laws: Is it really anomalous?

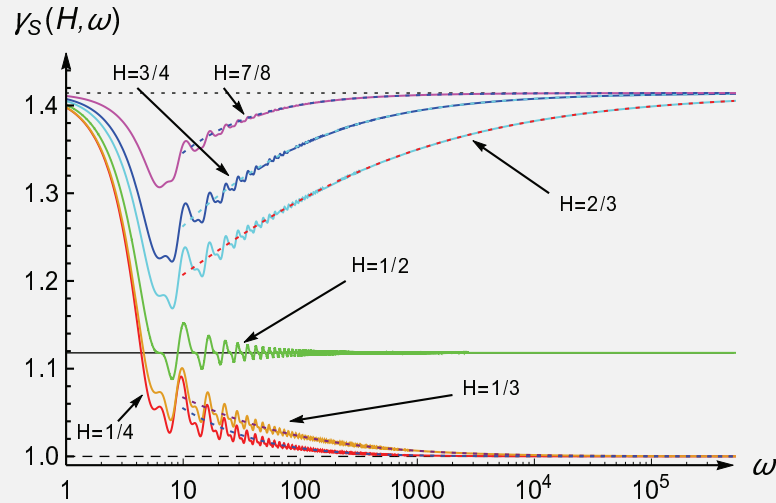
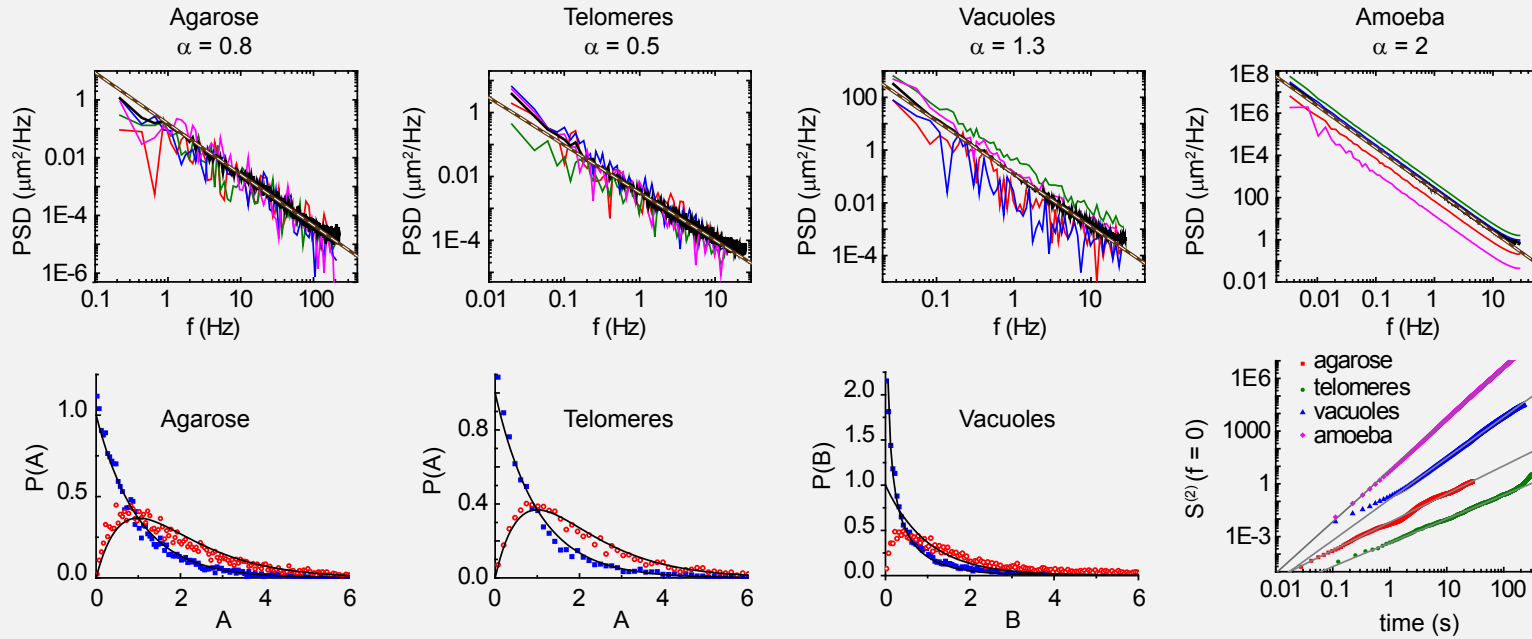
Coefficient of variation is smaller for MME PDF than for regular PDF:

$$\gamma = \frac{\sqrt{\langle \mathbf{r}^2(t) \rangle - \langle \mathbf{r}(t) \rangle^2}}{\langle \mathbf{r}(t) \rangle} \rightsquigarrow \frac{\gamma(\text{MSD})}{\gamma(\text{MME})} = 1.61 \text{ (1D)}, 1.44 \text{ (2D)}, 1.34 \text{ (3D)}$$



Analysis of an experimental set of 67 trajectories, the longest consisting of 210 points, for quantum dots freely diffusing in a solvent. MSD (black $\times$), fitted by a power law with exponents $\alpha = 0.81$ (red line). We also show a fit with fixed exponent $\alpha = 1$ (green line, expected behavior for Brownian motion). MME (blue $\times$), fitted by a power law (red line, $\alpha = 1.02$). Time is in seconds, distances are in μm^2 . Inset: double-logarithmic plot of the same data.

