

Simulating a Protein in a Non-Polar Solvent with Low Water Concentration

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Water plays a main role in the structural stability and function of proteins. In particular, the water molecules layer of a few Å wide, measured from the surface of a protein (the so called biological water), behaves quite different compared to the bulk water in terms of local order and dynamics. Amazing behaviors of enzymes like catalytic superactivity or sharp changes in the thermal stability have been ascribed to the use of different solvents. Much experimental work has been performed to study this matter with enzymes confined in reverse micelles or dispersed in organic solvents at low water concentration. A relationship between the flexibility, the thermal stability and the catalytic activity of proteins has been proposed on the base of such experiments. However, no information at molecular level exists for this kind of systems. In this work several molecular dynamics simulations of the Triosephosphate Isomerase of *Trypanosoma cruzi* (the parasite causing the Chagas' disease) in mixtures of decane with water at different relative concentrations are presented. The results show that the dynamic behavior of the protein does not change regardless the composition of the solvent if a thin layer of water is maintained around the protein. An analysis on the local structure of the protein, the redistribution and mobility of the solvent molecules, the intra and intermolecular hydrogen bonds (protein-protein and protein-solvent), the fluctuation of the protein residues through the trajectory, among other structural and dynamic properties is also presented. The methodology employed in this work could be useful for other macromolecules saving much computing time since simulations with non polar explicit solvents are much cheaper than simulations with explicit water.