Probing protein energy landscapes by quasielastic neutron scattering

Deutsche Neutronenstreutagung Kiel 20-22 Sept. 2016

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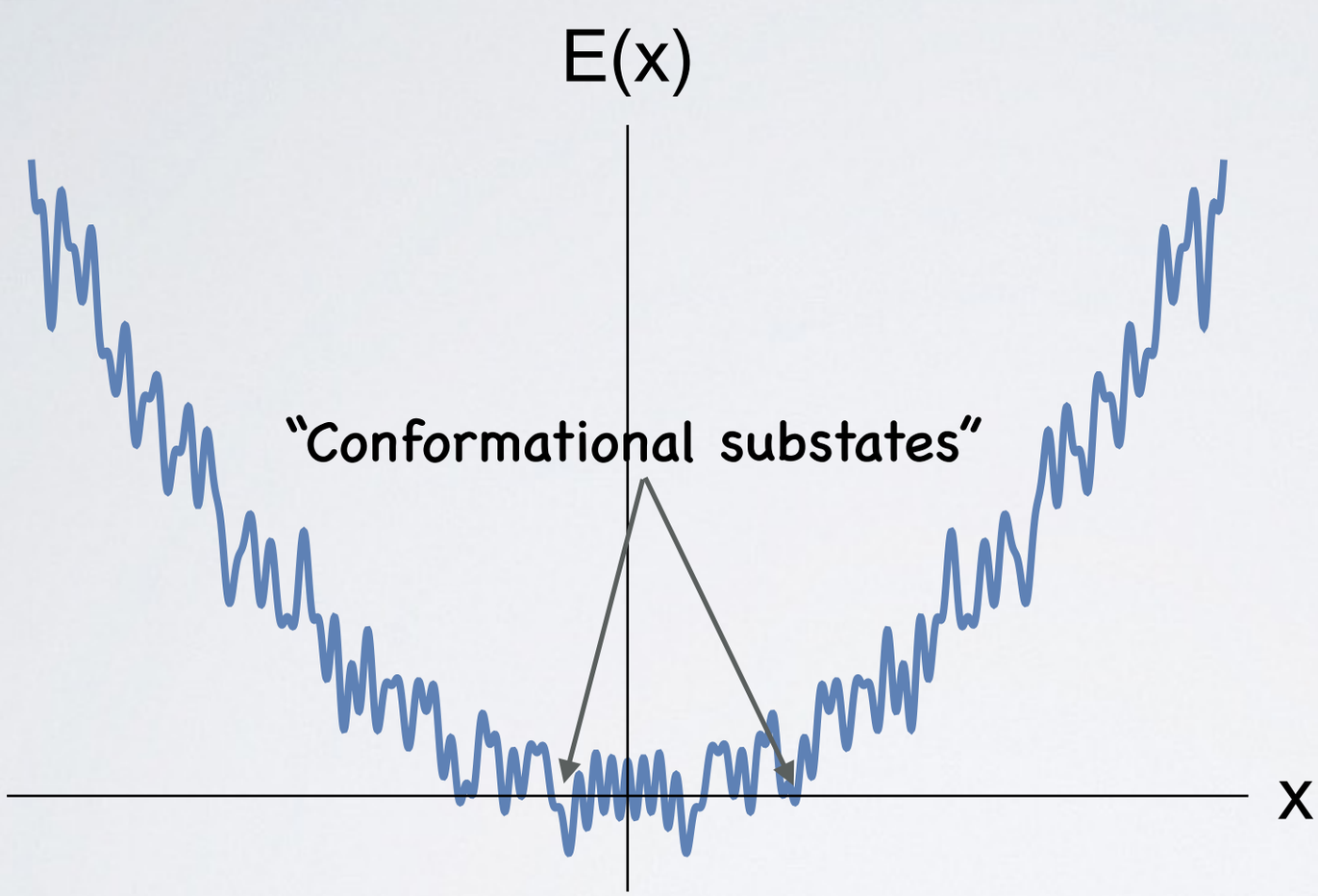
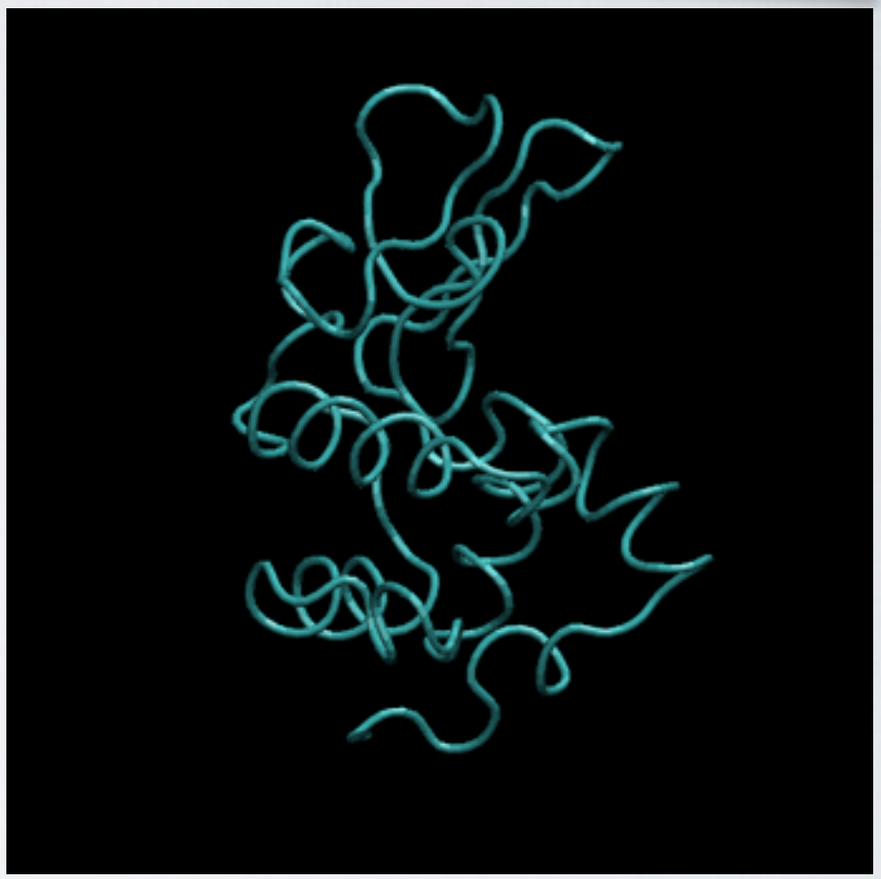
Energy landscapes - a qualitative picture of protein structural dynamics





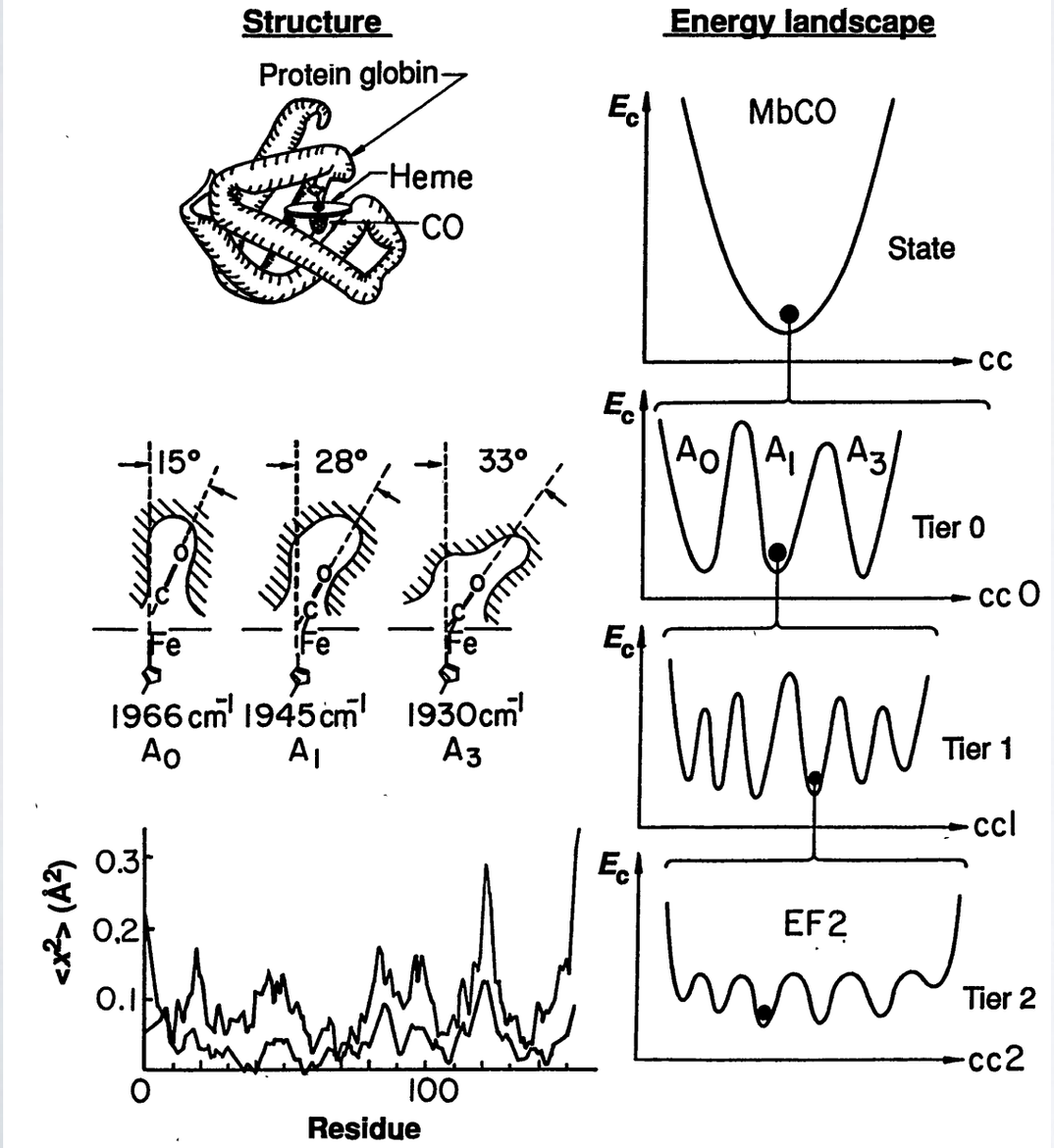
The protein jumps between different minima of the multidimensional (free) energy landscape which correspond to similar "conformational substates" (H. Frauenfelder et al, Science 254, 1598 (1991)).

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

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

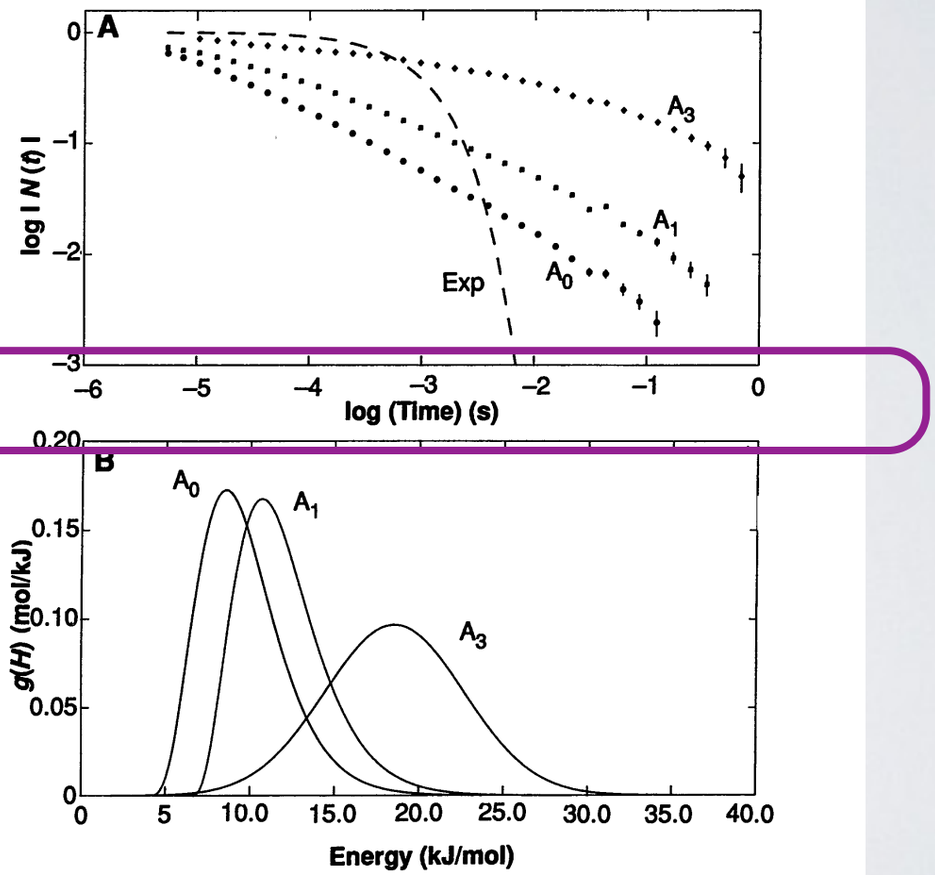


Fig. 2. Rebinding of CO to Mb after photodissociation, measured separately for the substates of tier 0 at pH 5.7. (**A**) $N(t)$ is the fraction of proteins that have not rebound a CO at the time t after photodissociation. All three substates (A_0, A_1, and A_3) rebind nonexponentially in time. (**B**)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

Relating relaxation and energy barriers

The distribution barrier heights corresponds to a distribution of rates for kinetic processes and conformational relaxation.

$$\lambda = \lambda_0 e^{-\frac{\Delta E}{k_B T}}$$

Relaxation and time correlation functions have a multi-exponential form:

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

For complex systems these functions decay for long times slowly with a power law and exhibit thus self-similarity:

$$\psi(t) \overset{t\to\infty}{\sim} (t/\tau)^{-\beta}, \quad 0 < \beta < 1$$

$$\Rightarrow \quad \psi(\lambda t) \overset{t\to\infty}{=} \lambda^{-\beta}\psi(t)$$

Modeling multi-scale reaction kinetics

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

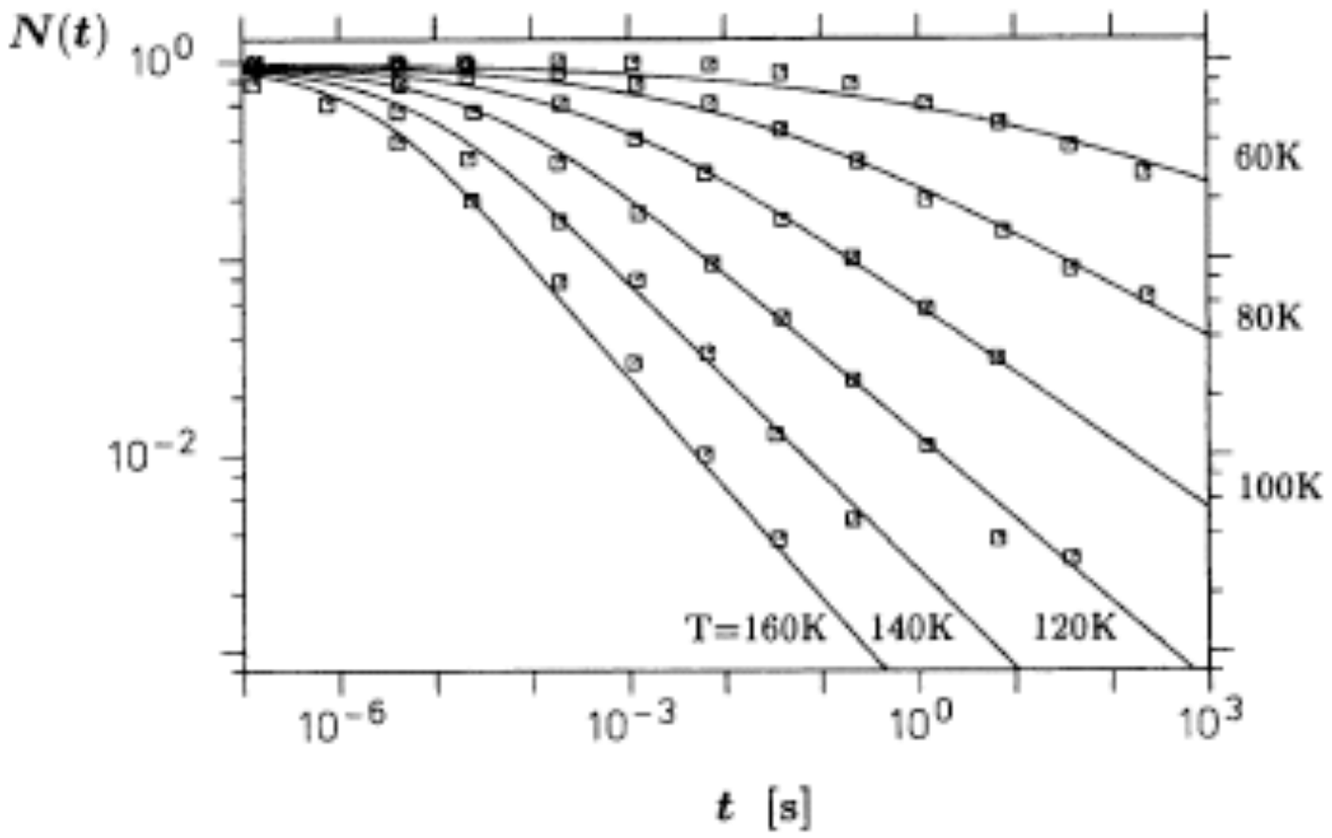


FIGURE 2 Three-parameter model Eq. 32 for rebinding of CO to Mb after photo dissociation. The parameters are $\tau_m = 8.4 \times 10^{-10}$s, $\alpha = 3.5 \times 10^{-3}\ K^{-1}$ and $k = 130$, the data points are from Austin et al. (1975).

