

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

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Contributed by Hans Frauenfelder, April 5, 2017 (sent for review August 22, 2016; reviewed by Robert H. Austin, Roger Pynn, and Giovanni Zocchi)

PNAS Vol. 114, 5130 (2017) Submitted in April 5, 2017 and published already in May 16 2017?? The authors have never done any research in bio-neutron scattering.

Reviewers: R. Austin: a pioneer collaborator of HF on optical spectroscopy, R. Pynn: a structural neutron scattering scientist (grazing incidence scattering from diffraction grating, 2010), G. Zocchi: biophysicist, viscoelastic properties of enzymes, plasmon resonance of DNA.

Comment by Wolfgang Doster, Dec. 8, 2017, expanded: Sept. 2018

This paper questions again the conventional theory of neutron scattering on proteins, termed as the “spatial motion” model (SMM) using Van Hove correlation functions, assuming that scattering reflects mainly density fluctuations. The alternative is to invoke scattering by diffusion within an energy landscape (ELM) via a push mechanism of energy-momentum exchange between sample and neutron. This paper deals specially with the Q-dependence of the elastic intensity versus the temperature.

- 1) There are some basic misconceptions about the scattering process:

“in the simplest case SMM assumes a Gaussian for “the elastic intensity”:

$$S(Q,0,T) = A \exp(-Q^2 \langle r^2 \rangle / 3) \quad \text{equ. 1}$$

which is in fact the dynamic structure factor. Now it is concluded that, since the n-p scattering is isotropic, the scattering from an isotropic sample should be Q-independent. Thus something is wrong with SMM. No, equ. 1 results from an isotropic sample since the Q-vector has been replaced by a scalar and the factor 1/3 reflects isotropic averaging. The Gaussian function results from a harmonic inelastic process, vibrations, which leads to a decrease of the elastic intensity with Q, while the inelastic intensity increases for compensation.

- 2) The elastic line and the inelastic line are thus not assigned to different processes as postulated. They reflect one and the same spatially constrained process (vibration, rotational transition, local jumps but not unconstrained diffusion). This particular property of SMM is quite essential and is not obtained with ELM.
- 3) In the case of overdamped motions, the linewidth of the broad band, centered at $\omega = 0$, indeed reflects the relaxation time of the process and does not lead to “unphysical fast life times” as postulated in the paper. For underdamped vibrational motions, the “broad band” is centered at $\omega > 0$, and its width reflects the vibrational density of states, it is indeed inhomogeneous but not as postulated in fig. 1b.

- 4) Their most important result is the temperature-dependent value of the elastic intensity extrapolated to $Q = 0$ (arrows). Fig. 5a) shows the original data of Nakagawa et al. which were normalized to the lowest temperature. Frauenfelder has denormalized the fig. 5 a) data somehow as shown I fig. 5 b). The supposedly real data displays a $Q \rightarrow 0$ intensity decreasing with the temperature (arrows).

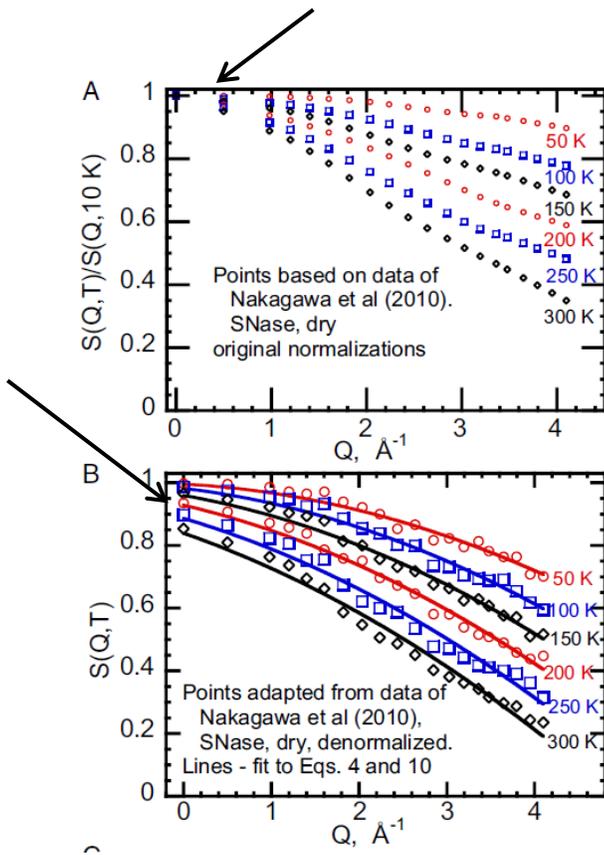


fig. 5 a), b)

Thus the dynamical structure factor at $Q = 0$, depends on the temperature: $S(Q = 0, T)$. This effect is interpreted as prove of the Frauenfelder energy landscape model (ELM).

