MODELING THE DYNAMICS OF BIOMOLECULES

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Outline

- Introduction
- Anomalous diffusive motions in proteins, examples from simulation and experiment
- Developing diffusion models through asymptotic analysis
- Anomalous lateral diffusion in lipid bilayers
- Conclusions

Nature Vol. 280 16 August 1979

Temperature-dependent X-ray diffraction as a probe of protein structural dynamics

Hans Frauenfelder, Gregory A. Petsko* & Demetrius Tsernoglou

Department of Physics, University of Illinois at Urbana-Champaign, Urbana, Illinois 61801
and
Department of Biochemistry, Wayne State University School of Medicine, Detroit, Michigan 48201

proteins have *dynamic* structures

Myoglobin

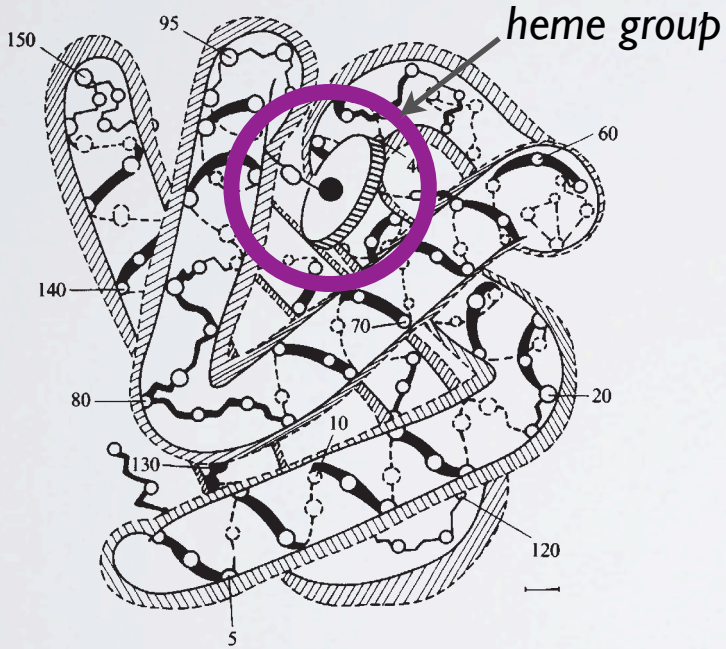
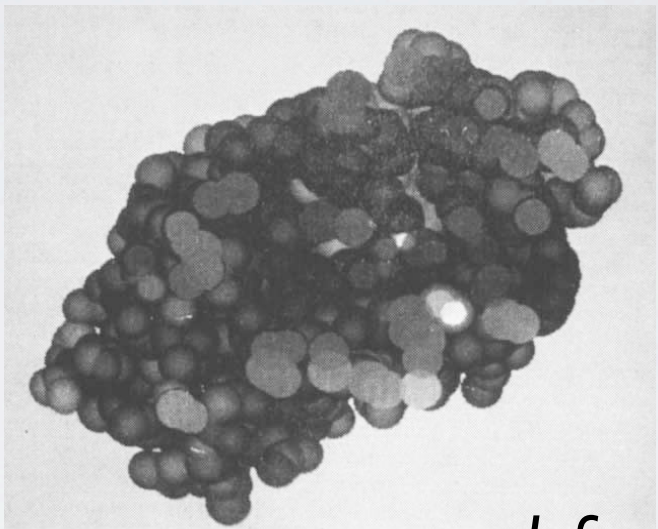
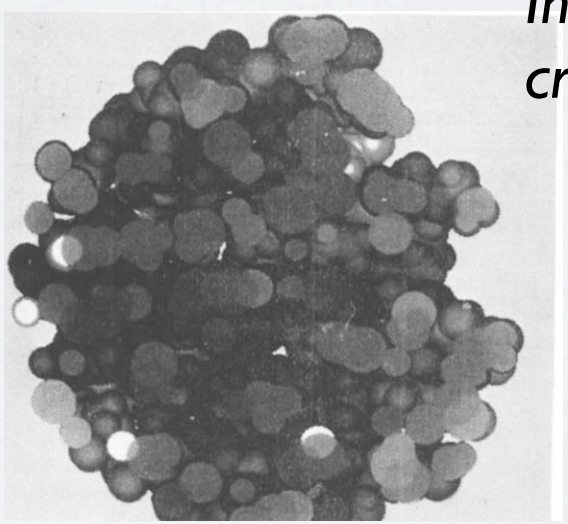


Fig. 3 Backbone (main chain) structure of myoglobin. The solid lines indicate the static structure as given in ref. 37. Circles denote the C^{α} carbons; some residue numbers are given. The shaded area gives the region reached by conformational substates with a 99% probability. Scale bar, 2 Å.





Inferring atomic motions from crystallgraphic B-factors

Conformational substates in a protein: Structure and dynamics of metmyoglobin at 80 K

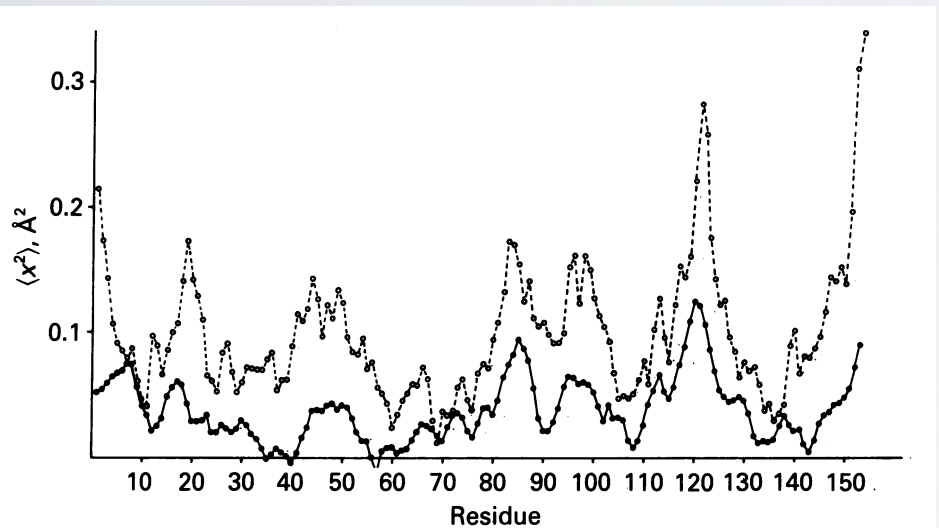
(low-temperature crystallography/Mössbauer absorption/Debye–Waller factor/intramolecular motion/lattice disorder)

H. Hartmann*, F. Parak*§, W. Steigemann*, G. A. Petsko†, D. Ringe Ponzi†, and H. Frauenfelder‡

Proc. Natl. Acad. Sci. USA
Vol. 79, pp. 4967–4971, August 1982
Biophysics

Protein dynamical transition

Average position fluctuations per residue from ***crystallography*** *at 80 K and 300 K*



Position fluctuation of the Fe atom from ***Mössbauer spectroscopy***

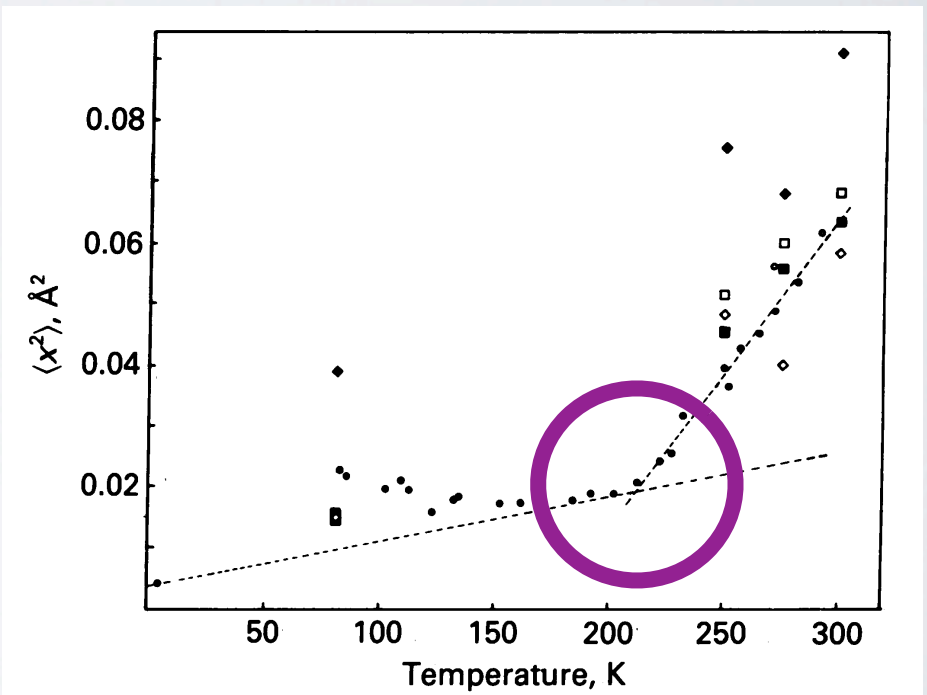


FIG. 3. Temperature dependence of $\langle x^2 \rangle$ values. ●, Fe measured by Mössbauer spectroscopy (13); ■, Fe determined by x-ray analysis; ◆, histidine-93(F8); ◇, histidine-64(E7).

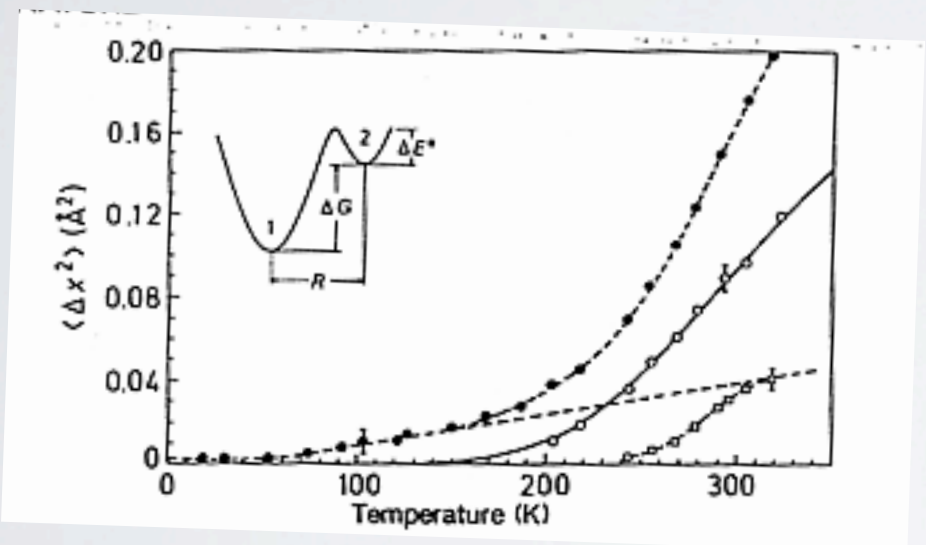
Dynamical transition of myoglobin revealed by inelastic neutron scattering

Wolfgang Doster*, Stephen Cusack† & Winfried Petry‡

NATURE VOL. 337 23 FEBRUARY 1989

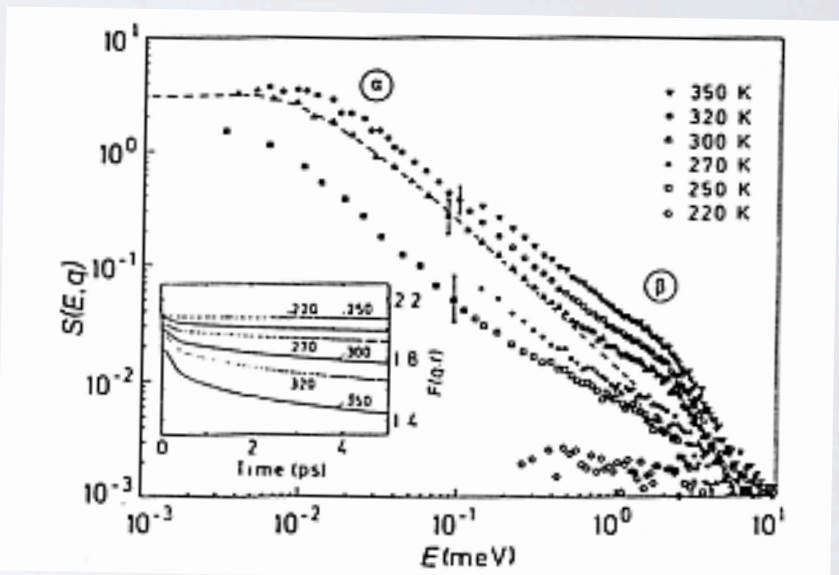
Dynamical transition by neutron scattering

Elastic scattering



Position fluctuation averaged over <u>all</u> (hydrogen) atoms

Quasielastic scattering



Onset of diffusive motions on the picosecond time scale

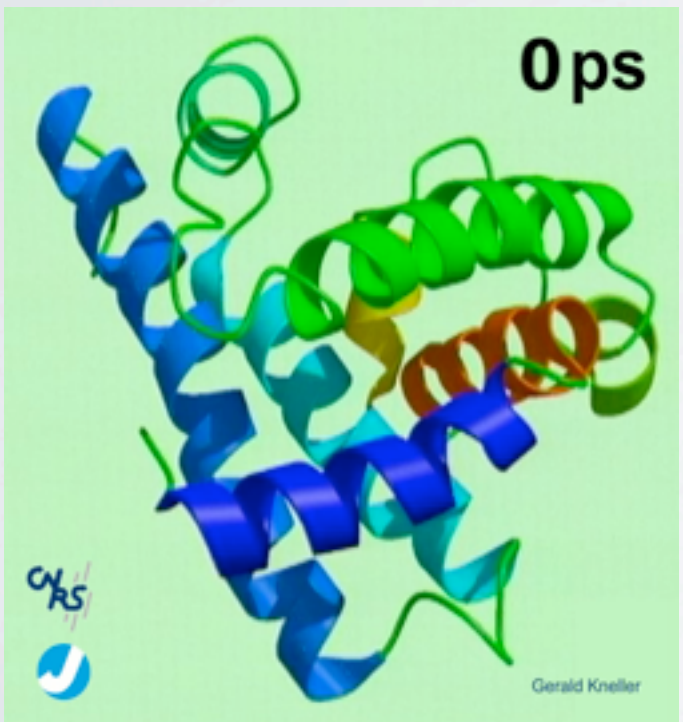
Classical MD simulations

Iterative solution of
Newton's equation of motion

$$\mathbf{r}_i(n+1) \leftarrow 2\mathbf{r}_i(n) - \mathbf{r}_i(n-1) + \frac{\Delta t^2}{M_i}\mathbf{F}_i(n)$$

$$\mathbf{v}_i(n) \leftarrow \frac{\mathbf{r}_i(n+1) - \mathbf{r}_i(n-1)}{2\Delta t}.$$

➜Access time scales < 100 ns



Forces: $\mathbf{F}_i = -\frac{\partial U}{\partial \mathbf{r}_i}$

$$\begin{aligned}
U &= \sum_{\text{bonds}\,\alpha\beta} k_{\alpha\beta}\left(r_{\alpha\beta} - r^{(0)}_{\alpha\beta}\right)^2 \\
&+ \sum_{\text{angles}\,\alpha\beta\gamma} k_{\alpha\beta\gamma}\left(\phi_{\alpha\beta\gamma} - \phi^{(0)}_{\alpha\beta\gamma}\right)^2 \\
&+ \sum_{\text{dihedrals}\,\alpha\beta\gamma\delta} k_{\alpha\beta\gamma\delta}\cos\left(n_{\alpha\beta\gamma\delta}\theta_{\alpha\beta\gamma\delta} - \delta_{\alpha\beta\gamma\delta}\right) \\
&+ \sum_{\text{pairs}\,\alpha\beta} 4\epsilon_{\alpha\beta}\left(\left[\tfrac{\sigma_{\alpha\beta}}{r}\right]^{12} - \left[\tfrac{\sigma_{\alpha\beta}}{r}\right]^{6}\right) \\
&+ \sum_{\text{pairs}\,\alpha\beta} \tfrac{q_\alpha q_\beta}{4\pi\epsilon_0 r_{\alpha\beta}}
\end{aligned}
\Bigg\} \text{non-bonded}$$

Simulated motions in myoglobin

J. Mol. Biol. (1994) **242**, 181–185

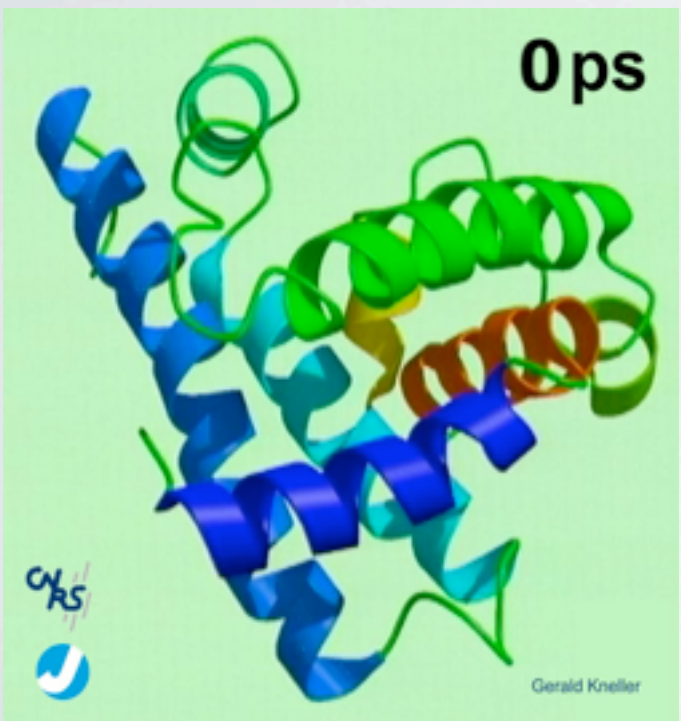
COMMUNICATION

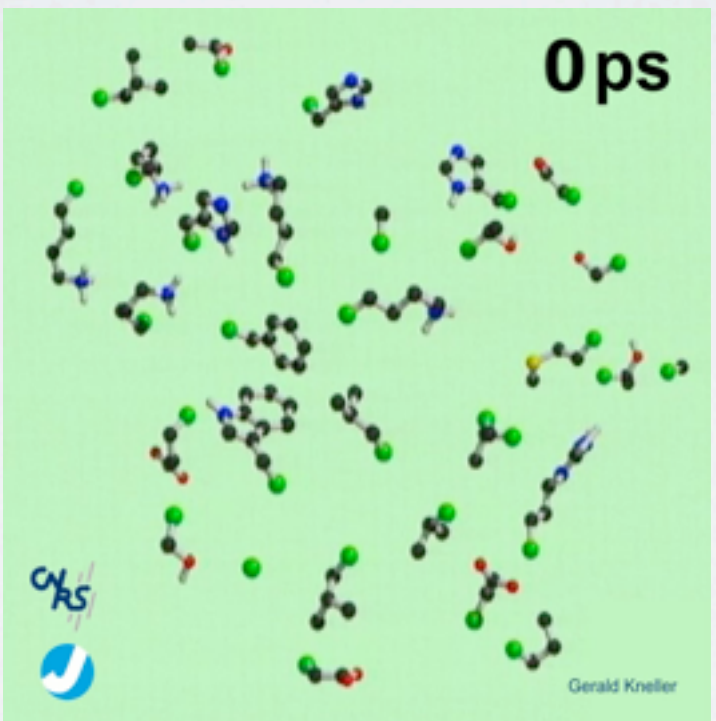
Liquid-like Side-chain Dynamics in Myoglobin

Gerald R. Kneller[1,2] and Jeremy C. Smith[2]