$$N(t) = N(0) E_\beta \left((-[t/\tau]^\beta \right)$$

Mittag-Leffler function

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

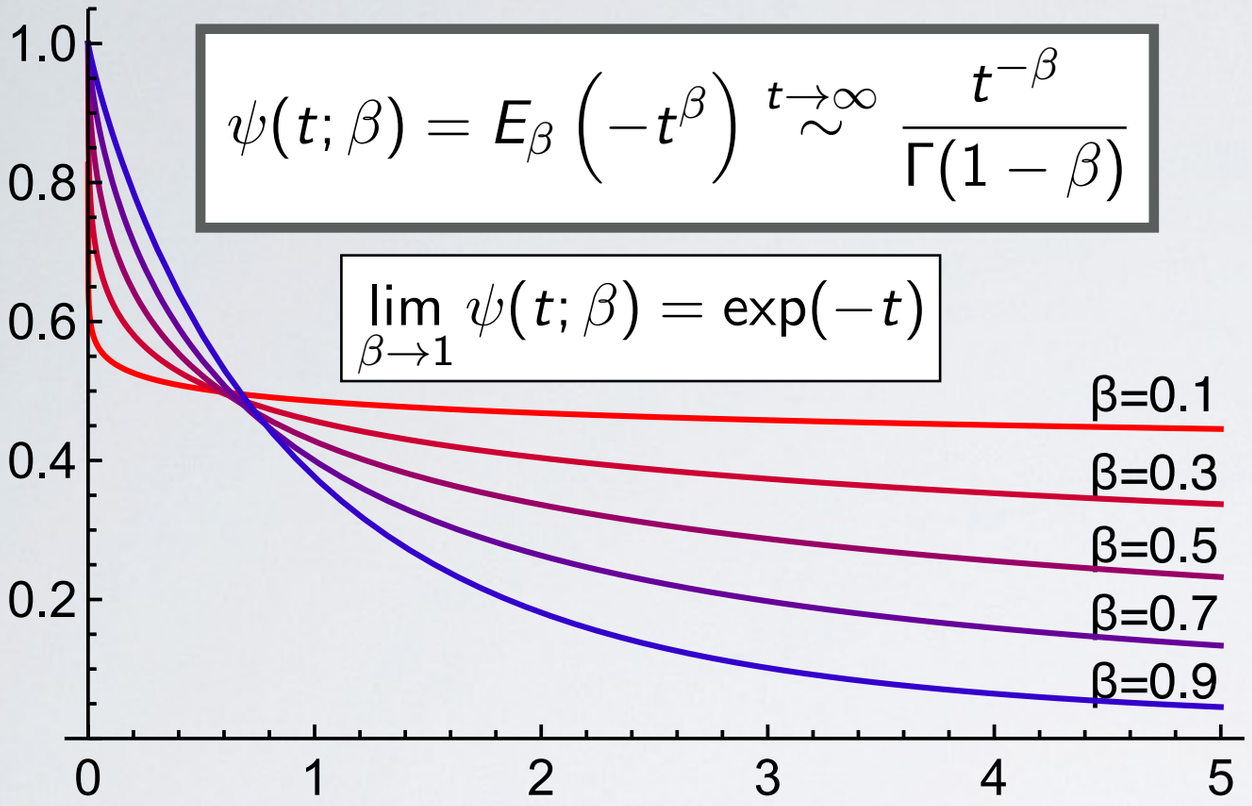
$$E_\beta\left(-t^\beta\right) \overset{t\to\infty}{\sim} \frac{t^{-\beta}}{\Gamma(1-\beta)}$$

"Stretched Mittag-Leffler function"

Relaxation function

$$\psi(t;\beta) = E_\beta\left(-t^\beta\right) \overset{t\to\infty}{\sim} \frac{t^{-\beta}}{\Gamma(1-\beta)}$$

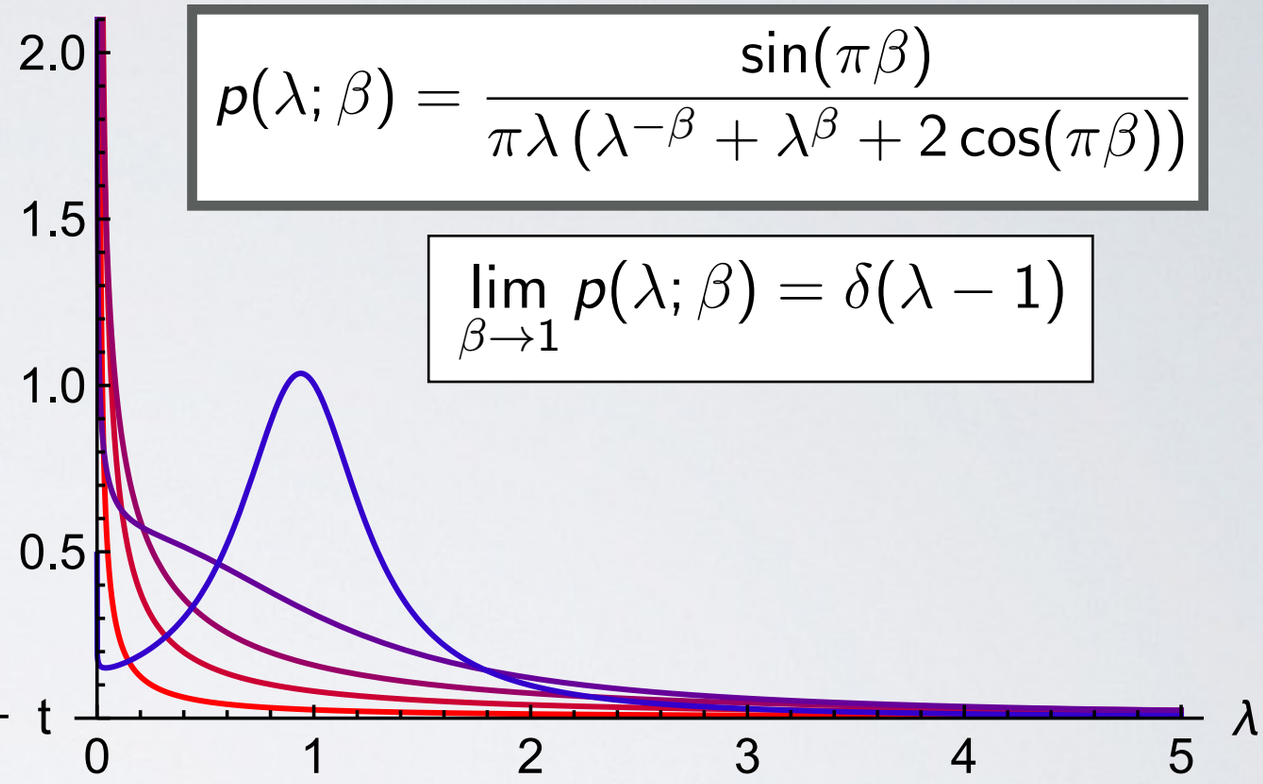
$$\lim_{\beta\to 1} \psi(t;\beta) = \exp(-t)$$



Relaxation rate spectrum

$$p(\lambda;\beta) = \frac{\sin(\pi\beta)}{\pi\lambda\left(\lambda^{-\beta}+\lambda^{\beta}+2\cos(\pi\beta)\right)}$$

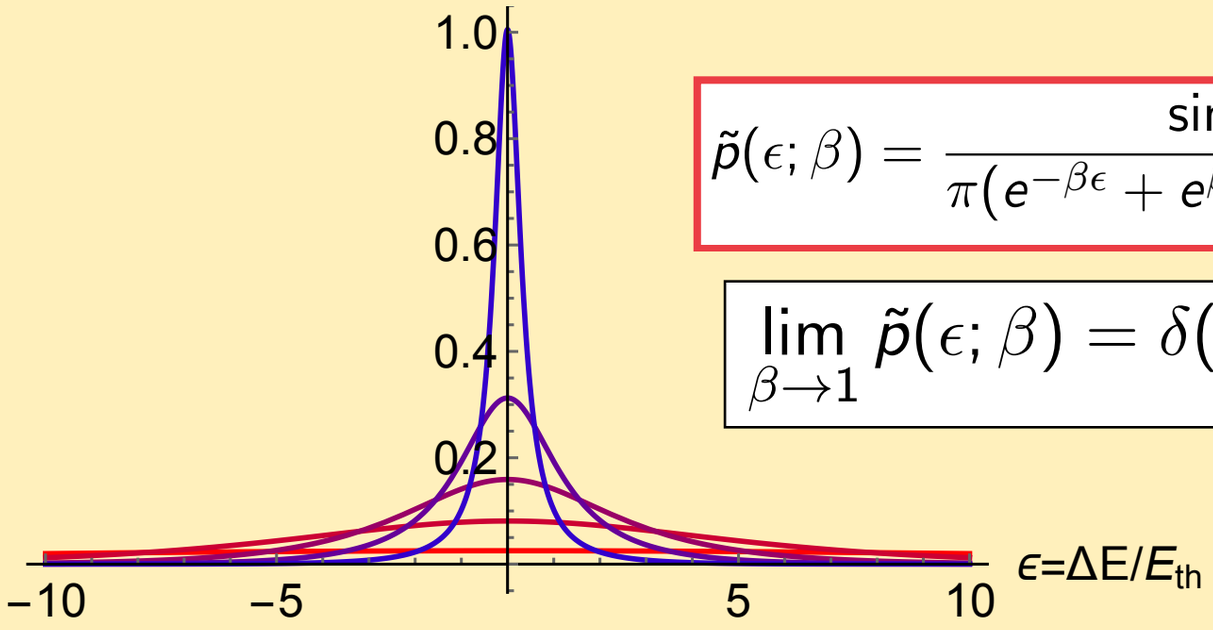
$$\lim_{\beta\to 1} p(\lambda;\beta) = \delta(\lambda-1)$$



Energy barrier distribution

$$\tilde{p}(\epsilon;\beta) = \frac{\sin(\pi\beta)}{\pi\left(e^{-\beta\epsilon}+e^{\beta\epsilon}+2\cos(\pi\beta)\right)}$$

$$\lim_{\beta\to 1} \tilde{p}(\epsilon;\beta) = \delta(\epsilon)$$



Relating energy landscapes to neutron scattering

A. Rahman, K. Singwi, and A. Sjölander, Physical Review 126, 986 (1962).
G.R. Kneller, J. Chem. Phys. 145, 044103 (2016).

Neutron scattering measures the dynamic structure factor of a condensed matter system

$$S(q,\omega) = \frac{1}{2\pi}\int_{-\infty}^{+\infty} dt\, e^{-i\omega t} F(q,t),$$

$$F(q,t) = \left\langle \exp\left(-iq\hat{x}(0)\right) \exp\left(iq\hat{x}(t)\right)\right\rangle.$$

At moderate momentum transfers, q, the neutron intermediate scattering function gives access to the mean square displacement of the diffusing scattering atom

$$F(q,t) \approx \exp\left(i\frac{\hbar q^2 t}{2m}\right) \exp\left(-q^2\mu_2(t)\right)$$

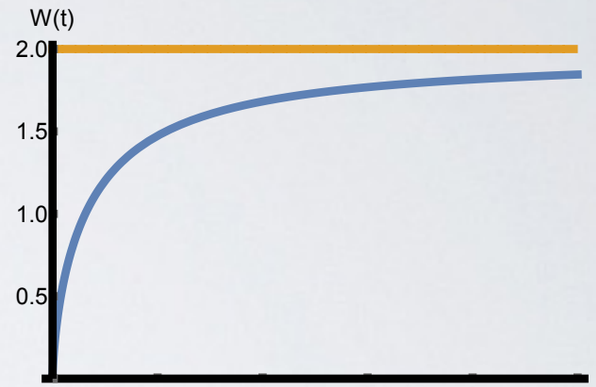
$$\mu_2(t) = \frac{1}{2}\left(1 - i\tan\left(\frac{\beta\hbar}{2}\frac{d}{dt}\right)\right) \underbrace{\left\langle (x(t)-x(0))^2\right\rangle}_{MSD \equiv W(t)}$$

Motions in proteins are confined in space and the atomic positions can be referred to a well-defined mean positions,

$$x(t) = u(t) + \langle x \rangle$$

The MSD for confined motions can be expressed in terms of the displacement autocorrelation function.

$$W(t) = \left\langle (u(t) - u(0))^2 \right\rangle = 2\left(c_{uu}(0) - c_{uu}(t)\right)$$
$$c_{uu}(t) = \langle u(t)u(0) \rangle$$



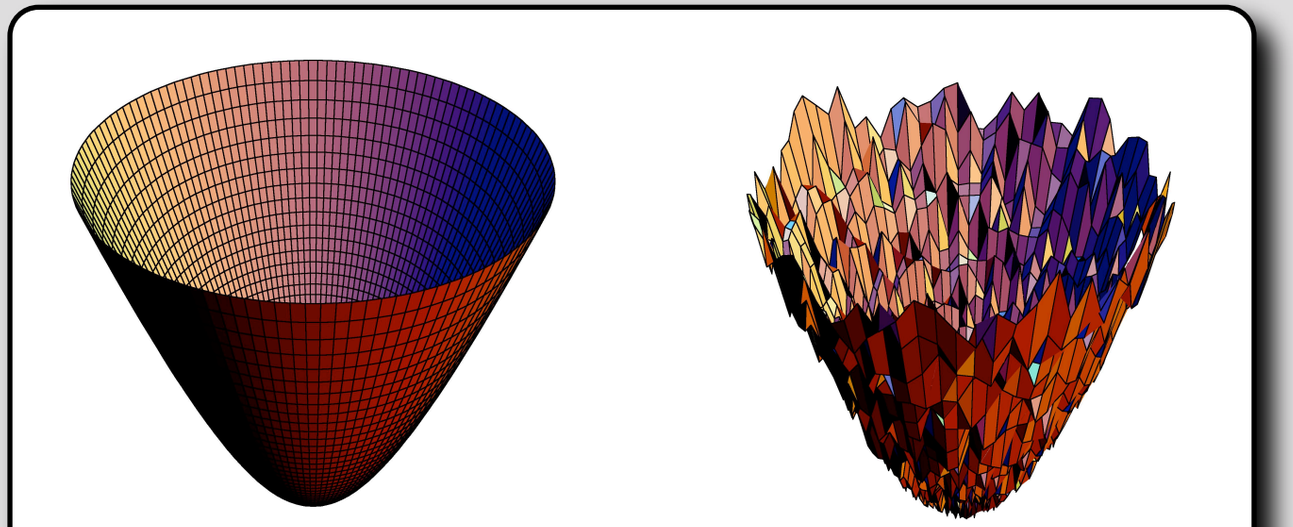
The displacement autocorrelation function has a multiexponential decay.

$$\frac{c_{uu}(t)}{c_{uu}(0)} \equiv \psi(t) = \int_0^\infty d\lambda\, p(\lambda) \exp(-\lambda t)$$

