A new spectroscopic perspective of neutron scattering - re-thinking the fundamentals

Presentation SNS Oakridge - July 2022

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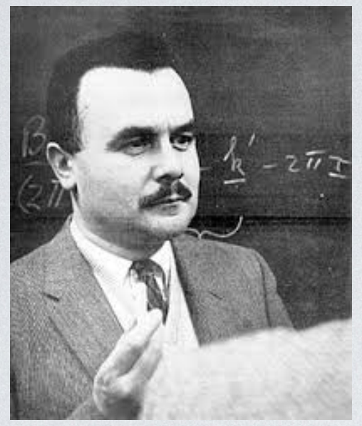
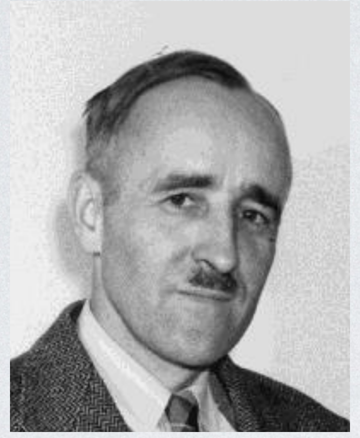
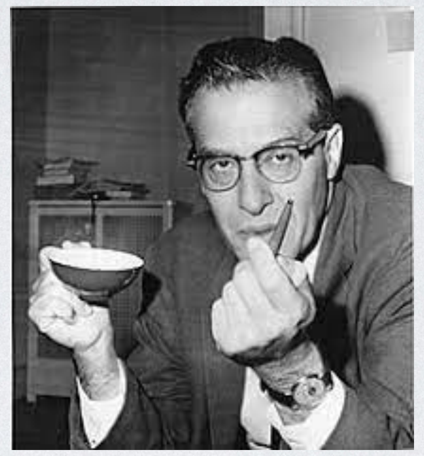
Thermal neutron scattering — probing the structural dynamics of condensed matter at the atomic scale

J. Chadwick

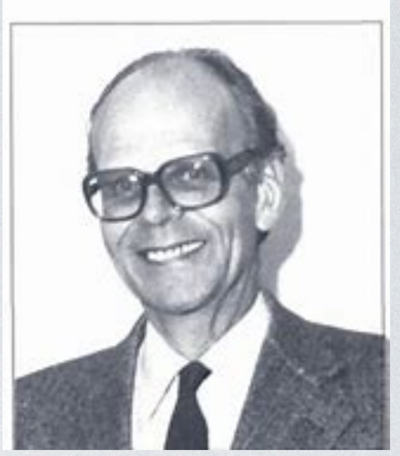
B.N. Brockhouse

C.G. Shull

E. Wollan

E. Fermi

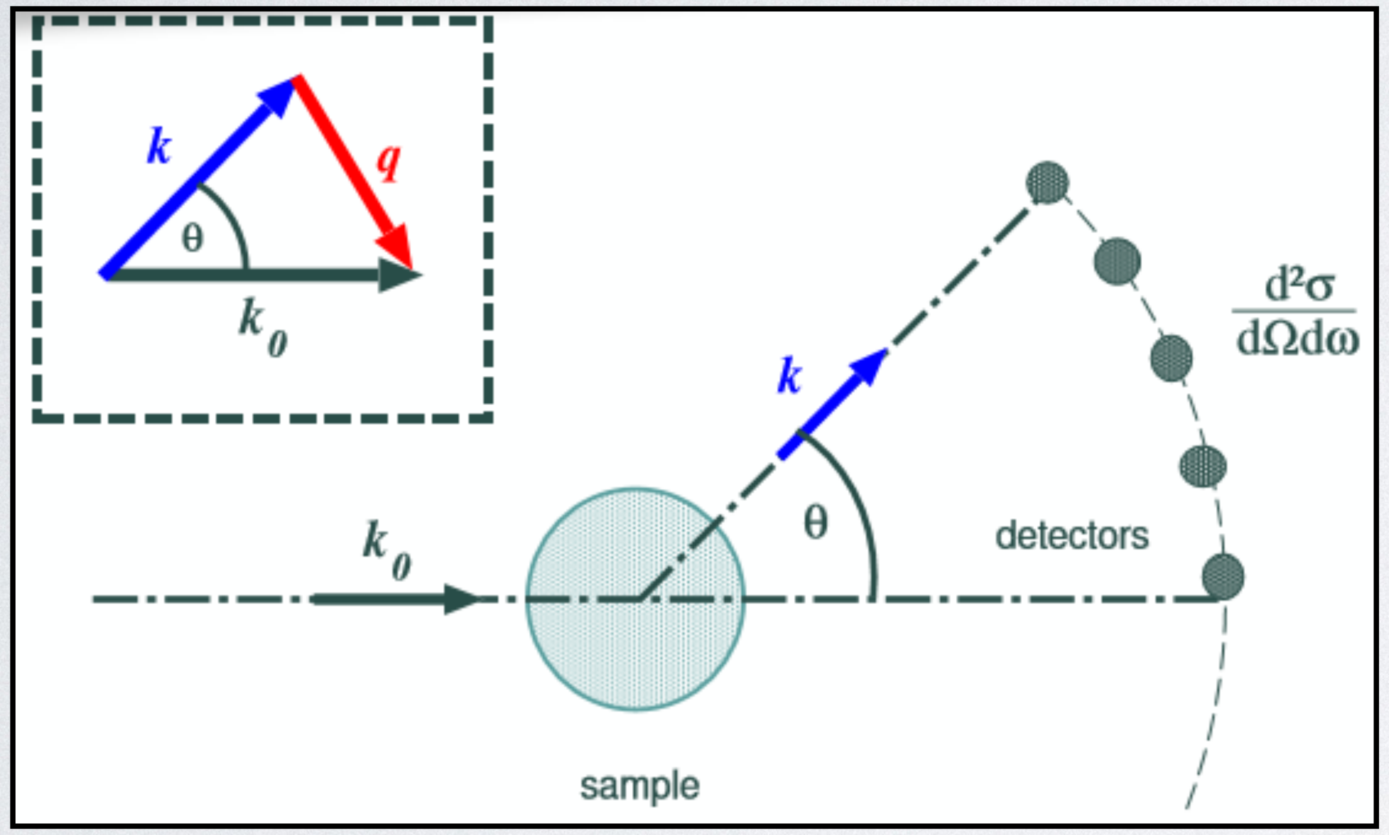
B. Lippmann

J. Schwinger

G. Placzek

G.C. Wick

L. Van Hove

A. Rahman


Scattering experiment



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

Differential scattering cross section

$$\hbar\mathbf{q} = \mathbf{p}_0 - \mathbf{p}$$

$$\hbar\omega = \frac{|\mathbf{p}_0|^2}{2m} - \frac{|\mathbf{p}|^2}{2m}$$

Momentum and Energy transfer

Scattering theory

Fermi pseudopotential

$$V(\mathbf{r}) = \frac{2\pi\hbar^2}{m}\sum_i b_i \delta(\mathbf{r} - \hat{\mathbf{R}}_i)$$

$$|b| \ll \lambda_n$$

Lippmann-Schwinger equation

$$|\Psi^{(+)}\rangle = |\Psi^{(0)}\rangle + \frac{1}{E - \hat{\mathbf{H}}_n - \hat{\mathbf{H}}_t + i\epsilon}\hat{\mathbf{V}}|\Psi^{(+)}\rangle$$

Interpretation

Dynamic structure factor

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

Intermediate scattering function

$$F(\mathbf{q},t) = \frac{1}{N}\sum_{j,k}\Gamma_{jk}\left\langle e^{-i\mathbf{q}\cdot\hat{\mathbf{R}}_j(0)} e^{i\mathbf{q}\cdot\hat{\mathbf{R}}_k(t)}\right\rangle$$

$$\Gamma_{jk} = \overline{b_j}^*\overline{b_k} + \delta_{jk}\overline{|b_j - \overline{b_j}|^2}$$

F(q,t) is a quantum time correlation function

Symmetries

$$F^*(\mathbf{q},t) = F(\mathbf{q},-t),$$
$$F(\mathbf{q},-t) = F(-\mathbf{q},t+i\beta\hbar)$$

⟺

$$S^*(\mathbf{q},\omega) = S(\mathbf{q},\omega),$$
$$S(\mathbf{q},\omega) = e^{\beta\hbar\omega} S(-\mathbf{q},-\omega)$$

Recoil moment

$$\int_{-\infty}^{+\infty} d\omega\, \omega S(\mathbf{q},\omega) = -i \left.\frac{\partial F(\mathbf{q},t)}{\partial t}\right|_{t=0} \propto \frac{\hbar|\mathbf{q}|^2}{2m}$$

Scattering kinematics

Motivation for a spectroscopy-oriented theory of neutron scattering

Time-dependent pair correlation function

PHYSICAL REVIEW VOLUME 95, NUMBER 1 JULY 1, 1954

Correlations in Space and Time and Born Approximation Scattering in Systems of Interacting Particles

LÉON VAN HOVE
Institute for Advanced Study, Princeton, New Jersey
(Received March 16, 1954)

From (q,ω)-space to (r,t)-space

$$G(\mathbf{r},t) = \frac{1}{(2\pi)^3}\int\int d^3q dt\, e^{i(\omega t - \mathbf{q}.\mathbf{r})} S(\mathbf{q},\omega)$$
$$= \frac{1}{N}\sum_{j,k}\Gamma_{jk}\int d^3r' \left\langle \delta\left(\mathbf{r}-\mathbf{r}'+\hat{\mathbf{R}}_j(0)\right)\delta\left(\mathbf{r}'-\hat{\mathbf{R}}_k(t)\right)\right\rangle$$

$$G^*(\mathbf{r},t) = G(-\mathbf{r},-t),$$
$$G(\mathbf{r},-t) = G(-\mathbf{r},t-i\beta\hbar)$$

Only for $\hbar \rightarrow 0$ G(r,t) becomes a time-dependent (real-valued) pair correlation function

$$G_{\rm cl}(\mathbf{r},t) = \frac{1}{N}\sum_{j,k}\Gamma_{jk}\left\langle\delta\left(\mathbf{r}-[\mathbf{R}_k(t)-\mathbf{R}_j(0)]\right)\right\rangle_{\rm cl}$$

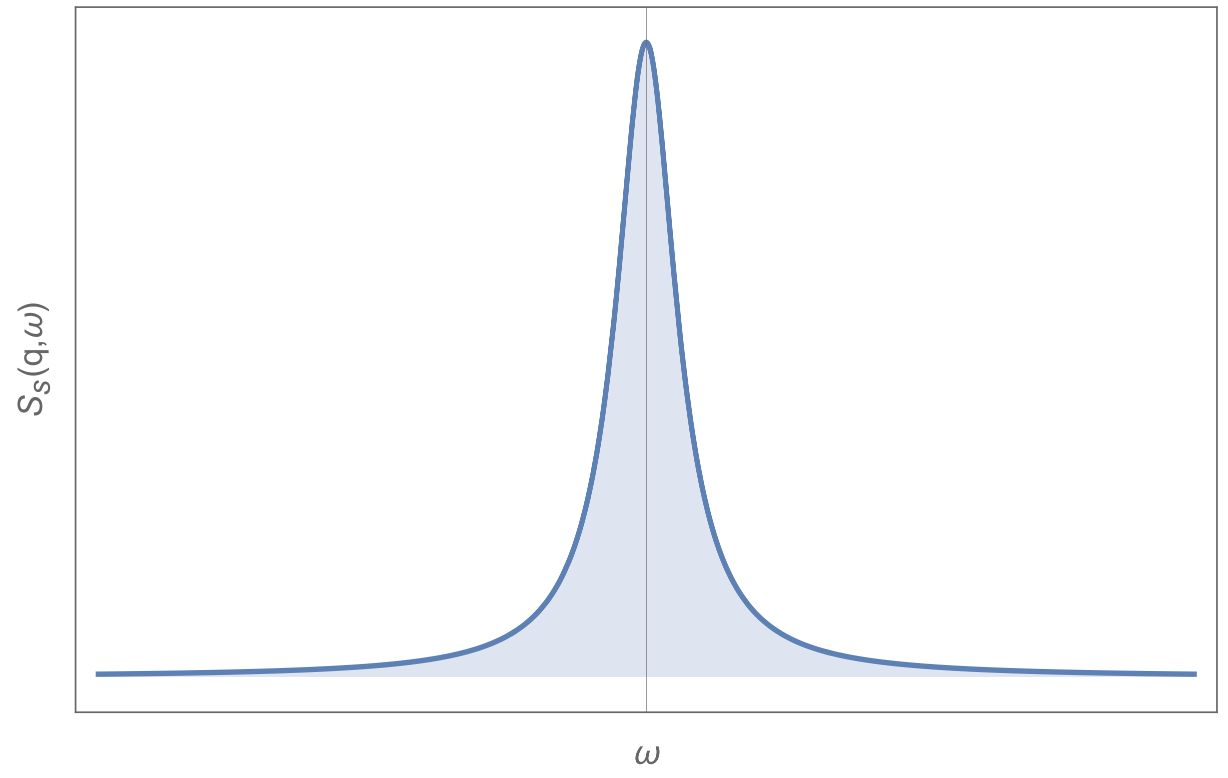
Classical statistical mechanics description of neutron scattering

"Spatial motion models"

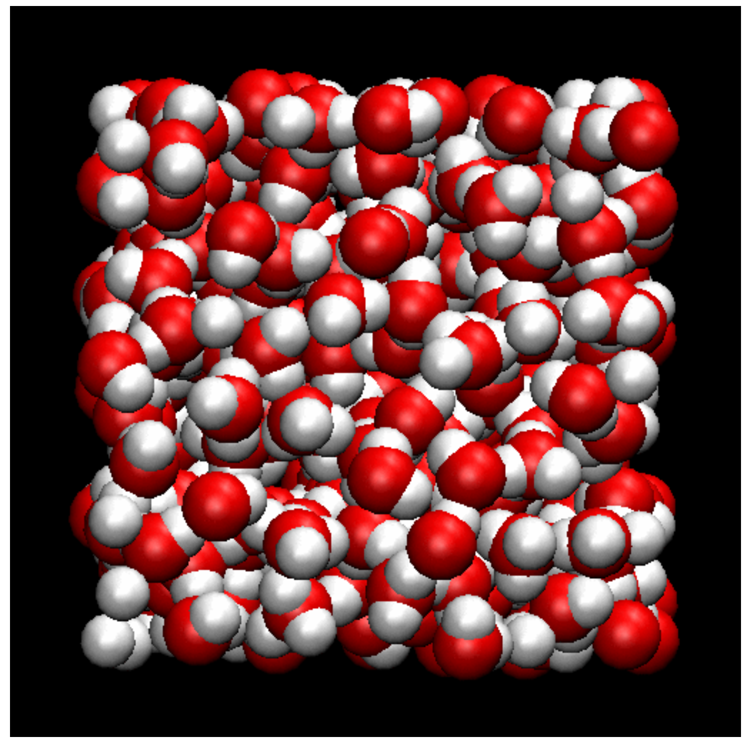
$$\partial_t G(\mathbf{r},t) = D\Delta G(\mathbf{r},t)$$

$$G(\mathbf{r},t) = \frac{e^{-\frac{|\mathbf{r}|^2}{4Dt}}}{(2\sqrt{\pi D t})^3}$$

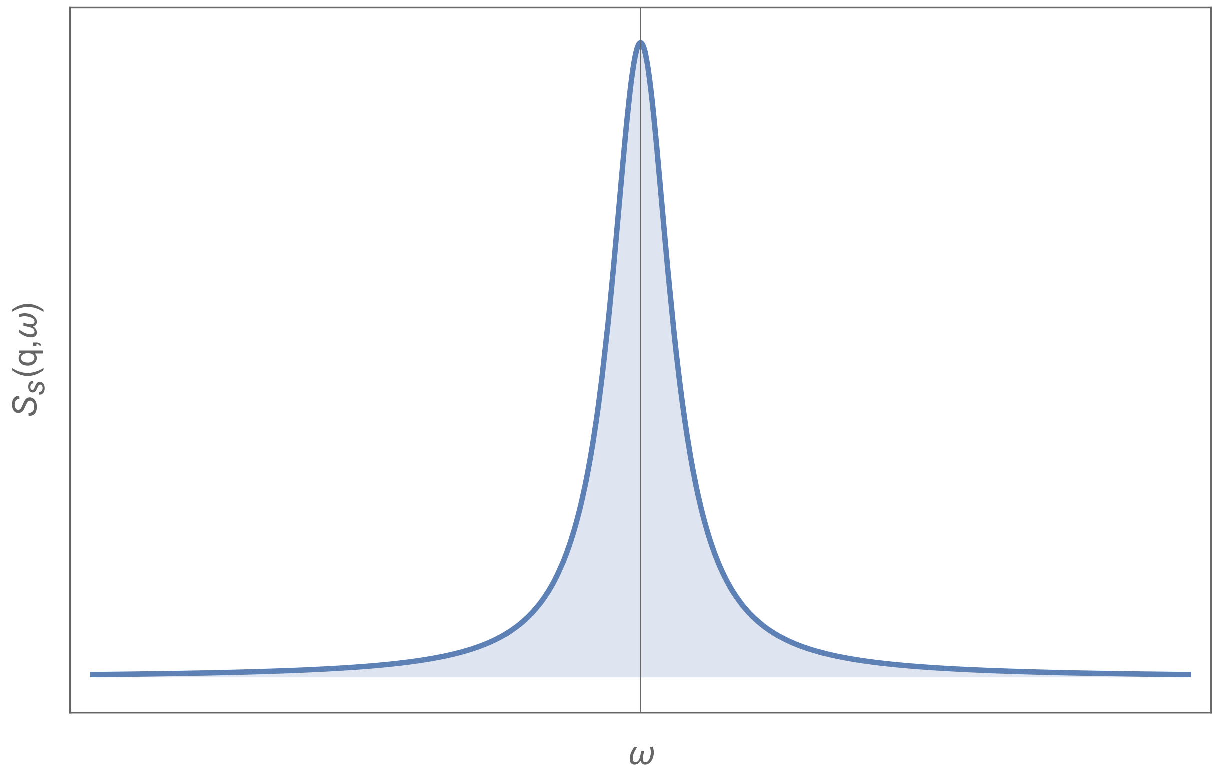
$$S(\mathbf{q},\omega) = \frac{1}{\pi}\frac{D|\mathbf{q}|^2}{(D|\mathbf{q}|^2)^2+\omega^2}$$



MD simulations / "trajectories"



$$F_{\mathrm{cl}}(\mathbf{q},t) \approx \frac{1}{N}\sum_{j,k}\Gamma_{jk}\,\frac{1}{T}\int_0^T d\tau\, e^{-i\mathbf{q}\cdot\mathbf{R}_j(\tau)}e^{i\mathbf{q}\cdot\mathbf{R}_k(\tau+t)}$$



Van Hove, Léon
1958

Physica XXIV
Zernike issue
404--408

A REMARK ON THE TIME-DEPENDENT PAIR DISTRIBUTION

by LÉON VAN HOVE

Instituut voor theoretische fysica der Rijksuniversiteit, Utrecht, Nederland

$$G(\mathbf{r}, t) = G_0(\mathbf{r}, t) + i\hbar G_1(\mathbf{r}, t)$$

$$n(\mathbf{r}, t) = \rho_0 - (2\pi a\hbar^2/m)\rho_0 \int_{-\infty}^{t} \mathrm{d}t' G_1(\mathbf{r} - \mathbf{r}_{t'}, t - t').$$

The imaginary (odd part in time) of G(r,t) describes the density perturbation of the sample due to the impact of the neutrons.

For $\hbar \to 0$ "impactless" scattering. The neutron is a passive probe.

Spotting the "kick" of the neutron

PHYSICAL REVIEW VOLUME 94, NUMBER 5 JUNE 1, 1954

The Scattering of Neutrons by Systems Containing Light Nuclei*

G. C. Wick
Carnegie Institute of Technology, Pittsburgh, Pennsylvania, and Institute for Advanced Study, Princeton, New Jersey

(Received January 21, 1954)

$$F_s(\mathbf{q},t) = \left\langle e^{-i\mathbf{q}\cdot\hat{\mathbf{x}}_1(0)} e^{i\mathbf{q}\cdot\hat{\mathbf{x}}_1(t)} \right\rangle = \boxed{\left\langle e^{it\hat{H}'(\mathbf{q})/\hbar} e^{-it\hat{H}/\hbar} \right\rangle}$$

"Positionless" representation of F(q,t)

$$\hat{H}'(\mathbf{q}) = \sum_k \frac{(\hat{p}_k + \hbar\mathbf{q}\delta_{1k})^2}{2m_k} + V\left(\hat{\mathbf{R}}_1, .., \hat{\mathbf{R}}_N\right)$$

"Kicked Hamiltonian"

Proof:

$$\left\langle e^{-i\mathbf{q}\cdot\hat{\mathbf{x}}_1(0)} e^{i\mathbf{q}\cdot\hat{\mathbf{x}}_1(t)} \right\rangle = \frac{1}{Z}\mathrm{tr}\Big\{ e^{-\beta\hat{H}} e^{-i\mathbf{q}\cdot\hat{\mathbf{x}}_1} \underbrace{e^{it\hat{H}/\hbar} e^{i\mathbf{q}\cdot\hat{\mathbf{x}}_1} e^{-it\hat{H}/\hbar}}_{e^{i\mathbf{q}\cdot\hat{\mathbf{x}}_1(t)}} \Big\}$$

$$= \frac{1}{Z}\mathrm{tr}\Big\{ e^{-\beta\hat{H}} \underbrace{e^{-i\mathbf{q}\cdot\hat{\mathbf{x}}_1} e^{it\hat{H}/\hbar} e^{i\mathbf{q}\cdot\hat{\mathbf{x}}_1}}_{e^{it\hat{H}'(\mathbf{q})/\hbar}} e^{-it\hat{H}/\hbar} \Big\}$$

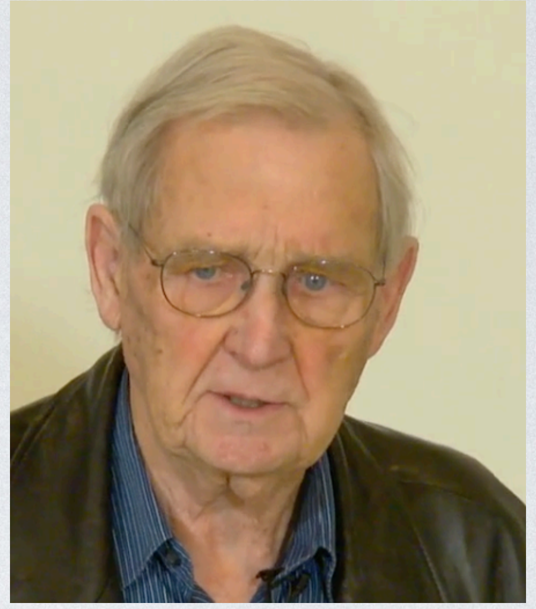
Energy landscape-based description of neutron scattering

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

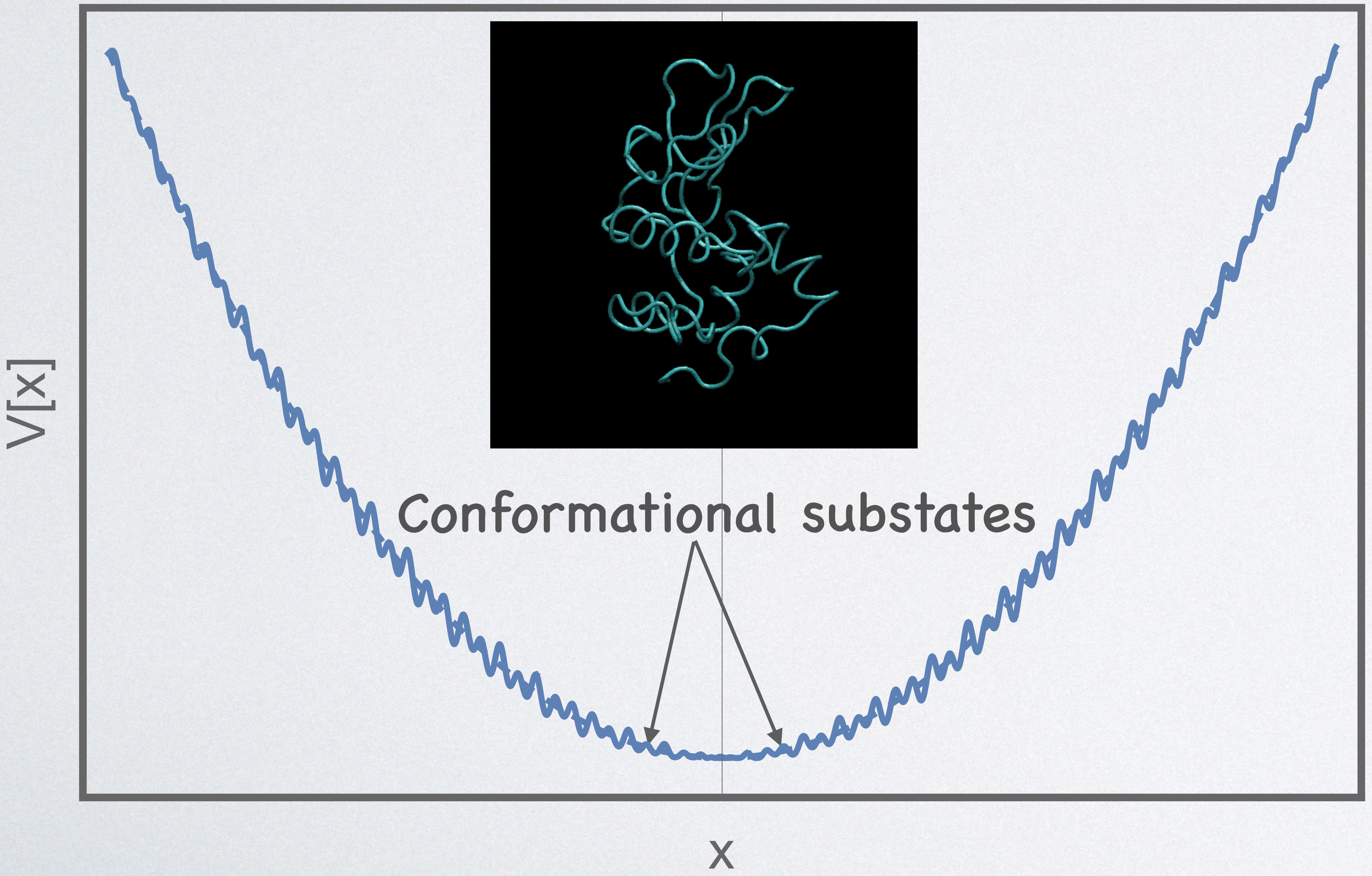
Hans Frauenfelder[a,1], Paul W. Fenimore[a], and Robert D. Young[b]

[a]Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, NM 87545; and [b]Center for Biological Physics, Arizona State University, Tempe, AZ 85287-1504

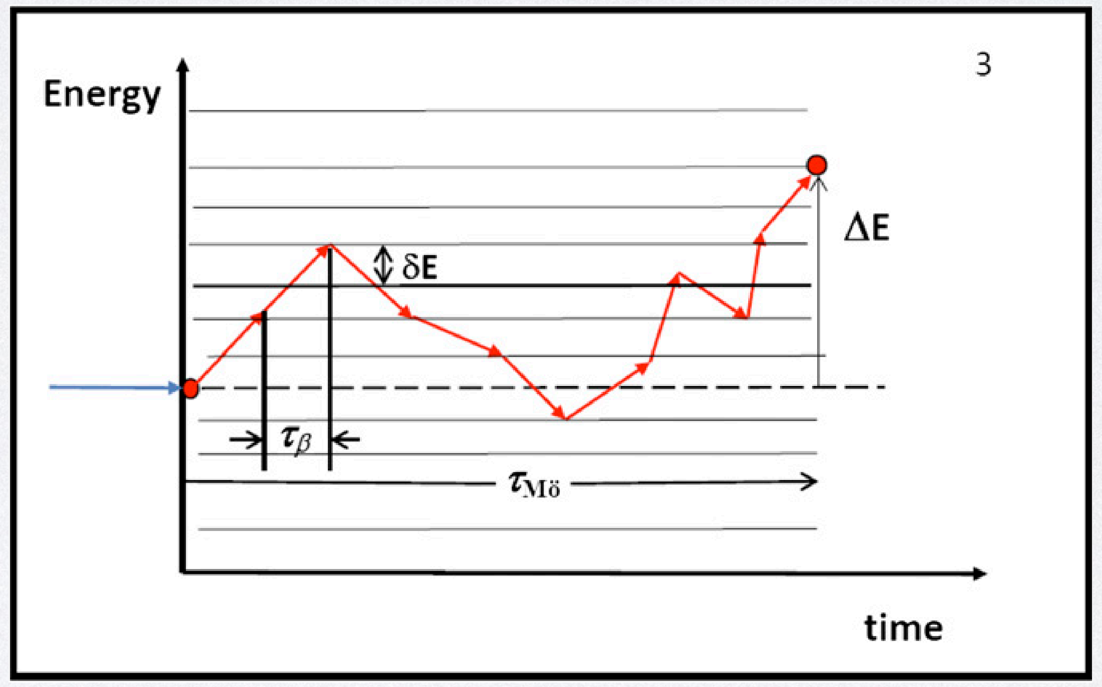
12764–12768 | PNAS | September 2, 2014 | vol. 111 | no. 35



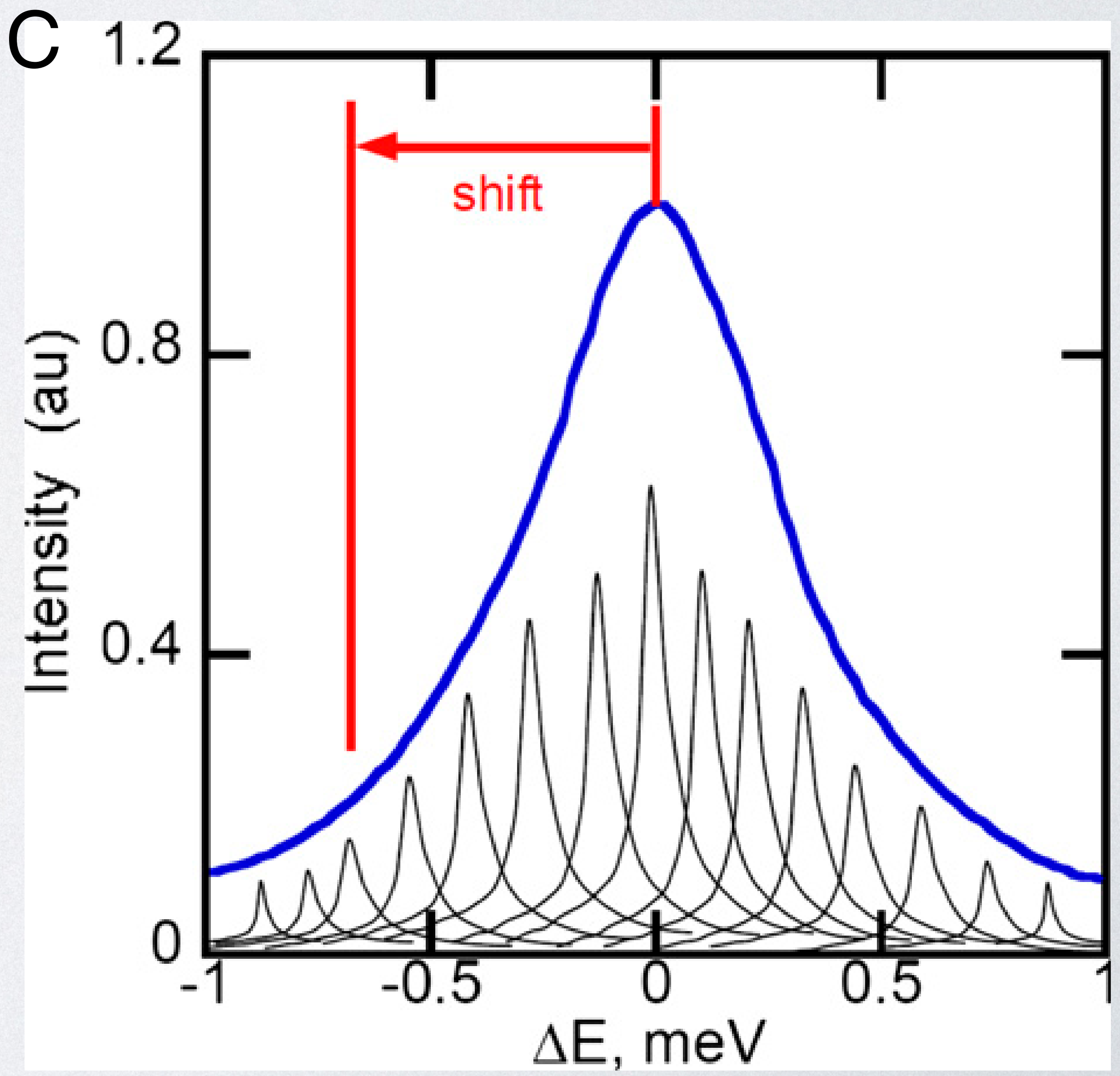
During its flight through the sample, the neutron wave packet records the net energy transition of the system from the initial energy level E to the final level E+ΔE.



H. Frauenfelder et al, Science 254, 1598 (1991).



QENS spectrum composed of many « Mössbauer lines »



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

The role of momentum transfer during incoherent neutron scattering is explained by the energy landscape model

Hans Frauenfelder[a,1], Robert D. Young[b], and Paul W. Fenimore[a,1]   PNAS 114, 5130 (2017).

- The neutron is an active probe : "Local heating" of the sample due to the momentum transfer.
- But: Momentum and energy transfer are not connected through scattering kinematics.

Develop a theory of neutron scattering, which

- is “spectroscopic”, in the sense that the neutron is an active probe, (de)exciting transitions in the scattering system
- integrates the concept of energy landscapes, which is adapted for complex systems

"Franck-Condon-interpretation" of neutron scattering

Franck–Condon picture of incoherent neutron scattering

Gerald R. Kneller[a,b,1]

PNAS, 115, pp. 9450 2018.

Use Wick's "kicked" Hamiltonian

$$F_s(\mathbf{q},t) = \frac{1}{Z}\sum_{m,n} \langle \phi_m | e^{-\beta \hat{H}} | \phi'_n(\mathbf{q})\rangle \langle \phi'_n(\mathbf{q}) | e^{it\hat{H}'(\mathbf{q})/\hbar} e^{-it\hat{H}/\hbar} | \phi_m \rangle$$

$$= \frac{1}{Z}\sum_{m,n} e^{-\beta E_m} e^{i(E'_n - E_m)/\hbar} \left| \langle \phi'_n(\mathbf{q}) | \phi_m \rangle \right|^2$$

$$\hat{H}|\phi_m\rangle = E_m|\phi_m\rangle$$

$$\hat{H}'(\mathbf{q})|\phi'_n(\mathbf{q})\rangle = E'_n|\phi'_n(\mathbf{q})\rangle$$

probabilities for a scattering-induced transition from the unperturbed energy level m to the perturbed energy level n.

Eigenfunctions and eigenvalues of the kicked Hamiltonian

$$\hat{H}'(\mathbf{q}) = \sum_k \frac{\left(\hat{p}_k + \hbar\mathbf{q}\delta_{1k}\right)^2}{2m_k} + V\left(\hat{\mathbf{R}}_1, .., \hat{\mathbf{R}}_N\right)$$

$$\langle \mathbf{P} \,|\phi_n'(\mathbf{q})\,\rangle = \tilde{\phi}_n\left(\mathbf{P} + \hbar\mathbf{Q}_1\right)$$

$$\langle \mathbf{R} \,|\phi_n'(\mathbf{q})\,\rangle = \phi_n(\mathbf{R})e^{-i\mathbf{Q}_1\cdot\mathbf{R}}$$

$$E_n' = E_n$$

$$\mathbf{Q}_1^T = (\underbrace{q_x, q_y, q_z}_{\text{atom 1}}, \underbrace{0, 0, 0}_{\text{atom 2}}, ..., \underbrace{0, 0, 0}_{\text{atom } N})$$

Select atom 1

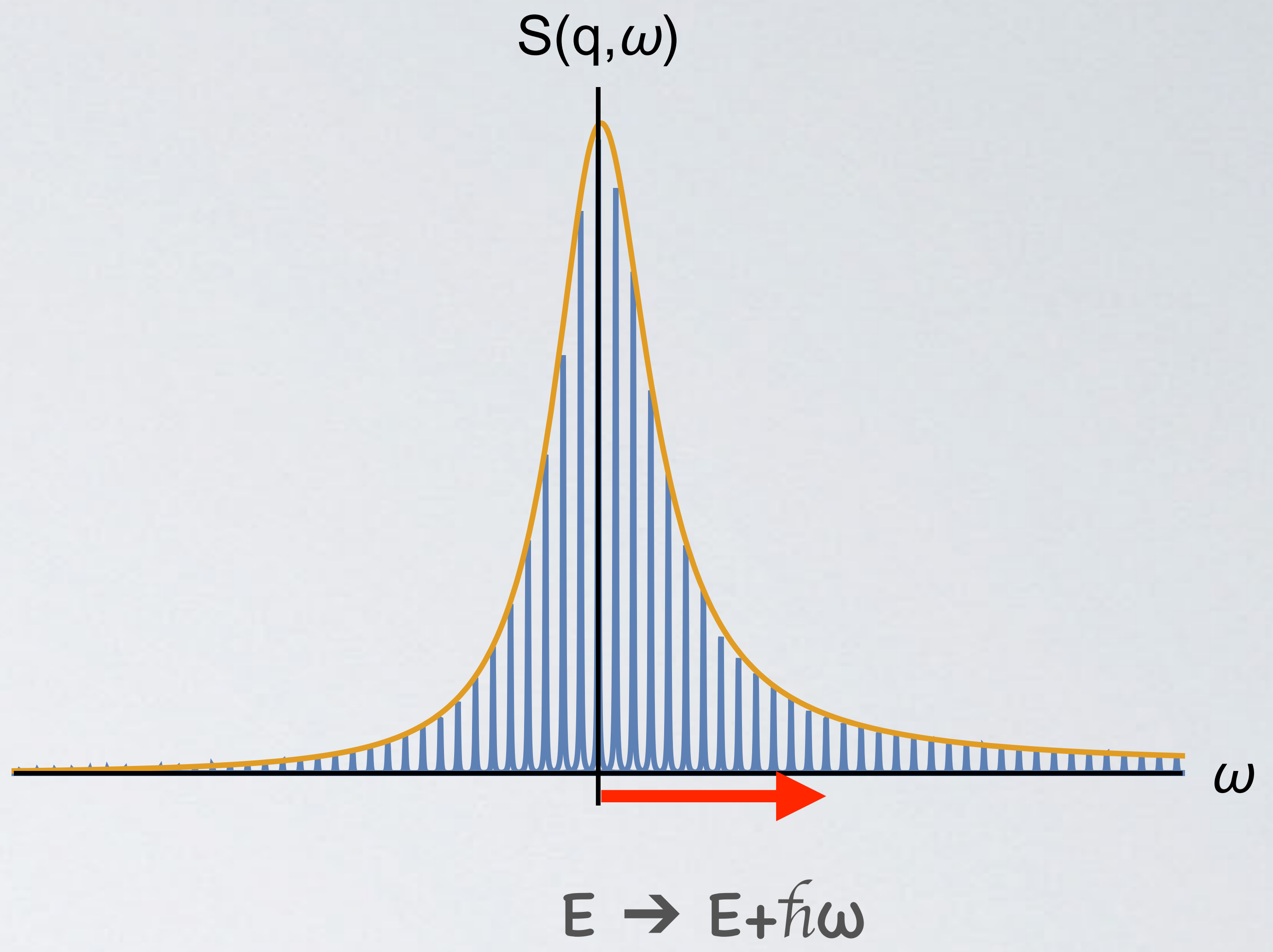
From the Brockhouse Nobel lecture (1994):

The neutron in being scattered "causes" transitions between the quantum states of the scattering system but does not change the states.