Power spectral density of a single FBM trajectory



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

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

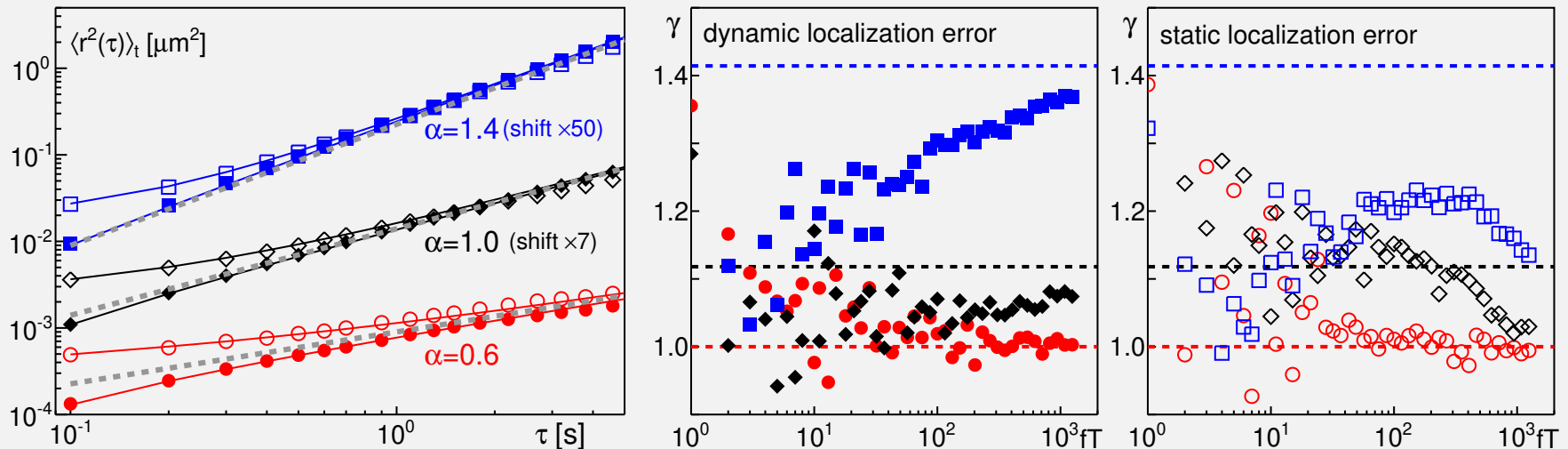
Robust criterion for anomalous diffusion

Two sources of noise: static (finite photon count, additive OU) & dynamic (finite measurement time). Static noise effect on γ :

$$H < 1/2 : \quad \gamma_Y^2(f, T) \sim 1; \quad \sigma_e = 0 : 1$$

$$H = 1/2 : \quad \gamma_Y^2(f, T) \sim 1 + \frac{1}{4} \left(1 + \frac{\sigma_e^2}{2u^2 D} f^2 \right)^{-2}; \quad \sigma_e = 0 : \frac{\sqrt{5}}{2}$$

$$H > 1/2 : \quad \gamma_Y^2(f, T) \sim 1 + \left(1 + \frac{\sigma_e^2}{u^2 D} T^{1-2H} f^2 \right)^{-2}; \quad \sigma_e = 0 : \sqrt{2}$$

