IV. Self-similar protein dynamics

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Fluorescence correlation spectroscopy

Protein Conformational Dynamics Probed by Single-Molecule Electron Transfer

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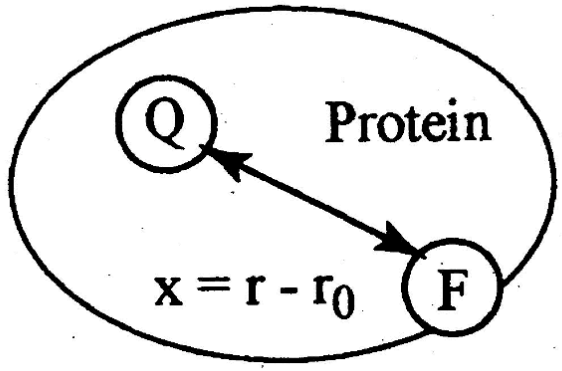
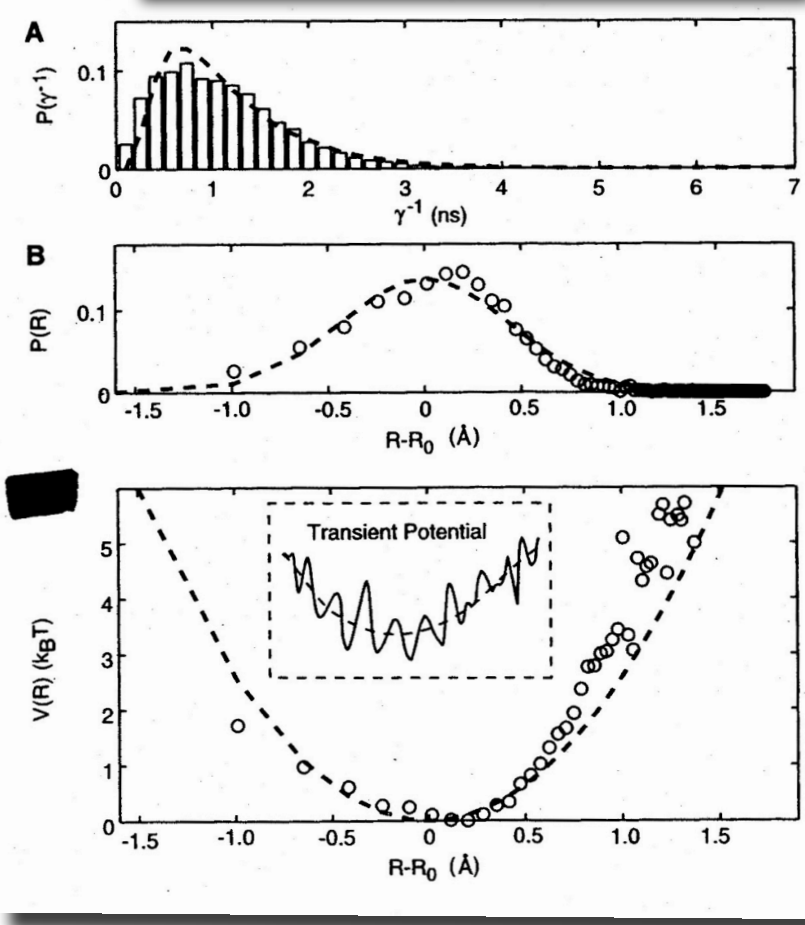
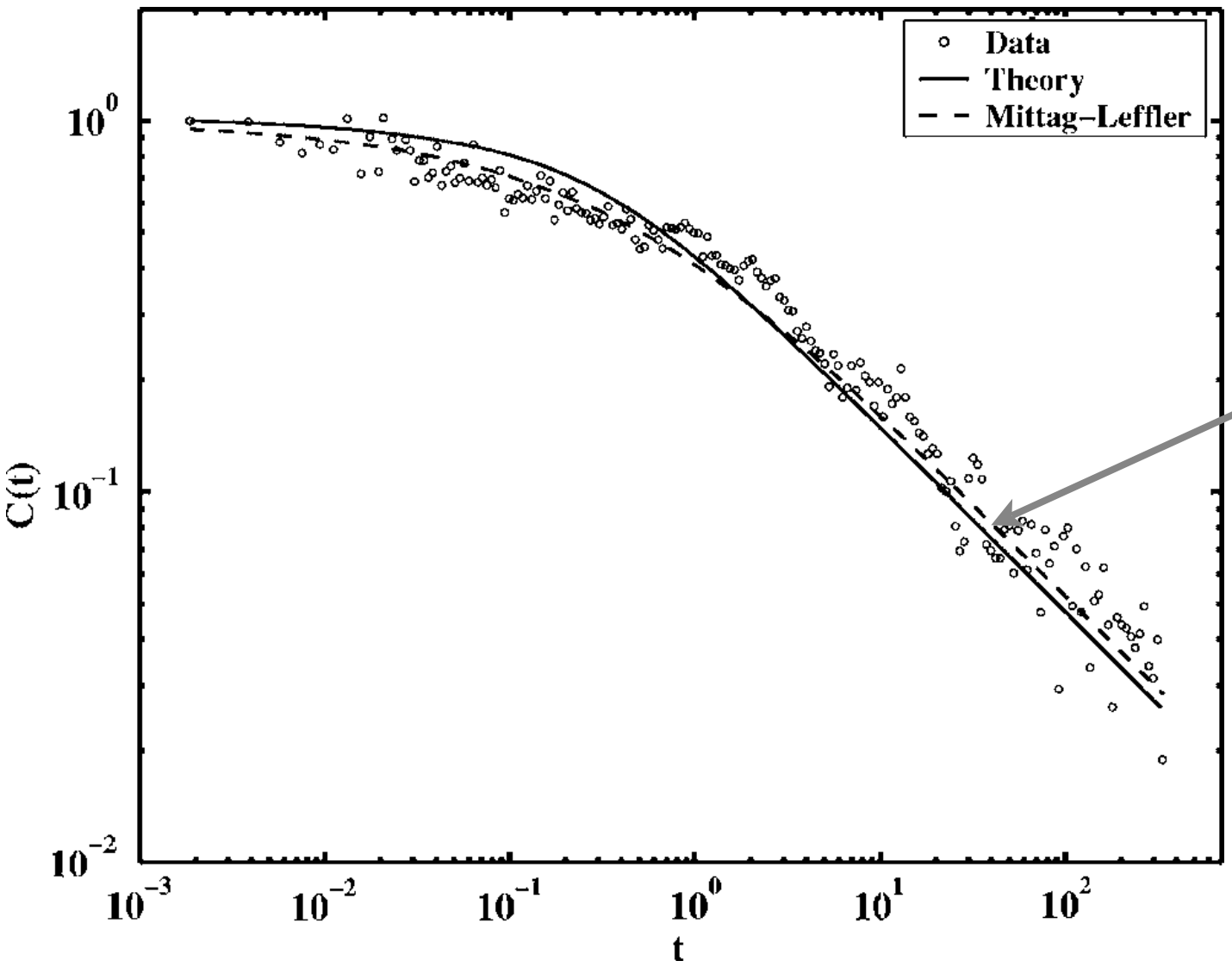
Electron transfer is used as a probe for angstrom-scale structural changes in single protein molecules. In a flavin reductase, the fluorescence of flavin is quenched by a nearby tyrosine residue by means of photo-induced electron transfer. By probing the fluorescence lifetime of the single flavin on a photon-by-photon basis, we were able to observe the variation of flavin-tyrosine distance over time. We could then determine the potential of mean force between the flavin and the tyrosine, and a correlation analysis revealed conformational fluctuation at multiple time scales spanning from hundreds of microseconds to seconds. This phenomenon suggests the existence of multiple interconverting conformers related to the fluctuating catalytic reactivity.

10 OCTOBER 2003 VOL 302 SCIENCE www.sciencemag.org





Distance autocorrelation function

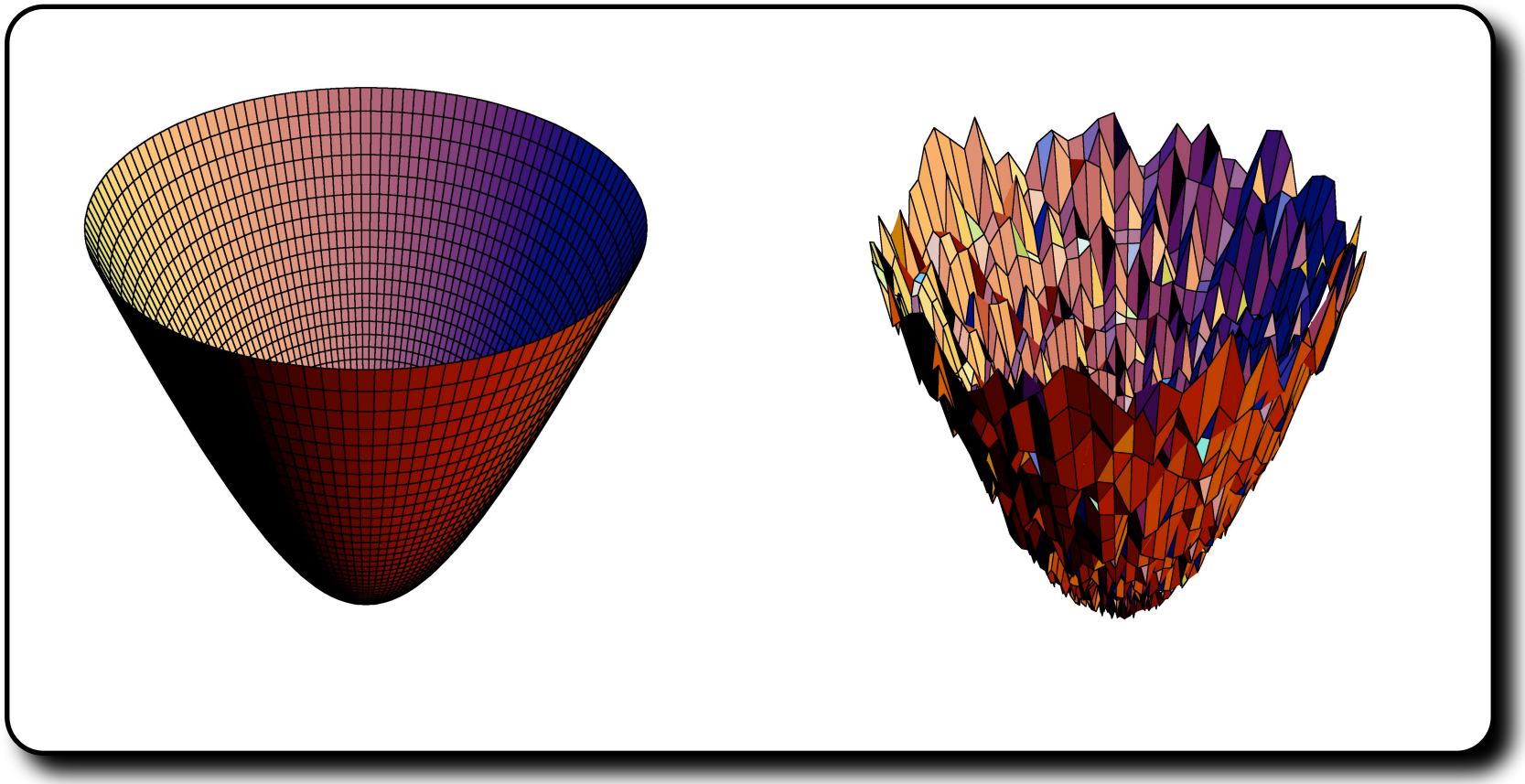


Non-exponential decay ("power law")

P. Debnath, M. Wei, S. Xie, and B.J. Cherayil. *J. Chem. Phys.*, 123:204903, 2005.

Diffusion in a harmonic potential : Ornstein-Uhlenbeck process [1]

Diffusion in a "rugged" harmonic potential Fractional O.U. process [2]



[1] M.C. Wang and G.E. Uhlenbeck. On the theory of Brownian motion II. Phys. Rev., 93(1):249–262, 1945.

[2] R. Metzler and J. Klafter. The random walk's guide to anomalous diffusion: A fractional dynamics approach. *Phys. Rep.*, 339:1–77, 2000.

Fractional Fokker-Planck equation

$$0 < \alpha \leq 1$$

$$\frac{\partial P(x,t)}{\partial t} = \tilde{\tau}^{1-\alpha}\, {}_0\mathcal{D}_t^{1-\alpha} \mathcal{L}_{FP} P(x,t)$$

Fractional Fokker-Planck equation

$${}_0\mathscr{D}_t^{1-\alpha} f(t) = \frac{\mathrm{d}}{\mathrm{d}t} \int_0^t \mathrm{d}\tau \frac{(t-\tau)^{\alpha-1}}{\Gamma(\alpha)} f(\tau)$$

fractional derivative

$$\mathscr{L}_{\mathrm{FP}} = \eta \frac{\partial}{\partial x} x + D \frac{\partial^2}{\partial x^2}$$

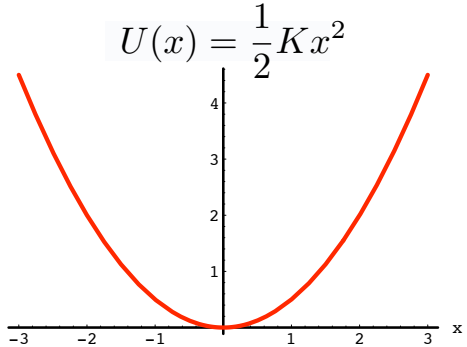
$$\frac{D}{\eta} = \frac{k_B T}{K} = \langle x^2 \rangle$$

[1] R. Metzler and J. Klafter. The random walk's guide to anomalous diffusion: A fractional dynamics approach. *Phys. Rep.*, 339:1–77, 2000.

Smoluchowski picture of fractional Brownian motion

"normal diffusion"

$$\frac{\partial P(x,t)}{\partial t} + \frac{\partial J(x,t)}{\partial x} = 0$$



$$F(x) = -\frac{\partial U}{\partial x}$$

$$J(x,t) = -D\frac{P(x,t)}{\partial x} + \frac{D}{k_B T}F(x)P(x,t)$$

"anomalous diffusion"

$$\frac{\partial P(x,t)}{\partial t} + \frac{\partial \tilde{J}(x,t)}{\partial x} = 0$$

fractional derivative of order 1-α

$$\tilde{J}(x,t) = \frac{d}{dt}\int_0^t d\tau \, \frac{(t-\tau)^{\alpha-1}}{\Gamma(\alpha)} J(x,\tau)$$

memory effects

Solution of FFPEs in terms of eigenfunctions

$$\frac{\partial P(y,t)}{\partial t} = \tilde{\tau}^{1-\alpha}\,{}_0\mathcal{D}_t^{1-\alpha}\mathcal{L}_{FP}P(y,t), \qquad 0 < \alpha \leq 1$$

$$P(t,y) - P(y,0) = \tilde{\tau}^{1-\alpha}\int_0^t d\tau \frac{(t-\tau)^{\alpha-1}}{\Gamma(\alpha)}\mathcal{L}_{FP}P(y,\tau)$$

Laplace transform

$$\hat{P}(s,y) - \frac{P(y,0)}{s} = \tilde{\tau}^{1-\alpha}s^{-\alpha}\mathcal{L}_{FP}P(y,\tau)$$

$$\hat{P}(y,s) = \frac{1}{s - [s\tilde{\tau}]^{1-\alpha}\mathcal{L}_{FP}}\delta(y-y_0)$$

$$\hat{P}(y,s) = \frac{1}{s - [s\tilde{\tau}]^{1-\alpha}\mathcal{L}_{FP}}\,\delta(y-y_0)$$

$$\begin{aligned}\mathcal{L}_{FP}P_n(y) &= -\lambda_n P_n(y)\\ \mathcal{L}^{+}_{FP}Q_n(y) &= -\lambda_n Q_n(y)\end{aligned}$$

$$\delta(y-y_0) = \sum_n P_n(y)Q_n(y_0)$$

$$\hat{P}(y,s) = \sum_n \frac{1}{s + (s\tilde{\tau})^{1-\alpha}\lambda_n} P_n(y)Q_n(y_0)$$

$$E_\alpha\left(-t^\alpha\right) = \frac{1}{2\pi i}\oint_C ds\,\frac{\exp(st)}{s(1+s^{-\alpha})}$$

$$\boxed{E_\alpha(z) = \sum_{k=0}^{\infty}\frac{z^k}{\Gamma(1+\alpha k)}}$$

$$\boxed{P(y,t) = \sum_n P_n(y)Q_n(y_0)E_\alpha\left(-\lambda_{\alpha,n}t^\alpha\right)}$$

$$\boxed{\lambda_{\alpha,n} := \tilde{\tau}^{1-\alpha}\lambda_n}$$

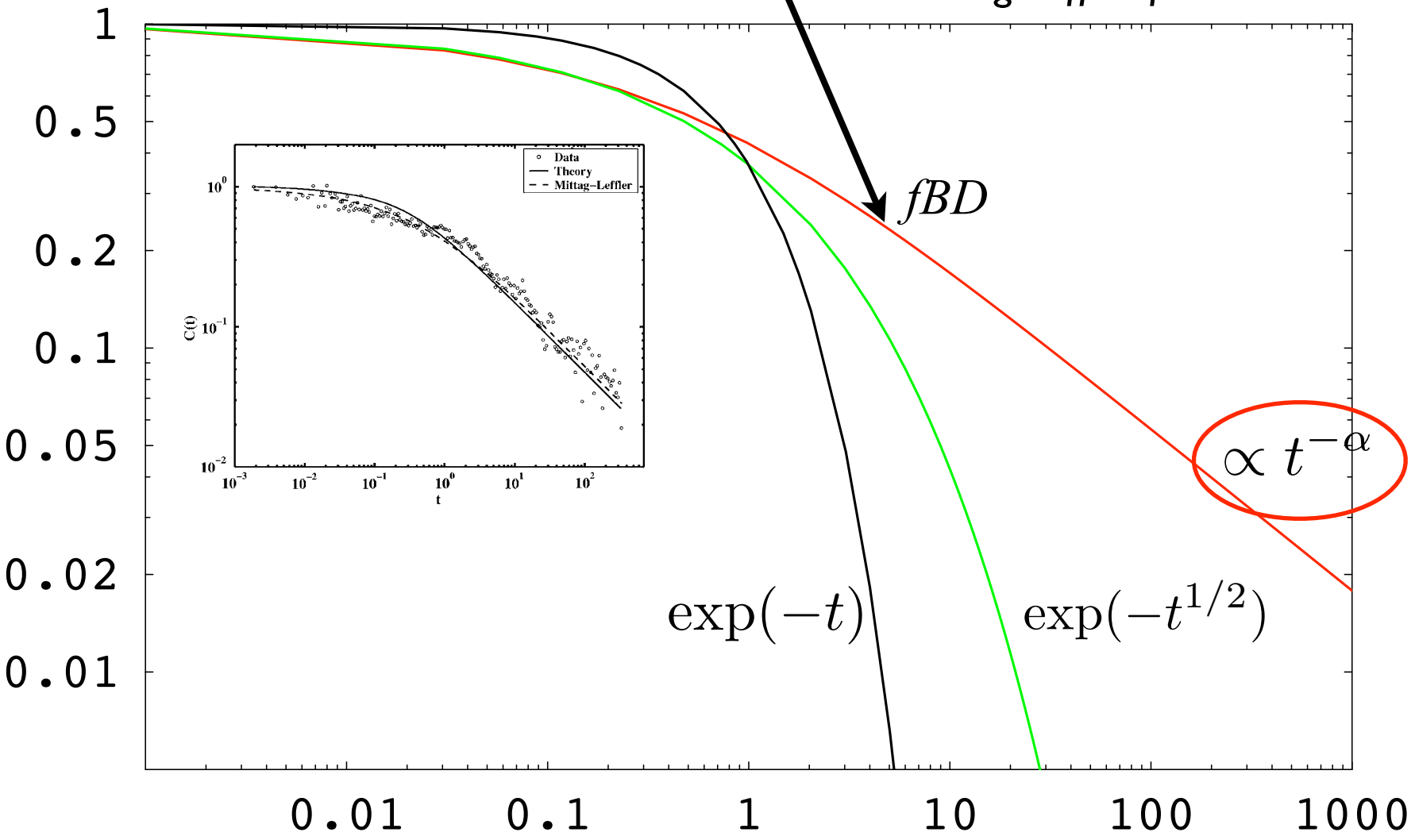
The exponential functions, $\exp(-\lambda_n t)$, are replaced by by Mittag-Leffler functions, $E_\alpha(-\lambda_{\alpha,n}t)$.