Scattering functions

$$F_s(\mathbf{q},t) = \frac{1}{Z}\sum_{m,n} e^{-\beta E_m} e^{it(E_n - E_m)/\hbar} |a_{m\to n}(\mathbf{q})|^2,$$

$$S_s(\mathbf{q},\omega) = \frac{1}{Z}\sum_{m,n} e^{-\beta E_m} |a_{m\to n}(\mathbf{q})|^2 \delta\left(\omega - [E_n - E_m]/\hbar\right).$$



Franck-Condon form of the transition amplitudes

$$a_{m\to n}(\mathbf{q}) = \int d^{3N}P\, \tilde{\phi}_n^*(\mathbf{P}+\hbar\mathbf{Q})\tilde{\phi}_m(\mathbf{P}) = \int d^{3N}R\, \phi_n^*(\mathbf{R})\phi_m(\mathbf{R})e^{i\mathbf{Q}_1\cdot\mathbf{R}}$$

Symmetry properties of the transition probabilities

$$w_{m\to n}(\mathbf{q}) \equiv |a_{m\to n}(\mathbf{q})|^2$$

$$w_{m\to n}(\mathbf{q}) = w_{n\to m}(-\mathbf{q})$$

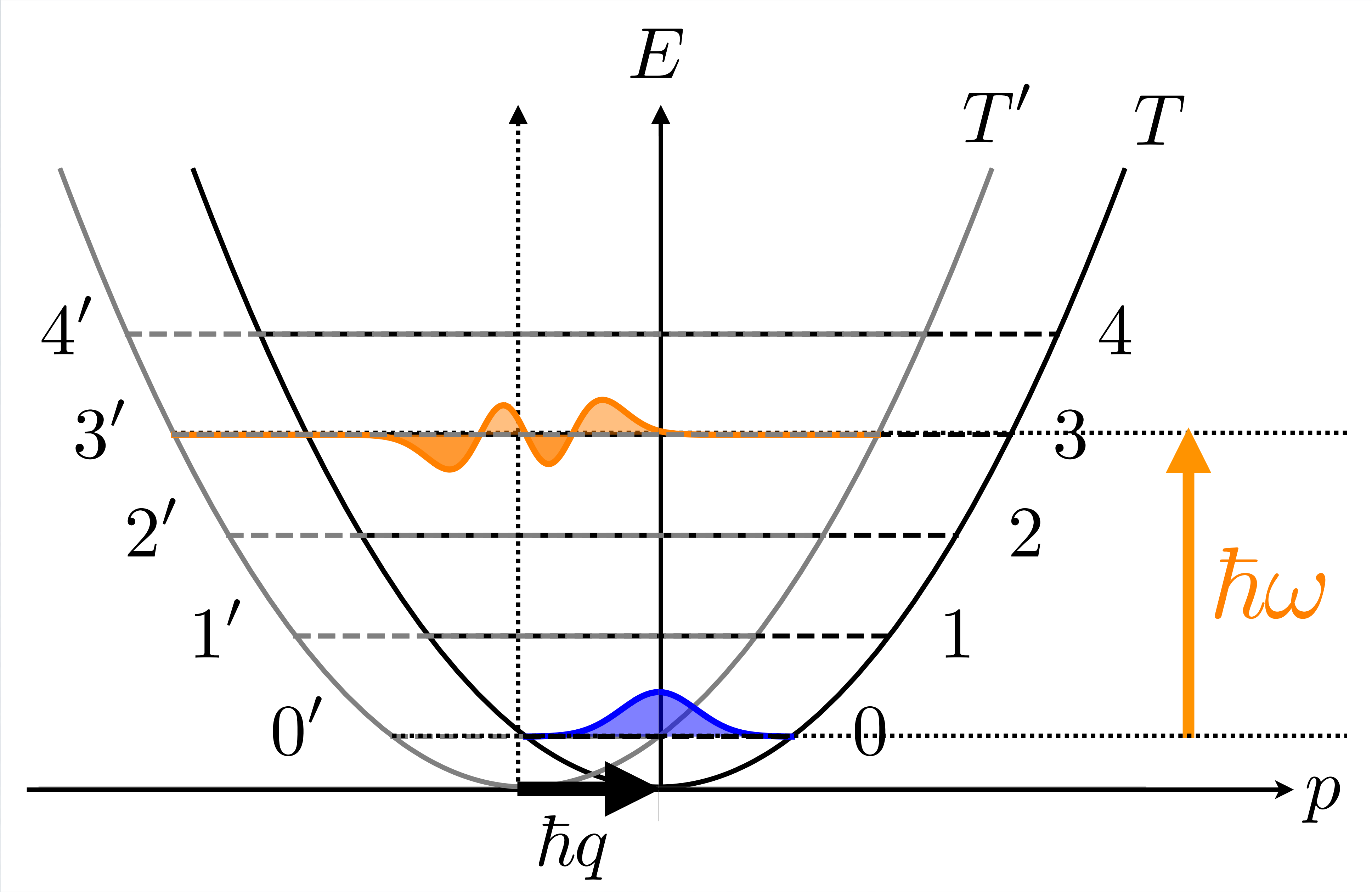
Detailed balance relation etc. fulfilled

$$F_s(\mathbf{q},t) = F_s(-\mathbf{q},-t+i\beta\hbar)$$

$$S_s(\mathbf{q},\omega) = e^{\beta\hbar\omega} S_s(-\mathbf{q},-\omega)$$

An analytical example - the harmonic oscillator

Wave functions for the 0→3′ transition



T **V**

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

Transition probabilities

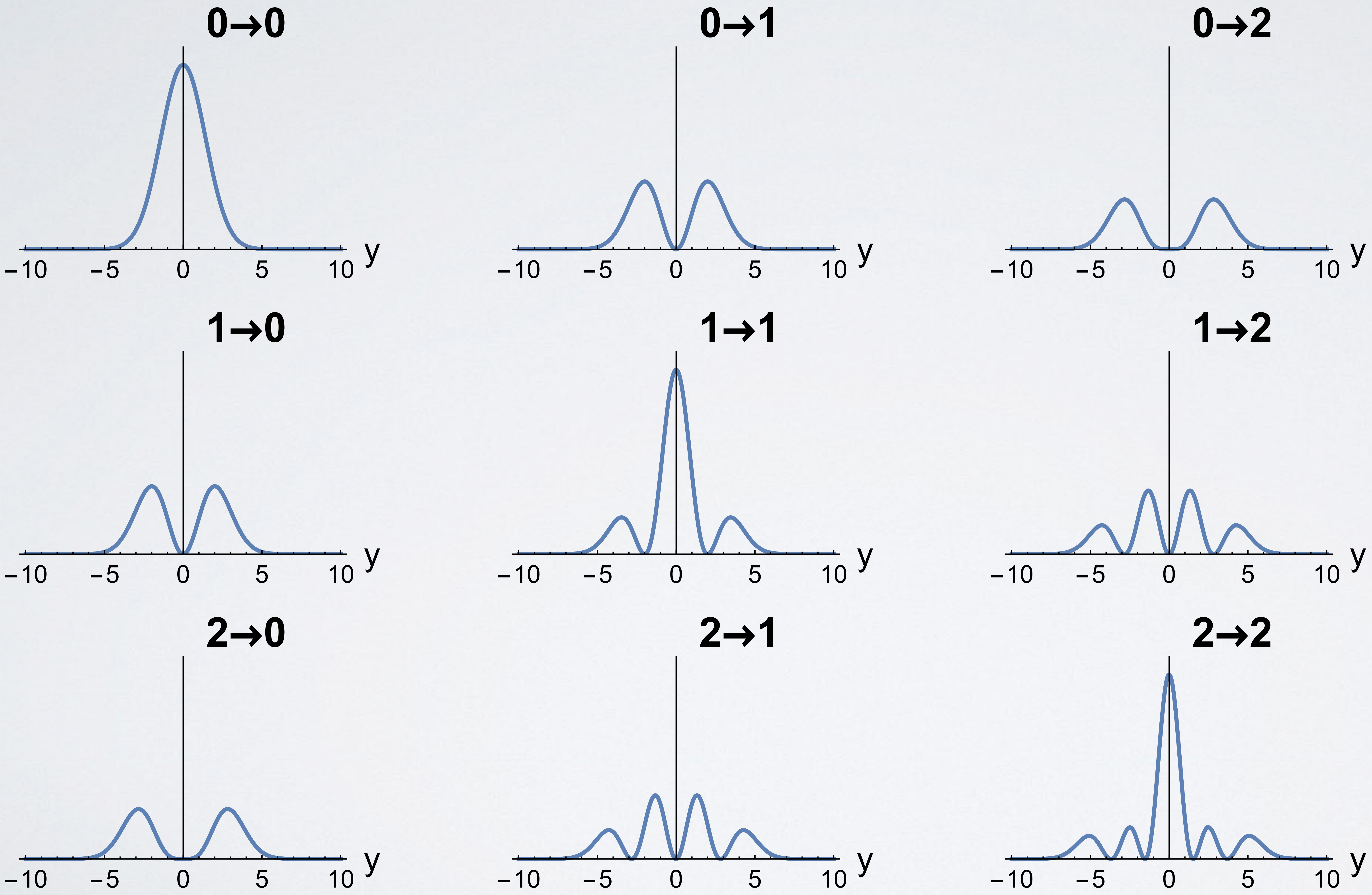
$$w_{m\to n}(q) = e^{-\frac{y^2}{4}} (-1)^{m+n} L_m^{(n-m)}\left(\frac{y^2}{4}\right) L_n^{(m-n)}\left(\frac{y^2}{4}\right)$$

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

Textbook result (c.f. Lovesey)

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

Some transition probabilities as a function of momentum transfer



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

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ARTICLE

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Quantum oscillations of nitrogen atoms in uranium nitride

A.A. Aczel[1], G.E. Granroth[1], G.J. MacDougall[1], W.J.L. Buyers[2], D.L. Abernathy[1], G.D. Samolyuk[3], G.M. Stocks[3] & S.E. Nagler[1,4]

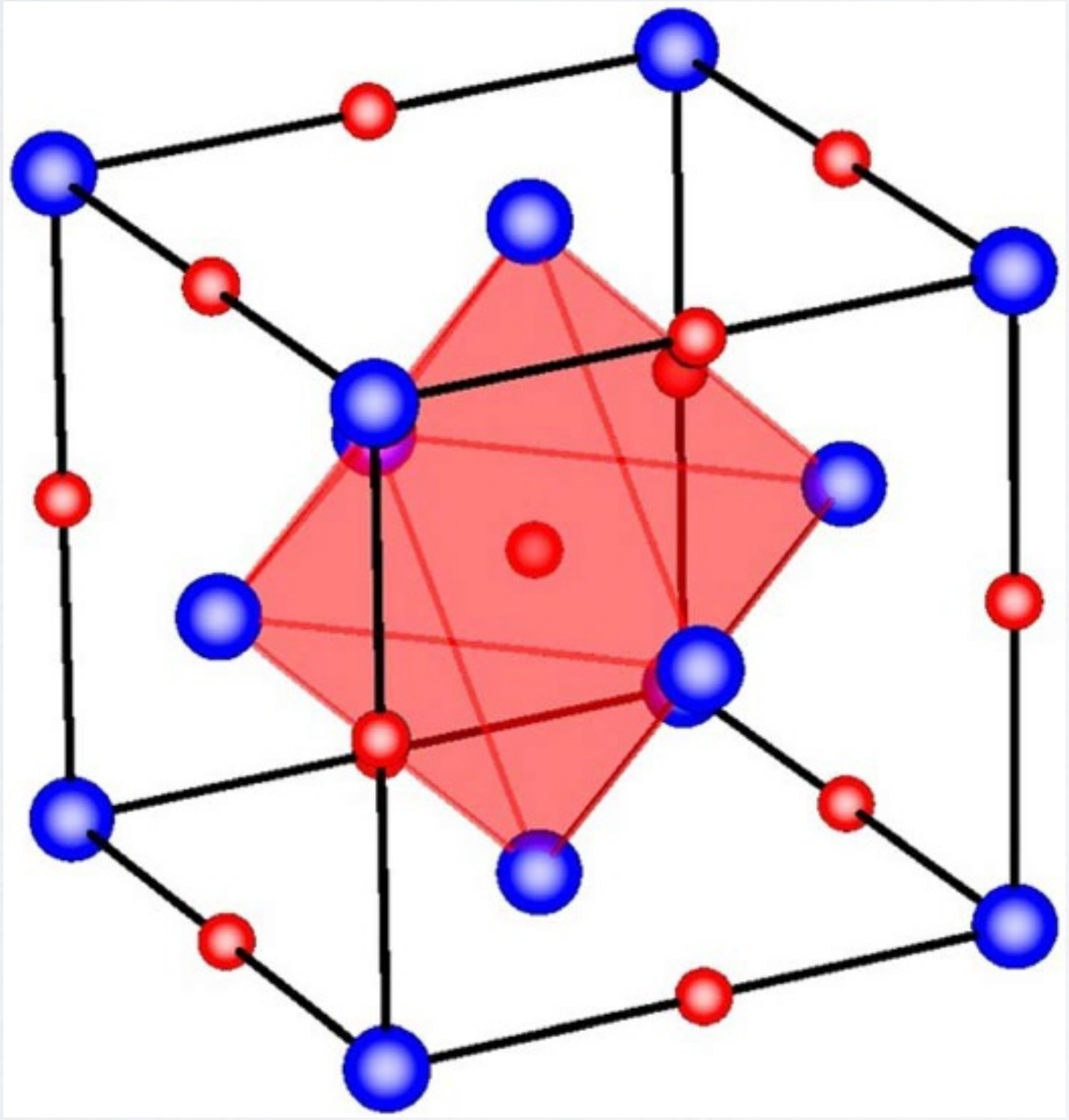
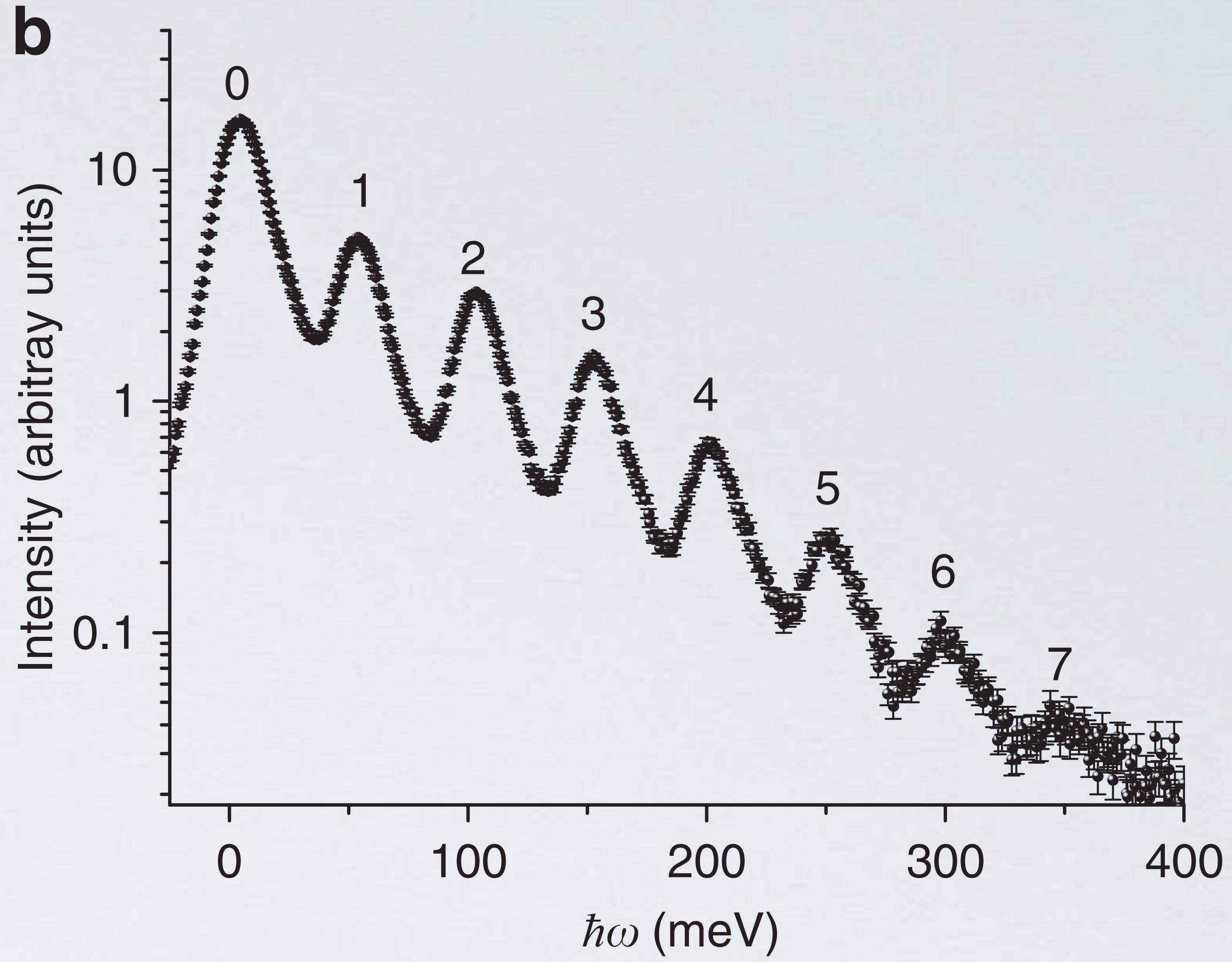
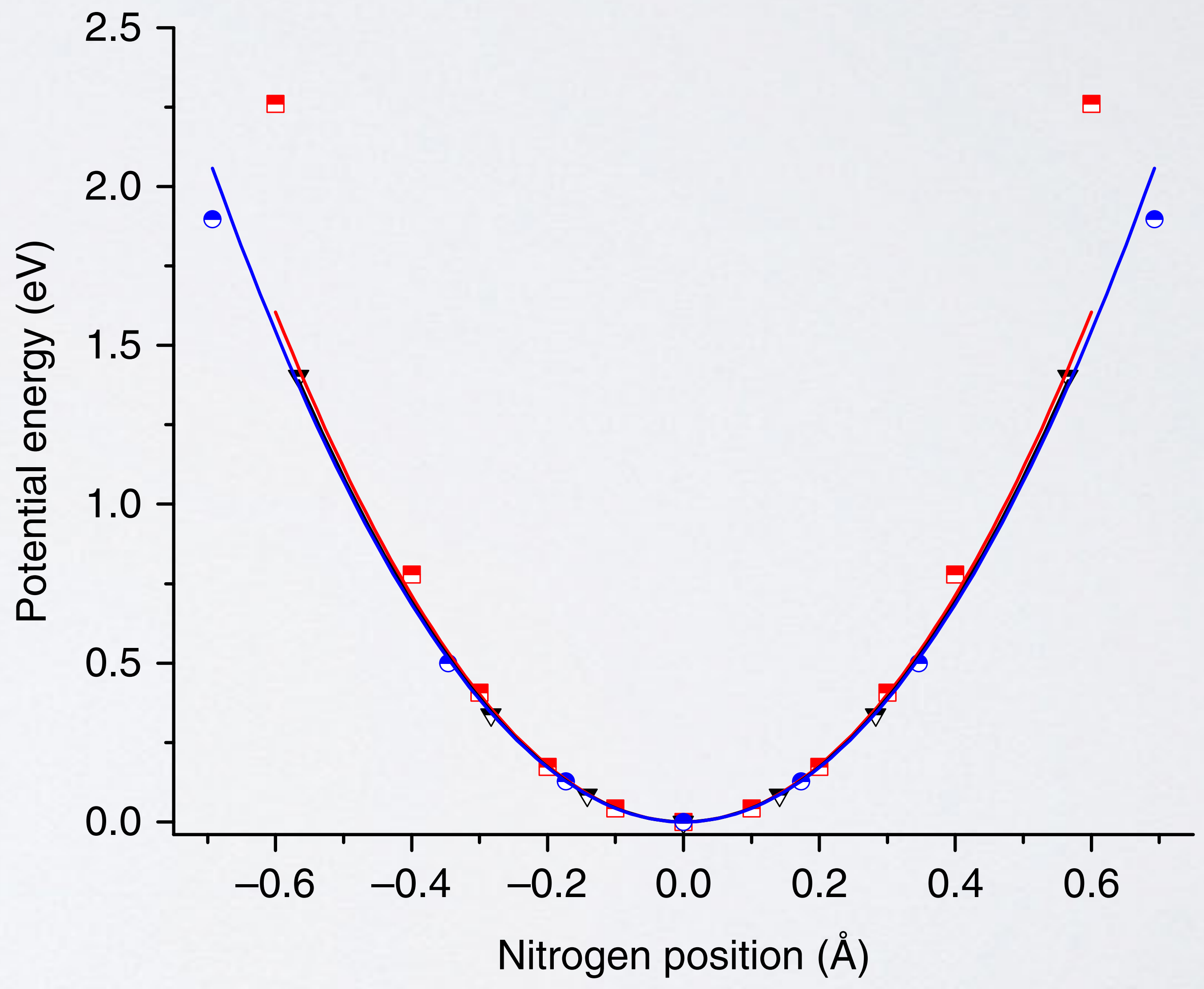


Figure 1 | Rocksalt crystal structure of uranium nitride. Each N atom (small red spheres) is centred in a regular octahedron of U atoms (large blue spheres).





Continuous energy spectra

$X \equiv \{x_1, \ldots, x_f\}$: variables describing the state of the scattering system

$$m \to dm = \rho(X) d^f X \qquad \langle \phi(X') | \phi(X) \rangle = \begin{cases} 1 & \text{if } X = X', \\ 0 & \text{otherwise.} \end{cases}$$

$$F_s(\mathbf{q}, t) = \int \int d^f X d^f X' \, W_{\text{eq}}(X) e^{i(E(X') - E(X))t/\hbar} W(X'|X; \mathbf{q})$$

$$S_s(\mathbf{q}, \omega) = \int \int d^f X d^f X' \, W_{\text{eq}}(X) W(X'|X; \mathbf{q}) \delta(\omega - [E(X') - E(X)]/\hbar)$$

$$W(X'|X; \mathbf{q}) = \rho(X') \left| \int d^{3N} p \, \tilde{\phi}^*(\mathbf{P} + \hbar \mathbf{Q}; X') \tilde{\phi}(\mathbf{P}; X) \right|^2$$

$$W_{\text{eq}}(X) = \rho(X) \frac{e^{-\beta E(X)}}{Z}$$

$$\lim_{|\mathbf{q}| \to 0} W(X'|X; \mathbf{q}) = \delta(X - X')$$

Dynamic structure factor for self-scattering and X=E

$$S_s(\mathbf{q},\omega) = \hbar \int dE\, W_{\text{eq}}(E) W(E+\hbar\omega|E;\mathbf{q})$$

$S(\mathbf{q},\omega)$ becomes a thermally averaged probability for a scattering-induced transition from $E \to E+\hbar\omega$ with a momentum transfer $\hbar\mathbf{q}$.

The dynamic structure factor has a true probabilistic interpretation.

A simple analytical example - the ideal gas:

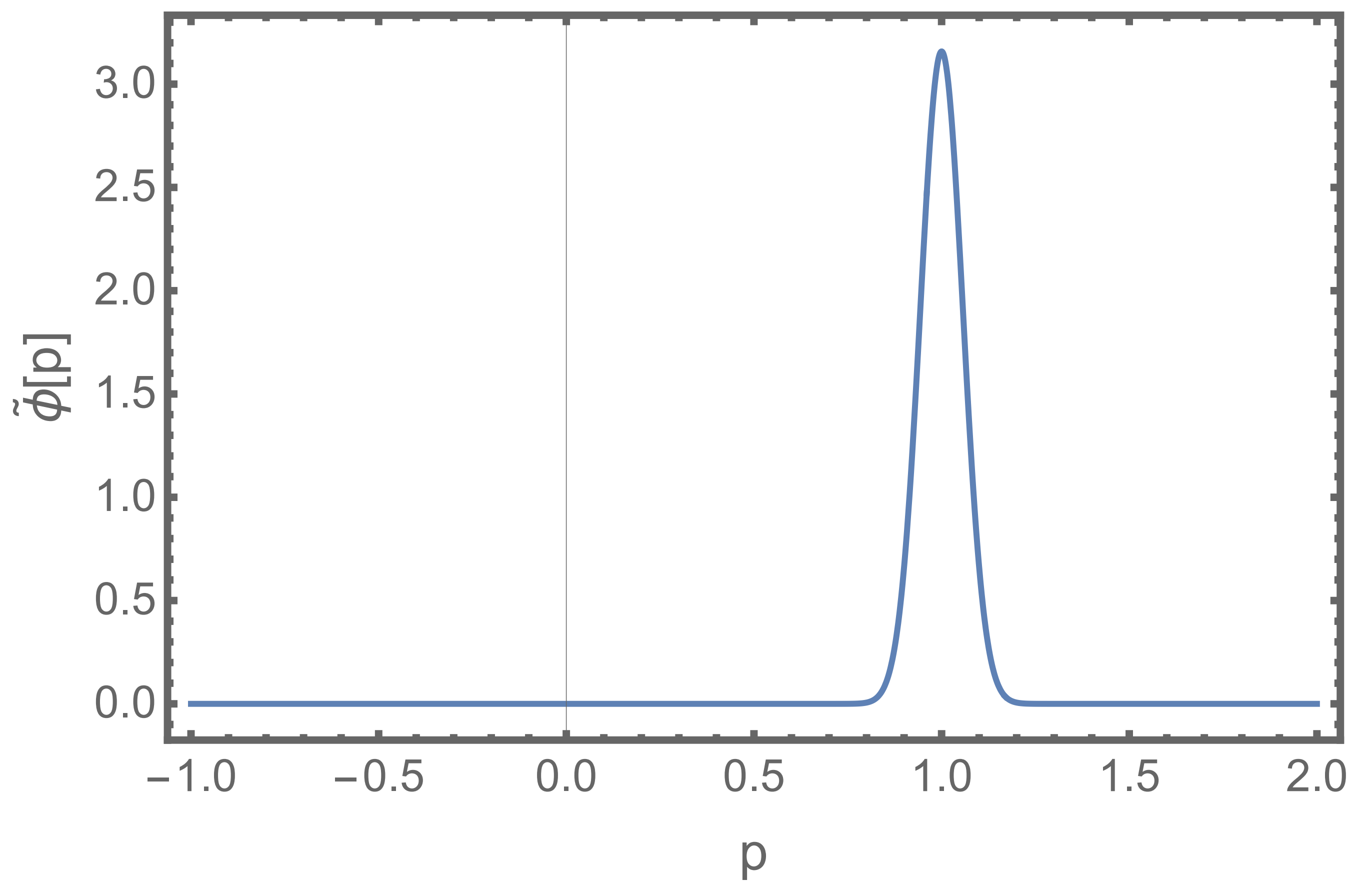
Quantum state

$$X = \{p_{0,x}, p_{0,y}, p_{0,z}\}$$

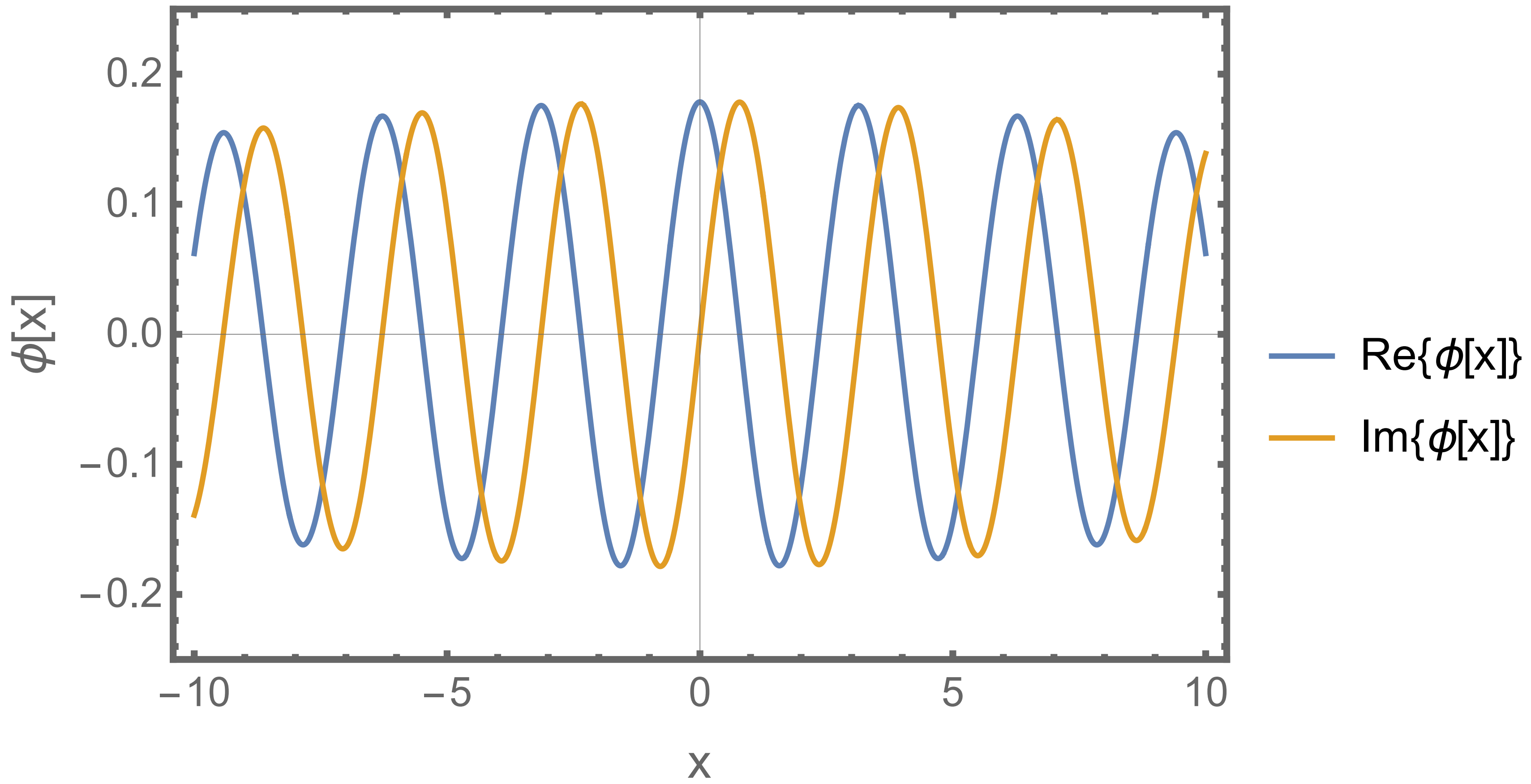
Momentum vector of a free particle

$$\rho(X) = 1/(2\sqrt{\pi}\epsilon)^3$$

$$\tilde{\phi}(\mathbf{p}) = \frac{1}{(2\pi\epsilon^2)^{3/4}} e^{-\frac{(\mathbf{p}-\mathbf{p}_0)^2}{4\epsilon^2}}$$



$$\phi(\mathbf{x}) = \left(\frac{2}{\pi}\frac{\epsilon^2}{\hbar^2}\right)^{1/4} e^{\frac{i}{\hbar}\mathbf{p}_0\cdot\mathbf{x}} e^{-\frac{x^2\epsilon^2}{\hbar^2}}$$



$$W(\mathbf{p}_1|\mathbf{p}_0;\mathbf{q}) = \frac{e^{-\frac{(\mathbf{p}_0-\mathbf{p}_1+\hbar\mathbf{q})^2}{4\epsilon^2}}}{(2\sqrt{\pi}\epsilon)^3} \overset{\epsilon\to 0}{=} \delta(\mathbf{p}_0+\hbar\mathbf{q}-\mathbf{p}_1)$$

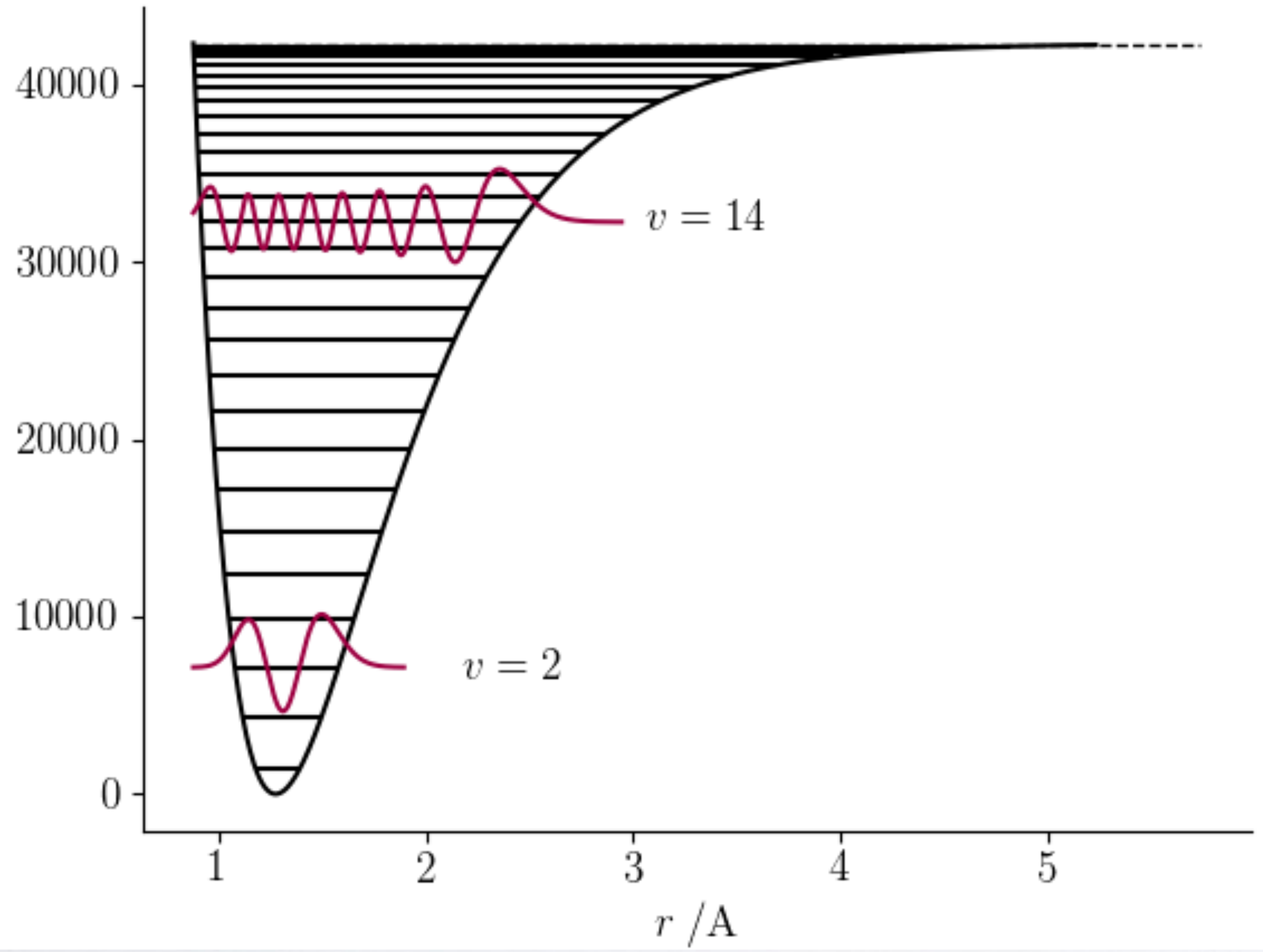
Momentum conservation

$$F_s(\mathbf{q},t) = e^{-\frac{q^2 t(t-i\beta\hbar)}{2\beta M}}$$

$$S_s(\mathbf{q},\omega) = \left(\frac{2\pi q^2}{\beta M}\right)^{-1/2} e^{-\frac{\beta\left(\hbar q^2-2M\omega\right)^2}{8Mq^2}}$$

From discrete to continuous distributions of energies

Morse potential [1)]



$$EISF(\mathbf{q}) = \lim_{\epsilon \to 0} \int dE\, W_{\text{eq}}(E) \int_{E-\hbar\epsilon}^{E+\hbar\epsilon} dE'\, W(E'|E;\mathbf{q}) \approx 0$$

Vanishes for any continuous wave function $\tilde{\phi}(\mathbf{P}; E)$.

$$EISF(\mathbf{q}) = \frac{1}{Z} \sum_m e^{-\beta E_m} w_{m\to m}(\mathbf{q})$$

Contributes for any continuous wave function $\tilde{\phi}_m(\mathbf{P})$.

