Time domain versus energy domain neutron scattering analysis of protein dynamics

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In PNAS, Kneller (1) suggests a quantum-theoretical justification of the “Frauenfelder energy landscape model” of protein dynamics applied to quasielastic neutron scattering (QENS) (2, 3). The diffusion-broadened QENS spectrum, centered at $\omega = 0$, is explained (Fig. 1 and ref. 2) by a distribution of narrow inelastic lines centered at $\omega \neq 0$, reflecting energetic transitions between discrete states of a “complex” landscape. Elastic scattering at $\omega = 0$ does not exist as a separate spectral component, contradicting standard scattering theory of spatially constrained motions (2) and most of the published literature (4). Kneller (1) rationalizes this picture by discrete quantum transitions within a Franck–Condon potential analogous to vibrational spectra of molecules (Fig. 1 and ref. 1). The ideas are applied to textbook examples, the quantum harmonic oscillator and the ideal gas. This ignores that the relevant structural relaxation processes in proteins are diffusive at ambient temperatures. The QENS energy transfers in such scattering experiments range between 0.1 and 200 μeV, which is much less than the thermal energy of 25.8 meV at 300 K. The resulting detailed balance symmetry correction is then less than 1,004 (1). In this case the classical Van Hove scattering functions provide a “very good approximation” to the real experimental data. An example of single-particle relaxation dynamics is presented in Fig. 1: $\Phi_S(Q, t)$ denotes the wave-vector-time self-correlation function of D_2O-hydrated myoglobin at 300 K (5). It represents the numerical Fourier transform of experimental energy exchange spectra to the time domain, combining experiments performed with three spectrometers, properly corrected for resolution and detailed balance effects. The structural relaxation process spreads across three time decades, which is a model-independent result. The next step is to analyze specific molecular models based on predictions of their time and Q dependence. The minimal model of Fig. 1 is composed of two major components, methyl rotational transitions and continuous residue diffusion. Local heterogeneity causes the respective time constants to be slightly distributed (4, 5). The fraction of elastic scattering can be estimated from the plateau of $\Phi_S(Q, t)$ at long times (Fig. 1, arrows). This contradicts the notion “that elastic and quasielastic scattering are practically not separable for complex systems” (1). For protein hydration water this separation was achieved by advanced fitting software (6). According to Wuttke (7), the energy landscape models present “no case against scattering theory” even for complex systems. In conclusion, the Franck–Condon model does not apply to protein structural relaxation at ambient temperatures. The question of separating elastic and quasielastic components should not be confused with a general exclusion of elastic scattering, especially for spatially constrained structural relaxation in proteins (1, 2).

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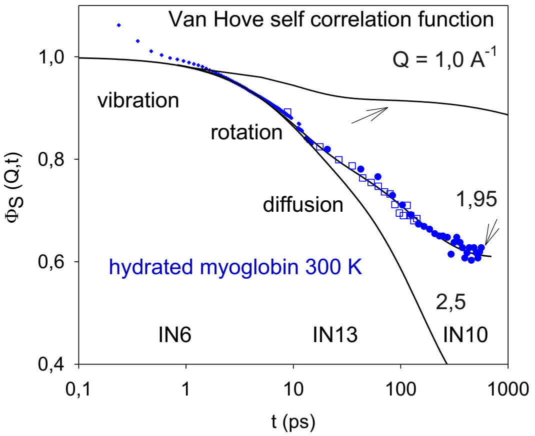

Fig. 1. **Blue symbols: self-correlation function $\Phi_S(Q, t)$ of D_2O-hydrated myoglobin (0.35 g/g), combining data of three spectrometers, IN6, IN13, and IN10 (Institut Laue–Langevin, Grenoble, France), at the wave vector $Q = 1{,}95$ Å^{-1}. Solid lines: theoretical predictions of a two-component model comprising rotational transitions of methyl groups and local residue diffusion versus Q. Reprinted from ref. 5. Arrows: elastic fraction.**

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