MS28.O06

X-ray scattering methods for accurate analyses of flexible complexes

R. Rambo[1], G. Hura[1], M. Hammel[1], J. Tainer[1,2]

[1]Lawrence Berkeley National Laboratory, Life Sciences Division, Berkeley, CA, [2]Department of Integrative Structural and Computational Biology, The Scripps Research Institute, La Jolla, CA

A grand challenge for structural biology is to efficiently inform macromolecular functions that involve flexible or unstructured regions and require multiple conformational states including membrane proteins and protein-nucleic acid complexes. Small angle X-ray scattering (SAXS) can probe at resolutions sufficient to distinguish conformational states, characterize flexible macromolecules, and screen in high-throughput under most solution conditions. However, methods for analyzing SAXS data and models have restricted progress. We are therefore developing SAXS methods that provide high-throughput, quantitative and superposition-independent evaluation of solution-state conformations and quantitatively define flexibility and disorder. The SIBYLS beamline provides hardware and software to integrate SAXS and crystal structure results. Our SAXS methods aim to improve crystallization and interpretation of crystal structures and NMR structure quality. We have invented a statistically robust method for assessing model-data agreements (chi-square free) akin to cross-validation. We also developed a metric and method for rapid quantitative and comprehensive assessment of molecular similarity suitable to examine functionally important conformational changes. To extend SAXS analysis to low concentrations and complex mixtures, we are developing SAXS with gold nano-crystal labels to enable examination of protein-induced DNA distortions along pathways key to the DNA repair, replication, transcription, and packaging. Collective results suggest SAXS can provide accurate shapes, assembly states, and comprehensive conformations of flexible complexes in solution that inform biology in fundamental ways.

[1] *G. Hura, H. Budworth, K. Dyer, et al. Nature Methods, 2013, 10, 453-454,* ***[2]*** *R. Rambo, J. Tainer, Nature, 2013, 496, 477-481,* ***[3]*** *G. Hura, C-L.Tsai, S. Claridge, et al., Proc Natl Acad Sci U S A 110: 17308-17313.*

Keywords: X-ray Scattering