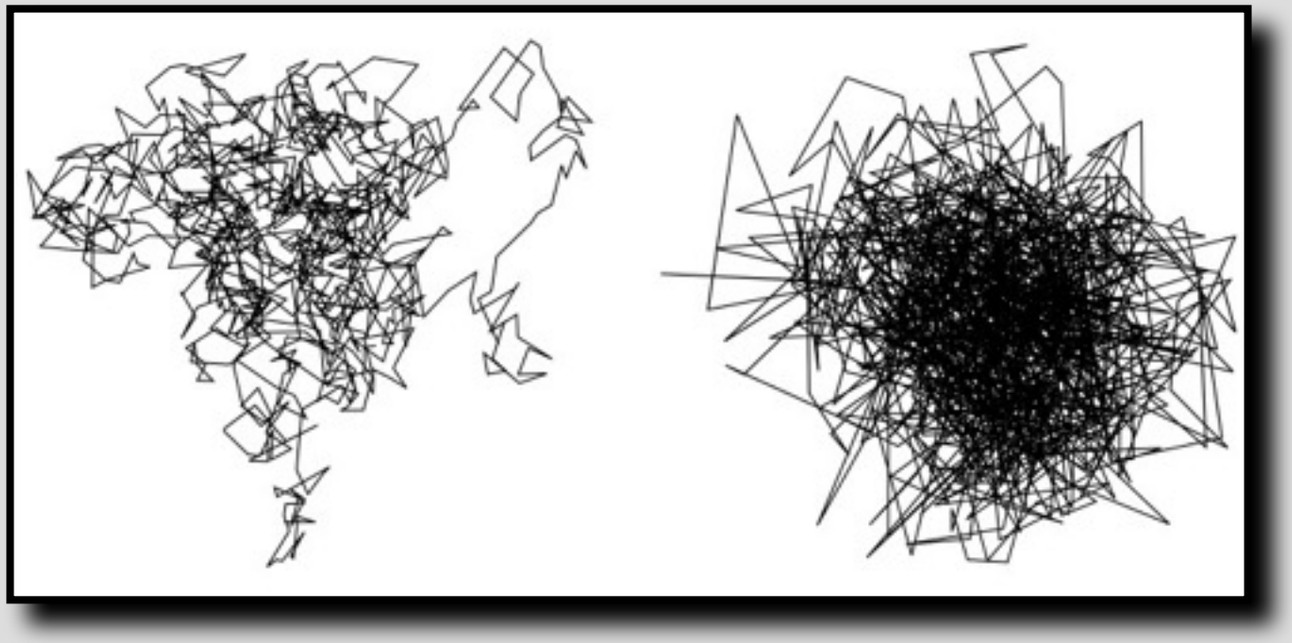
Distribution of relaxation rates/ barrier heights

Fractional Ornstein-Uhlenbeck process as a model for self-similar atomic dynamics in proteins

Normal Ornstein-Uhlenbeck process: Diffusion in a harmonic potential



Fractional Ornstein-Uhlenbeck process: Anomalous Diffusion in a "rugged" harmonic potential



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

1. Shao, Y. Physica D: Nonlinear Phenomena 83, 461–477 (1995).
2. Metzler, R. & Klafter, J. Phys Rep 339, 1–77 (2000).

Fractional Fokker-Planck equation for conditional probability

$$\frac{\partial}{\partial t} p(\mathbf{u}, t|\mathbf{u}_0, 0) = \partial_t^{1-\beta} \mathcal{L}\, p(\mathbf{u}, t|\mathbf{u}_0, 0), \quad 0 < \beta \leq 1$$

Time evolution operator

$$\mathcal{L} = D_\beta \frac{\partial}{\partial \mathbf{u}} \cdot \left\{ \frac{\partial}{\partial \mathbf{u}} + \frac{K\mathbf{u}}{k_B T} \right\}$$

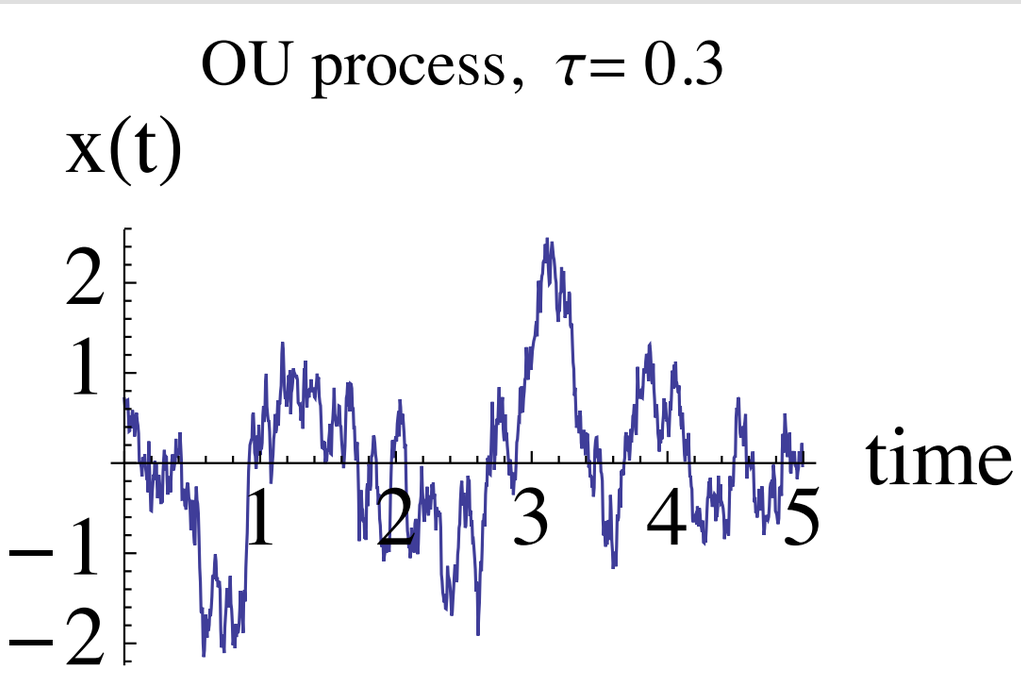
Harmonic potential

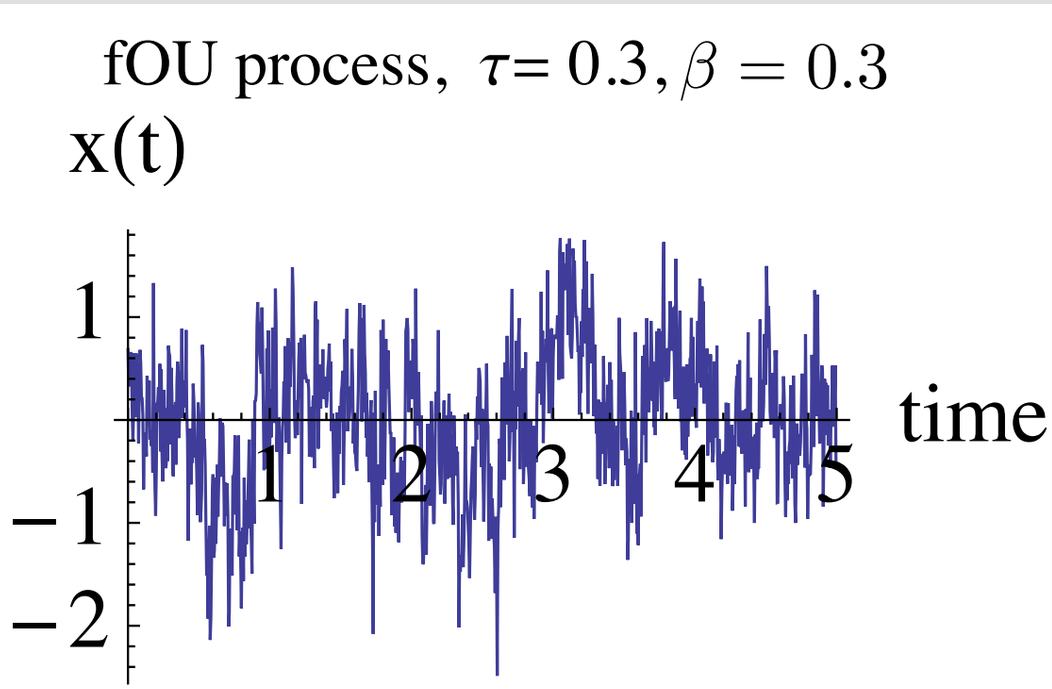
$$V(\mathbf{u}) = \frac{K}{2}|\mathbf{u}|^2$$

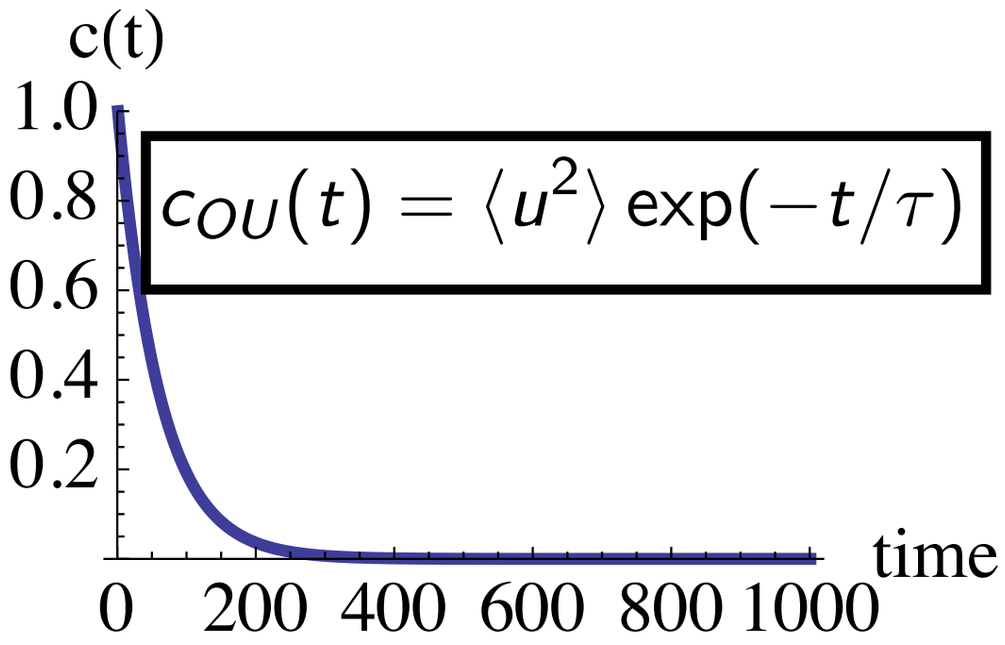
Fractional time derivative

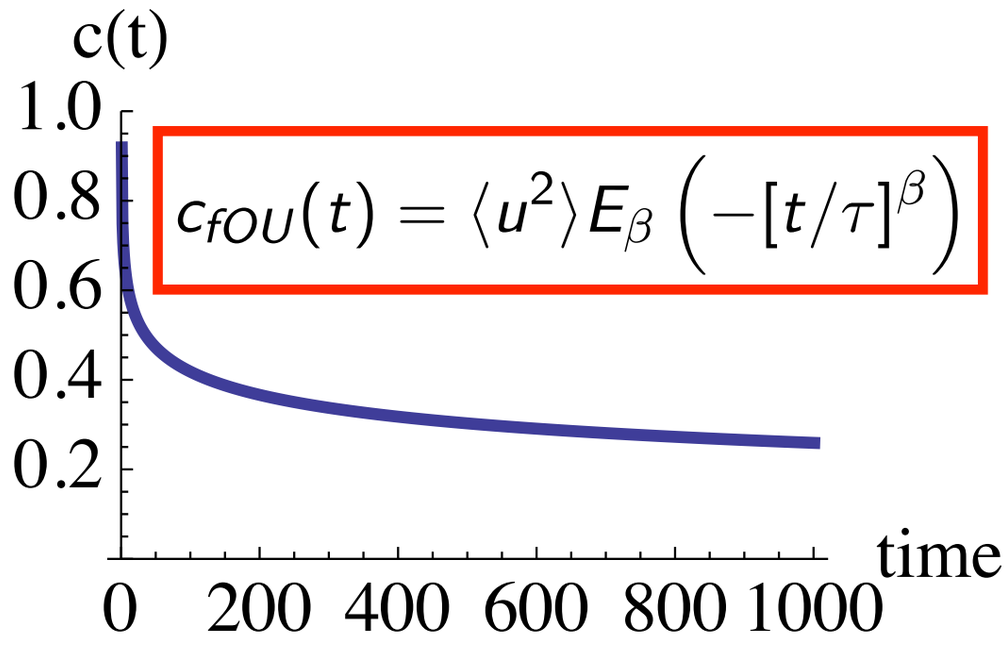
$$\partial_t^{1-\beta} g(t) = \frac{d}{dt} \int_0^t d\tau \, \frac{(t-\tau)^{\beta-1}}{\Gamma(\beta)} g(\tau)$$

Time series and autocorrelation functions for the fOU process







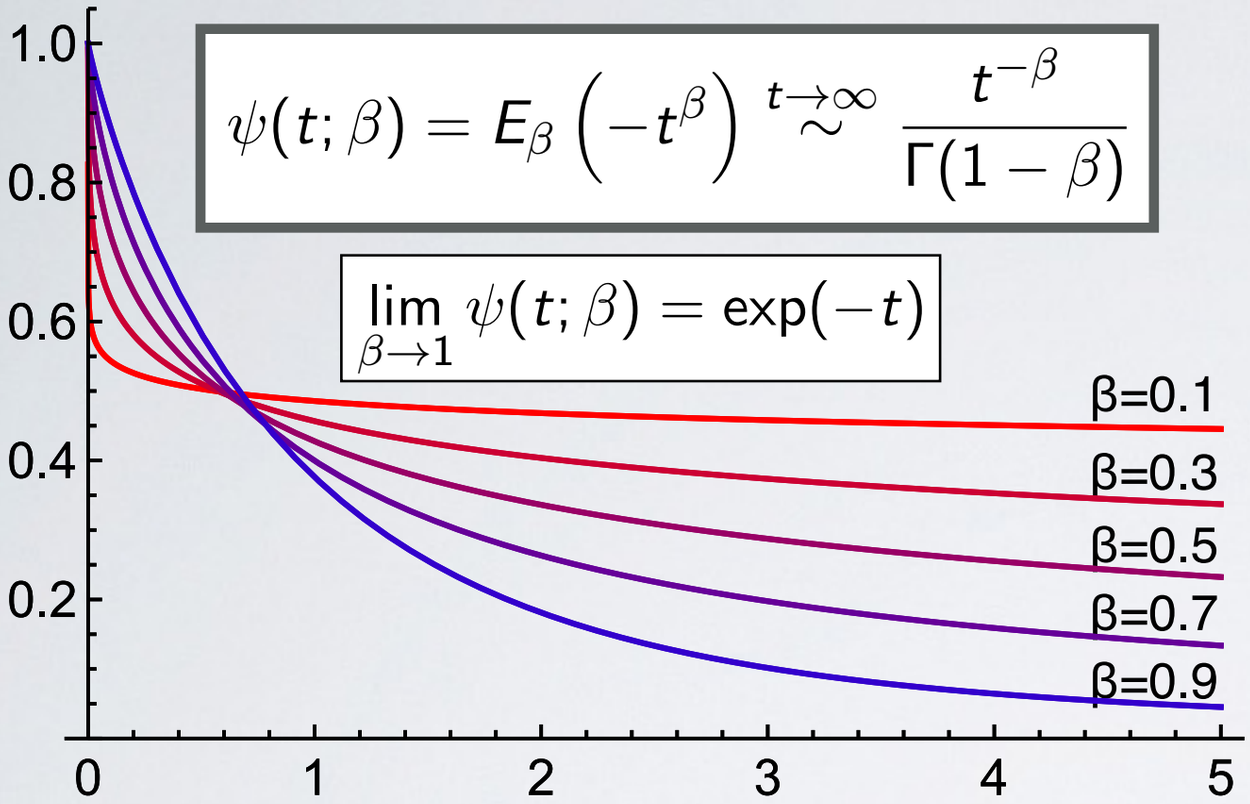


Fractional Ornstein-Uhlenbeck process

Position autocorrelation function

$$\psi(t;\beta) = E_\beta\left(-t^\beta\right) \overset{t\to\infty}{\sim} \frac{t^{-\beta}}{\Gamma(1-\beta)}$$

