Probing Protein Ensembles and Functional Intermediates with X-ray Solution Scattering

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X-ray solution scattering in the small angle (SAXS) and wide-angle (WAXS) regimes is making a substantial impact on our understanding of the way proteins move in solution. Proteins in solution exhibit an ensemble of structures which can be narrowly limited to those accessible through small thermal fluctuations or, alternatively, may include structurally and functionally distinct conformations. The conformations in solution may include intermediates in catalytic transformations; or structural forms imposed by regulatory interactions. Collection of data under conditions in which the relative abundances of structural variants are different provides the potential for teasing out structural information on each variant. For instance, we have shown that the scattering pattern from adenylate kinase undergoing catalytic cycling cannot be reconstructed as a linear sum of patterns from proteins in the endstates of this reaction. This implies the existence of intermediate states of sufficient abundance and lifetime to provide a detectable signal. To what extent will this signal allow characterization of the intermediates? We are currently pursuing a number of computational approaches to answering this question and developing strategies for generating structural information about important functional intermediates.