Enzyme Activity below the Dynamical Transition by Daniel et al (1998)

R. Daniel, J.Smith, M. Ferrand, S. Hery, R. Dunn, J. Finney, Biophys. J. 75 (1998) 2504

Comment by Wolfgang Doster at bioneutron.de

This paper is the first one of a series aiming to discredit the concept of a 'dynamical transition'. As their central message the authors announce, that the PDT is irrelevant to enzyme activity and thus to biology. This general statement is not based on experimental evidence. While the PDT, as defined by the authors, is measured on a time scale of picoseconds, the enzyme activity is recorded based on turn-over rates on the scale of seconds or days (Doster BBA 2005). The authors intentionally confuse the idea of a time-scale-dependent "dynamical transition" with a time-scale independent "structural transition". In physics the term "dynamical transition" comprises the glass transition and the percolation transition. The PDT was defined (Doster et al 1989) as the coupling of protein structural degrees of freedom to the structural relaxation of a glass forming solvent. The glass transition is by definition time-scale dependent. The PDT occurs in two steps, fast and slow, related to spectral properties. It is not just defined by the "anharmonic onset". 70 % methanol- water is not a glass forming solvent, it crystallizes around 200 K. Its viscosity is quite low even at low temperatures. The structural relaxation of the solvent is thus not rate limiting to the "enzyme activity", which is composed of several elementary steps. Some of them are solvent-independent.

Technical remarks:

(1) The tiny data base and the scientific quality of the data are shocking (fig. 1). The referee of this paper was either a good friend or totally incompetent or both. The elastic scattering curves versus Q and T are missing. Did they look too bad? The dynamic analysis involves only mean square displacements.

(2) The MSD(T) of the enzyme GDH 70 % methanol-water solution were derived from elastic neutron time-of-flight spectroscopy. With a good sample, it should be easily possible to derive MSDs at high precision. However the data in fig. 1 cannot even reproduce the harmonic linear increase of vibrational amplitudes at low temperatures, the MSDs even decrease! The drastic increase above 220 K is interpreted as a PDT, a cross-over of protein-

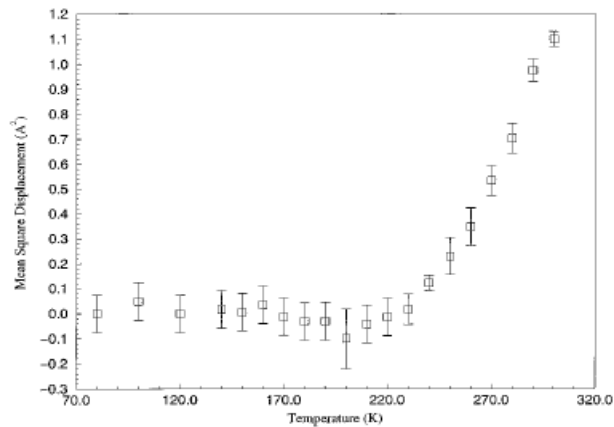internal harmonic to internal nonharmonic behaviour. Global protein diffusion and solvent

FIGURE 1   Effect of temperature on the dynamics of a glutamate dehydrogenase enzyme in 70% aqueous methanol, as measured by neutron scattering.

diffusion is ignored.

(3) The MSDs were derived assuming the dominance of incoherent scattering. In fact, at least 50% of the scattering is coherent (but not self-coherent?) due to the deuterated solvent.

(4)   However their methanol-water mixture is not a glass-forming solvent. The viscosity of this solvent has a regular Arrhenius behavior. The viscosity at 173 K is 540 cS, which is far from a glass, 10^{13} P. The correlation time is in the range of several hundred picoseconds not 100 s.

(5) The figure below compares the reciprocal viscosity ~ the solvent relaxation time to the enzyme activity measurement in the methanol-water solvent. This most relevant comparison is unfortunately not presented in the paper.

Result: The activity of GDH in liquid methanol-water is not limited in rate by the solvent relaxation. These processes are totally unrelated. Methyl groups in proteins rotate below 200 K!
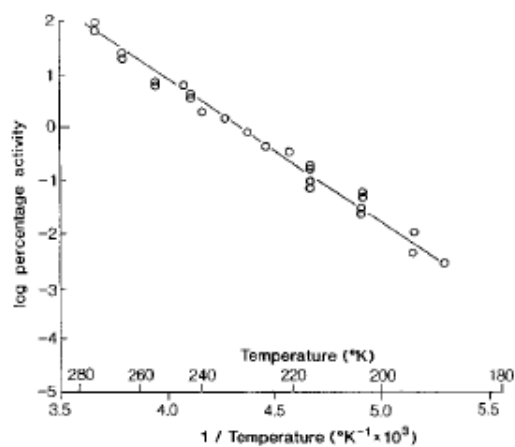
GDH in 70 % methanol-water
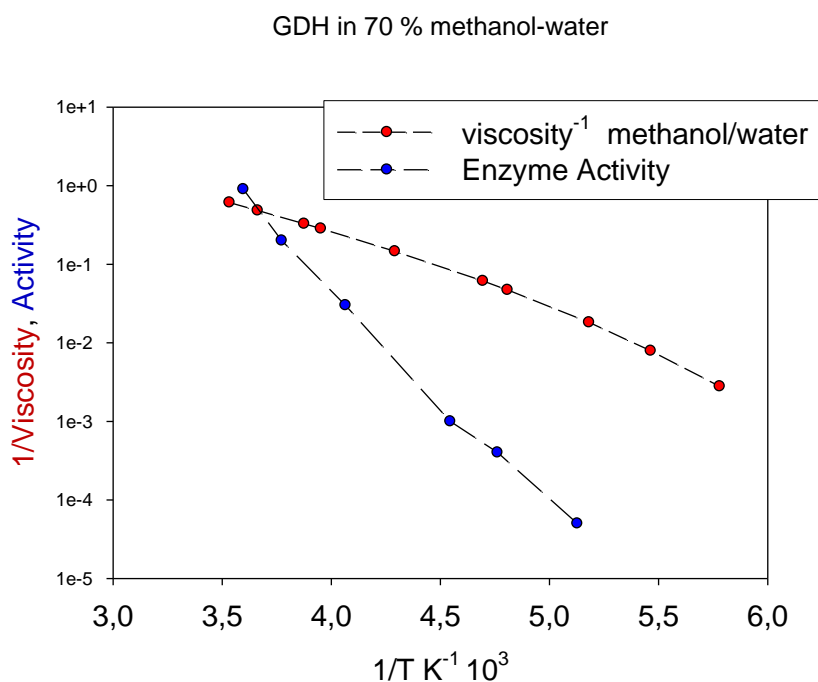
FIGURE 2 Effect of temperature on the activity of a glutamate dehy-
drogenase enzyme in 70% aqueous methanol. Activities are presented as a
percentage of the activity at 273 K (from More et al., 1995). Measurements
at selected temperatures in perdeuterated cryosolvent showed no signifi-
cant deviation from the results in Fig. 2.