Hydrogen atoms in proteins: Positions and dynamics

Niklas Engler*, Andreas Ostermann*†, Nobuo Niimura†, and Fritz G. Parak*‡

PNAS (2013) 100, 10243

This study is the intelligent experimental alternative to dynamical heterogeneity simulations of proteins. I cite this work because they came to the wrong conclusions not understanding incoherent neutron scattering and by ignoring the results of the original paper by Doster et al. 1989 Nature. The neutron structure of D-soaked myoglobin was determined including the hydrogen positions in the molecule. From the Debye Waller factors also the static mean square displacements were calculated. The H- displacement distribution was fitted by three Gaussian distributions.

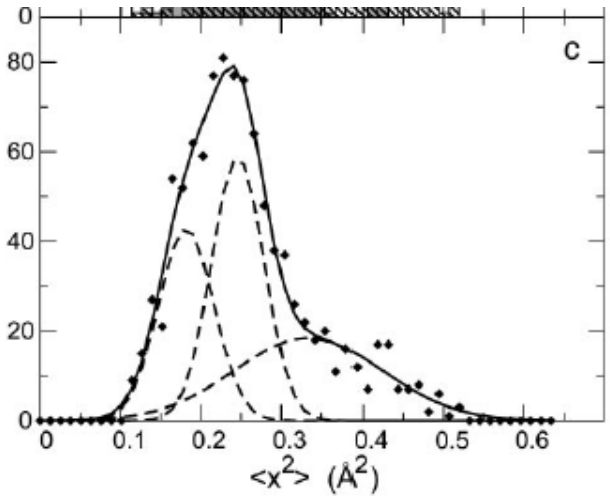


Table 3. Gaussian distributions

	Counted from structure	Gaussian 1	Gaussian 2	Gaussian 3	Sum within Gaussians
Position, Å²		0.182	0.246	0.333	
Width, Å²		0.034	0.033	0.092	
All ¹H	997 (194)	292	380	334	1,006
Main chain	161 (146)	122	26	11	159
Side chain	836 (48)	170	354	323	847
Methyl groups	282	21	226	40	287
Lysine side chains	152	0	4	140	144

First two rows, parameters for the Gaussian distributions. Following rows, number of hydrogens counted from

They discriminate between main chain, side chain, methyl groups, and lysine side chains.

28 % of all hydrogens belong to methyl groups mainly in G2 around $\langle\Delta x^2\rangle \cong 0{,}25\ A^2$. Rotational transitions involve much much larger displacements: around $1{,}5^2\ A^2$

In order to compare with dynamic neutron scattering experiments the displacements are divided according to fast (< 150 ps) and slow motions (> 150 ps), the resolution time of the spectrometer:

$$\langle\Delta x^2_j\rangle_{cryst} = \langle\Delta x^2_j\rangle_{fast} + \langle\Delta x^2_j\rangle_{slow} \quad j = 1,2,3$$

Now the authors use the three distributions to fit the elastic neutron scattering curves of myoglobin (Doster et al 1989).

For a comparison with the incoherent neutron-scattering data on myoglobin of Doster *et al.* (25), we used the expression

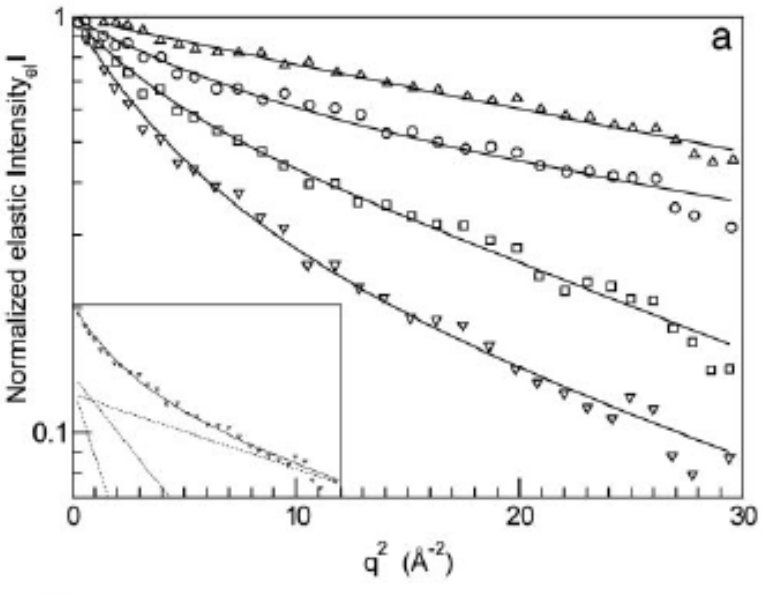
$$S[q, 0] = \sum_{j=1}^{3} c_j \exp[-q^2\langle x_j^2\rangle_{\text{fast}}^n]. \qquad [2]$$

The weight factor, c_j, for the contribution of atoms of class j is taken from the area of the Gaussian j (see Table 3). $\langle x_j^2\rangle_{\text{fast}}^n$ remain as free parameters for a fit of $S[q, 0]$ to the experimental data in ref. 25. The average mean-square displacement of the hydrogen atoms can be obtained from the slope of $\ln S[q, 0]/q^2$ for $q = 0$ (25). It can also be calculated by

$$\langle x^2\rangle = \sum_{j=1}^{3} c_j \langle x_j^2\rangle_{\text{fast}}^n. \qquad [3]$$