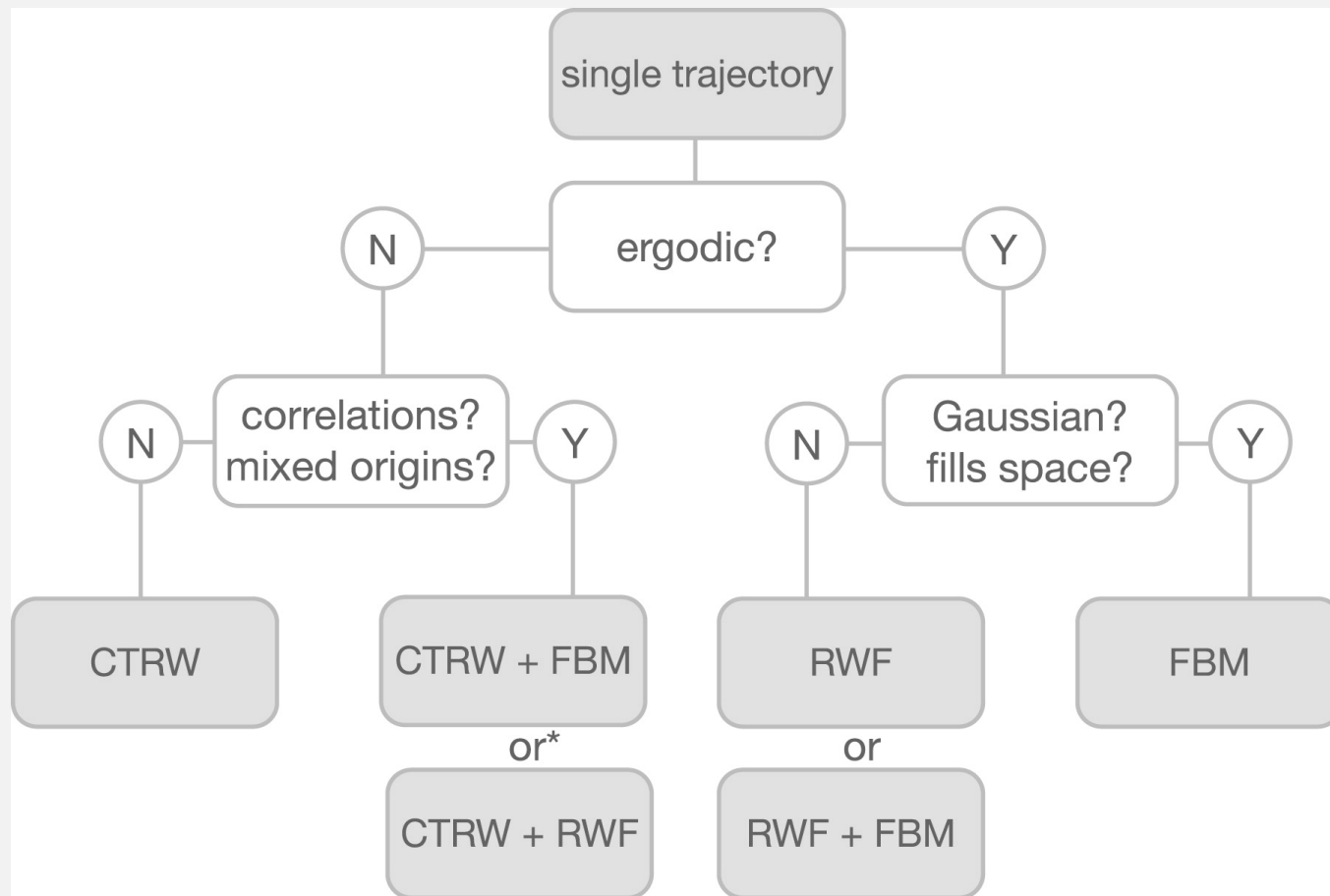


Complementary statistical observables enable decision trees

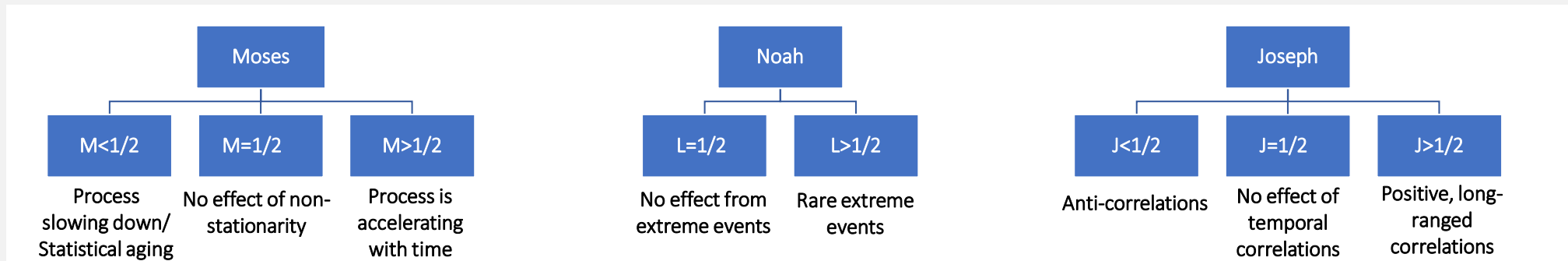
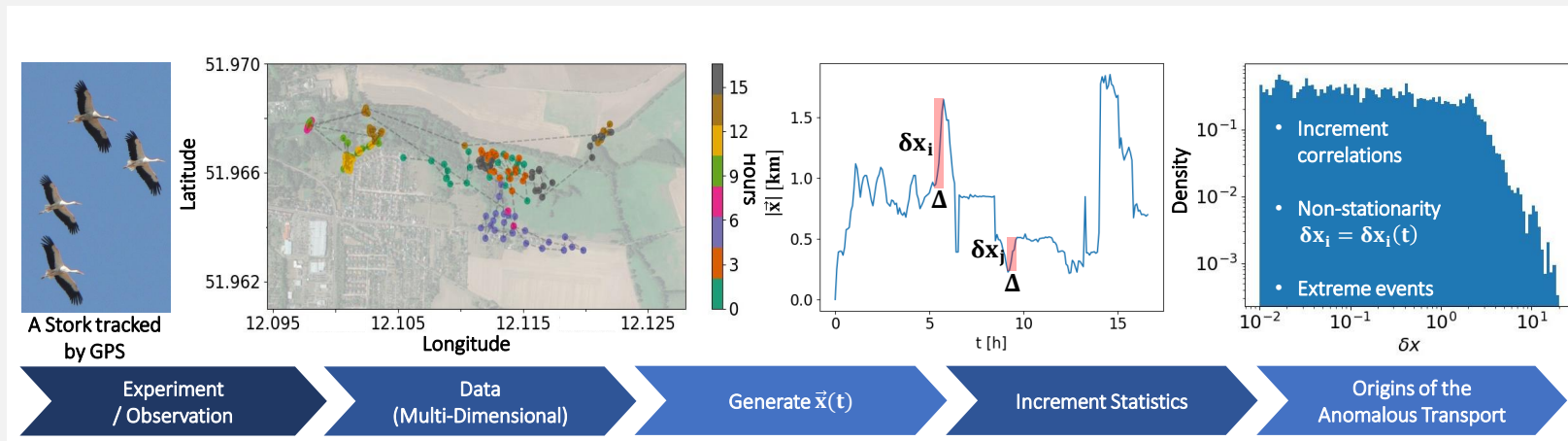
Central limit theorem (law of large numbers): emergence of “universal” Gaussian

