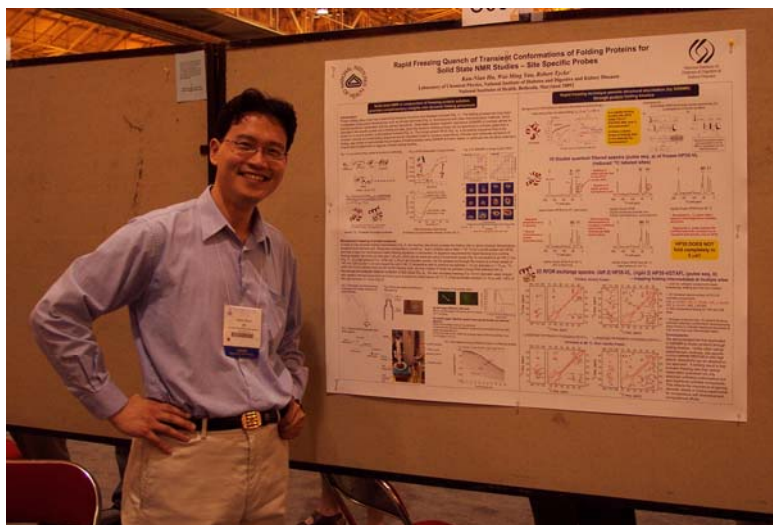


# SPECIAL SEMINAR

Date: Thursday  
December 10, 2009

Time: 3:30 pm  
Room 1315



**Dr. Kan-Nian Hu**

Laboratory of Chemical Physics, NIH

## **“Site-specific Structural Characterization of Protein Folding by Solid State NMR”**

Molecular structural information in solids can be obtained using a variety of solid state NMR (SSNMR) techniques under fast sample rotation at the magic angle. I will describe two unprecedented SSNMR applications to protein folding problems: quantitative conformational studies of unfolded proteins in an equilibrium state and observations of kinetic intermediates from nonequilibrium folding processes. In the equilibrium studies, quantitative torsion angle measurements on the model protein HP35 in frozen solutions reveal an unfolding “pathway” under chemical denaturation, in which alpha-helical segments convert to extended conformations and then to polyproline II conformations. In the nonequilibrium studies, transient states through HP35 folding were trapped using a submillisecond freezing apparatus; subsequent 1D and 2D SSNMR spectra indicated ‘non-cooperative’ folding with site-dependent rates toward the native conformations. Successful applications of SSNMR to protein folding studies rely on high sensitivity which can be significantly enhanced by dynamic nuclear polarization. The enhancements of NMR signals result from transferring electron spin polarization to nuclear spins under microwave irradiation. High transfer efficiency at strong magnetic fields ( $>5$  T) was achieved using biradicals (molecularly tethered nitroxides), generating an enhancement of  $\sim 300$  times.