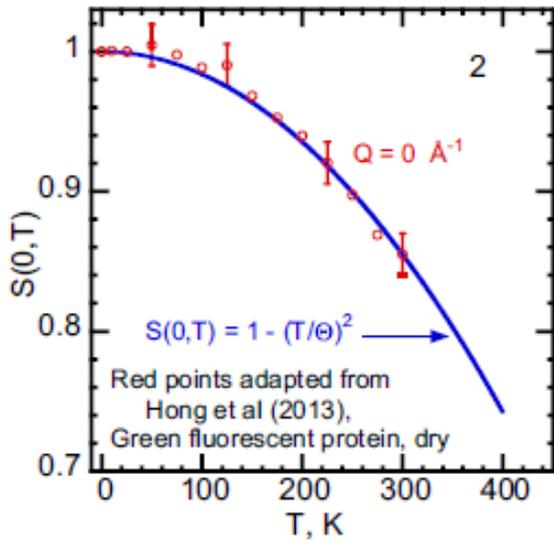


Fig. 2. The elastic fraction $S(Q, T)$ at $Q \rightarrow 0$ for dry green fluorescent protein. Red points are adapted from measured data in figure S1 of

Fig. 2 shows $S(Q=0, T)$ of another Frauenfelder denormalized data set of GFP by Hong et al.: The zero Q -elastic intensity decreases with T . This result is certainly not compatible with conventional single scattering theory. It violates the theorem of particle conservation. Before we go into details of scattering theory, we check the data set on which fig. 2 is based on:

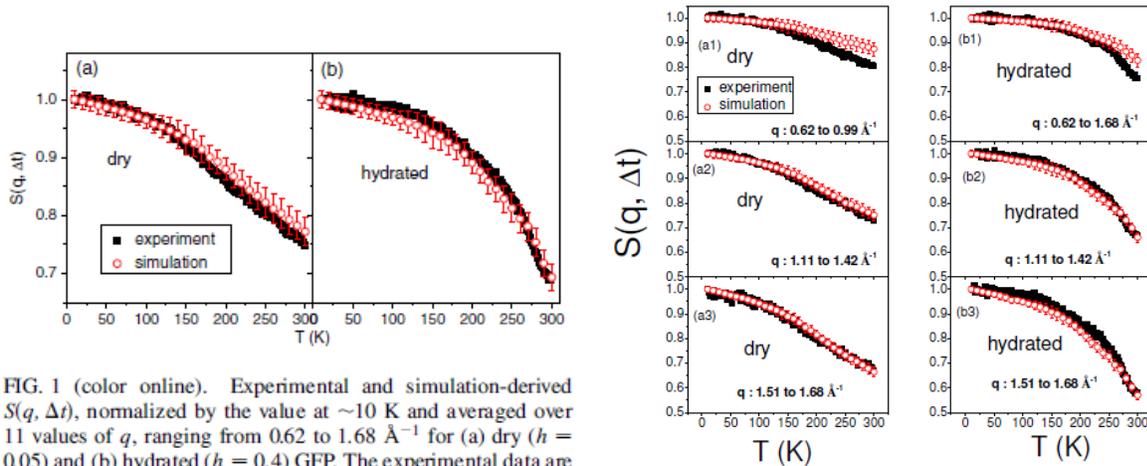


FIG. 1 (color online). Experimental and simulation-derived $S(q, \Delta t)$, normalized by the value at ~ 10 K and averaged over 11 values of q , ranging from 0.62 to 1.68 \AA^{-1} for (a) dry ($h = 0.05$) and (b) hydrated ($h = 0.4$) GFP. The experimental data are

Dry and hydrated GFP by Hong et al (PRL 2013, 110, 28104), experiments and simulation. In this paper all data are Q -averaged (fig.1), which means, the data quality is low and one should be very skeptical about the conclusions. HF refers to the supplement, where three data sets, covering a finite Q -range are shown: 0.62 - 0.99 , 1.11 to 1.42 and 1.5 to 1.68 \AA^{-1} (fig. S1).