Anomalous diffusion: universality broken, different processes effect $\langle \mathbf{r}^2(t) \rangle \simeq K_\alpha t^\alpha$

Physics from data? $\curvearrowright$ First-passage/reactions, parameter extraction . . .



Scaling analysis of anomalous diffusion: molecules $\rightarrow$ animals

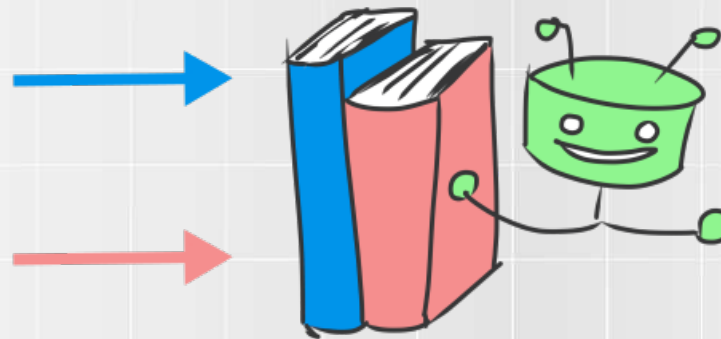


Machine learning approach to classification

Training data

Input (trajectories)

Output (diff. modes)



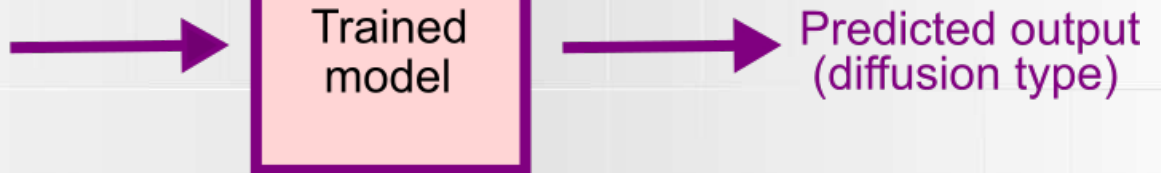
ML algorithm
learns the parameters and
produces a **trained model**
that could **generalize** data

Unseen data

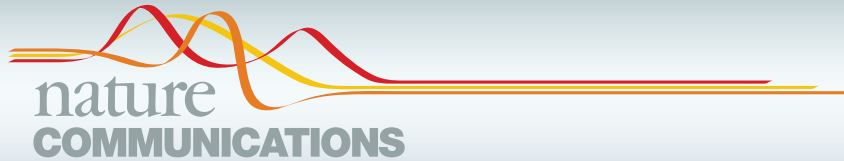
New input
(trajectory)

Trained
model

Predicted output
(diffusion type)