$$\lim_{\beta\to 1} \psi(t;\beta) = \exp(-t)$$



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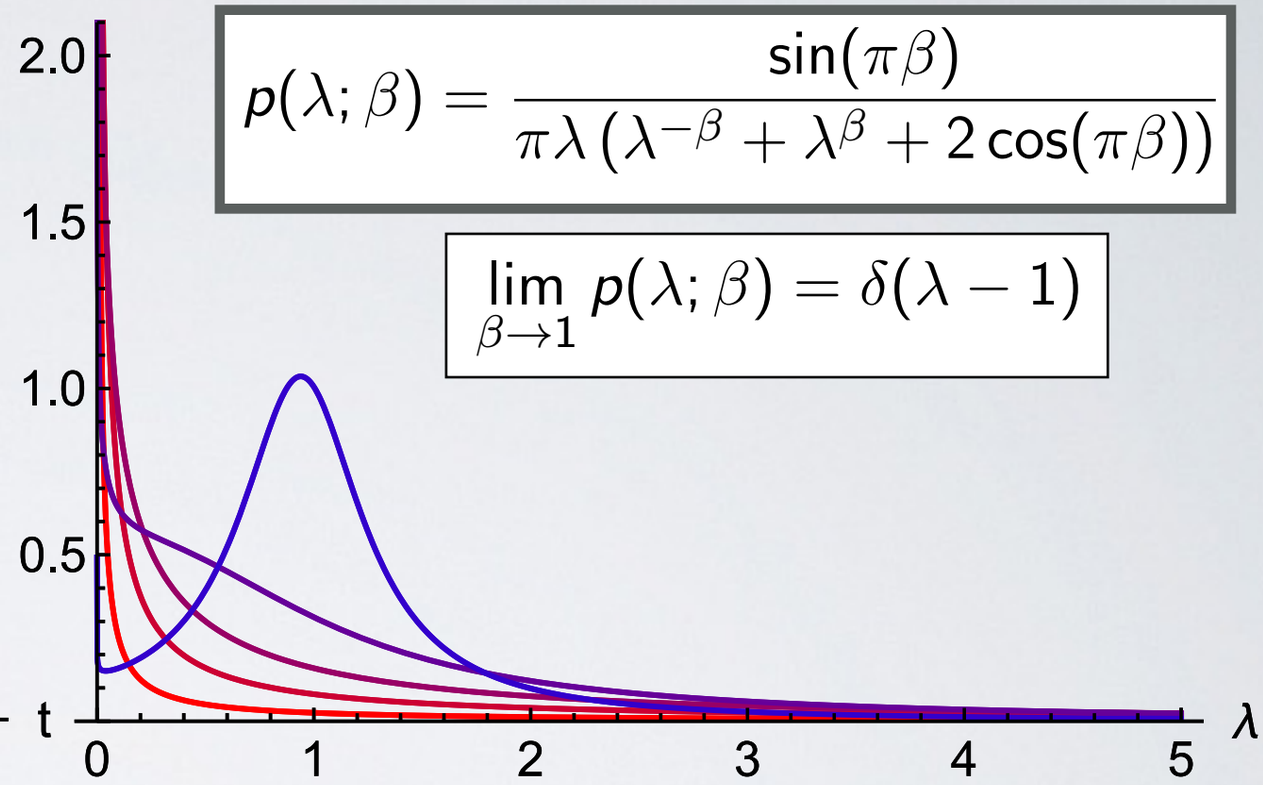

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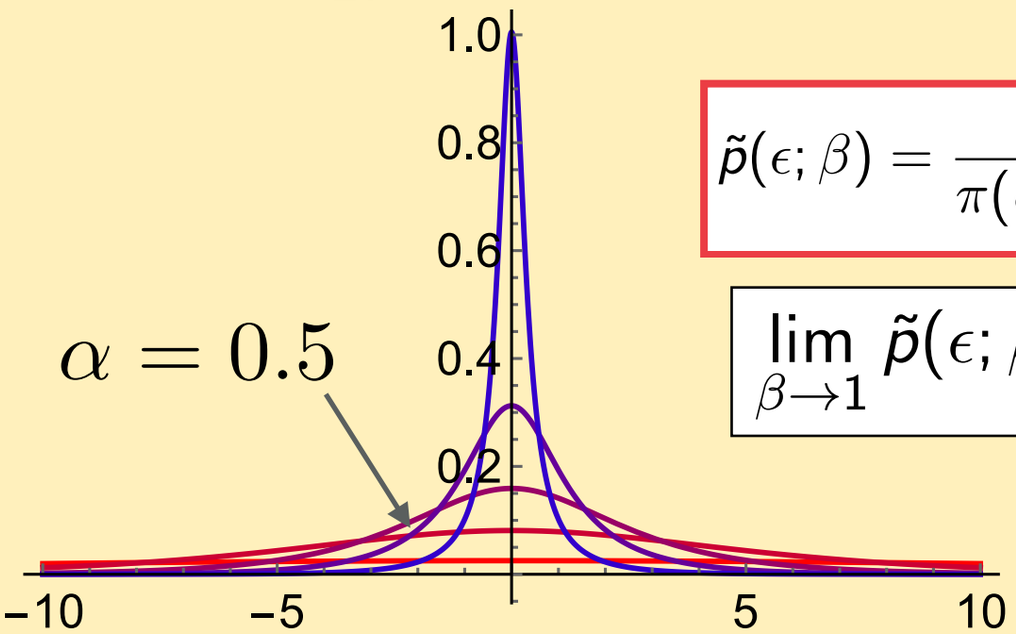
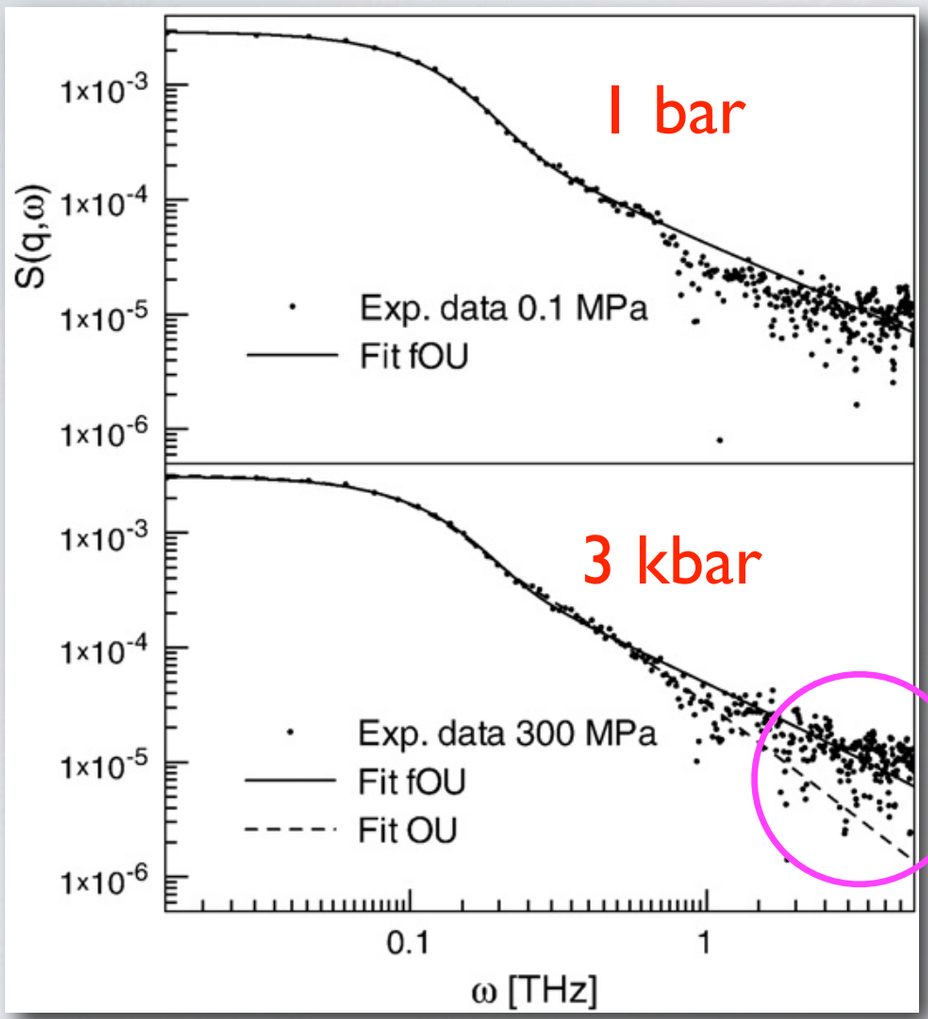
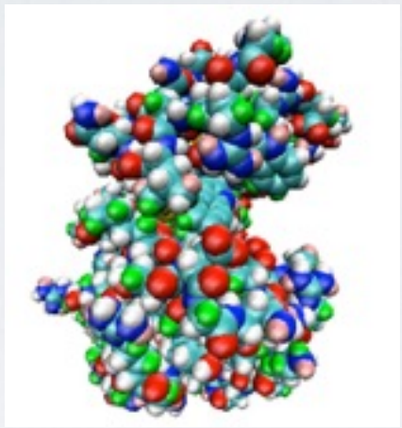


Application 1: Lysozyme under pressure by QENS and MD simulations

Neutron scattering

QENS dynamic structure factor

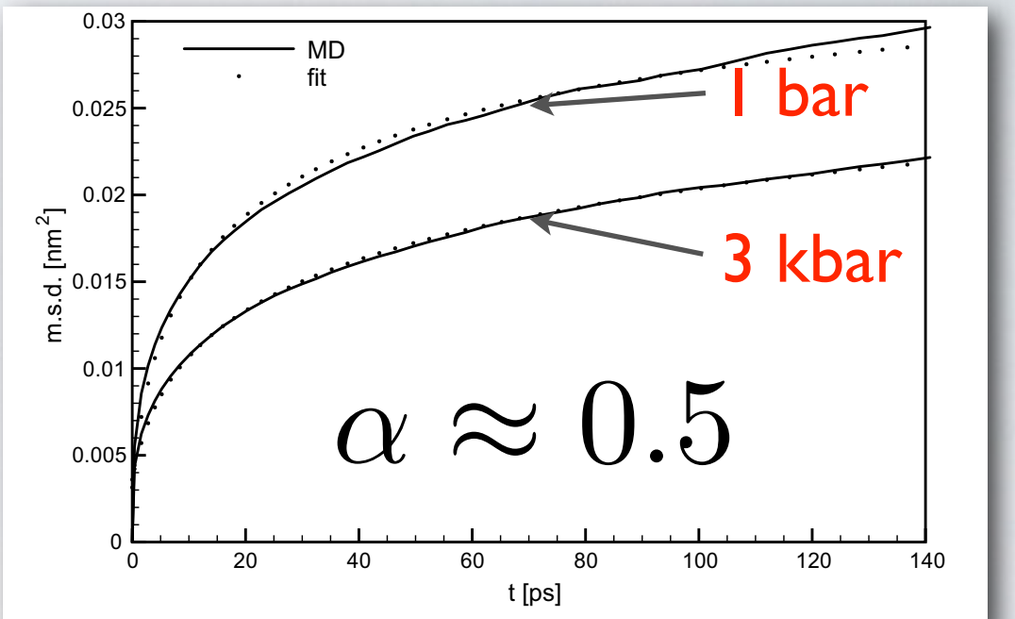




Lysozyme

MD simulation

Mean square displacement $\langle[x(t)-x(0)]^2\rangle$ of the H atoms in lysozyme MD simulation

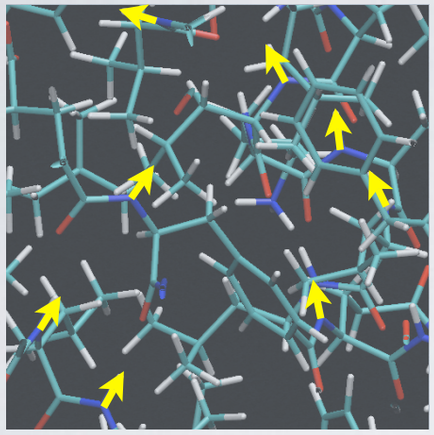


	0.1 MPa			300 MPa		
	$\langle x^2\rangle$ (nm^2)	α	τ (ps)	$\langle x^2\rangle$ (nm^2)	α	τ (ps)
MSD	6.17×10^{-3}	0.54	31.75	4.74×10^{-3}	0.54	39.08

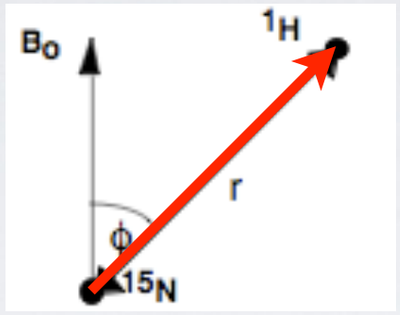
The form of the energy landscape does not change under pressure.

- 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.

Application 2: Protein dynamics by NMR relaxation spectroscopy



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



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

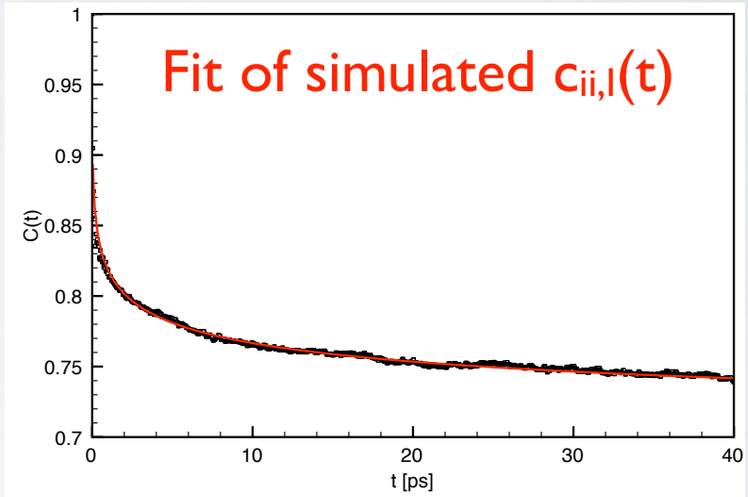
$$c_{ii}(t) = C_{ii,R}(t) C_{ii,I}(t)$$

Global rotation — Internal dynamics

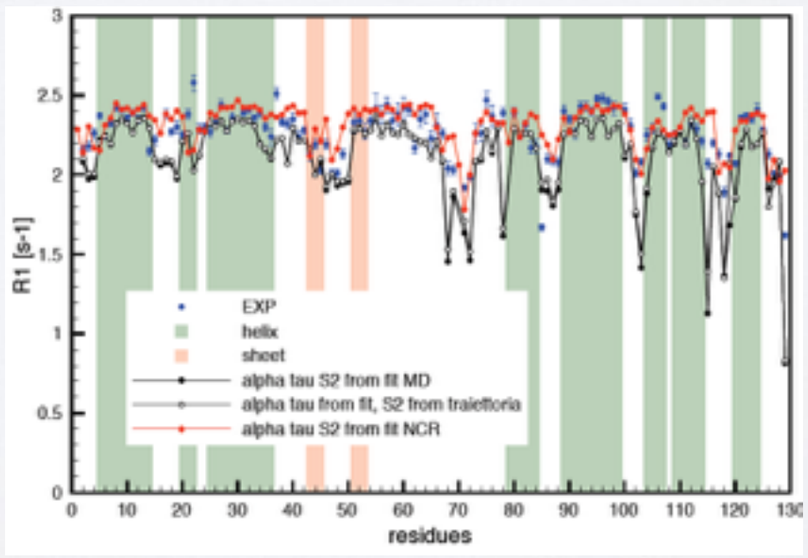
Model pour $c_{ii,I}(t)$:

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

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.

Limits of fractional Brownian Dynamics models

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

Velocity autocorrelation function

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

$$c_{vv}(t) = \sum_{k=0}^{\infty} c_{vv}^{(2k)}(0)\frac{t^{2k}}{(2k)!} \qquad \left(c_{vv}^{(2k)}(0) = (-1)^k\langle \mathbf{v}^{(k)}(0)\cdot\mathbf{v}^{(k)}(0)\rangle/3\right).$$

$$W(t) \overset{t\to 0}{\simeq} \langle \mathbf{v}^2\rangle t^2$$

Ballistic regime

Self-similarity cannot be true on arbitrarily small time scales, but must be seen as a model which holds **asymptotically**.

$$W(t) \overset{t\to\infty}{\simeq} 2D_\alpha t^\alpha$$

Asymptotic regime

Problem with the fOU process

- The model correlation functions have the experimentally observed power law decay for long times, but they are unphysical for short times.