Backbone

The "side-chain liquid"





flexible

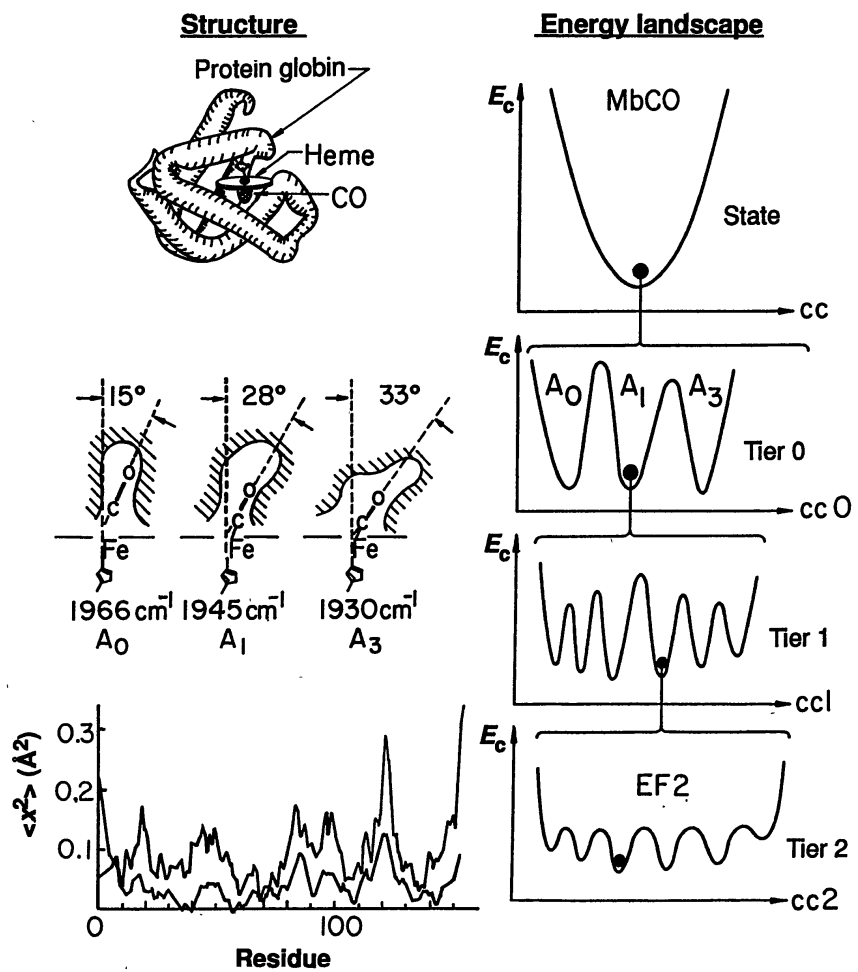
rigid

The Energy Landscapes and Motions of Proteins

HANS FRAUENFELDER, STEPHEN G. SLIGAR, PETER G. WOLYNES

SCIENCE, VOL. 254

Conformational substates



Non-exponential rebinding kinetics of CO

$$N(t) = \int dH\, g(H) \exp[-k(H)t]$$

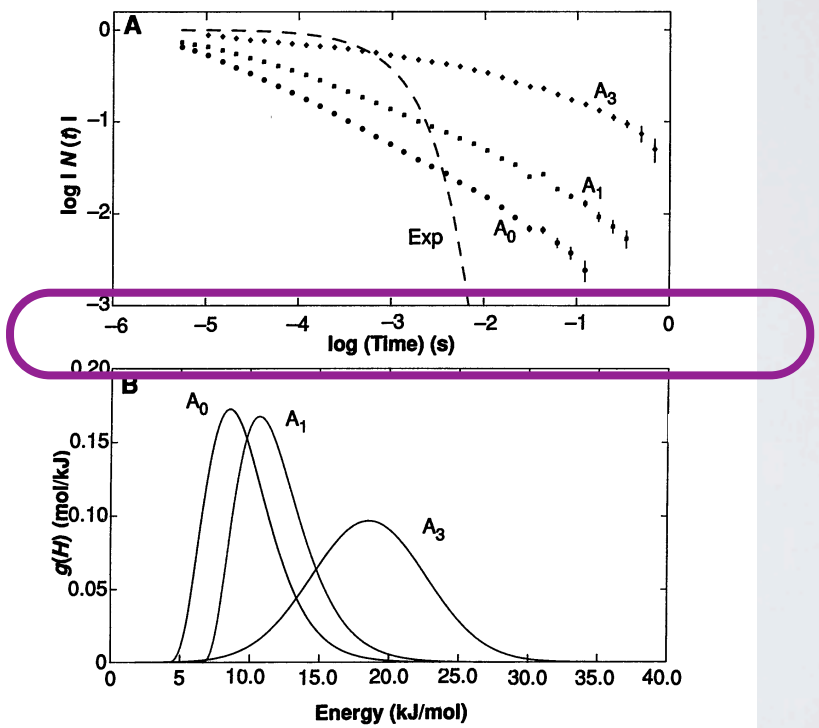


Fig. 2. Rebinding of CO to Mb after photodissociation, measured separately for the substates of tier 0 at pH 5.7. (**A**) $N(t)$ is the fraction of proteins that have not rebound a CO at the time t after photodissociation. All three substates (A_0, A_1, and A_3) rebind nonexponentially in time. (**B**) The activation enthalpy spectra, defined through Eq. 1.

46 Biophysical Journal Volume 68 January 1995 46–53

A Fractional Calculus Approach to Self-Similar Protein Dynamics

Walter G. Glöckle and Theo F. Nonnenmacher
Department of Mathematical Physics, University of Ulm, D-89069 Ulm, Germany

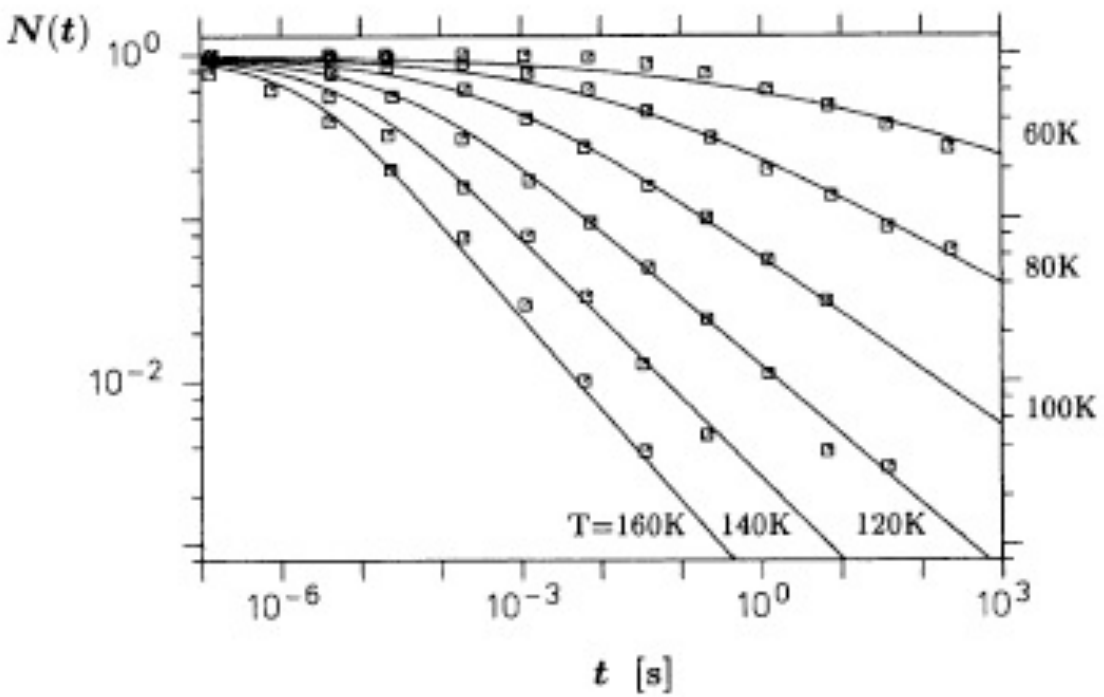


FIGURE 2 Three-parameter model Eq. 32 for rebinding of CO to Mb after photo dissociation. The parameters are $\tau_m = 8.4 \times 10^{-10}$s, $\alpha = 3.5 \times 10^{-3}\ K^{-1}$ and $k = 130$, the data points are from Austin et al. (1975).

$$\psi(t) = \frac{N(t)}{N(0)} = E_\beta(-[t/\tau]^\beta)$$

$$E_\beta(z) = \sum_{n=0}^{\infty} \frac{z^n}{\Gamma(1+\beta)}$$

Mittag-Leffler function

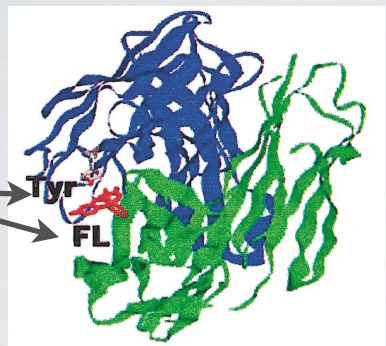
$$D_t^\beta \psi(t) + \tau^{-\beta}\psi(t) = \frac{t^{-\beta}\psi(0)}{\Gamma(1-\beta)}$$

Fractional differential equation

$$D_t^\beta \psi(t) = \frac{d}{dt}\int_0^t d\tau\, \frac{(t-\tau)^{-\beta}}{\Gamma(1-\beta)}\psi(\tau)$$

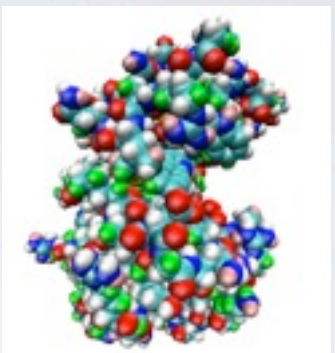
Self-similar relaxation dynamics of proteins

*The phenomenon of **self-similarity** on the time scale can be modeled by **stochastic processes with long-time memory**.*



FL/Anti-FL complex

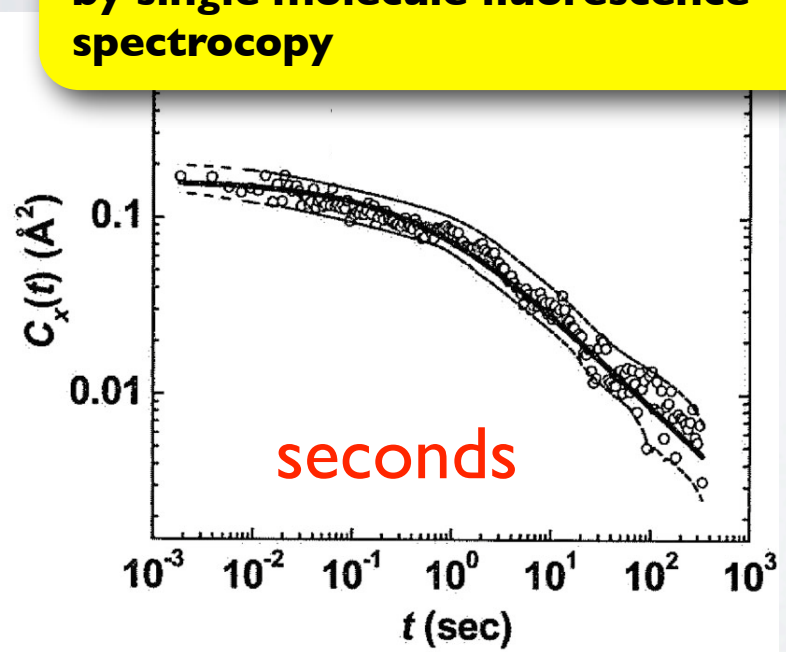
Min et al. PRL 94, 1983021



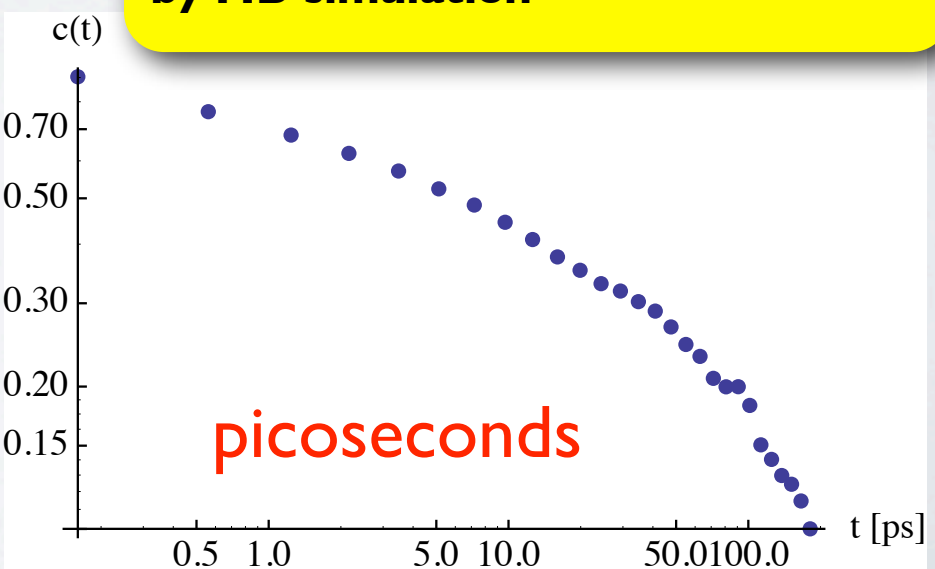
Lysozyme

G.R. Kneller,et al J Chem Phys 136, 191101 (2012).

Distance autocorrelation by single molecule fluorescence spectrocopy

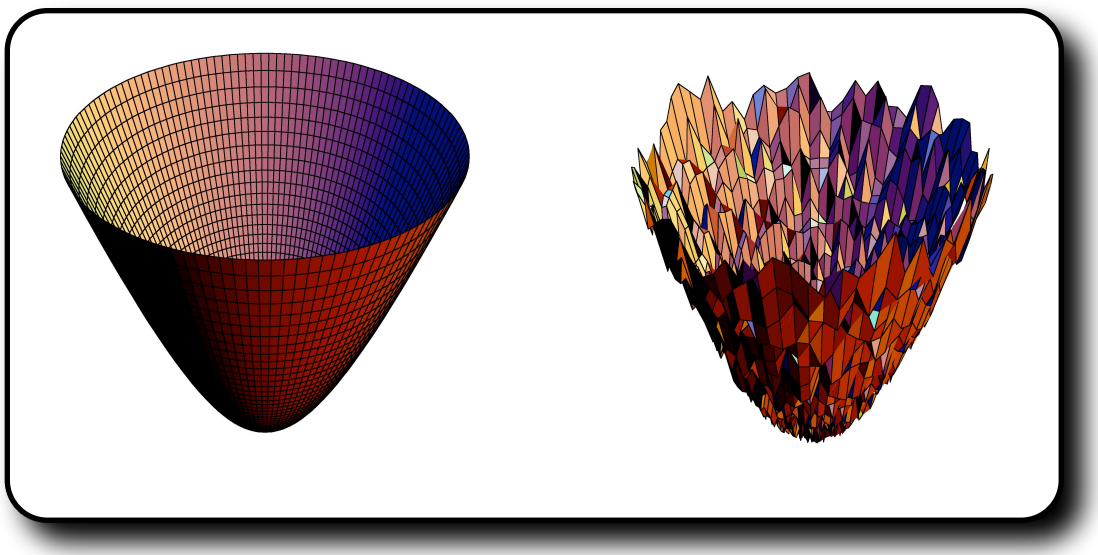


position-autocorrelation functions by MD simulation



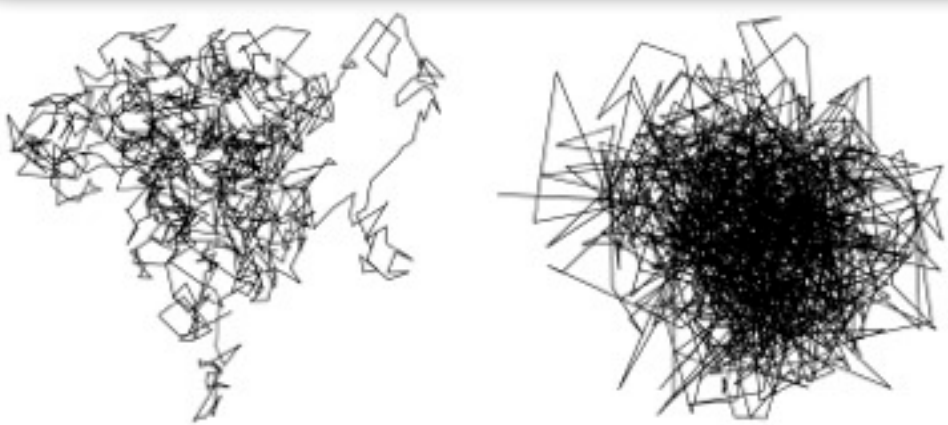
Fractional Ornstein-Uhlenbeck process as a simple model for atomic motions in proteins

smooth potential surface



"rugged" potential surface

Ornstein-Uhlenbeck process



Fractional Ornstein-Uhlenbeck process

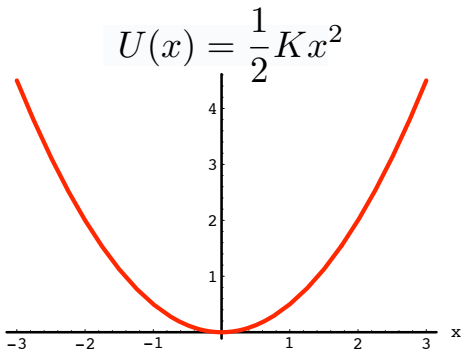
G.E. Uhlenbeck and L.S. Ornstein, Physical Review **36**, 823 (1930).