Elastic scattering from (low energy) bound states.

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1) https://scipython.com/blog/the-morse-oscillator/

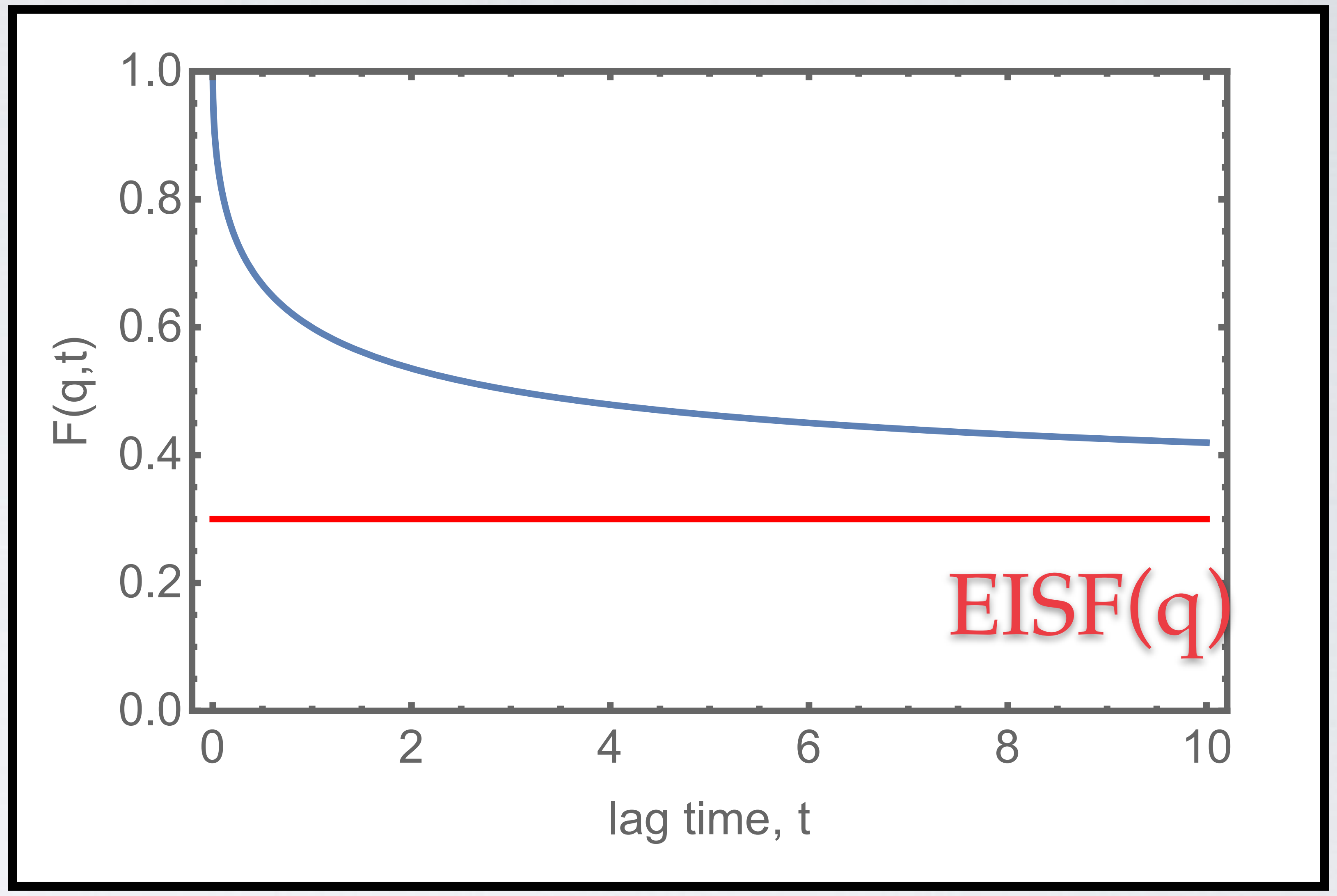
Elastic scattering — generic form of F(q,t)

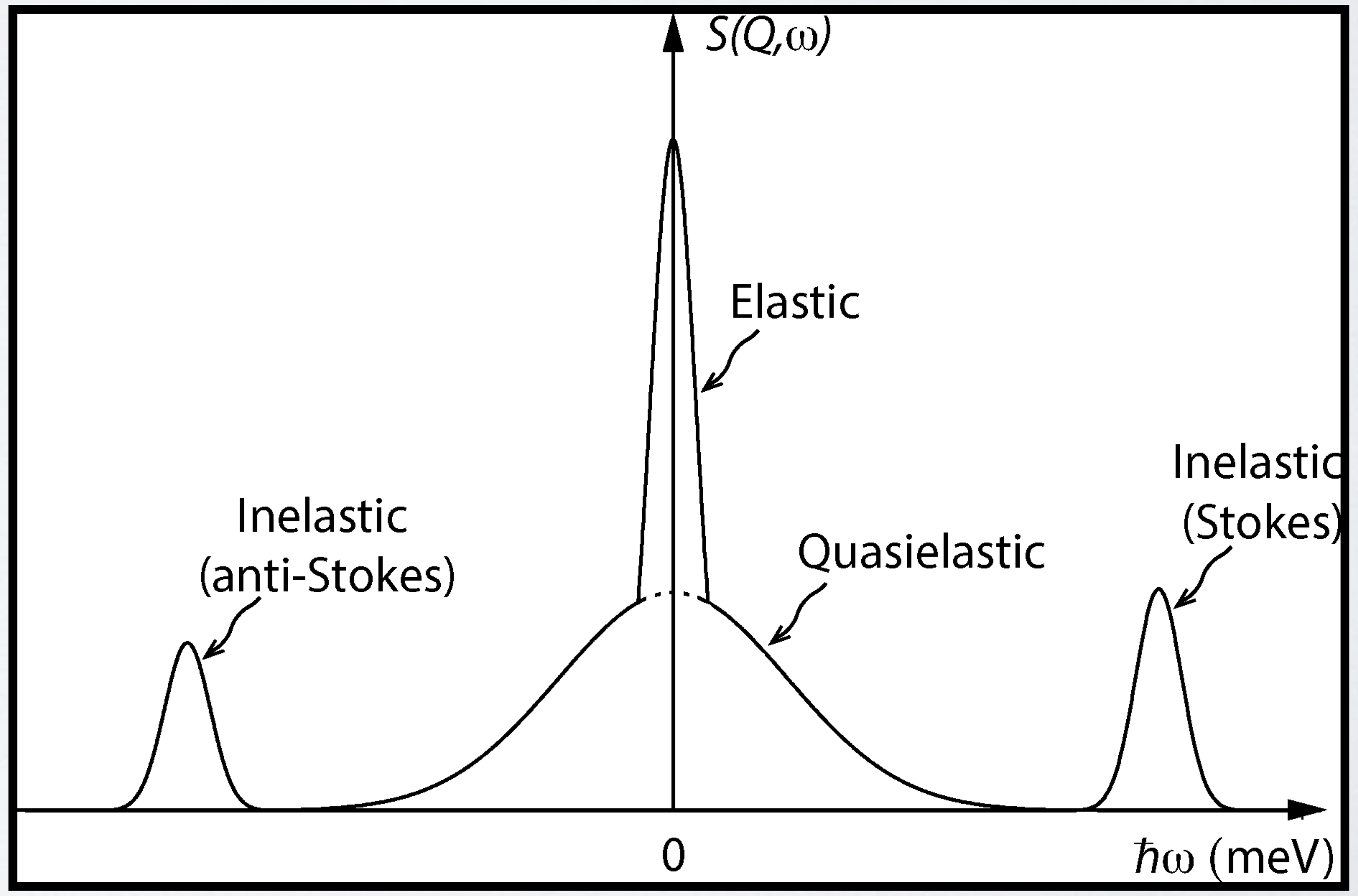
$$F(\mathbf{q},t) = EISF(\mathbf{q}) + (1 - EISF(\mathbf{q}))\phi(\mathbf{q},t)$$

$$\phi(0) = 1$$

$$\lim_{t\to\infty} \phi(t) = 0$$

$$S(\mathbf{q},\omega) = EISF(\mathbf{q})\delta(\omega) + (1 - EISF(\mathbf{q}))\tilde{\phi}(\mathbf{q},\omega)$$





Some maths : asymptotic analysis of F(q,t)

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

Von *J. Karamata* in Belgrad.

SUR UN MODE DE CROISSANCE RÉGULIÈRE. THÉORÈMES FONDAMENTAUX;

PAR M. J. KARAMATA

(Beograd).

$$h(t) \overset{t\to\infty}{\sim} L(t)t^{\rho} \longleftrightarrow \boxed{\hat{h}(s) \equiv \int_0^{\infty} dt\, e^{-st} h(t)} \overset{s\to 0}{\sim} L\left(\frac{1}{s}\right)\frac{\Gamma(1+\rho)}{s^{1+\rho}} \qquad (\rho > -1)$$

Tauberian theorem

$$\frac{L(\lambda t)}{L(t)} \overset{t\to\infty}{\sim} 1 \quad (\lambda > 0)$$

Slowly growing/ varying function

$$F(t) = EISF + (1 - EISF)\phi(t) \equiv L(t)$$

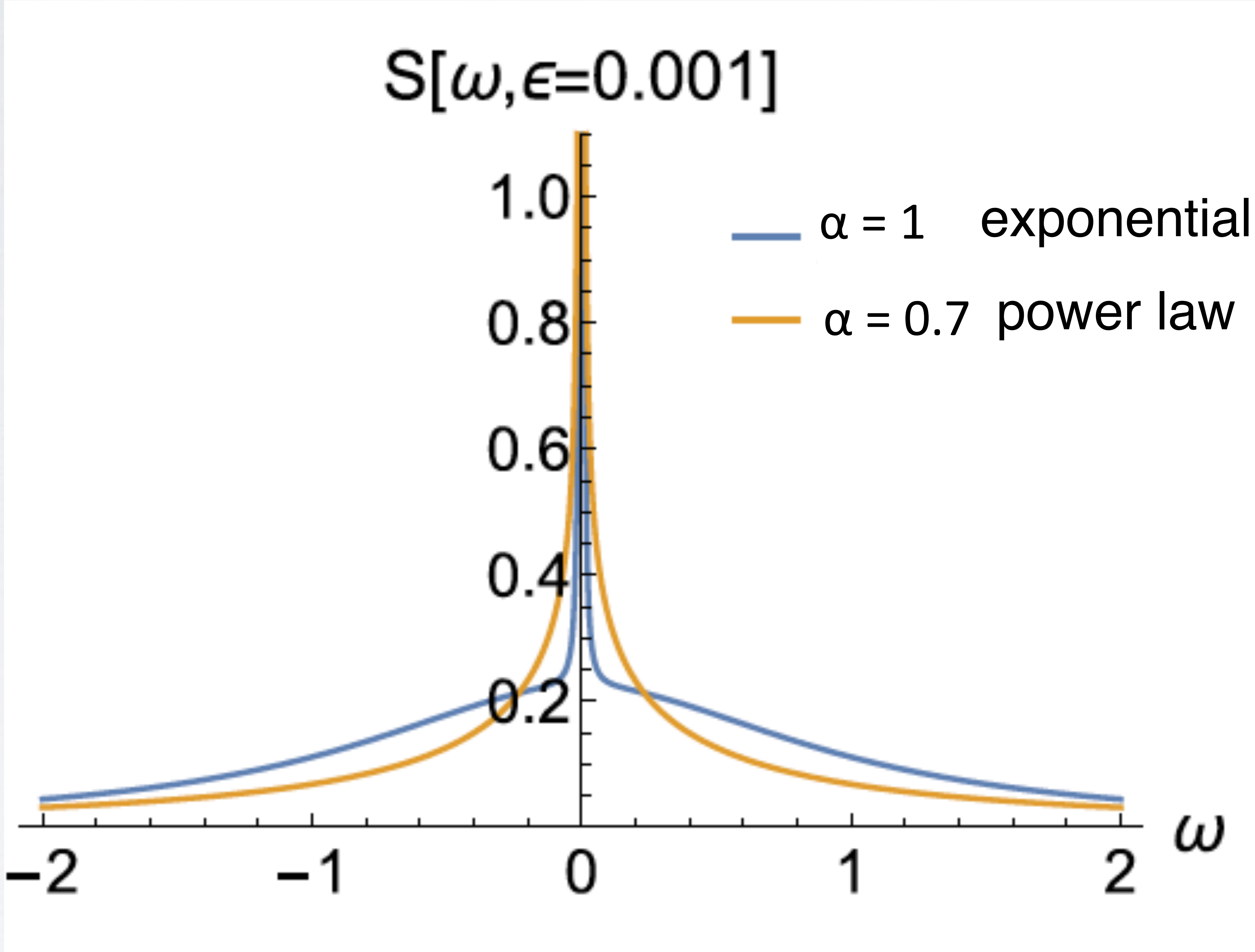
$$\hat{F}(s) \overset{s\to 0}{\sim} \frac{1}{s}F\left(\frac{1}{s}\right) = EISF\,\frac{1}{s} + (1 - EISF)\frac{1}{s}\phi\left(\frac{1}{s}\right)$$

Combined description of elastic and quasi-elastic scattering

$$F(t) = EISF + (1 - EISF)\phi(t)$$

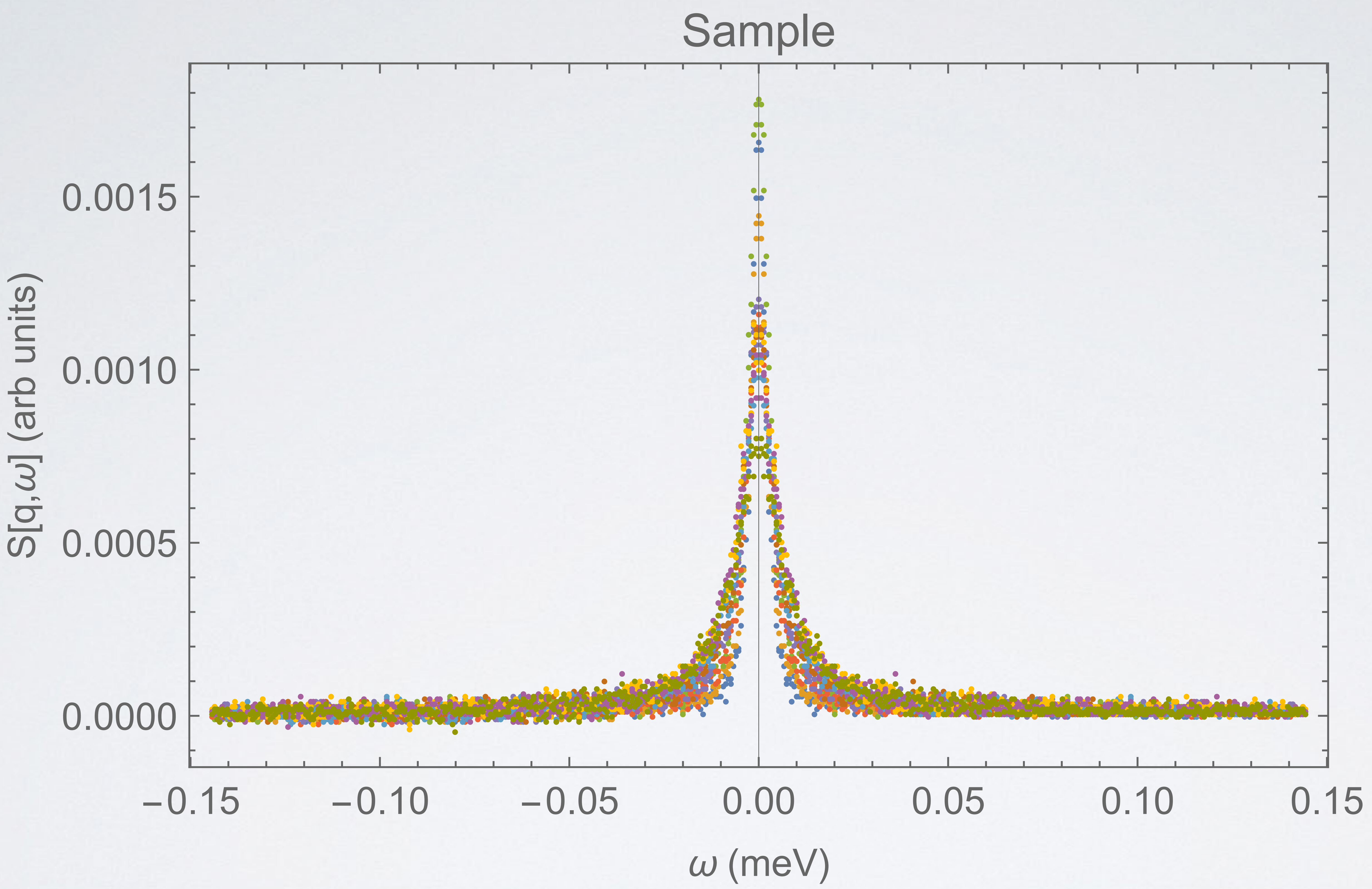
$$S(\omega) = \lim_{\epsilon \to 0} \frac{1}{\pi} \Re \left\{ \hat{F}(i\omega + \epsilon) \right\}$$

$$S_s(\omega) \overset{\omega \to 0}{\sim} \lim_{\epsilon \to 0+} \frac{1}{\pi} \Re \left\{ \frac{F_s(1/(i\omega + \epsilon))}{i\omega + \epsilon} \right\}$$



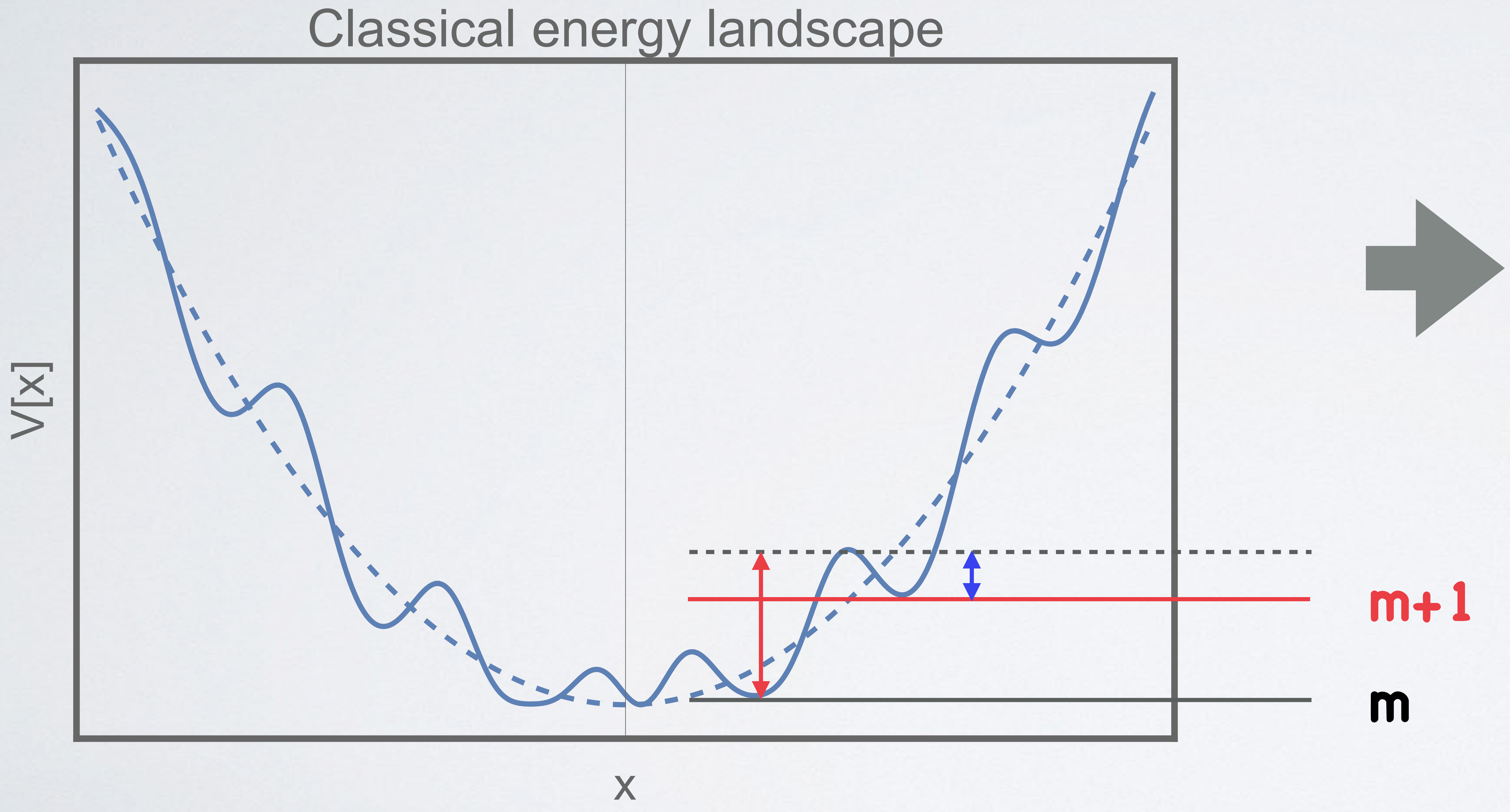
- The asymptotic form of the relaxation function for long times time determines the asymptotic form of the dynamic structure factor for small frquencies.
- For power law relaxation, the elastic and quasi-elastic lines are fused and the EISF must be adjusted with the parameters describing the relaxation function.
- Modeling essentially the asymptotic form of QENS spectra leads to «minimalistic models» describing the form of the spectra with few parameters.

Example: QENS from Phosphoglycerate kinase (A. Stadler)



Towards a quasi-classical picture of energy landscapes

Can quantum transition probabilities be replaced by classical ones ?



$$W_{cl}(E', E, \mathbf{q}) \propto \exp\left(-\frac{\Delta G_{E\to E'}}{k_B T}\right)$$

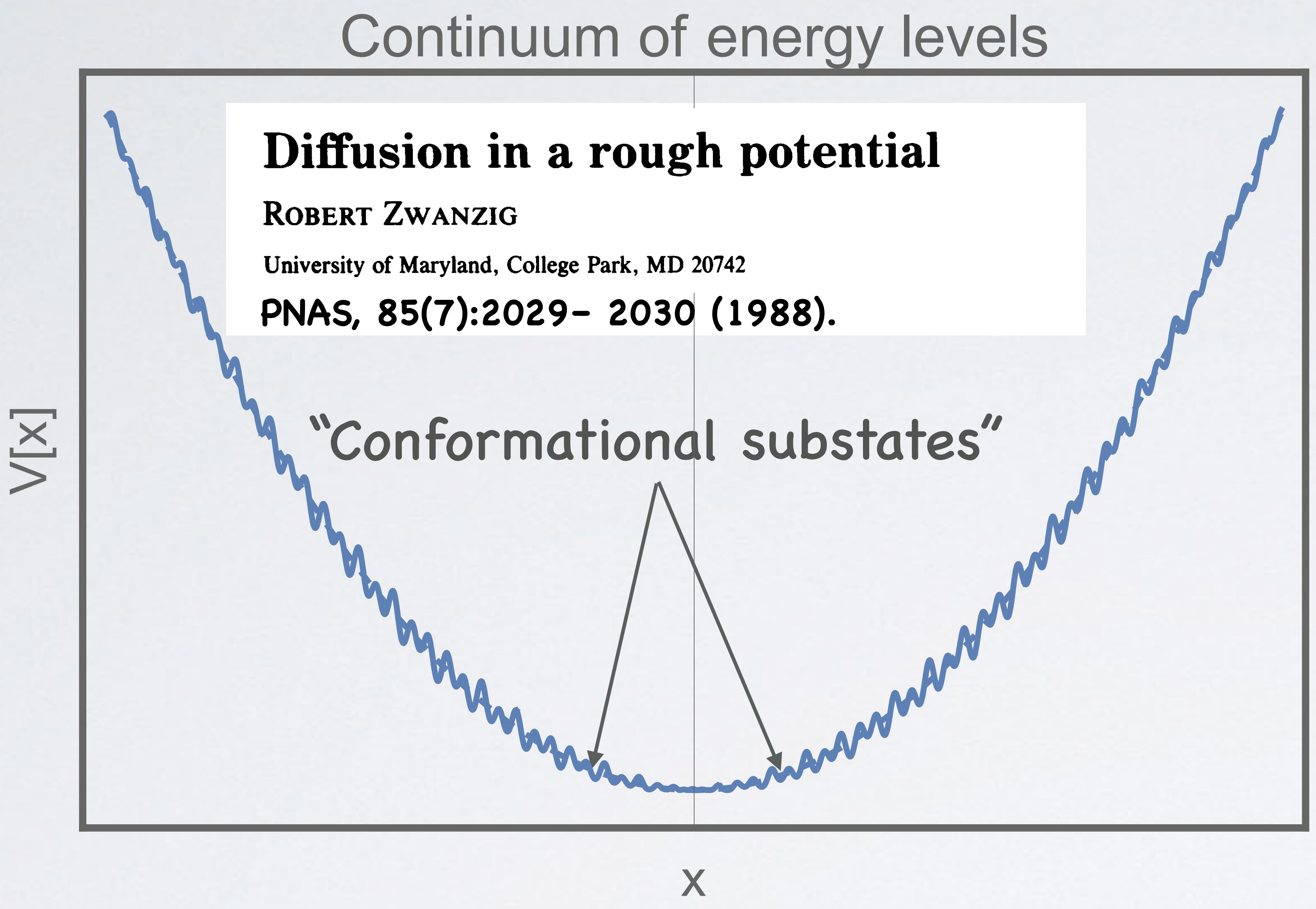
$$W_{cl}(E', E, \mathbf{q}) \neq W_{cl}(E, E', -\mathbf{q})$$

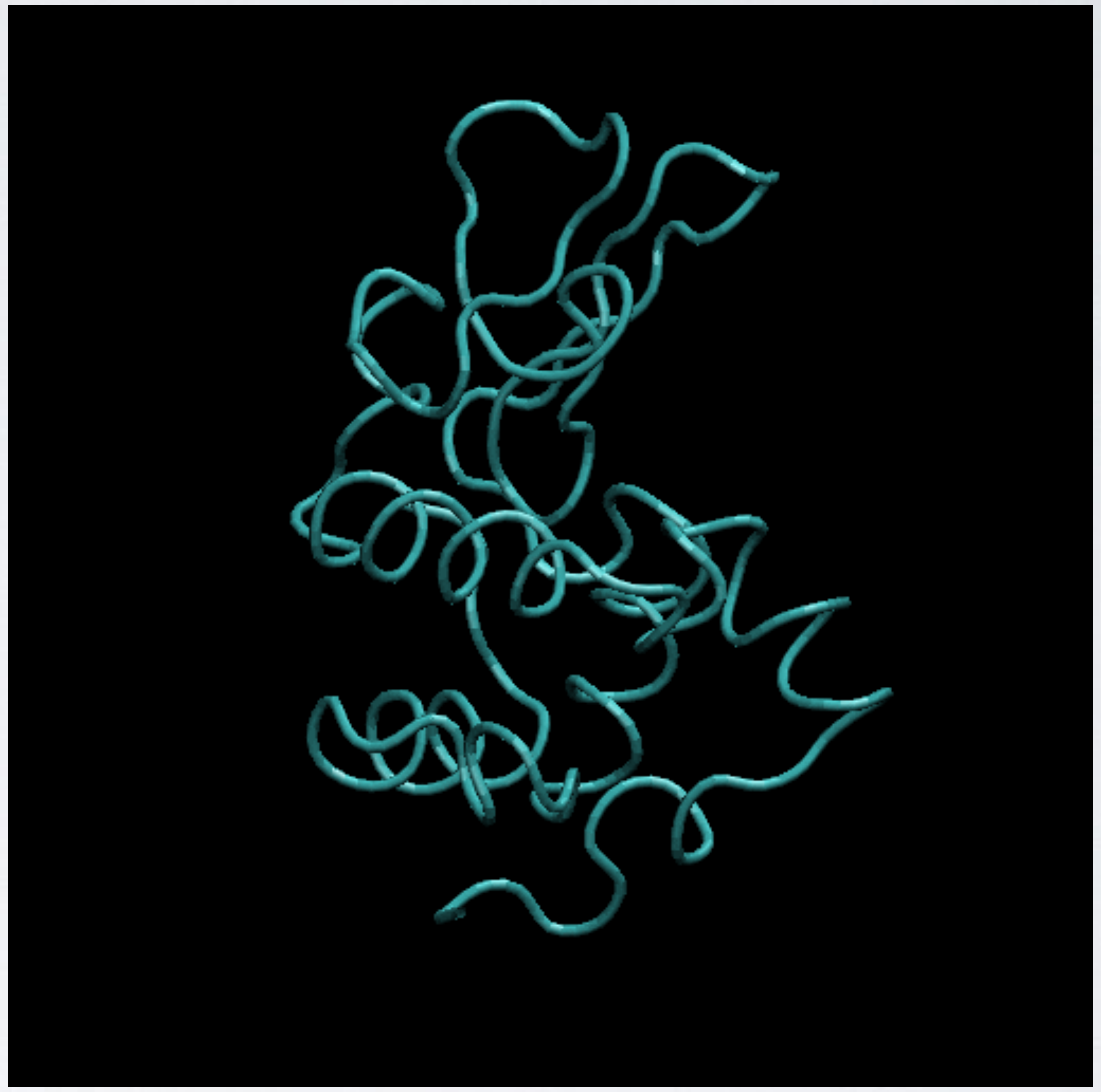
But

$$W_{qm}(E', E, \mathbf{q}) = W_{qm}(E, E', -\mathbf{q})$$

Semiclassical picture for a continuum of energy levels

Diffusion — jumps between almost equal neighboring energy minima





$$W_{cl}(E', E, \mathbf{q}) \approx W_{cl}(E, E', -\mathbf{q})$$

$$E' \approx E + \frac{\hbar^2 |\mathbf{q}|^2}{2M}$$

$$F(\mathbf{q}, t + i\beta\hbar/2) \approx F_{cl}(\mathbf{q}, t)$$

Non-exponential relaxation / anomalous diffusion in a rough potential

The Energy Landscapes and Motions of Proteins

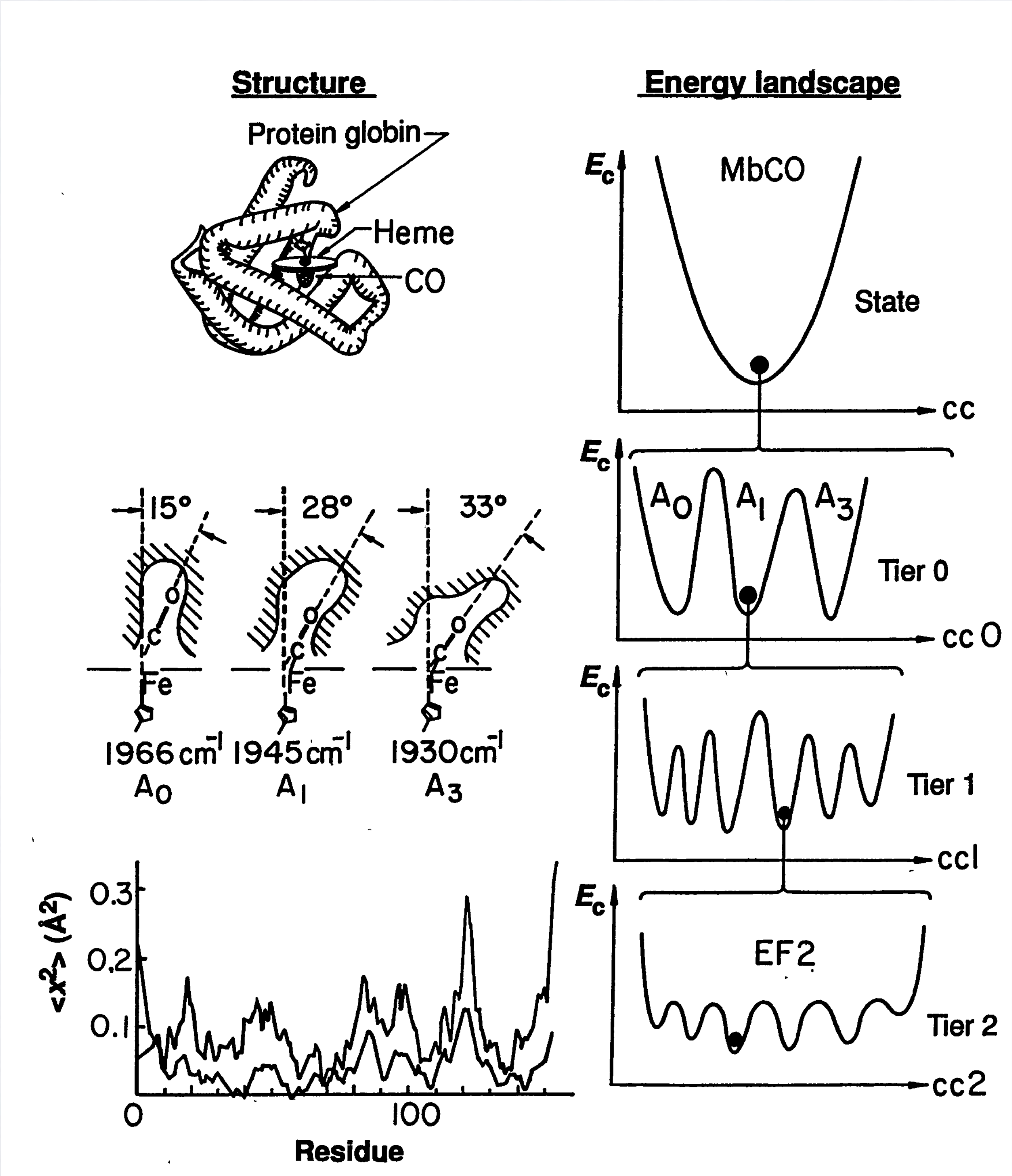
HANS FRAUENFELDER, STEPHEN G. SLIGAR, PETER G. WOLYNES

SCIENCE, VOL. 254

Non-exponential rebinding kinetics of CO

Conformational substates

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



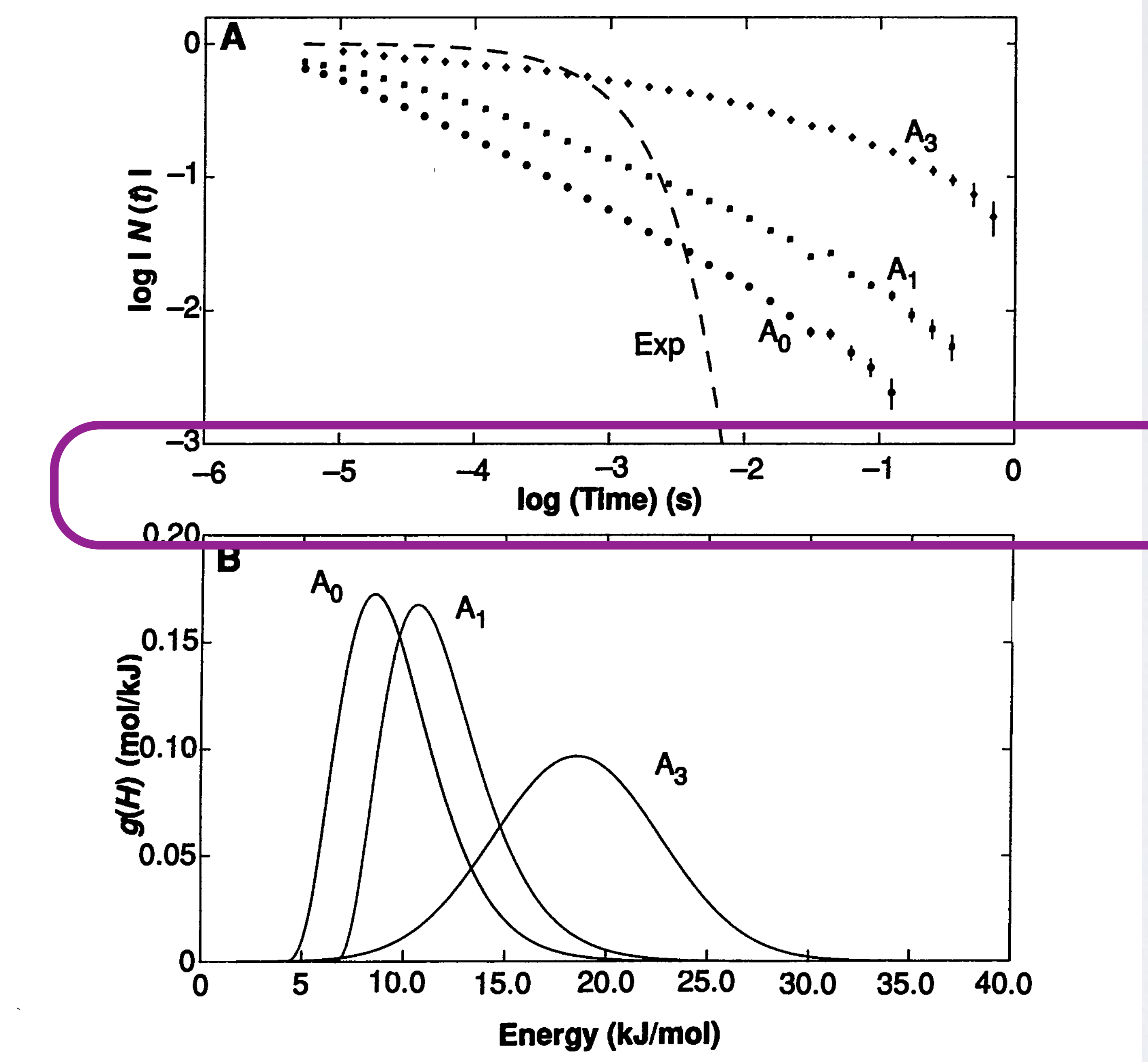


Fig. 2. Rebinding of CO to Mb after photodissociation, measured separately for the substates of tier 0 at pH 5.7. (**A**) $N(t)$ is the fraction of proteins that have not rebound a CO at the time t after photodissociation. All three substates (A_0, A_1, and A_3) rebind nonexponentially in time. (**B**)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

Protein dynamics displays self-similarity

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

$$\phi(t) = \int_0^\infty d\lambda \, p(\lambda) e^{-\lambda t}$$

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

$$\phi(t) \overset{t\to\infty}{\sim} (t/\tau)^{-\alpha} \quad \Rightarrow \quad \phi(\mu t) \overset{t\to\infty}{\sim} \mu^{-\alpha}\phi(t)$$

Self-similar relaxation dynamics seen in CO-rebinding 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

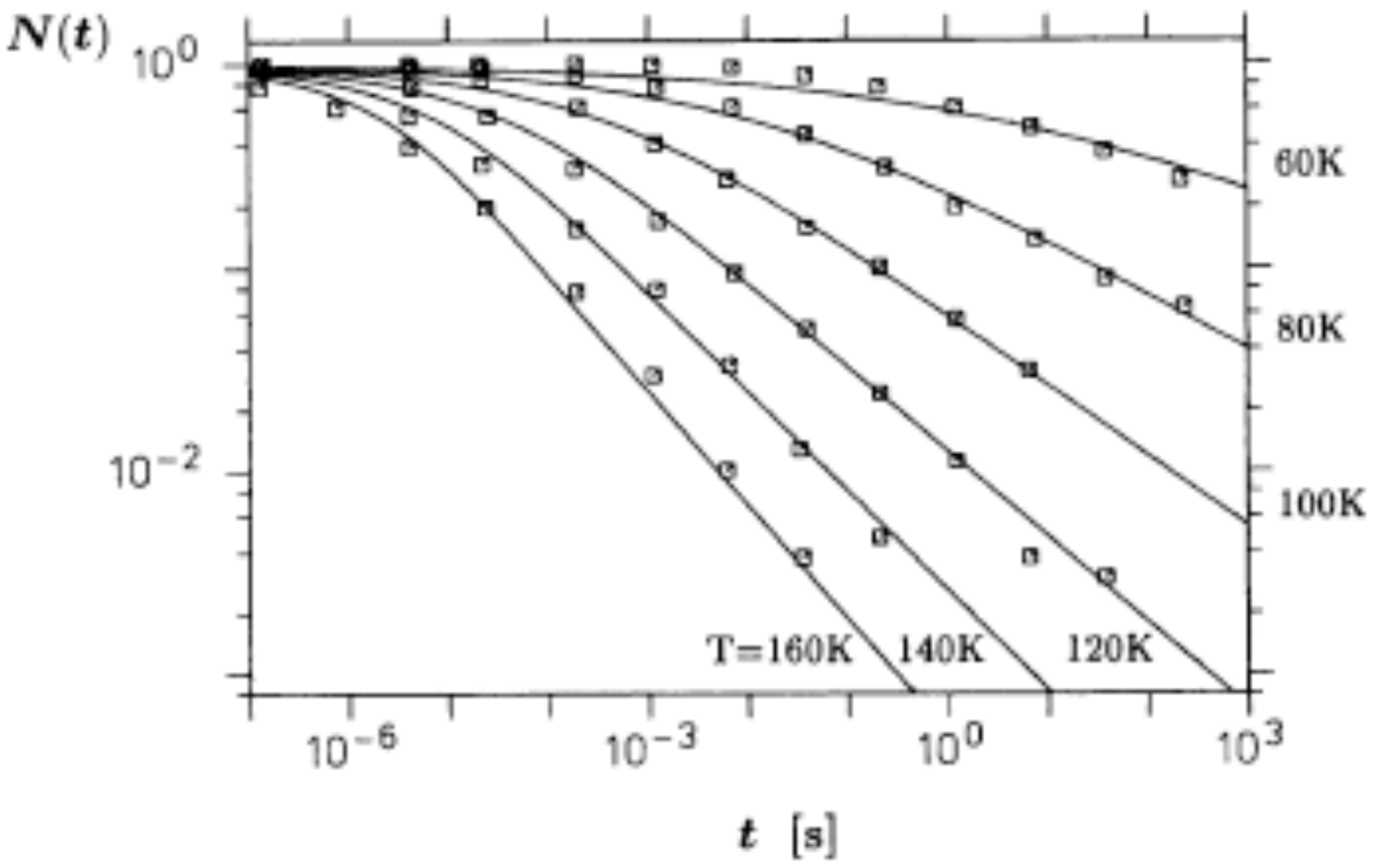


FIGURE 2 Three-parameter model Eq. 32 for rebinding of CO to Mb after photo dissociation. The parameters are $\tau_m = 8.4 \times 10^{-10}$s, $\alpha = 3.5 \times 10^{-3}\ K^{-1}$ and $k = 130$, the data points are from Austin et al. (1975).