Model autocorrelation function (α=0.5)

$$\psi(t) = \frac{\langle x(t)x(0)\rangle}{\langle x^2\rangle} = E_\alpha(-[t/\tau_\alpha]^\alpha)$$

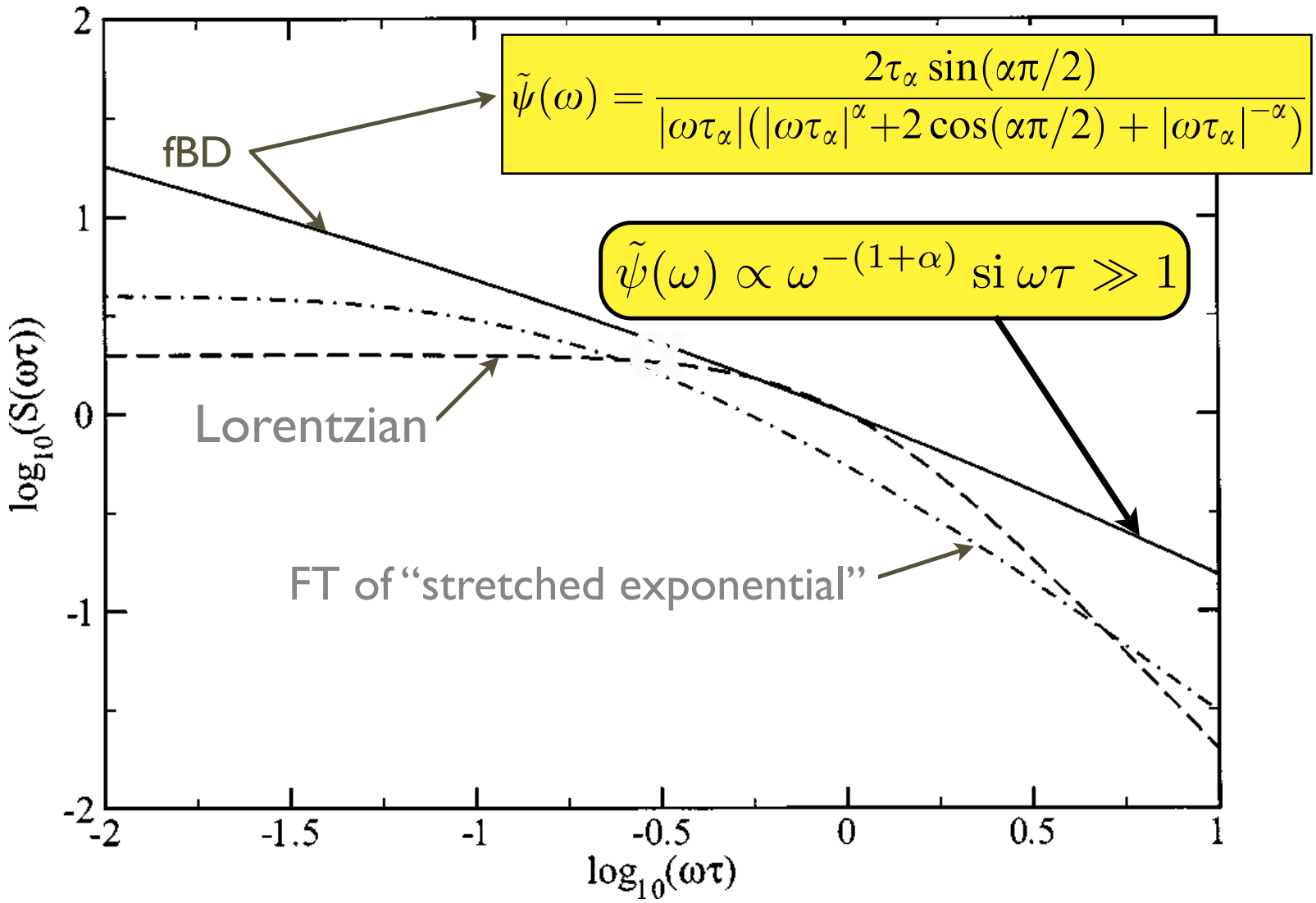
$$E_\alpha(z) = \sum_{k=0}^{\infty} \frac{z^k}{\Gamma(1+\alpha k)}.$$

Mittag-Leffler function



Fourier transform (α=0.5)

G.R. Kneller & K. Hinsen. *J. Chem. Phys.*, 121(20):10278–10283, 2004.



Memory function

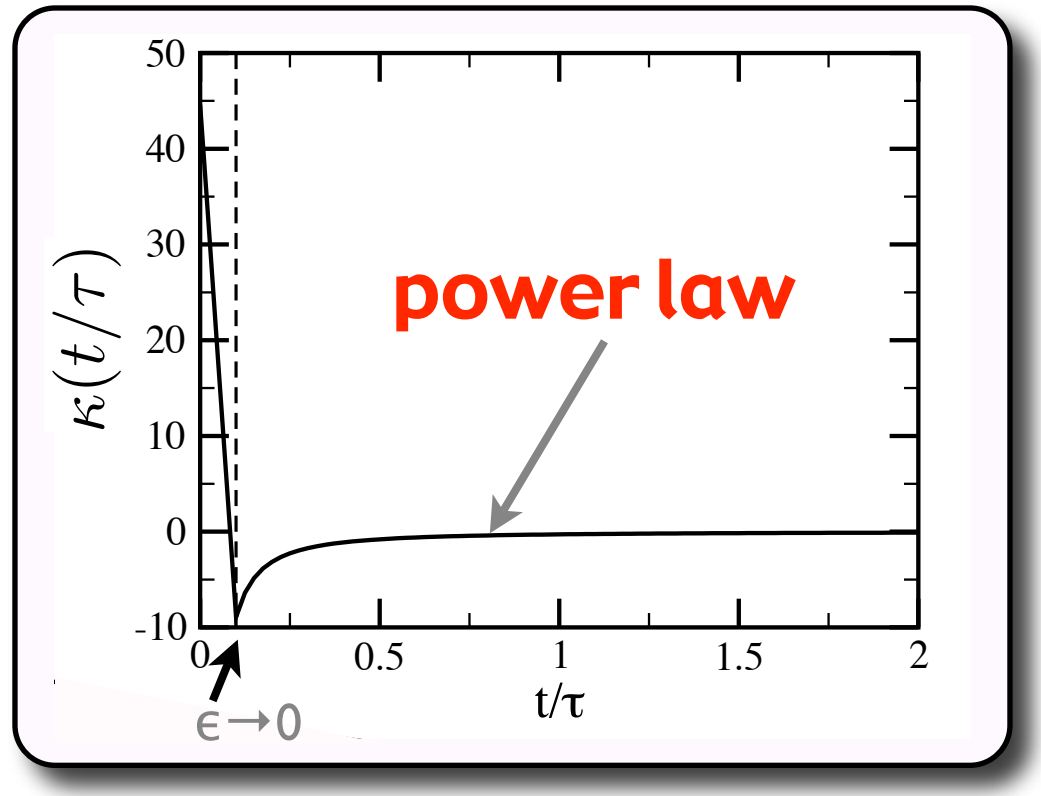
G.R. Kneller & K. Hinsen. *J. Chem. Phys.*, 121(20):10278–10283, 2004.

$$\hat{\psi}(s) = \frac{1}{s(1 + [s\tau_\alpha]^{-\alpha})}$$

$$\hat{\kappa}(s) = s(s\tau_\alpha)^{-\alpha}, \quad 0 < \alpha \leq 1$$

$$\kappa(t) = \frac{\alpha - 1}{\tau_\alpha^2 \Gamma(\alpha)} \left(\frac{t}{\tau_\alpha}\right)^{\alpha-2} \quad (t > 0)$$

$$\hat{\kappa}(0) = 0 \quad \Rightarrow \quad \int_0^\infty dt\, \kappa(t) = 0$$

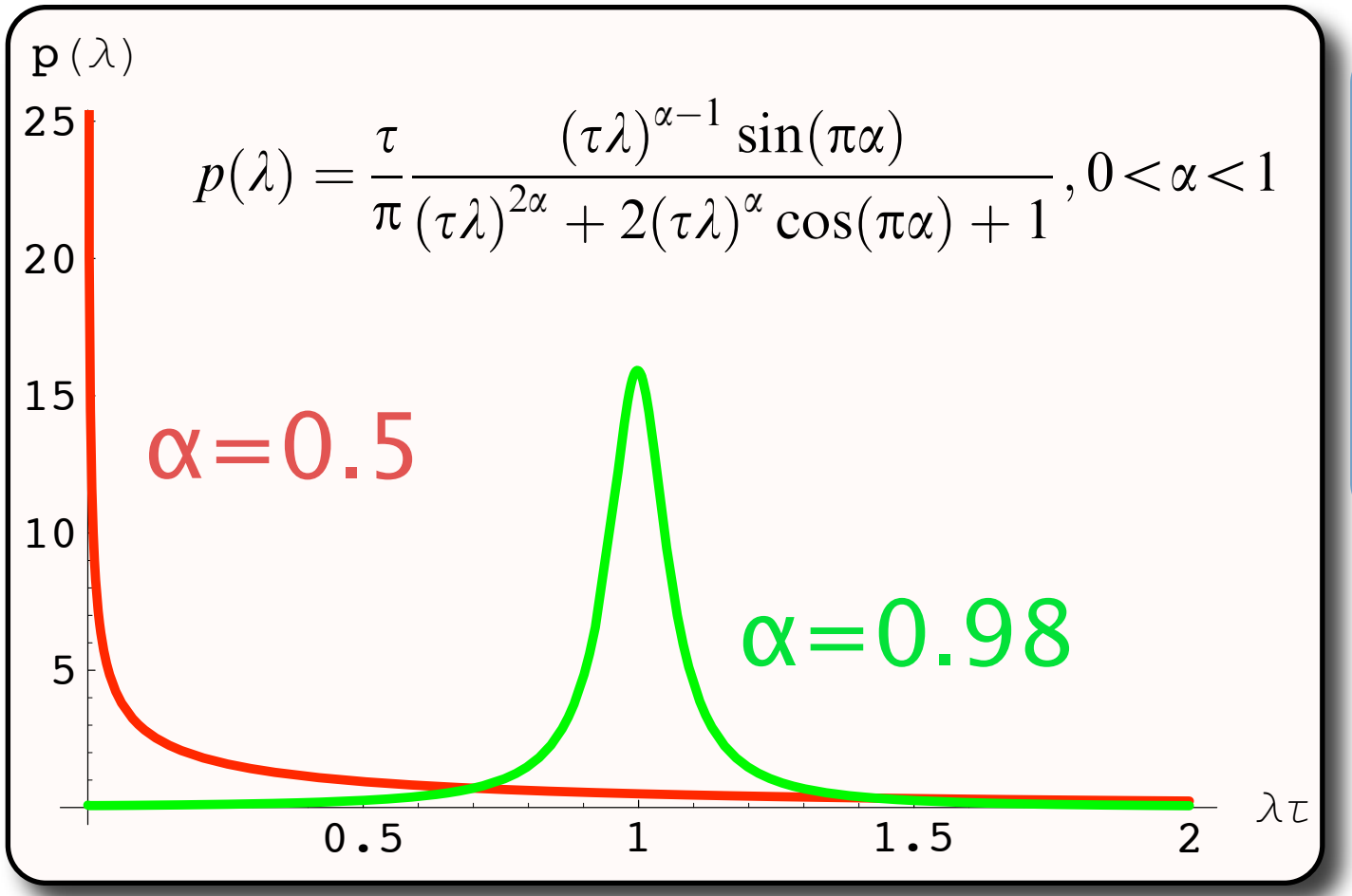


Relaxation rate spectrum

$$\psi(t) = \int_0^\infty d\lambda\, p(\lambda) \exp(-\lambda t)$$

[1] G.R. Kneller. *PCCP*, 7:2641 – 2655, 2005.

[2] V. Calandrini, D. Abergel, and G.R. Kneller. *J .Chem. Phys.*, 128(14): 145102, 2008.



$\lambda\tau = 1$ defines the median of the distribution

$$\int_0^{1/\tau} d\lambda\, p(\lambda) = 1/2$$

"Scaling" of the memory function

$$\psi_\lambda(t) = \frac{1}{2\pi i}\oint_C ds\,\frac{\exp(st)}{s+\lambda\hat{\kappa}(s)},$$

$$\overset{s\to s/\lambda}{=} \frac{1}{2\pi i}\oint_{C'} ds\,\frac{\exp(s\lambda t)}{s+\hat{\kappa}(\lambda s)} = \frac{1}{2\pi i}\oint_{C'} ds\,\frac{\exp(s\lambda t)}{s+\lambda^{1-\alpha}\hat{\kappa}(s)}.$$

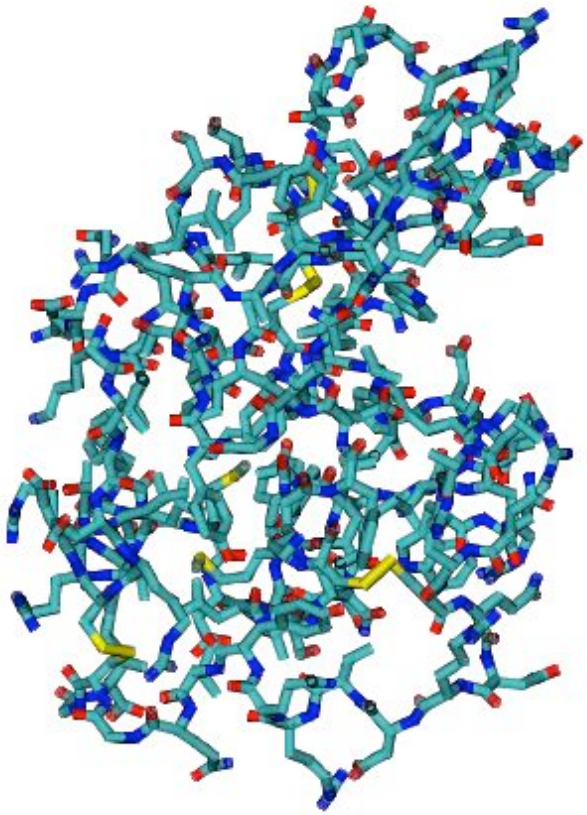
Fractional Brownian dynamics : $\hat{\kappa}(\lambda s) = \lambda^{1-\alpha}\hat{\kappa}(s)$

For *n* iterations :

$$\psi_\lambda(t) = \frac{1}{2\pi i}\oint_{C'} ds\,\frac{\exp\left(st\lambda^{\sum_{j=0}^{n-1}(1-\alpha)^j}\right)}{s+\hat{\kappa}(s\lambda^{(1-\alpha)^{n-1}})} \overset{n\to\infty}{\longrightarrow} = \psi(\lambda^{1/\alpha}t)$$

$\psi(t)$ does not change its form !