The ANomalous Diffusion challenge



ARTICLE



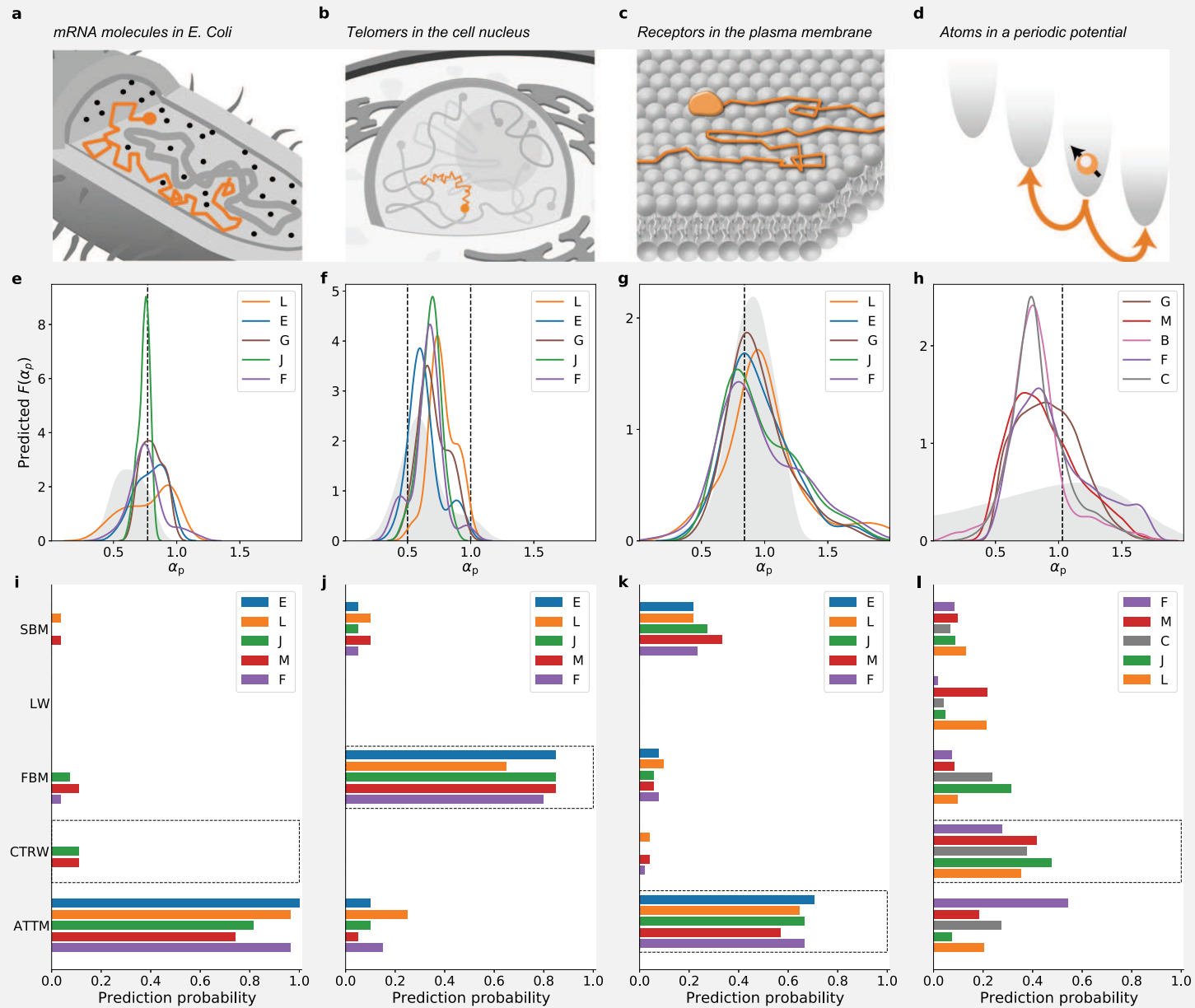
<https://doi.org/10.1038/s41467-021-26320-w>

OPEN

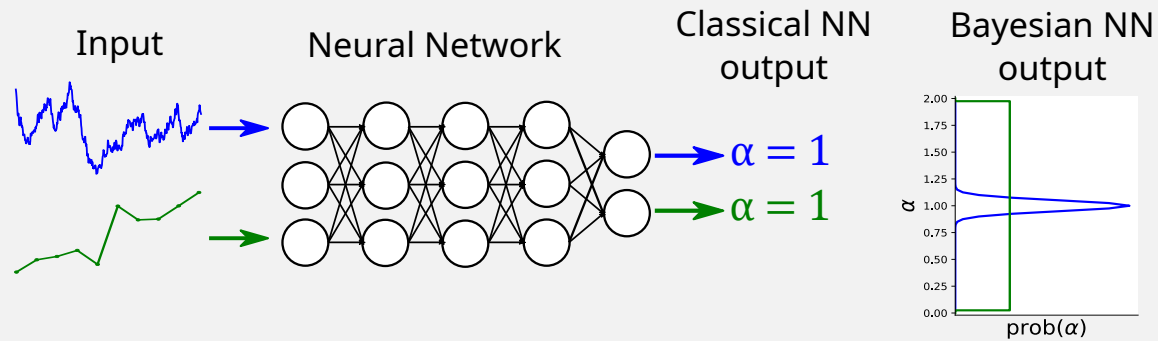
Objective comparison of methods to decode anomalous diffusion

Gorka Muñoz-Gil ¹, Giovanni Volpe ²✉, Miguel Angel Garcia-March³, Erez Aghion⁴, Aykut Argun², Chang Beom Hong⁵, Tom Bland⁶, Stefano Bo ⁴, J. Alberto Conejero³, Nicolás Firbas ³, Òscar Garibo i Orts ³, Alessia Gentili ⁷, Zihan Huang ⁸, Jae-Hyung Jeon ⁵, Hélène Kabbech ⁹, Yeongjin Kim⁵, Patrycja Kowalek ¹⁰, Diego Krapf ¹¹, Hanna Loch-Olszewska ¹⁰, Michael A. Lomholt¹², Jean-Baptiste Masson ¹³, Philipp G. Meyer ⁴, Seongyu Park ⁵, Borja Requena ¹, Ihor Smal⁹, Taegeun Song ^{5,14,15}, Janusz Szwabiński¹⁰, Samudrajit Thapa ^{16,17,18}, Hippolyte Verdier ¹³, Giorgio Volpe ⁷, Artur Widera ¹⁹, Maciej Lewenstein ^{1,20}, Ralf Metzler ¹⁶ & Carlo Manzo ^{1,21}✉