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

- **Therefore the moments of p(λ) diverge.**

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

Diffusion as an asymptotic dynamical regime

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

The laws for (anomalous) diffusion hold in the asymptotic regime

$$\boxed{\left\langle (x(t)-x(0))^2 \right\rangle \overset{t\to\infty}{\sim} 2L(t)D_\alpha t^\alpha \quad (0 \le \alpha < 2)}$$

L(t) is a "slowly growing function" with $\boxed{\lim_{t\to\infty} L(t) = 1}$

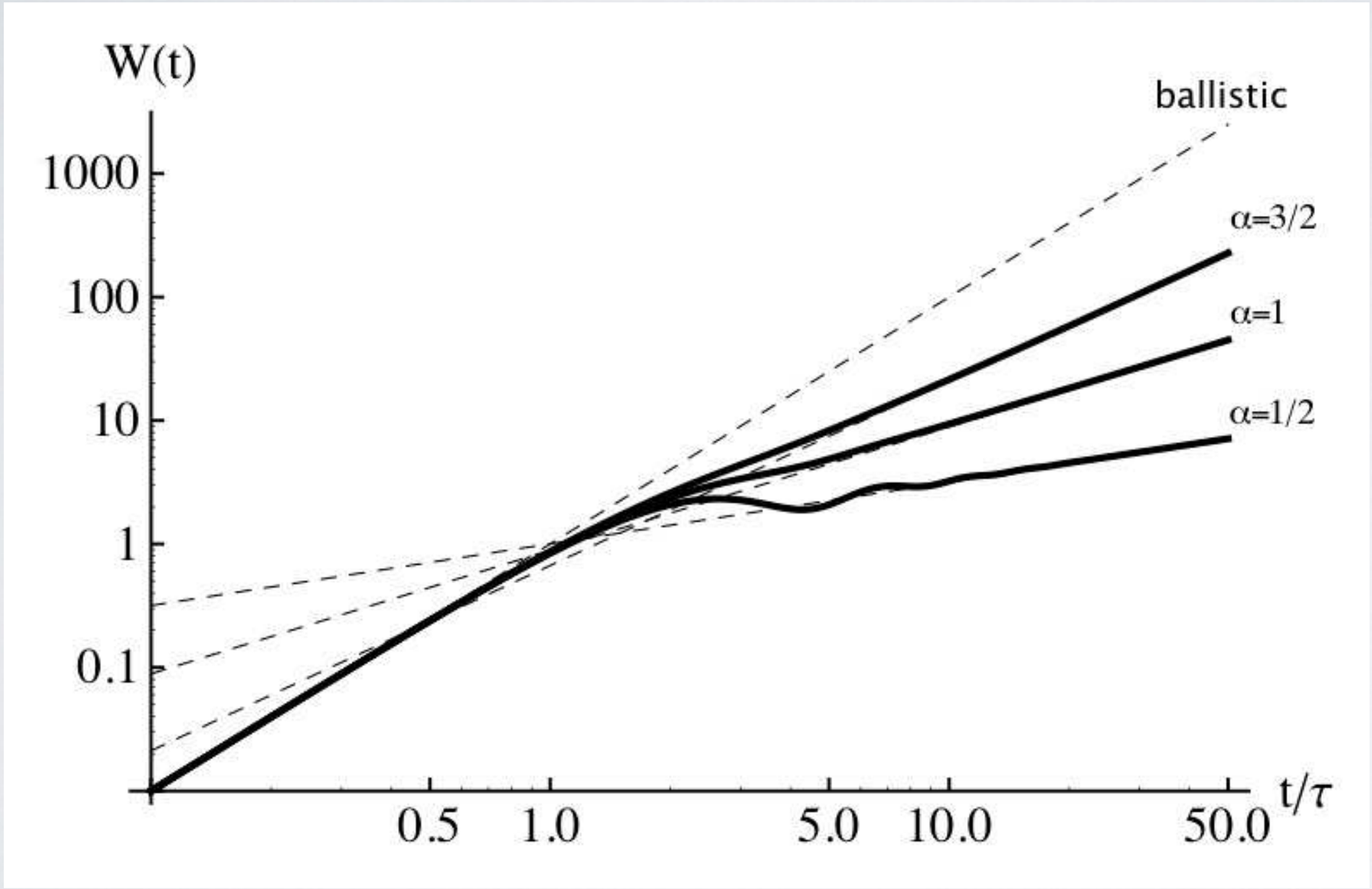
The diffusive regime is characterized by

$t \gg \tau_v$, where $\boxed{\tau_v = \left(\frac{D_\alpha}{\langle v^2 \rangle}\right)^{\frac{1}{2-\alpha}}}$ (in the ps regime).

A generalized Kubo relation expresses the diffusion constant

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

MSDs for free (anomalous) diffusion



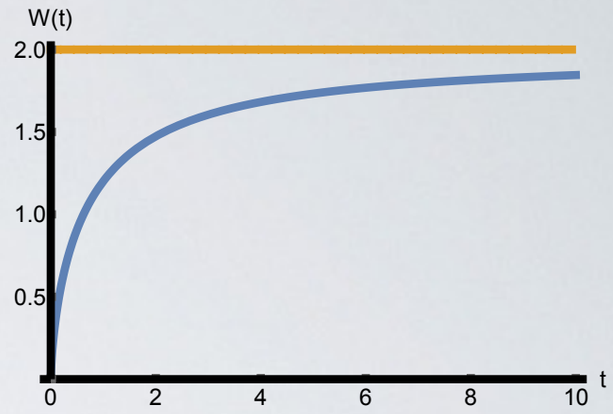
"superdiffusion"

normal diffusion

"subdiffusion"

The asymptotic form for the MSD includes explicitly the case of confined diffusion, α=0:

$$\langle (u(t) - u(0))^2 \rangle \overset{t\to\infty}{\sim} 2L(t)\langle u^2 \rangle$$

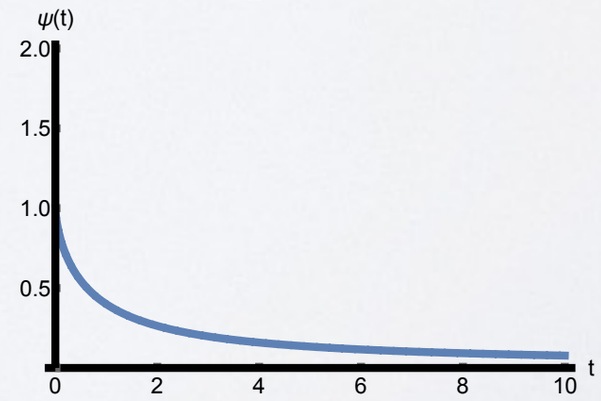


The "diffusion coefficient" is here $D_0 = \langle u^2 \rangle$

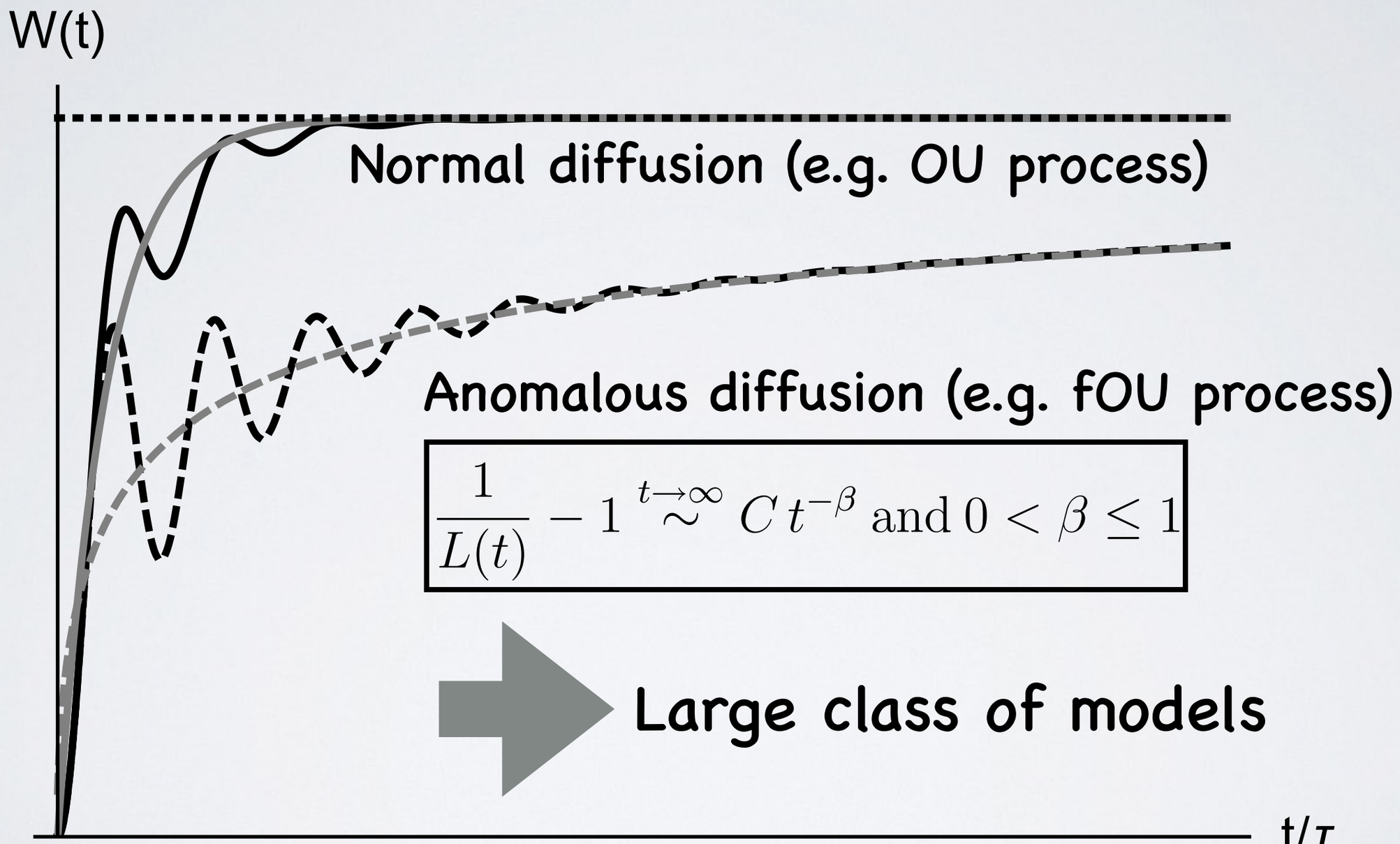
The characteristic time scales becomes $\tau_v = \left(\frac{\langle u^2 \rangle}{\langle v^2 \rangle} \right)^{\frac{1}{2}}$

The slowly growing functions is related to the decay of the position autocorrelation function for long times

$$\frac{\langle u(0)u(t) \rangle}{\langle u^2 \rangle} \overset{t\to\infty}{\sim} 1 - L(t)$$



MSDs for confined (anomalous) diffusion



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*

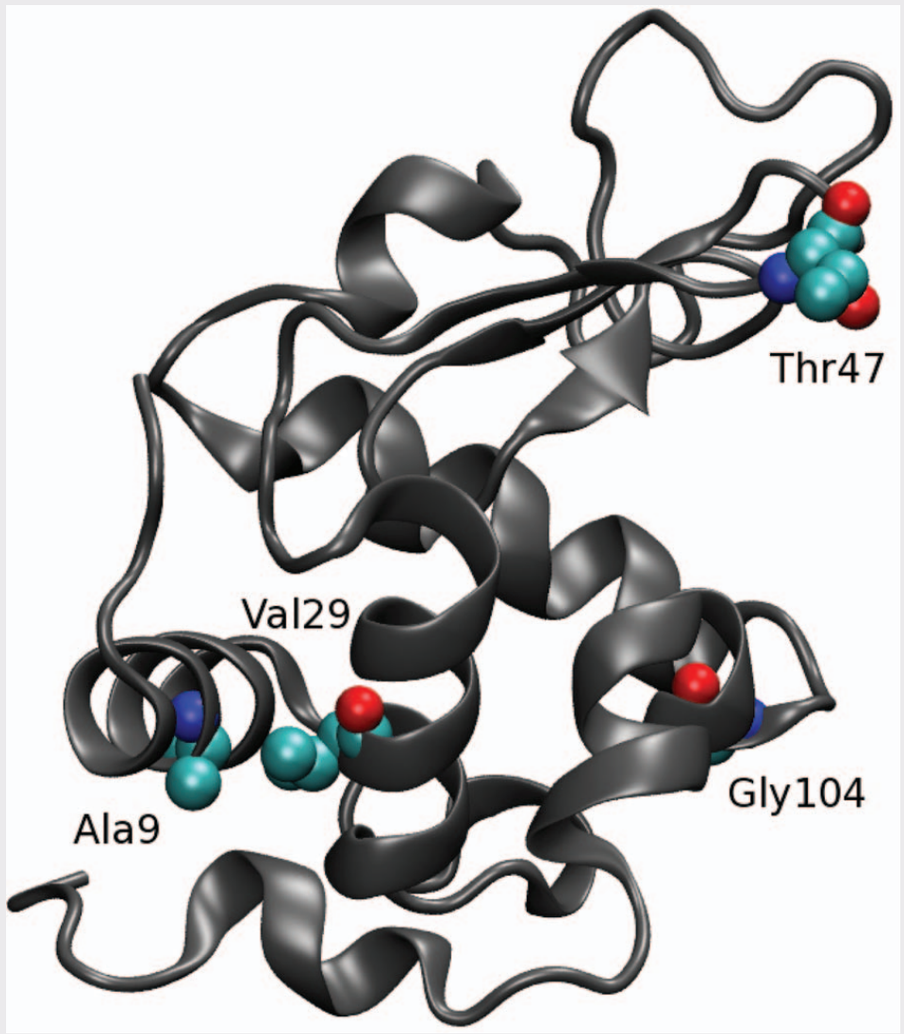


FIG. 1. Four selected residues in the lysozyme molecule.

Normalized position autocorrelation functions

$$\psi(t;\beta) = \frac{1}{(1 + t/\beta)^{\beta}} \qquad (0 < \beta < \infty)$$

- Accommodates exponential and power-law decay

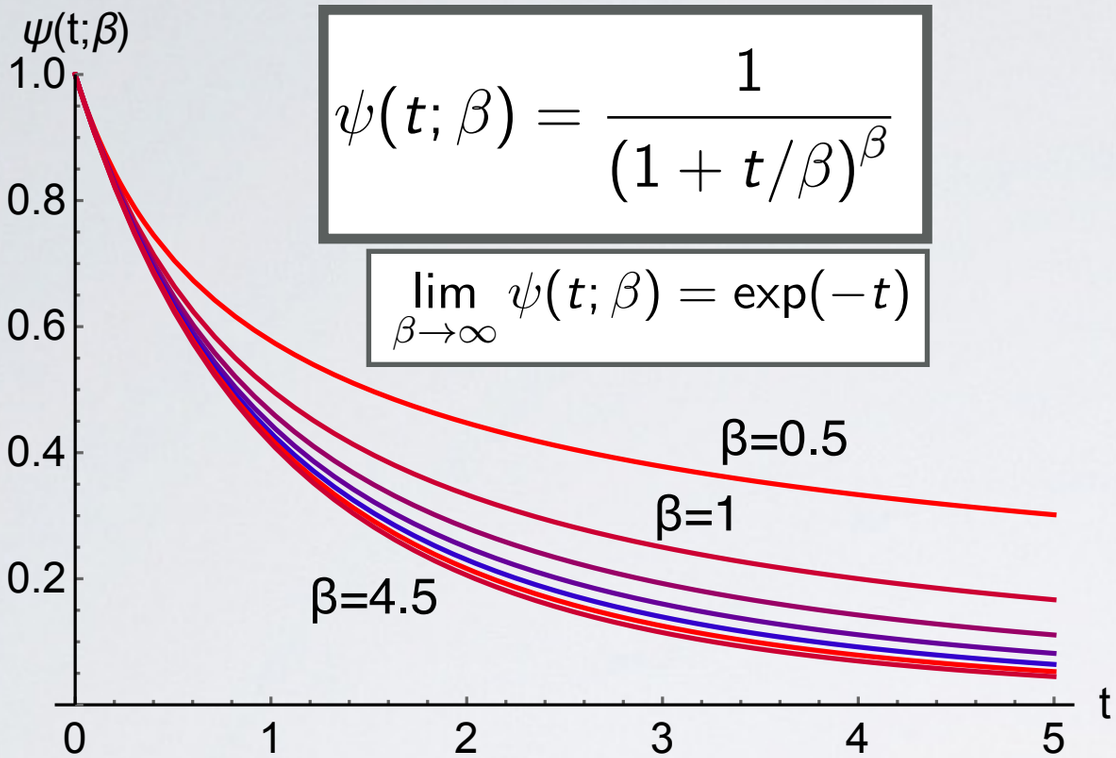
$$\lim_{\beta\to\infty} \psi(t;\beta) = \exp(-t)$$