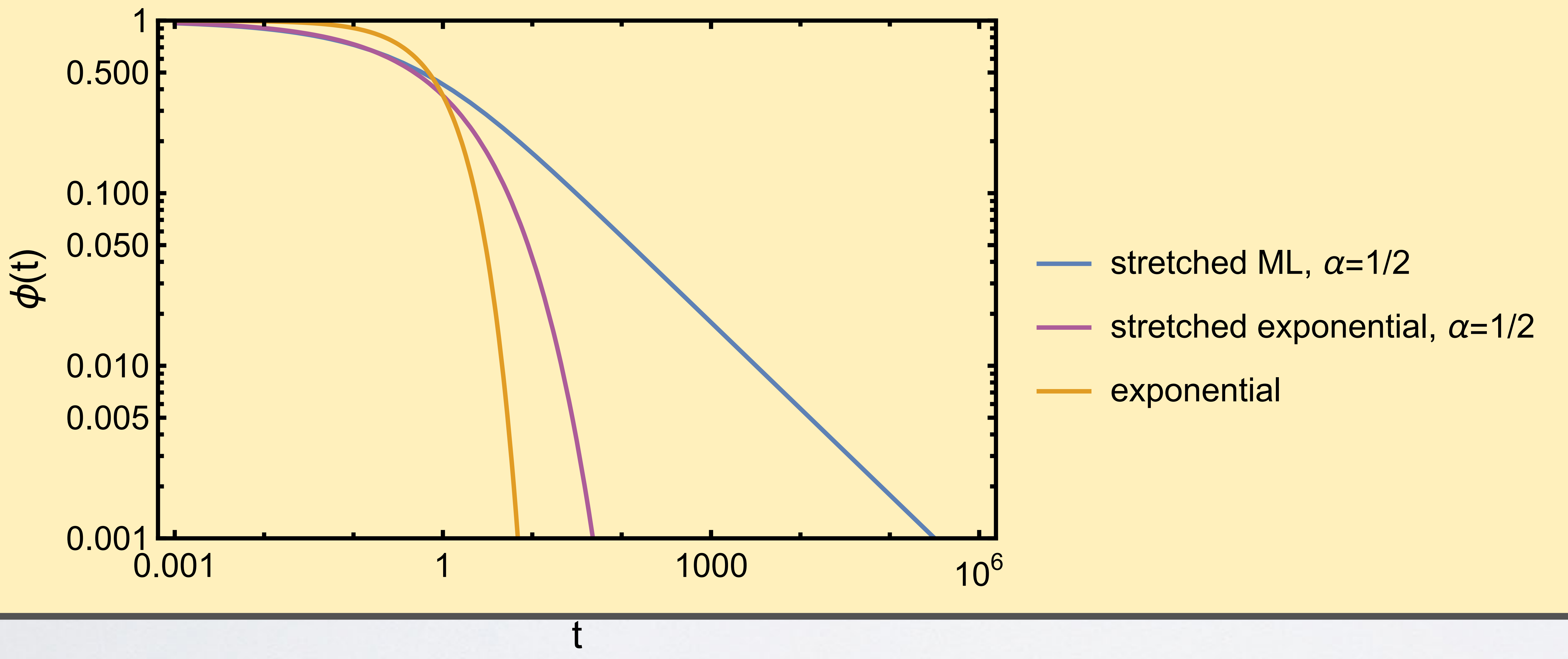
$$N(t) = N(0)E_\alpha(-(t/\tau)^\alpha)$$

Mittag-Leffler function

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

$$E_\alpha(-(t/\tau)^\alpha) \overset{t\to\infty}{\sim} \frac{(t/\tau)^{-\alpha}}{\Gamma(1-\alpha)}$$

Mittag-Leffler relaxation function



$$\frac{d\phi_{\mathrm{ML}}(t)}{dt} + \tau^{-\alpha}\, \boxed{{}_0\partial_t^{1-\alpha}}\, \phi_{\mathrm{ML}}(t) = 0$$

Fractional differential equation

$${}_0\partial_t^{1-\rho}\phi_{\mathrm{ML}}(t) \equiv \frac{d}{dt}\int_0^t dt' \, \frac{(t-t')^{\rho-1}}{\Gamma(\rho)}\phi_{\mathrm{ML}}(t')$$

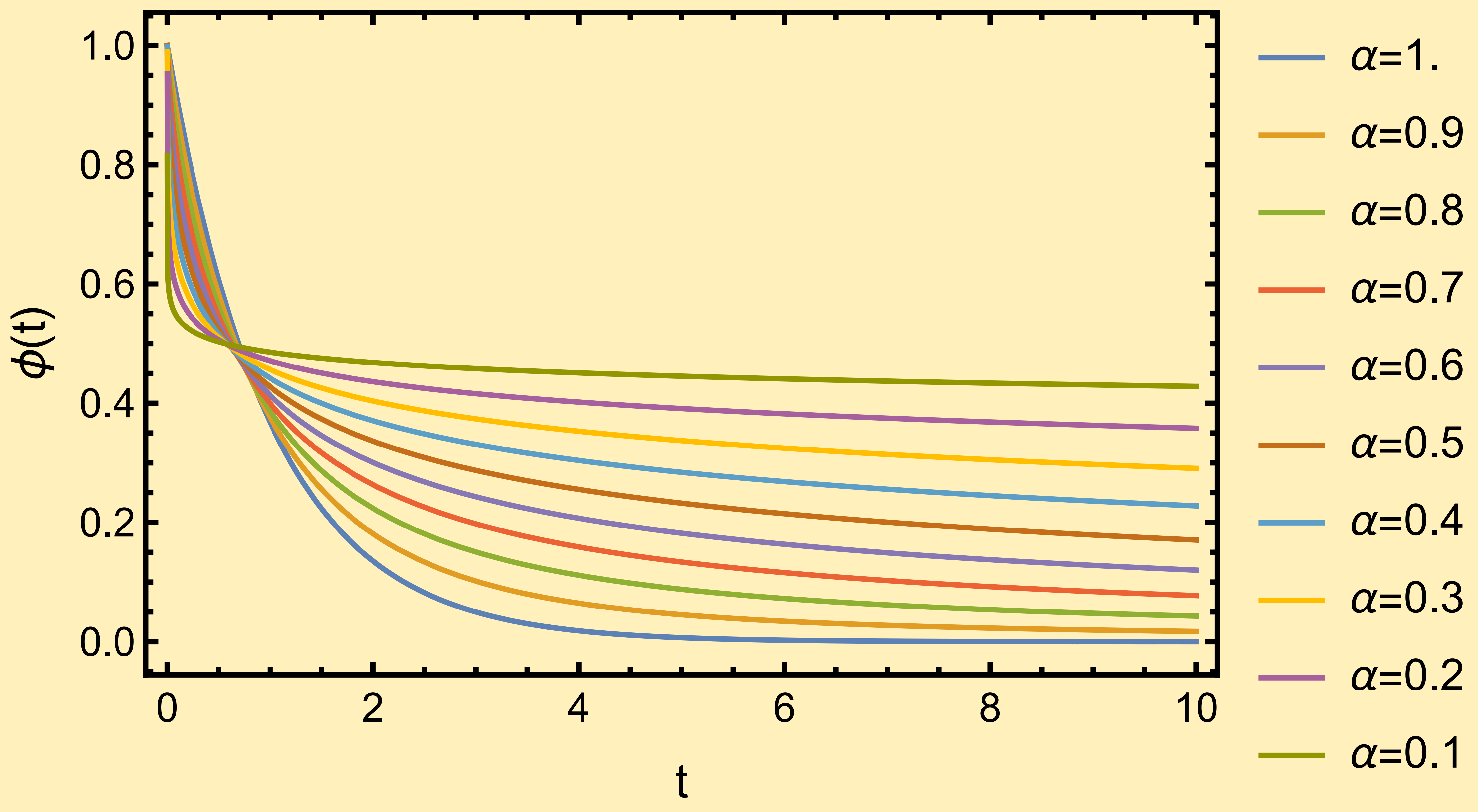
Fractional derivative = memory effects

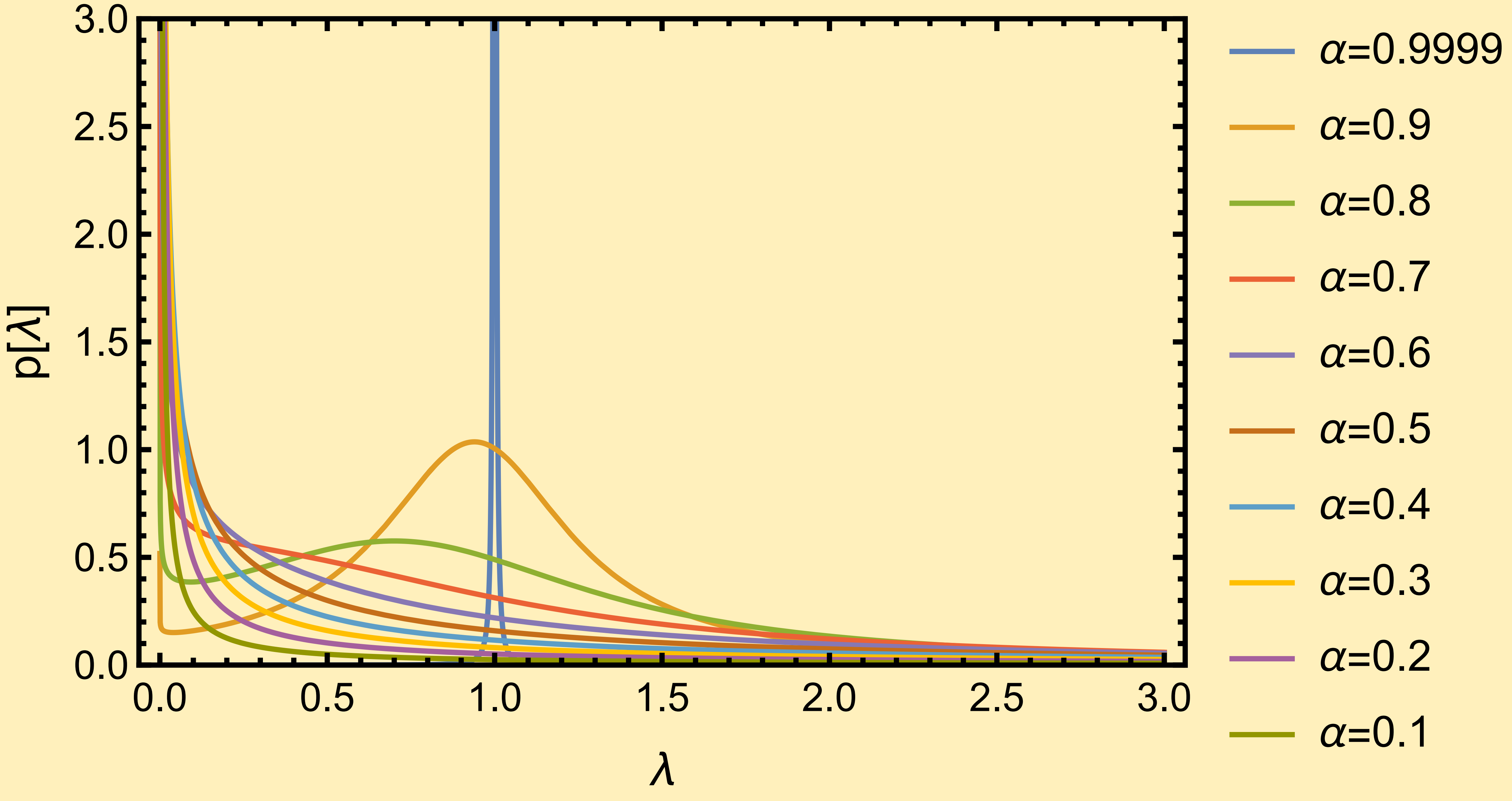
G. R. Kneller and M. Saouessi. Acta Physica Polonica B, 53(2):A–2, 2022.

“Stretched” ML function and relaxation rate spectrum

$$\phi(t) = E_\alpha(-t^\alpha)$$

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

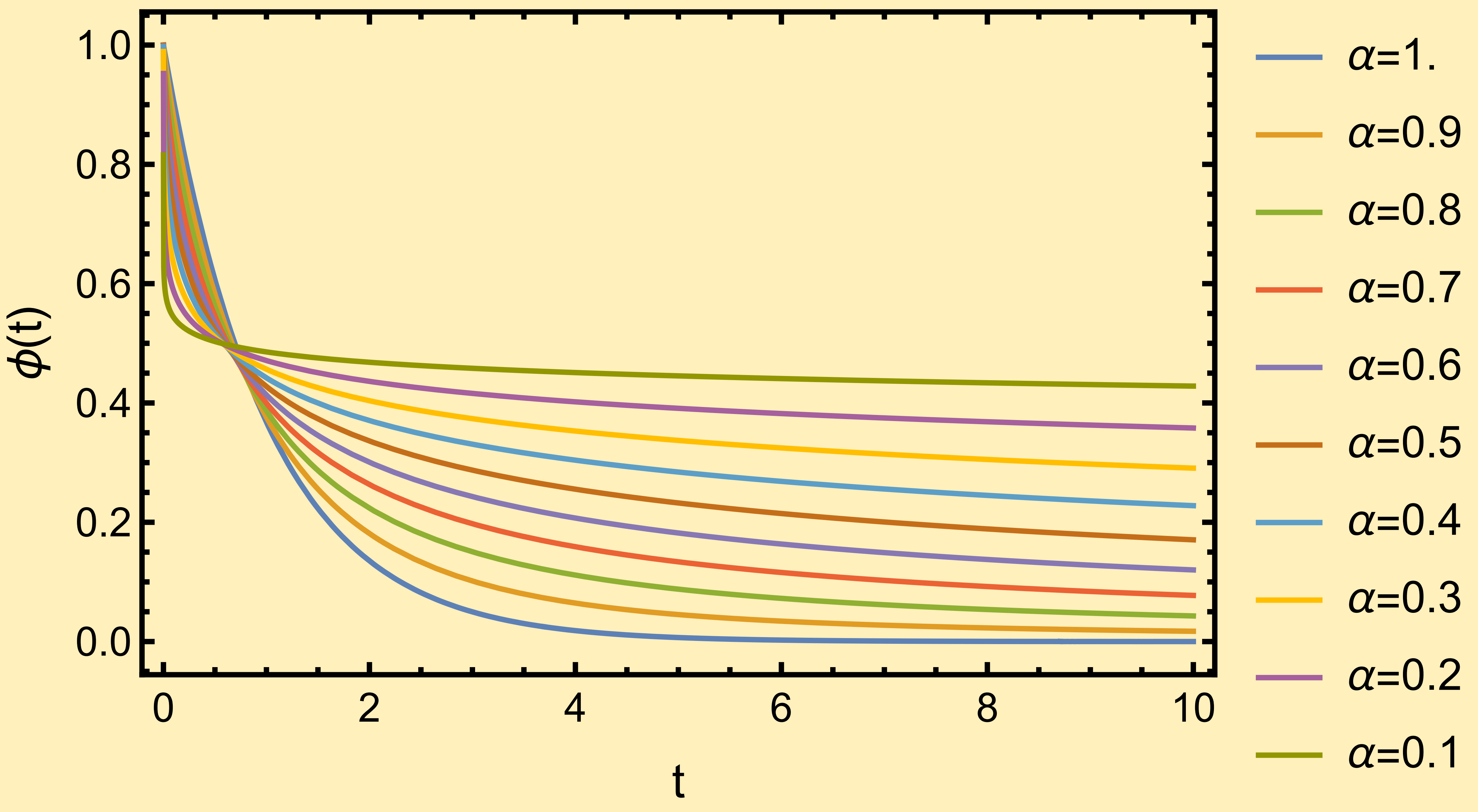


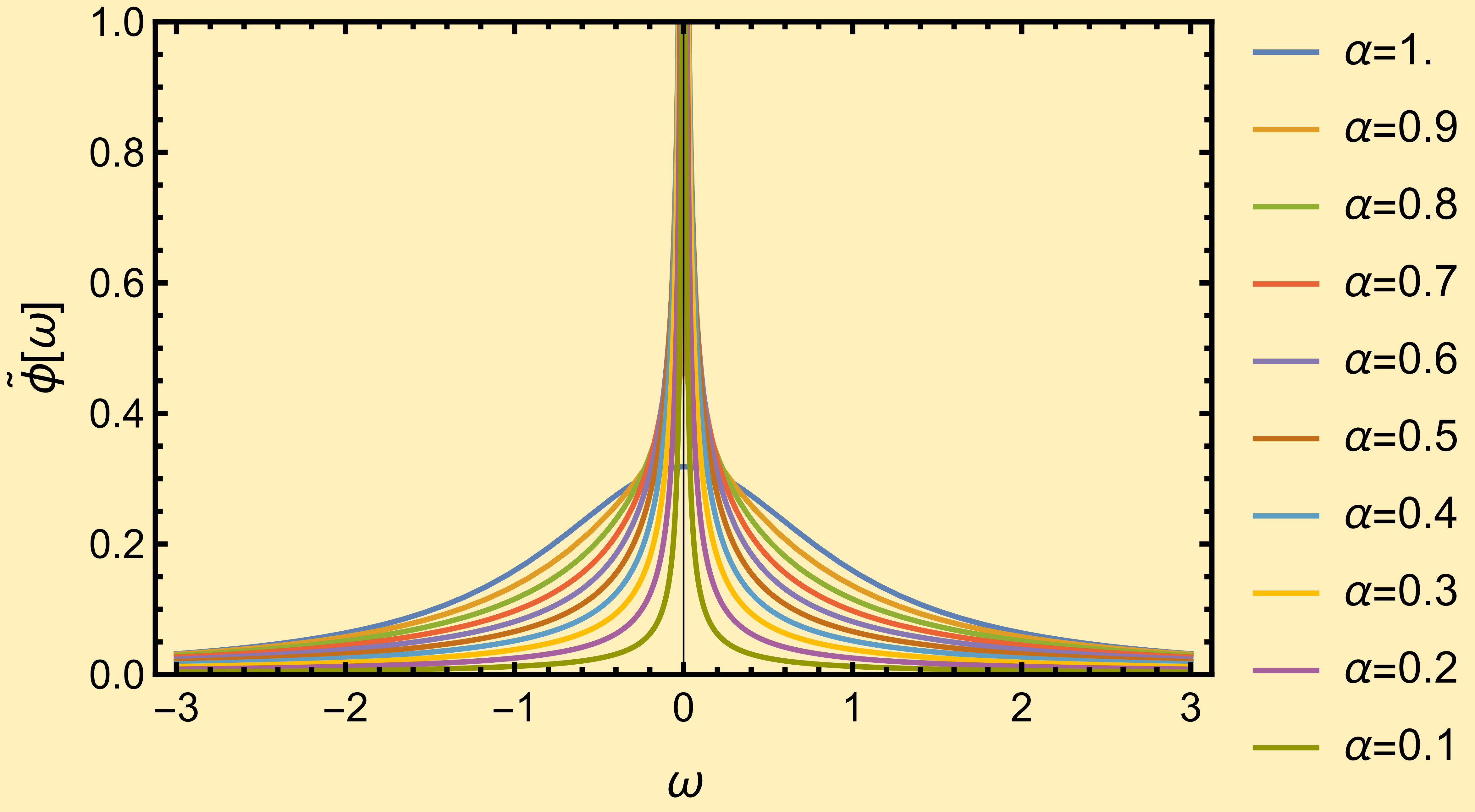


"Stretched" ML function and Fourier spectrum

$$\phi(t) = E_\alpha(-t^\alpha)$$

$$\tilde{\phi}(\omega) = \frac{\sin\left(\frac{\pi\alpha}{2}\right)}{\pi\omega\left(\omega^{-\alpha} + \omega^{\alpha} + 2\cos\left(\frac{\pi\alpha}{2}\right)\right)}$$





Relating relaxation rates to the "roughness" of the energy landscape

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

$$\lambda = f(\epsilon), \quad \epsilon = \frac{\Delta E}{k_B T}$$

$$\Rightarrow$$

$$p(\lambda) \rightarrow \tilde{p}(\epsilon)$$

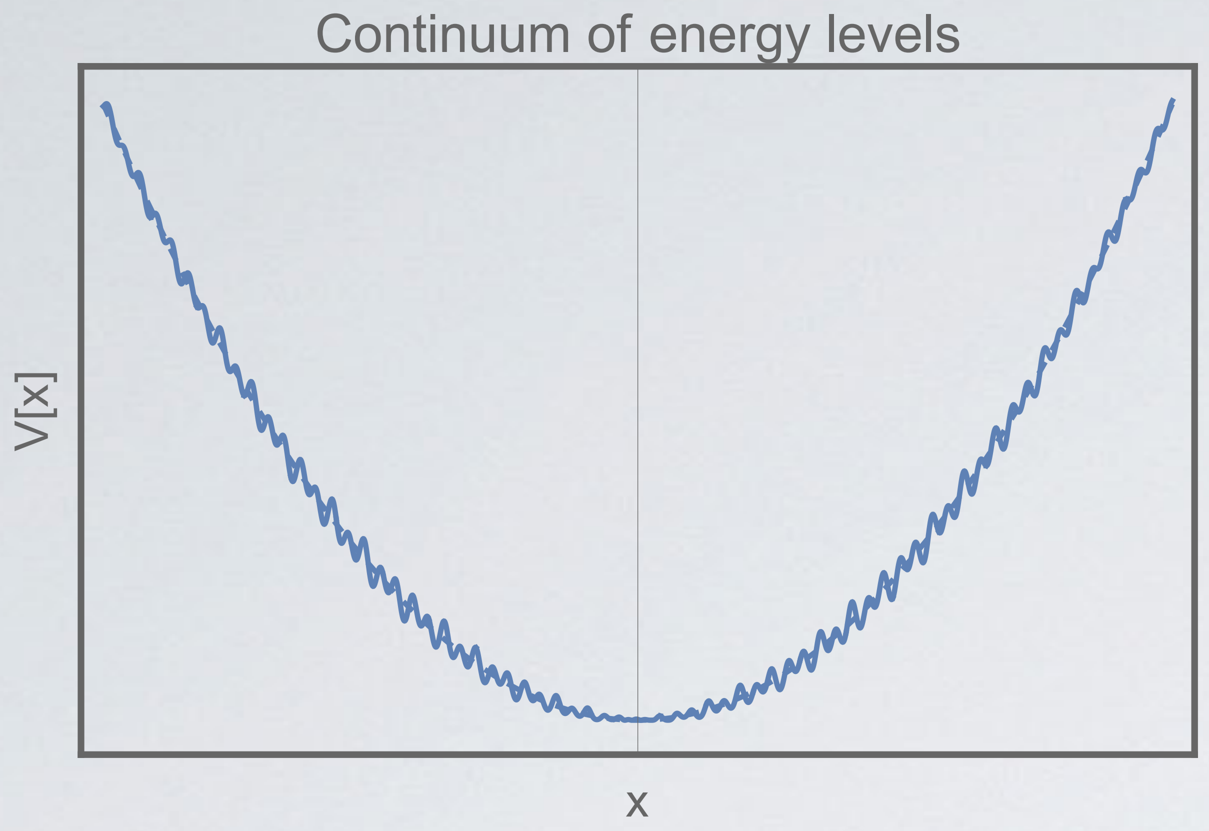
To relate barrier heights and relaxation rates, one needs a **model**.

$$\lambda = \lambda_0 e^{-\epsilon}$$

Arrhenius

$$\lambda = \lambda_0 e^{-\epsilon^2}$$

R. Zwanzig, PNAS 85,1988.

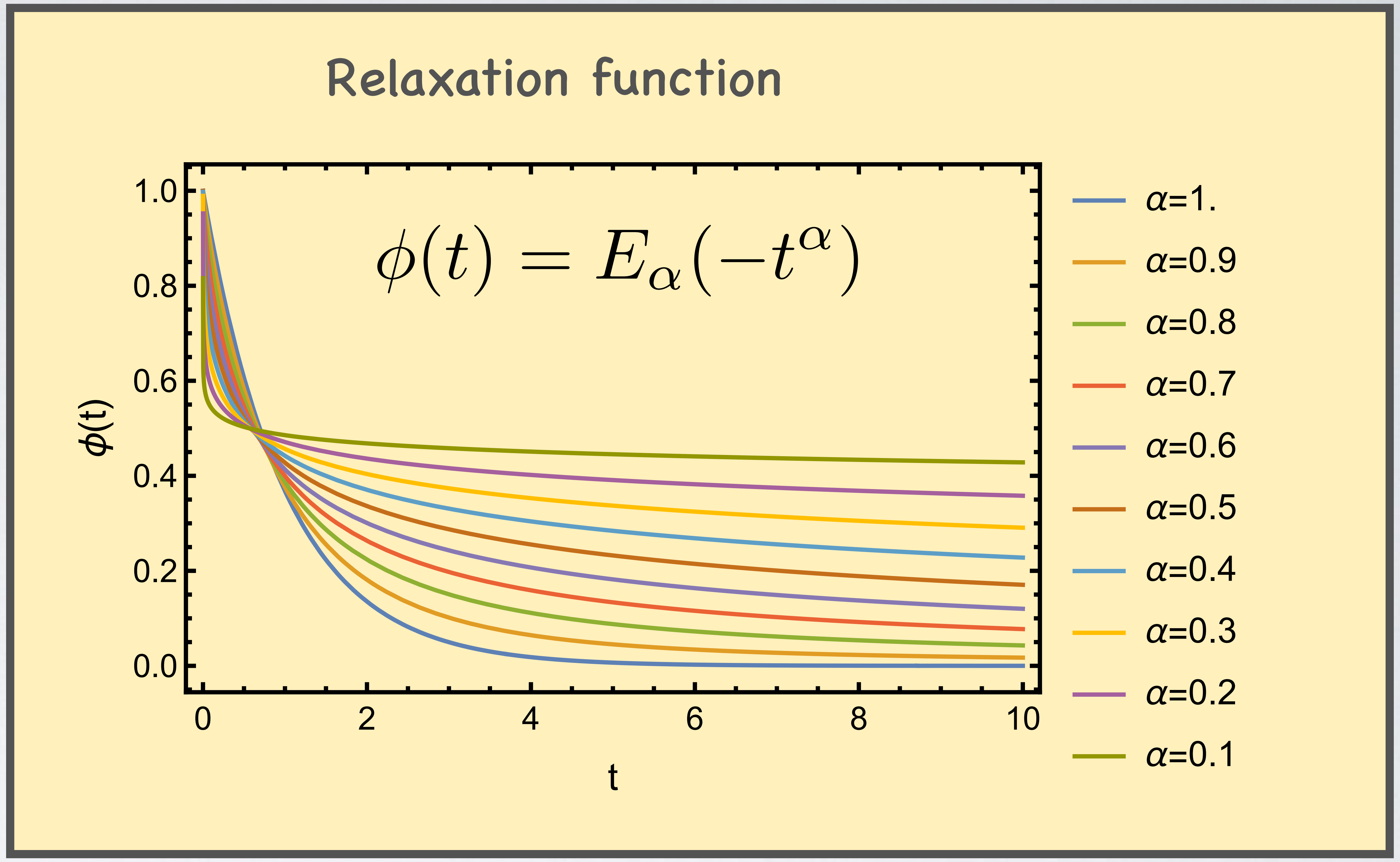


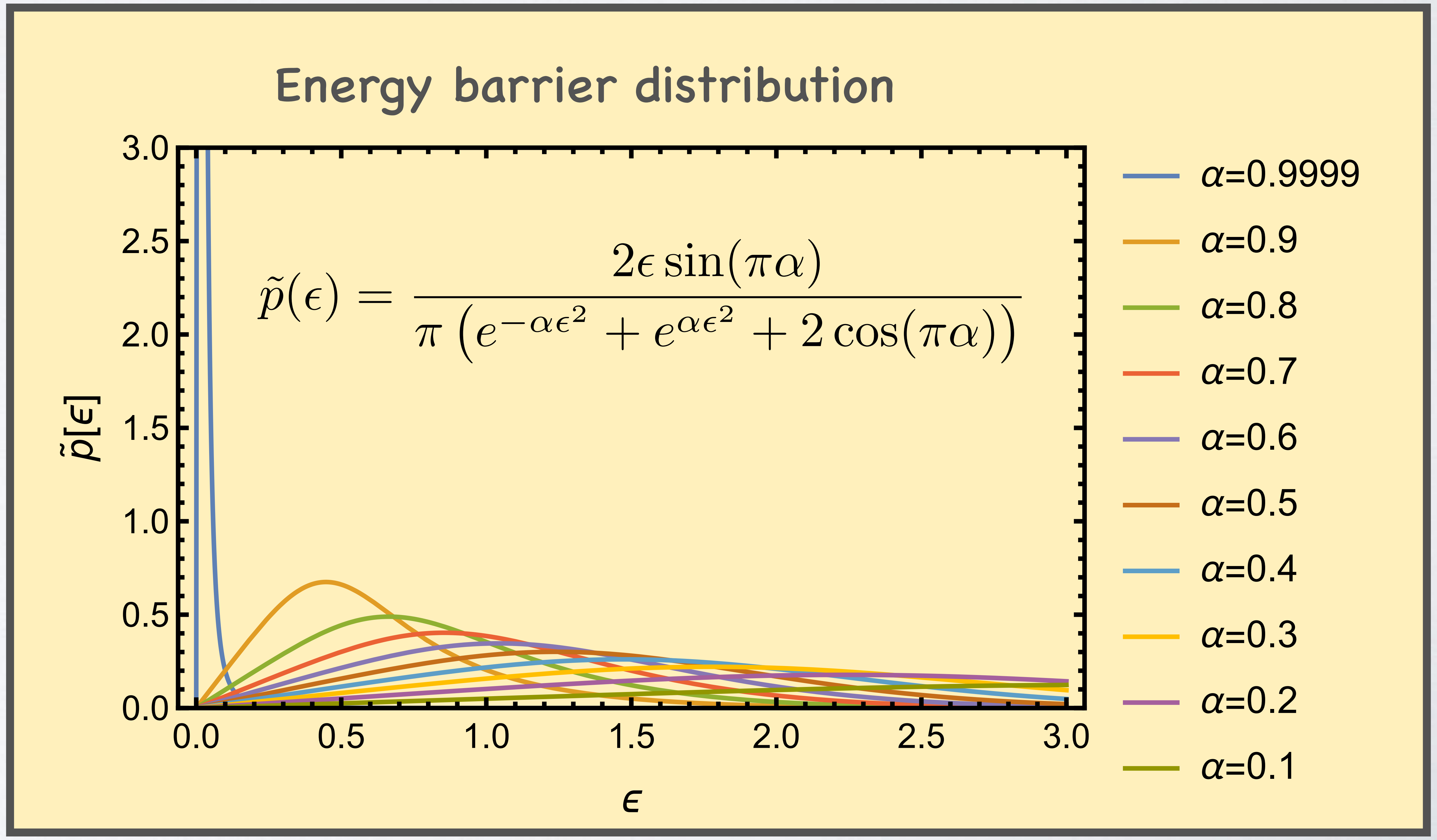
For diffusion in a harmonic potential

$$D_0 = \langle x^2 \rangle \lambda_0$$

$$\lambda = \lambda_0 e^{-\epsilon^2}$$

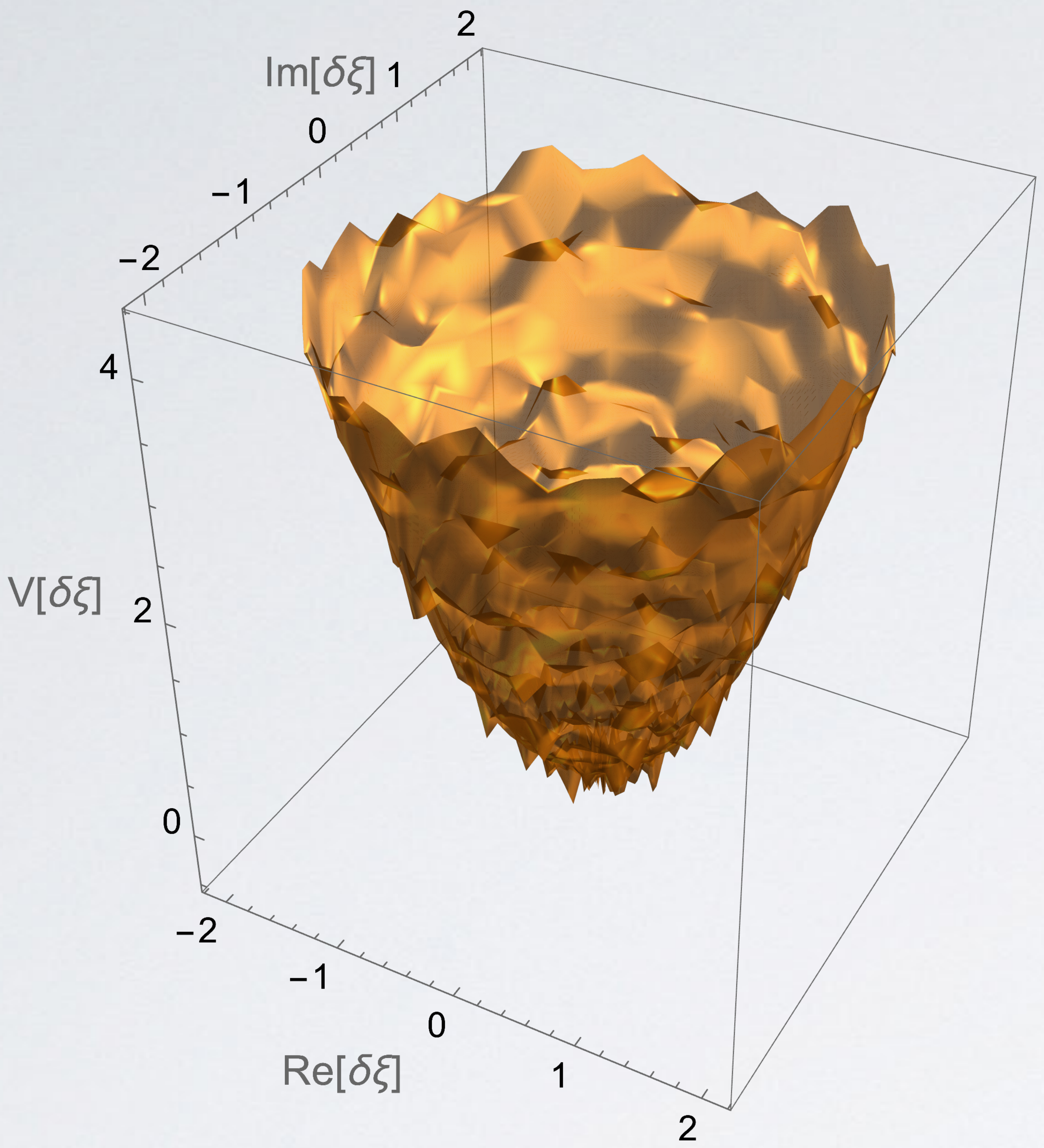
Saouessi, Peters & Kneller, JCP150, 2019.