Y. Shao, Physica D: Nonlinear Phenomena **83**, 461 (1995).
R. Metzler and J. Klafter, Phys Rep **339**, 1 (2000).

Diffusion with long-time memory

- **Standard case**

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



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

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

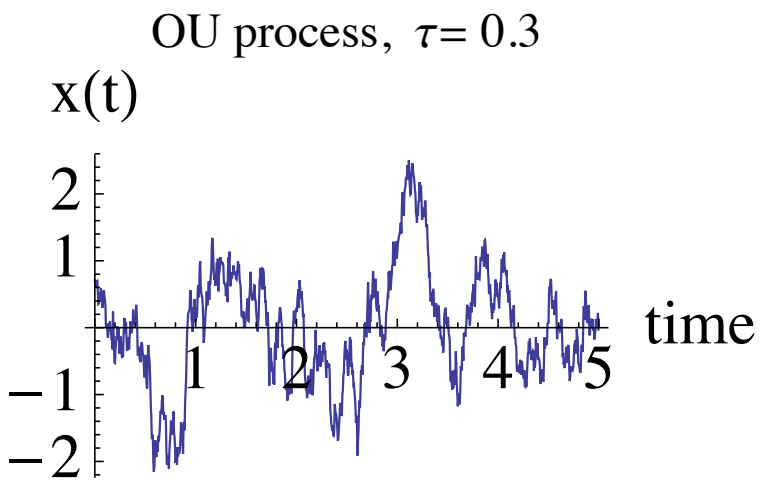
- **Fractional diffusion**

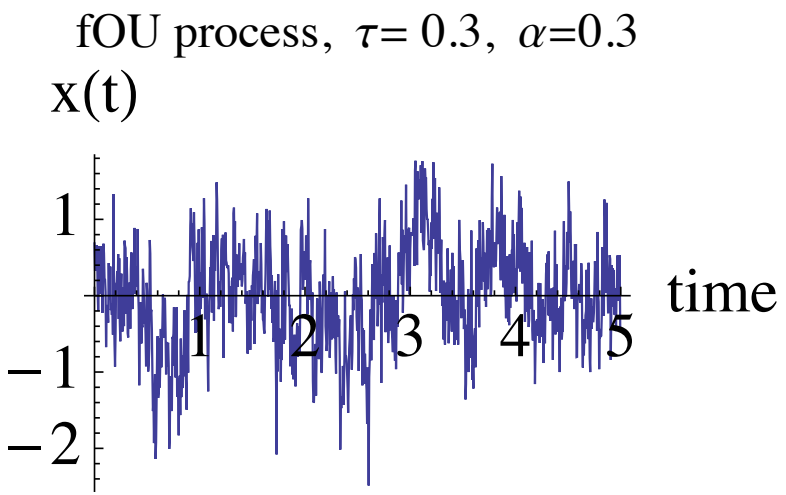
$$\frac{\partial P(x,t)}{\partial t} + \frac{\partial \tilde{J}(x,t)}{\partial x} = 0$$

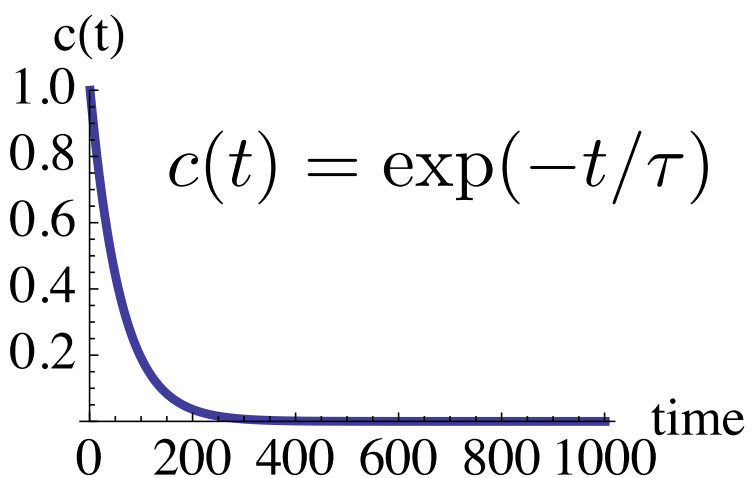
memory effects through fractional derivative

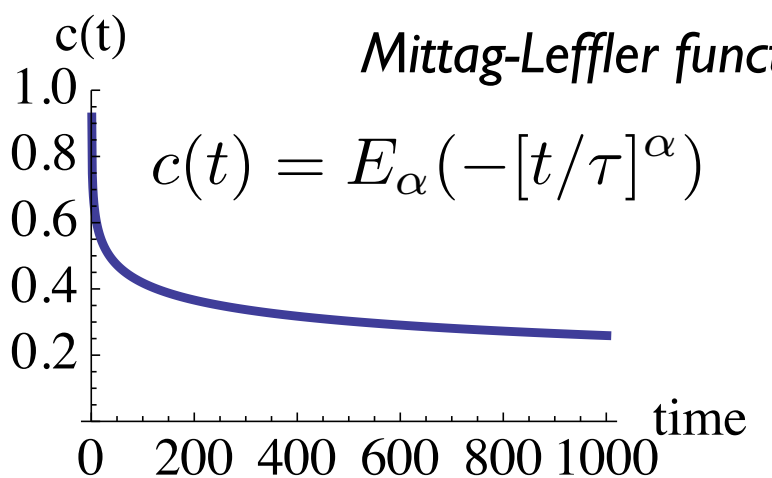
$$\tilde{J}(x,t) = \tilde{\tau}^{1-\alpha}\frac{d}{dt}\int_0^t d\tau \, \frac{(t-\tau)^{\alpha-1}}{\Gamma(\alpha)} J(x,\tau)$$

Time series and autocorrelation functions







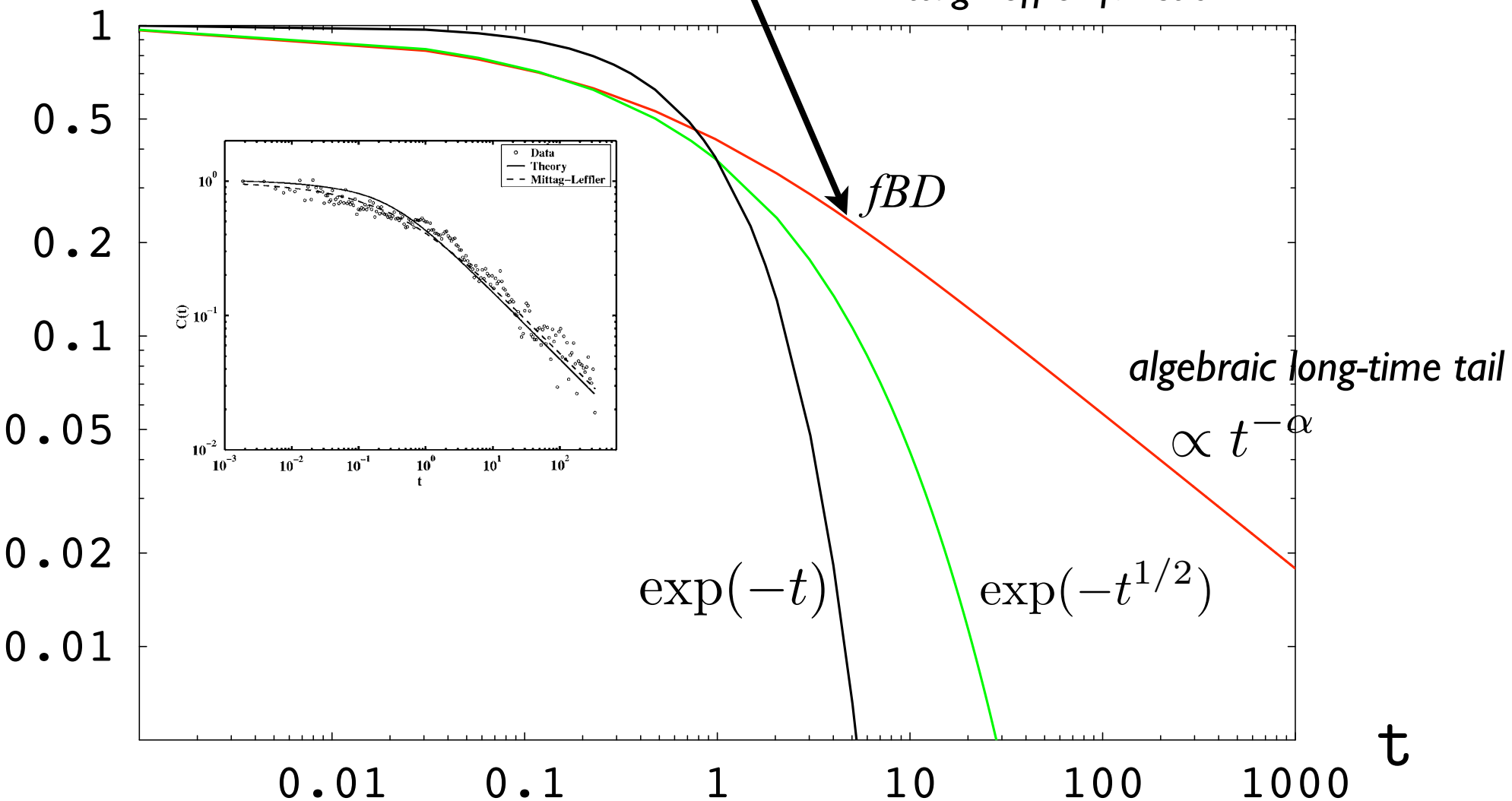


Model correlation function (α=0.5)

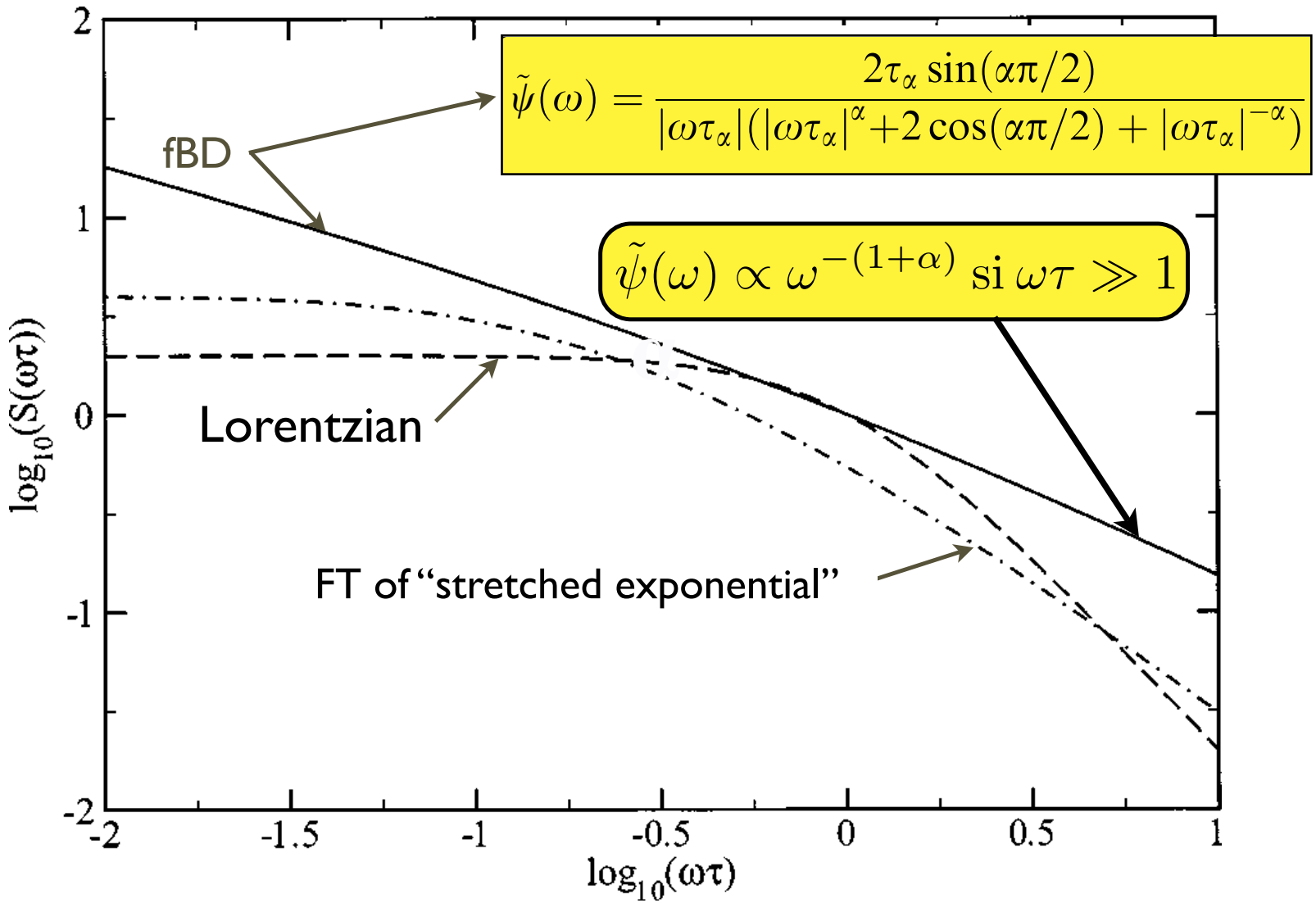
$$c_{xx}(t) = \langle x^2 \rangle E_\alpha(-[t/\tau]^\alpha)$$

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

Mittag-Leffler function



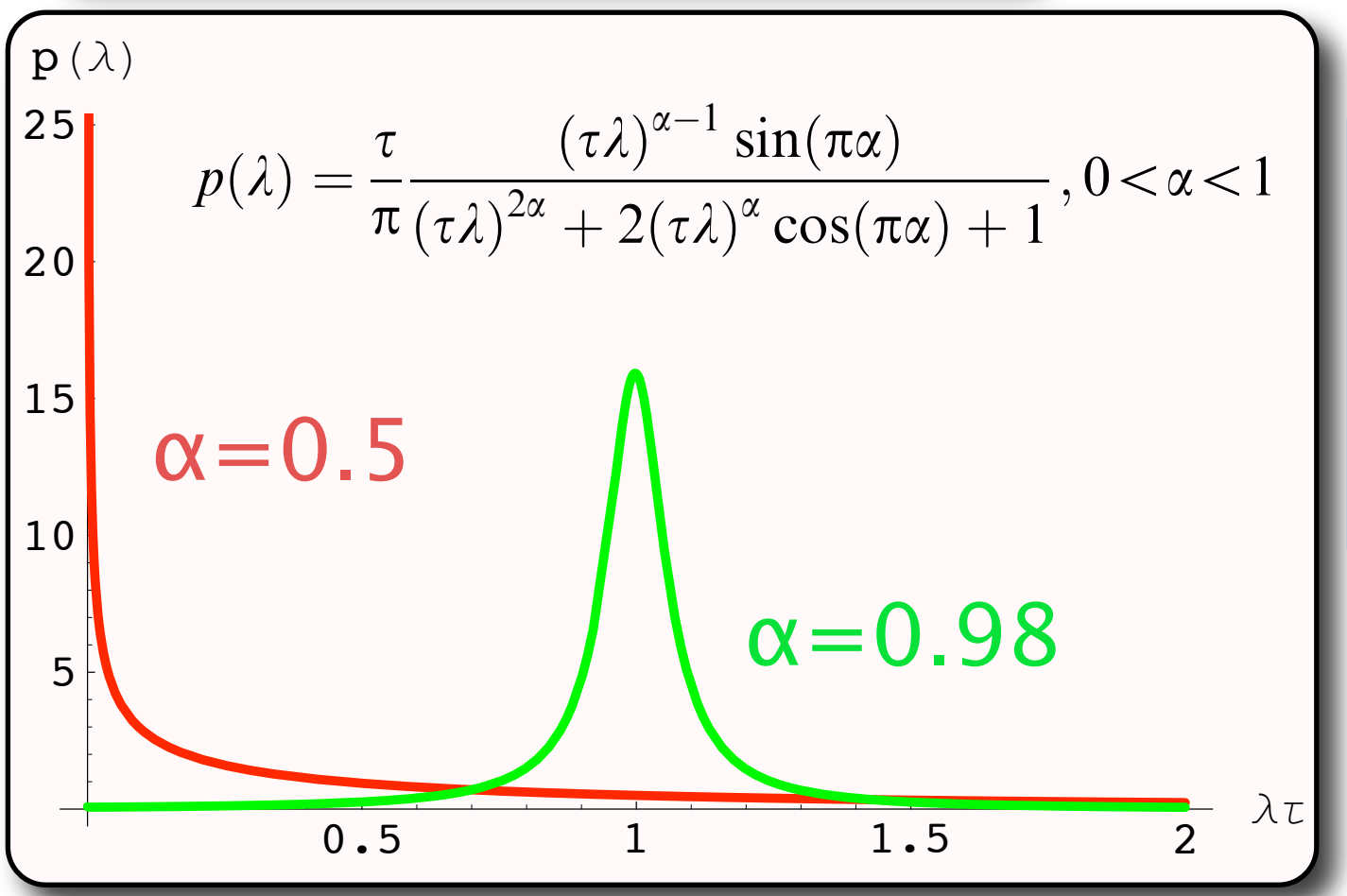
Self-similar «generalized» Lorentzian



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

Multiscale relaxation dynamics

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



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

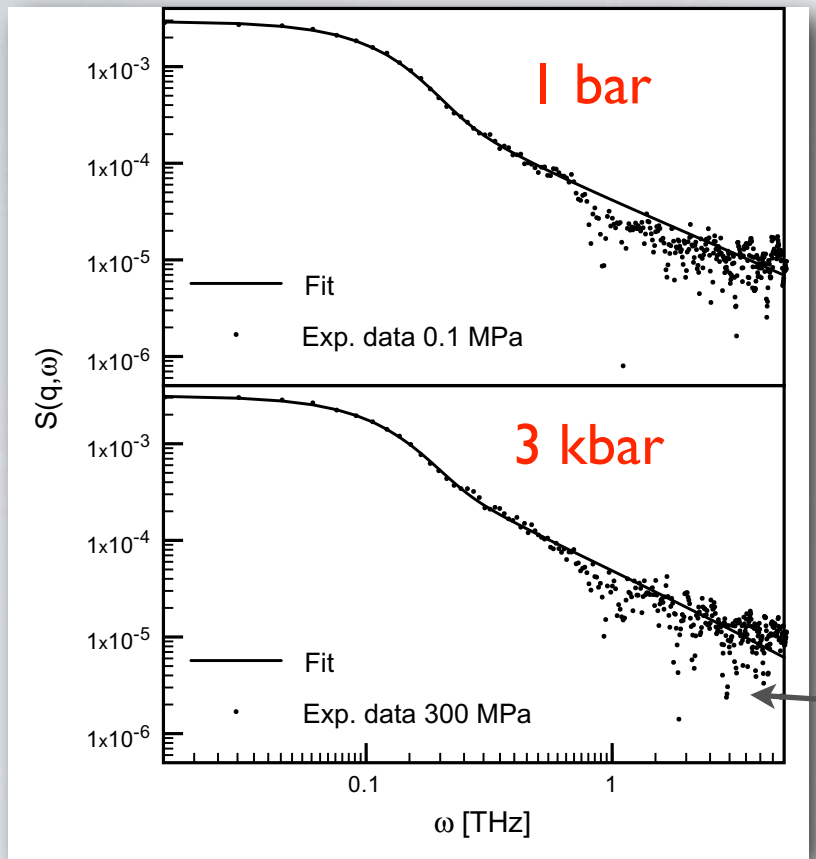
$$\int_0^{1/\tau} d\lambda\, p(\lambda) = 1/2$$

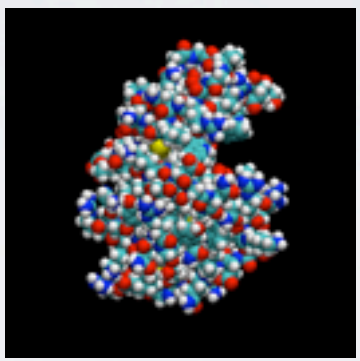
[1] W. Glöckle and T. Nonnenmacher, Biophysical Journal 68, 46 (1995).
[2] G.R. Kneller. *Physical Chemistry Chemical Physics*, 7:2641 – 2655, 2005.