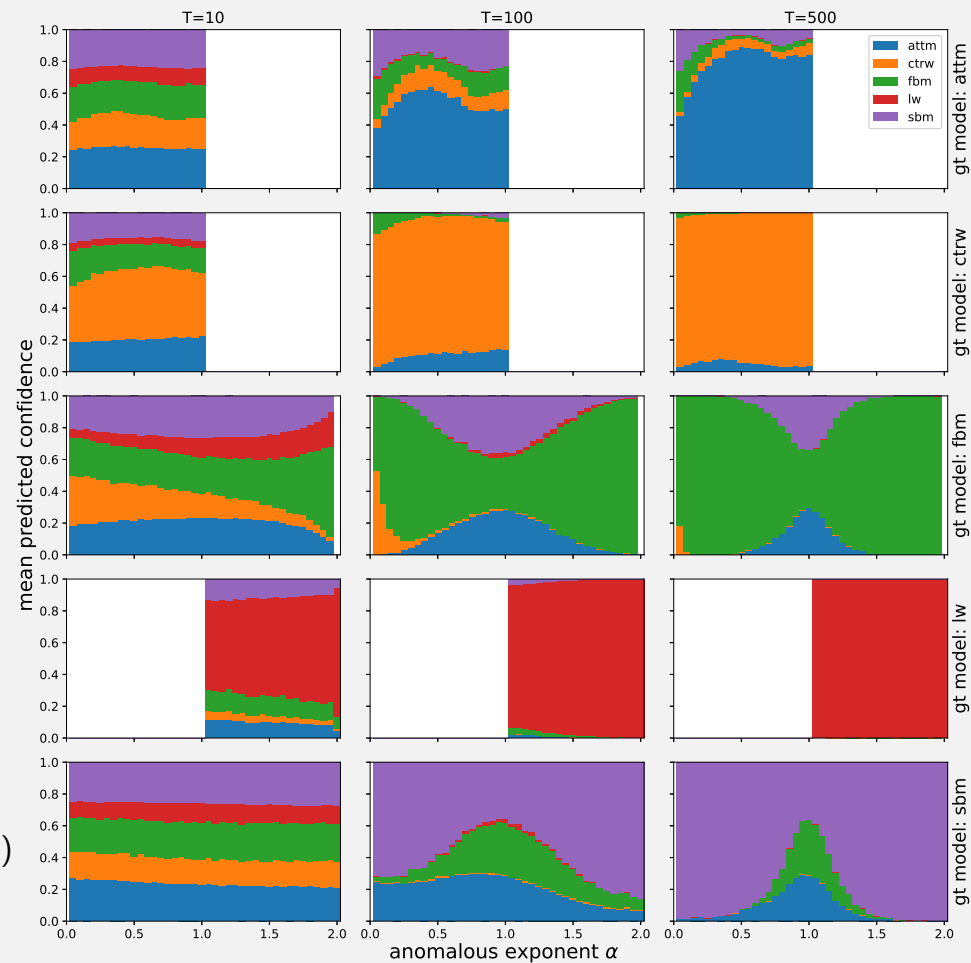
The ANomalous Diffusion challenge



Bayesian-weighted deep learning model selection



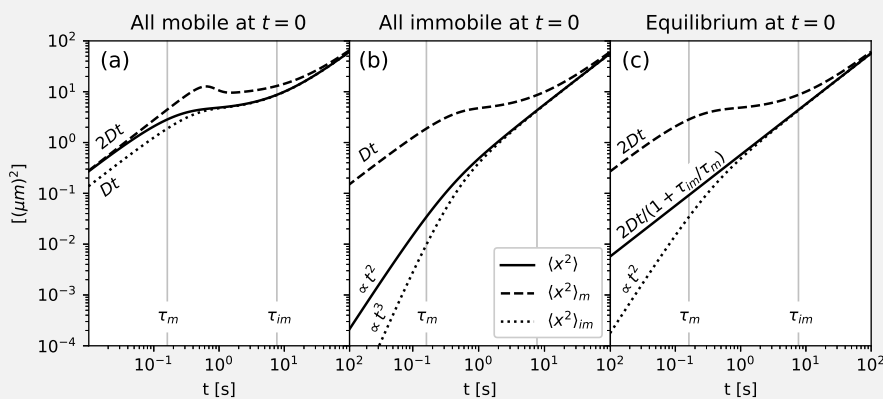