MD simulations



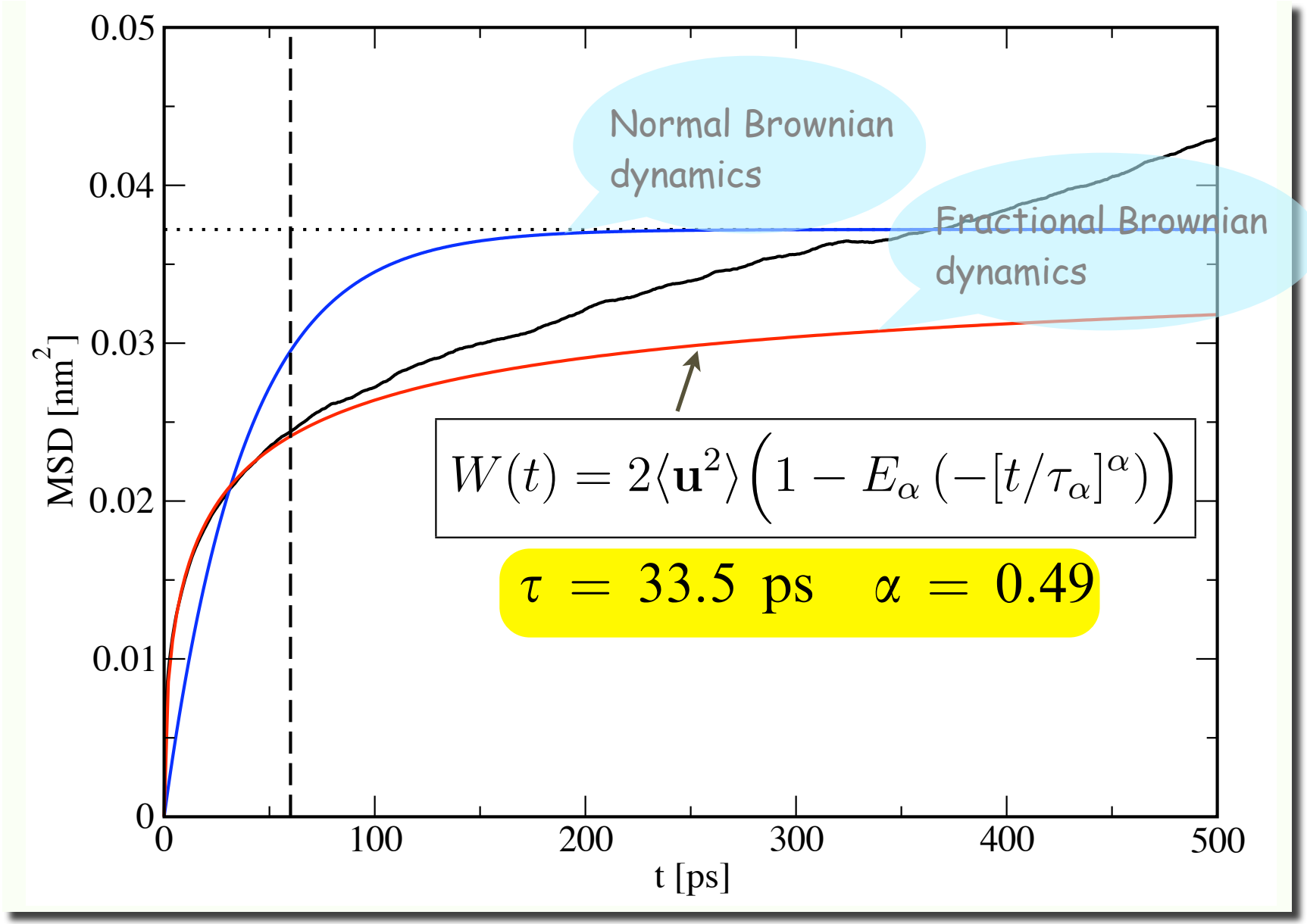
Lysozyme

$$
\begin{aligned}
U &= \sum_{\text{lisaisons } \alpha\beta} k_{\alpha\beta}\left(r_{\alpha\beta} - r_{\alpha\beta}^{(0)}\right)^2 \\
&+ \sum_{\text{angles } \alpha\beta\gamma} k_{\alpha\beta\gamma}\left(\phi_{\alpha\beta\gamma} - \phi_{\alpha\beta\gamma}^{(0)}\right)^2 \\
&+ \sum_{\text{dièdres } \alpha\beta\gamma\delta} k_{\alpha\beta\gamma\delta}\cos\left(n_{\alpha\beta\gamma\delta}\theta_{\alpha\beta\gamma\delta} - \delta_{\alpha\beta\gamma\delta}\right) \\
&+ \sum_{\text{paires } \alpha\beta} 4\epsilon_{\alpha\beta}\left(\left[\frac{\sigma_{\alpha\beta}}{r_{\alpha\beta}}\right]^{12} - \left[\frac{\sigma_{\alpha\beta}}{r_{\alpha\beta}}\right]^{6}\right) \\
&+ \sum_{\text{paires } \alpha\beta} \frac{q_\alpha q_\beta}{4\pi\epsilon_0 r_{\alpha\beta}}
\end{aligned}
\Bigg\} \text{ non-liées}
$$

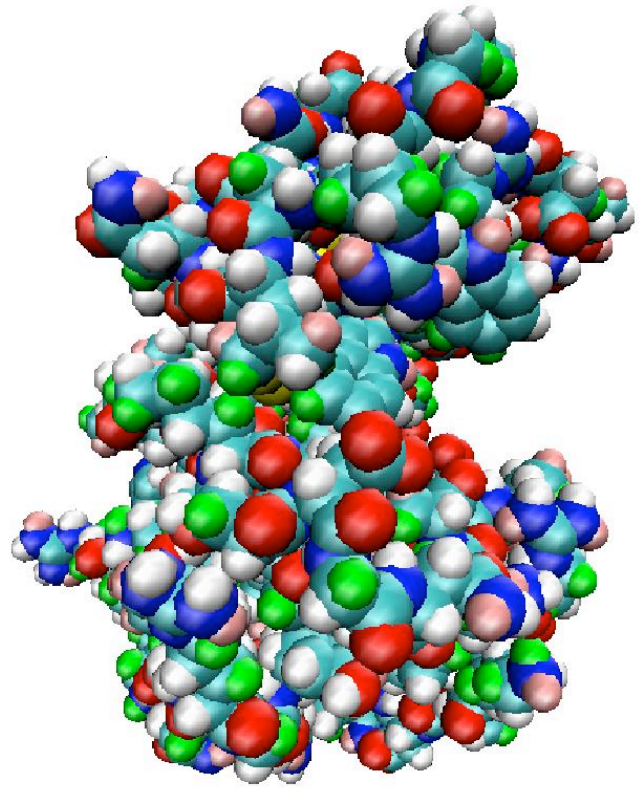
The force field (Amber)

Mean square displacement

G.R. Kneller. *PCCP*, 7:2641 – 2655, 2005.



Collective motions



- Correlation function

$$\psi(\mathbf{q},t) = \langle \delta\rho(\mathbf{q},t)\,\delta\rho(-\mathbf{q},0)\rangle$$

Density fluctuations $\delta\rho(\mathbf{q},t) = \rho(\mathbf{q},t) - \langle\rho(\mathbf{q},t)\rangle$

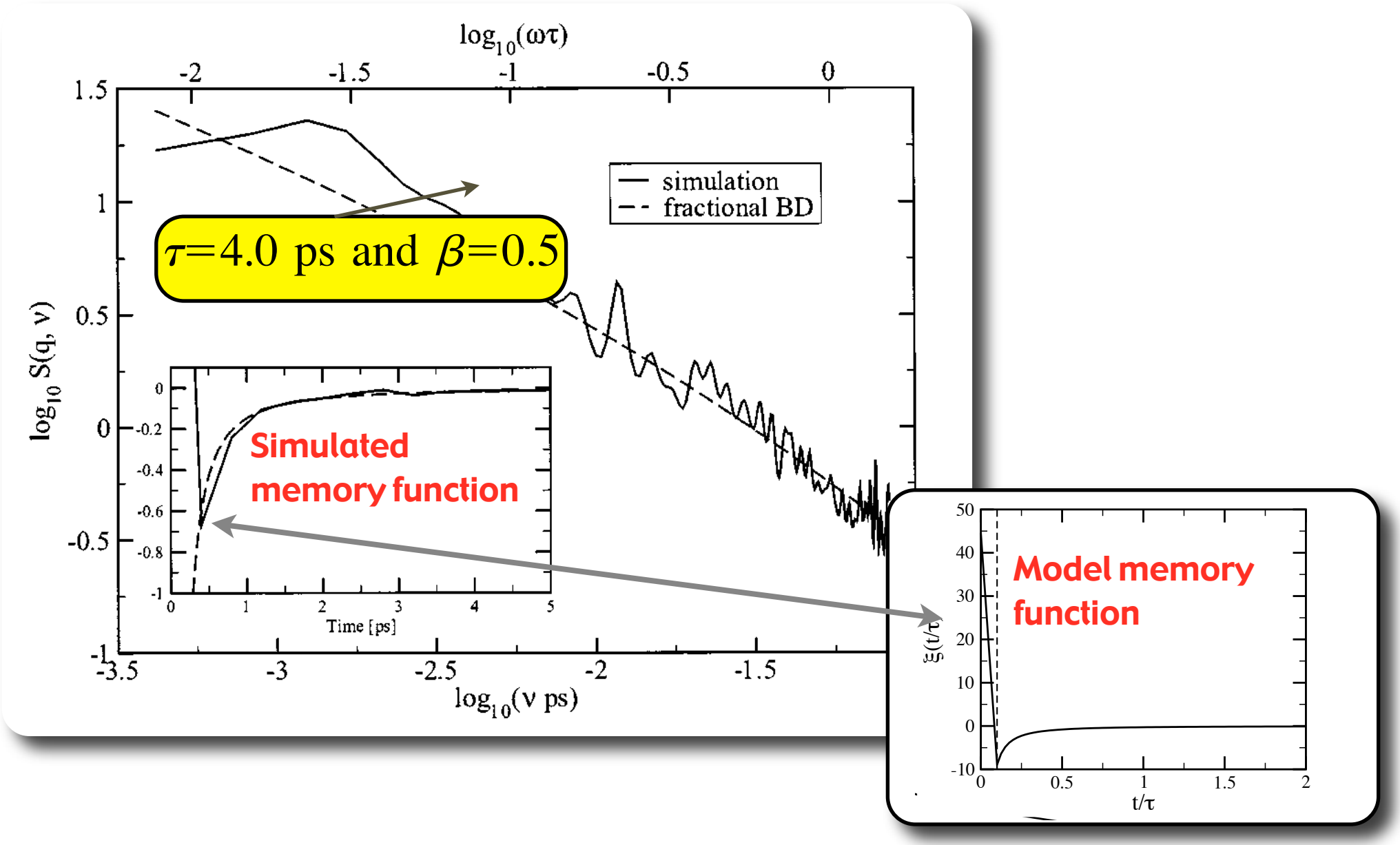
density $\rho(\mathbf{q},t) = \sum_{\alpha} \exp(i\mathbf{q}.\mathbf{R}_{\alpha}(t))$

- Memory function from AR model [1]

$$\frac{d}{dt}\psi(\mathbf{q},t) = -\int_0^t d\tau \xi(\mathbf{q},t-\tau)\,\psi(\mathbf{q},\tau)$$

[1] G. Kneller and K. Hinsen, *J .Chem. Phys.*, **121**(20) 10278–10283, 2004.

Fit of the model



G.R. Kneller & K. Hinsen. *J. Chem. Phys.*, 121(20):10278–10283, 2004.

Quasielastic neutron scattering and fractional Brownian dynamics

G.R. Kneller. *PCCP*, 7:2641 – 2655, 2005.

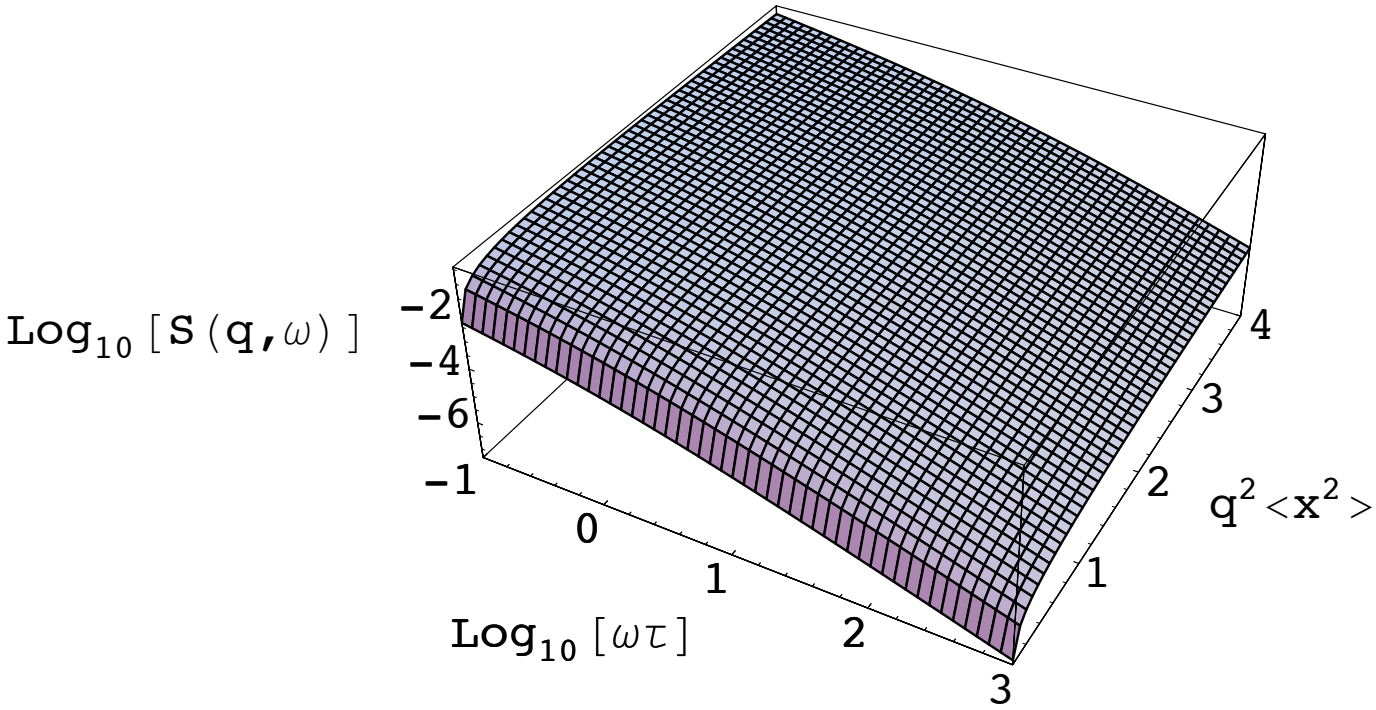
$$
\begin{aligned}
I(q,t) &= \int\int dx_0 dx \, \exp(iq[x-x_0]) P(x,t|x_0,0) P_{eq}(x_0) \\
&= \sum_{n=0}^{\infty} \left| \int dx \, \exp(iqx) P_n(x) \right|^2 E_\alpha\left(-\lambda_{\alpha,n} t^\alpha\right).
\end{aligned}
$$

$$
EISF(q) = \left| \int dx \, \exp(iqx) P_0(x) \right|^2
$$

$$
\boxed{I(q,t) = \exp(-q^2\langle x^2\rangle) \sum_{n=0}^{\infty} \frac{q^{2n}\langle x^2\rangle^n}{n!} E_\alpha\left(-n\eta_\alpha t^\alpha\right)}
$$

$$
\boxed{EISF(q) = \lim_{t\to\infty} I(q,t) = \exp\left(-q^2\langle x^2\rangle\right)}
$$

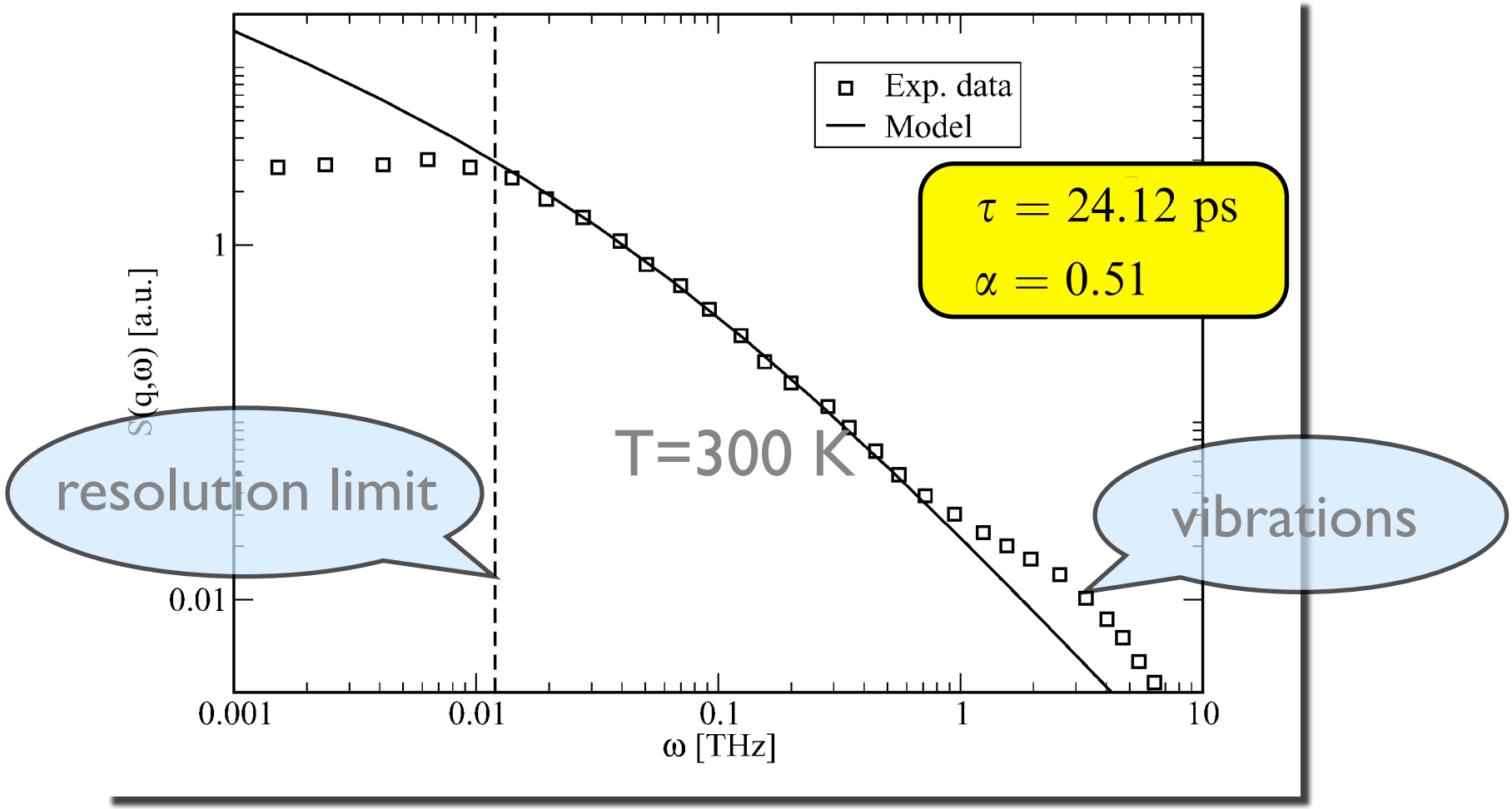
Dynamic structure factor


Log10[S(q,ω)]
-2
-4
-6
-1
0
1
2
3
Log10[ωτ]
4
3
2
1
q² <x²>
$S(q,\omega) = \exp(-q^2\langle x^2\rangle)\left\{\delta(\omega) + \sum_{n=1}^{\infty} \frac{q^{2n}\langle x^2\rangle^n}{n!}\frac{1}{2\pi}L_\alpha(\omega;\tau_{\alpha,n})\right\}$

$L_\alpha(\omega;\tau) = \frac{2\tau\sin(\alpha\pi/2)}{|\omega\tau|\left(|\omega\tau|^\alpha + 2\cos(\alpha\pi/2) + |\omega\tau|^{-\alpha}\right)}, \quad 0 < \alpha \leq 1$

$\tau_{\alpha,n} = \lambda_{\alpha,n}^{-(1/\alpha)}, \quad n \neq 0 \qquad \lambda_{\alpha,n} := \tilde{\tau}^{1-\alpha}\lambda_n \qquad \lambda_n = n\eta$

QENS of myoglobin



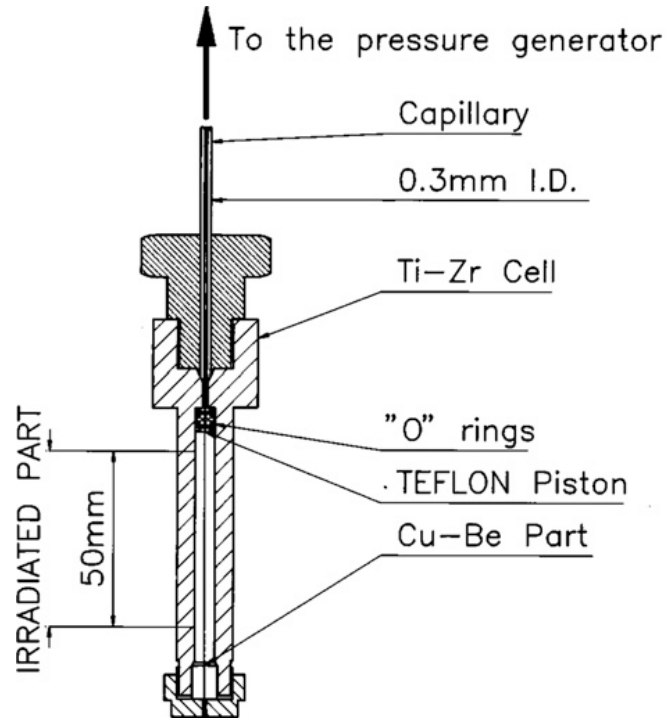
[1] W. Doster, S. Cusack, and W. Petry. *Nature*, 337:754–756, 1989.

