

## W0165

**Chain Collapse and Hydrogen Bond Formation in Protein Folding.** Tobin R. Sosnick<sup>1,2</sup>, Jaby Jacob<sup>1,3</sup>, Bryan Krantz<sup>1</sup>, Robin S. Dothager<sup>1</sup>, & P. Thiyagarajan<sup>3</sup>, <sup>1</sup>Dept. of Biochemistry and Molecular Biology, <sup>2</sup>Inst. for Biophysical Dynamics, Univ. of Chicago, Chicago, IL 60637, <sup>3</sup>Intense Pulsed Neutron Source, Argonne National Laboratory, Argonne, IL 60439.

Two fundamental events in protein folding are collapse and hydrogen bond formation. We have measured these events using synchrotron-based small-angle X-ray scattering, circular dichroism and kinetic amide isotope effects. Even upon a jump to strongly native conditions, the proteins ubiquitin and ctAcP do not contract or form secondary structure prior to the major folding event. Hence, collapse and secondary structure formation are not energetically downhill processes even under aqueous conditions for these proteins. Using amide isotope effects, we find that hydrophobic association cannot be divorced from helix formation in the transition state. Therefore, folding models describing an incremental build-up of structure are more consistent than are models that posit the extensive formation of one quantity before the other.

Jacob, J., et al. (2004). "Early Collapse is not an Obligate Step in Protein Folding." J. Mol. Biol. 338(2): 369-82.

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