The Mechanisms of Hydration-Dependent Modulation of Protein Reactivity through Confinement and Addition of Osmolytes. Joel M. Friedman, Professor, Dept of Physiology and Biophysics, Albert Einstein College of Medicine, Bronx, New York 10461. Tel.718 430 3591. Email jfriedma@aecom.yu.edu

Understanding the molecular mechanisms through which environmental factors modulate protein reactivity and stability is a core issue for biophysics and biotechnology. Both reactivity and stability are directly connected to protein dynamics which in turn are strongly coupled to the dynamical properties of the surrounding water. We have adopted a two pronged approach to this issue. First we expose how different categories of functionally important dynamics are coupled to specific water dynamics. Second we expose how different environmental factors including confinement in either sol-gels or glassy matrices and addition of osmolytes perturb properties of water in the hydration layer that are linked to the modulation of protein dynamics. The framework for organizing and studying hydration-sensitive protein dynamics is the Protein Dynamic State Model(Samuni and others 2007a; Samuni and others 2007b) which is based on the concept of solvent slaved protein motions(Fenimore and others 2002; Fenimore and others 2004). Using this model we can directly monitor how specific categories of functionally important protein dynamics respond to environmentally-induced specific changes in hydration waters. In parallel we use a range of spectroscopic tools to probe the changes in the hydration waters as a function of these same environmental perturbations. These tools include: i) fluorescence from hemoglobin-associated pyranine (HPT) to monitor changes in water activity/mobility(Roche and others 2006); ii) fluorescence from BADAN coordinated to proteins and peptides to monitor changes in polarity within the hydration layer; and iii) Gd(+3) vibronic luminescence spectroscopy(Iben and others 1991; Roche and others 2006; Stavola and others 1981) to monitor changes in the hydrogen bonding between first and second shell hydration waters on the surface of calcium binding peptides, chelates and proteins.

References.

Fenimore PW, Frauenfelder H, McMahon BH, Parak FG. 2002. Slaving: solvent fluctuations dominate protein dynamics and functions. Proc Natl Acad Sci U S A 99(25):16047-51.

Fenimore PW, Frauenfelder H, McMahon BH, Young RD. 2004. Bulk-solvent and hydration-shell fluctuations, similar to alpha- and beta-fluctuations in glasses, control protein motions and functions. Proc Natl Acad Sci U S A 101(40):14408-13.

Iben IE, Stavola M, Macgregor RB, Zhang XY, Friedman JM. 1991. Gd3+ vibronic side band spectroscopy. New optical probe of Ca2+ binding sites applied to biological macromolecules. Biophys J 59(5):1040-9.

Roche CJ, Guo F, Friedman JM. 2006. Molecular Level Probing of Preferential Hydration and Its Modulation by Osmolytes through the Use of Pyranine Complexed to Hemoglobin. J Biol Chem 281(50):38757-68.

Samuni U, Dantsker D, Roche CJ, Friedman JM. 2007a. Ligand recombination and a hierarchy of solvent slaved dynamics: the origin of kinetic phases in hemeproteins. Gene 398(1-2):234-48.

Samuni U, Roche CJ, Dantsker D, Friedman JM. 2007b. Conformational dependence of hemoglobin reactivity under high viscosity conditions: the role of solvent slaved dynamics. J Am Chem Soc 129(42):12756-64.

Stavola M, Friedman AJ, Stepnoski RA, Sceats MG. 1981. Hydrogen bonding between solvation shells around Gd^{3+} from cooperative vibronic spectra. Chem. Phys. Lett. 80:192-194.