Interpreting neutron

Neutron scattering

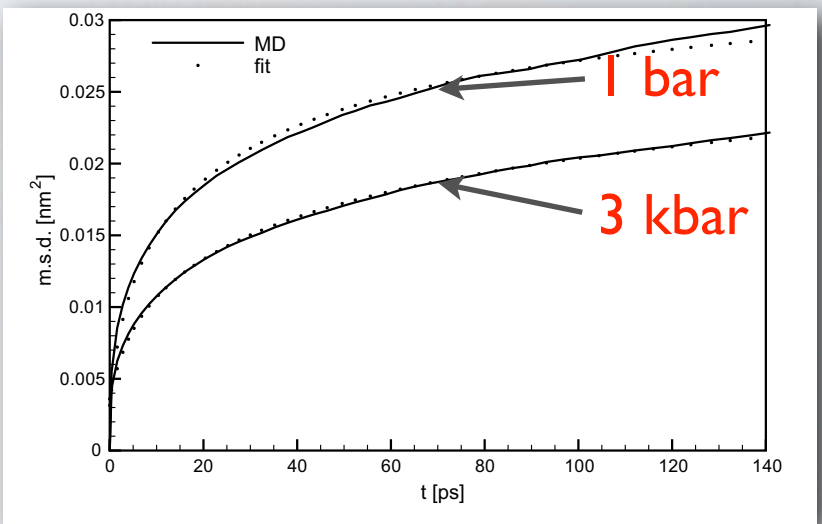
QENS dynamic structure factor





MD simulation

Mean square displacement <[x(t)-x(0)]^2> of the H atoms in lysozyme MD simulation



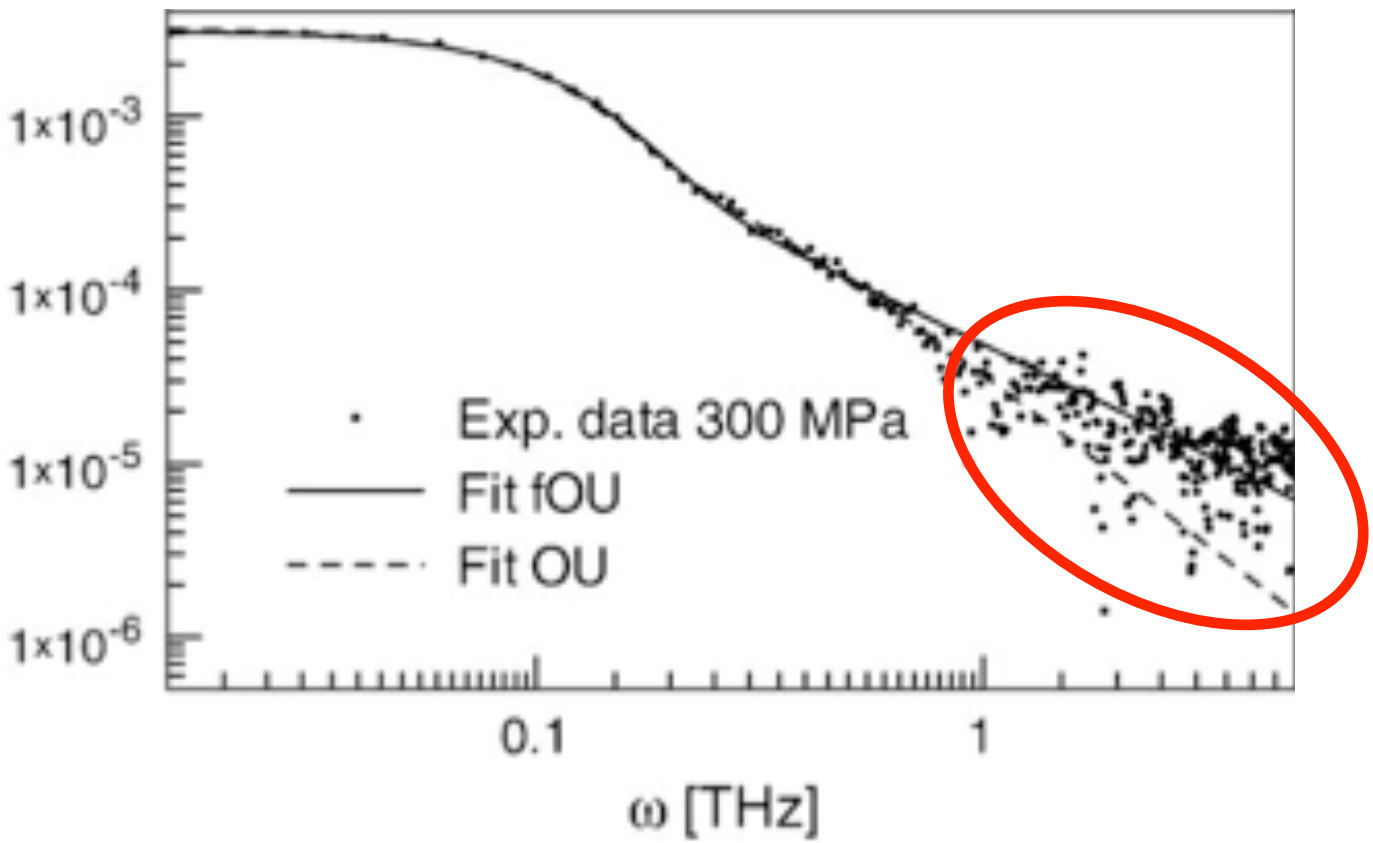
$$S(q,\omega) = \exp(-q^2\langle x^2\rangle)\left\{\delta(\omega) + \sum_{n=1}^{\infty} \frac{q^{2n}\langle x^2\rangle^n}{n!}\frac{1}{2\pi}L_\alpha(\omega;\tau_{\alpha,n})\right\}$$

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

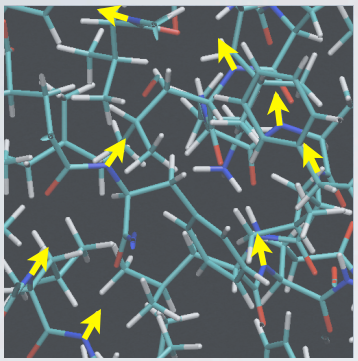
$$\tau_{\alpha,n} = \lambda_{\alpha,n}^{-(1/\alpha)}, \quad n \neq 0 \qquad \lambda_{\alpha,n} := \tilde{\tau}^{1-\alpha}\lambda_n \qquad \lambda_n = n\eta$$

- Calandrini, Kneller, *J. Chem. Phys.*, vol. 128, no. 6, p. 065102, 2008.
- Calandrini et al,, *Chem. Phys.*, vol. 345, pp. 289–297, 2008.
- Kneller, Calandrini, *Biochimica et Biophysica Acta,* vol. 1804, pp. 56–62, 2010.

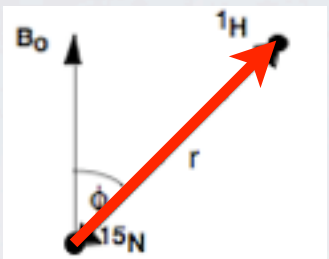
A fractional OU process fits better than a normal one ....



Protein dynamics & NMR



Relaxation $^{15}N - ^{1}H$



$$C_{ii}(t) = \langle P_2(\boldsymbol{\mu}_i(t) \cdot \boldsymbol{\mu}_i(0)) \rangle,$$

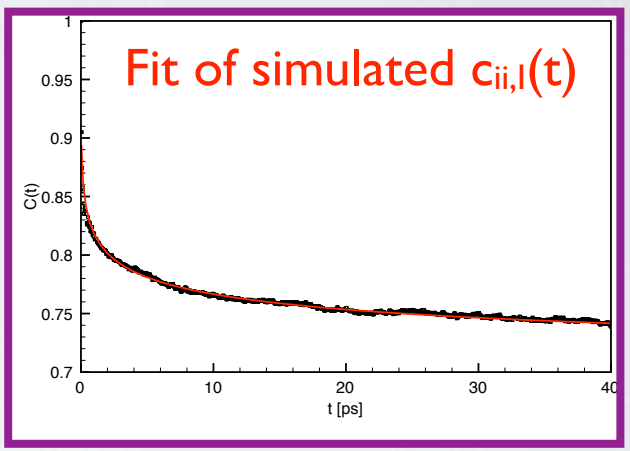
$$c_{ii}(t) = C_{ii,R}(t) C_{ii,I}(t)$$

Global rotation — Internal dynamics

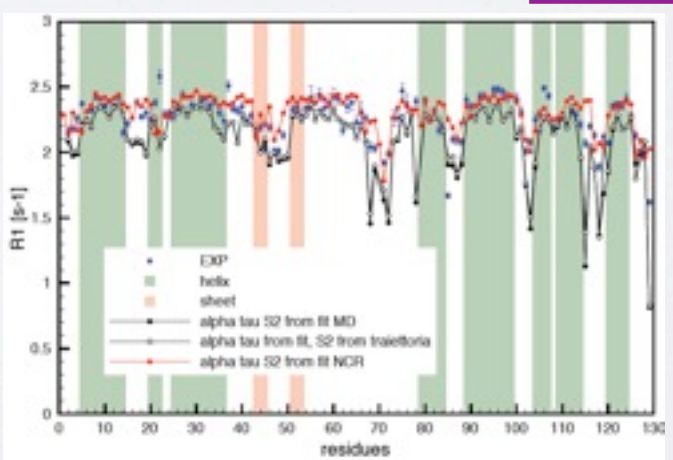
Model pour $c_{ii,I}(t)$:

$$c_{ii,I}(t) = S_{ii}^2 + (1 - S_{ii}^2) E_\alpha(-[t/\tau]^\alpha)$$

Mittag-Leffler function



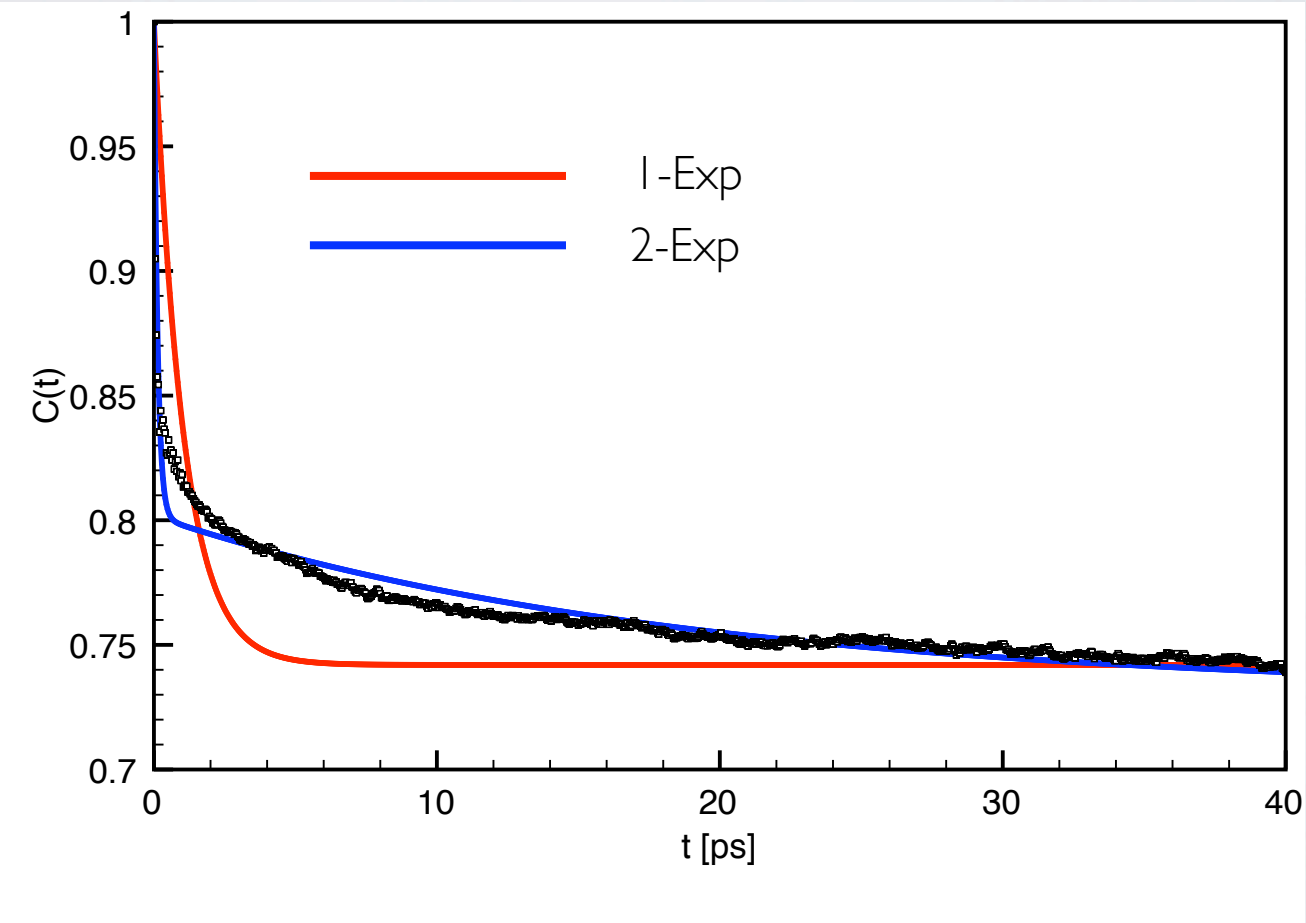
Prediction of Expérimental data (T1, T2, NOE)



- Calandrini, Abergel, Kneller, *J. Chem. Phys.*, vol. 128, p. 145102, 2008.
- Calandrini, Abergel, Kneller, *J. Chem. Phys.*, vol. 133, p. 145101, 2010.

Try fits with 1 & 2 exponentials ("model free", Liparo-Szabo)

Lysozyme, res 104



Limits of fractional Brownian dynamics and asymptotic modeling of anomalous diffusion

The fBD model correlation functions have the experimentally observed power law decay, but they are not analytic and thus unphysical at t=0.

$$\left.\frac{d^n c(t)}{dt^n}\right|_{t=0} = (-1)^n \infty$$

Consider "normal" and "anomalous" relaxation and diffusion as **asymptotic** form of relaxation and diffusion processes, respectively.

Asymptotic form of the mean square displacement

$$W(t) = \langle (\mathbf{x}(t) - \mathbf{x}(0))^2 \rangle$$

Mean square displacement

$$W(t) \overset{t\to\infty}{\sim} 2D_\alpha L(t) t^\alpha \quad (0 \le \alpha < 2)$$

$$\lim_{t\to\infty} L(t) = 1, \qquad \lim_{t\to\infty} t\frac{dL(t)}{dt} = 0.$$

Slowly growing function

- Anomalous free diffusion for $\alpha \neq 1$
- Anomalous confined diffusion for $\alpha = 0$

and $\dfrac{1}{L(t)} - 1 \overset{t\to\infty}{\sim} t^{-\beta}$ with $0 < \beta \le 1$

Slow approach of W(∞)

Using a theorem from asymptotic analysis

Journal für die Reine und Angewandte Mathematik (Crelle's Journal) **1931**, 27–39 (1931).

Neuer Beweis und Verallgemeinerung der Tauberschen Sätze, welche die Laplacesche und Stieltjessche Transformation betreffen.

Von *J. Karamata* in Belgrad.

Laplace transform

$$W(t) \overset{t\to\infty}{\sim} 2D_\alpha L(t)t^\alpha \quad \Leftrightarrow \quad \hat{W}(s) \overset{s\to 0}{\sim} 2D_\alpha L(1/s)\frac{\Gamma(\alpha+1)}{s^{\alpha+1}}$$

$$W(t) = 2\int_0^t dt'\,(t-t')c_{vv}(t') \quad \Leftrightarrow \quad \hat{W}(s) = \int_0^\infty dt\,\exp(-st)W(t) = \frac{2\hat{c}_{vv}(s)}{s^2}$$

velocity autocorrelation function

$$c_{vv}(t) = \langle \mathbf{v}(t)\cdot\mathbf{v}(0)\rangle$$

Define the fractional diffusion constant

Asymptotic form of the VACF

G. Kneller, *J. Chem. Phys.*, vol. 134, p. 224106, 2011.

Diffusion and the generalized Langevin equation

$$W(t) = 2\int_0^t dt'\,(t-t')c_{vv}(t')$$

Velocity autocorrelation function

$$c_{vv}(t) = \langle \mathbf{v}(t)\cdot\mathbf{v}(0)\rangle$$

Generalized Langevin equation

$$\dot{\mathbf{v}}(t) = -\int_0^t dt'\,\kappa(t-t')\mathbf{v}(t') + \mathbf{f}^{(+)}(t)$$

Memory kernel

$$\langle \mathbf{v}(t)\cdot\mathbf{f}^{(+)}(t')\rangle = 0$$

$$\partial_t c_{vv}(t) = -\int_0^t dt'\,c_{vv}(t-t')\kappa(t')$$

R. Zwanzig, *Nonequilibrium statistical mechanics*. Oxford University Press, 2001.

Interpretation of the memory function as a «cage»

$$\dot{\mathbf{v}}(t) = -\int_0^t dt'\, \kappa(t-t')\mathbf{v}(t') + \mathbf{f}^{(+)}(t)$$

$$\kappa(t) \equiv \Omega^2 \Rightarrow c_{vv}(t) = \langle v^2 \rangle \cos \Omega t$$

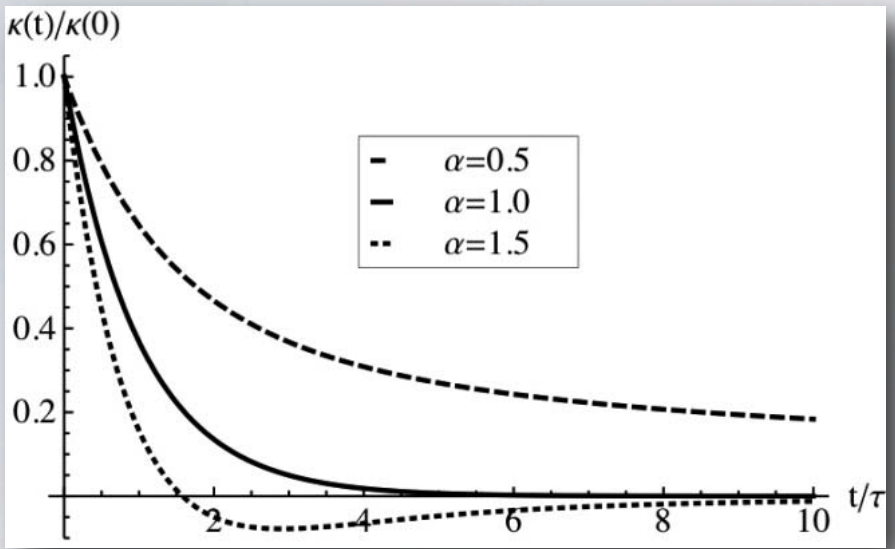
special choice of constant memory

oscillatory «rattling» motions in the «cage» of nearest neighbors

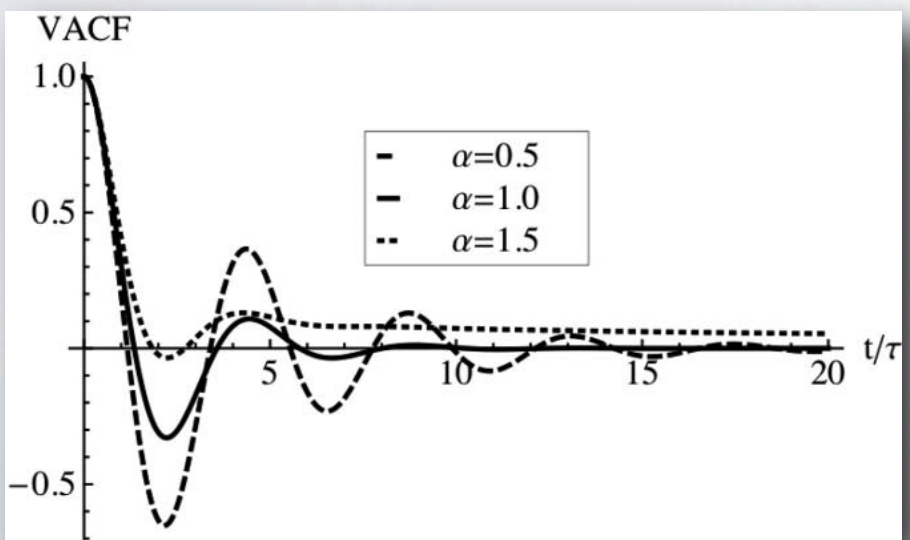
The asymptotic decay of this cage determines the type of diffusion which is observed (normal, anomalous).