[2] G.R. Kneller. Physical Chemistry Chemical Physics, 7:2641 – 2655, 2005.

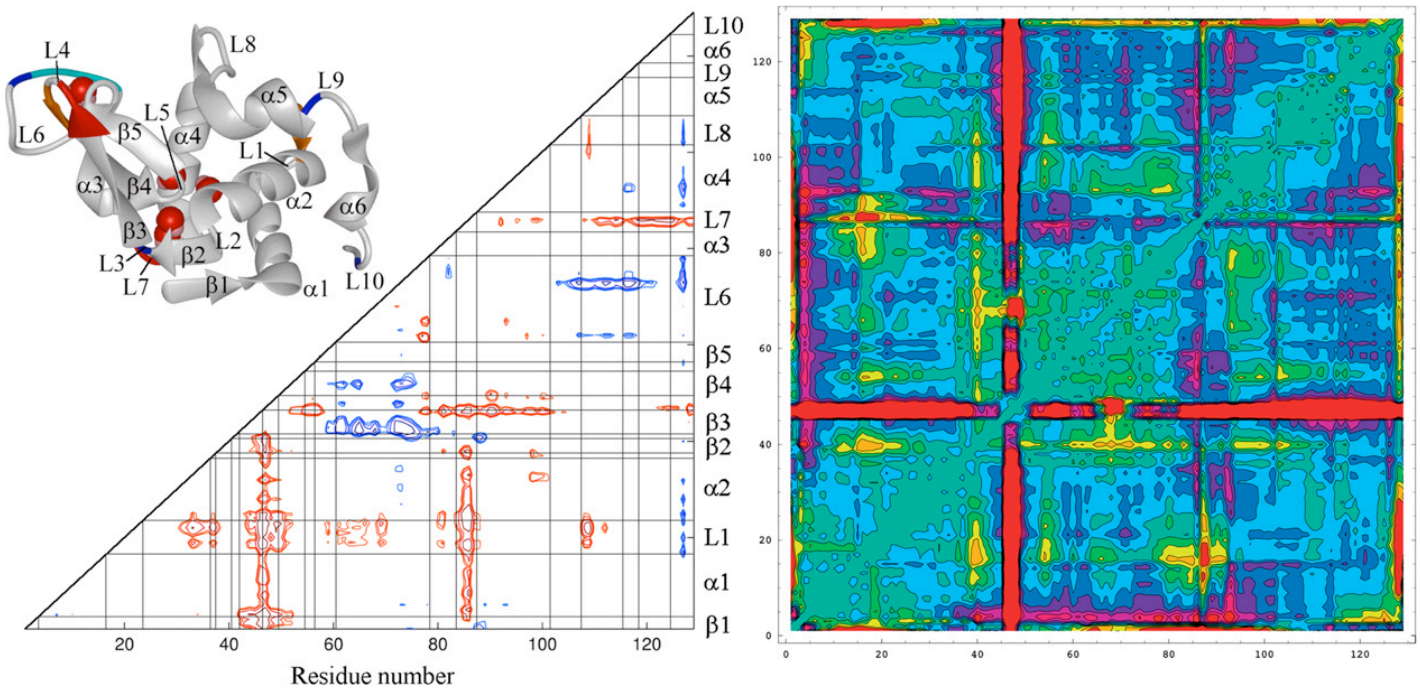
Dynamics of lysozyme under pressure : neutron scattering, NMR, simulation

Quantify the influence of a non-denaturing pressure (< 3kbar) on the internal dynamics of lysozyme

Pressure cell (Ti-Zr, b_{coh} = 0),
M.-C. Bellissent-Funel



Change of volume and structure



NMR[1]

Simulation[2]

Compression:

$$\frac{\Delta V_{exp}}{V_{exp}} = -2\%$$

$$\frac{\Delta V_{MD}}{V_{MD}} = -2.25\%$$

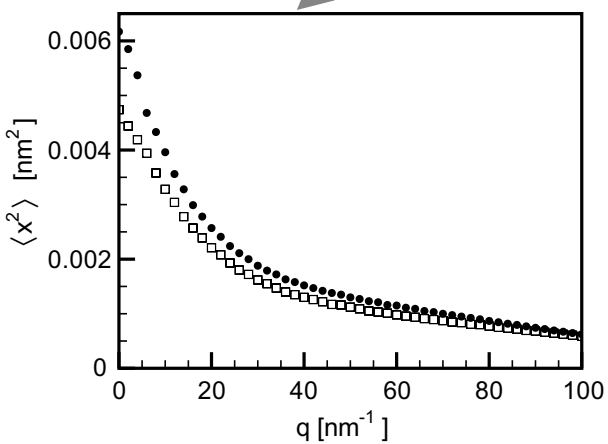
[1] M. Refaee, T. Tezuka, K. Akasaka, and M.P. Williamson. *J. Mol. Biol.*, 327:857–865, 2003.

[2] V. Hamon, P. Calligari, K. Hinsen, and G.R. Kneller. *Journal of Non-Crystalline solids*, 352:4417–4423, 2006.

Data analysis

$$S(q,\omega) = \exp(-q^2\langle x^2\rangle)\left\{\delta(\omega) + \sum_{n=1}^{\infty} \frac{q^{2n}\langle x^2\rangle^n}{n!2\pi} L_{\alpha,\tau_n}(\omega)\right\}$$

Dynamic structure factor



Apparent position fluctuation

$$EISF(q) = \exp(-q^2\langle x^2\rangle(q))$$

$$L_{\alpha,\tau}(\omega) = \frac{2\tau\sin(\alpha\pi/2)}{\omega\tau((\omega\tau)^{\alpha} + 2\cos(\alpha\pi/2) + (\omega\tau)^{-\alpha})}$$

"generalized Lorentzian"

$$\tau_n = \tau n^{-1/\alpha}$$

$$S_{\mathrm{m}}(q,t) = (S * l * r)(\omega)$$

$$l(\omega) = \frac{1}{\pi}\frac{Dq^2}{(Dq^2)^2 + \omega^2}$$

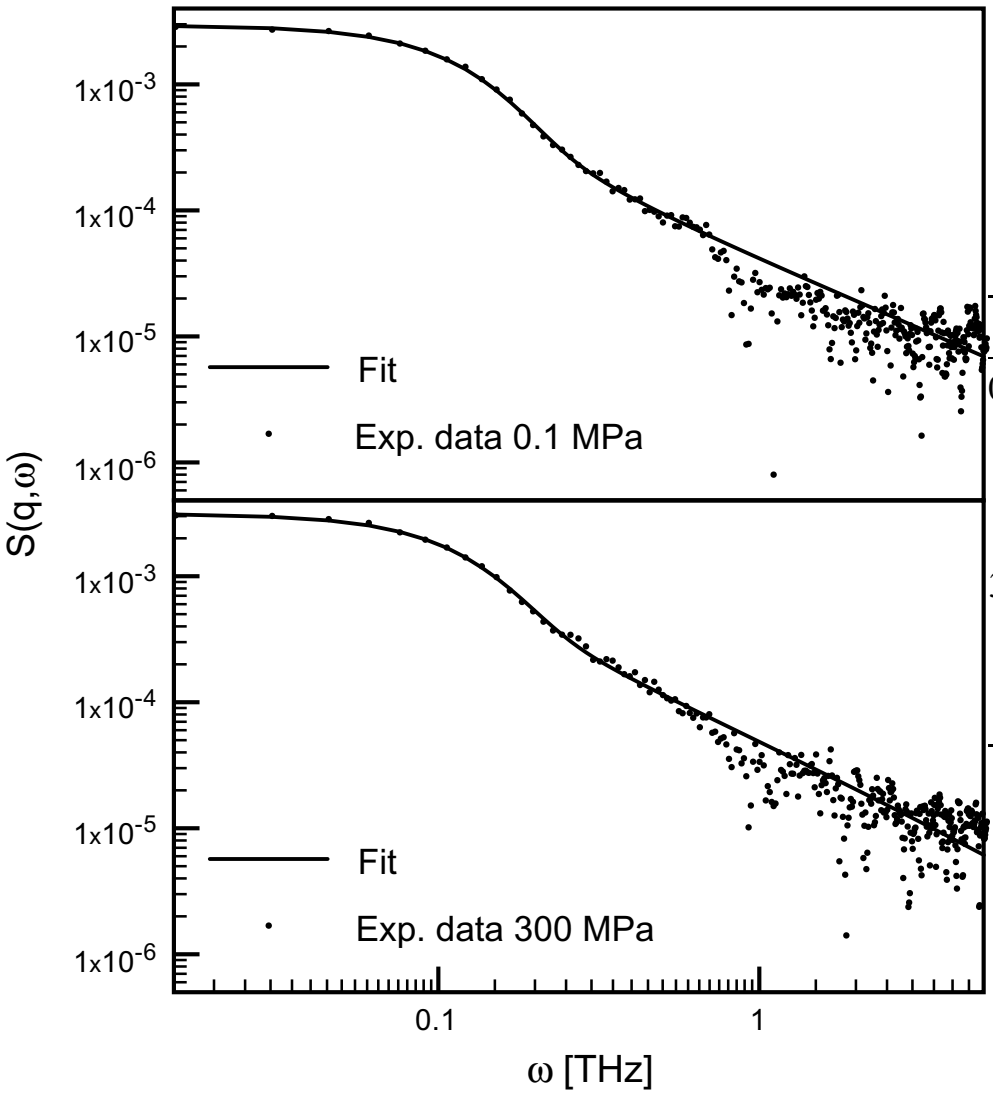
Translational diffusion

$$r(\omega) = \frac{\exp\left(-\frac{\omega^2}{2\sigma^2}\right)}{\sqrt{2\pi}\sigma}$$

resolution function

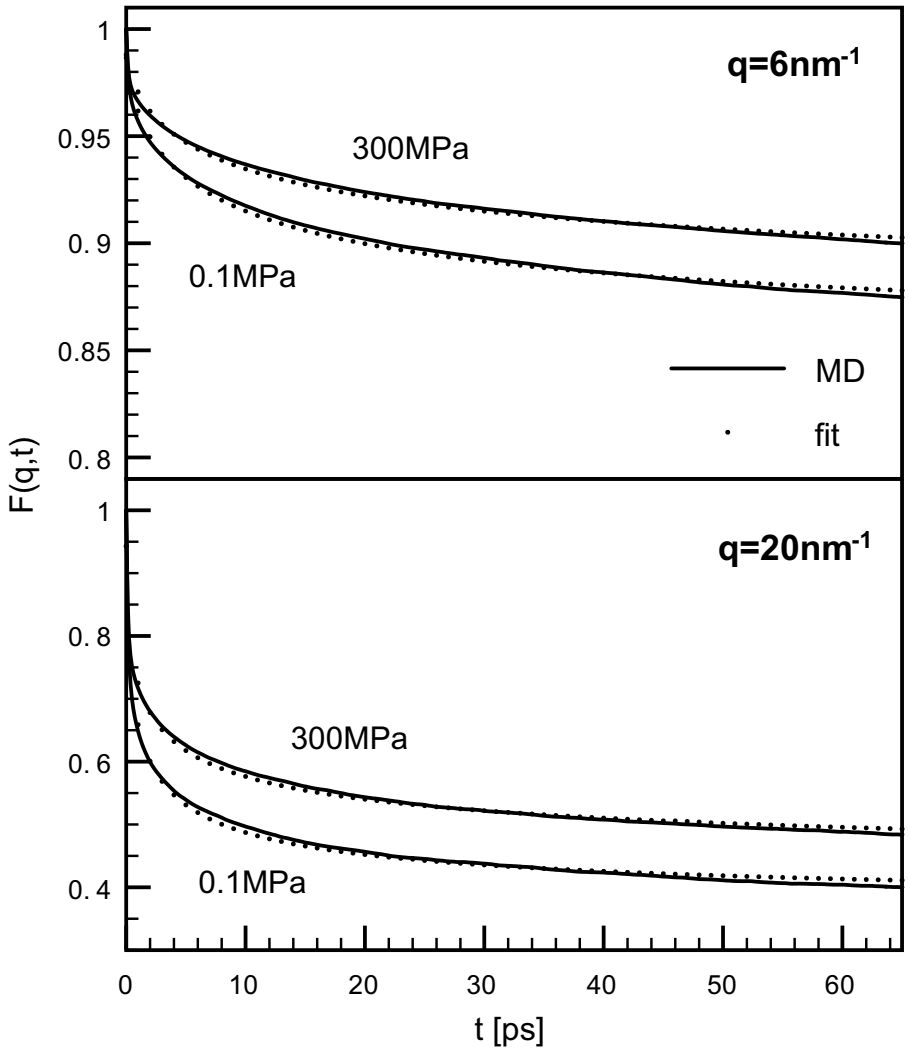
Fit of the model to experimental QENS spectra

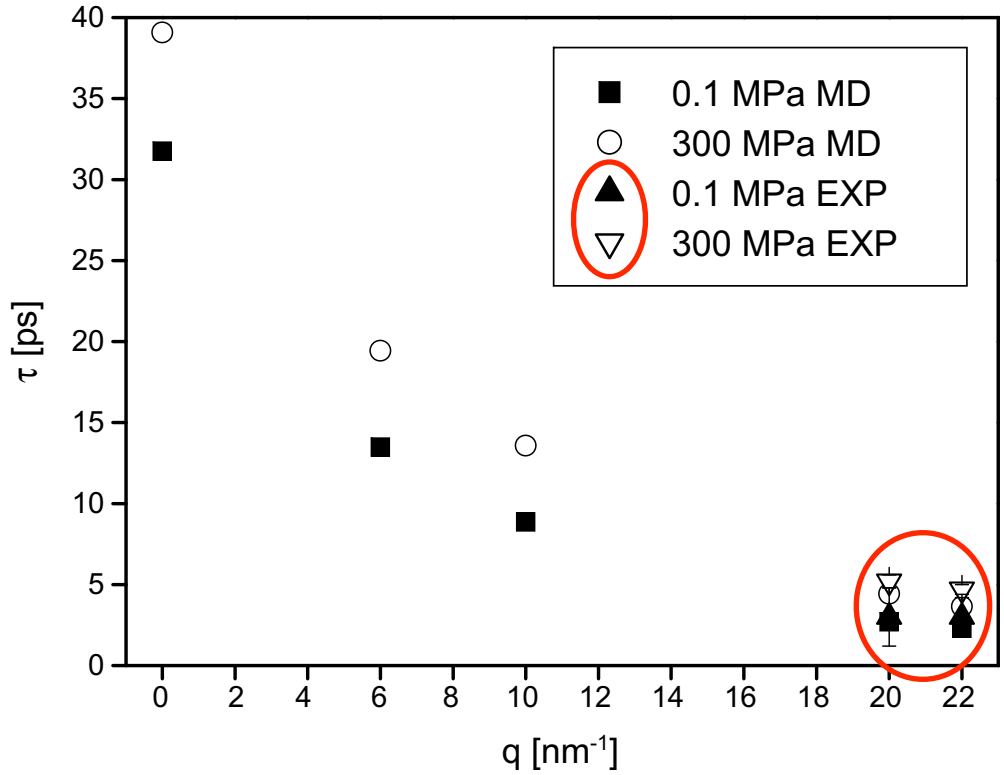
V. Calandrini, V. Hamon, K. Hinsen, P. Calligari, M.-C. Bellissent-Funel, and G.R. Kneller.
Chem. Phys., 345:289–297, 2008.



