Comment by Wolfgang Doster on

"a wave mechanical model of incoherent quasielastic scattering in complex systems"

By Hans Frauenfelder et al. PNAS vol 111 , p 12764 (2014)

Most remarkable to me is that this model is supported by three open reviewers with neutron scattering expertise, Gerald Kneller, E. Mamontov and Roger Pynn (above). However there was no reviewer with Mössbauer expertise, which is the essential part. Frauenfelder can get published in PNAS without passing a decent review, he just names his friends.

Sept. 10, 2018

1) The "wave mechanical model" is not new

It is often used to explain conventional quasi-elastic neutron scattering to students. In 2003, we wrote in Chem. Phys. 282, 487: "TOF-elastic resolution spectroscopy, time domain analysis of weakly scattering (biological) samples":

> If the primary spectrometer could select a sharp wavelength, λ_0, an infinite plane neutron wave without time limitation would result. Instead, a narrow distribution of wavelengths of width $\Delta\lambda$ is selected, which leads to a finite coherence length. The finite length of the neutron wave packet, which moves with average velocity $v = h/(m_N\lambda_0)$ across the scattering centres, limits the scattering
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> time to $t \leqslant \hbar/\Delta E_0 = m_N\lambda_0^3/(h\Delta\lambda)$. "$m_N$" is the neutron mass and ΔE_0 denotes the width of the initial energy distribution. Choosing $\lambda_0 = 5.1$ Å and $\Delta\lambda = 0.1$ Å, yields a time window of 33 ps. By varying λ_0 and $\Delta\lambda$ or E_0 and ΔE (resolution), one is scanning the time window of observation [3,7].

which is remarkably close to the Frauenfelder version.

2) Whats wrong with scattering theory?

The well known specialist of neutron scattering theory and instrumentation, Joachim Wuttke, wrote a counter-letter, "No case against scattering theory" (PNAS vol.114, E8318, 2017): *"In a series of papers , Frauenfelder et al. (see also comment in 2013) propose a radical reinterpretation of incoherent neutron scattering (and the Mössbauer effect) by complex systems, proteins, hydration water, drawing into doubt the "currently" accepted model which was highly successful for > 50 years.."* Wuttke concludes *" that there is nothing wrong with the accepted Van Hove space time scattering theory"*.

In contrast Frauenfelder writes: "*At present the QENS spectra are separated into a narrow elastic peak and a broad quasi-elastic band as in fig. 1A. As sketched in fig. 1B the broad band is taken to consist of Lorentzians of different width centered at ΔE = 0, the sum is shown in red.*
The broadening it attributed to **the spatial motion** *of the target atoms, diffusion, jumps, conformational changes.This is called the "SMM model". The "radically" different "energy landscape model ELM is illustrated in fig. 1 C: There is no separate elastic line, pinned to the center. The entire spectrum is composed of a very large number of spectral lines with twice the natural line width. Such a spectrum is called* **inhomogeneous.** *The lines are shifted from the center by transitions among the conformational substates of the ELM. Different proteins experience different energy shifts.*".
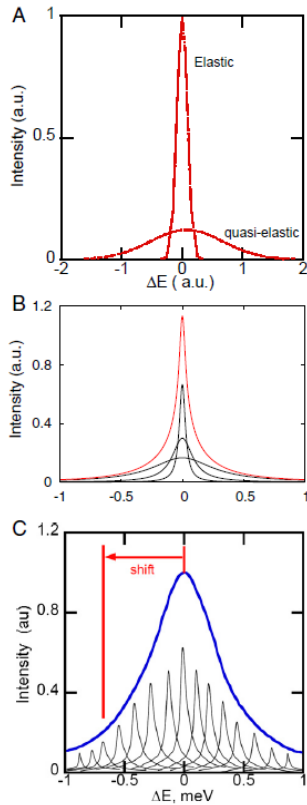
which gives the series of shifted sharp lines of fig. 1C with the envelope of the vibrational density $\rho(Q, \omega_i)$ centered also at $\omega = 0$

$$S(Q,\omega, \omega_i) = \Sigma\rho(Q, \omega_i)\, \delta(\omega - \omega_i)\,, \quad E_i = h\omega_i$$

In a recent paper in PNAS (2018) G. Kneller has developed a Franck Condon picture of this model.

This is a quantum mechanical model, which does not apply however to overdamped diffusion within a **free-energy** landscape. For such a classical situation the spectral lines are symmetrically centered around $\omega = 0$, after correction for detailed balance, the linewidth is dominated by relaxation times and not by heterogeneity.