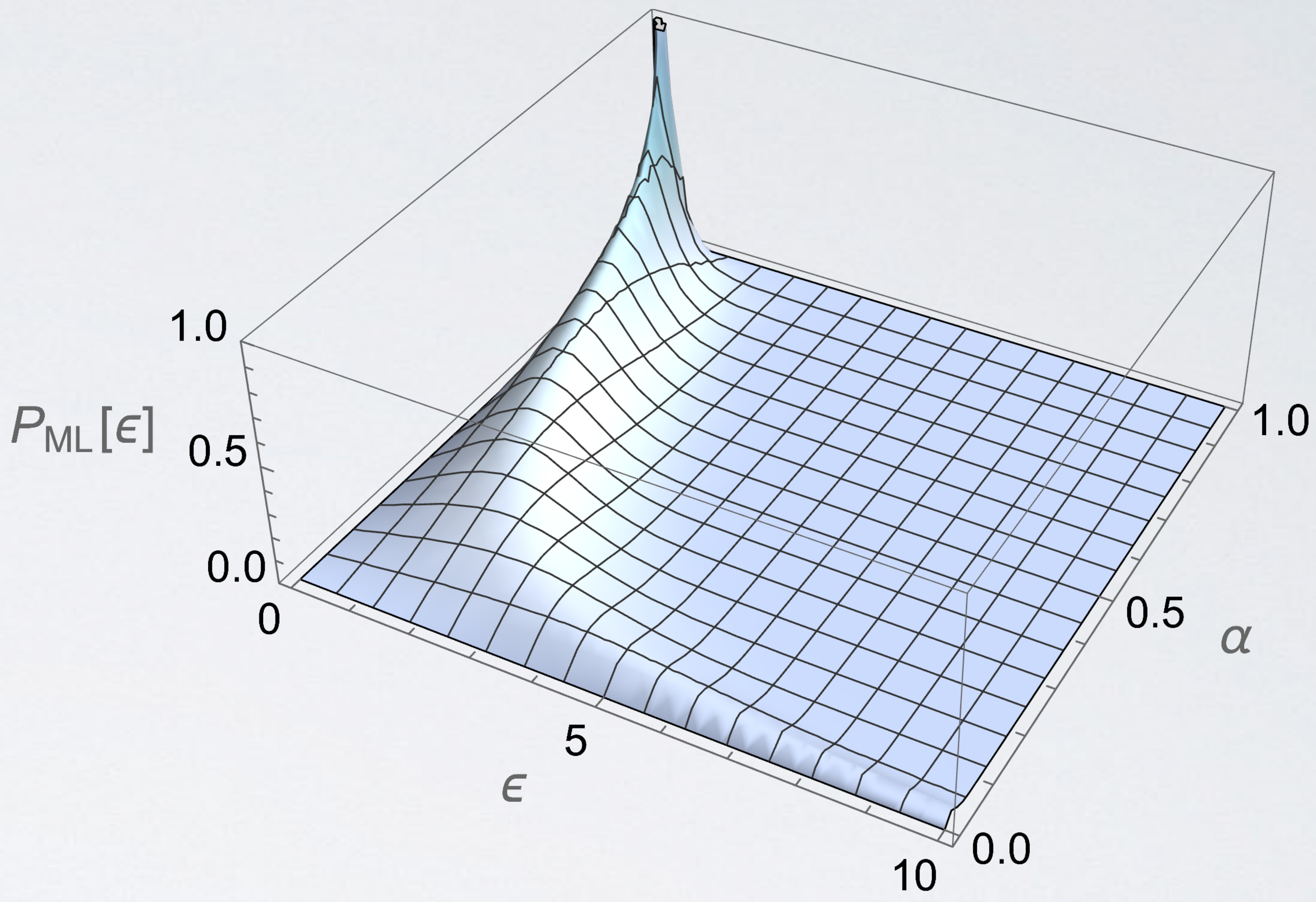




Integrate the momentum transfer q

[1] R. Zwanzig. PNAS USA, 85(7):2029– 2030, Apr. 1988.
[2] M. Saouessi, J. Peters, and G. R. Kneller. J. Chem. Phys. 150(16):161104, 2019.
[3] A. N. Hassani, et al. J. Chem Phys., 152(2):025102, 2022.





Dynamical variable:

$$\xi(\mathbf{q}, t) = e^{i\mathbf{q}\cdot\mathbf{R}_j(t)}$$

$$\delta\xi(\mathbf{q}, t) = \xi(\mathbf{q}, t) - \langle \xi(\mathbf{q}, t) \rangle$$

Distribution of barrier heights

$$P_{ML}(\epsilon, \alpha) = \frac{2\epsilon \sin(\pi\alpha)}{\pi \left(e^{-\alpha\epsilon^2} + e^{\alpha\epsilon^2} + 2\cos(\pi\alpha)\right)}$$

Modeling QENS for concrete examples

A. N. Hassani, L. Haris, M. Appel, T. Seydel, A. M. Stadler, and G. R. Kneller. J. Chem. Phys., 156(2):025102, Jan. 2022.

Myelin basic protein — an intrinsically disordered protein

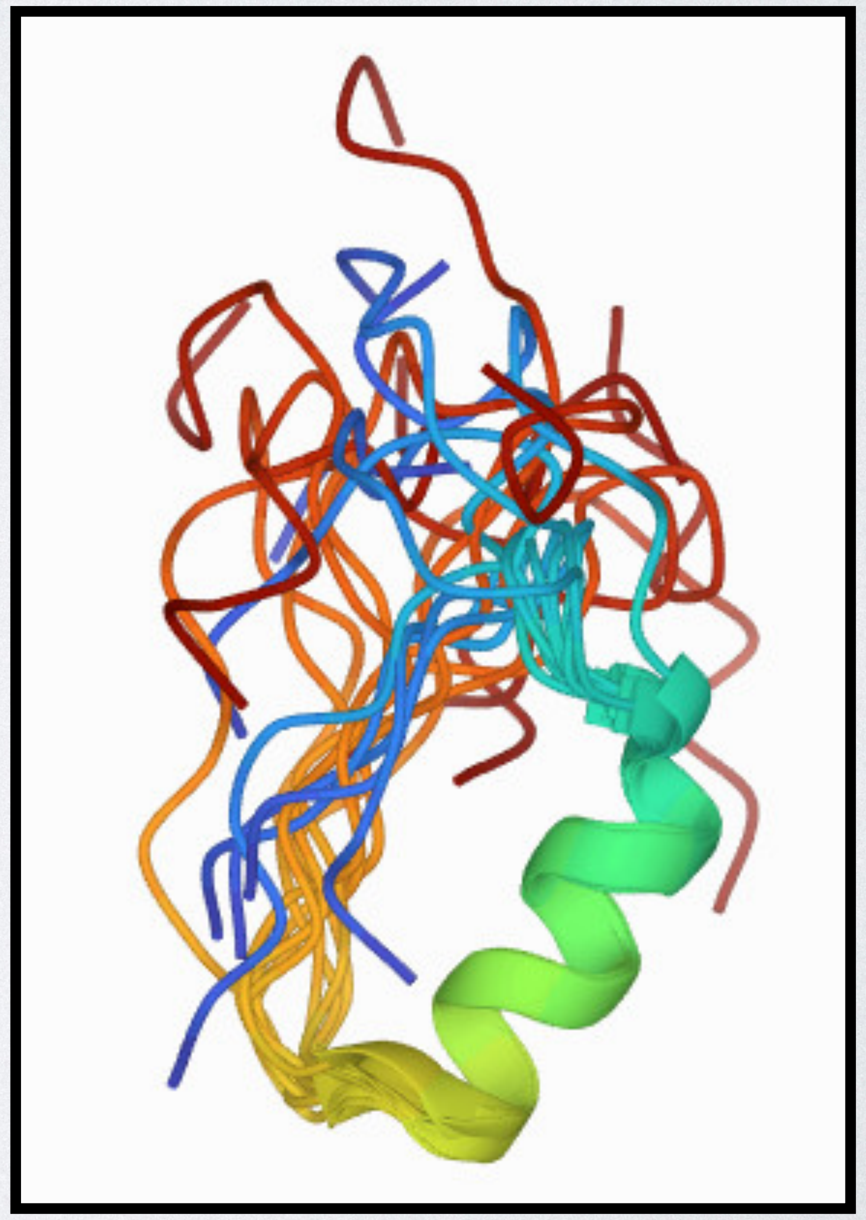
(Thesis Abir Nesrine Hasssani, with Andreas Stadler, JCNS Jülich)

- Essential component of the myelin sheath of the central nervous system
- Intrinscially disordered in aqueous solution

Motivation

Understand the internal dynamics of MBP in two solutions :

- D2O buffer
- D2O buffer + 30% trifluoro ethanol (TFE)



Neutron Scattering experiment

IN16B at Institut Laue-Langevin with BATS (backscattering + time of flight) with time scales 2 ps < t < 600 ps

Basic data treatment

Subtract the solvent

$$S(q,\omega) = S(q,\omega)_{\text{protein solution}} - (1-\phi)\cdot S(q,\omega)_{\text{buffer}}$$

Volume fraction $$\phi = \bar{\nu}\cdot c$$ ≈ 4 %

Symmetrize and normalize the QENS spectra

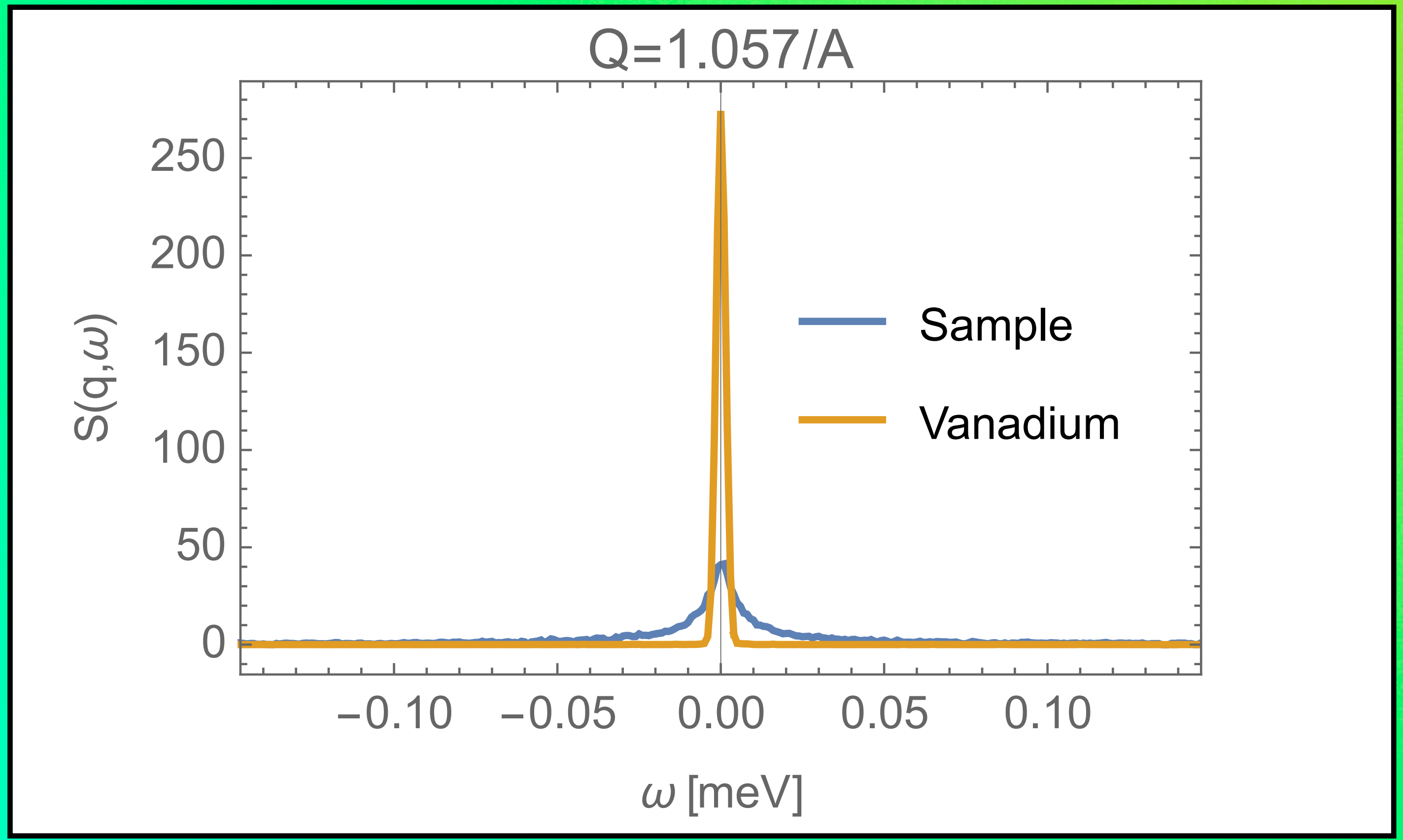
$$S^{(+)}(q,\omega) = \frac{e^{-\beta\hbar\omega/2}S(q,\omega)}{\int_{-\infty}^{+\infty} d\omega\, e^{-\beta\hbar\omega/2}S(q,\omega)} \iff F^{(+)}(q,t) = \frac{F(q,t-i\beta\hbar)}{F(q,-i\beta\hbar)}$$

Semiclassical approximation

$$F^{(+)}(q,t) \approx F_{cl}(q,t)$$

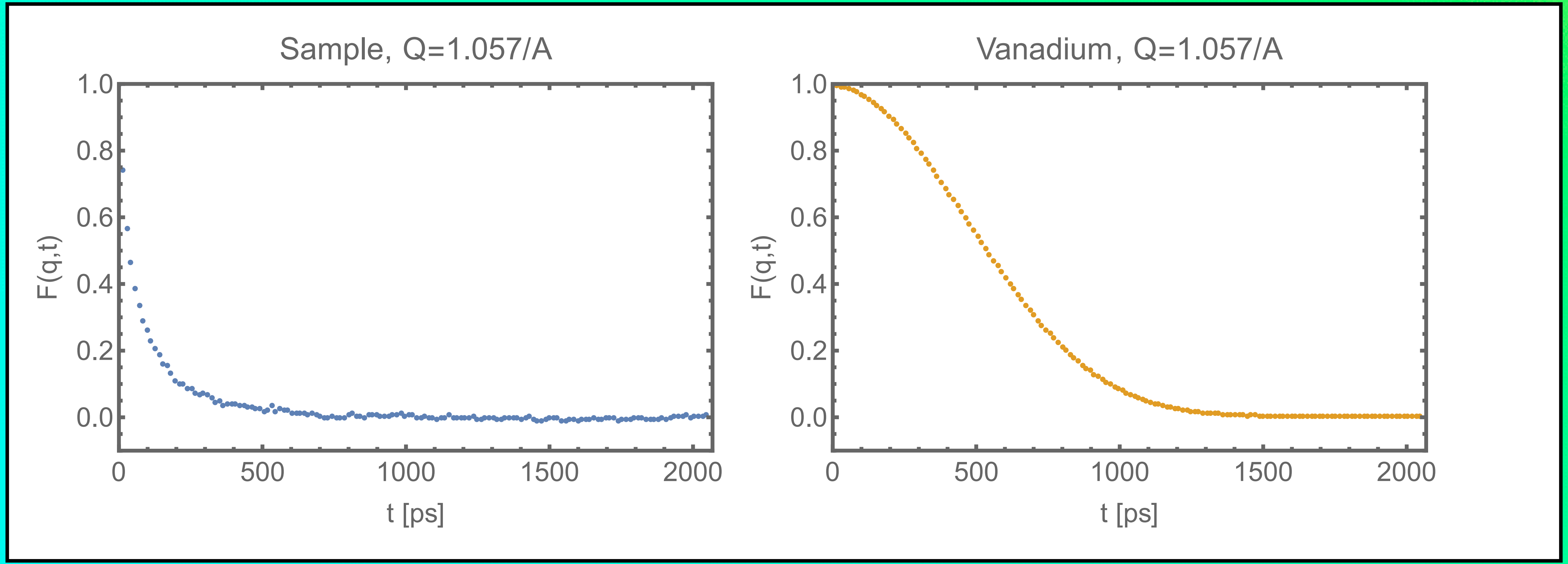
P. Schofield, Phys. Rev. Lett. 4, 239 (1960)

Instrument deconvolution



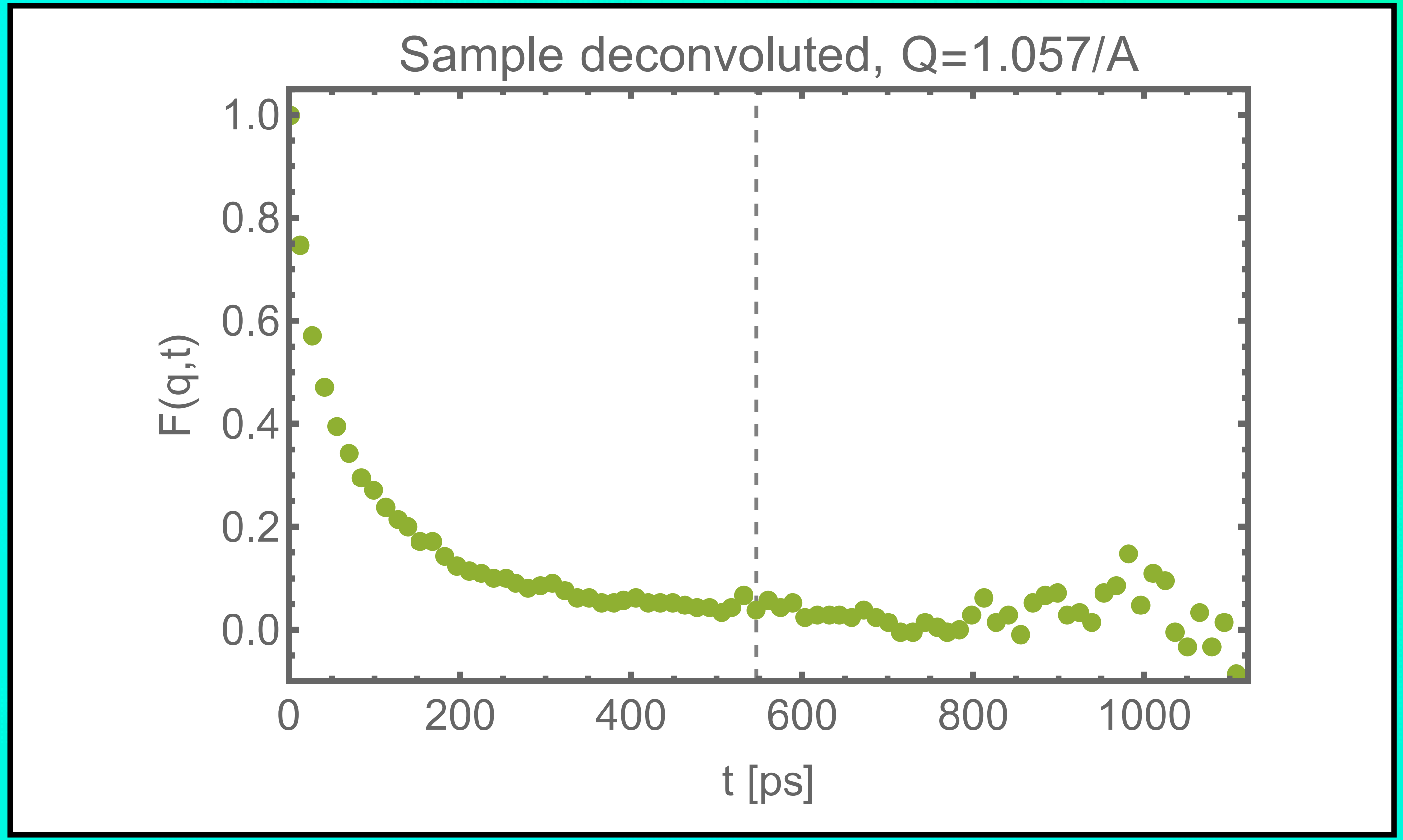
$$S_m^{(+)}(q,\omega) = \int_{-\infty}^{+\infty} d\omega' \, \tilde{R}(q,\omega-\omega') S^{(+)}(q,\omega') + \tilde{N}(q,\omega)$$

Discrete Fourier transform



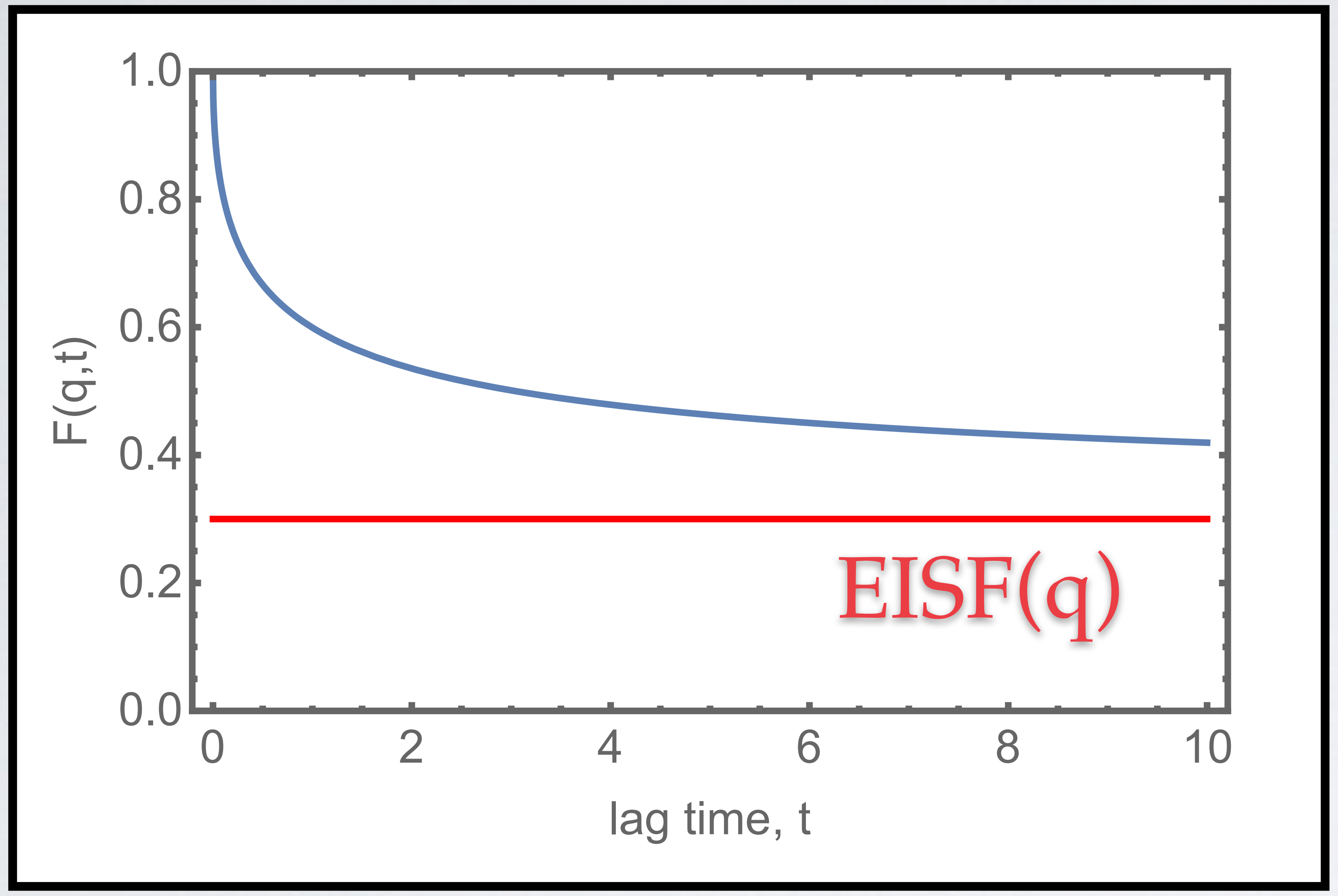
$$F_m^{(+)}(q,t) = F^{(+)}(q,t) R(q,t) + N(q,t)$$

Instrument deconvolution in the time domain



$$F^{(+)}(q,t) = \frac{F_m^{(+)}(q,t)}{R(q,t)} - \frac{N(q,t)}{R(q,t)}$$

The "minimalistic model" for F(q,t)



$$F_{\text{int}}(q,t) = EISF(q) + (1 - EISF(q)\phi(q,t))$$

$$\phi(t) = E_\alpha\left(-[t/\tau_R]^\alpha\right)$$

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

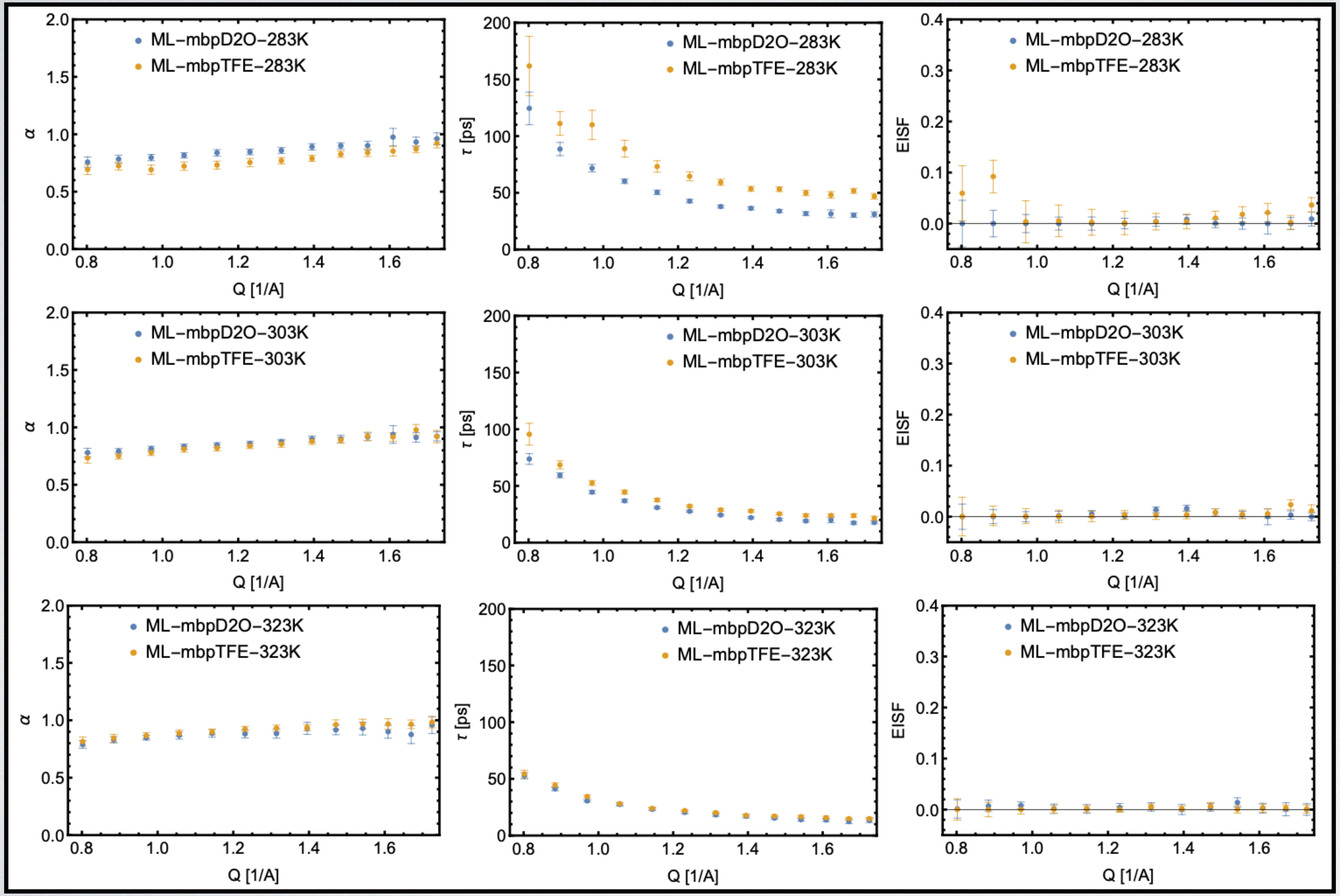
Mittag-Leffler function

Parameters

1. α
2. τ
3. EISF

Fitted parameters

$$F_{\text{int}}(q,t) = EISF(q) + (1 - EISF(q)\phi(q,t))$$



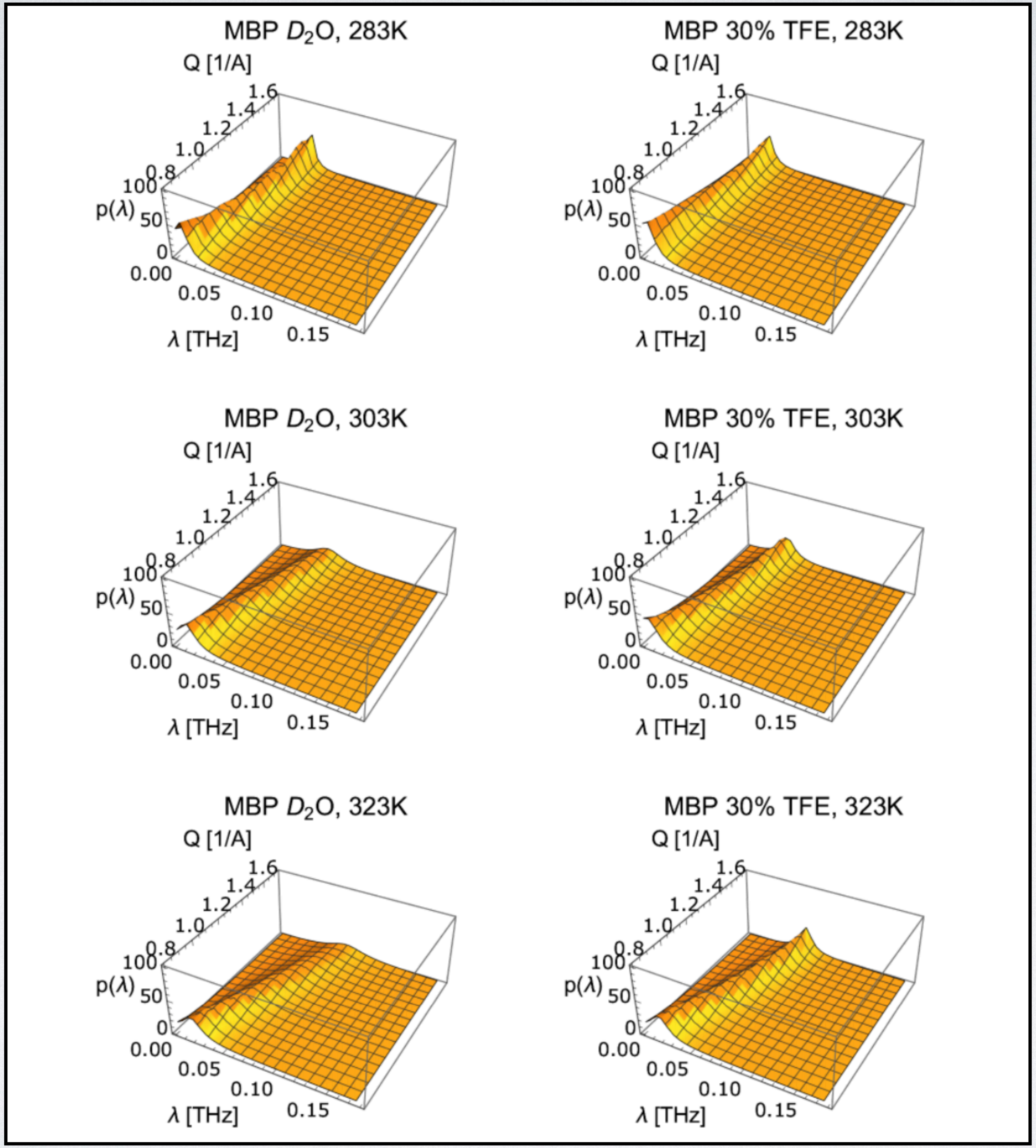
Parameters

1. α
2. τ
3. EISF ≈ 0

Relaxation rate spectra
283 K

Relaxation rate spectra
303 K

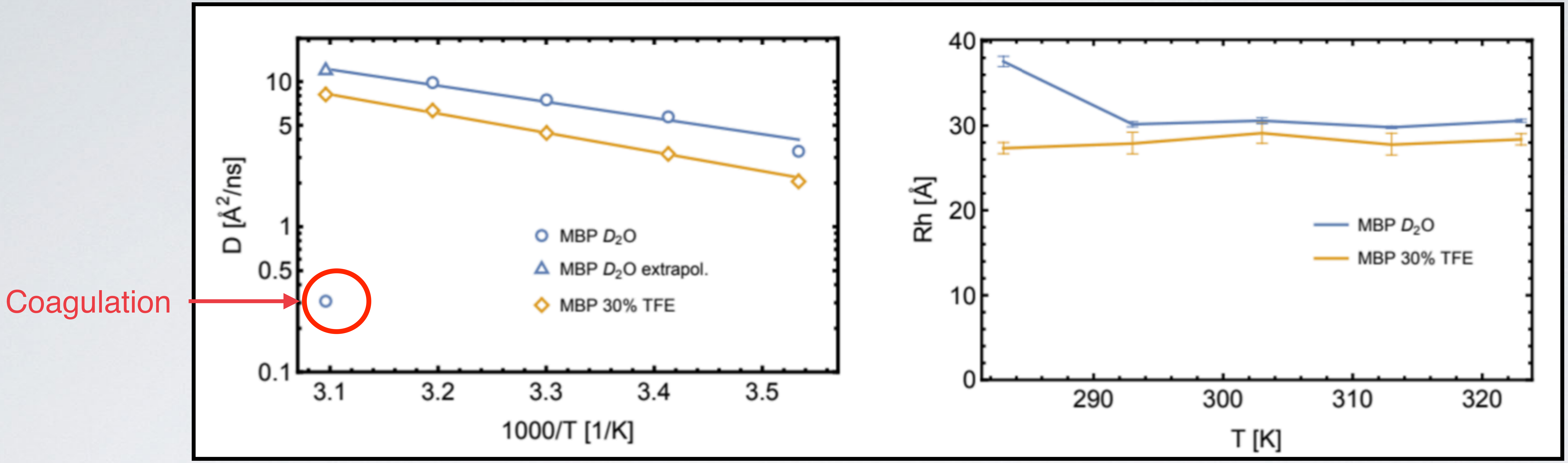
Relaxation rate spectra
323 K



TFE induces a less heterogeneous relaxation dynamics

Global diffusion observed by DLS

Diffusion constant   Hydrodynamic radius



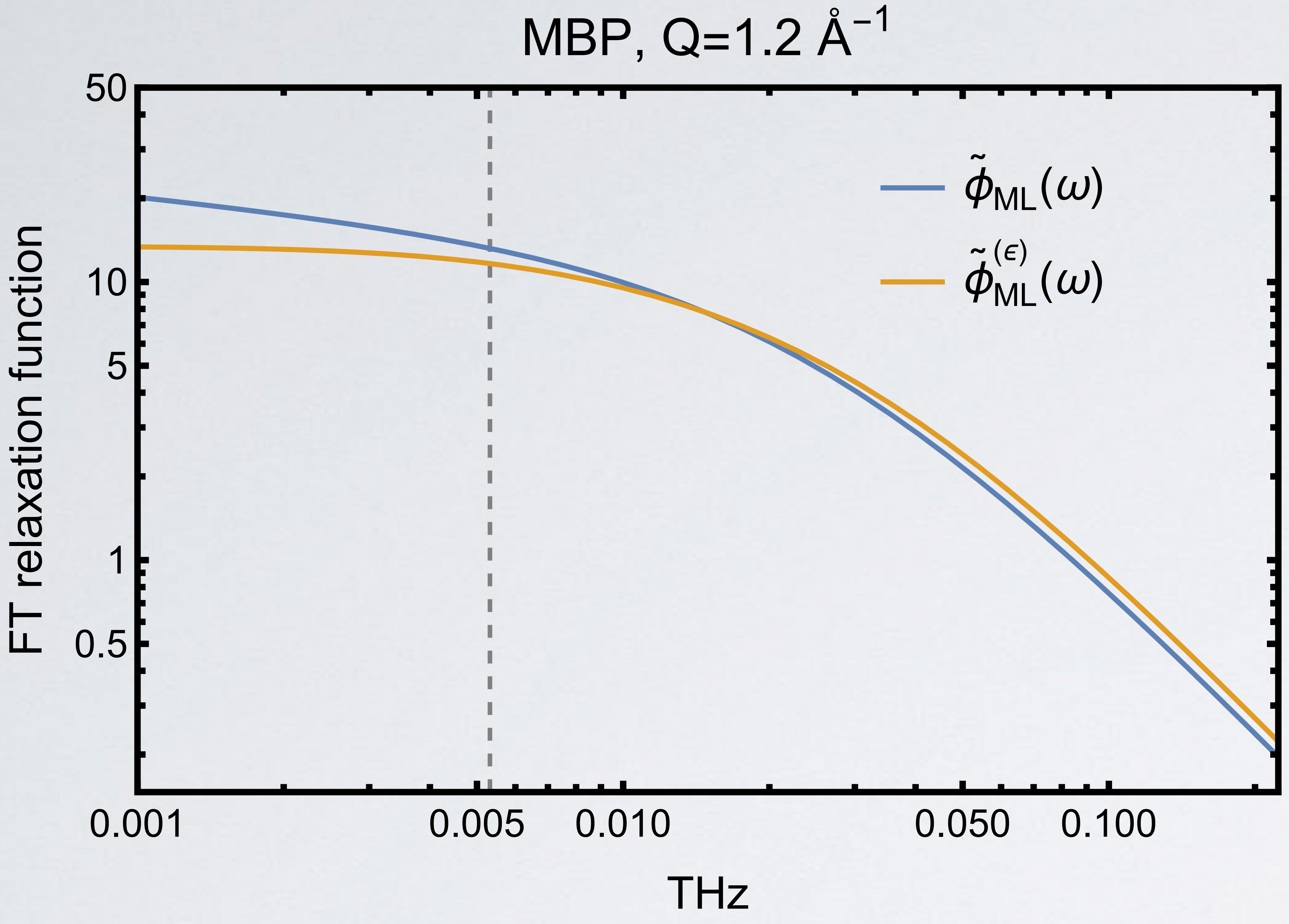
$$D(T) = D_0 e^{-\frac{\Delta G}{k_B T}}$$