		$S_{\mathrm{inc}}(20\ \mathrm{nm}^{-1},\omega)$	$S_{\mathrm{inc}}(22\ \mathrm{nm}^{-1},\omega)$
0.1 MPa	$\langle x^2\rangle$ (nm^2)	2.57×10^{-3}	2.41×10^{-3}
	α	0.35(2)	0.40(2)
	τ (ps)	3(2)	3(1)
	$\overline{D}$ (nm^2 ps^{-1})	$0.53(3)\times10^{-4}$	
300 MPa	$\langle x^2\rangle$ (nm^2)	2.21×10^{-3}	2.08×10^{-3}
	α	0.52(1)	0.55(1)
	τ (ps)	5.2(2)	4.7(3)
	$\overline{D}$ (nm^2 ps^{-1})	$0.50(3)\times10^{-4}$	

Simulated intermediate scattering function

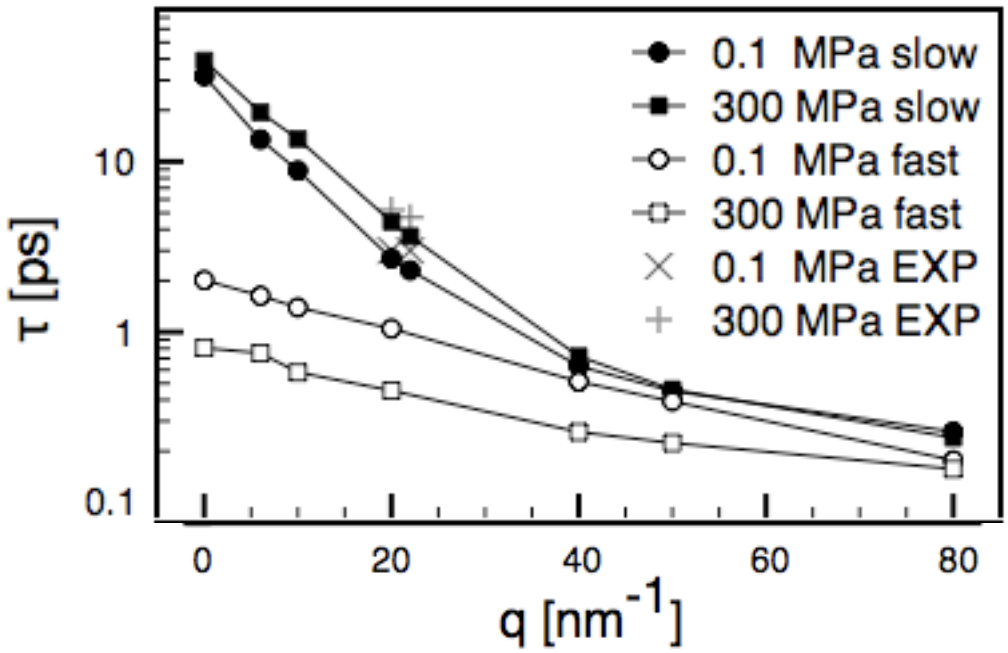




$$I(q,t) = \exp(-q^2\langle x^2\rangle)\sum_{n=0}^{\infty}\frac{q^{2n}\langle x^2\rangle^n}{n!}E_\alpha(-[t/\tau_n]^\alpha)$$

Detailed analysis of fast (20 ps) localized motions and collective slow (1 ns) motions

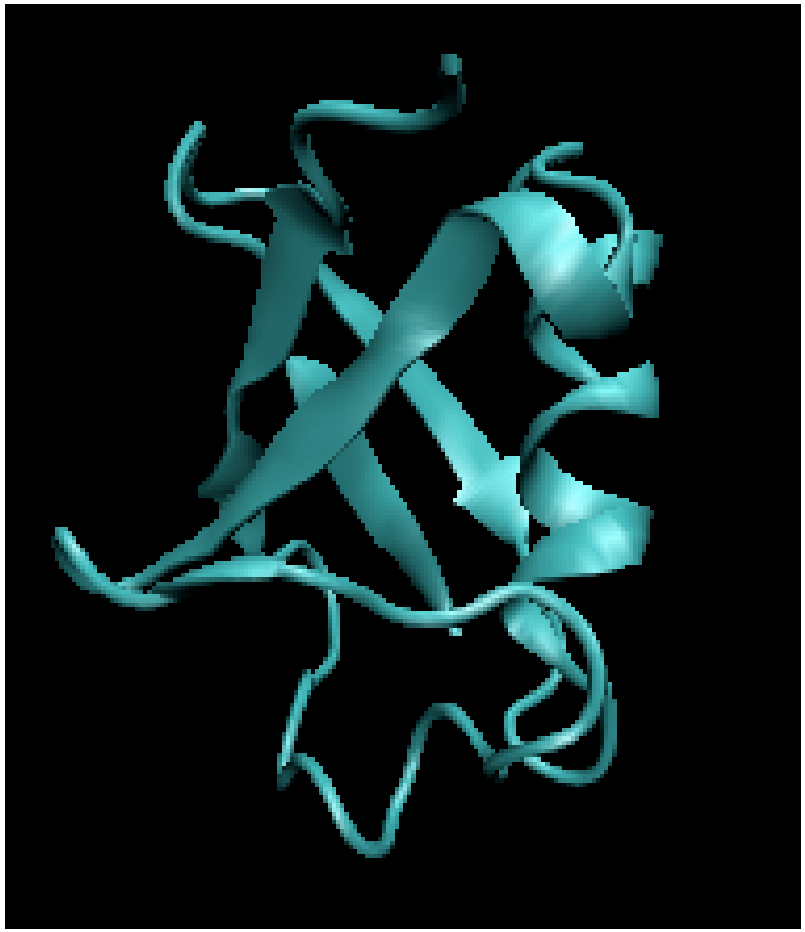
V. Calandrini and G.R. Kneller. *J. Chem. Phys.*, 128(6):065102, 2008.



- Slow collective motions are slowed down

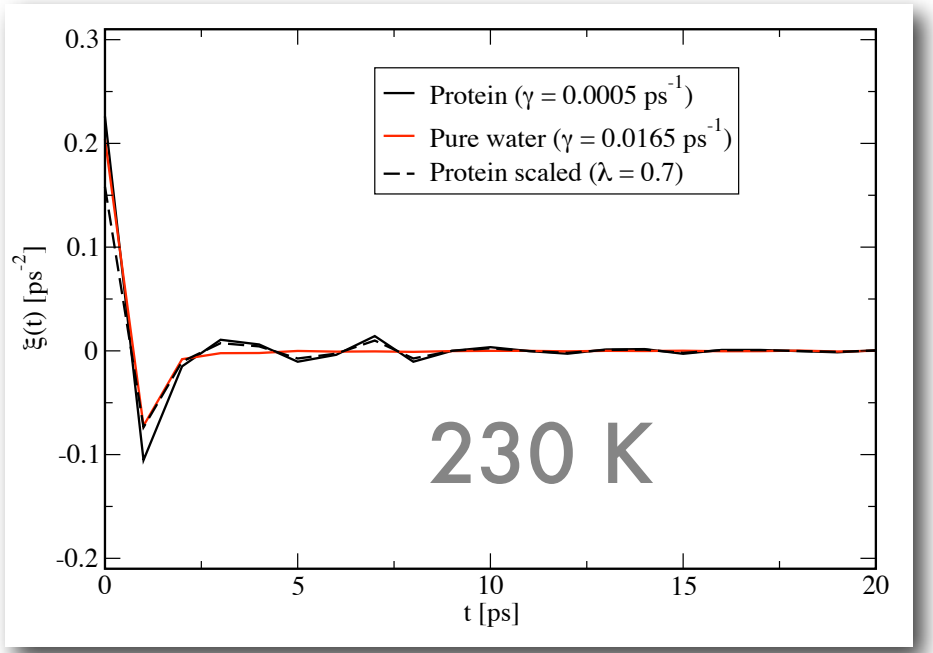
- Fast localized motions are accelerated

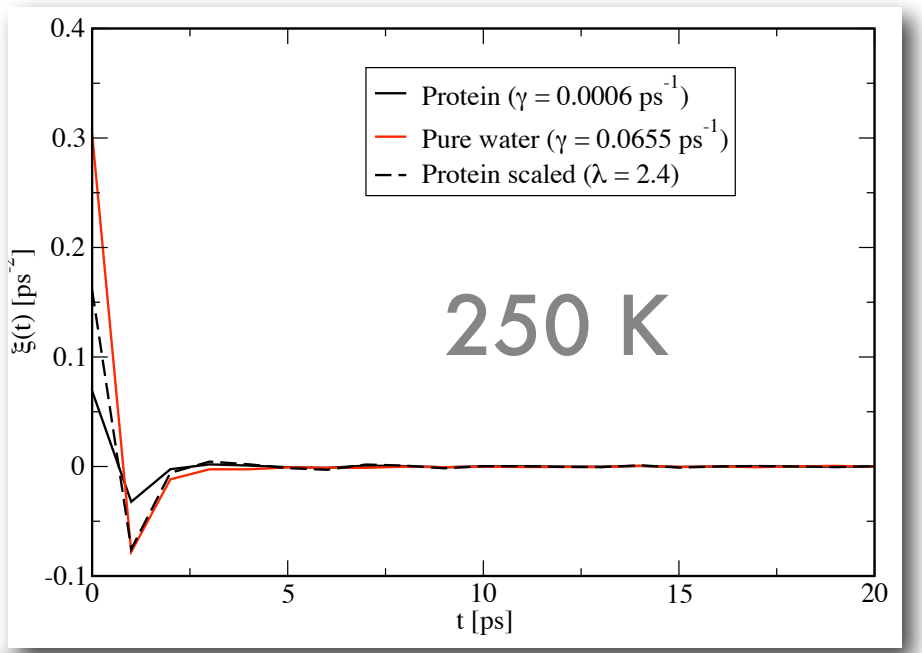
Fractional BD and solvent

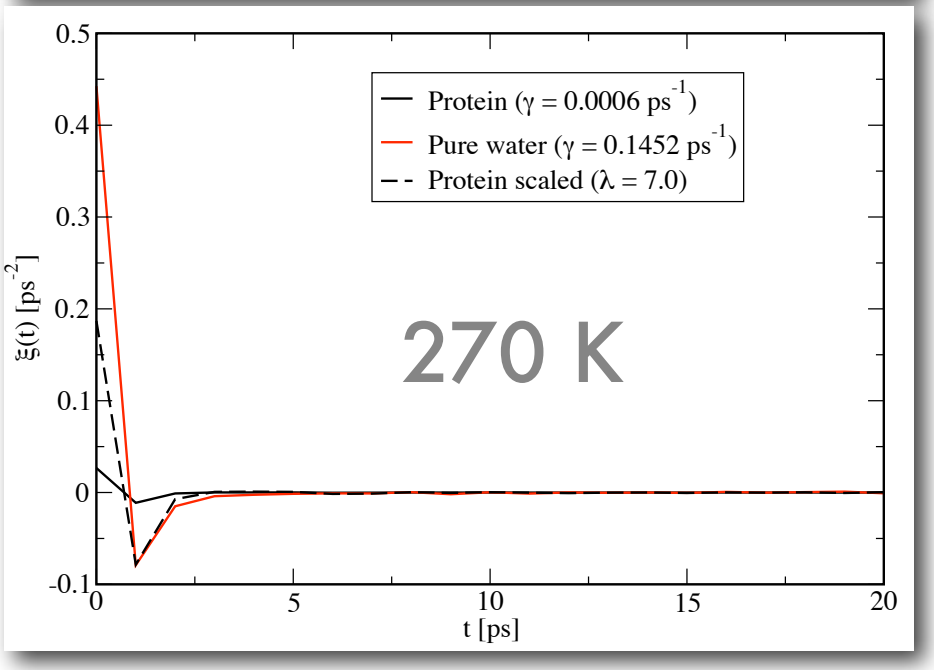


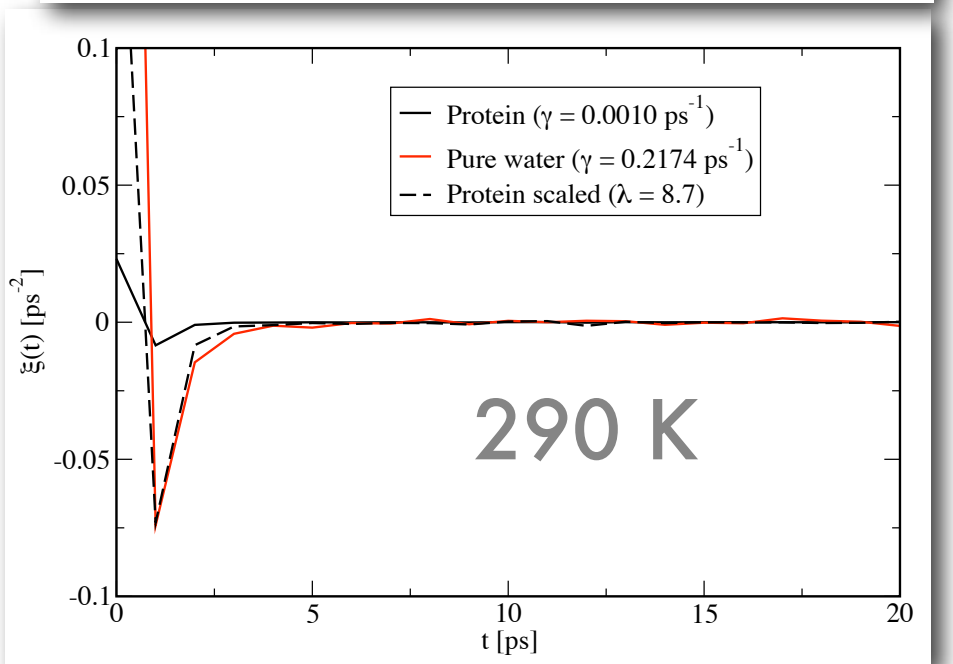
Simulation study of colective motions in Ubiquitine in aqueous solution (TIP4P) and comparison with bulk water

→ $F_{coh}(q,t)$ and its memory function


Protein (γ = 0.0005 ps^{-1})
Pure water (γ = 0.0165 ps^{-1})
Protein scaled (λ = 0.7)
230 K
ξ(t) [ps^{-2}]
t [ps]


Protein (γ = 0.0006 ps^{-1})
Pure water (γ = 0.0655 ps^{-1})
Protein scaled (λ = 2.4)
250 K
ξ(t) [ps^{-2}]
t [ps]


Protein (γ = 0.0006 ps^{-1})
Pure water (γ = 0.1452 ps^{-1})
Protein scaled (λ = 7.0)
270 K
ξ(t) [ps^{-2}]
t [ps]


Protein (γ = 0.0010 ps^{-1})
Pure water (γ = 0.2174 ps^{-1})
Protein scaled (λ = 8.7)
290 K
ξ(t) [ps^{-2}]
t [ps]