Fig. 1. (A) Conventionally the elastic line and the quasielastic band in neutron scattering are treated as separate phenomena. (B) The broad band is usually assumed to be composed of Lorentzians of different widths and amplitudes, centered at ΔE = 0 (black curves). The sum is shown in red. (C) The proposed model (ELM) is composed of a very large number of narrow, shifted Lorentzians and has no separate elastic line. B and C adapted from ref. 4.

Spectral heterogeneity for overdamped relaxation processes

1) **The heterogeneous relaxation model of the intermediate scattering function:**
   $$I(Q,t) = \Sigma A_i(Q)\exp(-t/\tau_i) + A_\infty.$$
   An elastic line emerges only if $A_\infty > 0$. The resulting spectrum will be a heterogeneous superposition of Lorentzian lines with width $\Gamma_I = 1/\tau_i$, centered at $\omega = 0$, fully compatible with SMM, fig. 1 a and b

2) **Homogeneous nonexponential relaxation (fig. 1 b):**
   $$I(Q,t) = A(Q)\exp(-t/\tau_{KWW})^\beta$$
   The Kohlrausch function accounts for relaxtion in complex systems, such as liquids. The homogeneous spectrum will be centered at $\omega = 0$. $1 > \beta > 0$ is the inhomogeneity coefficient.

What is the main difference between SMM and ELM heterogeneity?

The SMM treats essentially overdamped relaxation or diffusion processes. Thus all spectral components are centered at $\omega = 0$, as a simple consequence of the Fourier transform of exponential functions. The width of the spectrum reflects the average relaxation time. There is no necessity of an "elastic line" in SMM as postulated here: Liquids do not exhibit an elastic line, since there are no spatial constraints at long times. For short times or low resolution, a partial localisation of particles may persist, depending on the relaxation time distribution, which leads to a resolution dependent elastic line. The existence of an elastic line allows to decide whether the system is in a liquid or a glassy state.

The ELM postulates underdamped vibrational transitions with a density of states $\rho(\omega_i)$, which is centered at $\omega = 0$. The individual components are displaced from $\omega = 0$ by $\omega_i = \Delta E_i/h$, which is the energy change due a move in the landscape. The width of the spectral components is very narrow due to vibrational dephasing (T_2), unrelated to a relaxtion time (T_1). The width of the combined spectrum does not reflect an average relaxation time. Instead it is the width of the frequency distribution $\rho(\omega_i)$.

With NMR spectra one has also two components: The width can be inhomogeneously broadened due to dephasing of spins (T_2), or it can be homogeneously broadened due to longitudinal relaxation T_1. The neutron and Mössbauer case are quite different from NMR. With incoherent neutron scattering, the neutron spins are dephased by the random spin orientations of the scattering protons. In practice it is very easy to decide with neutrons, whether the spectrum is motionally broadened according to an average relaxation time or whether it is broadened by multiple energetic transition as for a quantum harmonic oscillator. Structural relaxation in proteins is not well characterized by quantum transitions.

Lichtenegger et al wrote in their Mössbauer study on "heme solvent coupling" (Biophys. J. 76, 414, 1999): *The ME in proteins has the two characteristic features of a rapid decrease of the Debye-Waller factor above a characteristic temperature T_C ($\cong 200$ K) and the parallel appearance of quasi-elastic line-broadening in the energy range of a few neV (Parak and Formanek, 1971; Keller and Debrunner, 1980; Parak et al., 1981, 1982; Nowik et al., 1983). These results were interpreted in terms of protein-specific structural jumps and diffusion between conformational substates (Knapp et al. 1982; Nadler and Schulten, 1984).*

The common ground of QENS and Mössbauer spectroscopy

a) **The ME and NS approach to molecular dynamics:**
   ME and NS record density fluctuation around their reporter groups, which can be understood on the same basis: The spatial interference of the scattered (absorbed) waves generates the signal: More precisely, it is the loss of coherence in space and time giving rise to a dynamical structure factor $S(Q,\omega)$ as a function of momentum and energy exchange. It is reflecting exclusively the properties of the sample and is defined by the Fourier transform of the phase (factor) correlation function:

$$S(Q,\omega) = FT\{\Sigma_{ij}<e^{iQr_i(0)}e^{-iQr_j(t)}>R(t/\tau_{res})\} \qquad (equ.\ 1)$$

Incoherent scattering implies that waves scattered from different nuclei, i, j do not interfere. The signal with incoherent scattering is generated by the self- coherence of ii waves scattered from the same center i versus time and space. The modulation of the signal originates from motions of the nuclei $r_i(t)$ during the time τ_{res}, defined by the coherence length and the velocity (energy) of the neutron, see above. $R(t/\tau_{res})$ denotes the resolution function. The momentum parameter Q sets the spatial scale $1/Q$, over which the displacements are probed. The elastic structure factor S(Q,0), more precisely its Fourier transform, the density correlation function $G(r, t = \tau_{res})$ reflects the distribution of displacements (Doster/Settles BBA 2005, Doster et al. JCP 2013, 139,45105).

