

## W0104

**SANS Reveals that Protein Kinase A RI $\alpha$  Dimer Undergoes a Large Conformational Change upon Binding C Subunits.** W.T. Heller<sup>1</sup>, D. Vigil<sup>2</sup>, S. Brown<sup>2</sup>, D.K. Blumenthal<sup>3</sup>, S.S. Taylor<sup>2</sup>, J. Trehwella<sup>4</sup>, <sup>1</sup>Center for Structural Molecular Biology, ORNL, Oak Ridge, TN 37831, <sup>2</sup>Dept. of Chemistry & Biochemistry & HHMI, Univ. of California, San Diego, La Jolla, CA 92037, <sup>3</sup>Depts. of Pharmacology & Toxicology, & Biochemistry, Univ. of Utah, Salt Lake City, UT 84112, <sup>4</sup>Bioscience Div., LANL, Los Alamos, NM 87545.

Small-angle neutron scattering with contrast variation was used to study the type I $\alpha$  isoform of the cAMP-dependent protein kinase A (PKA) holoenzyme, which consists of a pair of catalytic (C) subunits bound to a regulatory (R) subunit dimer. Information on the shapes and dispositions of the C subunits and deuterated R subunit dimer within the holoenzyme was derived from the data. The study demonstrates that a large conformational change occurs within the R subunit dimer upon binding the C subunits. The results infer that inhibition of C subunit activity involves both local conformational changes in the cAMP-binding domains and large changes in the linker region of the R subunit dimer. A model of the holoenzyme was constructed to fit the SANS data using available structures of the subunits and domains. The result is a flattened V shape with the R subunit dimerization domain at the point and the cAMP-binding domains of the R and C subunits at the ends.