Memory function

$0.7 < \lambda < 8.7$

$$\xi_{\mathrm{water}}(t) = \lambda \xi_{\mathrm{UBQ}}(t) + \gamma\delta(t)$$

Glassy dynamics, represented by the fBD model

zero friction constant

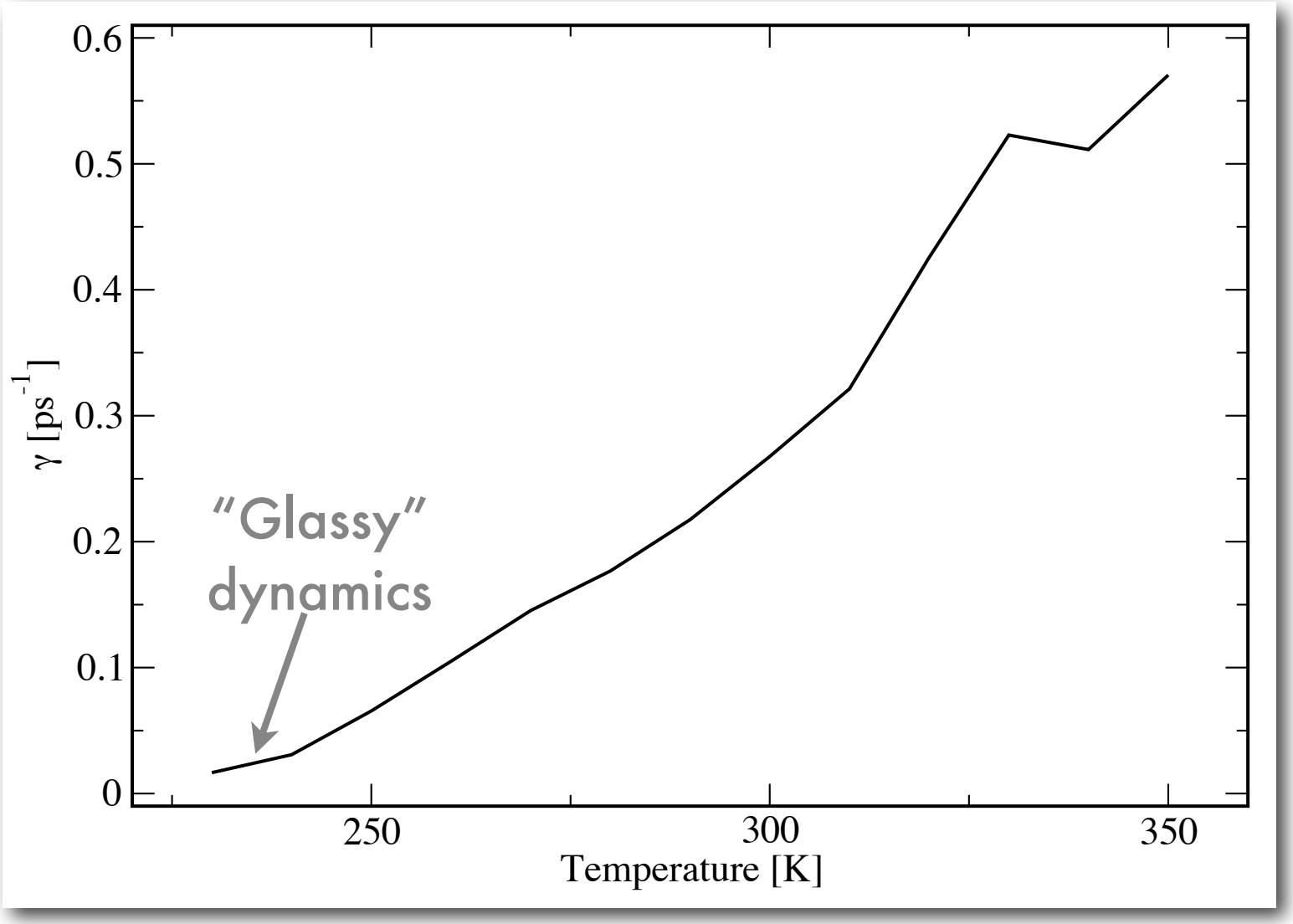
➔ infinite relaxation time

Normal Brownian dynamics for molecular diffusion

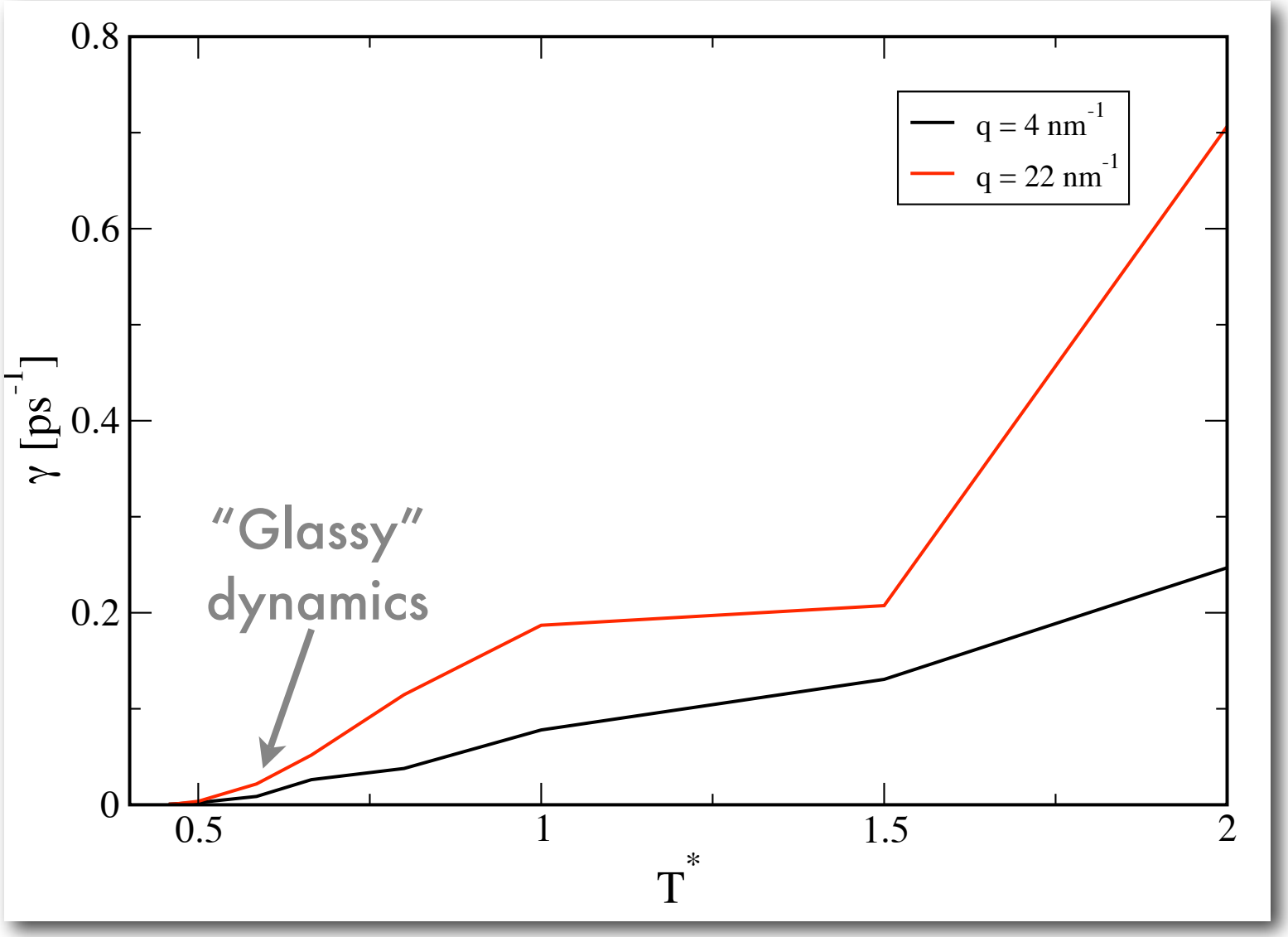
finite friction constant

➔ finite relaxation time

Friction constant of $F_{coh}(q,t)$ for TIP4P water

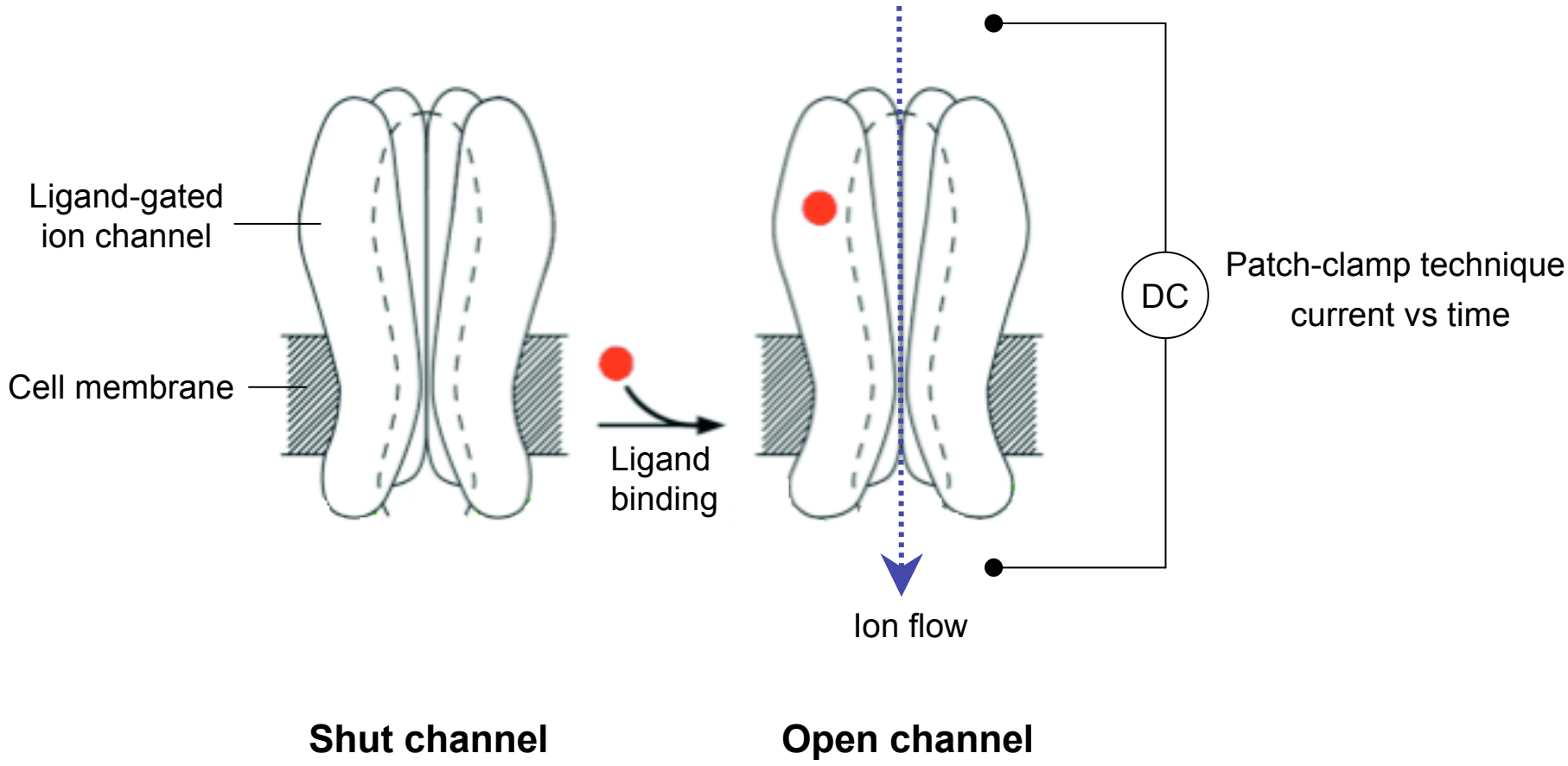


Friction constant of $F_{coh}(q,t)$ for a model glass-forming liquid (binary Lennard-Jones mixture)



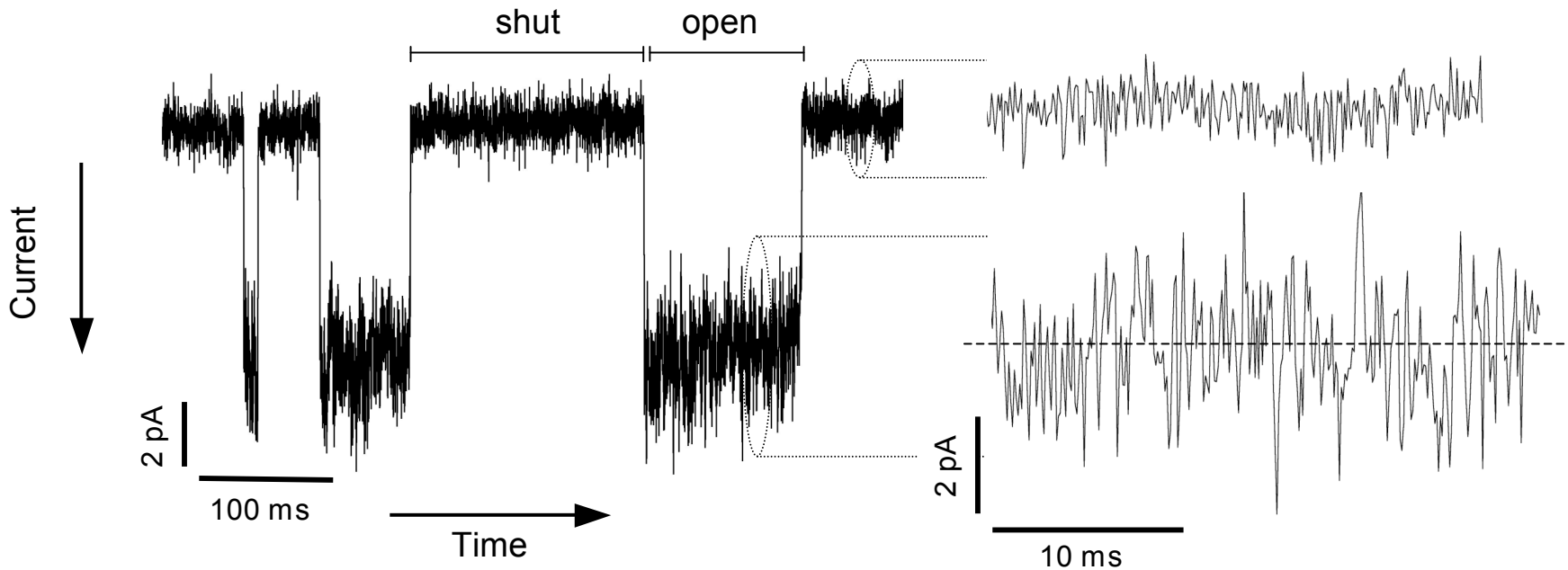
Anomalous diffusion in other systems

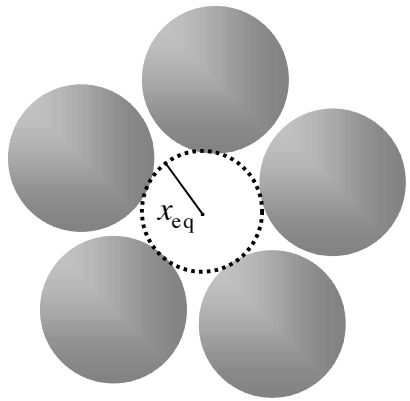
Fluctuating currents in ion channels



With permission of C. Danelon, EPFL Lausanne

From current fluctuations to protein dynamics





View of the protein along channel axis

Current fluctuations, δi, can be related to the displacement δx: $\delta i = V\left(\frac{\partial g}{\partial x}\right)_{x_{eq}} \delta x$

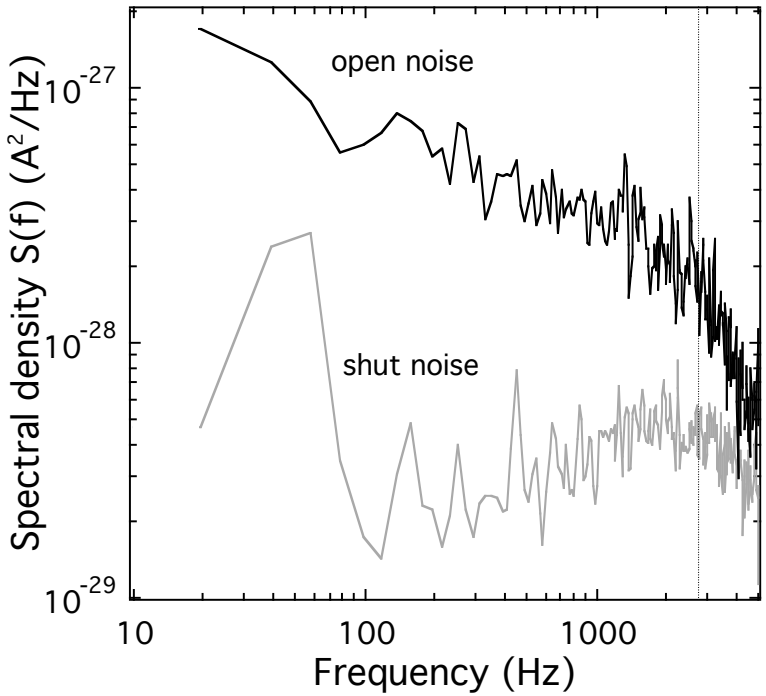
V applied voltage ≈ −100 mV

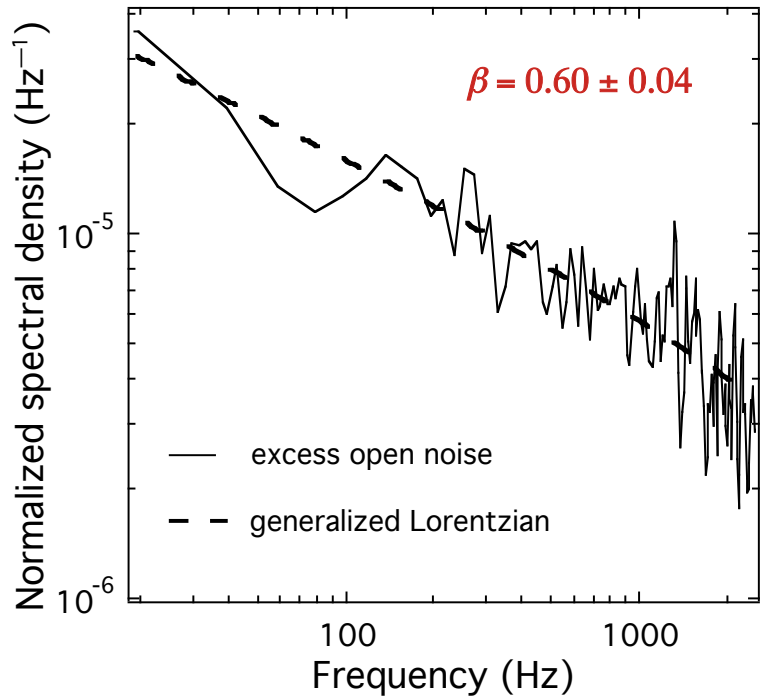
δx = $x - x_{eq}$

x_{eq} equilibrium domain coordinate

$(\partial g/\partial x)_{x_{eq}}$ conductance change as a function of δx

Power spectrum of current fluctuations





Spectral density of the current, $S_i(\omega)$, is related to the spectral density of protein dynamics, $S_x(\omega)$, by:

$$S_i(\omega) = \left(\frac{\partial g}{\partial x}\right)^2 V^2 S_x(\omega)$$

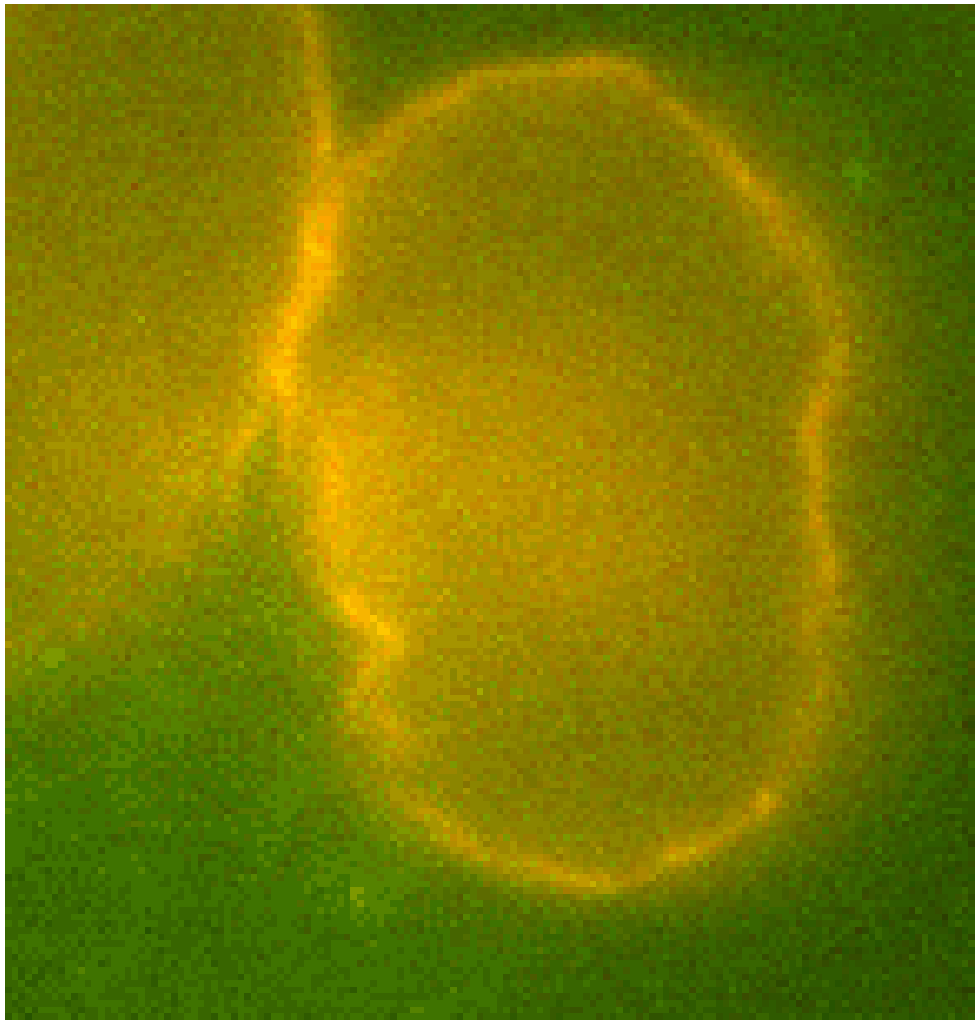
Fractional Brownian dynamics:

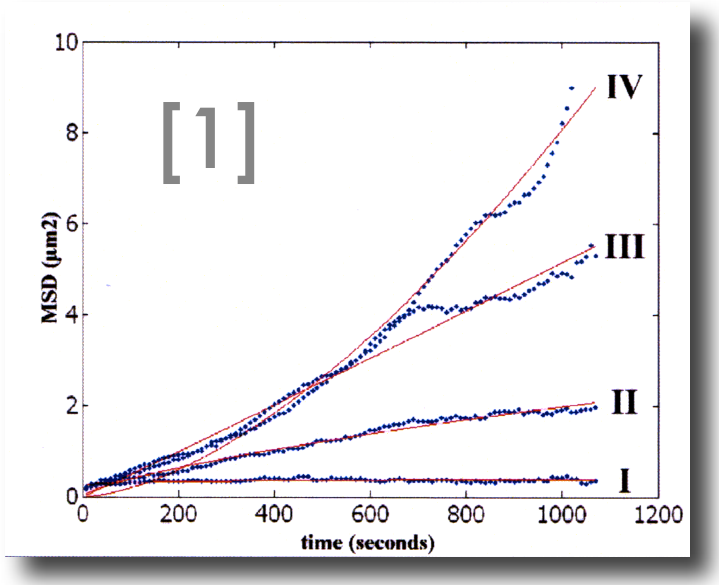
$$C_x^{\mathrm{FBD}}(t) = \langle \delta x(0)\delta x(t) \rangle = C_x^{\mathrm{FBD}}(0) E_\beta\left[-(t/\tau)^\beta\right] \qquad 0 < \beta \le 1$$

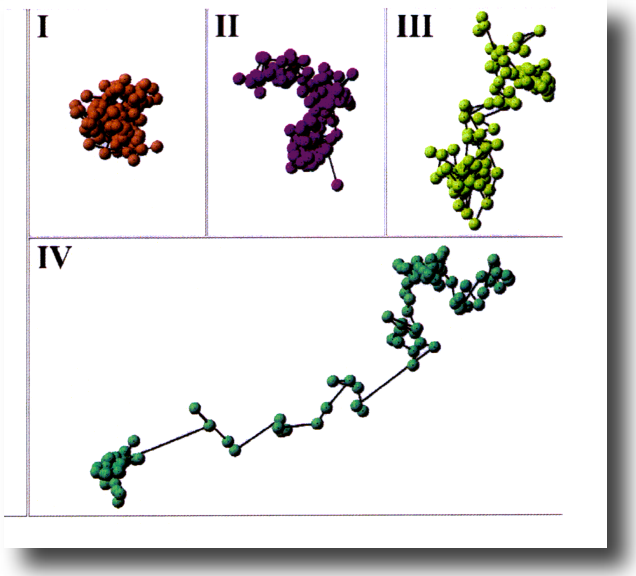
$$S_x^{\mathrm{FBD}}(\omega) = C_x^{\mathrm{FBD}}(0) \frac{2\tau \sin(\beta\pi/2)}{|\omega\tau|\left(|\omega\tau|^\beta + 2\cos(\beta\pi/2) + |\omega\tau|^{-\beta}\right)}$$

Diffusion processes in a cell

"Superdiffusion" - another type of anomalous diffusion







* Animation of Spencer Shorte, Institut Pasteur, Paris

[1] C.P. Bacher et al. 4d single particle tracking of synthetic and proteinacous microspheres reveals preferential moveme of nuclear particles along chromatin - poor tracks. BMC Cell Biology, 5:45, 2004.