Besides the Q -uncertainty, one has a small total Q -range available with the instrument HFBS. Moreover HF refers to dry PFC, the three plots on the left of Fig. S1, thus only three data points

can be used for extrapolation to zero Q. Taken together this yields at best qualitative information, even the most sophisticated software cannot remove this restriction. The extrapolated elastic fraction is given in fig. 2 as $S(Q = 0, T)$. That the elastic intensity decreases with temperature even at zero Q has been observed previously with back-scattering instruments. It is usually removed by normalization (fig. 2 a).

With conventional scattering theory one has for the dynamical structure factor at zero frequency: $S(Q, \omega = 0) = \text{EISF}(Q) \delta(\omega)$, the elastic incoherent structure factor times a delta function with

$$\text{EISF}(Q) = | \langle e^{iQr} \rangle |^2 = | \int d^3r G(r, t \rightarrow \infty) e^{iQr} |^2 \quad (2)$$

$G(r, t)$ denotes the density correlation function, which is normalized for reasons of particle conservation, it follows: $\text{EISF}(Q = 0) \equiv 1$. Thus, in single scattering theory there can be no T-dependence of the elastic scattering function at $Q = 0$. Do we need a new theory, is HF right?

Most likely not, since multiple scattering effects predict such a decline with T even at $Q = 0$. Second scattering produces a noticeable Q-independent background, which decreases with the temperature (Cusack, Doster, Biophys.J. 1990, 58,243, M. Settles and W. Doster in Biological Macromolecular Dynamics, H. Büttner et al. (Eds.) Adenine, New York, 1996, 307-331. Multiple scattering effects are rarely discussed in the bio-molecular neutron literature. By contrast, our elastic and inelastic NS data (Doster, Settles, BBA 2005, 1749,173) were corrected for MS. A very important parameter of a neutron scattering experiment is the transmission coefficient, which is again rarely published:

$$\text{Tr} = \exp(- \Sigma_0 r_0) \quad (3)$$

With r_0 being the thickness of the sample along the wave vector \mathbf{k}_0 and Σ_0 is the total scattering probability integrated over all energies and directions.

For various sample geometries, M. Bee (Quasi-elastic neutron scattering) has calculated the transmission due to multiple scattering (p. 107ff) according to the theory of Sears. For often used (infinite) slab samples we have performed the respective calculations up to third order scattering, which is shown in fig. 3 assuming only elastic scattering.

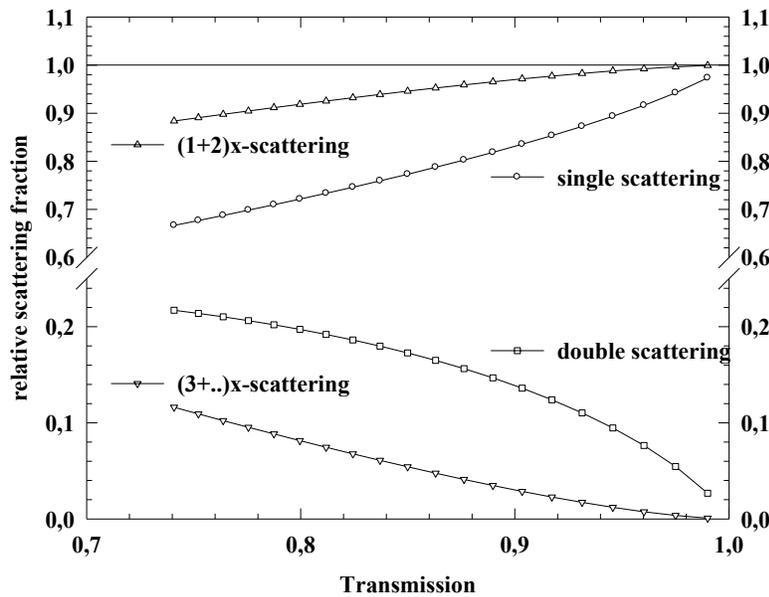


Fig. 3 Relative multiple scattering fraction calculated for pure elastic scattering and a flat cell at 45° oriented with respect to the beam

Conventionally one tries to keep the sample transmission above 0.9, which implies about 17 % of double scattering, too big to be ignored. Second scattering (elastic-elastic) is most strong at low temperatures decreasing with increasing temperature in proportion to the single scattering elastic intensity.