Free diffusion for a model system

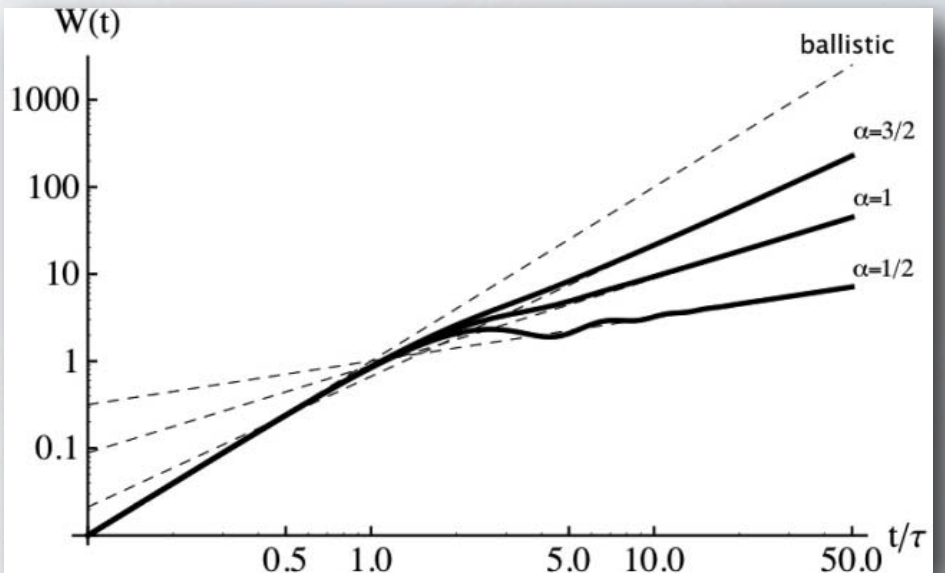
memory $\kappa_f(t) = \Omega^2 M(\alpha, 1, -t/\tau),$



VACF



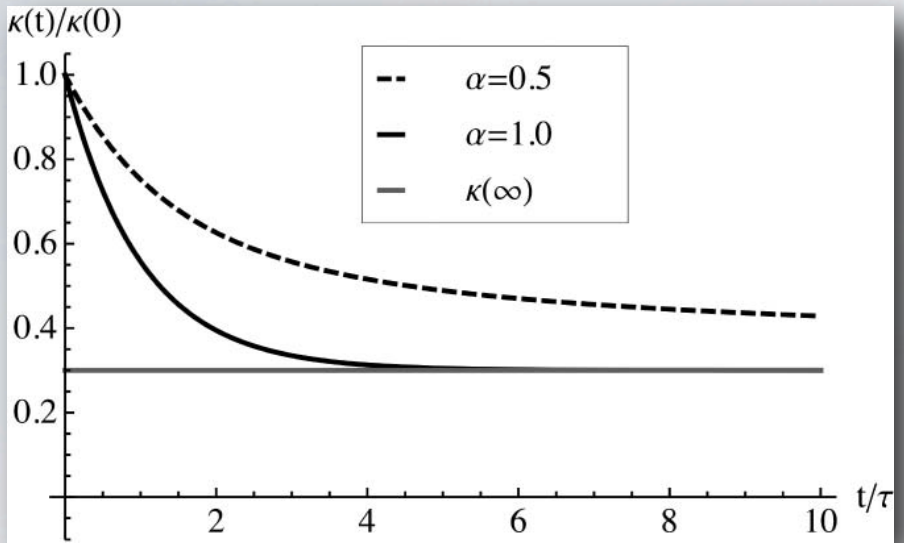
MSD



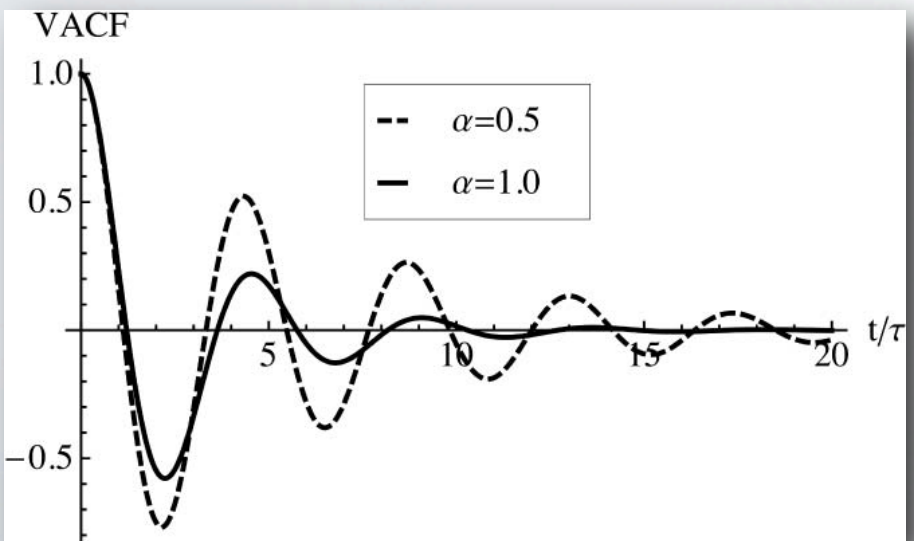
Confined diffusion for a model system

memory

$$\kappa_c(t) = \Omega^2 \{r + (1-r)M(\beta, 1, -t/\tau)\}$$



VACF



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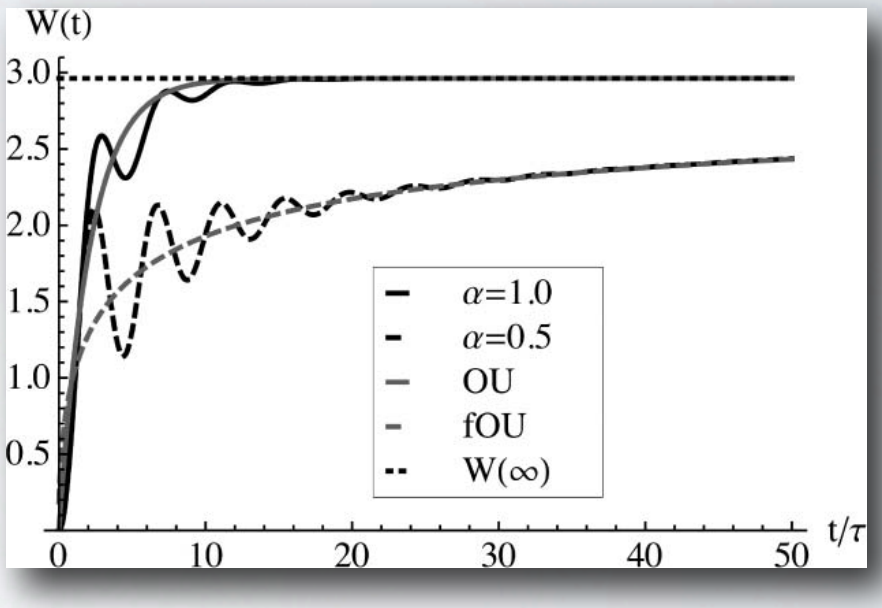


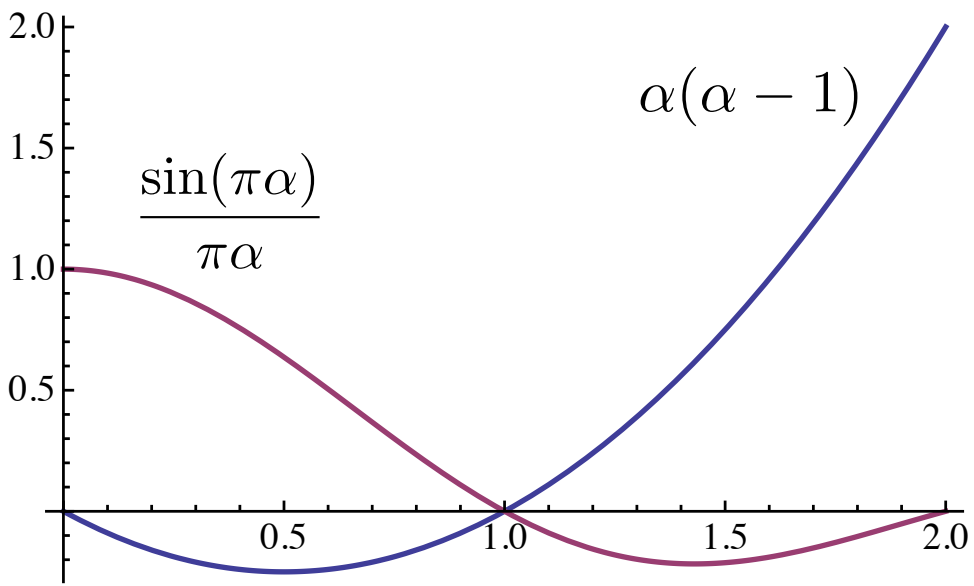
Conditions for anomalous diffusion

$$c_{vv}(t) \overset{t\to\infty}{\sim} D_\alpha \alpha(\alpha-1) L(t) t^{\alpha-2},$$

also sufficient for $1 < \alpha < 2$

$$\kappa(t) \overset{t\to\infty}{\sim} \frac{\langle \mathbf{v}^2 \rangle}{D_\alpha} \frac{\sin(\pi\alpha)}{\pi\alpha} \frac{1}{L(t)} t^{-\alpha}.$$

also sufficient for $0 < \alpha < 1$



Signs of the VACF and its memory function

Fractional diffusion constant

$$\hat{c}_{vv}(s) \overset{s\to 0}{\sim} D_\alpha \Gamma(\alpha+1) L(1/s) s^{1-\alpha}.$$

$$\Rightarrow \quad D_\alpha = \lim_{s\to 0} s^{\alpha-1}\hat{c}_{vv}(s)/\Gamma(1+\alpha).$$

Generalized Kubo relation

$$\Rightarrow \quad D_\alpha = \frac{1}{\Gamma(1+\alpha)} \int_0^\infty dt \; {}_0\partial_t^{\alpha-1} c_{vv}(t).$$

Fractional relaxation constant

$$\hat{\kappa}(s) \overset{s\to 0}{\sim} \frac{\langle \mathbf{v}^2 \rangle}{D_\alpha \Gamma(\alpha+1)} \frac{s^{\alpha-1}}{L(1/s)}.$$

$$\eta_\alpha = \Gamma(1+\alpha) \lim_{s\to 0} s^{1-\alpha} \hat{\kappa}(s),$$

Generalized Kubo relation

$$\eta_\alpha = \Gamma(1+\alpha) \int_0^\infty dt \; {}_0\partial_t^{1-\alpha} \kappa(t)$$

Fractional fluctuation-dissipation theorem

$$D_\alpha = \frac{\langle \mathbf{v}^2 \rangle}{\eta_\alpha}.$$

Fluctuation

Dissipation

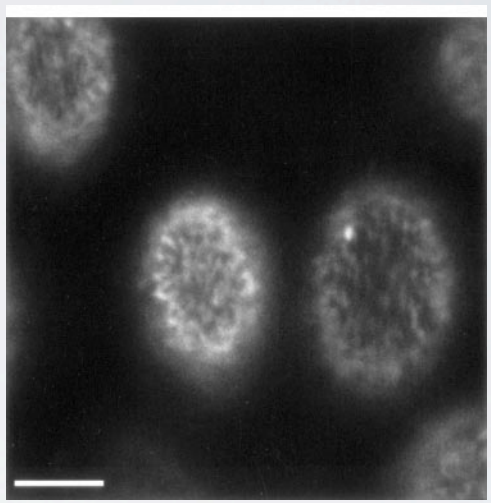
G. Kneller, *J. Chem. Phys.*, vol. 134, p. 224106, 2011.

Anomalous lateral diffusion In lipid bilayers on the ms-s time scale

Cytometry 36:176–182 (1999)

Fluorescence Correlation Spectroscopy With Single-Molecule Sensitivity on Cell and Model Membranes

Petra Schwille,* Jonas Korlach, and Watt W. Webb
Cornell University, School of Applied and Engineering Physics, Ithaca, New York



$$\langle \Delta r^2 \rangle = \Gamma \tau^{\alpha}$$

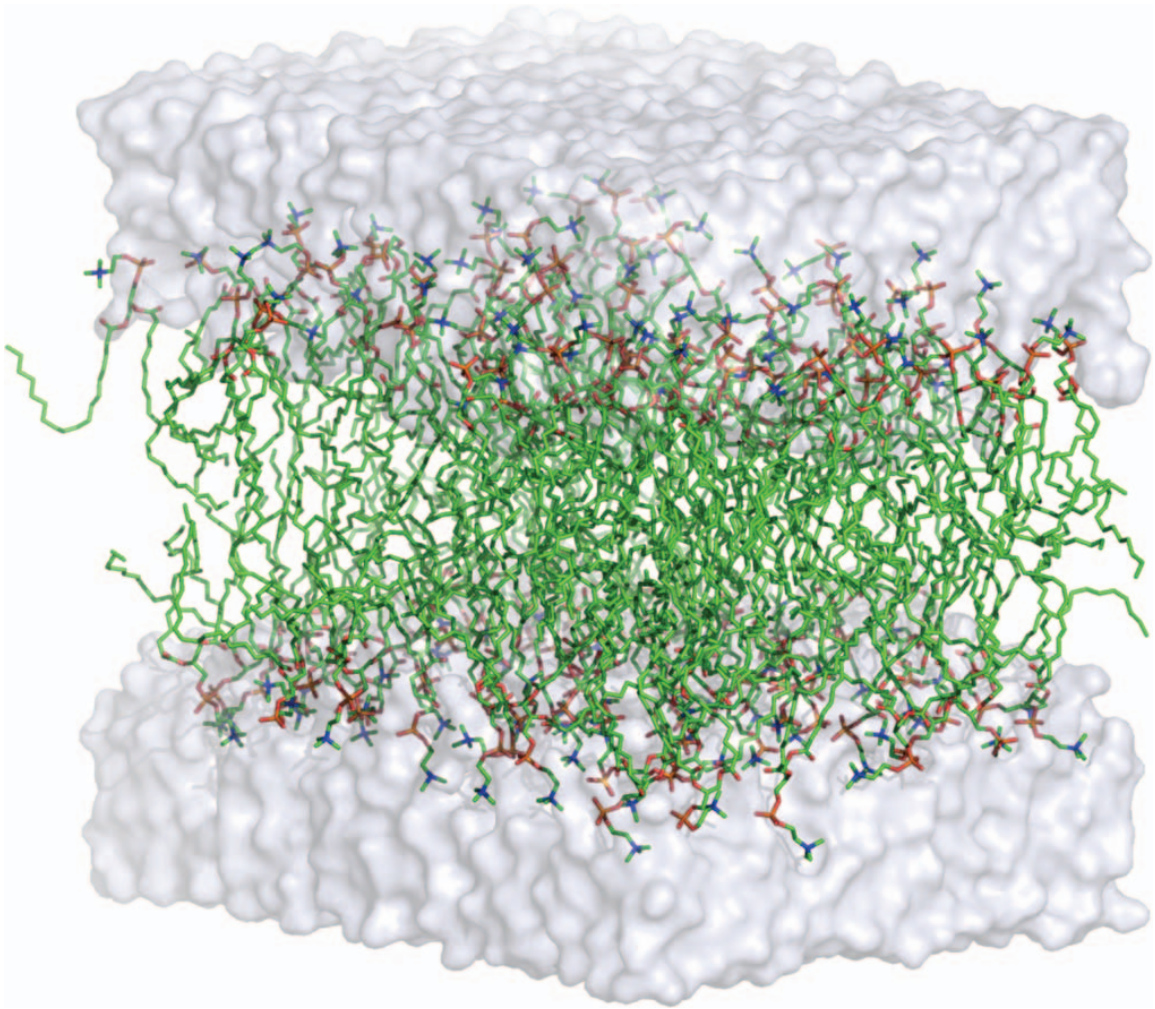
$$P[\underline{r}', (t+\tau)|\underline{r},t] = \frac{1}{(4\pi D\tau)^{n/2}} e^{\frac{-(\underline{r}-\underline{r}')^2}{4D\tau}}$$

Normal Brownian motion

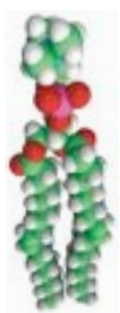
$$P_{anom}[\underline{r}', (t+\tau)|\underline{r}, t] = \frac{1}{(\pi\Gamma\tau^{\alpha})^{n/2}} e^{\frac{-(\underline{r}-\underline{r}')^2}{\Gamma\tau^{\alpha}}}$$

Anomalous Brownian motion

Lateral subdiffusion in a DOPC membrane by MD simulation



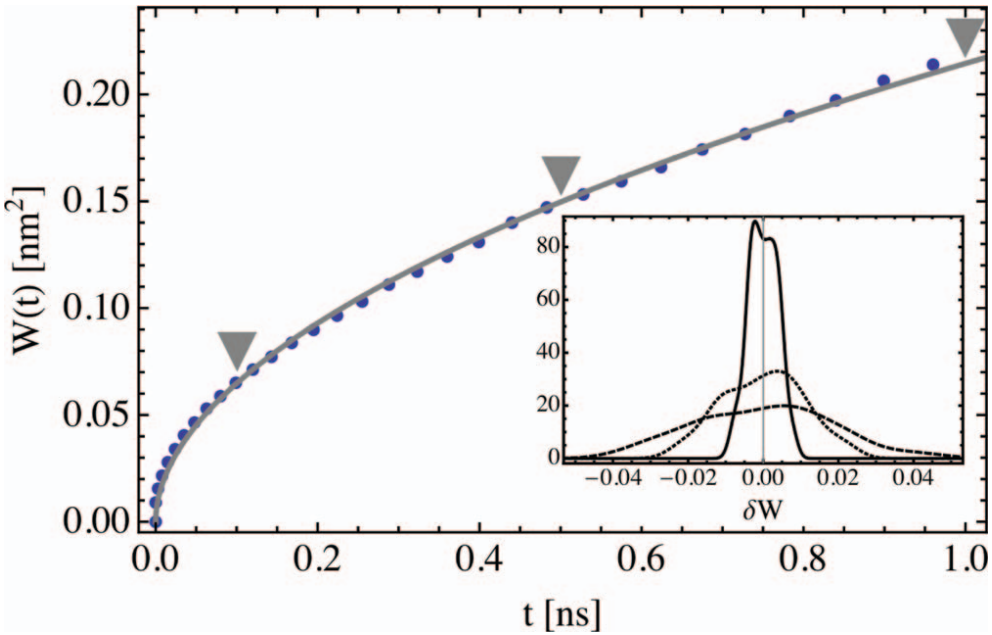
Simulated system consisting of a bilayer of 2 × 64 DOPC lipid molecules and 3840 water molecules (light-grey).



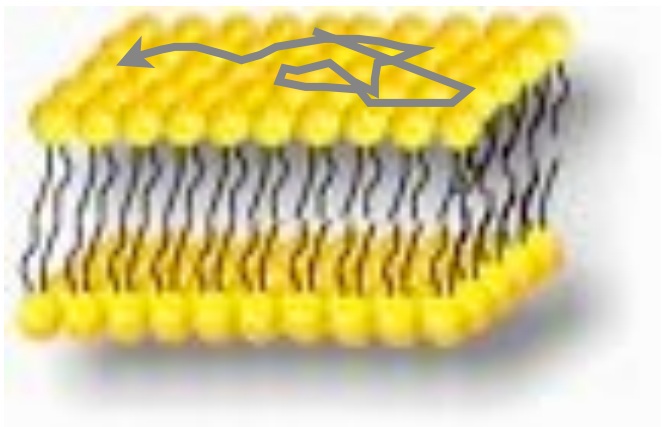
DOPC molecule

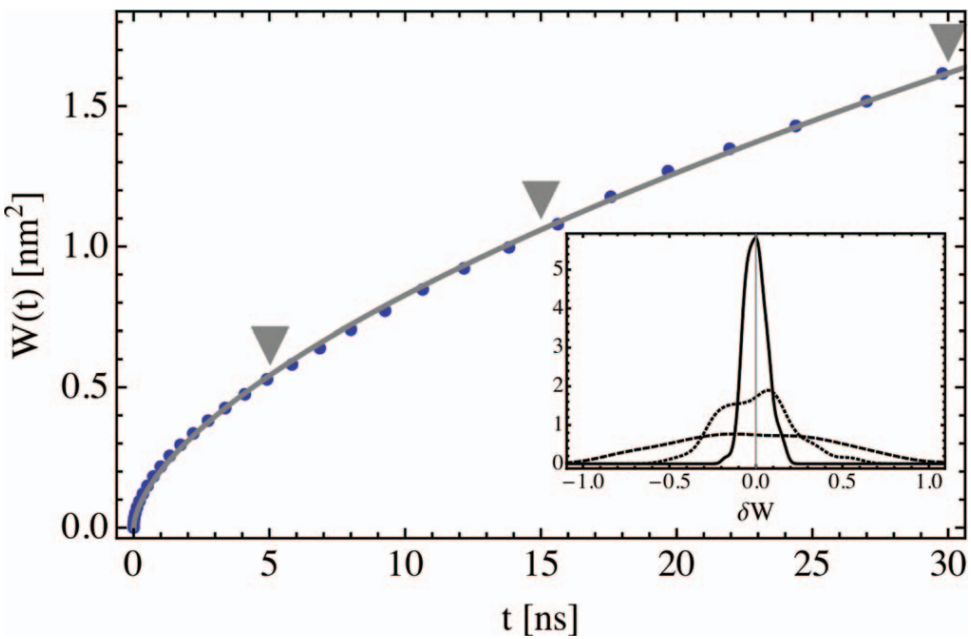
G. R. Kneller, K. Baczynski, and M. Pasenkiewicz-Gierula. *J. Chem. Phys.*, 135(14):141105, 2011.

Lateral mean square displacements



$D_\alpha = 0.107\ nm^2/ns^\alpha$ for $\alpha = 0.52$.