- Is analytical everywhere, such that all moments of p(λ) exist

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

2nd diffusion model

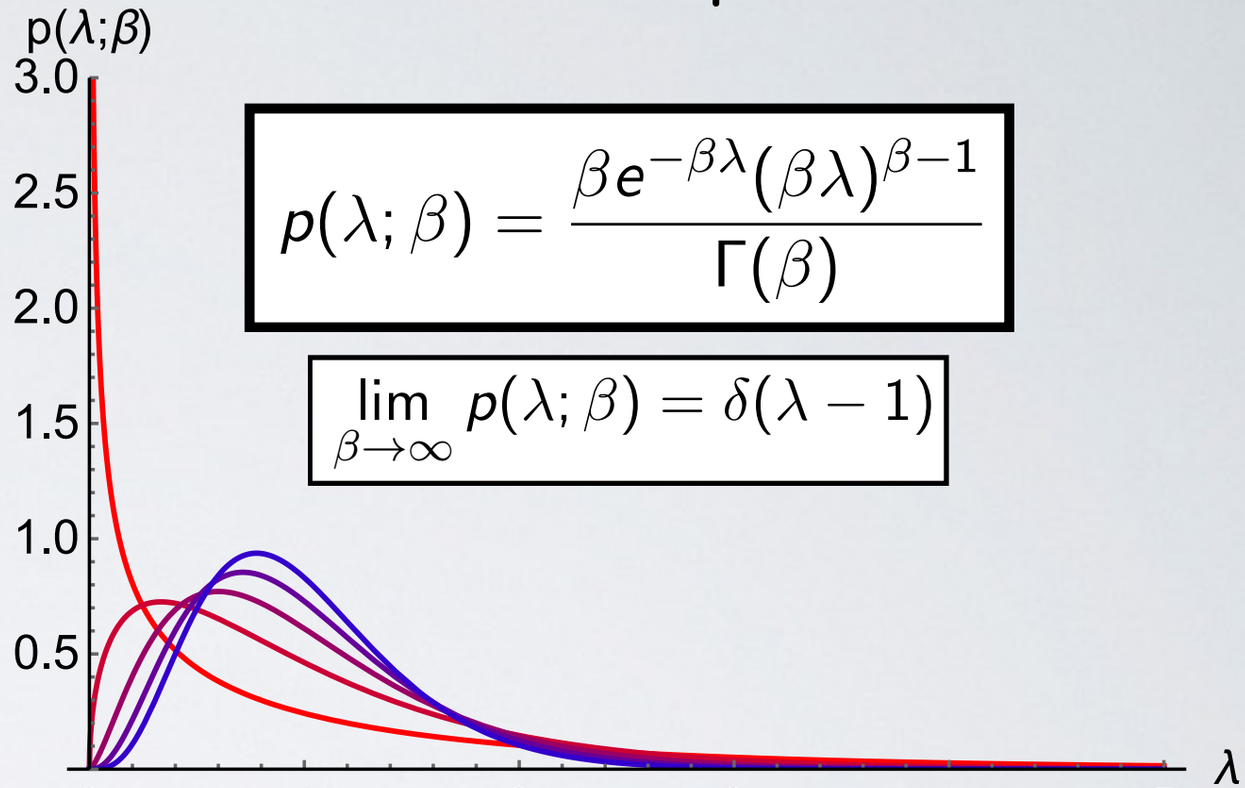
Position auticorrelation function



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

$$\lim_{\beta\to\infty} \psi(t;\beta) = \exp(-t)$$

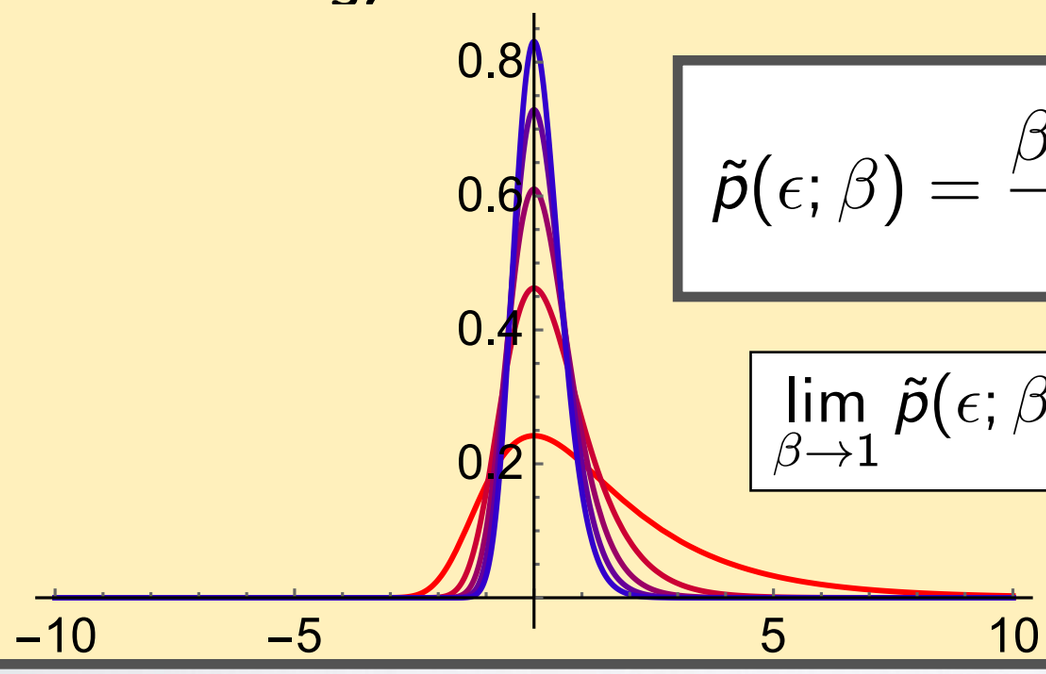
Relaxation rate spectrum



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

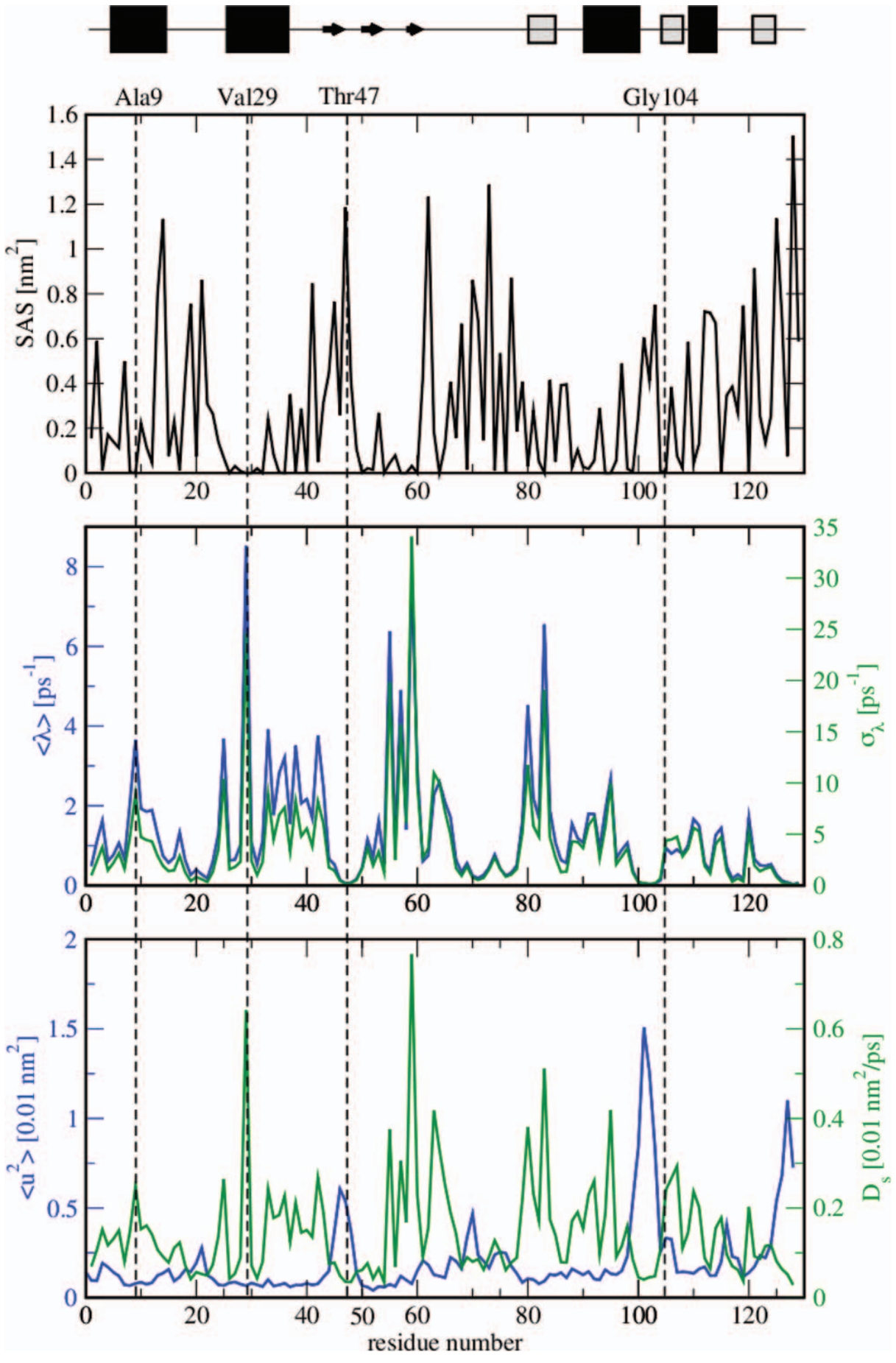
$$\lim_{\beta\to\infty} p(\lambda;\beta) = \delta(\lambda-1)$$

Energy barrier distribution



$$\tilde{p}(\epsilon;\beta) = \frac{\beta^{\beta} e^{-\beta\left(\epsilon+e^{-\epsilon}\right)}}{\Gamma(\beta)}$$

$$\lim_{\beta\to 1} \tilde{p}(\epsilon;\beta) = \delta(\epsilon)$$



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

Solvent-accessible surfaces.

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

$$\overline{\lambda} = \frac{1}{\tau} \qquad \overline{\lambda^2} - \overline{\lambda}^2 = \frac{1}{\beta\tau^2}$$

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

$$D_s = \frac{\langle u^2 \rangle}{\tau}$$

"Universal" asymptotic form of the QENS intermediate scattering function

G.R. Kneller, The Journal of Chemical Physics 145, 044103 (2016).

$$F_{\mathrm{GA}}(q,t) \overset{t\to\infty}{\sim} \underbrace{e^{i\frac{\hbar q^2}{2m}t}}_{\text{recoil}} \underbrace{e^{-q^2 L(t) D_\alpha t^\alpha}}_{\text{cl. diffusion}} \underbrace{e^{iq^2 L(t) D_\alpha \alpha \frac{\beta\hbar}{2} t^{\alpha-1}}}_{\text{quantum effects}}$$

In the special case of confined diffusion this becomes

$$F_{\mathrm{GA}}(q,t) \overset{t\to\infty}{\sim} e^{i\frac{\hbar q^2 t}{2m}} e^{-q^2\langle u^2\rangle L(t)}$$

New perspectives on QENS and energy landscapes seen by neutrons

A wave-mechanical model of incoherent quasielastic scattering in complex systems

Hans Frauenfelder[a,1], Paul W. Fenimore[a], and Robert D. Young[b]

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Contributed by Hans Frauenfelder, July 9, 2014 (sent for review April 15, 2014; reviewed by Angel E. Garcia, Gerald Kneller, Eugene Mamontov, and Roger Pynn)

Significance

Quasielastic incoherent neutron scattering (QENS) is a key tool for the exploration of complex systems, such as liquids, polymers, glasses, and biomolecules. A considerable number of neutron facilities exist and more are being planned. Understanding QENS is important, both for comprehending and applying the science and making efficient use of the facilities. We claim that the present explanation of QENS is incomplete. We propose a wave-mechanical model, consistent with neutron diffraction. It is based on the free-energy landscape and treats the neutrons as de Broglie wave packets. The model is supported by experiments and has predictive power. It provides significant insight into the dynamics of proteins and may lead to a better understanding of biological processes.

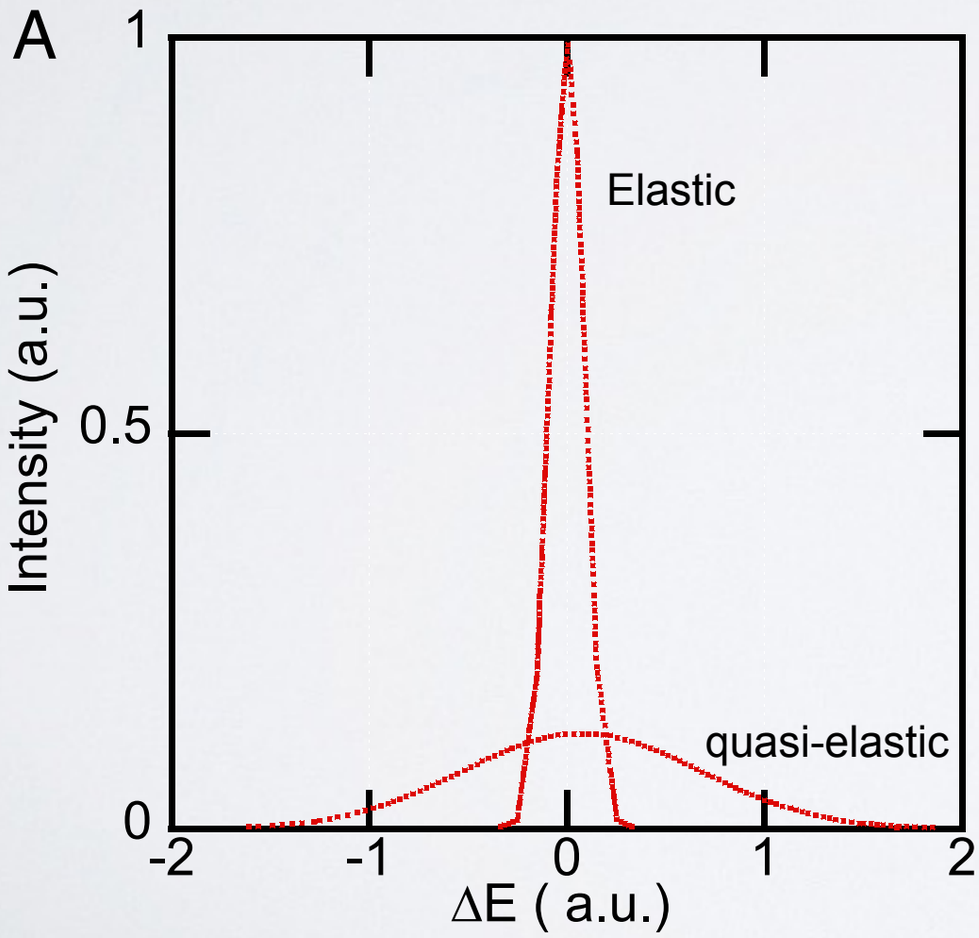
PNAS 111, 12764 (2014).