Cyto-skeleton and "crowding"

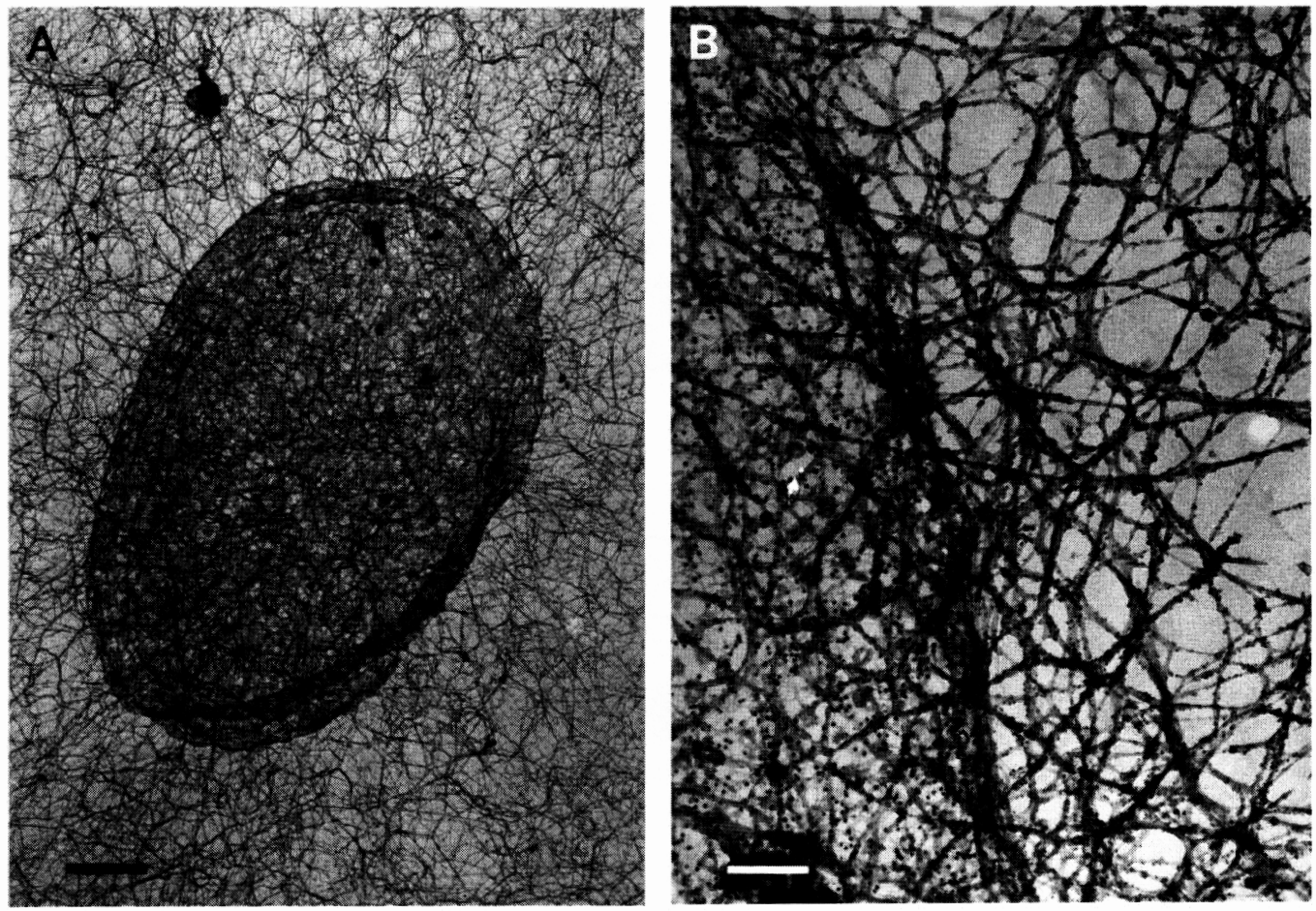


Fig. 7. (A) Overview of a mouse skin fibroblast cytoskeleton. Bar, 0.3 µm. (B) The nucleus/cytoplasm border of a mouse skin cytoskeleton. Bar, 0.15 µm. These photos show the intermediate filament network. B was prepared using anti-vimentin antibody/5 nm gold and anti-lamin antibody/18 nm gold complexes. This photo strongly suggests continuity between the cytoplasmic and nuclear assemblies. (Photo kindly provided by X. Wang and P.Traub, Max- Planck-Institute für Zellbiologie, 68526 Ladenburg, Germany.)

A simple explanation for "superdiffusion"

$$\langle [x(t) - x(0)]^2 \rangle = 2Dt + v_D^2 t^2$$

$$v_D = \frac{DF_0}{k_B T}$$

Drift under the influence of a constant external force

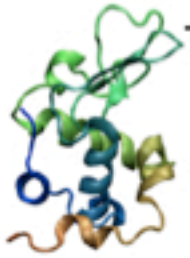
"Subdiffusion" could be explained by anomalous, fractinal Brownian dynamics in a crowded environment.

Thans to

- Konrad Hinsen, CBM Orléans/SOLEIL
- Vania Calandrini, CBM Orléans/SOLEIL
- Paolo Calligari, CBM Orléans/SOLEIL
- Véronique Hamon, CBM Orléans
- Marie-Claire Bellissent, LLB CEA Saclay
- Roger Fourme, SOLEIL
- Eric Girard, IBS Grenoble
- Godehard Sutmann, NIC, FZ Jülich
- F. Affouard, LDSMM, CNRS Lille
- Christophe Danélon, EPFL Lausanne
- Spencer Shorte, Institut Pasteur, Paris

Agence Nationale de la Recherche
ANR
programme "Calcul intensif et Simulation"

http://dirac.cnrs-orleans.fr



Theoretical Biophysics, Molecular Simulation, and Numerically Intensive Computation

navigation

- Accueil
- Projects
- Publications
- Software
  - MMTK
  - nMOLDYN
  - DomainFinder
  - ScrewFit
  - ScientificPython
  - DensityFit
  - HYDROLIB
  - DigiPlot

Software

Aller au niveau supérieur

Numerical methods are of little use without ready-to-use and tested implementations. Our policy is to make all methods developped in the group freely available to the scientific community.

MMTK — Par Konrad Hinsen — Dernière modification 13/02/2007 18:28

The Molecular Modelling Toolkit is a library which contains a wide range of algorithms that are used in molecular simulations and modelling. It is particularly useful for data analysis and visualization, but also contains standard techniques such as energy minimization and Molecular Dynamics. All our recently developped techniques for biomolecules have been implemented in MMTK.

nMOLDYN — Par Gerald Kneller — Dernière modification 14/02/2007 09:28

nMOLDYN is an interactive analysis program for Molecular Dynamics simulations. It is especially designed for the computation and decomposition of neutron scattering spectra, but also computes other quantities.

DomainFinder — Par Konrad Hinsen — Dernière modification 13/02/2007 18:29

DomainFinder is an interactive program to analyze collective motions in large proteins, either by comparing two experimental structure, or by applying an efficient normal mode technique to a single structure. Proteins up to a few thousand residues can be treated on a desktop computer in a few minutes.

ScrewFit — Par Paolo Calligari — Dernière modification 16/02/2007 18:22

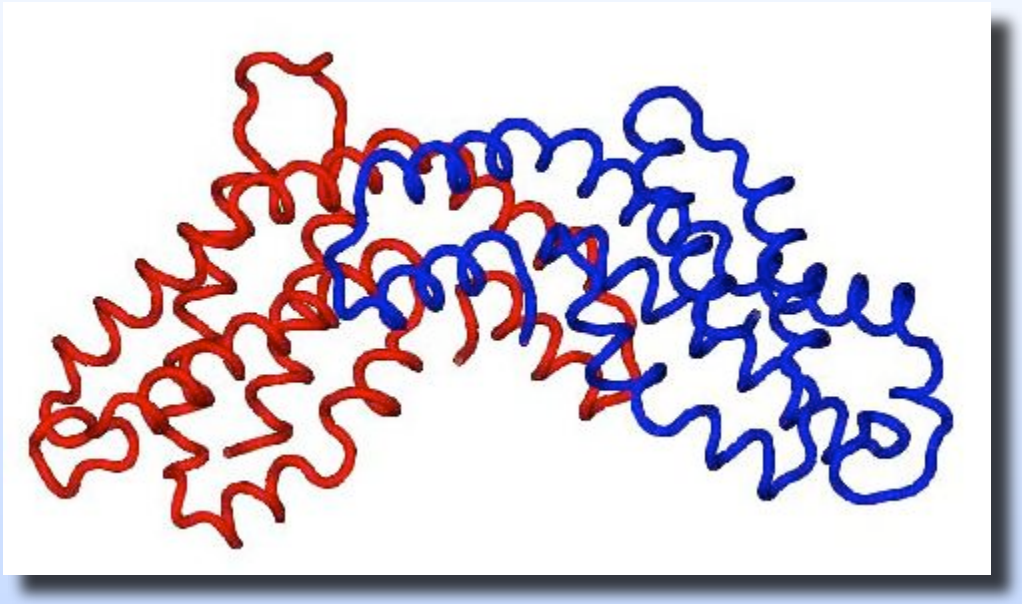
ScrewFit is a program for the characterization of protein secondary structures. It provides an efficient description of structural

Supplementary material

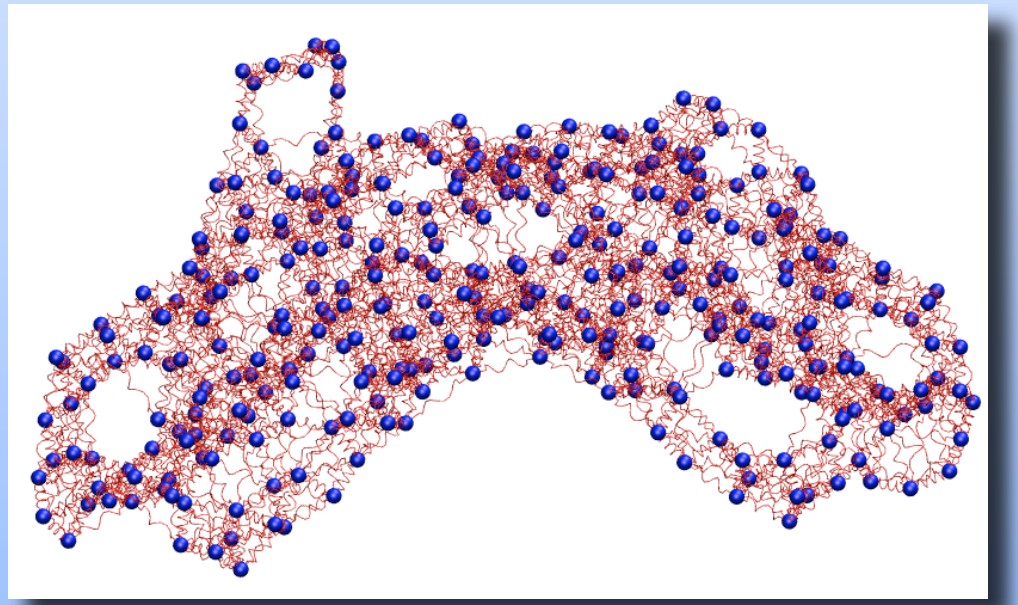
Simulation-based model for protein dynamics

Protein dynamics without explicit simulation

Coupled Brownian oscillators



Backbone of
C-phycocyanine
(2 chains)



Effective harmonic model. Each residue is a harmonic oscillator with friction

[1] K. Hinsen, A.-J. Petrescu, S. Dellerue, M. Bellissent-Funel, and G. Kneller. *Chem. Phys.*, 261(1+2):25–38, 2000.

High friction limit

$$\frac{\partial P(\tilde{\mathbf{x}},t)}{\partial t} = \frac{\partial}{\partial \tilde{\mathbf{x}}} \cdot \left\{ \tilde{\boldsymbol{\eta}} \cdot \tilde{\mathbf{x}} \, P(\tilde{\mathbf{x}},t) \right\} + k_B T \frac{\partial}{\partial \tilde{\mathbf{x}}} \cdot \frac{\partial}{\partial \tilde{\mathbf{x}}} P(\tilde{\mathbf{x}},t)$$

Multidimensional Fokker-Panck equation

$$\tilde{\mathbf{x}} = \boldsymbol{\gamma}^{1/2} \cdot \mathbf{x}$$

Friction matrix

$$\tilde{\boldsymbol{\eta}} = \boldsymbol{\gamma}^{-1/2} \cdot \boldsymbol{\kappa} \cdot \boldsymbol{\gamma}^{-1/2}$$

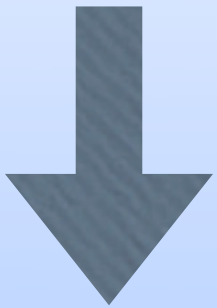
Elasticity matrix

$$\mathbf{c}_{\tilde{x}\tilde{x}}(t) = \exp(-\boldsymbol{\eta} t) \langle \tilde{\mathbf{x}} \cdot \tilde{\mathbf{x}}^T \rangle$$

Multiexponential relaxation

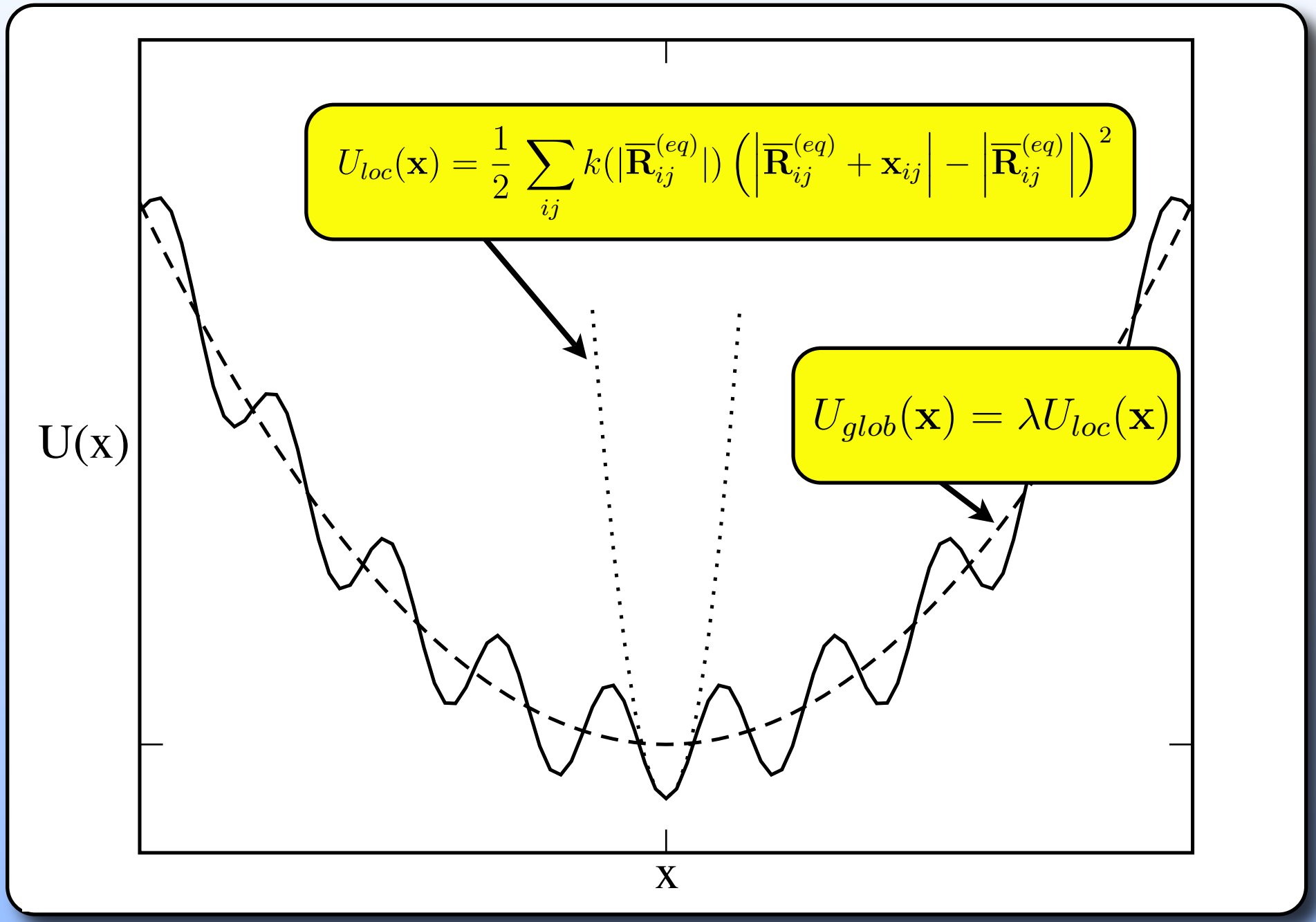
Brownian modes

$$\tilde{\boldsymbol{\eta}} \cdot \mathbf{u}_\nu = \lambda_\nu \mathbf{u}_\nu, \qquad \nu = 1, \ldots, 3N$$

