

## **Review of Protein Dynamics, Simulation and Experiment by Smith Qu.Rev.Bioph. (1991)**

Comment by Wolfgang Doster at [bioneutron.de](http://bioneutron.de)

This now completely obsolete review article is still cited by Smith and company today (see recent articles 2012, 2013). Its main purpose at the time was to regain control of the field after the seminal papers by Doster/Cusack et al. in Nature 1989, PRL 1990, Bioph.J. 1990.

The main deficiency was again that vacuum simulations of myoglobin were compared with hydrated myoglobin and lysozyme experiments. Still the data were reproduced. What is wrong? Smith writes:

*This data suggests that the hydration water undergoes a dynamical transition in a similar temperature range to that observed in the protein in the neutron-scattering experiments (Doster et al. 1989). However, the fact that a similar dynamical transition was seen in the simulations of myoglobin without water molecules suggests that water is not required for the dynamical transition to occur in the protein (Smith et al. 1990).*

By contrast, the simulations by Loncharich and Brooks, J.Mol. Biol. (1990) 215, 439 of hydrated myoglobin **are not cited**. Here the experimental data were reproduced because of including the hydration water.

Smith misunderstood our 1989 definition of a “dynamical transition”: Only a single transition is discussed in analogy to the Mössbauer effect of the heme iron:

the anharmonic onset of displacements characterized by an asymmetric two-state model

By contrast in the neutron scattering experiments two transitions in the displacements were revealed:

- (1) a pretransition near 180 K due rotational transitions of side chains, characterized by a two-state model
- (2) a water-induced **dynamical transition** due to motions which are resolved only above 240 K.

This misunderstanding persists up to today.

To lump everything together, dry with hydrated proteins, the Mössbauer effect with neutron scattering, simulation with experiment is a typical feature of this article.

How water-induced spectral properties can be reproduced with vacuum simulations is still an unclarified question.

Smith correctly writes in 1991 (around 2000 this is sold as a new idea):

*Motions in proteins on a time-scale longer than that accessible by the instrument will not contribute to the experimentally determined mean-square displacement. In the Gaussian approximation we have (elastic intensity)*

$$S(q,0) = \sum b_i^2 \exp(-q^2 \langle R_i^2 \rangle)$$

*This equation is exact in the limit as  $q \rightarrow 0$ .*

Note that the factor 1/3 is missing in the exponent, the equation is not exact, since the quasi-elastic part at  $\omega = 0$  is ignored (Doster et al. JCP (2013)139, 45105).

The Lamb-Mössbauer factor applies to self-motions and should have the same form but according to Smith one has

*The Lamb-Mössbauer factor  $f$  which is the fraction of the  $\gamma$  radiation scattered without energy transfer, the recoilless fraction, is then given by*  
$$f = \exp(-q^2 \langle R^2 \rangle / 6)$$
*where  $\langle R^2 \rangle$  is the mean-square displacement of the iron ion.*

Note that there is now a factor of 1/6 in the exponent. The correct factor would be 1/3 (see paper by Parak et al.).

This confusion about the prefactors in the exponent of the Lamb Mössbauer factor persists until today.