5) Correction of elastic scattering data from multiple scattering (Placzek expansion)

The application of the Placzek expansion to protein data was discussed in Doster, Settles BBA (2005). For correction of the elastic scattering one has:

$$S_{el}(Q,T) = f_{ms}^{el}(T) + (1 - f_{ms}^{el}) * (1 - B(T) * Q^2 + C(T) * Q^4) \quad (4)$$

$f_{ms}^{el}(T)$ is the multiple scattered fraction, shown in fig. 2 as a function of the transmission Tr and the temperature. $B(T)$ and $C(T)$ are defined by the second and the fourth moment of the displacement distribution.

With the moment this expansion we fit the true elastic scattering data with known transmission. The coefficients yield the second and fourth moment of the displacement correlation function and a temperature dependent multiple scattering fraction, shown in fig. 6 below (Doster, Settles BBA 2005). With the theory of Sears (as discussed by Marc Bee in his book on Quasi-elastic Neutron Scattering, pp 107), we calculated the second scattering effect at various temperatures from the known myoglobin-D₂O single scattering structure factor, $S(Q,T)$. The result is shown in fig. 6 as $S^2(T)$, the full line. Also shown are the extrapolated experimental data, $S(Q = 0,T)$.

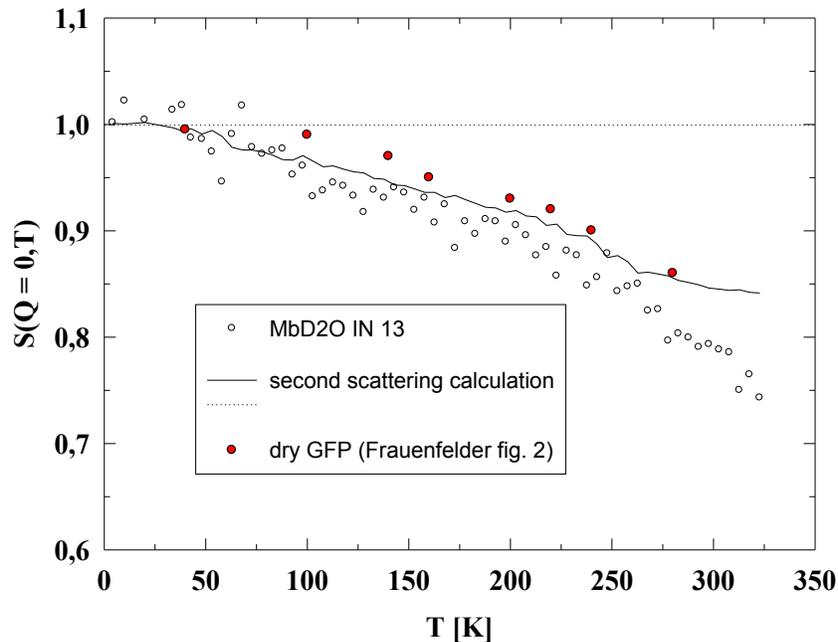


Fig. 6 shows that the second scattering calculation reproduces the temperature dependent Mb-D₂O data rather well. The discrepancy at high temperature results from problems with the low angle detectors and the presence of quasi-elastic scattering. We superimpose the Frauenfelder GFP analysis of fig. 2 (red dots). Given the qualitative nature of the HF analysis, the unknown transmission, our second scattering calculations agree quite well the T-dependent GFP elastic data at zero Q. Thus there is no discrepancy between zero Q data and conventional scattering theory if multiple scattering effects are included.

Conclusion:

On page 5131 HF concludes, “*the central intensity $S_{el}(0, T)$ decreases and a line appears at E (fig.1), E can be positive and negative, the result is an inhomogeneous spectrum..*” We have shown above, that this effect is well explained by classical multiple scattering. I agree with Joachim Wuttke, ELM is no case against scattering theory (PNAS vol 114, E8318, 2017). Just to the contrary, scattering theory is a case against ELM. The three HF papers dealing with NS and ME do not prove the ELM. However they still imply a significant progress. ELM belongs to the non-Popper models, which cannot be falsified. ELM is always right, all physical systems, even gases, exhibit or are even defined by free energy sub-states. With the three PNAS papers and his neutron /Mössbauer model, HF has changed the situation. Now it has become possible to test certain assumptions and predictions of ELM. Hans Frauenfelder once said to me, *I might be wrong, but it will take them a long time to find out.* But not forever!