Abstract for an Invited Paper
for the MAR10 Meeting of
The American Physical Society

Water in the Protein Interior

JAYENDRAN RASAIAH, University of Maine

Water expulsion from protein cores is a key step in protein folding, but there is experimental evidence for water in specific protein cavities. Calculations of the thermodynamics of transfer of bulk water into cavities, using MD simulations, have shown that filling of non-polar cavities with water is favored by dispersion forces at the walls of cavities large enough to contain a hydrogen-bonded cluster of at least three water molecules. The free energy of transfer is driven by the energy and not by the entropy. I will discuss the thermodynamics of water transfer into three different protein cavities: (a)a 4-water molecule cluster formed at high pressures in the large cavity of an L99A mutant of T4lysozyme studied previously by Collins et al (PNAS 102,16668-71 (2005)) (b) a 9-water molecule cluster formed at 92C in the largest cavity of the thermostable bacterial protein tetrabrachion predicted to dry at 110C and (c) water in the nonpolar cavity of interleukin 1-β. The presence of water in the first two proteins was determined in X-Ray crystallographic studies and is supported by negative free energies of transfer. X-Ray and NMR evidence for water in interleukin 1-β is less conclusive. Attempts to resolve this problem by calculating the transfer free energy of water from the bulk phase into the cavity will be described.