

CBIMMS Invited Seminar

“The Comprehensive Hydrophobic Effect in Protein Engineering and Function”

Dan W. Urry, Ph.D.

Chairman

Bioelastics Research, Ltd. (1272-0875-1)

2800 Milan Court, Suite 386

Birmingham, AL 35211-6918

Professor

Biological Process Technology Institute

240 Gortner Laboratory, 1479 Gortner Avenue,

College of Biological Sciences, University of Minnesota,

St. Paul, MN 55108

Friday, January 24, 2003

1:00 PM

203 Teer Building

ABSTRACT

The relevance of hydrophobic interactions in proteins has been appreciated since the classical 1959 paper of Walter Kauzmann in *Advances in Protein Chemistry*. Over the last three decades this realization of relevance has been expanded into the comprehensive hydrophobic effect by means of the study and further design of a family of elastic-contractile model proteins beginning with the sequence, (GVGVP)_n. These model proteins exhibit a phase separation of hydrophobic association that provides for contraction and for the set of energy conversions exhibited by proteins in biology that involve the six intensive variables of the free energy of mechanical force, pressure, temperature, chemical potential, electrochemical potential and electromagnetic radiation.

Calorimetric studies of a hydrophobic folding and assembly transition yield a plot of the sigmoidal relationship between the onset temperature of the inverse temperature (phase) transition, $T_{(b)}$, and the Gibbs free energy for hydrophobic association, ΔG_{HA} , as one embodiment of the comprehensive hydrophobic effect. The central part of the sigmoid is defined by the aliphatic side chains of the amino acid residues, L, I, V, P, A, and G with a slope of 80 cal/deg-mol(GXGVP), the low temperature segment defined by the aromatic hydrocarbons, W and F, with a slope of 14 cal/deg-mol(GXGVP), and a high temperature segment defined by the charged residues, K^+ and E^- , with a 7 cal/deg-mol(GXGVP) slope that arises from the competition for hydration between hydrophobic and charged residues called an apolar-polar repulsive free energy of hydration.

The above-described comprehensive hydrophobic effect is proposed to provide the dominant basis for the description of protein structure formation and function and for protein engineering. In short hydrophobic association occurs when there is too much hydrophobic hydration. Formation of charged species destroys hydrophobic hydration with the results of hydrophobic dissociation and increase in free energy of the charged species. The phosphate group is the most potent charged species for disrupting hydrophobic association and thereby can be most energized. One signature of this competition for hydration is a positive cooperativity that in the model proteins increases dramatically with increase in hydrophobicity. During the discussion this perspective can be discussed in terms of examples of protein function and dysfunction.