$\Delta G = 5.10$ kcal/mol	D_2O
$\Delta G = 6.05$ kcal/mol	$70\%\ D_2O + 30\%\ dTFE$

Stokes-Einstein relation

$$D = \frac{k_B T}{6\pi\eta R_h}$$

Classical method of treating global diffusion



$$\tilde{\phi}_{\mathrm{ML}}(\omega) = \frac{1}{\pi} \frac{\sin\left(\frac{\pi\alpha}{2}\right)}{|\omega|\left((|\omega|\tau_R)^{-\alpha} + (|\omega|\tau_R)^{\alpha} + 2\cos\left(\frac{\pi\alpha}{2}\right)\right)}$$

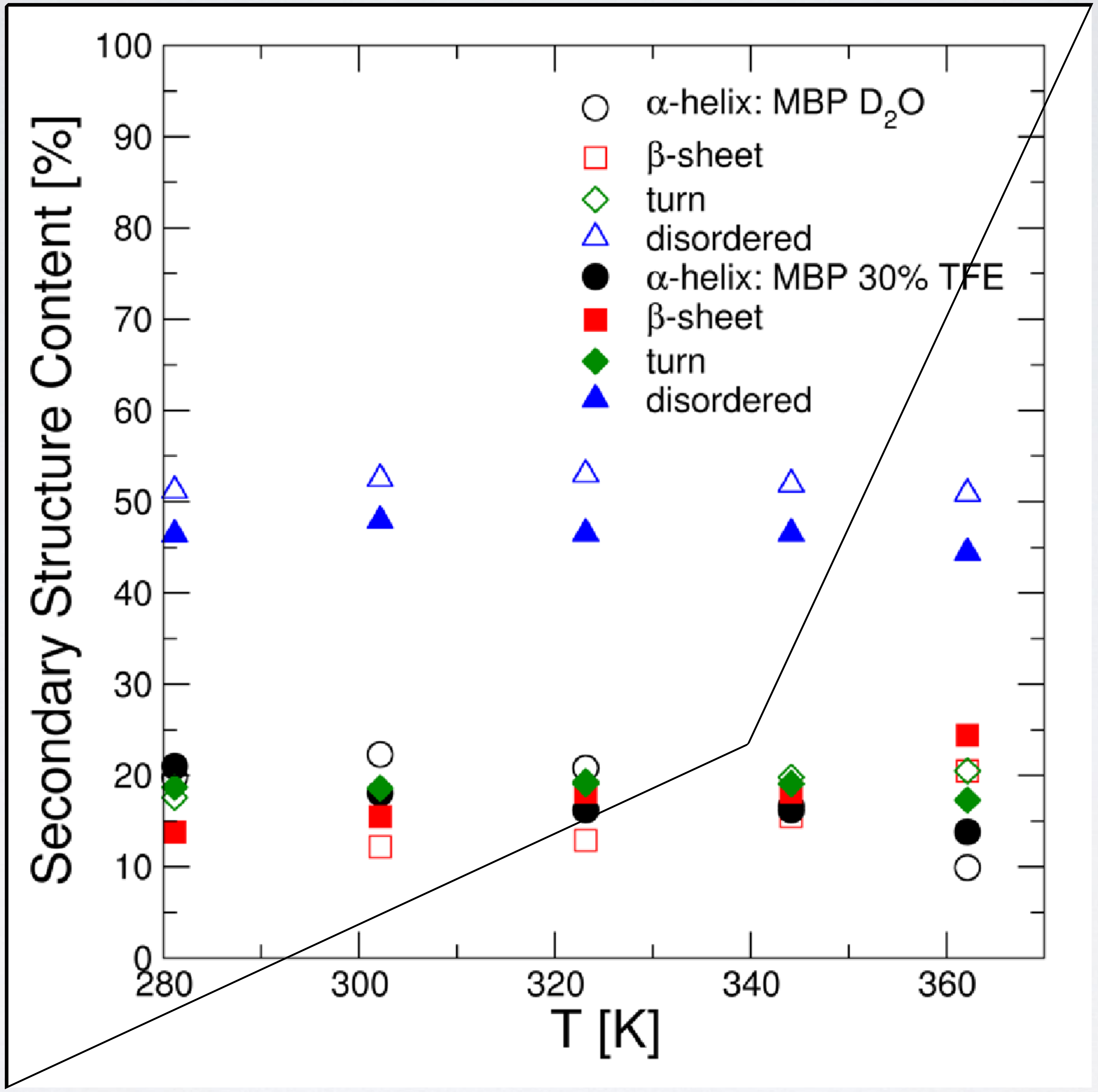
$$\phi^{(\epsilon)}_{\mathrm{ML}}(t) = e^{-Dq^2|t|}\phi_{\mathrm{ML}}(t)$$

$$\tilde{\phi}^{(\epsilon)}_{\mathrm{ML}}(\omega) = \frac{\epsilon\left(\omega^2+\epsilon^2\right)^{\alpha/2} + \omega\sin(\alpha\arg(\epsilon+i|\omega|)) + \epsilon\cos(\alpha\arg(\epsilon+i|\omega|))}{(\omega^2+\epsilon^2)\left(\left((\omega^2+\epsilon^2)^{\alpha}+1\right)(\omega^2+\epsilon^2)^{-\alpha/2} + 2\cos(\alpha\arg(\epsilon+i|\omega|))\right)}$$

$$\epsilon = Dq^2$$

Setting $D = 0$ has very little influence on the fit parameters $\alpha, \tau, EISF$.

CD analysis (DISCO beam line SOLEIL)

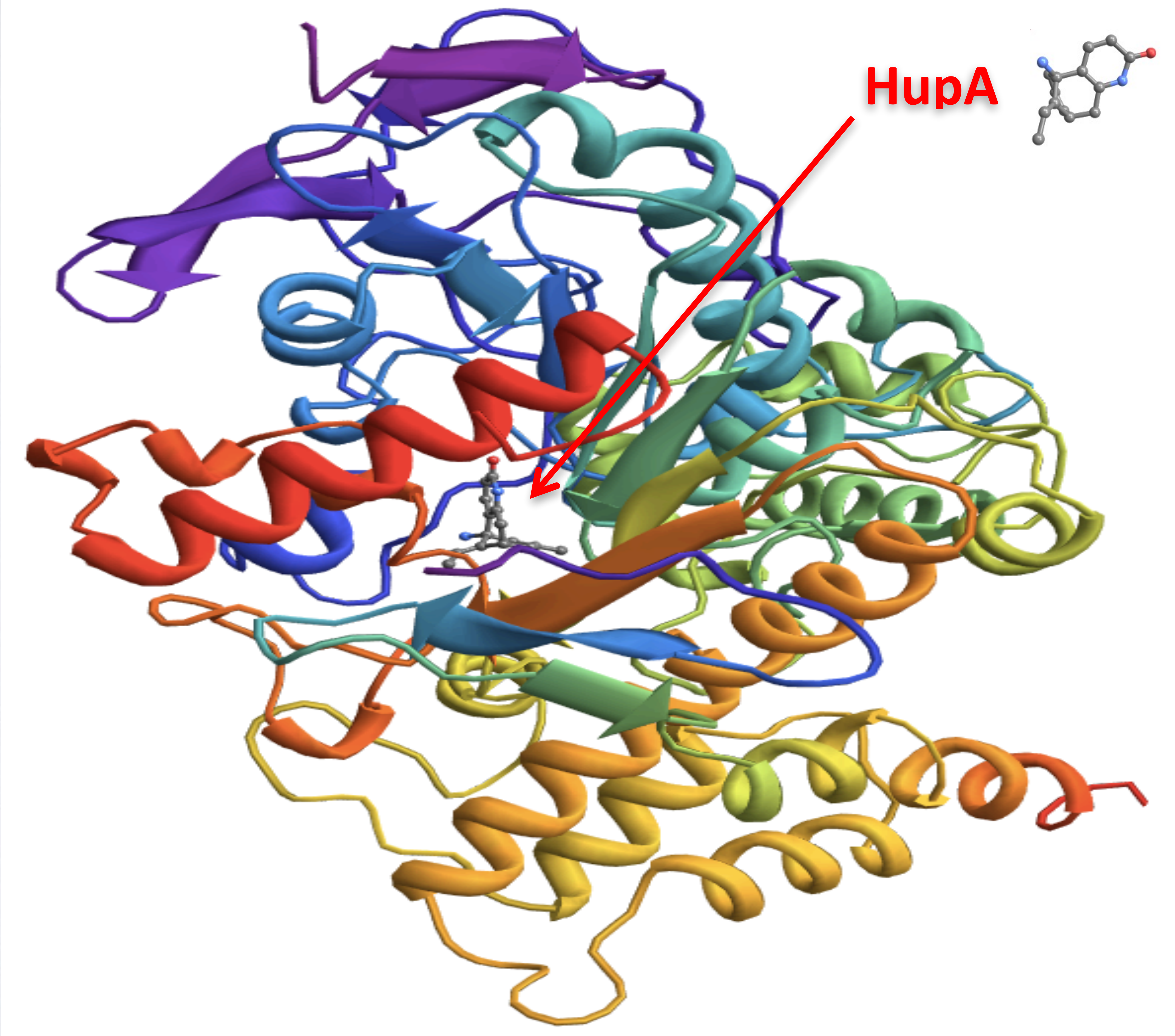


Dynamical changes of human acetylcholinesterase in presence of a reversibly bound inhibitor – Huperzine A

Hydrated powder samples

Thesis Melek Saouessi, with Judith Peters, ILL/UGA Grenoble

AChE catalyzes the degradation of acetyl choline at neuro-muscular junctions



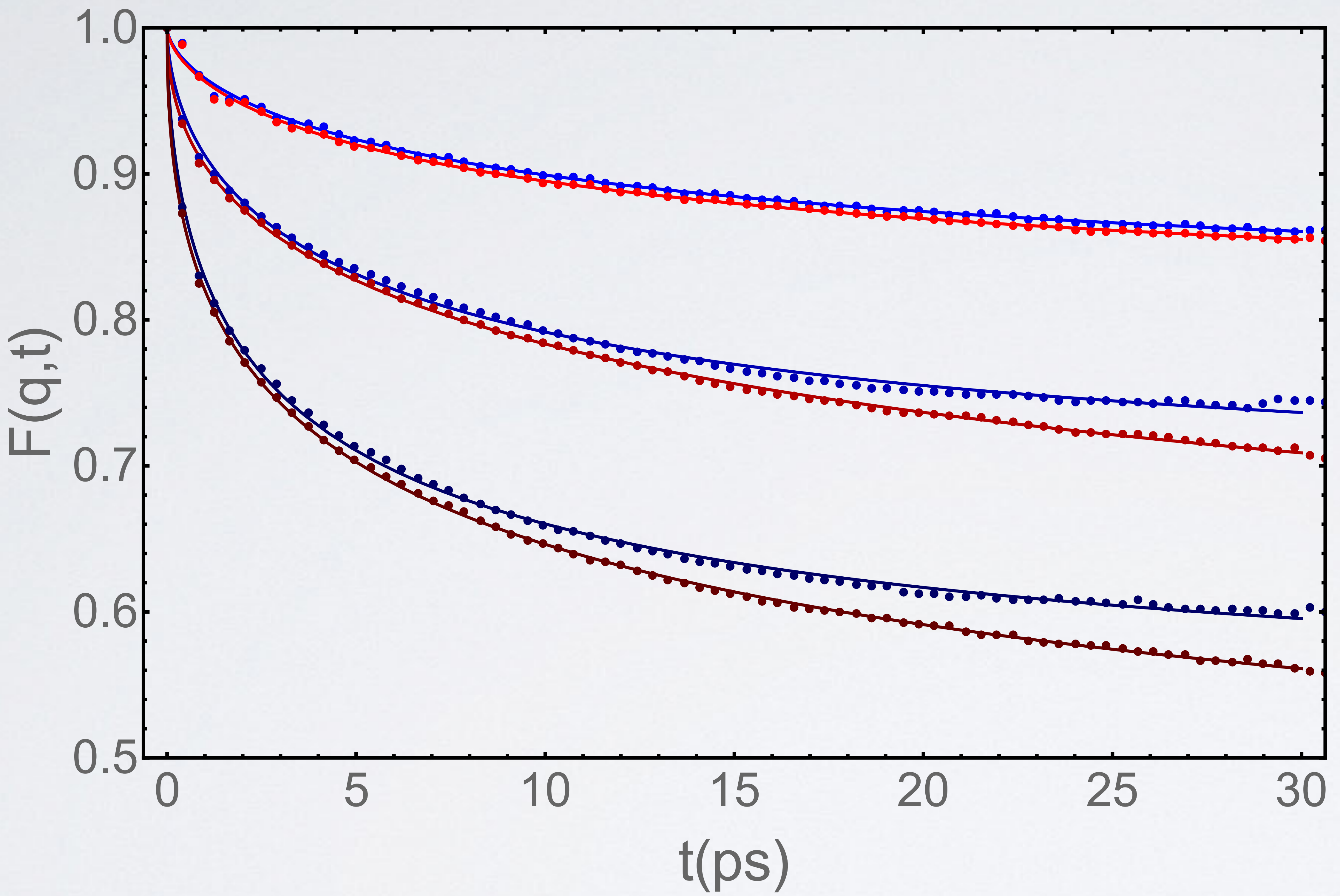
[1] M. Saouessi, J. Peters, and G. R. Kneller. J. Chem. Phys. 150(16):161104, Apr. 2019.

[2] M. Saouessi, J. Peters, and G. R. Kneller. J. Chem. Phys. 151(12):125103, Sept. 2019.

The enzyme hAChE

PDB entry 4EY5

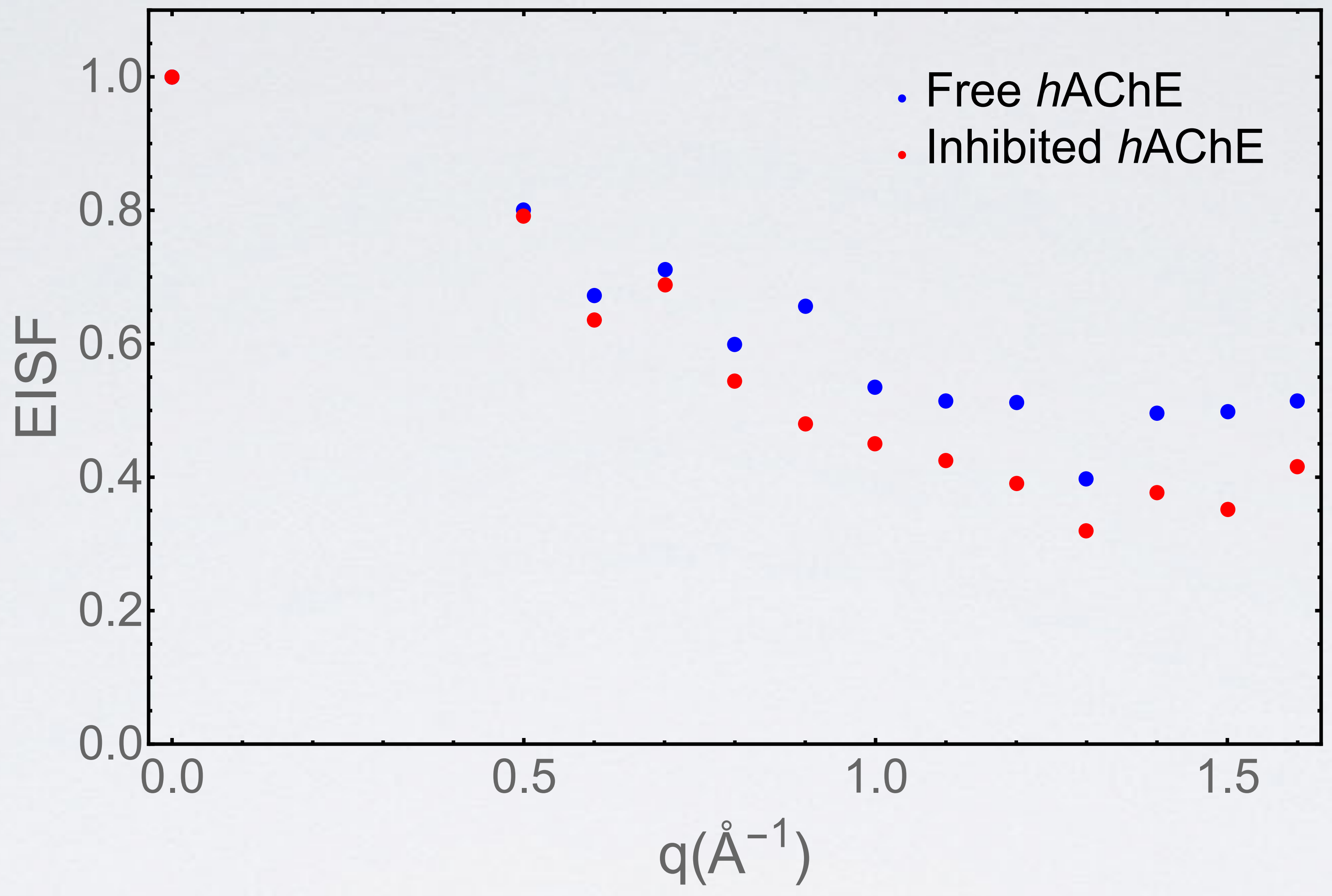
Fitted intermediate scattering functions of resolution-deconvolved spectra reveal differences between free and HupA-inhibited hAChE



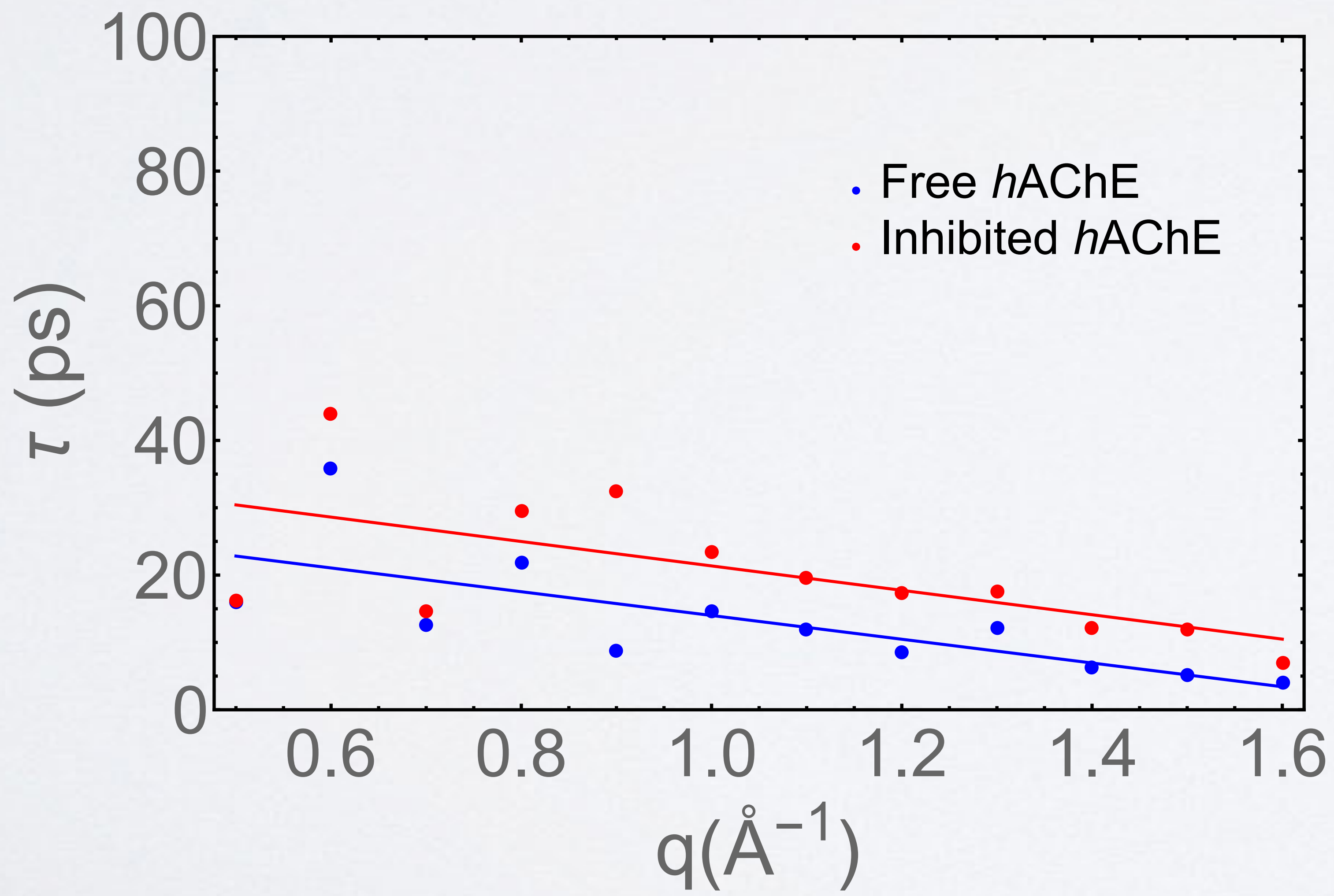
Blue : free hAChE

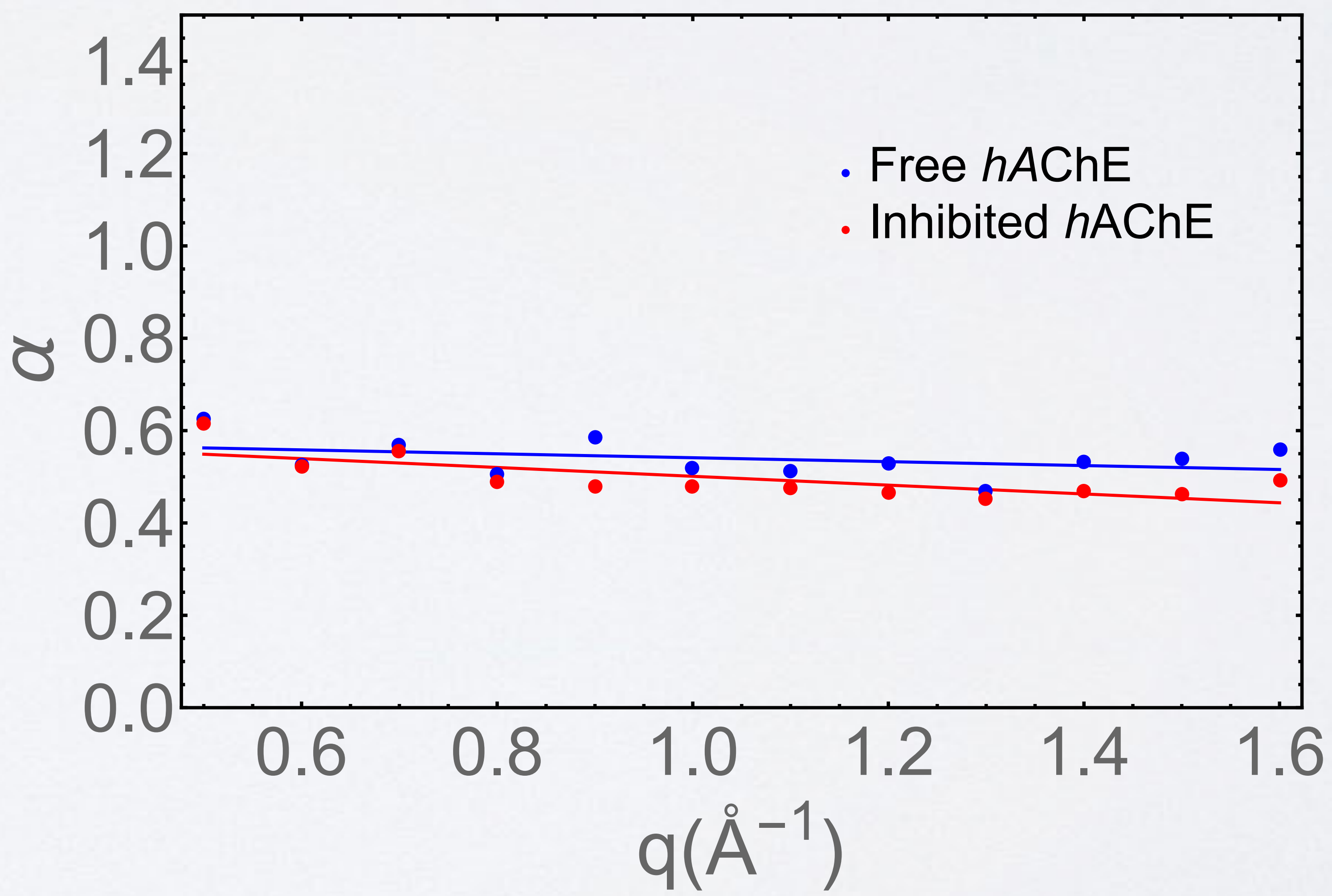
Red : HupA-inhibited hAChE

Fit parameters

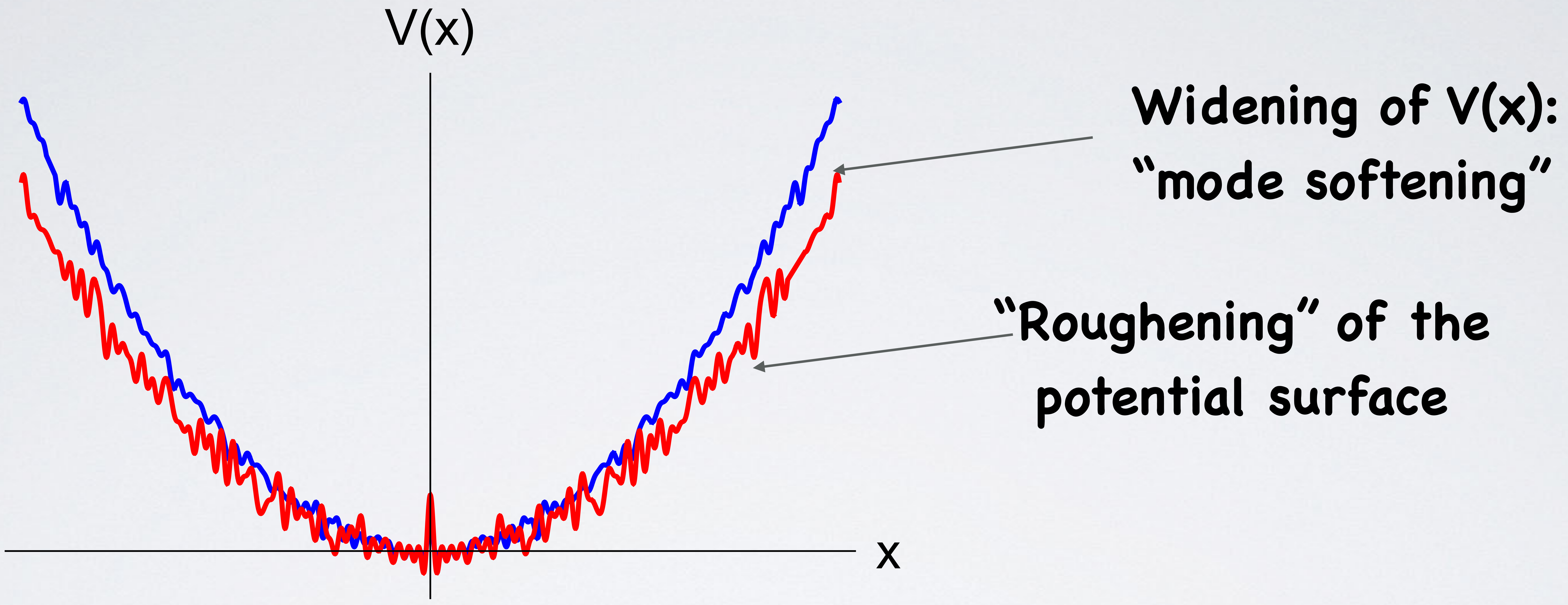


Non-vanishing EISF

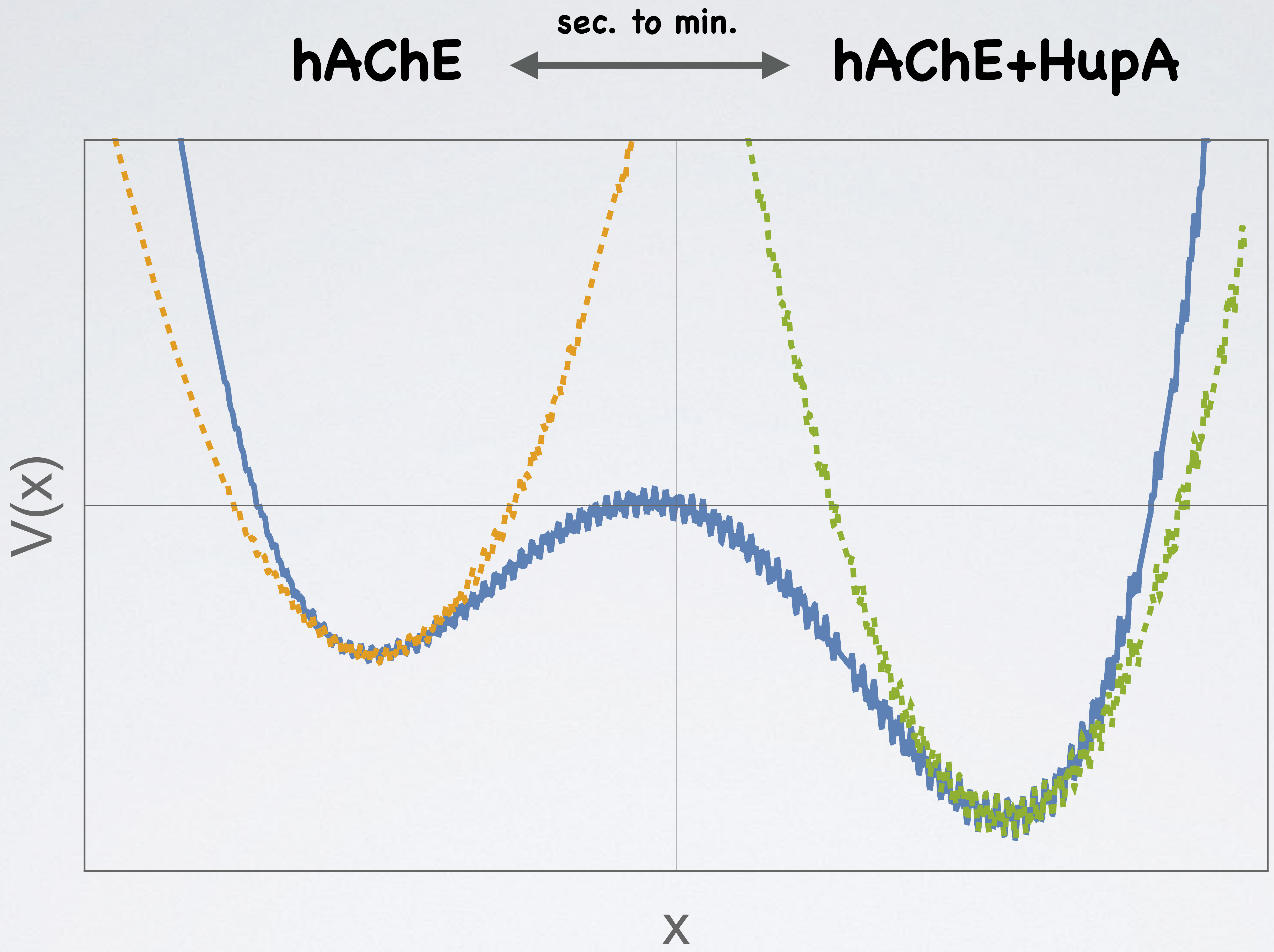




The effect of ligand binding



Possible explanation of the "mode softening"



The widened, softer potential is effectively a double-well potential. The neutrons see a superposition of the fast ps dynamics in the two wells and motional amplitudes determined by the envelope potential.

Work in progress : integrate coherent scattering

$$F(\mathbf{q},t) = \underbrace{\frac{1}{N}\sum_{j,k}\Gamma_{jk}\left\langle e^{-i\mathbf{q}\cdot\hat{\mathbf{R}}_j(0)}e^{i\mathbf{q}\cdot\hat{\mathbf{R}}_k(t)}\right\rangle}_{f_{jk}(\mathbf{q},t)}$$

$$f_{jk}(\mathbf{q},t) = \frac{1}{Z}\sum_{m,n} e^{-\frac{E_m}{k_B T}} e^{it(E_n - E_m)/\hbar} a^*_{m\to n}(\mathbf{q},j) a_{m\to n}(\mathbf{q},k)$$

Interference terms for j ≠ k

$$a_{m\to n}(\mathbf{q},j) = \int d^{3N}P\,\tilde{\phi}^*_n\left(\mathbf{P}+\hbar\mathbf{Q}_j\right)\tilde{\phi}_m(\mathbf{P}) = \int d^{3N}R\,\phi^*_n(\mathbf{R})\phi_m(\mathbf{R})e^{\mathrm{i}\mathbf{Q}_j\cdot\mathbf{R}}$$

Work in progress : integrate "ballistic" short time dynamics

Construct analytical and symmetrical relaxation functions

- Find a an even function in time, $f(t) = g(t^2)$, such that $f(t) \overset{t\to\infty}{\sim} t^\alpha$ and $f(0) = 0$. Defining $\theta(t) = f(t/\tau_0)(\tau_0/\tau)^\alpha$ it follows that

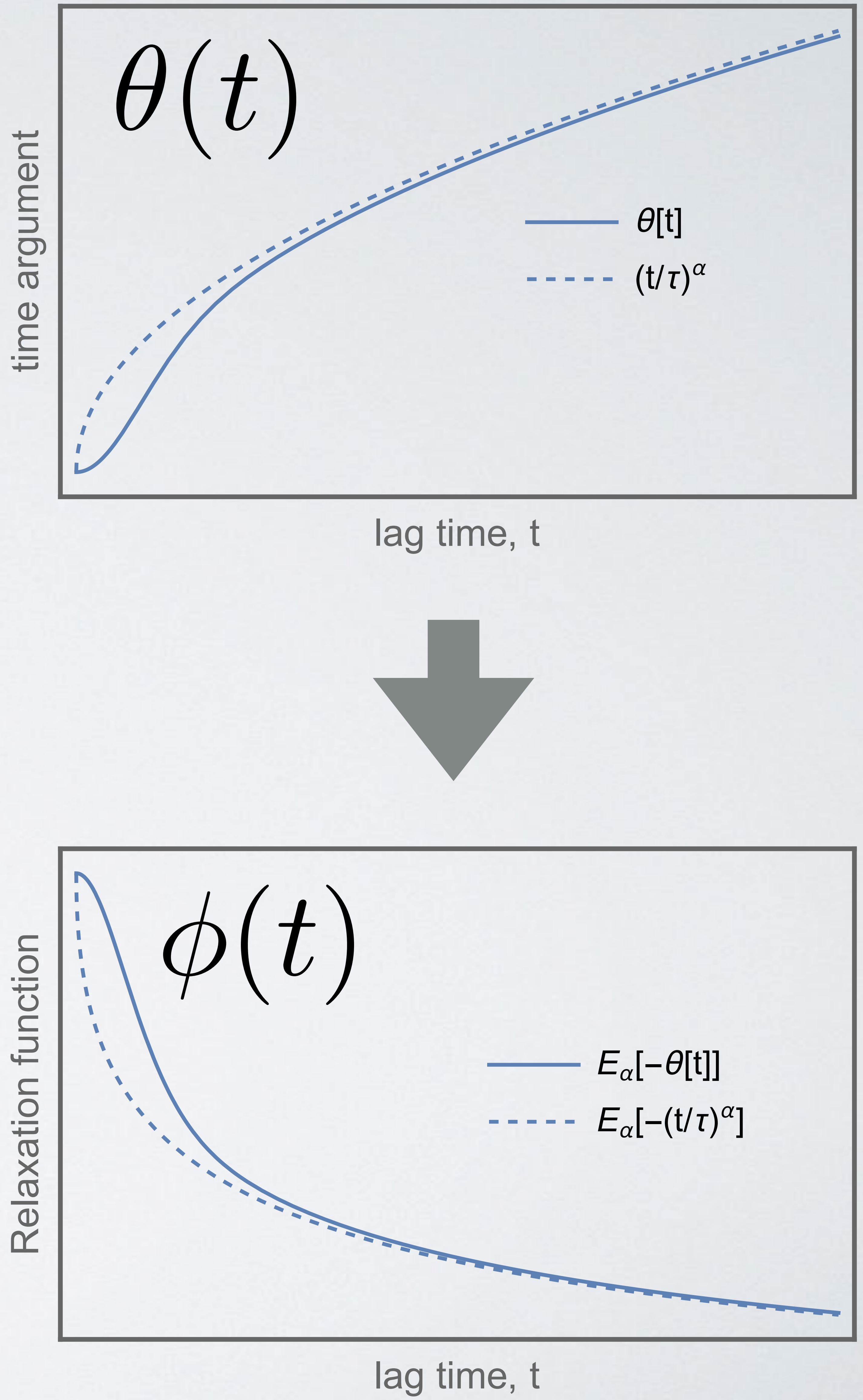
$$\phi(t) = E_\alpha(-\theta(t)) \overset{t \gg \tau_0}{\sim} E_\alpha(-(t/\tau)^\alpha)$$

is an analytical function of t^2.

