Protein Motions in Catalysis, Binding, and Folding

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NMR spectroscopy is a powerful approach for characterizing protein conformational dynamics on multiple time scales with applications to folding, binding, and catalysis. These applications will be discussed through examples. The villin headpiece domain HP67 is a model for subglobal protein folding. At pH 7.0, the N-terminal subdomain of HP67 exists in equilibrium between folded (98.5%) and unfolded (1.5%) states while the C-terminal subdomain remains stably folded. ATP-binding cassette (ABC) transporters move solutes across membranes and are associated with diseases including cystic fibrosis and multi-drug resistance. Solution NMR spectroscopy of a soluble model ABC, *Methanococcus jannaschii* protein MJ1267, shows that ADP-Mg binding alters the flexibilities of key ABC motifs and induces allosteric changes in conformational dynamics more that 30 Å away from the ATPase active site. Ribonuclease HI enzymes from the mesophilic bacterium *Escherichia coli* and the thermophilic bacterium *Thermus thermophilus* are highly homologous, but differ greatly in thermodynamic stability and catalytic activity. Nuclear spin relaxation measurements identify conformational dynamics on picosecond-nanosecond and microsecond-millisecond time scales that may contribute to these differences.