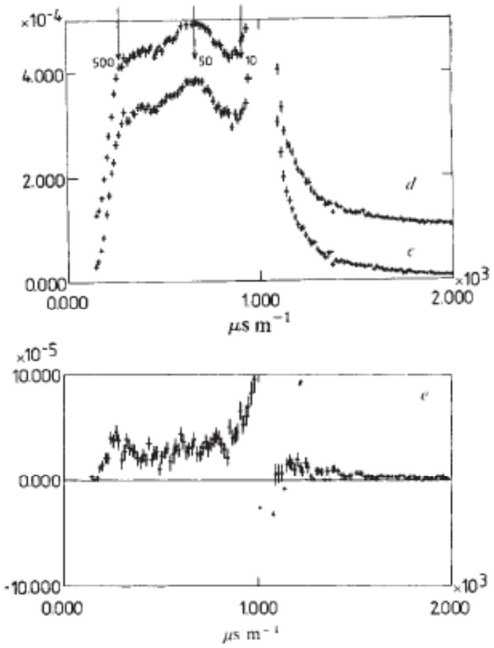
Ligand Binding to Hexokinase, effect on low frequency modes, by Jacrot et al. Nature 1982



Time of Flight Spectrum of hexokinase with and without glucose bound and the difference spectrum

Dynamic analysis of biomolecules often works by the principle of difference spectroscopy: What is the qualitative difference in structural flexibility of a protein with and without ligand? This method, illustrated elsewhere in this book, is quite useful considering the complexity of biomolecules. Sometimes, however, differences between different samples are easier to obtain than reproducable identical results. This chapter is addressed to students of biophysics,

(W. Doster in Brownian Oszillator Analysis of Molecular Motions in Biomolecules, Neutron Scattering in Biology, Techniques and Applications Springer Book (2006) Ed. Katsaras, Fitter, Gutberlet)

The spectral difference between the two protein solutions could not be reproduced (Cusack 1986, Comm. molec. Cell Biophys. 3, 243. The difference was due to sample preparation. At this time the difficulties of neutron scattering with protein solutions were not know. A similar faulty experiment was published in 2004 by the Smith, Lechner, Finney group in PRL 93, 28103, on changes of the low frequency motions induced by ligand binding. We have shown that the Boson peak region is independent of protein structure (Cusack, Doster 1990, Biophys.J. and Diehl et al. (1997) Biophys. J. 73, 2726.

The unpublished figure below shows a TOFTOF experiment (FRM2, Munich) in the low frequency Boson peak region of three equally hydrated proteins with very different structures: myoglobin (helices), lysozyme (helices, beta sheets) and casein (disordered). **Inelastic neutron scattering is not the appropriate method to study structural changes in proteins at low frequency.**