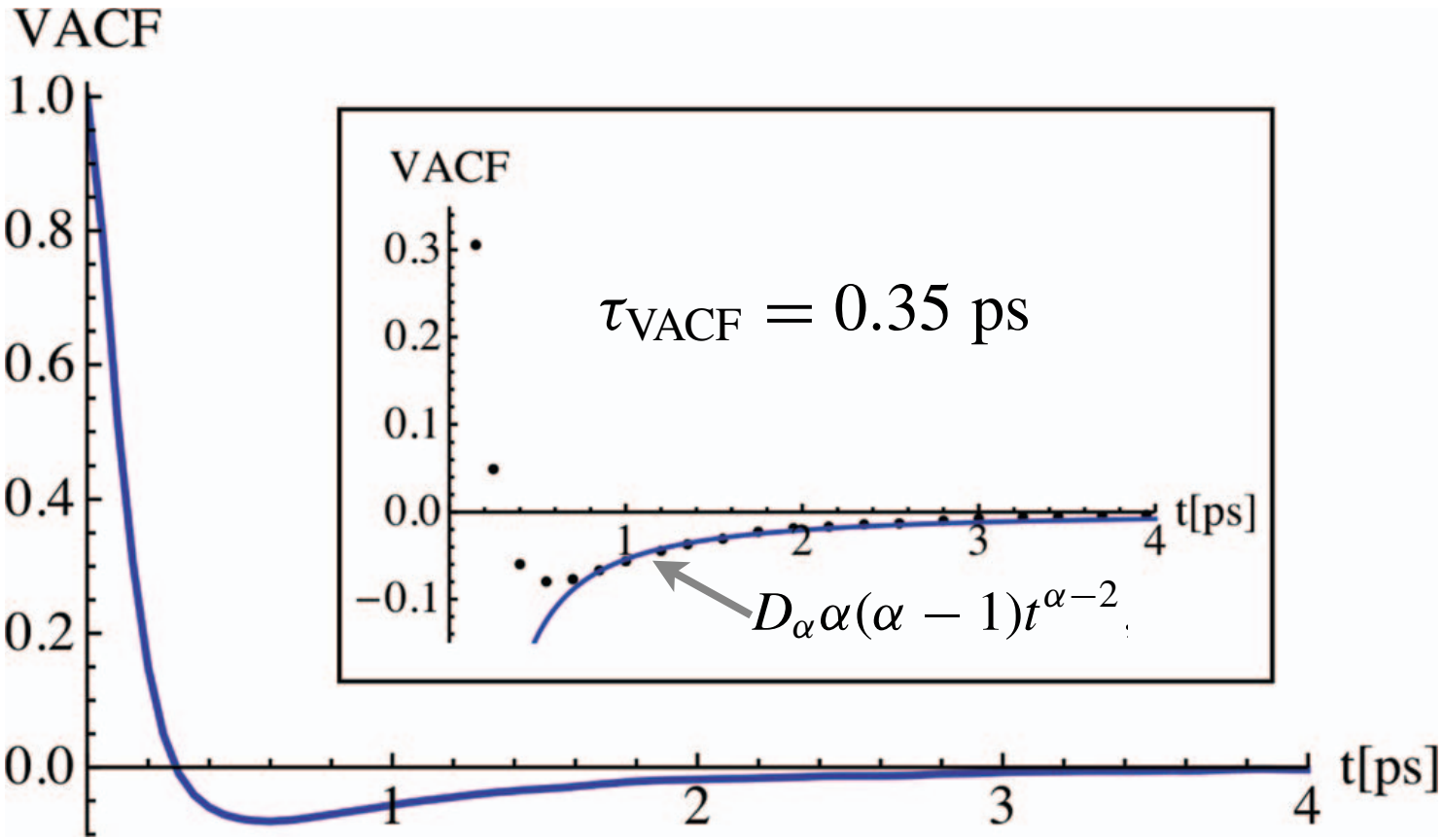




$D_\alpha = 0.101\ nm^2/ns^\alpha$ for $\alpha = 0.61$.

Experimental value for DLPC:
$D_\alpha = 0.088 \pm 0.007\ nm^2/ns^\alpha$
for $\alpha = 0.74 \pm 0.08$.

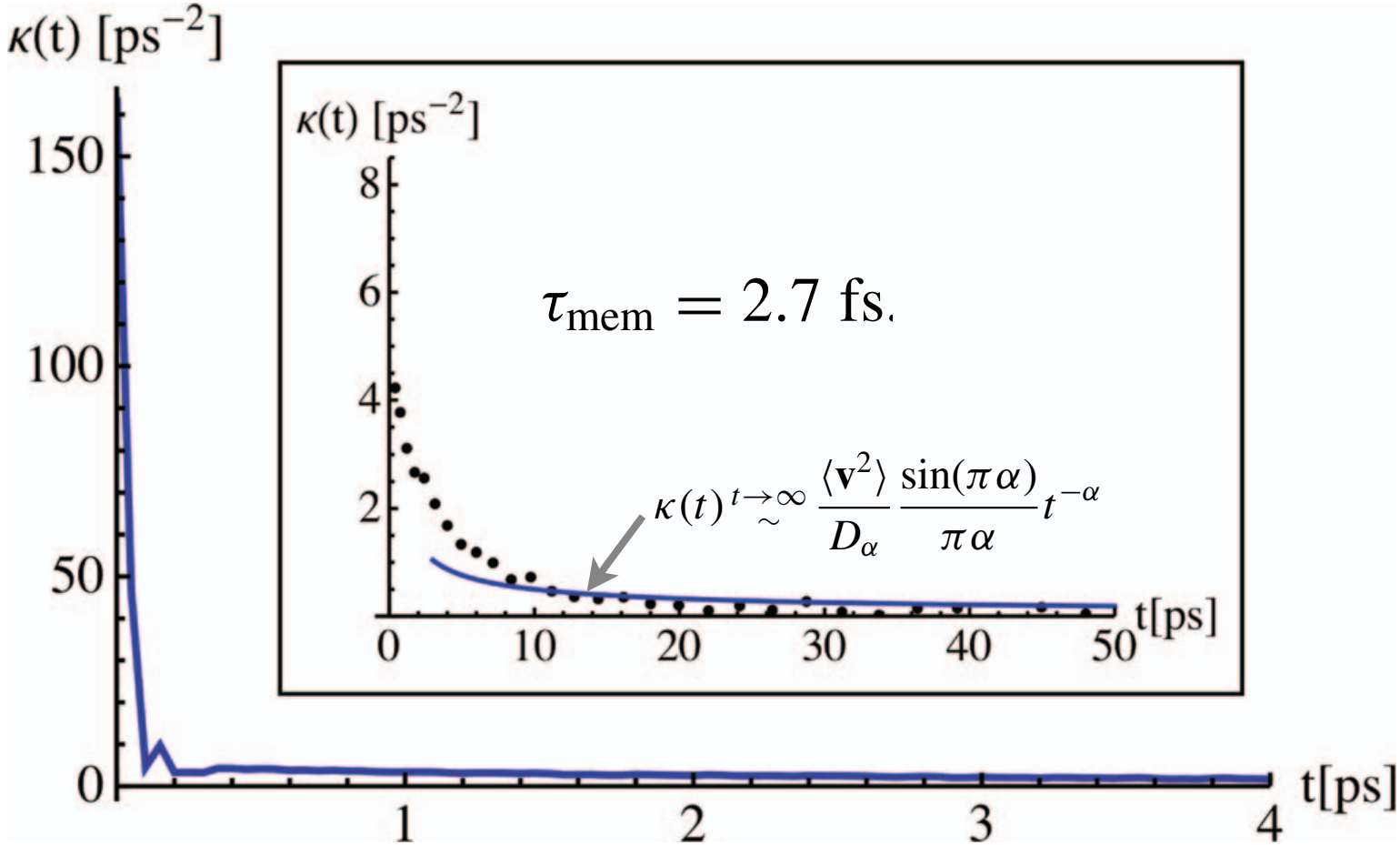
Velocity autocorrelation function of the DOPC bilayer :



Characteristic time scale:

$$\tau_{\mathrm{VACF}} = \left(\frac{D_\alpha}{\langle \mathbf{v}^2 \rangle} \right)^{1/(2-\alpha)}$$

Memory kernel of the VACF



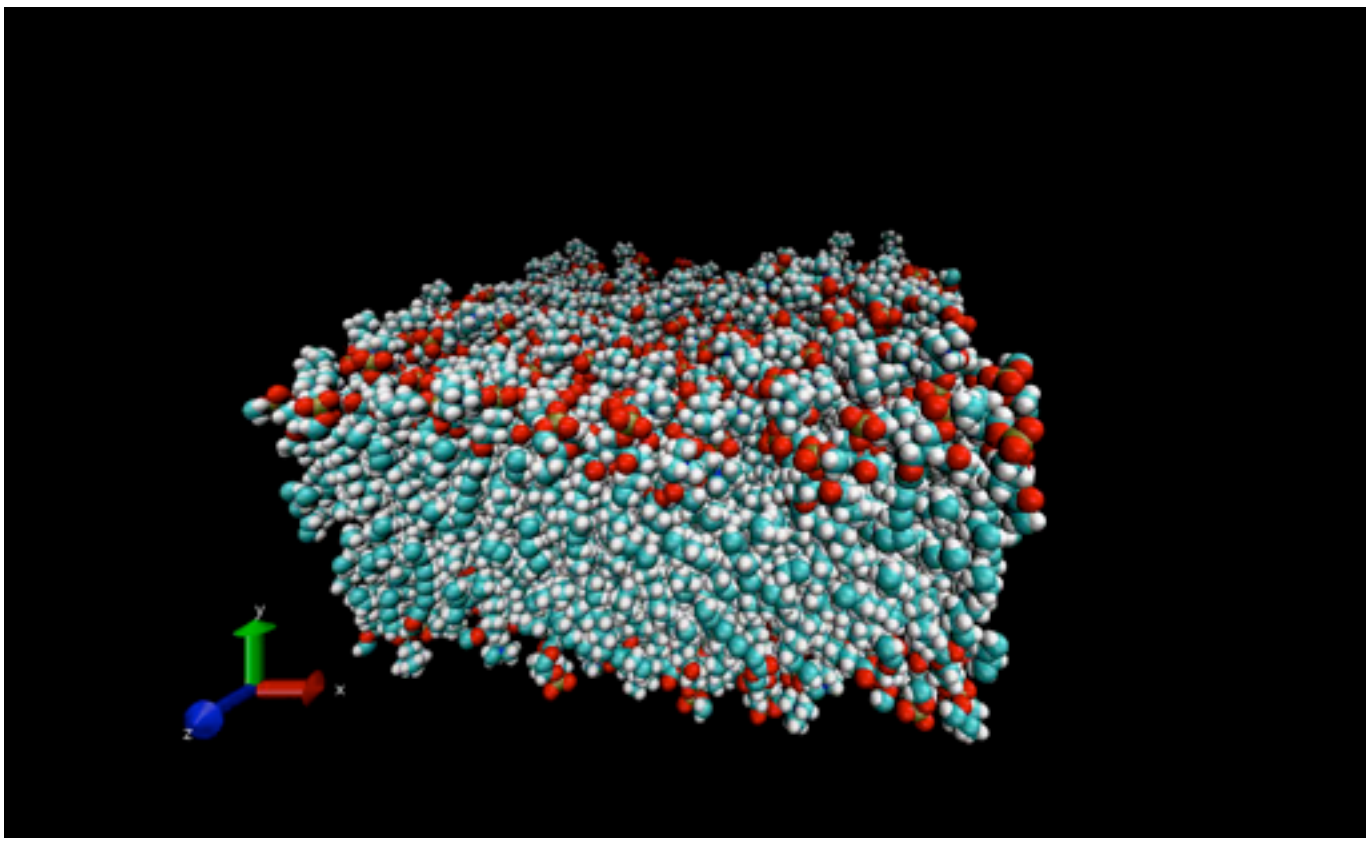
Characteristic time scale:

$$\tau_{\mathrm{mem}} = \left(\frac{\eta_\alpha}{\Omega^2} \right)^{1/\alpha}$$

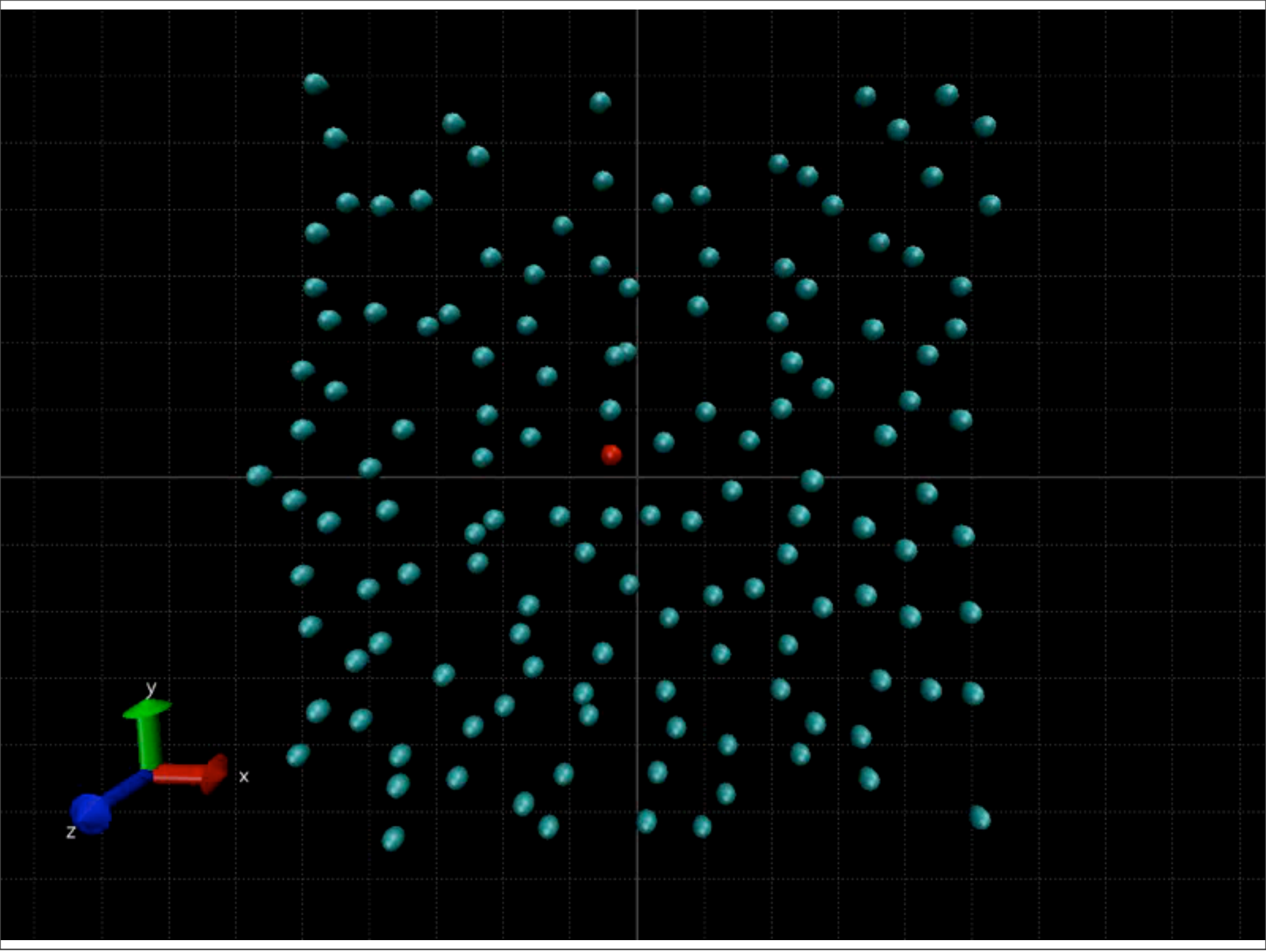
$$\eta_\alpha = \frac{\langle \mathbf{v}^2 \rangle}{D_\alpha}$$

$$\Omega \equiv \sqrt{\kappa(0)}.$$

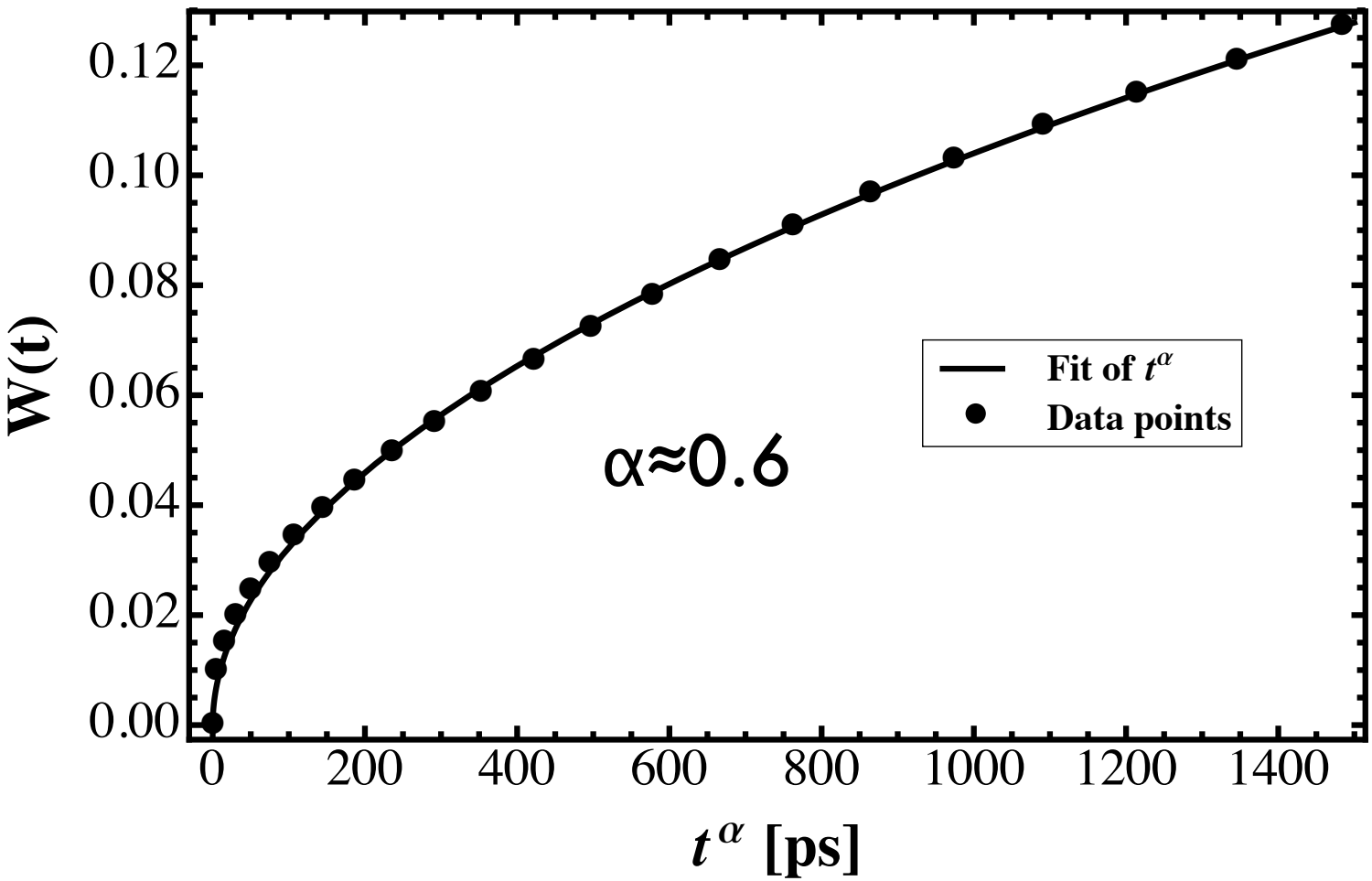
Cage effect for lateral subdiffusion in a POPC bilayer



- 2x137 POPC molecules (10 nm × 10 nm in the XY-plane)
- 10471 water molecules (fully hydrated)
- OPLS force field
- T=310 K


y
x
z

The average lateral MSD



Mean Square Displacement of POPC lipids after 15ns simulation (dots) and fit of the model for anomalous diffusion (thick line).

Van Hove correlation function and the „cage" of nearest neighbours

- The pair Distribution Function (PDF), g(r), is proportional to the probability of finding a particle between distances „r+dr", from a tagged central particle in a liquid.
- Time-dependent PDFs (van Hove PDFs), $G_D(r,t)$, display the dynamic structure in a liquid.

