

## Microsymposium

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*SAXS, WAXS, MD, Protein fluctuations and function*

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Conformational mobility is essential to many protein functions and design of therapies for a broad spectrum of human diseases depends on a deep understanding the linkage between protein structure, intramolecular motions and function. Methods for screening small molecules and mutations that alter fluctuations are essential for improved understanding of this linkage. To what extent do changes in intramolecular motions lead to changes in function? To address this question, we are using a combination of wide-angle x-ray solution scattering (WAXS) and molecular dynamics (MD) to generate novel insights into the magnitude, form and functional consequences of intramolecular motions of proteins in solution. WAXS has proven unexpectedly sensitive to the intramolecular motions of proteins in solution and can detect changes in flexibility generated by single amino acid replacements or binding of small molecule ligands. Here we formulate the effect of structural fluctuations on WAXS data in such a way as to make possible direct experimental assessment of the range of motion that proteins explore in solution. The approach differs from other strategies by treating it as an inverse source problem, deriving flexibility parameters directly from data rather than from an ensemble of structures generated to predict the data.

**Keywords:** WAXS, protein fluctuations, protein function