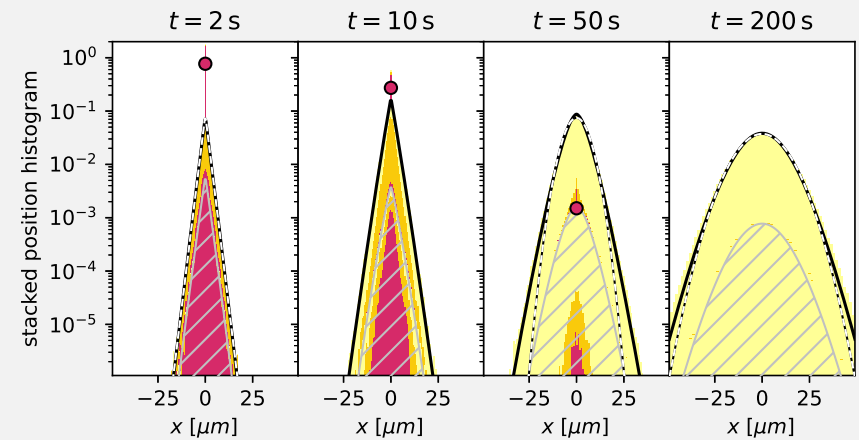
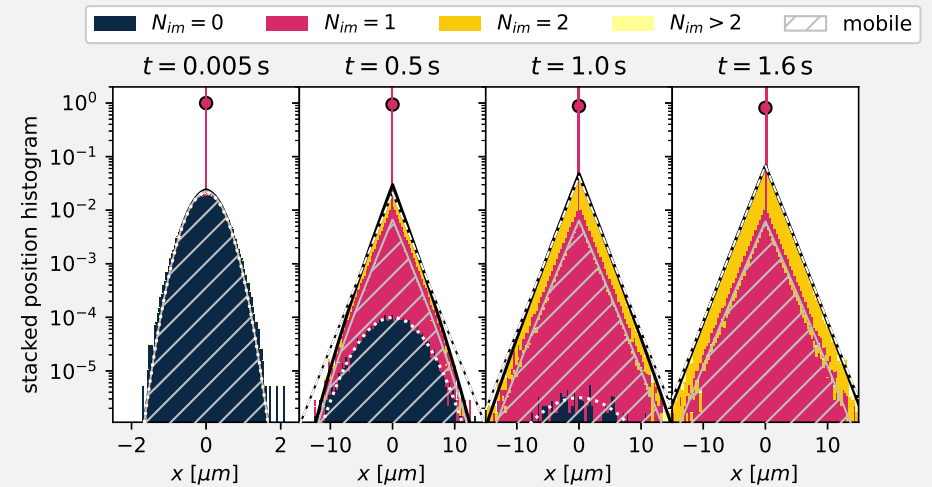
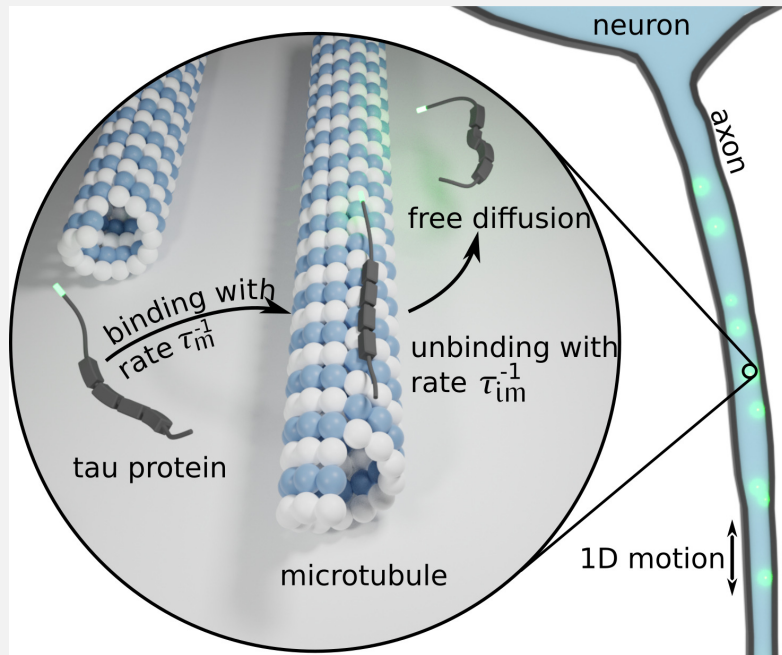
“Beyond the Black Box problem”



H Seckler & RM, Nat Comm (2022)