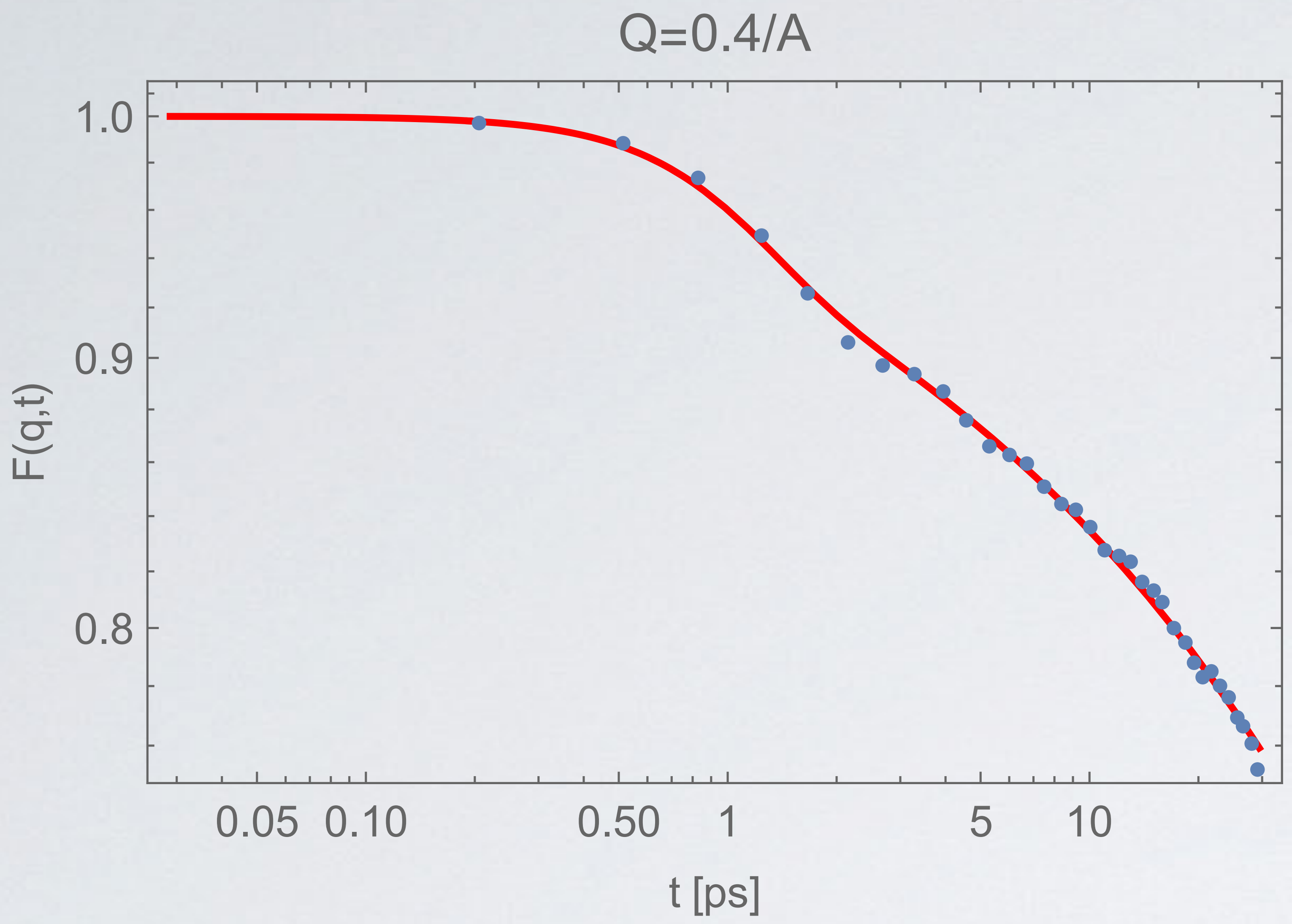
- Concrete choice $f(t) = \frac{\Gamma\left(\frac{\alpha}{2}+\beta\right)\left({}_1F_1\left(-\frac{\alpha}{2};\beta;-t^2\right)-1\right)}{\Gamma(\beta)}$

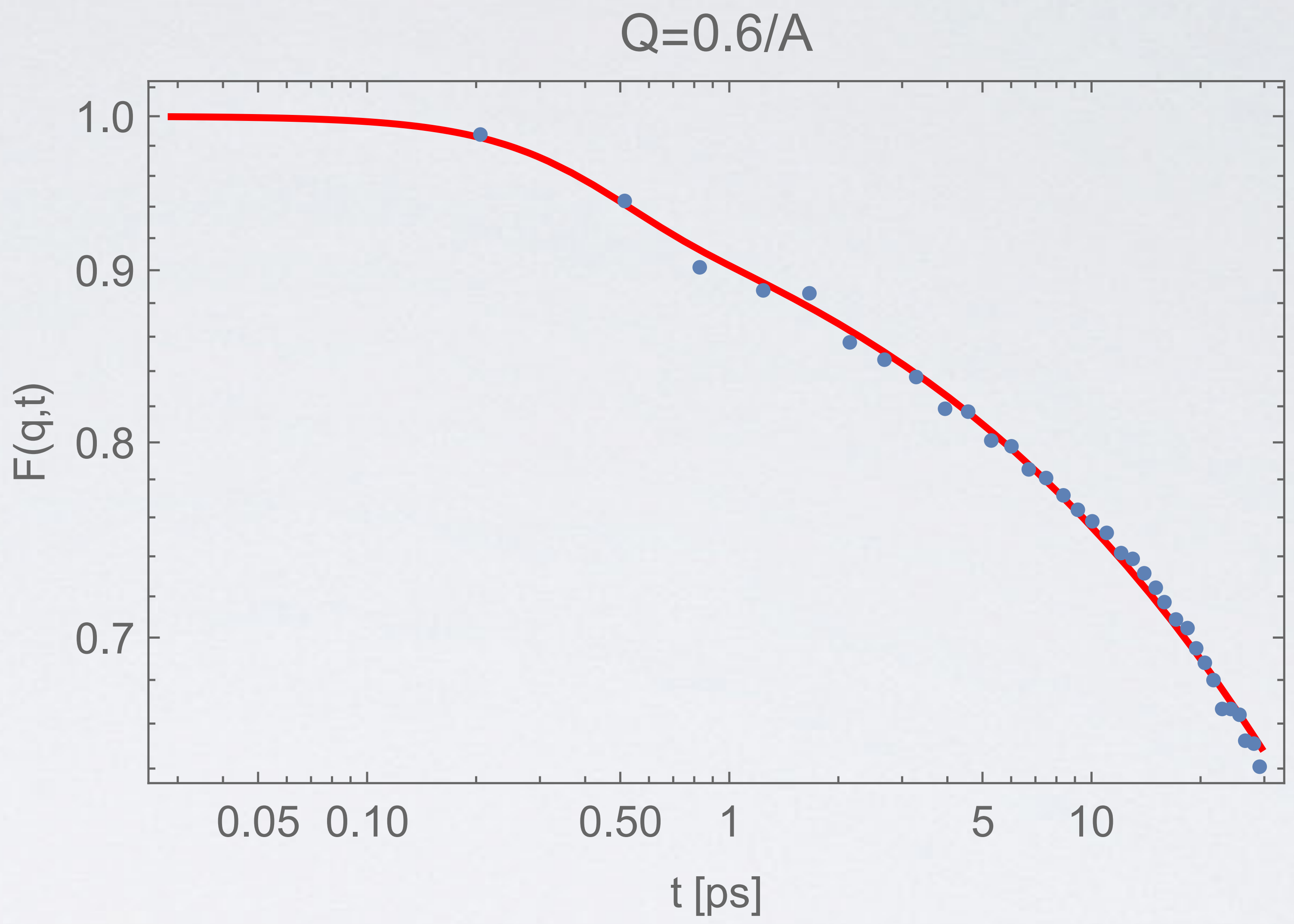
  such that $f(t) \overset{t\to\infty}{\sim} -\frac{\Gamma\left(\frac{\alpha}{2}+\beta\right)}{\Gamma(\beta)} + t^\alpha + \frac{e^{-t^2}(-1)^{-\frac{\alpha}{2}-\beta}\Gamma\left(\frac{\alpha}{2}+\beta\right)t^{2\left(-\frac{\alpha}{2}-\beta\right)}}{\Gamma\left(-\frac{\alpha}{2}\right)}$. Note that the shift $-\frac{\Gamma\left(\frac{\alpha}{2}+\beta\right)}{\Gamma(\beta)} \to 0$ for $\beta \to 0$.

- **Quantum correction**: $t^2 \longrightarrow t(t - i\beta\hbar)$.

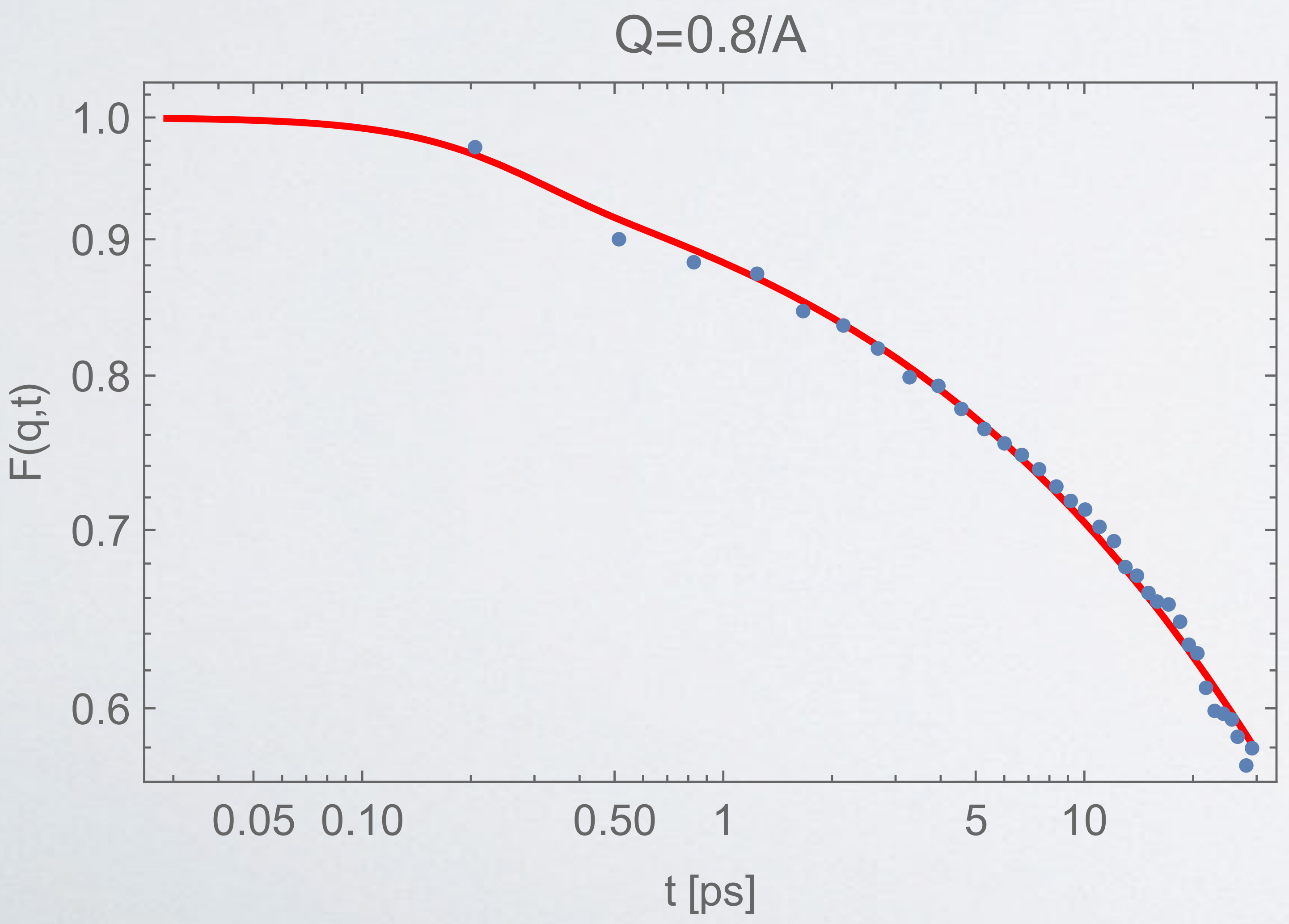


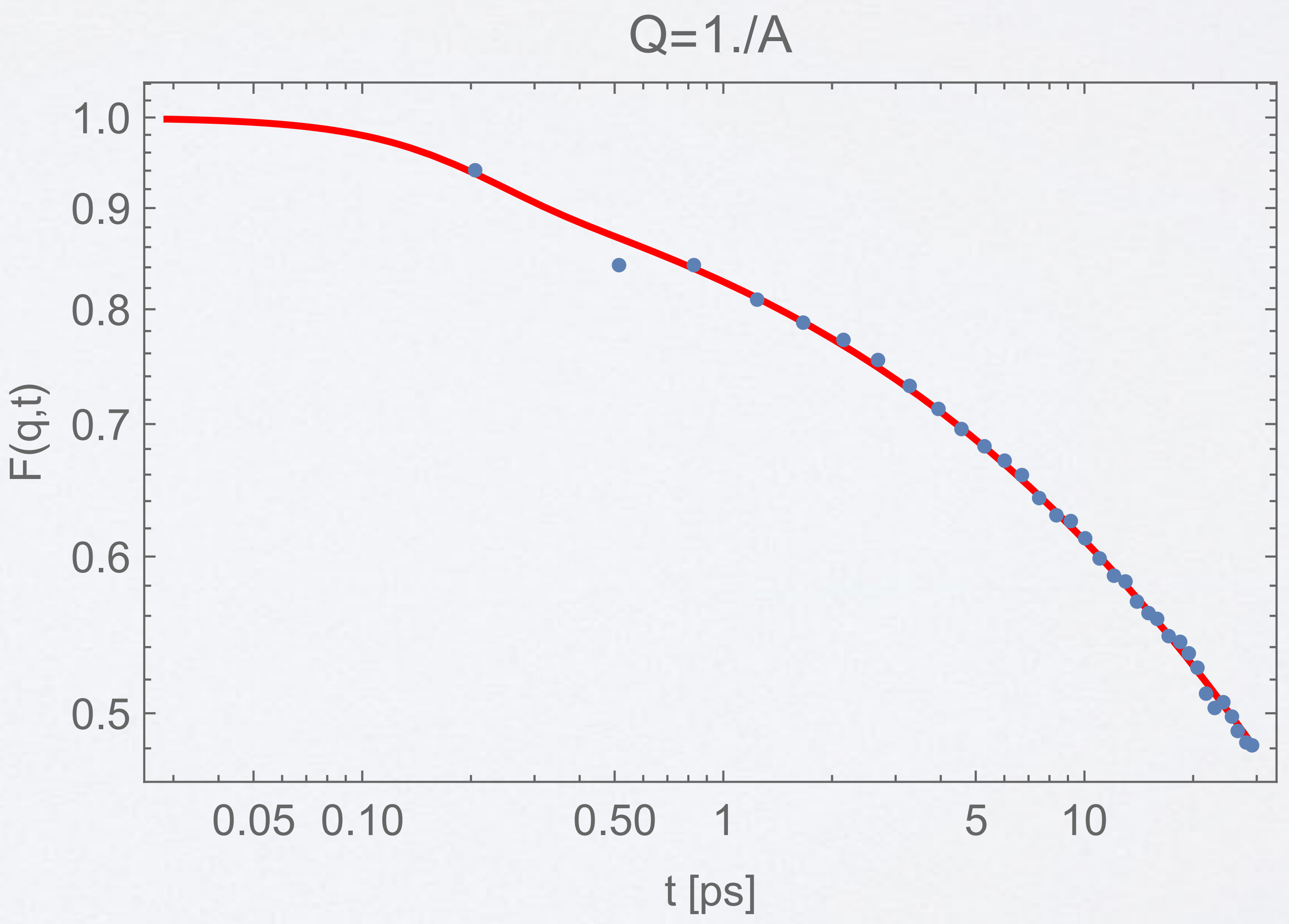
$$f(t^2) = \frac{\Gamma\left(\frac{\alpha}{2}+\beta\right)\left({}_1F_1\left(-\frac{\alpha}{2};\beta;-t^2\right)-1\right)}{\Gamma(\beta)}$$





QENS data from Myoglobin in D2O at 293 K from IN6





nature physics

LETTERS

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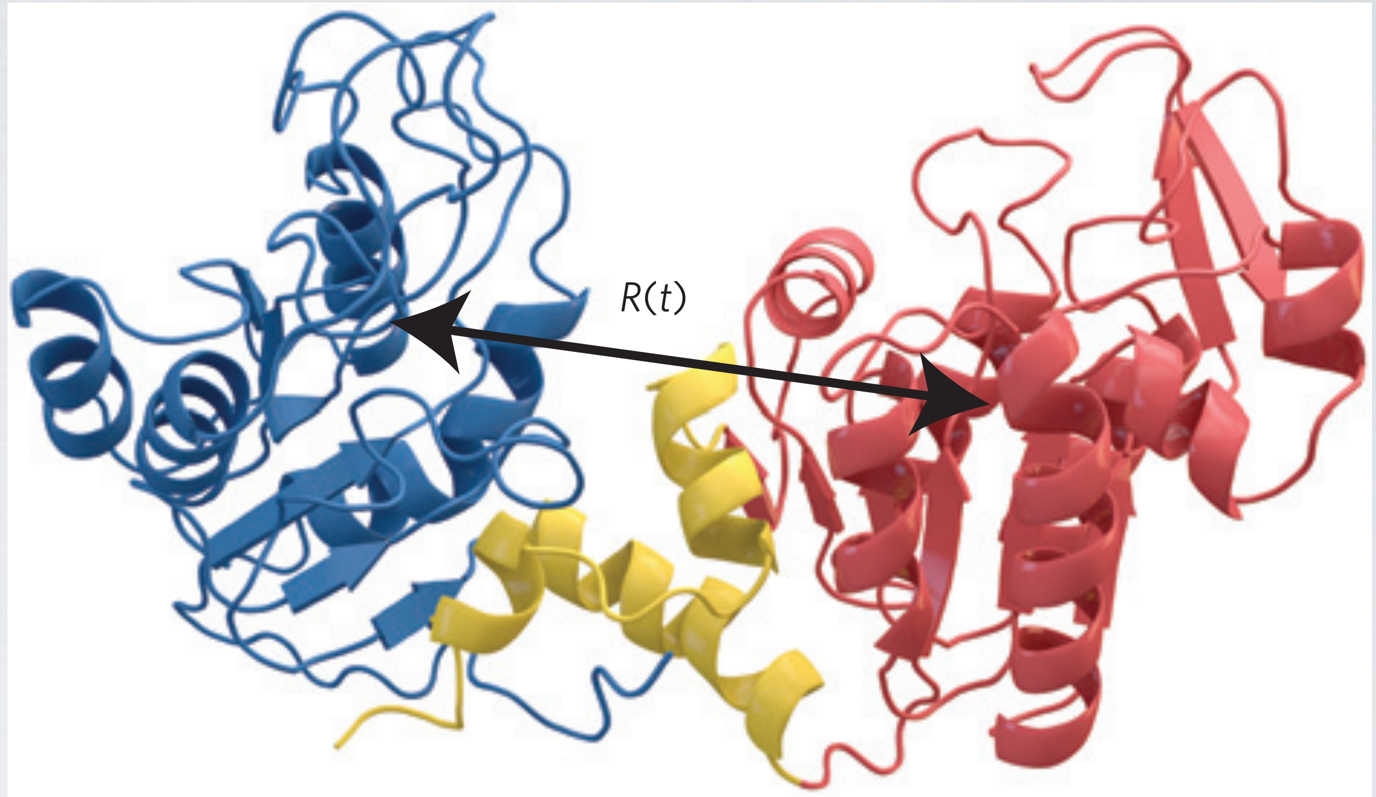
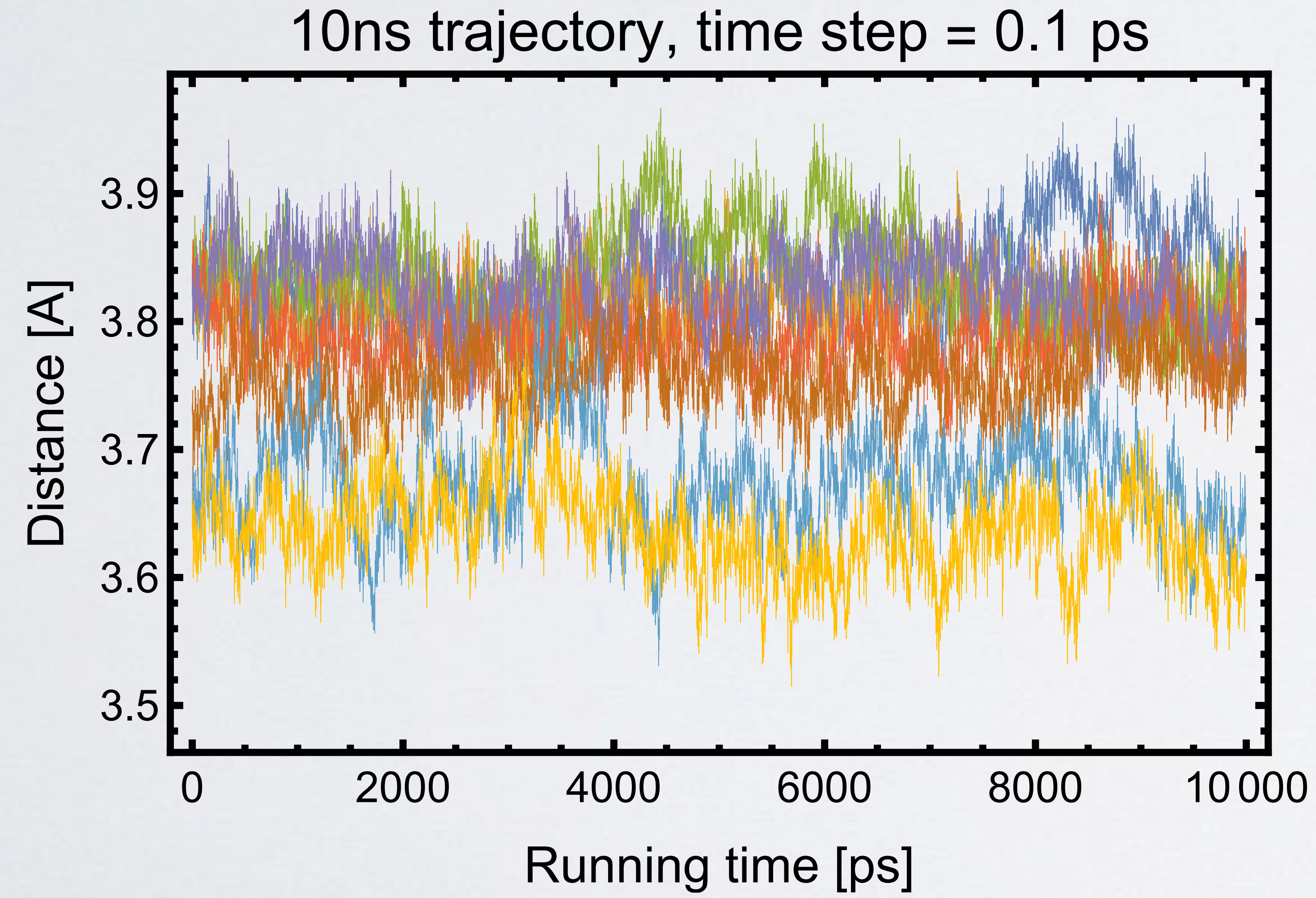
The dynamics of single protein molecules is non-equilibrium and self-similar over thirteen decades in time

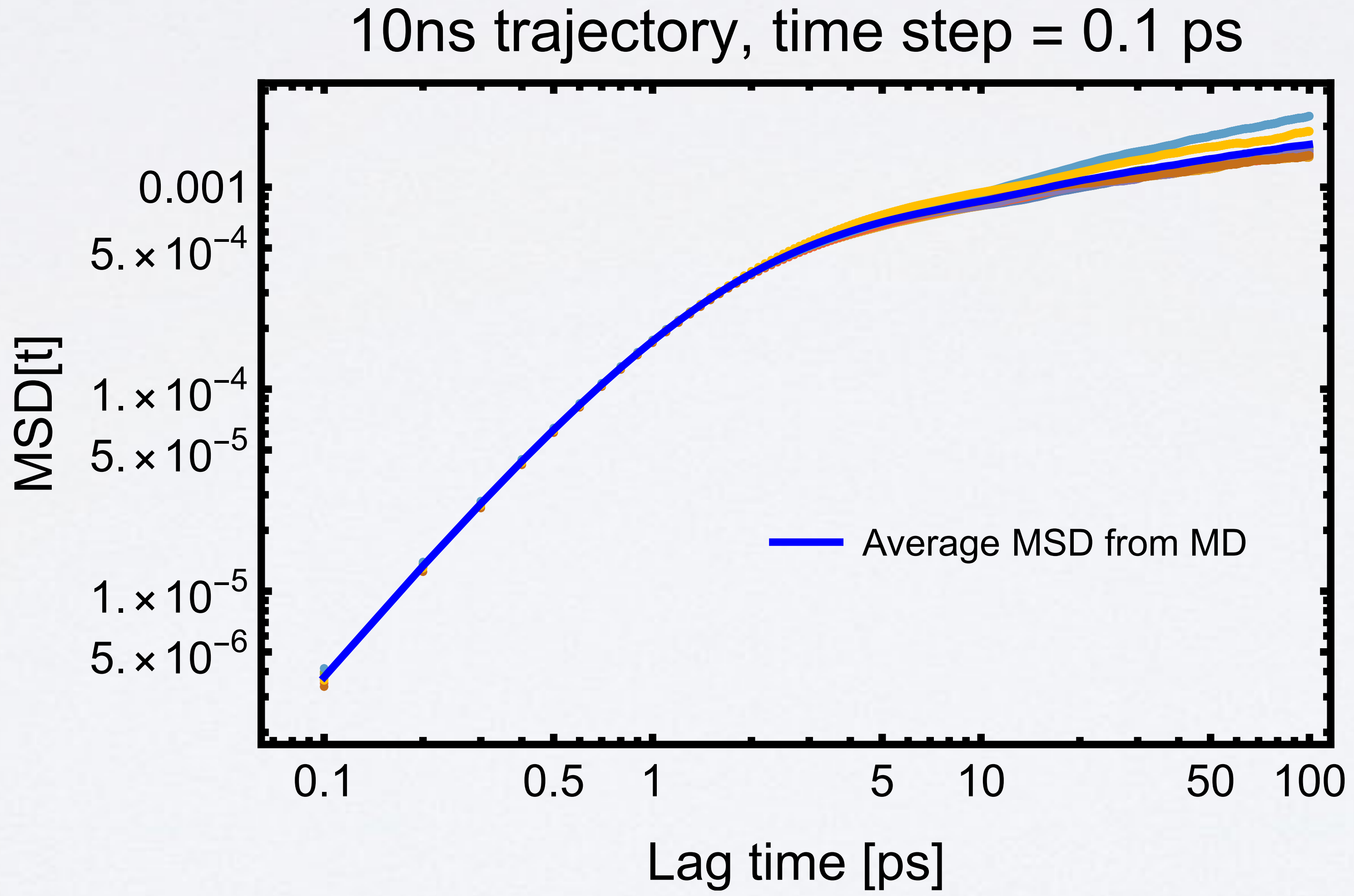
Xiaohu Hu[1,2], Liang Hong[3], Micholas Dean Smith[1], Thomas Neusius[4], Xiaolin Cheng[1] and Jeremy C. Smith[1,5]*

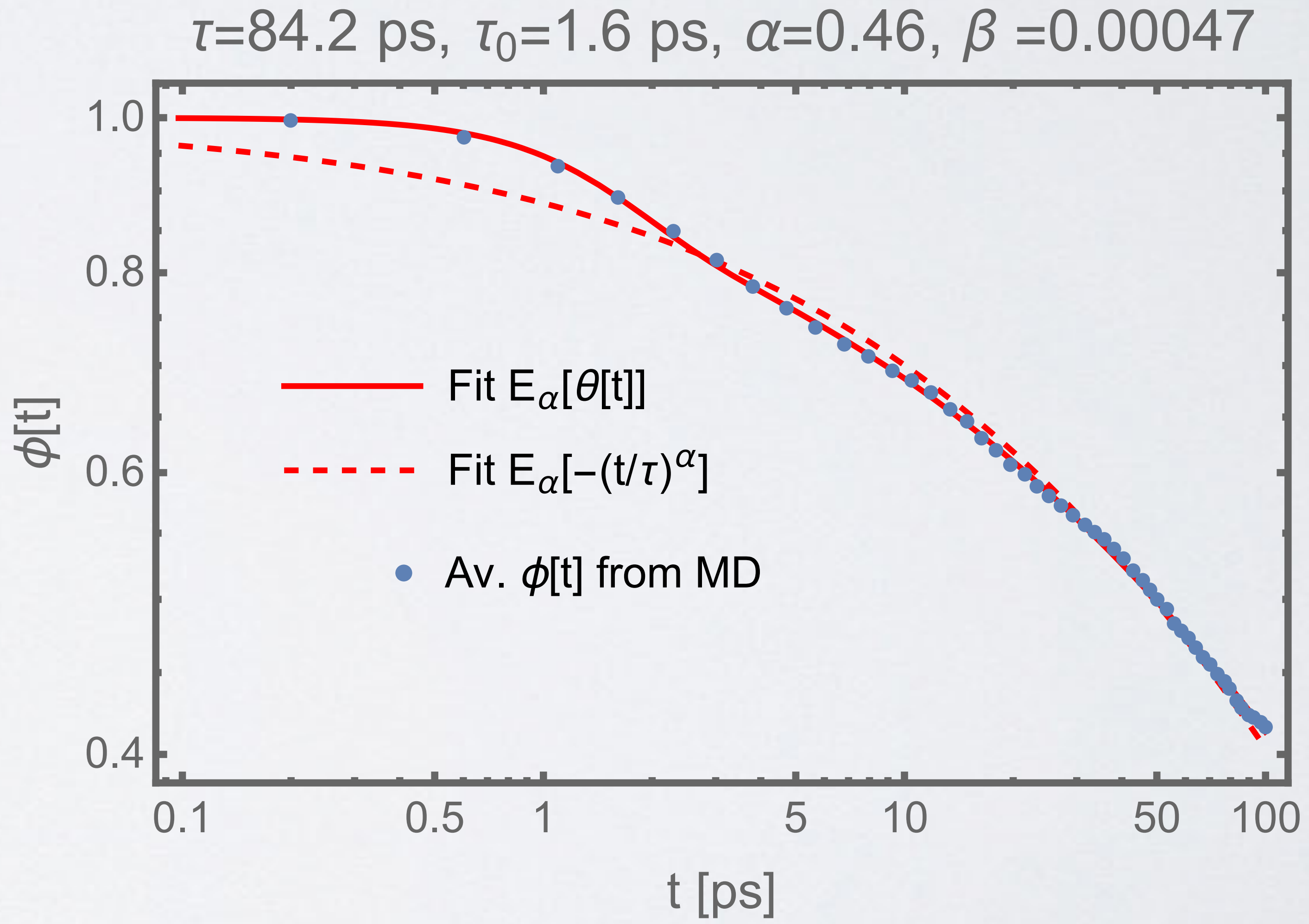


$$MSD(t) = \langle (\mathbf{R}(t) - \mathbf{R}(0))^2 \rangle$$

$$\phi(t) = \frac{\langle \mathbf{R}(t) \cdot \mathbf{R}(0) \rangle}{\langle \mathbf{R}(0) \cdot \mathbf{R}(0) \rangle}$$



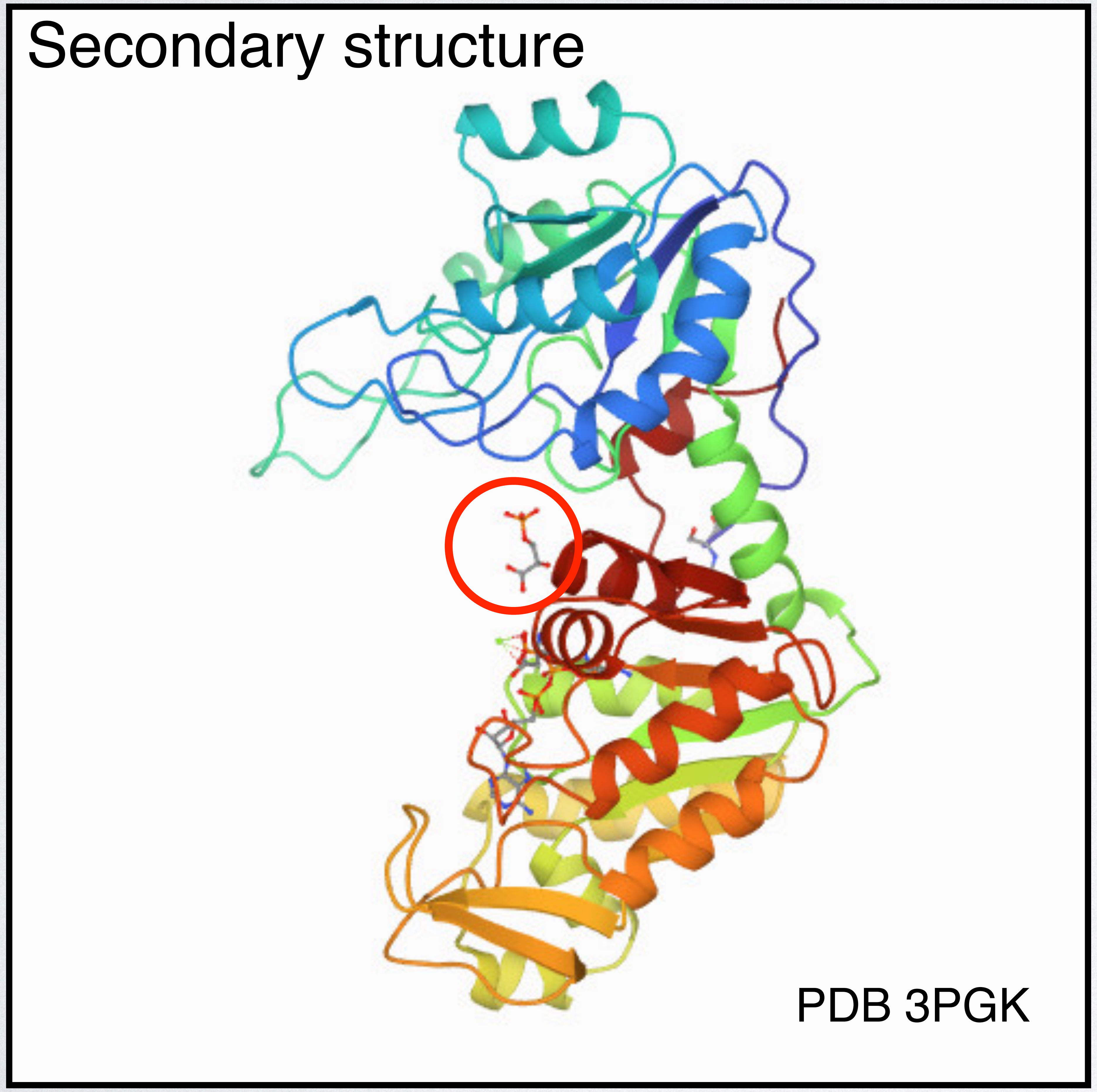


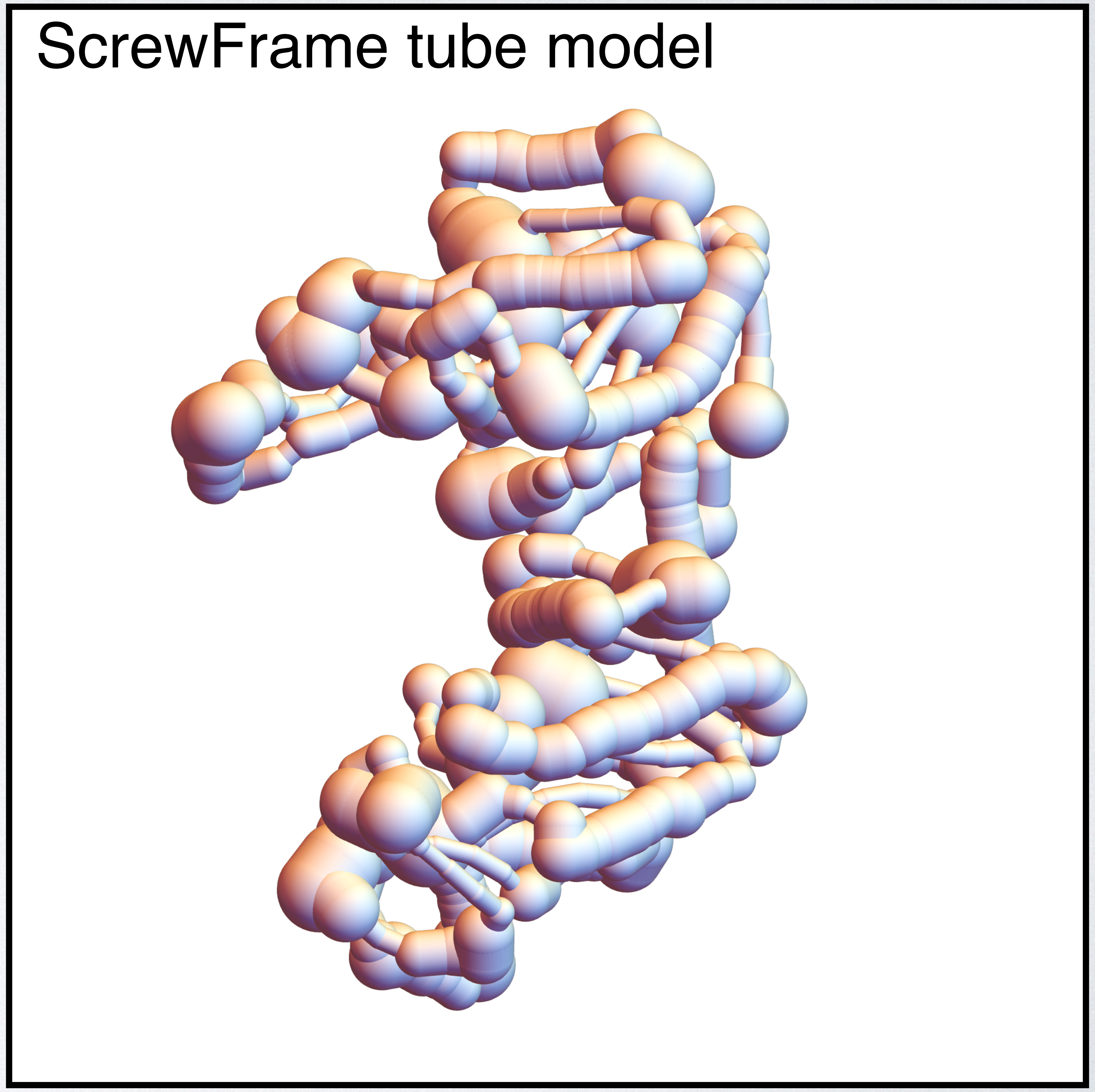


QENS from Phosphoglycerate Kinase (with A. Stadler JCNS Jülich)