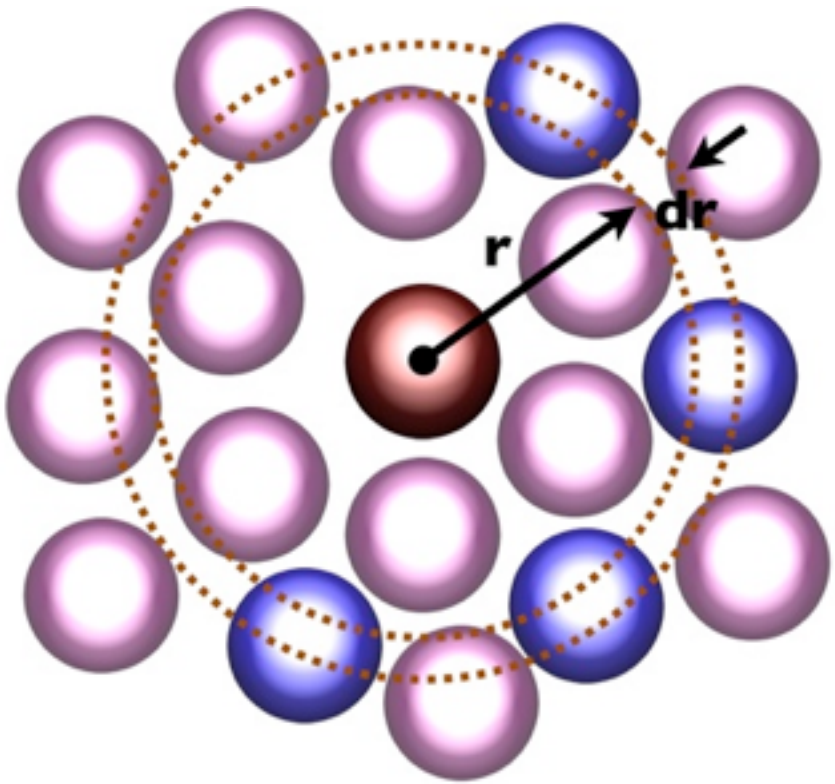
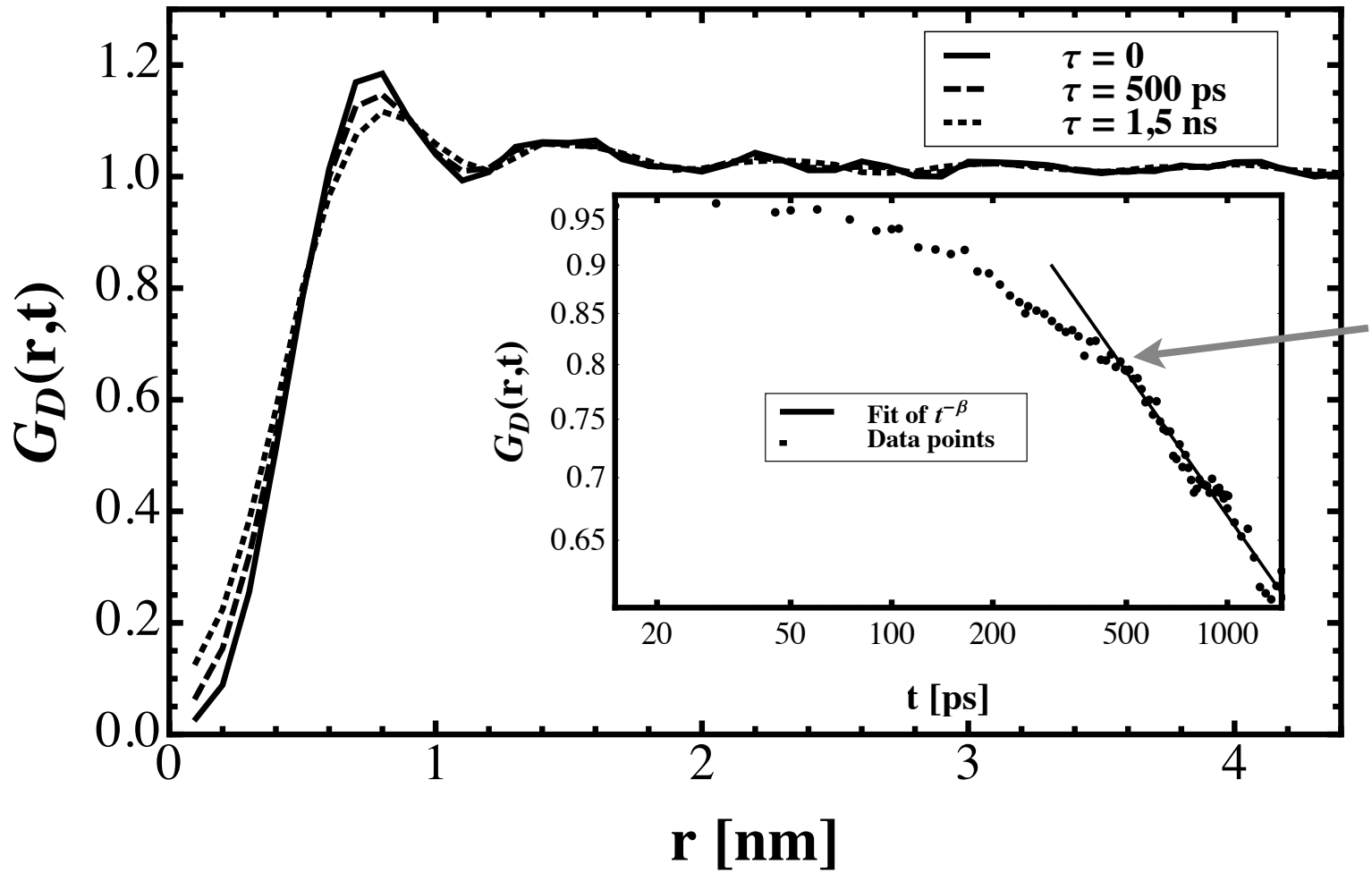


Image: "The structure of the cytoplasm" from Molecular Biology of the Cell. Adapted from D.S. Goodsell, Trends Biochem. Sci. 16:203-206, 1991.

- (Van Hove) PDFs can be obtained from scattering experiments (neutron scttering, inelastic X-ray scattering)

Time-dependent pair correlation function for POPC

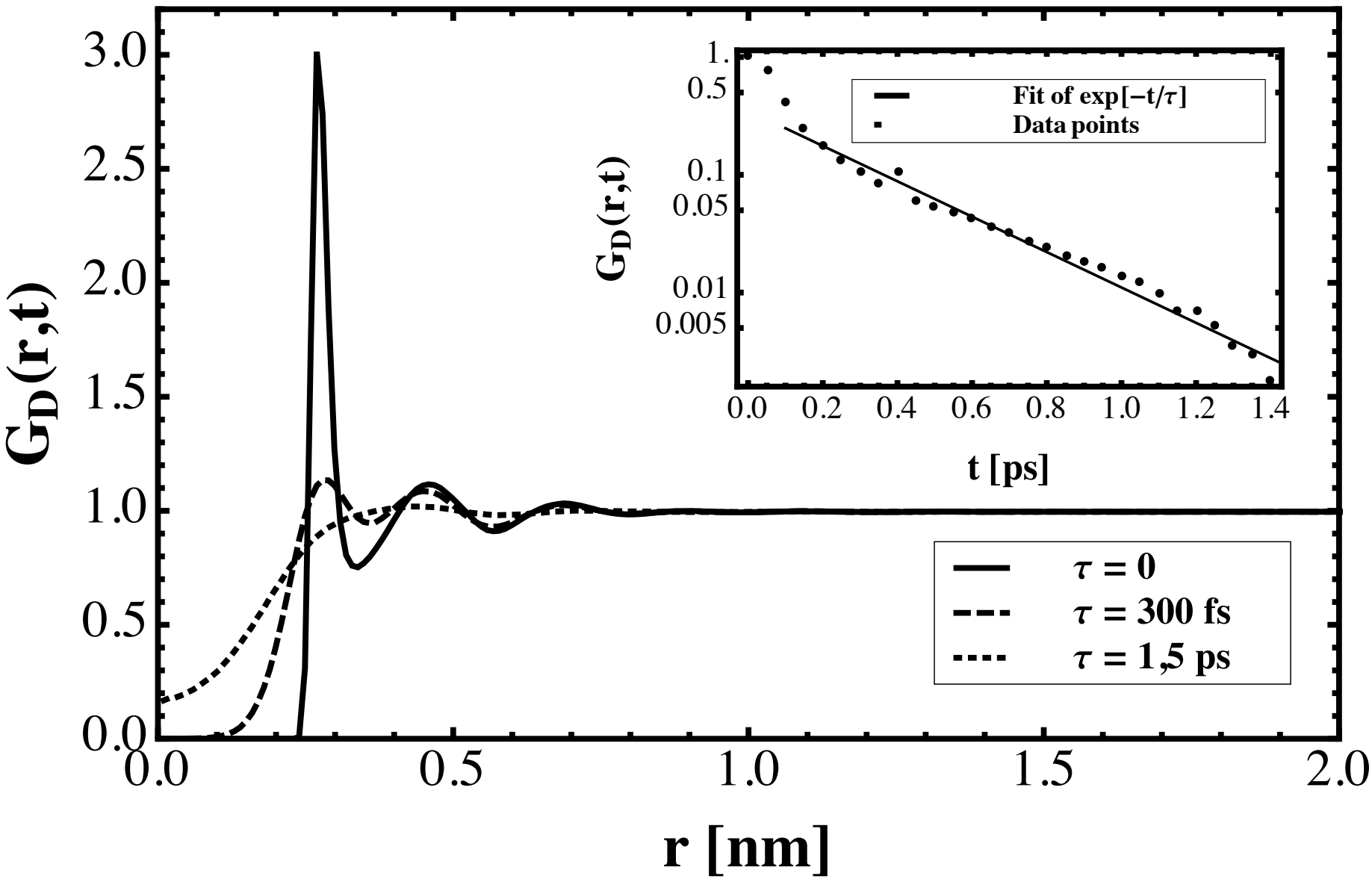


$\propto t^{-\beta}$

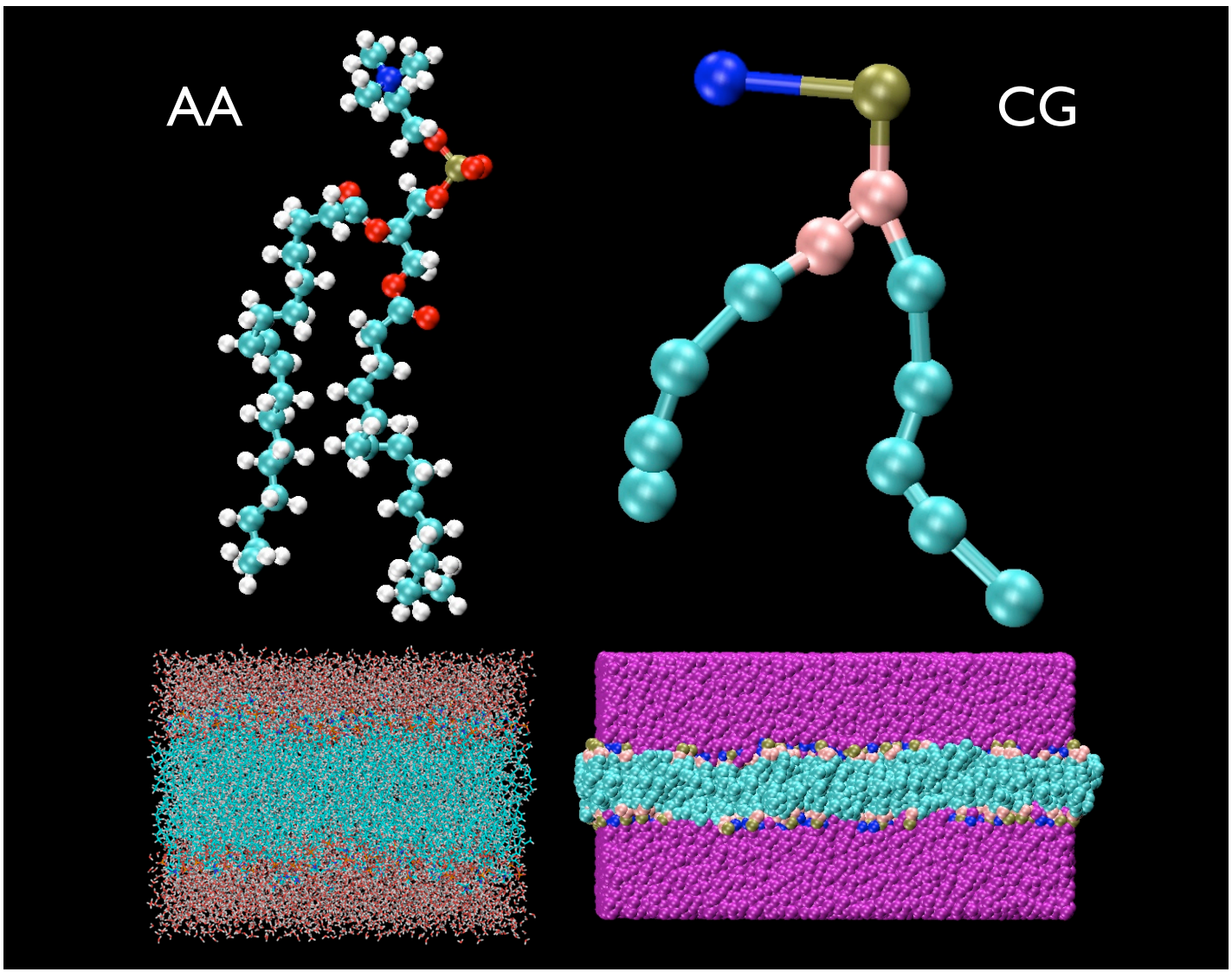
$\beta = 0.34$

Time-dependent Pair Correaltion Function $G_d(r,t)$ of centre of mass of POPC lipids for three time slices : t=0 (thick line), t=500 ps (dashed line) and for t=1.5 ns (dotted line). **Inset:** Log-log plot for the decay of Gd(r,t) as a function of time for r =0.8 nm.

Bulk water for comparison....



All-atom versus coarse-grained (Martini) force field



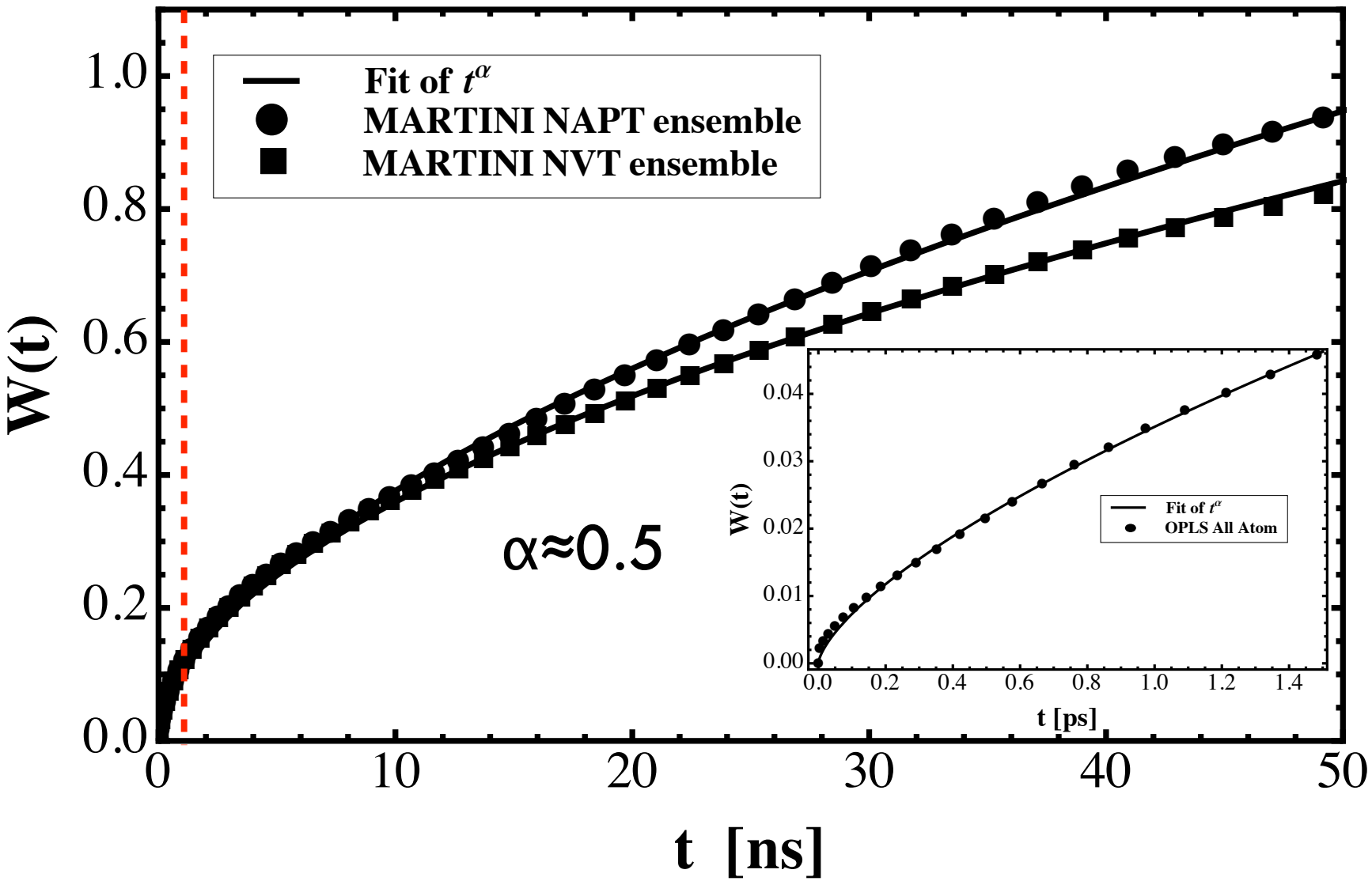
CG (MARTINI):

- 2033 POPC molecules (27.23 nm × 27.23 nm)
- 57952 P4 water molecules
- T=320 K

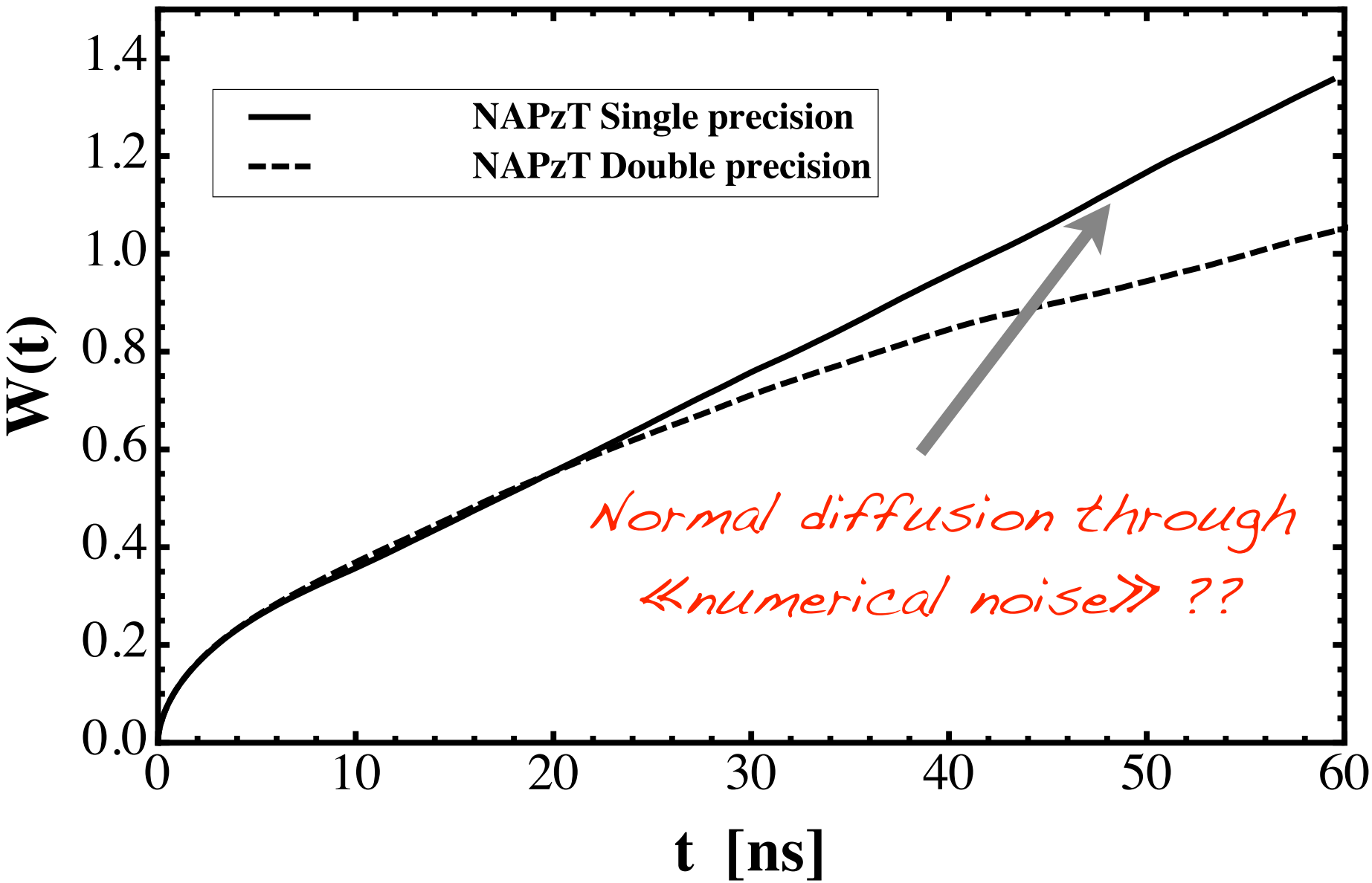
AA (OPLS):

- 2x137 POPC molecules (10 nm × 10 nm)
- 10471 water molecules
- T=310 K

Subdiffusion in both systems - but on a different time scale !