QENS from a Mössbauer perspective

H. Frauenfelder at al., PNAS 111, 12764 (2014).

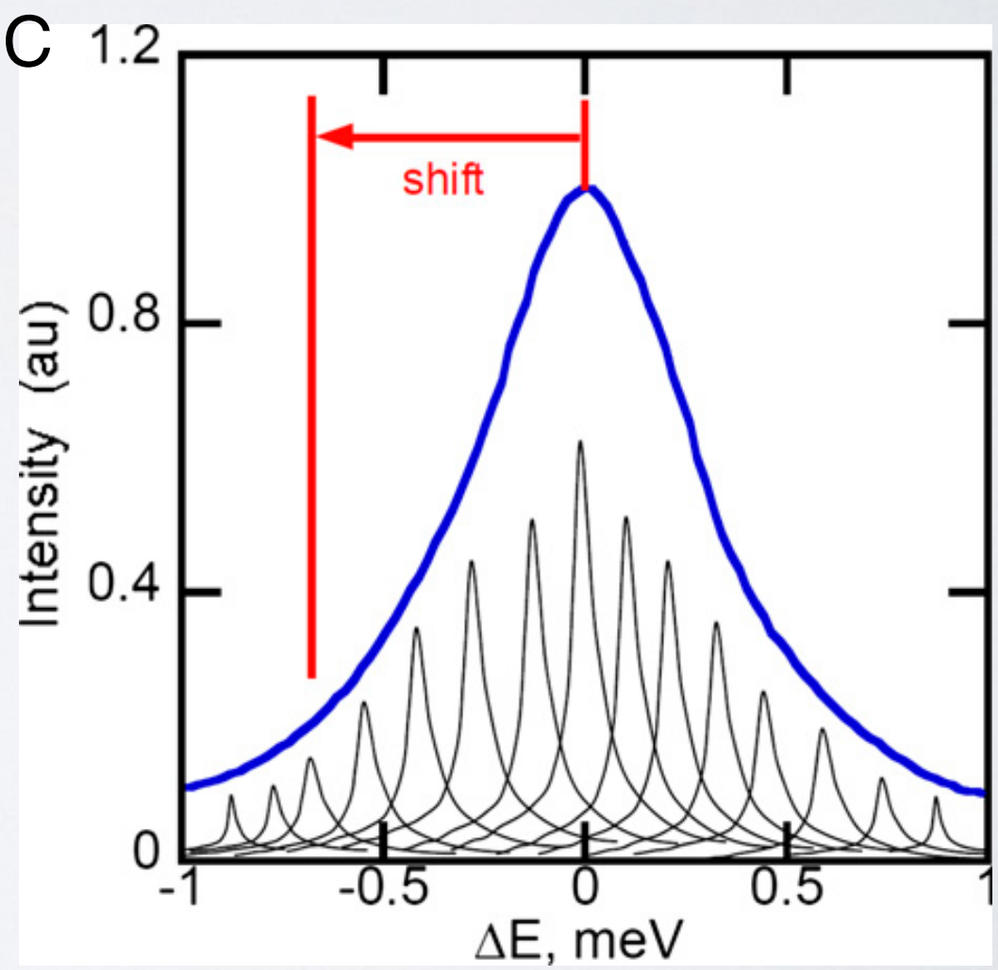
Spatial motion model

Homogeneous QENS spectrum from a diffusion model based on Van Hove's theory

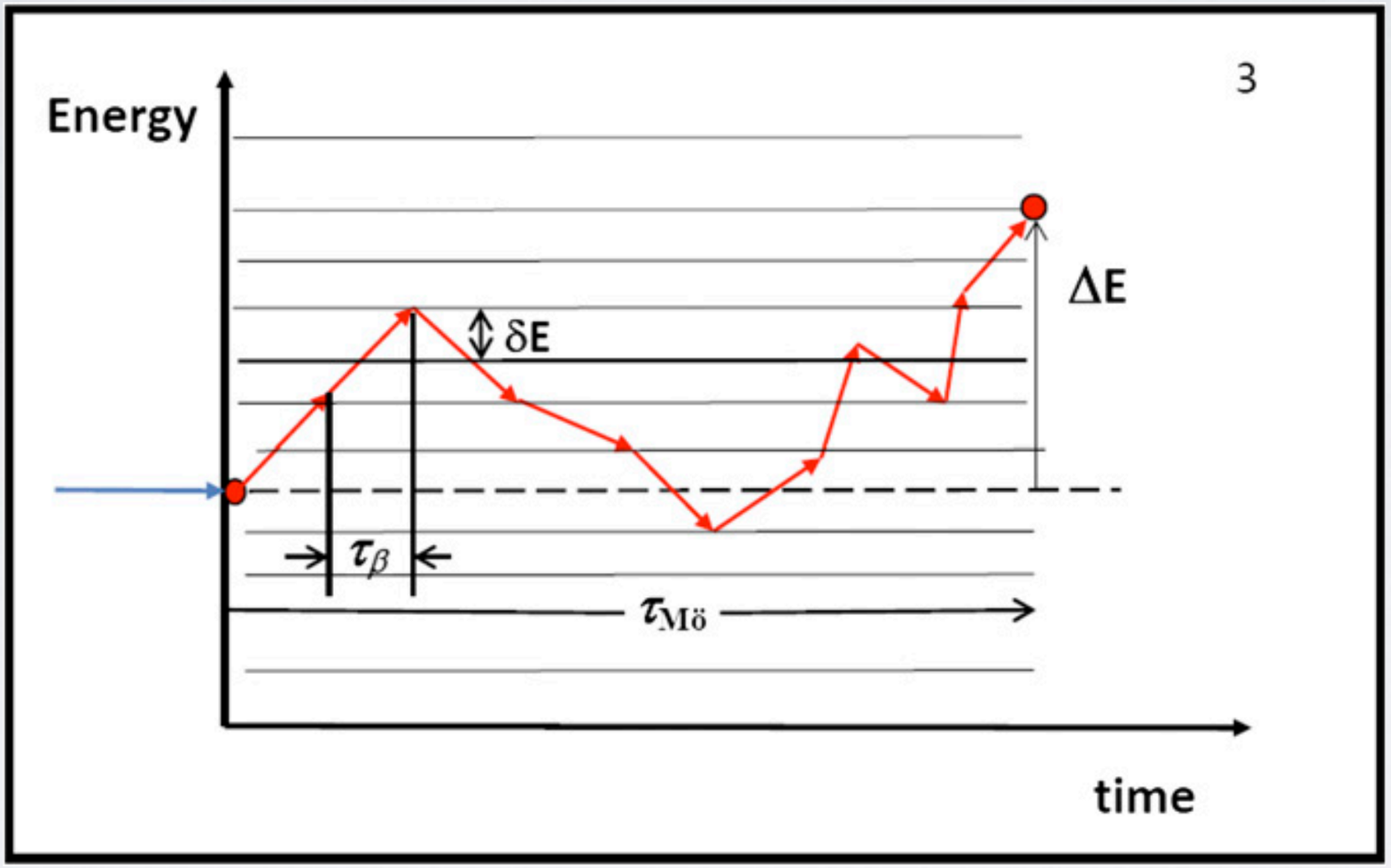


Energy landscape model

Heterogeneous QENS spectrum composed of many « Mössbauer lines »



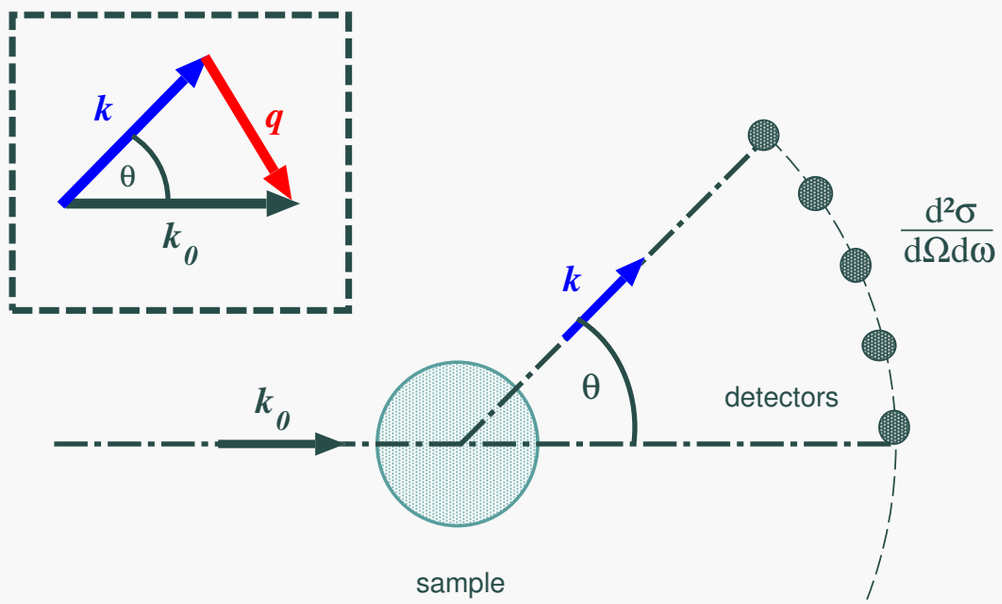
During its flight through the sample, the neutron wave packet records the net energy transition of the system from the initial energy level E to the final level E+ΔE.



- The description is not quantitative
- The neutron is considered as a passive probe
- Momentum transfer is not considered

Conventional interpretation of QENS

Plane wave neutron scattering



$$\frac{d^2\sigma}{d\Omega d\omega} = \frac{k}{k_0} S(\mathbf{q},\omega)$$

momentum transfer:

$$\mathbf{q} = \mathbf{k}_0 - \mathbf{k} = (\mathbf{p}_0 - \mathbf{p})/\hbar$$

energy transfer:

$$\omega = (E_0 - E)/\hbar$$

Information content

$$\mathcal{S}(\mathbf{q},\omega) = \frac{1}{2\pi}\int_{-\infty}^{+\infty} dt\, e^{-i\omega t}\mathcal{F}(\mathbf{q},t)$$

Dynamic structure factor

$$\mathcal{F}(\mathbf{q},t) = \frac{1}{N}\sum_{\alpha\beta}\Gamma_{\alpha\beta}\left\langle e^{-i\mathbf{q}\cdot\hat{\mathbf{r}}_\alpha(0)} e^{i\mathbf{q}\cdot\hat{\mathbf{r}}_\beta(t)}\right\rangle$$

Intermediate scattering function

Self-Scattering from hydrogen dominates

$$\mathcal{F}(\mathbf{q},t) \approx |b_{H,inc}|^2 F_s(\mathbf{q},t)$$

$$F_s(\mathbf{q},t) = \left\langle e^{-i\mathbf{q}\cdot\hat{\mathbf{R}}(0)} e^{i\mathbf{q}\cdot\hat{\mathbf{R}}(t)} \right\rangle$$

Van-Hove theory in the classical limit

$$F_s(\mathbf{q},t) \approx \left\langle e^{-i\mathbf{q}\cdot[\mathbf{R}(0)-\mathbf{R}(t)]} \right\rangle_{cl}$$

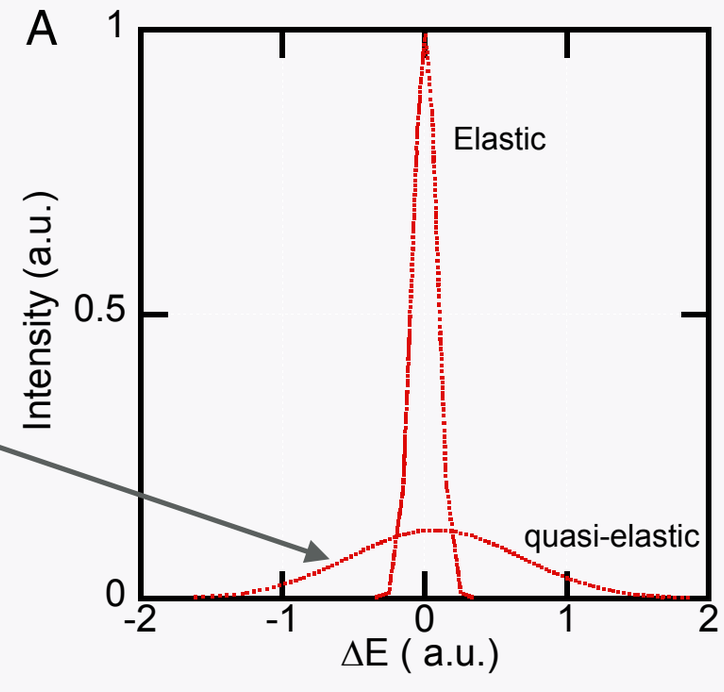
$$= \frac{1}{(2\pi)^3} \int d^3r\, e^{i\mathbf{q}\cdot\mathbf{r}} \underbrace{\langle \delta\left(\mathbf{r} - [\mathbf{R}(0) - \mathbf{R}(t)]\right) \rangle_{cl}}_{G_s(\mathbf{r},t)}$$

No impact of the neutron on the sample !

Diffusion models for the Van Hove correlation function (➜ "spatial motion models")

$$\partial_t G_s(\mathbf{r},t)) = D\Delta G_s(\mathbf{r},t)$$

Spatial Fourier Transform



Franck-Condon picture of neutron scattering

From plane wave scattering to energy landscapes

A somewhat forgotten paper....

G. Wick, The scattering of neutrons by systems containing light nuclei;
Physical Review 94, 1228 (1954).

ISF in the Heisenberg picture

$$F_s(\mathbf{q},t) = \frac{1}{Z}\mathrm{tr}\left\{e^{-\beta\hat{H}}e^{-i\mathbf{q}\cdot\hat{\mathbf{r}}}e^{it\hat{H}/\hbar}e^{i\mathbf{q}\cdot\hat{\mathbf{r}}}e^{-it\hat{H}/\hbar}\right\}$$

$$= \frac{1}{Z}\mathrm{tr}\left\{e^{-\beta\hat{H}}e^{it\hat{H}'(\mathbf{q})/\hbar}e^{-it\hat{H}/\hbar}\right\}$$

"Kicked" Hamiltonian

$$\hat{H}'(\mathbf{q}) = \sum_{\alpha=1}^{N}\frac{(\hat{\mathbf{p}}_\alpha + \delta_{1\alpha}\hbar\mathbf{q})^2}{2m_\alpha} + V(\hat{\mathbf{r}}_1,\ldots,\hat{\mathbf{r}}_N)$$

Normal Hamiltonian

$$\hat{H} = \sum_{\alpha=1}^{N}\frac{\hat{\mathbf{p}}_\alpha^2}{2m_\alpha} + V(\hat{\mathbf{r}}_1,\ldots,\hat{\mathbf{r}}_N)$$

$$F_s(\mathbf{q},t) = \left\langle e^{\frac{it}{\hbar}\hat{H}'(\mathbf{q})}e^{-\frac{it}{\hbar}\hat{H}}\right\rangle$$

Eigenvalues and eigenfunctions for the Hamiltonians

$$\hat{H}\phi_n(\mathbf{p}) = E_n\phi_n(\mathbf{p})$$
$$\hat{H}'(\mathbf{q})\phi_n(\mathbf{p}+\hbar\mathbf{Q}) = E_n\phi_n(\mathbf{p}+\hbar\mathbf{Q})$$

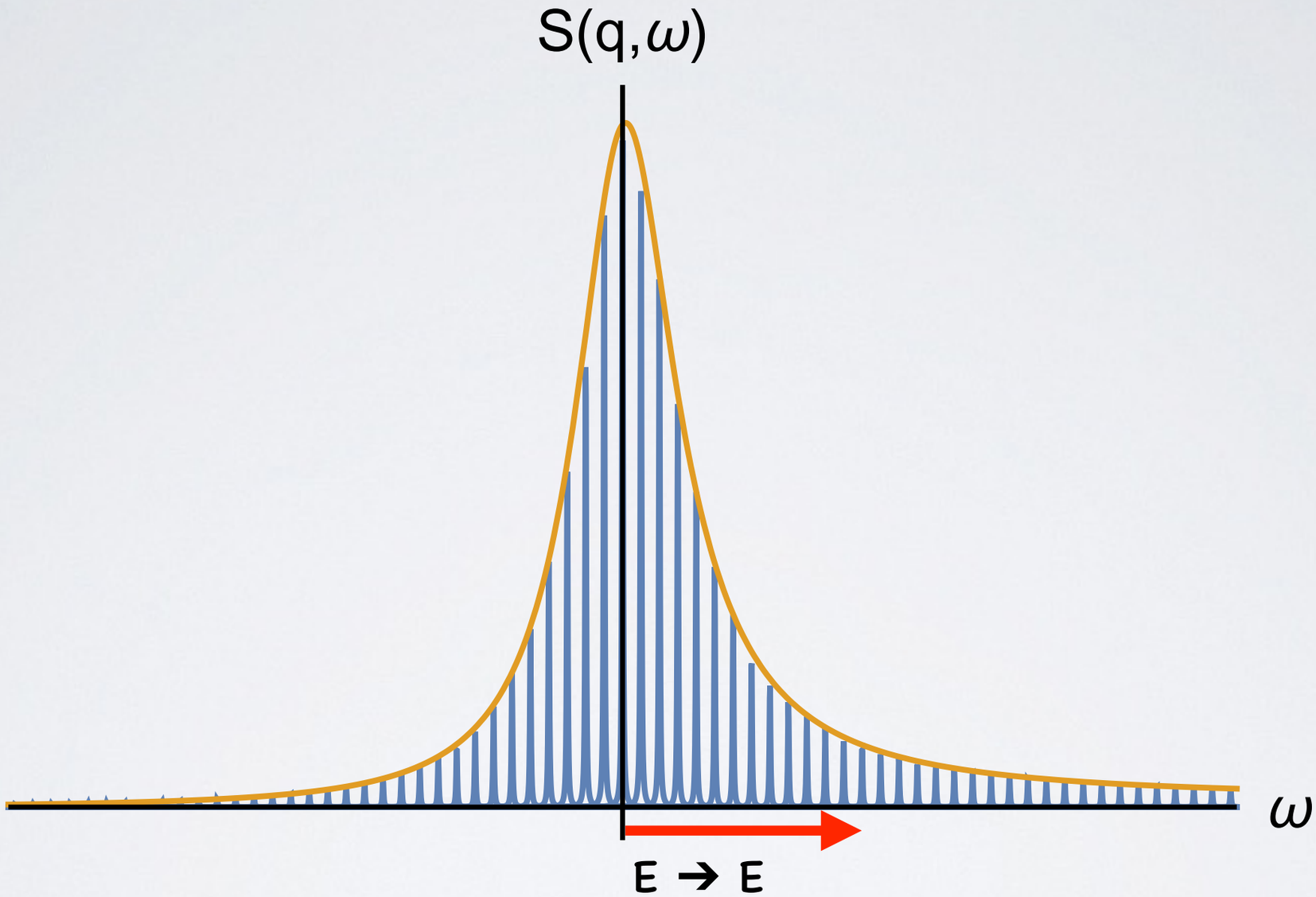
→ Franck-Condon type transition probabilities in momentum space

$$p_{mn}(\mathbf{q}) = \left| \int d^{3N}p\, \phi_n^*(\mathbf{p}+\hbar\mathbf{Q})\phi_m(\mathbf{p}) \right|^2$$

