Time domain versus energy domain neutron scattering analysis of protein dynamics

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G. Kneller presented in a recent PNAS article (1) a quantum-theoretical justification of the "energy landscape model" of protein dynamics for the case of neutron scattering. There it was claimed that the established Van Hove space- time correlation function formalism does not apply to proteins (2, 3): For "complex systems" the concept of structural diffusion across a multilevel energy surface seems more appropriate. Proteins, however, are not true quantum systems at physiological temperatures, where the thermal energy is near 25 **meV**. The relevant motional energy transfers in such scattering experiments range between 0,1 and 100 **μeV**. It is thus well justified, to employ the classical scattering functions to experimental spectra made symmetric by the detailed balance factor. It is somewhat disappointing, that the new Franck-Condon approach is applied only to simple model systems as the quantum harmonic oscillator and the ideal gas, which have little to do with protein complexity. Moreover, incoherent neutron scattering of protein protons provides a spatially averaged picture of motions, which does not satisfy spatial heterogeneity models. Thus, instead of elaborating on energetic complexity, it seems more promising to focus on specific molecular motions in the time domain. Fig. 1 shows as an example a numerical Fourier transform (after performing the relevant corrections) of experimental spectra of D_2O-hydrated myoglobin at 300 K (4, 5). $\Phi(Q, t)$ denotes the classical wave-vector-time correlation function of hydrated myoglobin, combining the experiments performed with three spectrometers of overlapping time window. The system is indeed complex in the sense that the relaxation processes cover three decades in time. On the contrary, it is also simple, since $\Phi(Q, t)$ can be reduced to two known dynamic components (rot, trans), which are affected differently by the degree of hydration (4, 5). The question of separating elastic and inelastic scattering is now reduced to the problem of determining a plateau at long times. In ref. (2) the existence of elastic scattering is all together denied. For thermal motions in proteins around 1 to 1000 ps I don't recognize an advantage of a description based on energy landscapes.

References

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Figure Legends

Fig. 1: Φ(Q, t) of hydrated myoglobin derived from three spectrometers IN6, IN13 and IN10 at Q = 1,9 $Å^{-1}$ and theoretical predictions of a two-component model comprising rotational transitions of methyl groups and local residue diffusion (red line) (4 ,5).