

The Department of Chemical Engineering welcomes

# Carol Hall

North Carolina State University

March 11, 2008 - Warnock 102- 10:45 A.M.

Presenting a lecture entitled

## *“Computer Simulation of Protein Aggregation”*

### **ABSTRACT:**

Protein aggregation is a cause or associated symptom of a number of neurodegenerative diseases including Alzheimer's, Parkinson's and prion disease. It can also interfere with the recovery of recombinant proteins during processing and can limit the stability of protein-based drugs during their packaging, shipping, storage and administration. We are engaged in a computational study aimed at understanding the basic physical principles that govern the competition between protein aggregation and protein folding. A novel off-lattice, intermediate-resolution protein model, PRIME, has been developed that is simple enough to allow the simulation of multi-protein systems over relatively long time scales, yet contains enough genuine protein-like character to mimic real protein dynamics when used in conjunction with constant-temperature discontinuous molecular dynamics, a fast alternative to conventional molecular dynamics. We are using PRIME to investigate the formation and properties of fibrillar protein aggregates, the structures that have been implicated in the pathology of many neurodegenerative diseases including Alzheimer's and Parkinson's diseases. Simulations have been performed on systems containing 12 to 96 model polyalanine peptides, each containing 16 residues. Polyalanine was chosen for study because synthetic polyalanine-based peptides, which form  $\alpha$ -helical structures at low temperatures and low peptide concentrations, have been found to form  $\beta$ -sheet complexes (fibrils) in vitro at high temperatures and high peptide concentrations. In our simulations we find that at a low peptide concentration, a system of peptides initially in the random coil state forms  $\alpha$ -helices at low temperatures and assembles into large  $\beta$ -sheet structures at high temperatures. When the concentration is increased at high temperatures, the system again forms  $\beta$ -sheets but these assemble into fibrils as the simulation progresses. The effect of temperature, peptide concentration and chain length on the kinetics and thermodynamics of fibril formation is being explored. Movies of the simulation will be shown.

### *Short Biography*

Professor Carol K. Hall is Camille Dreyfus Distinguished University Professor of Chemical and Biomolecular Engineering at North Carolina State University. She received her B.A. in physics from Cornell University and her Ph.D. in physics from the State University of New York at Stony Brook. After postdoctoral training in the Chemistry Department at Cornell and a brief stint as an economic modeler at Bell Laboratories, she joined the Chemical Engineering Department at Princeton University in 1977 as one of the first women to be appointed to a chemical engineering faculty in the U.S. In 1985 she joined the Chemical Engineering Department at North Carolina State University. Hall's research focuses on applying statistical thermodynamics and molecular-level computer simulation to topics of chemical, biological or engineering interest involving macromolecules or complex fluids. Current research activities include modeling of: polymer adsorption on heterogeneous surfaces, self assembly of dipolar colloidal particles, self assembly of nanoparticles for the delivery of cancer drugs, solid-fluid phase equilibria, hybridization of DNA on microarrays, and the formation of fibrils and other molecular aggregates of peptides and proteins. She is the author of over 180 publications and was elected to the National Academy of Engineering in 2005.

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