Poster Presentation

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Analysis of macromolecular flexibility in solution by combining SAXS with MX

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Proteins containing significant disordered regions are difficult for crystallization. Consequently, individual structured domains or subunits are often crystallized to determine their high resolution structures. These structures, not containing the disordered parts, are available from the protein databases. Small-Angle X-ray Scattering (SAXS) in solution is a complementary structural technique offering the possibility to characterize full length proteins including inter-domain disordered regions. Modern approaches for the analysis of the SAXS data from flexible systems utilize the representation of the system as ensembles of co-existing structures (e.g. Ensemble Optimization Method (EOM), Bernado et al. 2007). Here, the high resolution models of the domains are employed as rigid bodies together with the flexible parts represented by chains of dummy residues in order to construct models covering the configurational space of the full length proteins. Until now, the use of the ensemble approach was mostly limited to relatively simple cases like single chain proteins. We present improvements for the SAXS modeling including the possibilities to characterize flexible particles for complicated scenarios, in particular, for the cases when disorder comes in combination with point group symmetry. A new strategy for missing sections generation allows a rapid and accurate construction of the full length protein. Further, two metrics, Rflex and Rrat, are introduced for a quantitative assessment of the EOM results. Rflex is used as a measure of flexibility – based on the concept of entropy (information communication) – whereas Rrat is employed as a control parameter to detect potential artifacts. These developments implemented in the new version EOM 2.0 further promote the hybrid approach synergistically employing SAXS and MX in the analysis of complicated flexible systems. The capacity of the enhanced method will be illustrated by practical examples.

[1] *Bernado, P., E. Mylonas, M. V. Petoukhov, et al, 2007. "Structural characterization of flexible proteins using small-angle X-ray scattering." J Am Chem Soc no. 129 (17):5656-64. doi: 10.1021/ja069124n*

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