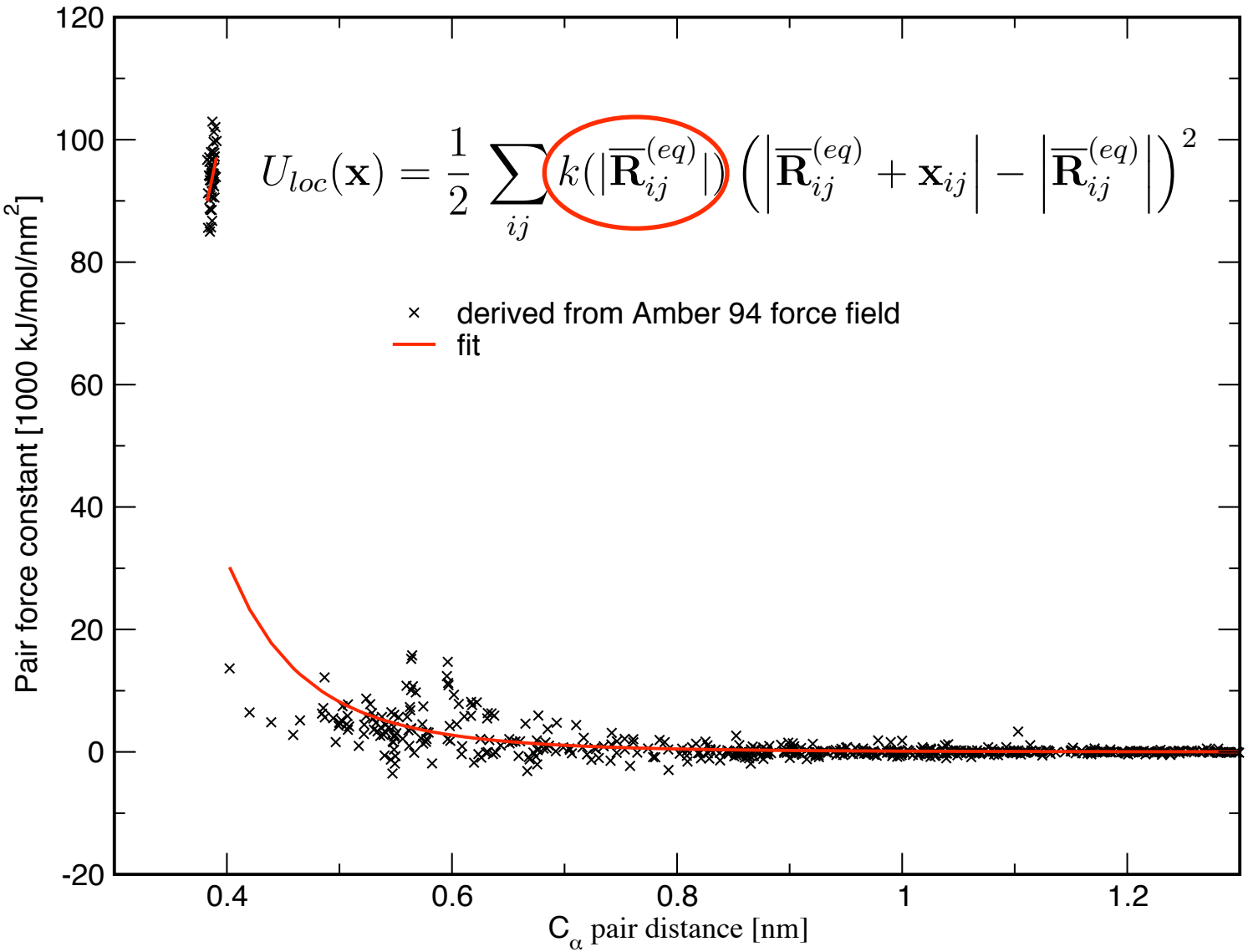


$$\mathbf{c}_{\tilde{x}\tilde{x}}(t) = k_B T \sum_{\nu=1}^{3N} \frac{\exp(-\lambda_\nu t)}{\lambda_\nu} \mathbf{u}_\nu \cdot \mathbf{u}_\nu^T$$

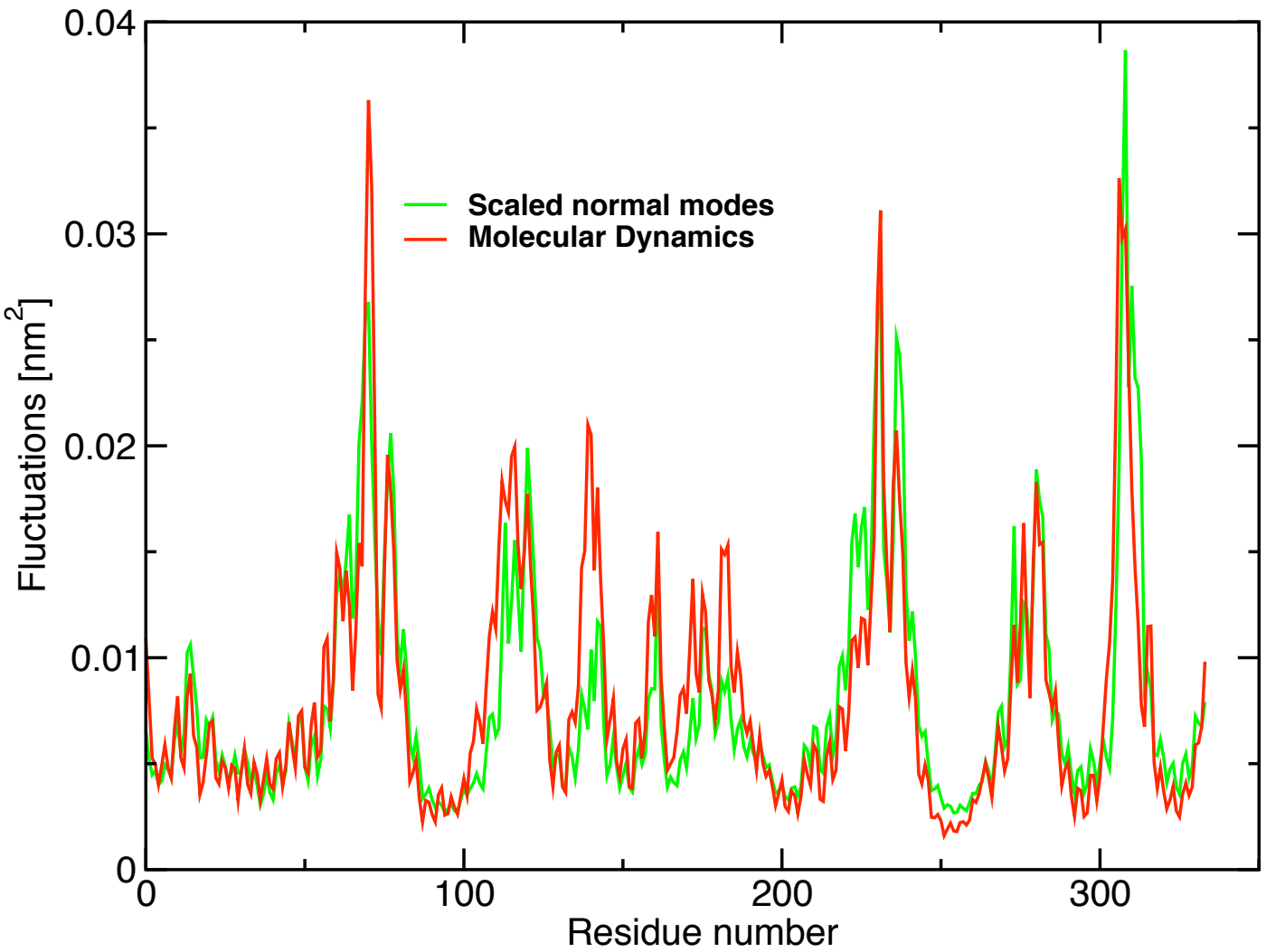
Effective harmonic potential



Effective force constants



Adapting the scaling parameter



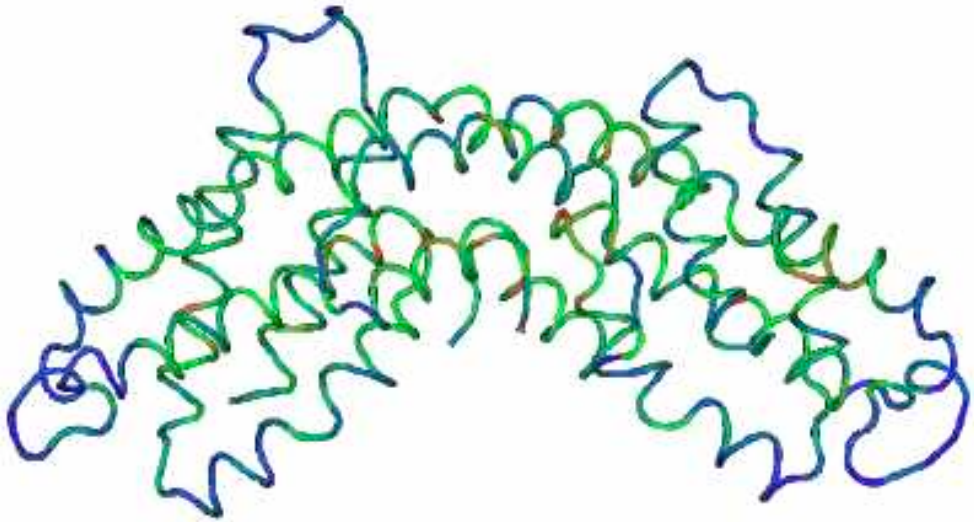
$$U_{glob}(\mathbf{x}) = \lambda U_{loc}(\mathbf{x})$$

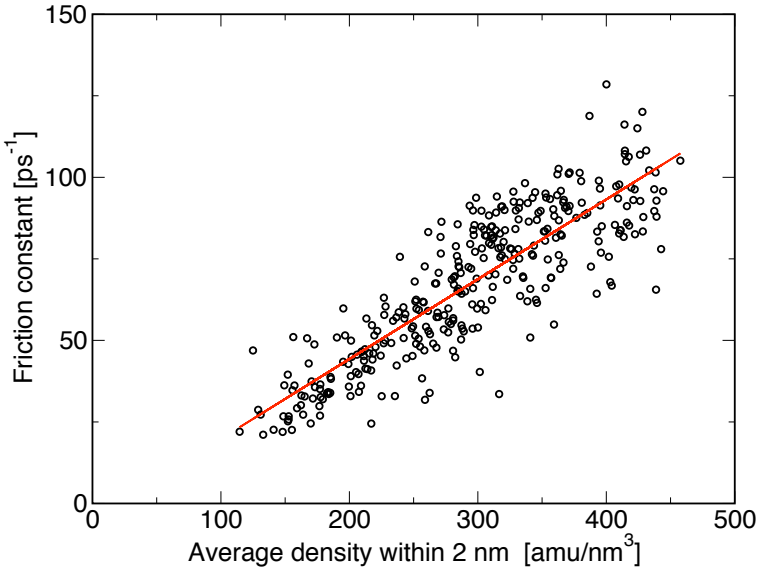
$$\lambda = 0.115$$

Friction matrix

$$\gamma = \begin{pmatrix} \gamma_1 & 0 & \dots & 0 \\ 0 & \gamma_2 & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \dots & \gamma_N \end{pmatrix}$$

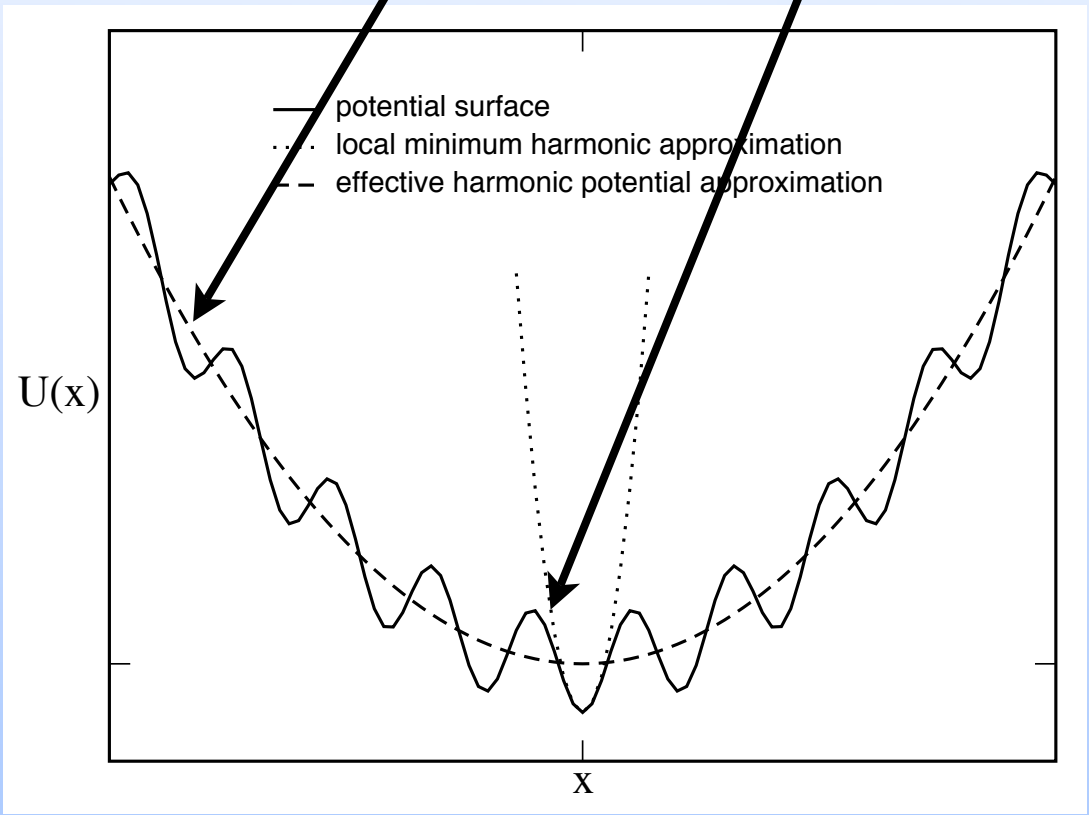
$$\gamma_i = \gamma_i \mathbf{1}$$





Intermediate scattering function

$$F_{\mathrm{inc}}(\mathbf{q},t) = F_{\mathrm{inc,bm}}(\mathbf{q},t)F_{\mathrm{inc,vib}}(\mathbf{q},t)$$



- Diffusion in a global potential well

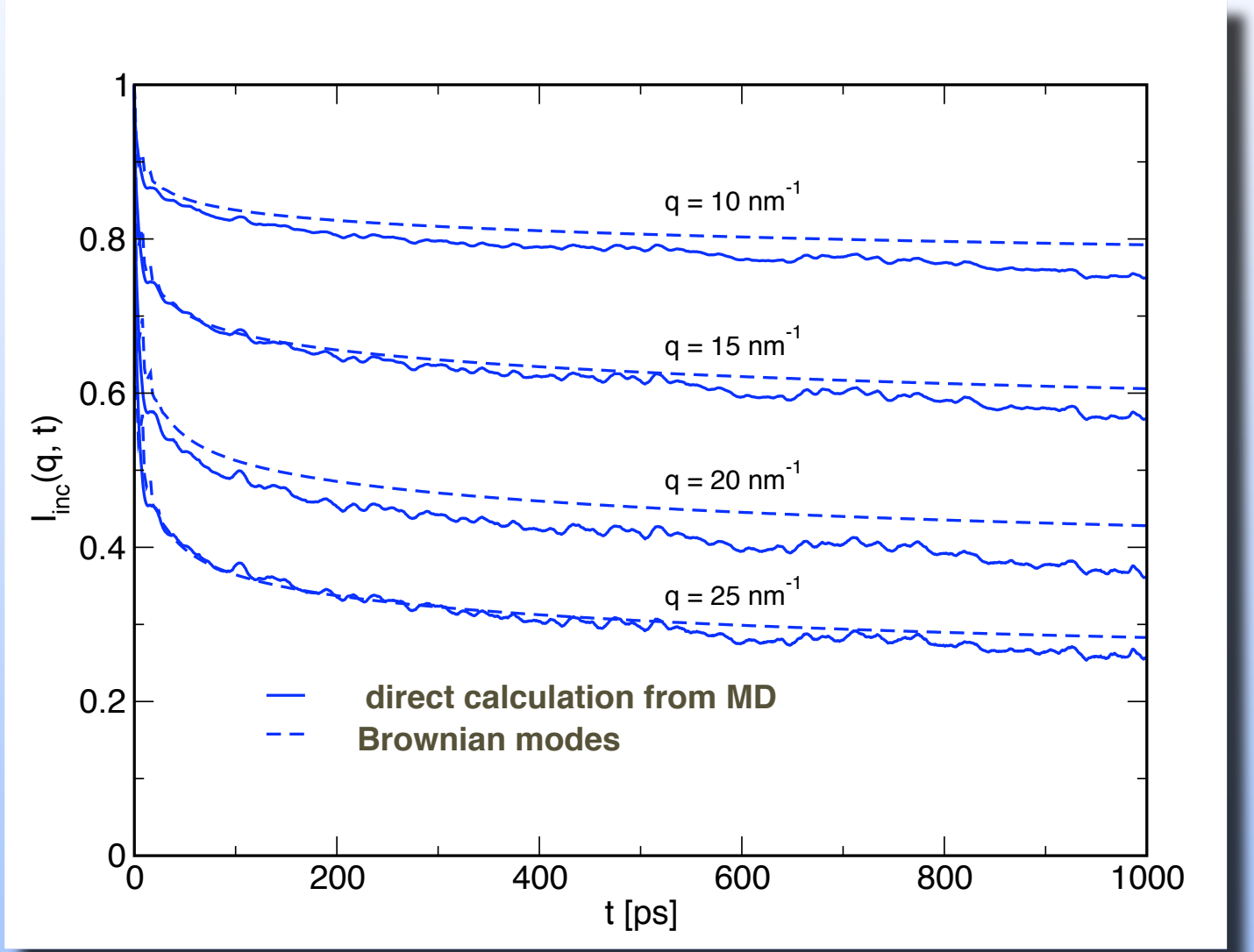
+

- Damped oscillations in a local potential well

[1] G.R. Kneller. *Chem. Phys.*, 261(1+2):1–24, 2000.

[2] K. Hinsen, A.-J. Petrescu, S. Dellerue, M.C. Bellissent-Funel, and G.R. Kneller. *Chem. Phys.*, 261(1+2):25–38, 2000.

MD compared to Brownian modes



K. Hinsen, A.-J. Petrescu, S. Dellerue, M.C. Bellissent-Funel, and G.R. Kneller. *Chem. Phys.*, 261(1+2):25–38, 2000.