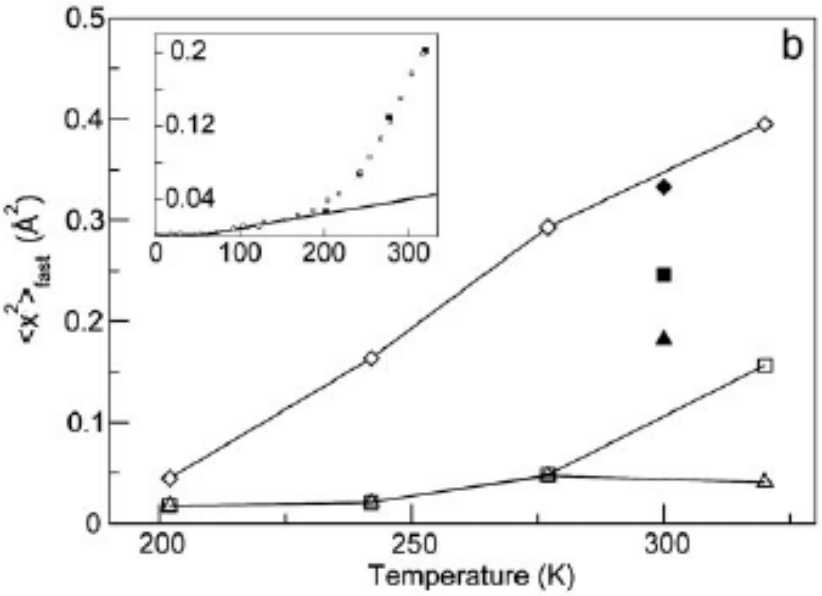
The data for $S[q, 0]$ and the average mean-square displacement at each temperature were fitted simultaneously. The weight for the fit to $S[q, 0]$ and $\langle x^2\rangle$ was adjusted equally.

Results are shown in Fig. 5*a* for different temperatures. The contributions of the three different hydrogen classes are shown as dashed lines for the 320 K data in *Inset*. The result for the average mean-square displacement $\langle x^2\rangle$ in comparison with the data of Doster *et al.* (25) is shown in Fig. 5*b Inset*. Smith *et al.* (33) have shown by an analysis of molecular dynamics trajectories that the description of $S[q, 0]$ by a sum of Gaussians similar to Eq. 2 is in qualitative agreement with the data.



The non-Gaussian scattering functions are adjusted by a sum of three Gaussians, with

$\langle \Delta x^2_j \rangle_{fast}$ as free parameters. There are enough free parameters to fit the smooth scattering curves.



Dynamic fits: open

Lysine

Static Values (closed)

Methyl

Main Chain

The striking result is that the main fast displacement of dynamic neutron scattering should result from the charged lysine side chain.

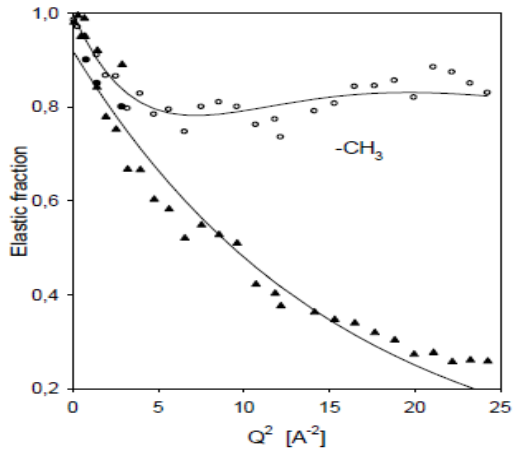
By contrast it is well established that the methyl group rotation gives a major contribution to the total mean square displacement (Doster, Settles BBA 2005, Sokolov BJ 2006).

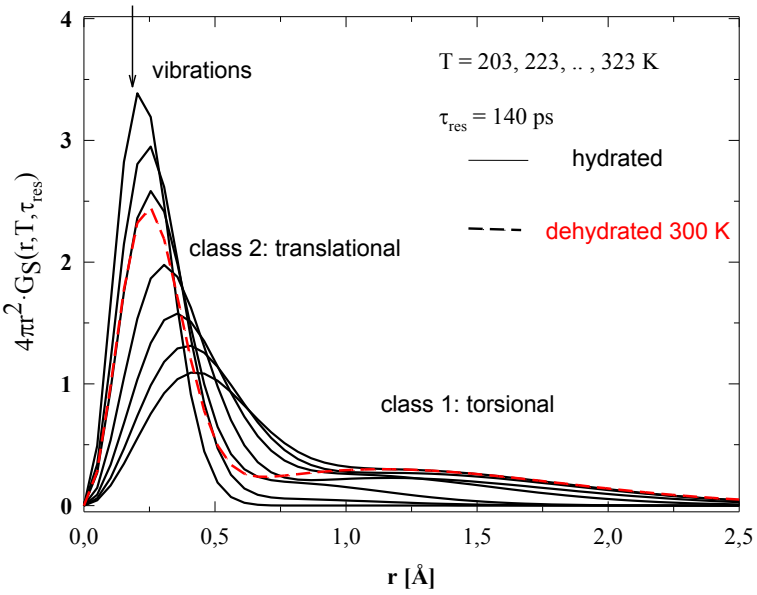
What is wrong? The Gaussian distribution does not apply to rotational transitions!

The elastic structure factor of methyl group rotation is not distributed and is given by

$S_{el}(CH_3) = 1/3(1+ 2\ \sin(Q\sqrt{3}r)/(Q\sqrt{3}r))$

Decomposition of the neutron elastic structure factor of hydrated myoglobin at 300 K: Gaussian + rotation





Displacement distribution of a two-Gaussian approximation: the two components are Methyl group rotation (class 1) and water coupled translational displacements (class 2). From: Doster, Settles BBA 2005.