Comment on "Glass Transition in Biomolecules and the Liquid-Liquid Critical Point of Water"

A recent Letter [1] investigated the relationship between dynamic transitions of biomolecules (lysozyme and DNA) and dynamic and thermodynamic properties of hydration water. This seminal work demonstrated that the so-called "protein glass transition" is (in two ways) ill-defined: It is not properly a glass transition nor due to the protein's behavior. Rather, this phenomenon is shown to occur at the dynamic crossover in the diffusivity of the hydration water as a result of crossing the hypothesized liquid-liquid critical point (Widom line). One piece of evidence provided was the demonstration that the rate of change with temperature of the local order of hydration water molecules for both lysozyme and DNA presents a maximum at such crossover temperature [1]. However, there exist two problems on their way to this result which could lead to misleading results.

The first and main concern regards the use of the tetrahedral order parameter Q (a quantitative measure of local structure by the extent to which a water molecule and its four nearest neighbors adopt a tetrahedral arrangement), defined for bulk water but clearly not suited for interfacial water [2]. The hydrogen bond network of water is disrupted close to a surface and these vicinal water molecules tend to be surrounded by three (hydrogen bonded) water molecules instead of the four first neighbors typical of the bulk [2,3]. Thus, the calculation of Q would force the consideration of a complete fourfold coordination arrangement [1], yielding in this case a lower than bulk unrealistic value, inconsistent with the better than bulk structuration shown both experimentally and computationally [2,3].

The second point involves the number of molecules included in the calculation. $N = 1242$ TIP5P water molecules [1] implies that roughly only half of them belong to the first hydration shell of lysozyme. The structuring effect of the surface usually does not go much beyond the first hydration layer (upper layers tend to show bulklike structure [2,3]) and its temperature dependence can be different (less T sensitive) from that of the bulk [2]. Hence, in the calculations of Ref. [1] bulklike behavior could be interfering with a typical surfacelike one.

Thus, to properly test the picture of Ref. [1] we reproduced their simulations for lysozyme (now hydrated with 12600 TIP5P water molecules). In Fig. 1 we show the derivative with respect to temperature of the local structure index (LSI [2,4], which at variance from Q can be safely applied to interfacial water [2]). For convenience, we divided hydration water into "biological" (that whose distance to the protein is less than $r = 4.25$ Å, comprising the first hydration shell) and "bulk" (the rest). We can see that both curves present a peak close to $T = 250$ K, the crossover temperature value indicated in Ref. [1]. Thus, free from the problems involved in the calculations of Ref. [1], our procedure indeed validates the conclusions reported therein, furnishing support to the beautiful hypothesis put forth by Stanley's group [1,5].

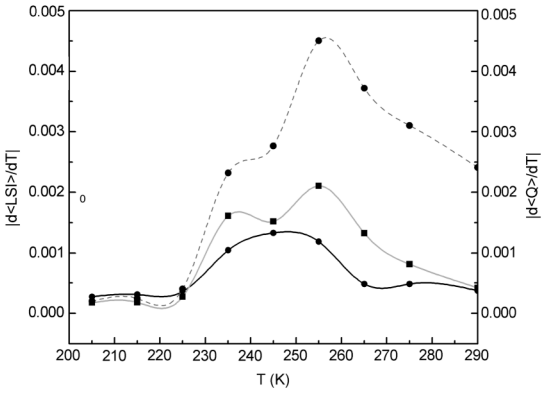

FIG. 1. $|d\langle \mathrm{LSI} \rangle / dT|$ for lysozyme hydration water: biological (solid black line) and bulk (solid gray line). The dashed gray line shows the corresponding curve for Q in bulk water, the only valid region for its calculation.

S. R. Accordino, D. C. Malaspina, J. A. Rodríguez Fris, and G. A. Appignanesi
Sección Fisicoquímica INQUISUR-UNS-CONICET and Departamento de Química
Universidad Nacional del Sur
Av. Alem 1253, 8000 Bahía Blanca, Argentina

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