→ Line spectrum for the dynamic structure factor

$$F_s(\mathbf{q},t) = \frac{1}{Z}\sum_{m,n} e^{-\beta E_m} e^{it(E_n-E_m)/\hbar} p_{mn}(\mathbf{q})$$
$$S_s(\mathbf{q},\omega) = \frac{1}{Z}\sum_{m,n} e^{-\beta E_m} p_{mn}(\mathbf{q})\delta\left(\omega - [E_n - E_m]/\hbar\right)$$

Line spectrum for S(q,ω)



Detailed balance and recoil

It follows from the symmetry properties of the transition properties

$$\boxed{p_{mn}(\mathbf{q}) = p_{nm}(-\mathbf{q})}$$

that the detailed balance relations are fulfilled

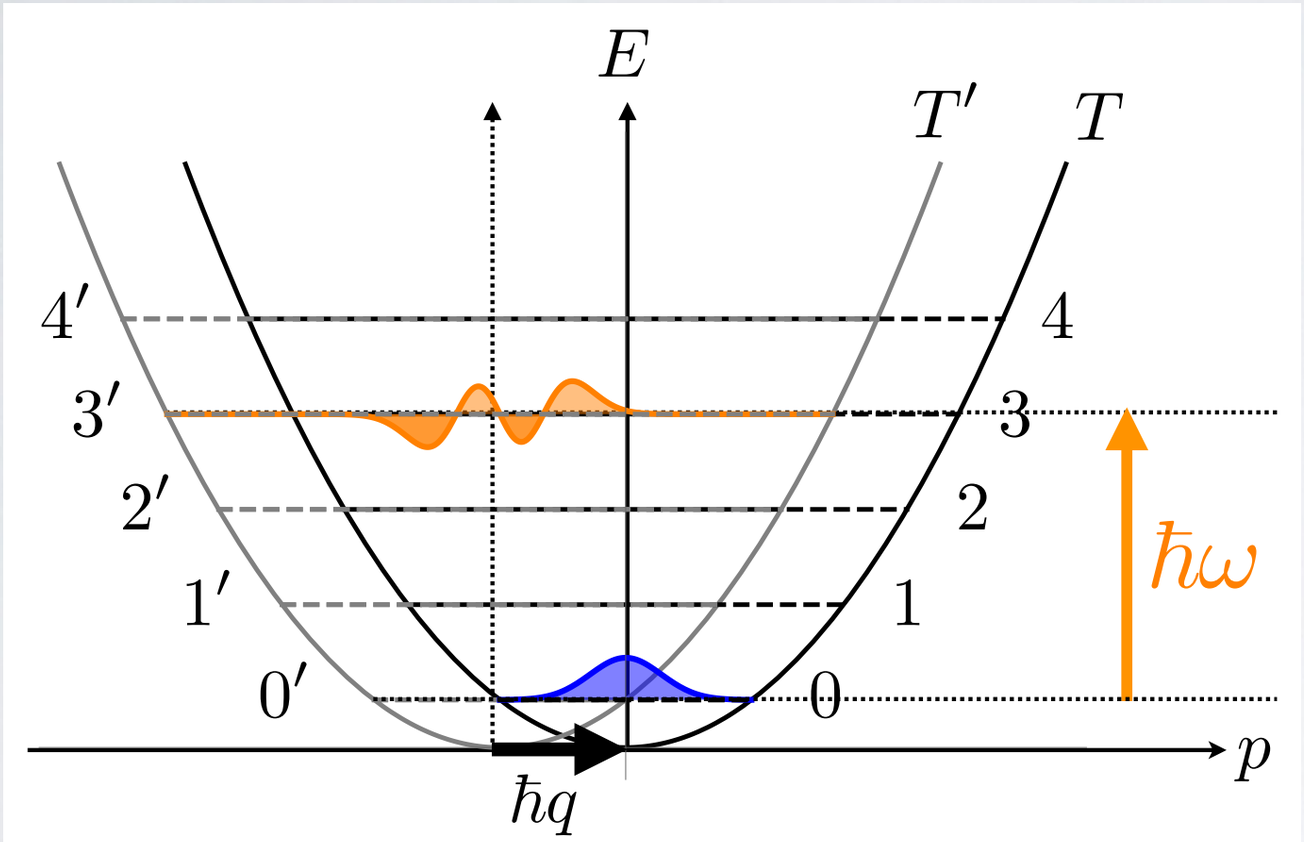
$$\boxed{\begin{aligned} F_s(\mathbf{q},t) &= F_s(-\mathbf{q},-t+i\beta\hbar) \\ S_s(\mathbf{q},\omega) &= e^{\beta\hbar\omega} S_s(-\mathbf{q},-\omega) \end{aligned}}$$

The scattering kinematics is reflected in the recoil moment

$$\boxed{\int_{-\infty}^{+\infty} d\omega\, \omega S_s(\mathbf{q},\omega) = \frac{\hbar q^2}{2m}}$$

An analytical example - harmonic oscillator

Wave functions for the 0→3′ transition



T V

$$E = \frac{p^2}{2m} + \frac{1}{2} m \Omega^2 x^2$$

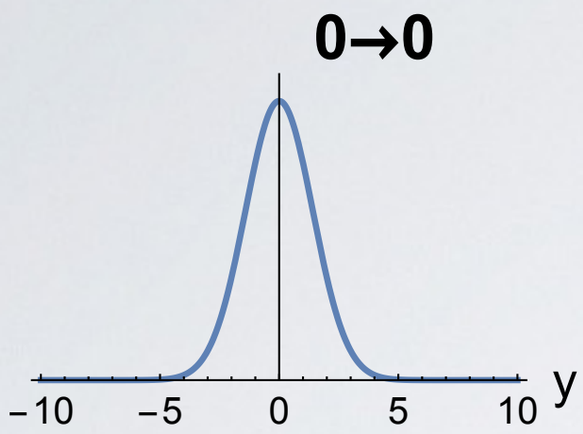
$$p_{mn}(q) = e^{-\frac{y^2}{4}} (-1)^{m+n} L_m^{(n-m)}\left(\frac{y^2}{4}\right) L_n^{(m-n)}\left(\frac{y^2}{4}\right)$$

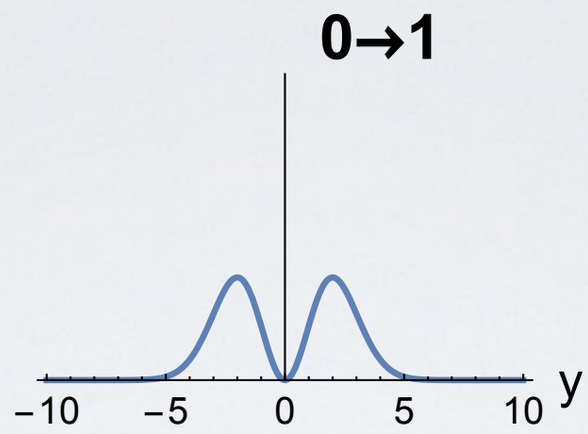
Transition probabilities

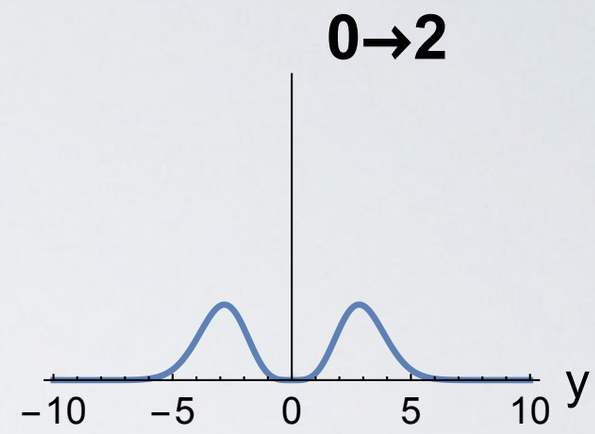
$$y(q) = \sqrt{\frac{2\hbar}{M\Omega}} q$$

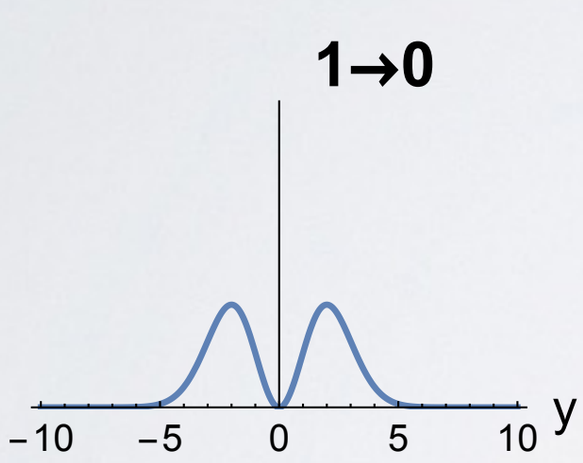
Dimensionless momentum transfer

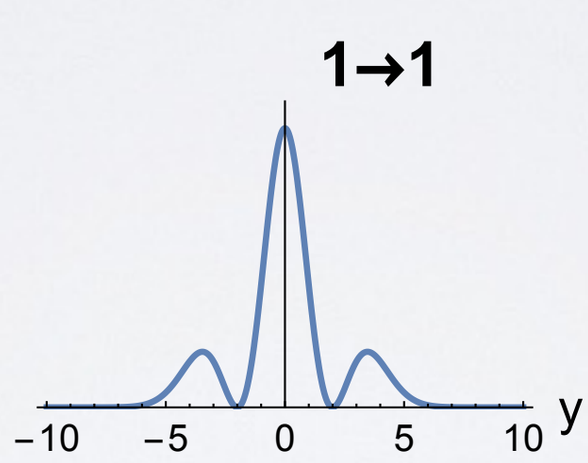
Some transition probabilities as a function of momentum transfer

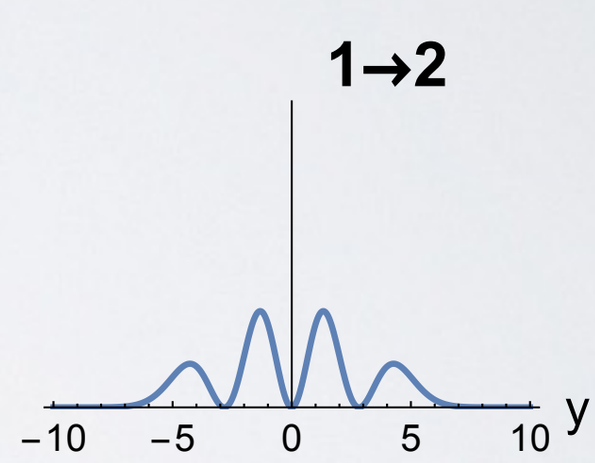


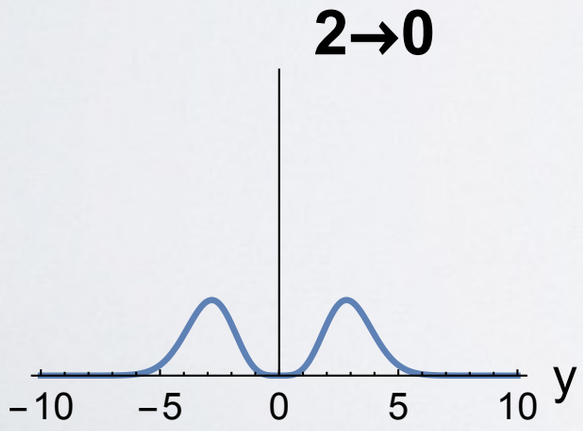


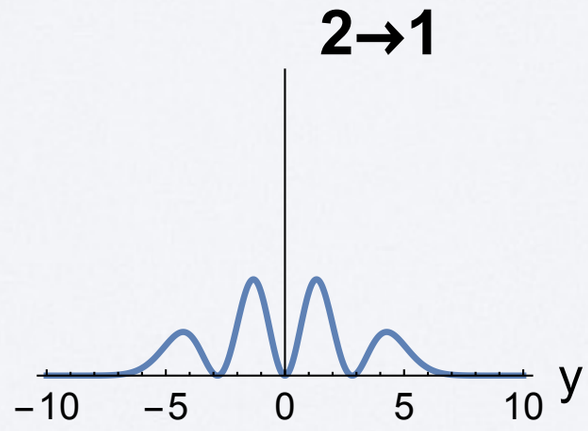


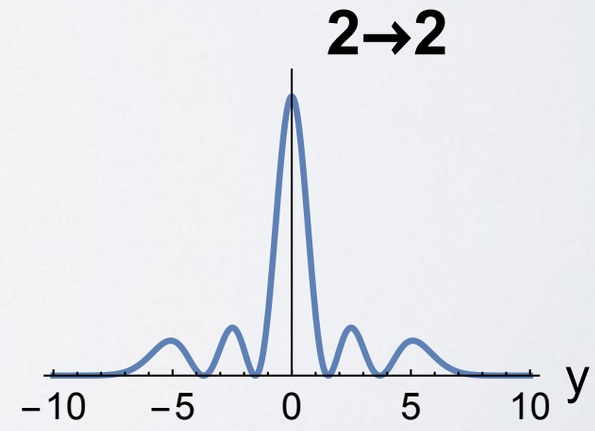












Intermediate scattering function

$$F_s(q,t) = \frac{1}{Z}\sum_{m,n} e^{-\beta\hbar\Omega(m+1/2)} e^{i(n-m)\Omega t} p_{mn}(q)$$

Textbook result (c.f. Lovesey)

$$F_s(q,t) = e^{i\frac{y(q)^2}{4}\left(\sin(\Omega t)+i(1-\cos(\Omega t))\coth\left(\frac{\beta\Omega\hbar}{2}\right)\right)}$$

Dynamic structure factor

$$S_s(q,\omega) = \frac{1}{Z}\sum_{m,n} e^{-\beta\hbar\Omega(m+1/2)} \delta\big(\omega - [n-m]\Omega\big) p_{mn}(q)$$

Complex systems

The energy levels of complex systems are quasi-continuously distributed.

$$\hat{H}|\phi(X)\rangle = E(X)|\phi(X)\rangle$$

X is a set of variables describing the state of the system

$$\langle\phi(X')|\phi(X)\rangle = \begin{cases} 1 & \text{if } X = X', \\ 0 & \text{otherwise} \end{cases}$$

Continuous counting $m \to dm = \rho(X)d^f X$

ρ(X) is the density of states of the system.

The scattering functions are determined by the transition probabilities and the density of states, ρ(X).

The dynamic structure factor is a continuous function in ω

$$S_s(\mathbf{q},\omega) = \int\int d^f X d^f X' \rho(X) p_{\mathrm{eq}}(X) \rho(X') p(X'|X,\mathbf{q}) \delta(\omega - [E(X') - E(X)]/\hbar)$$

Conclusions

- Energy landscapes are an intuitive concept to understand protein structural dynamics, but they are NOT directly probed by neutron scattering.
- Diffusion-based EL models tacitly the classical limit, where recoil effects are absent and the neutron acts an "observer".
- What is really measured in neutron scattering experiments is the reaction of the target to the impact of the neutron. The scattering of neutrons induces transitions on the energy landscape and the corresponding momentum transfer-dependent transition probabilities determine the measured intensities.

Merci à

- Hans Frauenfelder, LANL
- Konrad Hinsen, CBM Orléans/SOLEIL
- Vania Calandrini, CBM ➟ FZJ Jülich (D)
- Paolo Calligari, CBM ➟ SISSA (I)
- Daniel Abergel, ENS Paris
- Marie-Claire Bellissent-Funel, CEA Saclay

Agence Nationale de la Recherche ANR programme "Conception et Simulation"

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