Even in the simplest case of a single exponential relaxation, identical to all sites, a homogeneous broad spectrum results. The line width $\Gamma = 1/\tau$, as illustrated in fig. 1 A above. The existence of site heterogeneity in the parameters of a single process or the involvement of several processes for each site would lead to non-exponential relaxation, or a superposition of Lorentzian spectra as suggested in fig.1 B. There could be a distribution of amplitudes and correlation times. There is enough sensitivity to heterogeneity build into the method. By contrast the model of Fig. 1C would imply that the local phase-correlation function of an overdamped relaxation process has oscillatory components. "Chemical shifts" occur only with resonance absorption methods, where well defined energy levels are modulated as with ME, NMR or optical spectroscopy but not with NS. The ELM model shares some features with "single molecule optical spectroscopy": With a variable narrow laser line one can resolve the inhomogeneous broadening of a macroscopically averaged absorption band into life-time broadened narrow lines of individual molecules. By selecting a single molecule, one can even record the jumps between different conformational states. With NS and ME, this kind of information cannot be extracted.

The elastic line at $\omega = 0$ (NS, ME) reflects the spatial localization of the scattering centers at long times: The long time spatial memory does not decay to zero in contrast to diffusion in liquids. The FT of a constant leads to a δ-line at $\omega = 0$: $S(Q, 0) = EISF(Q)\delta(Q)$, the EISF(Q) denotes the normalized elastic structure factor:

$$EISF(Q) = | <e^{iQr}> |^2 = | \int d^3r\ G(r,t\rightarrow\infty)e^{iQr}|^2$$

For $Q \rightarrow 0$, one obtains $EISF(Q) \equiv 1$ quite generally for reasons of particle conservation. Therefore the correlation function is normalized at all times. The observed decrease in elastic intensity at low Q with increasing temperature, which plays such a big role in Frauenfelder et al. PNAS 2017, is thus not compatible with conventional single scattering theory. But it is well explained by multiple scattering. In fact we use the extrapolated zero Q value of $S(Q\rightarrow0,0)$ routinely to correct our elastic and quasi-elastic scattering data from multiple scattering (Doster, Settles BBA 2005). The details will be discussed in the next comment (HF 2017).

A suitable starting point for the evaluation of Mössbauer spectra is the self part of the intermediate scattering function by (Knapp et al. J. Chem. Phys. 78,4701, 1983) similar to incoherent neutron scattering, equ. 1. The ME absorption cross-section is then given:

$$\sigma(k,\omega) \sim FT\{\ \Sigma_j <e^{ikr_j(t)}\ e^{-ikr_j(0)}> R(t/\tau_{M\ddot{o}})\ \}\qquad\text{equ. (2)}$$

where **k** is the wave vector the gamma radiation and $h\omega = E - E_a$ with E_a being the resonance energy of the nuclear transition, $\tau_{M\ddot{o}} \cong 141$ ns is the nuclear life time (Chong et al. Eur. Biophys. J. (2001) 30,319). The resolution $R(t/\tau_{ME})$ is an exponential with a resulting Lorentzian half with of $1/\tau_{ME}$: If the phase correlation function in equ.(2) has an exponential decay due to spatial motion of the iron with time τ_c , the combined half width of the Lorentzian $\sigma(k,\omega)$ will be $\Gamma = 1/\tau_{ME} + 1/\tau_c$. This is standard ME theory. If there is a finite long time value of the intermediate scattering function, $EISF_{ME}(k)$ as in solids, there will be an elastic line in addition to the Lorentzian broad line as with NS.

$$\sigma(k,\omega) = EISF_{ME}(k_0) \cdot \delta(\omega)\ + (1 - EISF_{ME}(k_0))\ \Lambda\ (\omega, \Gamma)\quad\text{equ. (3)}$$

$\Lambda(\omega, \Gamma)$ is a Lorentzian line. So the decomposition into elastic and quasi-elastic components is unavoidable if these methods record the decay of the phase correlation function. The similarity between equ. (1) and equs. (2,3) is the main reason, why some experimental results look so similar. The quasi-elastic lines are homogeneous for diffusive processes with both methods in contrast to what is proposed with ELM. Static broadening due to a distributed Fe environment is often observed at low temperatures (Lichtenegger, 1999).

In conclusion: That the Energy Landscape model explains Mössbauer and Neutron data sets together is a misconception. Both methods show different things . Not a single evidence of heterogeneous Mössbauer or quasi-elastic neutron scattering spectra was presented. The NS linewidth is not 4,7 neV but ranges around 1 µeV for back-scattering spectrometers.