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Comment

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Comment on "Puzzle of the Protein Dynamical Transition"

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I comment on the article entitled "Puzzle of protein dynamical transition" by Magazu et al.[1] appearing in a recent issue of the *Journal of Physical Chemistry B*. The protein dynamical transition (PDT) is a well established feature of solvent-coupled protein dynamics usually identified from a striking increase of apparent molecular displacements above a certain onset temperature, $T_{\mathrm{on}} \approx 200{-}240$ K. It is suggestive to invoke a scenario, originally proposed by Parak and Frauenfelder,[2,3] of enhanced fluctuation amplitudes due to a detrapping transition, controlled by a multiple energy minima landscape: At a characteristic temperature T_{on}, the thermally activated protein changes its dynamic properties from rigid to flexible. This model predicts a fixed T_{on}, if the energy traps are deep and if the trapping rate is fast enough compared to the instrumental resolution. This model of the PDT was fully adopted by the elastic neutron scattering community[4] and is now dismissed in ref 1 based on three statements:

(i) "The PDT is a finite resolution effect, it appears, when the characteristic system relaxation time intersects the resolution time"; thus, T_{on} varies with the observation time.
(ii) "The PDT does not imply any transition in the dynamical properties of the system...", such as the escape out of energy traps.
(iii) The apparent fragile-to-strong crossover described by Chen et al.[5] is interpreted instead as a switch between primary and secondary structural relaxation.

(ai) Magazu et al. essentially criticize the detrapping model of their "so-called PDT". By contrast, the originally proposed concept of the PDT, first suggested by us in 1986,[6,7] is quite different from a simple detrapping mechanism: We developed a glass-transition scenario of protein hydration water and of other glass forming liquids, coupled to protein side-chain motions by hydrogen bond fluctuations. This model predicts onset temperatures, which vary with the instrumental resolution, if the main structural relaxation is probed at different time scales.[6−8] Moreover, the PDT, as originally defined, comprises two steps:[7,9] (1) a pre(detrapping) transition due to increasing amplitudes of fast hydrogen bond fluctuations around the glass temperature $T_g \approx 170$ K (fast β-relaxation) and (2) the main transition at $T_{\mathrm{on}} \approx 210{-}240$ K, caused by slow translational displacements of hydration water (α-process), which arrest at T_g.[7,9] Only the second onset, which is the one discussed in ref 1, varies with the instrumental resolution.[9]

(aii) The claim that the dynamical properties of the sample do not change at T_{on} is supposed to be the "killer argument" to deny the existence of a PDT altogether. The authors overlook, however, that their central statements (i) and (ii) also apply to the conventional calorimetric glass transition at T_g: Neither the structure of the liquid nor its long-time dynamic properties change at T_g. In spite of this continuity, a step in the specific heat is observed, signaling structural arrest and the freezing of translational degrees of freedom. The fallacy in Magazu's argument is contained in the idea that dynamic system properties can be defined independently of the observation time. This applies to a local molecular process but fails in the case of collective structural relaxation, which restores the ergodicity of the liquid. Ergodic behavior is a prerequisite to defining equilibrium properties. The GT thus represents the physical change from ergodic to nonergodic behavior. It occurs at the crossover of structural relaxation and observation time: The properties of a "silly putty ball" (silicon based polymer) vary from a brittle glass to a viscous liquid, depending on the speed of external perturbation. Whether an amorphous material behaves like a glass or a liquid thus depends on the time scale of observation. The Challenger catastrophe happened because the slow structural relaxation of a rubber ring could not adjust to the fast oscillatory stress imposed by the rockets. The protein glass transition was first demonstrated by Morozov et al., based on the Young modulus of hydrated lysozyme crystals (and the thermal expansion of hydrated lysozyme films), which displays a step-like change near $T_g \approx 170$ K, varying with the probe frequency.[10] Walter Kauzmann wrote in 1948:[11] *"It is widely agreed that this "glass transformation" is caused by a relaxation effect, through which some process in the amorphous material occurs too slowly at low temperatures to permit thermodynamic equilibrium to be established in all degrees of freedom. It is shown that the molecular movements involved in the relaxation process must resemble closely the movements in viscous flow and dielectric relaxation. Movements of this type permit the liquid structure to change following temperature and pressure changes...The glass transformation temperature T_g could then be "defined" in a very general way as the temperature below which the relaxation time for structural degrees of freedom are long compared with the duration of the experiment."* The neutron scattering experiment probes the glassy relaxation of the protein−water system on a picosecond to nanosecond time scale; thus, T_{on} (ns) $\gg T_g$ (s) and T_{on} (s) $\approx T_g$. The specific heat will display a corresponding step at T_{on} (ns), if probed on this time scale.[8] Moreover, the characteristic time of a supercooled liquid diverges from picoseconds to seconds according to a super-Arrhenius law, more than 12 decades within a narrow T interval. This time span is longer than the age of the universe, which may justify the notion of a "dynamical transition".

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(aiii) On the basis of elastic scattering information, plotting T_{on} versus instrumental resolution, Magazu et al. derive a crossover in the Arrhenius plot of the structural relaxation time. According to our full dynamic analysis of inelastic neutron scattering spectra of protein hydration water, no such kink is observed.[12] Their "crossover" is supported by a single data point, which was taken from the literature, and no error bar is given. The kink disappears if, instead of their assigned T_{on} = 200 K, the literature value of 220 K is taken.[12]

In conclusion, Magazu et al. disprove the detrapping model of the PDT[2,3] but confirm the original glass transition scenario.[6−9,12] The puzzle originates from mixing up two incompatible views of the PDT and the incorrect citation of the relevant literature. The neutron scattering data do not support a fragile to strong crossover in the average relaxation times between the main structural relaxation and a Johari−Goldstein secondary process.

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Notes

The authors declare no competing financial interest.

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