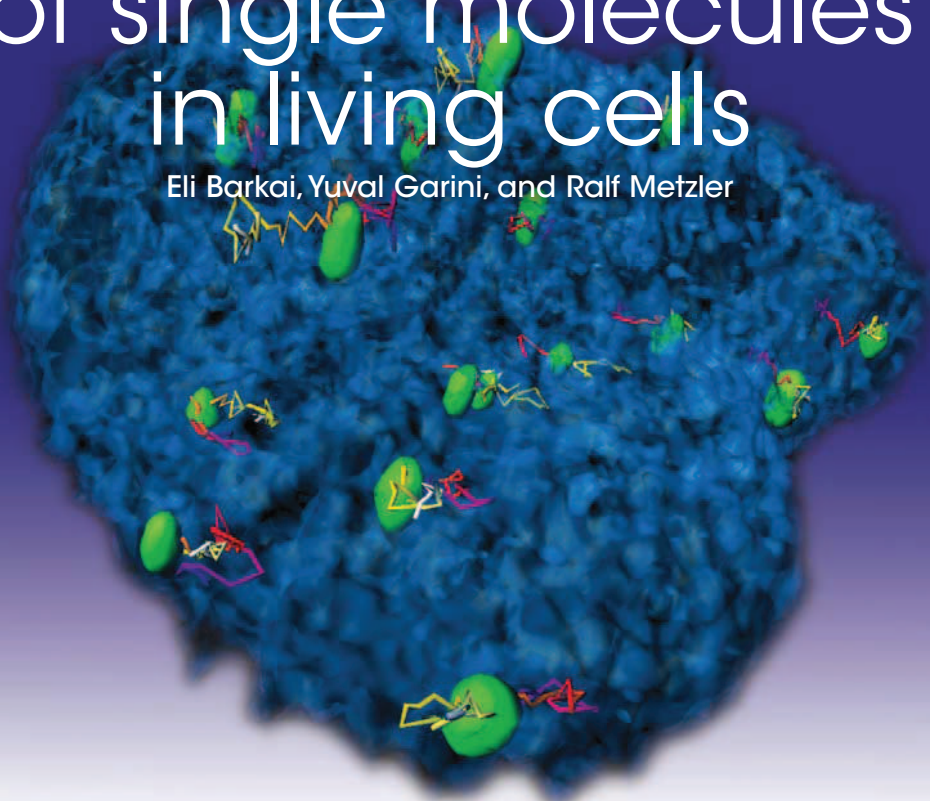
Non-Gaussianity & apparent anomalous diffusion

Mobile-immobile model with fixed exchange rates for $\tau_{im} \gg \tau_{mob}$

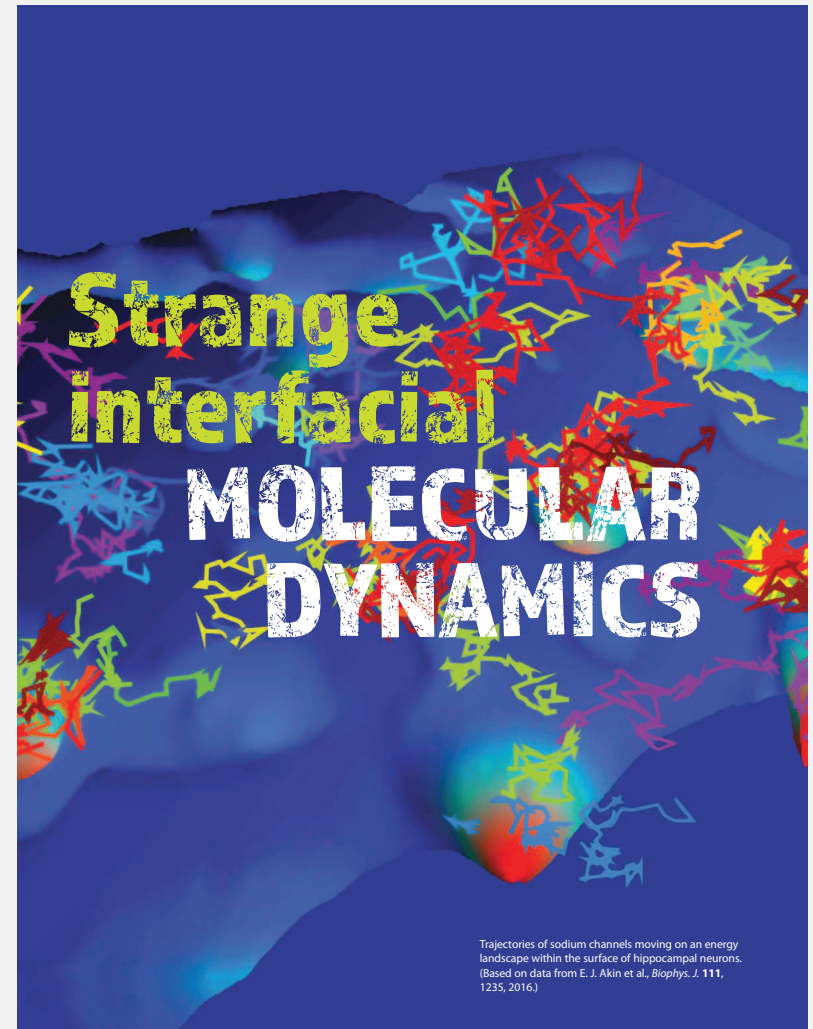


STRANGE KINETICS of single molecules in living cells

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.



Σ ummary

- I Lévy flights & superdiffusive FBM exhibit non-Boltzmannian, multimodal PDFs in superharmonic confining external potentials
- II Lévy flights & superdiffusive FBM have critical potential scaling exponent above which stationary states exist: $c = 2 - 1/H$ ($H = \alpha/2$ for FBM, $H = 1/\mu$ for LFs)
- III FBM next to hard walls or steep potentials shows accretion/depletion for superdiffusive/subdiffusive dynamics
- IIII Lévy walks have multimodal PDFs in harmonic potentials
- IIII Objective data analysis methods aid in identification of models & parameters: Bayesian-maximum likelihood, deep learning, & their combinations. Measurement error! AnDi challenge special issue of JPA & AnDi 2!

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

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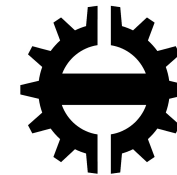
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