Experimental report

08/08/2018

Proposal: CRG-2485 **Council:** 4/2017

Title: Testing the Validity of Current Models to Describe the Protein Dynamics from EFWS data

Research area:

This proposal is a new proposal

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Samples: a-lactalbumin at different hydration levels in D2O

Instrument	Requested days	Allocated days	From	To
IN13	6	6	09/03/2018	15/03/2018

Abstract:

Experimental report: CRG 2485 on IN13 - From 09/03/2018 to 15/03/2018

Experimenters: Dominik Zeller, L. Misuraca, Judith Peters

Testing the Validity of Current Models to Describe the Protein Dynamics from EFWS data

Background

In 2013, following the ideas which led to the creation of the very successful Protein Data Bank (pdb) for structures, G. Zaccai and coworkers proposed to build up a neutron Dynamics Data Bank (nDDB)[1] which would be populated with primarily dynamical data of biological macromolecules measured with different neutron spectrometers as well as some NMR and molecular dynamics (MD) simulation data. The ultimate goal is to enable us to find trends in the experimental data over a range of different systems and instruments and under many different conditions like temperature, pressure, hydration, pH/pD or crowding, hopefully leading to a global picture of the dynamics of biomolecules One important aspect of this task is to figure out to what extent such trends may depend on sample preparation, data reduction and data analysis, to have accurate comparisons between data sets. For instance, so-called elastic window scans typically performed on neutron backscattering spectrometers are often used to compute mean square displacements (MSD) as a measure of protein flexibility. Typically MSDs are derived from fitting the Q-dependence of the measured elastic intensity on a given neutron spectrometer (so at a given energy resolution and Q-range), with the Gaussian Approximation (GA). In the last few years, the validity of such models has been questioned and models that go beyond the Gaussian approximation have been proposed [2-5]. Despite a large number of proteins measured at specific conditions, and even for one of the most studied systems, lysozyme, there is no systematic study to cover a complete set of measurements (EINS, QENS, INS), time scales and conditions. We propose to perform a systematic study on a relatively simple molecule, bovine alpha-Lactalbumin (123 amino acids, 14.2 kDa), commercially available and easily amenable to simulation, making it feasible to perform a systematic analysis of its dynamics both experimentally and computationally.

Experiment

We measured alpha-lactalbumin with (holo-form) and without (apo-form) calcium in powder form in two different hydration levels of D_2O. As ratio h = g D2O/g we used h=0, h=0.4 for the holo-form and h=0 for the apo-form (h=0 equals a dry sample and 0.4h equals ~ one hydration layer [6]). For all samples, we measured elastic fixed window scans (EFWS) from 20 to 315K. All samples were cooled down and then the data was registered under an angle of 135 degree by slowly heating the flat aluminum sample holder.

Result

The elastic data were analyzed using three of the models cited above, the GA, the Peters and Kneller model [2] and Yi et al. model [3]. The GA models was used for the low Q-range and the other two models for an extended Q-range. The value at EISF(Q=0) was fixed to the result obtained by the GA. All three models evaluate to an average MSD/MSPF (mean square position fluctuation [2]) for each temperature. The preliminary results are shown in figure 1-3.

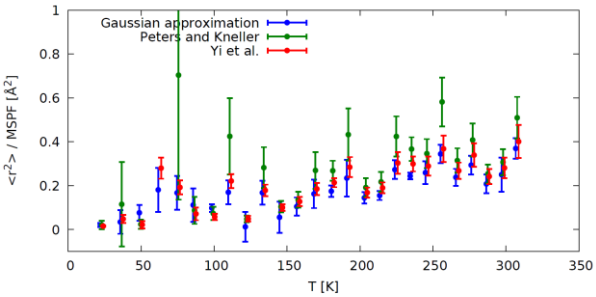

Figure 1: *MSD/MSPF for dry alpha-lactalbumin with calcium.*

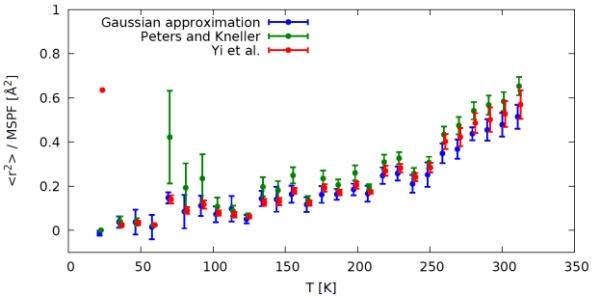

Figure 2: *MSD/MSPF for 0.4h alpha-lactalbumin with calcium.*

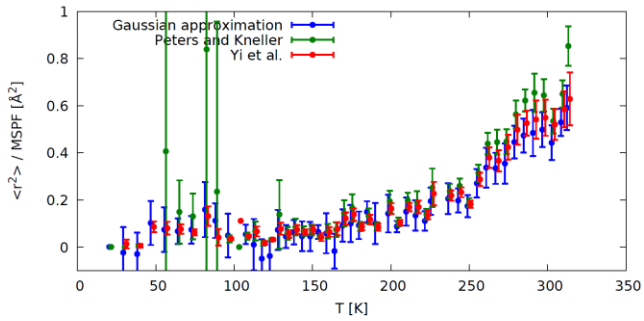

Figure 3: *MSD/MSPF for 0.4h alpha-lactalbumin without calcium.*

The preliminary results suggest a small difference between the holo- and apo-form considering the Peters and Kneller model. The other two models are rather similar.

References

[1] L. Rusevich et al., *Eur. Phys. J. E*, 36, 80, 2013; [2] J. Peters and G.R. Kneller, *JCP*, 139, 16, 2013 ; [3] Zheng Yi et al., *JPCB*, 116, 16, 5028-5036, 2012 ; [4] A. Tokuhisa et al., *Phys. Rev.* E, 75, 04, 2007 ; [5] D. Vural et al., *Phys. Rev. E*, 88, 052706, 2013 ; [6] S. Perticaroli et al., *JACS*, 139, 3, 1098–1105, 2017.