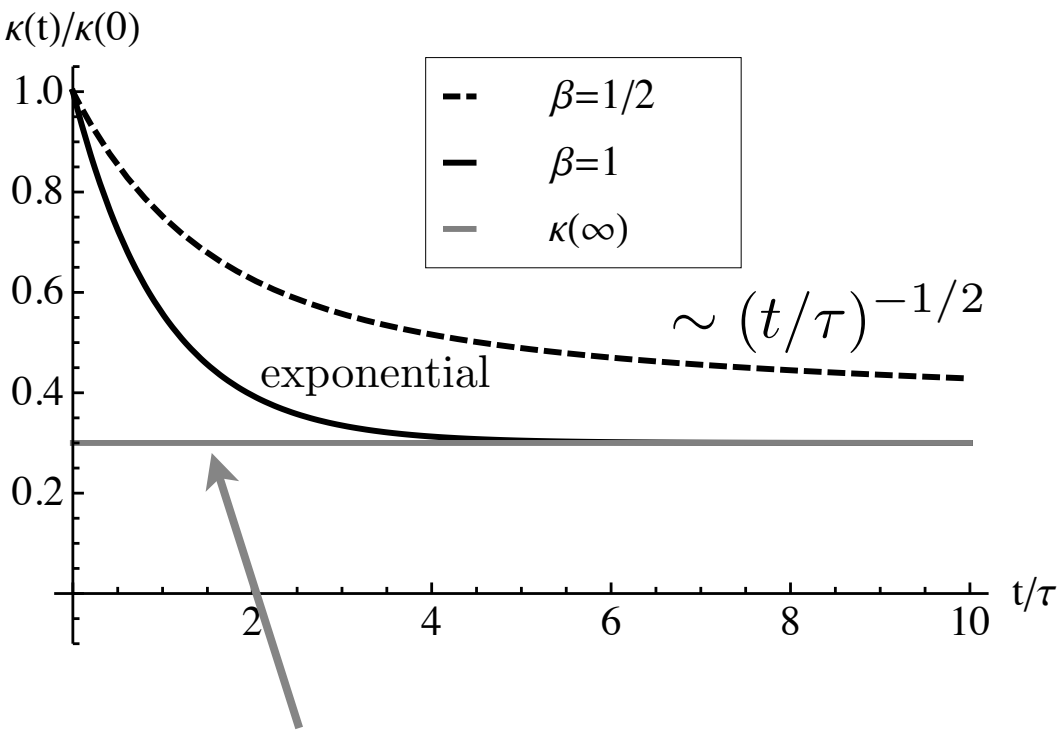
The impact of single and double precision



Back to protein dynamics: Cage effect and confined anomalous diffusion

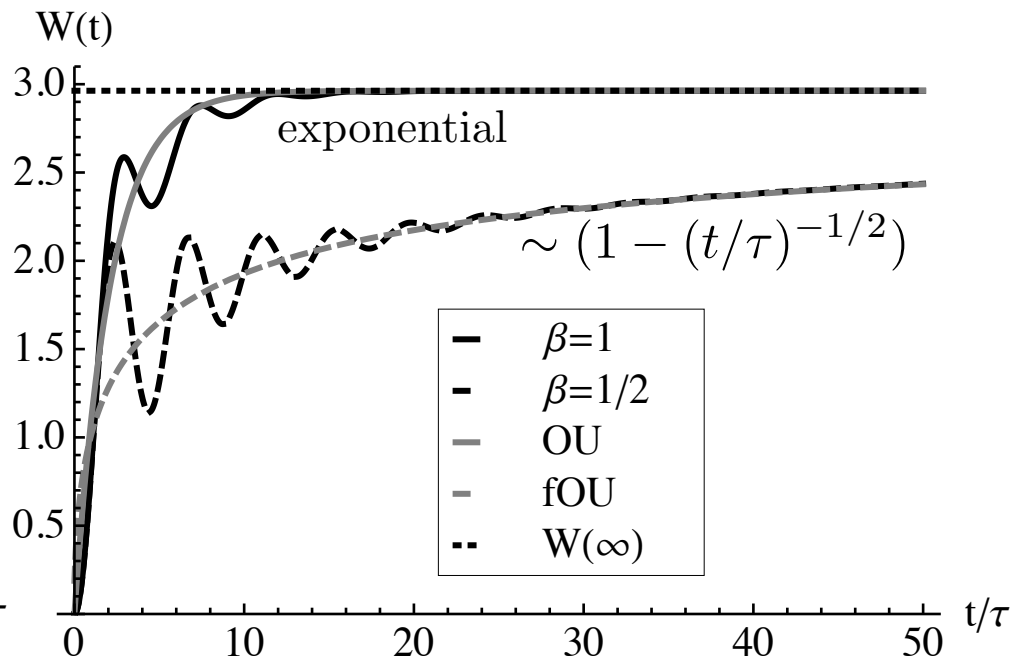
Model memory function

$$\kappa_c(t) = \Omega^2 \{r + (1-r)M(\beta, 1, -t/\tau)\}$$



Constant asymptotic memory

Mean-square displacement

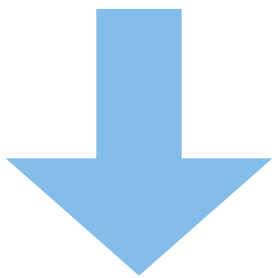


$$\langle x(t)x(0)\rangle \overset{t\to\infty}{\sim} \begin{cases} (t/\tau)^{-\beta} & \text{if } 0 < \beta < 1 \\ \exp(-(t/\tau)) & \text{if } \beta = 1 \end{cases}$$

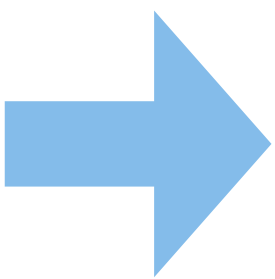
G.R. Kneller, J Chem Phys **134**, 224106 (2011).

General form of relaxation rate spectra in case of anomalous relaxation

$$\psi(t) = \int_0^\infty d\lambda\, p(\lambda) \exp(-\lambda t) \overset{t\to\infty}{\sim} t^{-\beta}$$



$$p(\lambda;\beta) = f(\lambda)\frac{\sin(\pi\beta)}{\pi}\frac{\Gamma(1-\beta)}{\lambda^{1-\beta}} \quad (0<\beta<1)$$



Construct models for $f(\lambda)$.

THE JOURNAL OF CHEMICAL PHYSICS **136**, 191101 (2012)

Communication: A minimal model for the diffusion-relaxation backbone dynamics of proteins

Gerald R. Kneller,[1,2,3,a)] Konrad Hinsen,[1,2] and Paolo Calligari[4]
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[2]*Synchrotron Soleil, L'Orme de Merisiers, 91192 Gif-sur-Yvette, France*
[3]*Université d'Orléans, Chateau de la Source-Av. du Parc Floral, 45067 Orléans, France*
[4]*Département de Chimie, associé au CNRS, Ecole Normale Supérieure, 24, rue Lhomond, 75231 Paris Cedex 05, France*

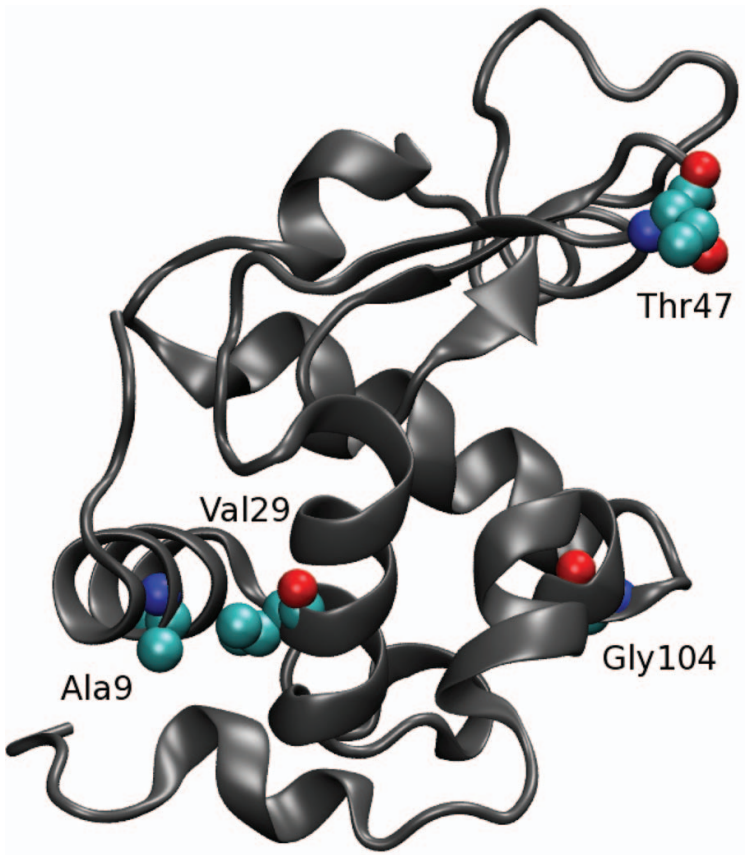


FIG. 1. Four selected residues in the lysozyme molecule.

Position autocorrelation functions

$$\frac{c(t)}{c(0)} \approx \psi(t/\tau;\alpha,\beta).$$

$$\psi(t;\alpha,\beta) = \frac{\exp(-\alpha t)}{(1+t/\beta)^{\beta}}$$

- Acommodates exponential and power-law decay

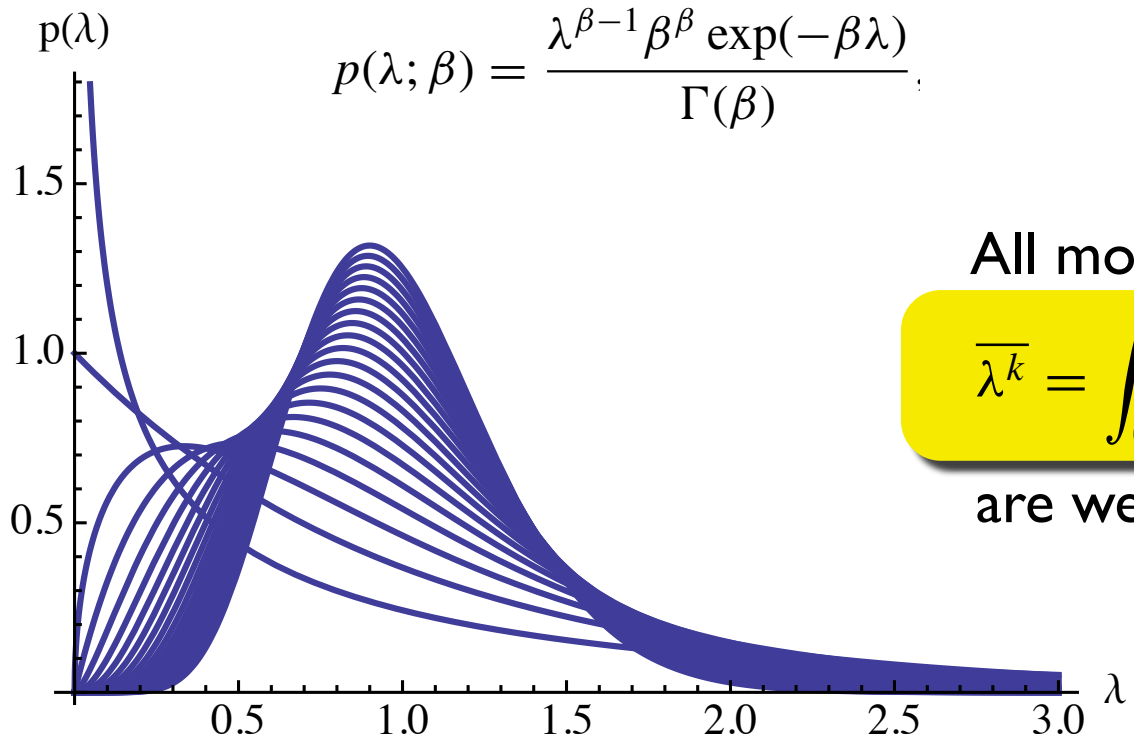
$$\lim_{\beta\to\infty} \psi(t;\alpha,\beta) = \exp(-[1+\alpha]t)$$

- Is analytical everywhere.

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

$$p(\lambda; \alpha, \beta) = \theta(\lambda - \alpha) p(\lambda - \alpha; \beta)$$

$$p(\lambda; \beta) = \frac{\lambda^{\beta-1} \beta^\beta \exp(-\beta\lambda)}{\Gamma(\beta)}$$

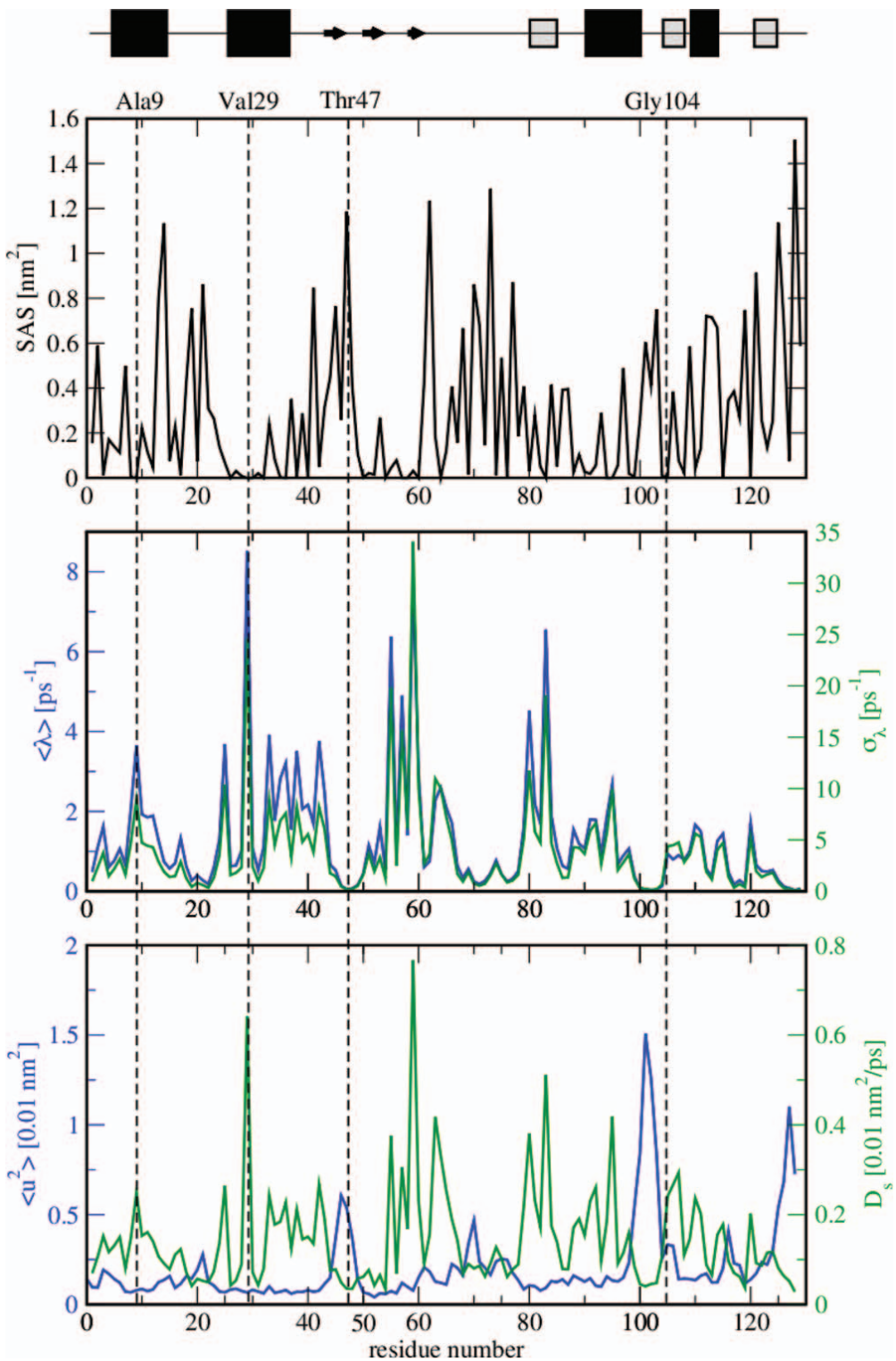


All moments

$$\overline{\lambda^k} = \int_0^\infty d\lambda\, \lambda^k p(\lambda) = (-1)^k \psi^{(k)}(0)$$

are well defined

FIG. 3: Relaxation rate spactrum $p(\lambda; \beta)$ for $\beta = k/2$, with $k = 1, 20$.



Helices (black) and beta-sheets (grey).

Solvent-accessible surfaces.

Mean relaxation rates, $\overline{\lambda}$, and corresponding spreads (green).

Mean square position fluctuations, $\langle \mathbf{u}^2 \rangle$, and short-time diffusion coefficients, D_s (green).

Conclusions

- Molecular simulation plays a crucial role the development of models for the dynamics of biomolecular systems (validation versus experiment and theory).
- (Anomalous) diffusion in membranes and proteins must be understood as an asymptotic behavior.
- Dynamical Models should be physical on all time scales. Fractional Brownian dynamics is an asymptotic model and becomes unphysical for short times.

Test coarse-graining methods (Martini force field etc.) for their capapibility to reproduce the correct dynamical behavior of the simulated systems.

Merci à

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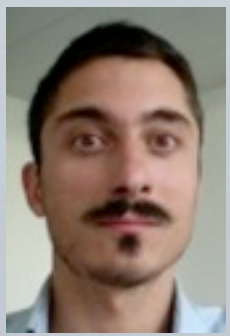
http://dirac.cnrs-orleans.fr/sputnik/home/

Theoretical Biophysics Group at the Centre de Biophysique Moléculaire, CNRS Orléans & SOLEIL

G. Kneller

K. Hinsen



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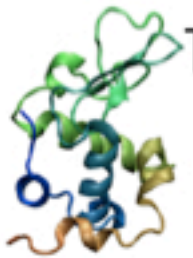

Theoretical Biophysics, Molecular Simulation, and Numerically Intensive Computation

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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