1,3-bisphosphoglycerate + ADP ⇌ glycerate 3-phosphate + ATP

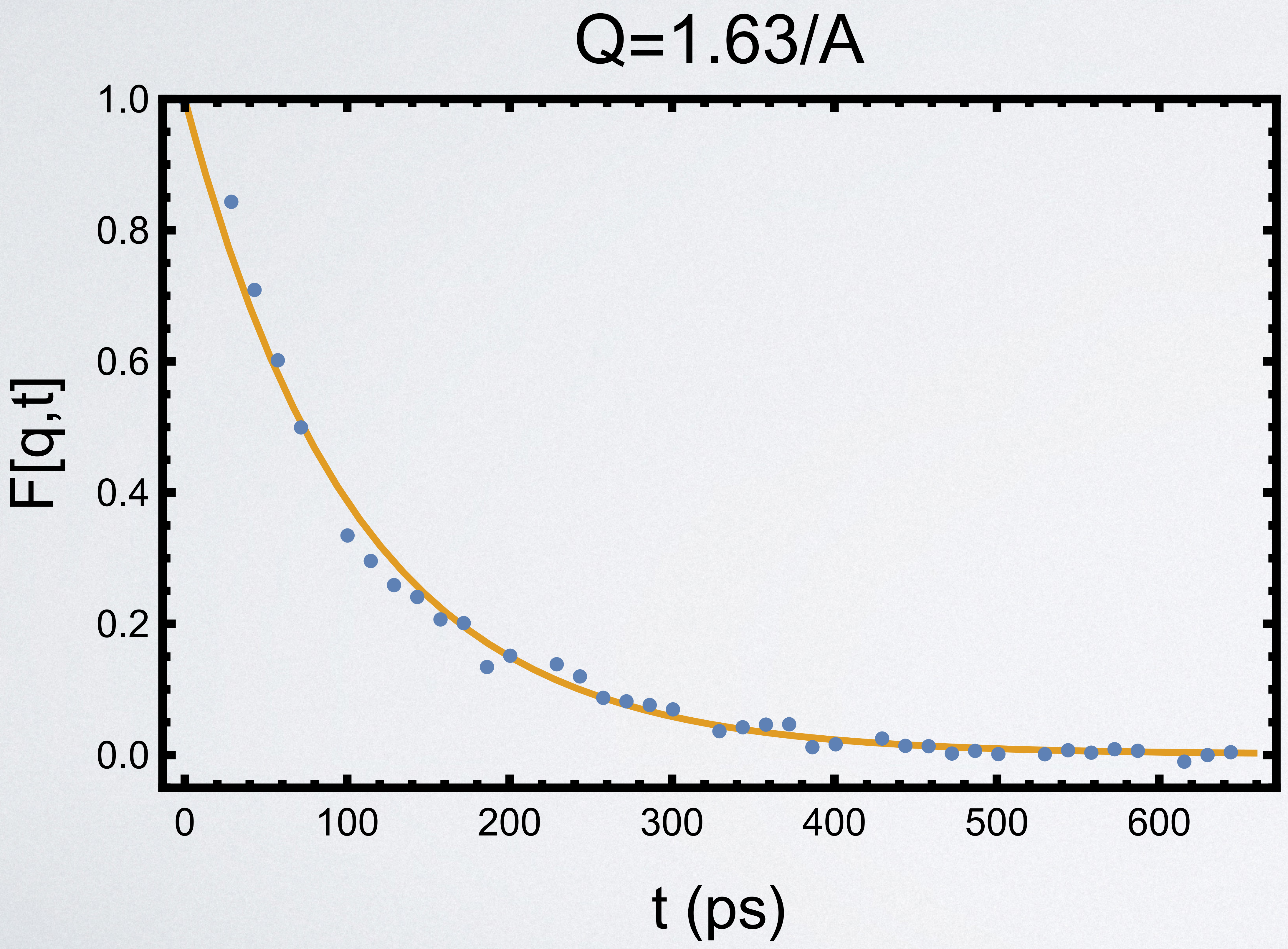
Influence of ATP on the internal dynamics seen by QENS



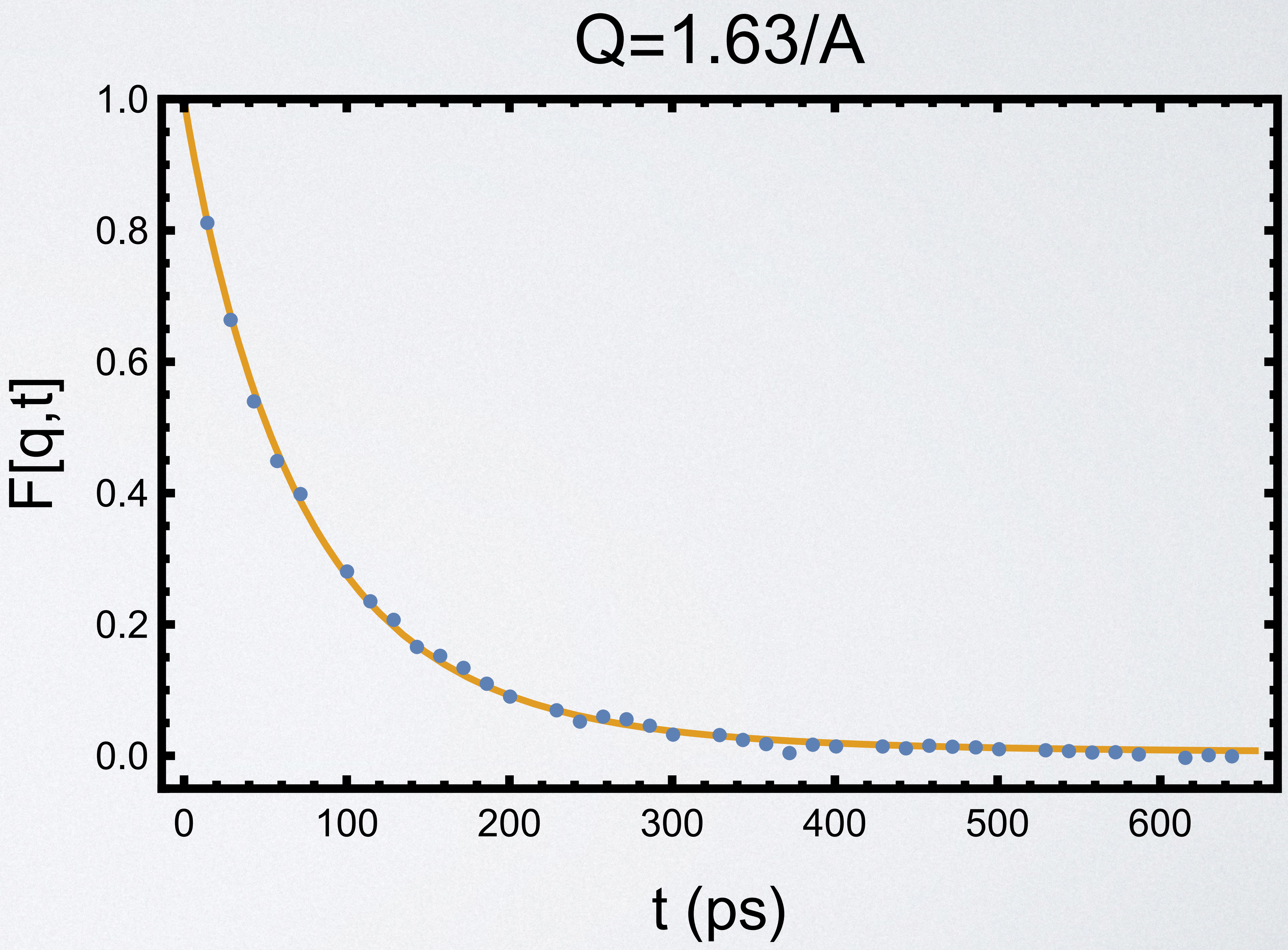


Data from A. Stadler obtained on IN16B, ILL

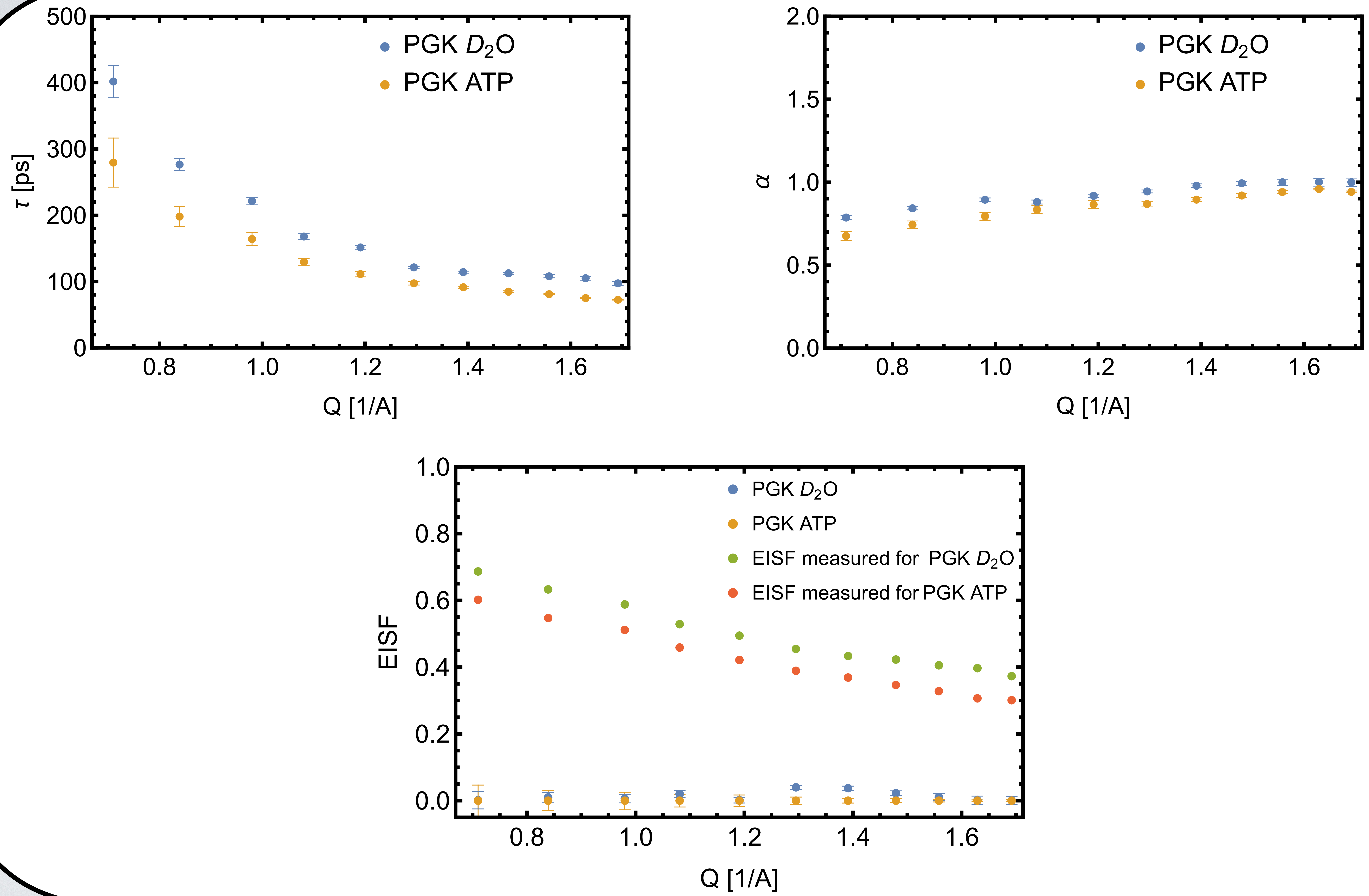
PGK in D2O buffer



PGK in D2O buffer + ATP



PGK 283 K



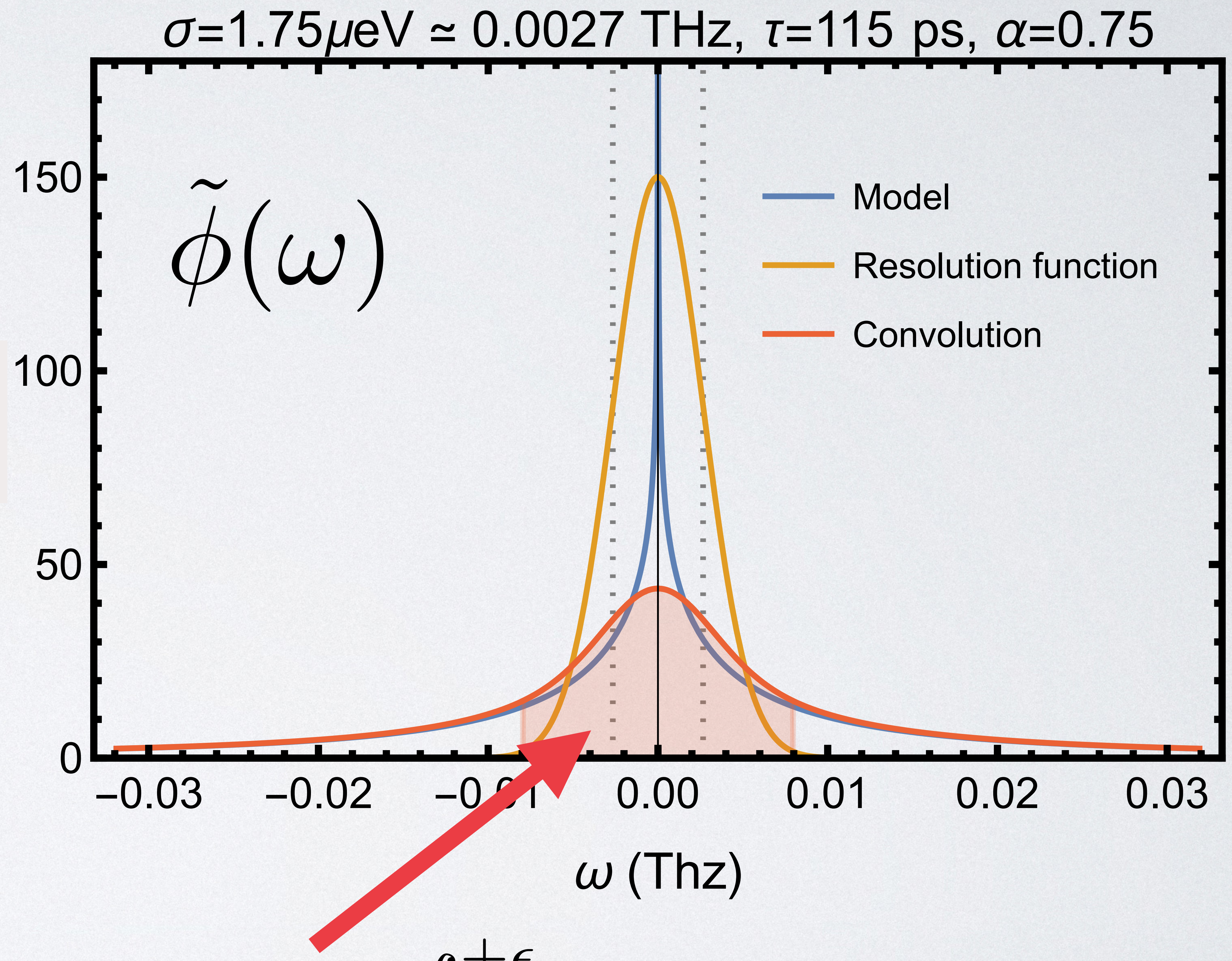
500
400
300
200
100
0
τ [ps]
0.8
1.0
1.2
1.4
1.6
Q [1/A]
PGK D_2O
PGK ATP
2.0
1.5
1.0
0.5
0.0
α
0.8
1.0
1.2
1.4
1.6
Q [1/A]
PGK D_2O
PGK ATP
1.0
0.8
0.6
0.4
0.2
0.0
EISF
0.8
1.0
1.2
1.4
1.6
Q [1/A]
PGK D_2O
PGK ATP
EISF measured for PGK D_2O
EISF measured for PGK ATP

Pseudoelastic scattering due to finite resolution

$$S_m(\omega) = (R * S)(\omega) \equiv \int_{-\infty}^{+\infty} d\omega' \, R(\omega - \omega') S(\omega')$$

$$F_m(\infty) \equiv \int_{-\epsilon}^{+\epsilon} d\omega \, S_m(\omega) \approx F(\infty) + (F_m(0) - F(\infty))\xi$$

$$\boxed{F(\infty) \approx \frac{F_m(\infty) - \xi F_m(0)}{1 - \xi}}$$

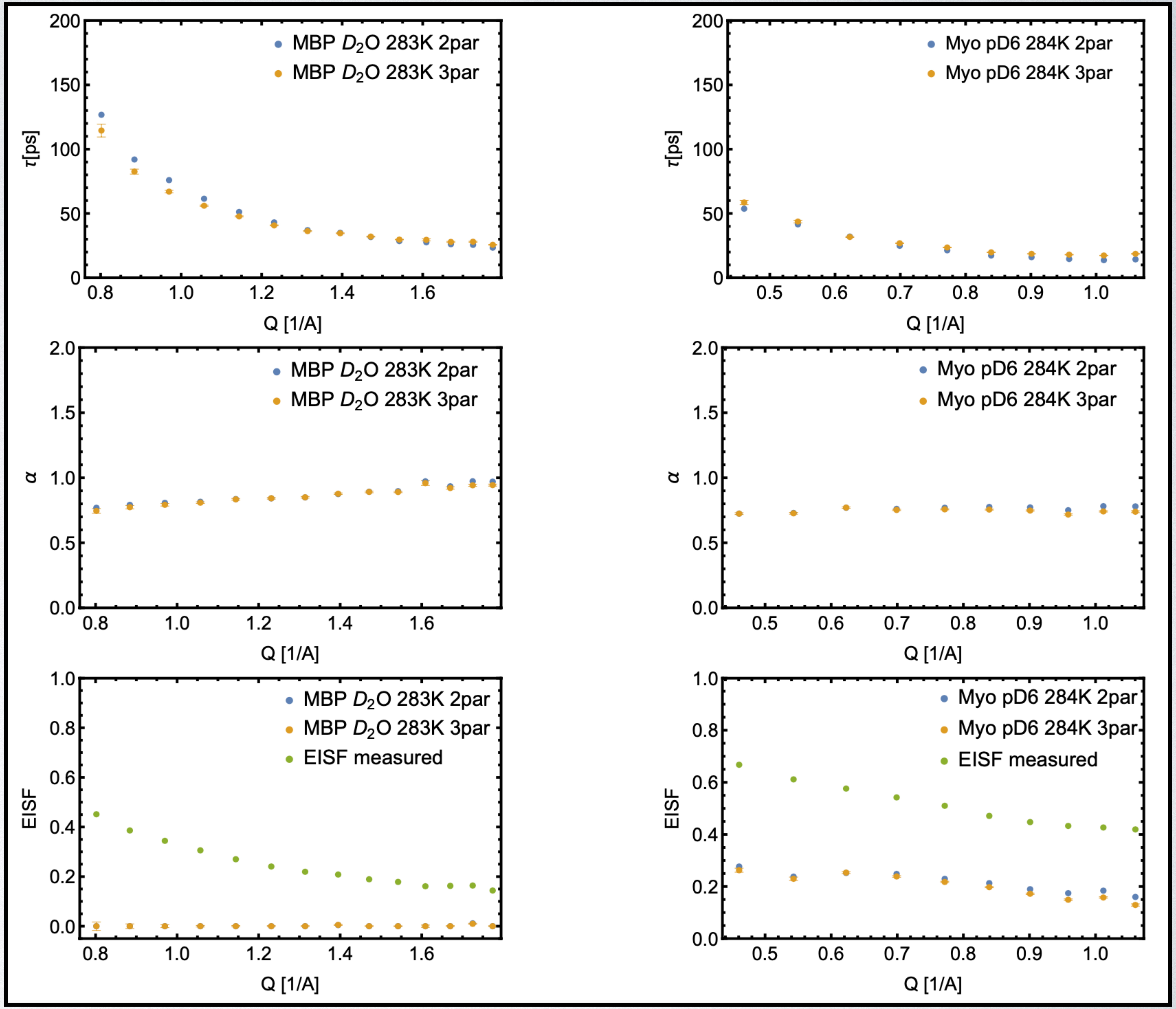


$$\xi = \int_{-\epsilon}^{+\epsilon} d\omega \, (\tilde{R} * \tilde{\phi})(\omega)$$

$$F^{(+)}(t) = F(\infty) + (F(0) - F(\infty))E_{\alpha}(-(|t|/\tau)^{\alpha})$$

MBP **Myoglobin**

Fit parameter



Conclusions

- The Franck-Condon formulation of neutron scattering links the concepts of energy landscapes of complex systems and scattering theory/spectroscopy.
- A quasi-classical interpretation beyond "$\hbar \to 0$" (impactless scattering) is possible and corresponds to diffusion in "rough potentials".
- Coherent inelastic scattering has no classical interpretation and probes correlated wave function-based conformational changes.
- The FC formulation enables a combined description of elastic and quasi-elastic scattering through asymptotic analysis of $F(q,t)$.
- MD simulations are most useful to probe and understand the transition to the asymptotic regime of self-similar protein dynamics in the ps regime.
- "Minimalistic" few parameter for QENS spectra can capture the signature of slight changes in the conformational dynamics of proteins due to external stress.

Merci à

- Hans Frauenfelder, LANL
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- Judith Peters, UGA/ILL Grenoble

Integrate the neutron kick into a trajectory-based description of neutron scattering

G. R. Kneller. Inelastic Neutron Scattering from Classical Systems. Mol Phys, 83(1):63–87, 1994.

Propagator form of the intermediate scattering function

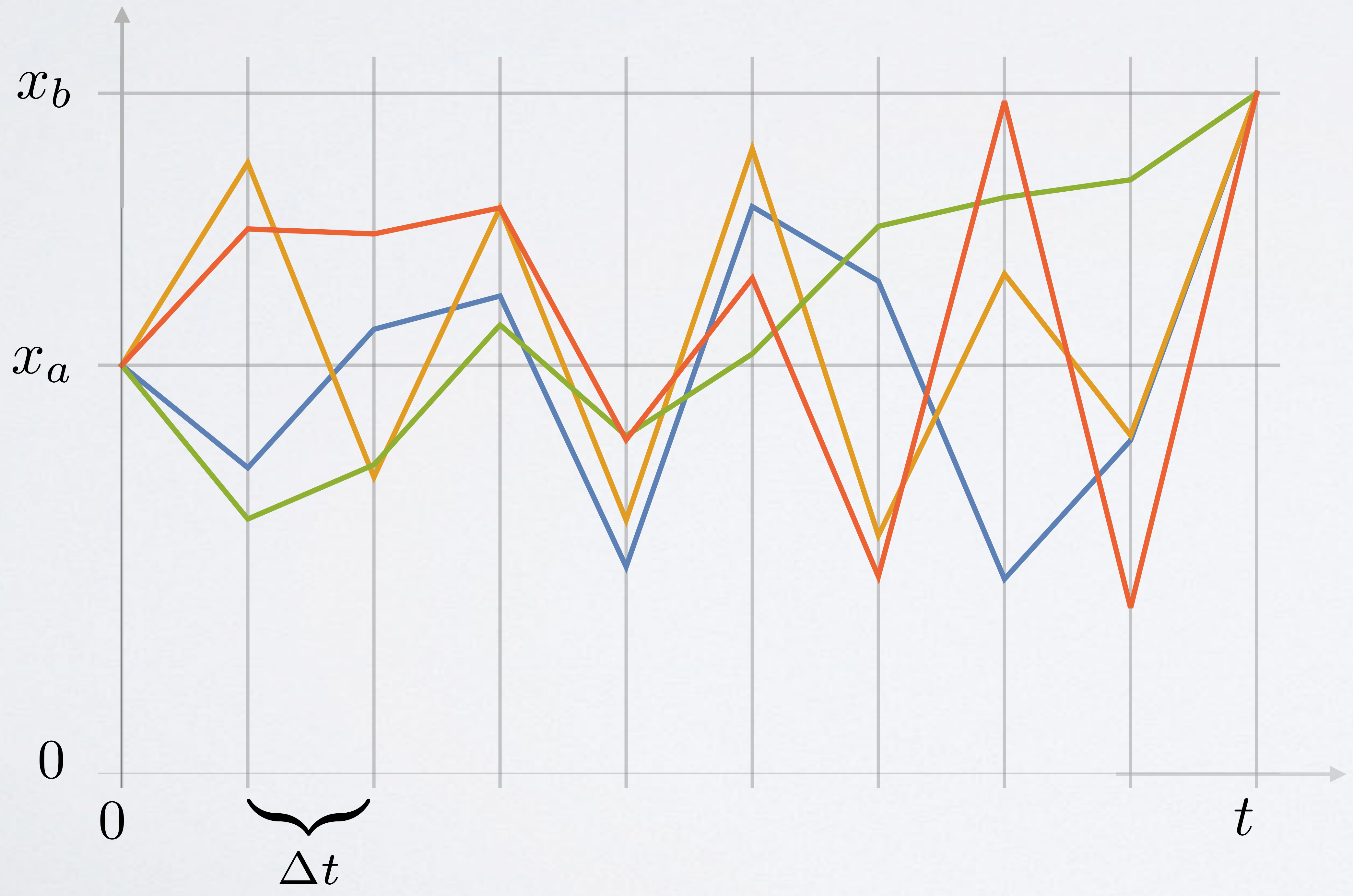
$$F_s(\mathbf{q}, t) = \frac{1}{Z} \int\int\int dx dx' dx'' \underbrace{\langle x | e^{-\beta \hat{H}} | x' \rangle}_{K(x,x',-i\beta\hbar)} \underbrace{\langle x' | e^{it\hat{H}'(\mathbf{q})/\hbar} | x'' \rangle}_{K_q(x',x'',-t)} \underbrace{\langle x'' | e^{-it\hat{H}/\hbar} | x \rangle}_{K(x'',x,t)}$$

➔ Retrieve trajectories through a **path integral representation** of the propagators

Real time propagator

Setting $\Delta t = t/n$

$$K(x_b, x_a, t) = \langle x_b | e^{-it\hat{H}/\hbar} | x_a \rangle = \langle x_b | \left(e^{-i\frac{\Delta t}{\hbar}\hat{H}} \right)^n | x_a \rangle$$
$$= \int \dots \int dx_1 \dots dx_n \langle x_b | \left(e^{-i\frac{\Delta t}{\hbar}\hat{H}} \right) | x_1 \rangle \langle x_1 | \left(e^{-i\frac{\Delta t}{\hbar}\hat{H}} \right) | x_2 \rangle \dots$$
$$\dots \langle x_n | \left(e^{-i\frac{\Delta t}{\hbar}\hat{H}} \right) | x_b \rangle \overset{n \to \infty}{\longrightarrow} \int \mathcal{D}[x(\tau)] e^{iA[x(\tau)]/\hbar}$$



Path action integral

$$A[x(\tau)] = \int_0^t d\tau \underbrace{\left(M\dot{x}(\tau)^2/2 - V(x(\tau) \right)}_{L(\dot{x}(\tau), x(\tau))}$$

"Kicked" real time propagator

Phase factor form

$$K_q(x_b, x_a, t) = K(x_b, x_a, t)e^{iq(x_b - x_a)}$$

Path integral form

$$K(x_b, x_a, t) = \int \mathcal{D}[x(\tau)]e^{iA_q[x(\tau)]/\hbar}$$

"Kicked" path action integral

Coupling to the neutron

$$A_q[x(\tau)] = \int_0^t d\tau \underbrace{\left(M\dot{x}(\tau)^2/2 - V(x(\tau)) + \hbar q\dot{x}(\tau)\right)}_{L_q(\dot{x}(\tau),x(\tau))}$$

Imaginary time propagator

Setting $t_{th} = \beta\hbar$ and $\Delta t_{th} = t_{th}/n$

$$K(x_b, x_a, -i\beta\hbar) = \langle x_b | e^{-\beta\hat{H}} | x_a \rangle = \langle x_b | \left(e^{-\frac{\Delta t_{th}}{\hbar}\hat{H}} \right)^n | x_a \rangle$$

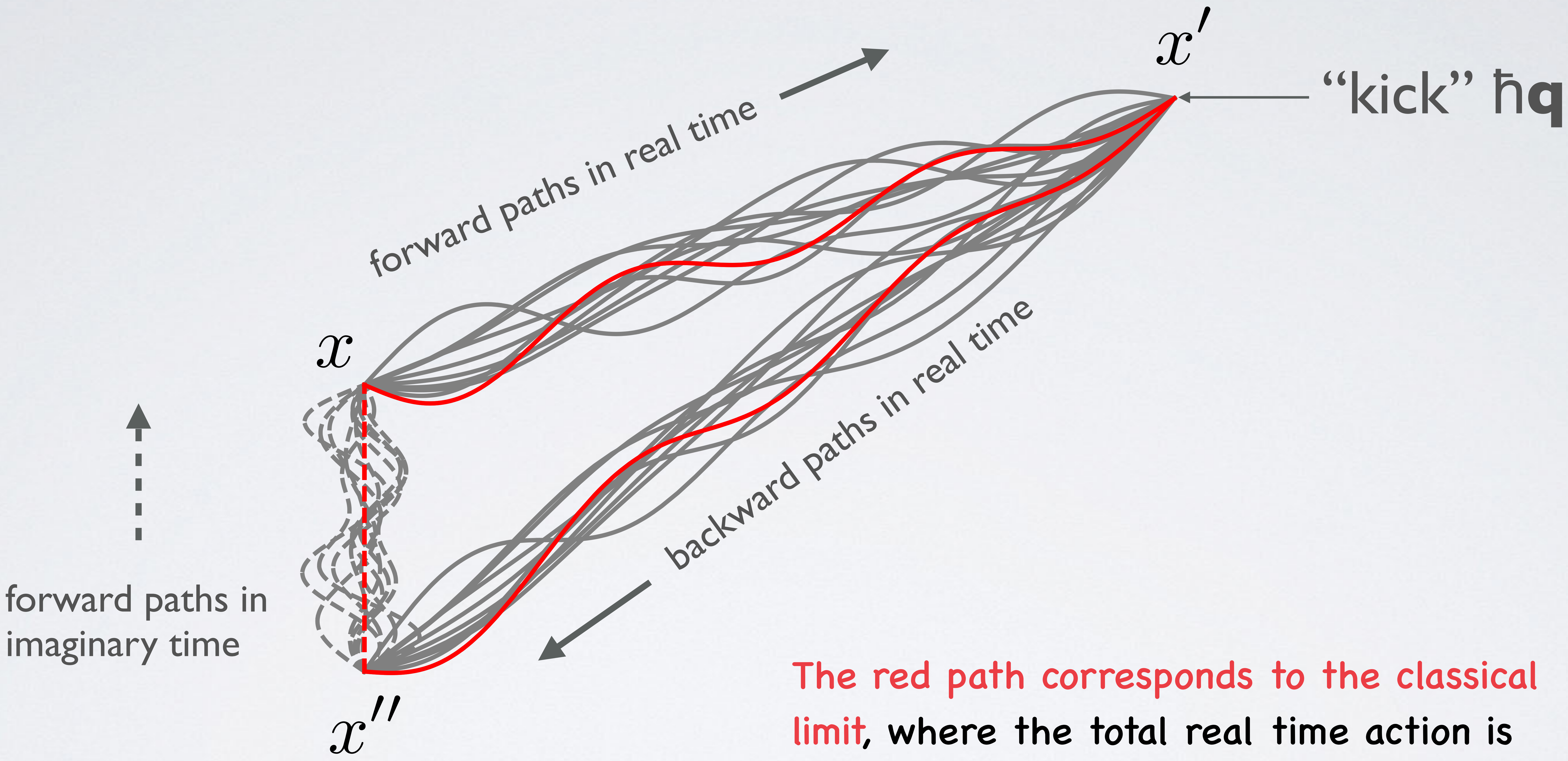
$$= \int \ldots \int dx_1 \ldots dx_n \langle x_b | \left(e^{-\frac{\Delta t_{th}}{\hbar}\hat{H}} \right) | x_1 \rangle \langle x_1 | \left(e^{-\frac{\Delta t_{th}}{\hbar}\hat{H}} \right) | x_2 \rangle \ldots$$

$$\ldots \langle x_n | \left(e^{-\frac{\Delta t_{th}}{\hbar}\hat{H}} \right) | x_b \rangle \overset{n\to\infty}{\to} \int \mathcal{D}[x(\tau)] e^{-\beta \overline{H}[x(\tau)]/\hbar}$$

Average path energy

$$\overline{H}[x(\tau)] = \frac{1}{\beta\hbar} \int_0^t d\tau \underbrace{\left(M\dot{x}(\tau)^2/2 + V(x(\tau)) \right)}_{H(\dot{x}(\tau), x(\tau))}$$

$$F_s(\mathbf{q},t) = \frac{1}{Z}\int\int\int dx dx' dx'' \, K(x,x',-i\beta\hbar)K_q(x',x'',-t)K(x'',x,t)$$



The red path corresponds to the classical limit, where the total real time action is minimized and the high temperature/short time limit is used for the propagation in imaginary time. The "neutron kick" is taken into account.

Classical limit of the intermediate scattering function

Expressing the density matrix through the classical limit of the Wigner function and retaining only the classical path ($A \gg \hbar$) yields

$$\tilde{F}_{cl}(\mathbf{q},t) = \frac{1}{Z_{cl}} \int\int d^3p d^3x \, e^{-\beta H(\mathbf{p},\mathbf{x})} e^{-\beta \Delta V(\mathbf{p},\mathbf{x};\hbar\mathbf{q},t)} \times e^{i\Delta\Phi(\mathbf{p},\mathbf{x};\hbar\mathbf{q},t)/\hbar} e^{i\mathbf{q}\cdot(\mathbf{x}'(\mathbf{p},\mathbf{x},t)-\mathbf{x})}$$

$$\Delta V(\mathbf{p},\mathbf{x};\hbar\mathbf{q},t) = V((\mathbf{x}+\mathbf{x}'')/2) - V(\mathbf{x})$$

$$\Delta\Phi(\mathbf{p},\mathbf{x};\hbar\mathbf{q},t) = A(\mathbf{x},\mathbf{x}',t) - A(\mathbf{x}',\mathbf{x}'',t) + (\mathbf{p}_0 + \hbar\mathbf{q})\cdot(\mathbf{x}-\mathbf{x}'')$$

where $\mathbf{x}' \equiv \mathbf{x}'(\mathbf{p},\mathbf{x},t)$ and $\mathbf{x}'' \equiv \mathbf{x}''(\mathbf{p},\mathbf{x};\hbar\mathbf{q},t)$.

The standard classical limit reads

$$\lim_{\hbar\to 0} \tilde{F}_{cl}(\mathbf{q},t) = \frac{1}{Z_{cl}} \int\int d^3p d^3x \, e^{-\beta H(\mathbf{p},\mathbf{x})} e^{i\mathbf{q}\cdot(\mathbf{x}'(\mathbf{p},\mathbf{x},t)-\mathbf{x})}$$

Outlook - Energy landscape entropy

Based on the probabilistic interpretation of the dynamic structure factor

$$S_s(\mathbf{q},\omega) = \hbar \int dE\, W_{\mathrm{eq}}(E) W(E + \hbar\omega | E; \mathbf{q}).$$

one can define a Shannon entropy **for the** neutron scattering explored energy landscape of proteins

$$H(\mathbf{q}) = -\int_{-\infty}^{+\infty} d\omega\, S_s(\mathbf{q},\omega) \log\Big(S_s(\mathbf{q},\omega)\Big)$$