1992 PROGRAM

A.M.

9:00 **Registration and Coffee—Room 137, Chemistry-Physics Building**

9:30 **Welcome by Dr. Lee Magid, Vice President for Research and Graduate Studies, University of Kentucky, Room 139, Chemistry-Physics Building**

9:40 **Introductory Remarks—Dr. Mark Meier, University of Kentucky**

9:45 **Dr. Robert L. Baldwin, Stanford University "Pathways of Protein Folding"**

There is general agreement today that structured folding intermediates are populated in favorable conditions on the kinetic pathways of folding of small proteins. A principal tool for characterizing their structures is by pulse exchange with solvent ($^1H \rightarrow ^2H$) of the peptide NH protons in the polypeptide backbone, followed by 2D ^1H-NMR analysis after folding is complete. Results of this technique show that native-like secondary structures, both α-helices and β-sheets, are formed early in folding. Equilibrium "molten globule" intermediates are attractive subjects for study because it is possible to characterize in detail their structures and the interactions that determine these structures. Molten globule forms of different proteins exhibit a compact conformation, a high content of apparent secondary structure, and few if any fixed tertiary interactions. Two classes of molten globule forms are observed: structured molten globule intermediates, with α-helices at the same location as in the fully folded forms, and collapsed unfolded forms, which show no significant protection of any amide proton.

10:45 **Discussion**

10:50 **Dr. Barry Honig, Columbia University "Hydrophobic and Electrostatic Contributions to Protein Stability"**

The balance of forces that determine the denaturation free energies of globular proteins will be discussed. Our major conclusions are: a) Ionizable amino acids are slightly destabilizing but make only a marginal contribution to the net free energy balance. b) The fact that the enthalpies of unfolding are quite small despite experimental evidence for a large stabilizing enthalpy suggests that there must be a "missing" destabilizing enthalpic contribution. c) the hydrophobic effect is quite large and its magnitude points to the existence of a large compensating free energy contribution. d) Both b and c can be explained by the cost associated with "burying" polar groups (including those that form hydrogen bonds) in the polar interior. Finally, our breakdown of free energy contributions has led to the development of a relatively fast algorithm which distinguishes stable from unstable protein conformations.

11:50 **Discussion**

P.M.

12:15 **Buffet Lunch, Faculty Club (Please return card by April 9, 1992 for reservations. Cost $7.00 to be paid at registration.)**

1:30 **Dr. Kenneth Dill, University of California, San Francisco "The Stabilities and Kinetics of Protein Folding"**

We are interested in the forces that determine the relationship between the amino acid sequence of a protein and its structure and kinetics. Using simple models of short chains on lattices, we search conformational and sequence spaces to find the relationships between sequences and structures. We assume the dominant forces are hydrophobic interactions and conformational entropies. We find that some sequences collapse in poor solvents to compact conformations with hydrophobic cores, secondary structure, and few native states (often only one). A significant fraction of all possible sequences are relatively protein-like in water, i.e., compact and with much secondary structure. They fold along kinetic pathways, the cooperativity being due to conformational entropy. Interestingly we find that the problem of protein design (i.e. inverse folding: given a desired native structure, find a good sequence that folds to it) has much lower computational complexity than the protein folding problem, which is computationally difficult.

2:40 **Discussion**

2:50 **Dr. Saskia van der Vies, DuPont Central Research and Development "Molecular Chaperones and their Role in Protein Folding"**

Molecular chaperones are defined as a family of unrelated classes of protein that mediate the correct assembly of other polypeptides, but are not themselves components of the final functional structures. The concept of molecular chaperones suggests that interactions within and between polypeptides and other molecules need to be controlled to reduce the probability of formation of incorrect structures. This control is exerted by pre-existing proteins acting as chaperones to inhibit incorrect molecular interactions. It is argued that in the assembly process there is a certain probability that incorrect interactions will produce nonfunctional structures. Where this probability is small, self-assembly needs no assistance, but where it is high, molecular chaperones are essential to produce sufficient correct structures for cellular needs.

3:50 **Discussion**

4:00 **Mixer.**

Department of Chemistry
University of Kentucky
Lexington, Ky. 40506-0055

Eighteenth Annual
Symposium on

Chemistry & Molecular Biology

established in the memory of
Anna S. Naff

PROTEIN FOLDING

SPEAKERS

Robert L. Baldwin
Barry Honig
Kenneth Dill
Saskia van der Vies

Monday, April 13, 1992
Department of Chemistry
University of Kentucky
Lexington, Kentucky 40506-0055