

Small-angle x-ray scattering for biological macromolecules

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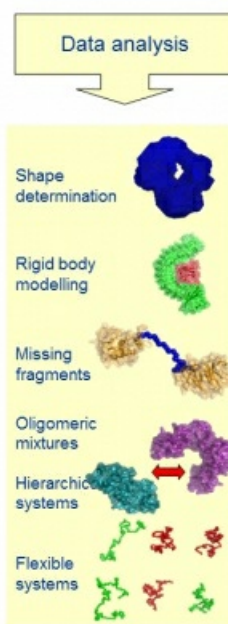
Small-angle X-ray scattering (SAXS) is an established method to study the overall structure of biological macromolecules and complexes in solution, allowing one to also rapidly analyze structural changes in response to variations in external conditions [1]. The last decade saw a major progress both in data analysis methods and instrumentation, and these developments significantly enhanced the possibilities of SAXS and quality of structural models provided by the method. Large scale structural studies in molecular biology are now possible on high brilliance synchrotrons thanks to the automation of the experiment, data processing and interpretation. Importantly, SAXS is directly applicable to medical formulations raising the popularity of the technique for pharmaceutical industry. Hybrid applications are gaining momentum where SAXS is combined with the high resolution methods like crystallography, NMR and electron microscopy, but also with computational, biophysical and biochemical techniques. In these applications, rapid validation of predicted or experimentally obtained high resolution models in solution, identification of biologically active oligomers and addition of missing fragments to high resolution models are possible. The quaternary structure of macromolecular complexes, can be modelled by rigid body movements/rotations of individual subunits, but, very importantly, SAXS can also account for potential flexibility of the objects. The method can help visualizing flexible portions of the structures, not seen by the high resolution methods, and also characterize (partially) disordered macromolecules like intrinsically unfolded proteins. SAXS is very effective in quantitative analysis of equilibrium mixtures of states in combination with on-line size-exclusion chromatography and in time-resolved studies of processes. The broad spectrum of the structural information that can be gained about about macromolecules in solution is presented in Figure 1. In the talk, main principles and recent developments in SAXS will be presented and illustrated by examples of application to various macromolecular systems. The perspectives of the synergistic use of SAXS for hybrid structural modelling using other methods will be discussed.

[1] Svergun, D. I., Koch, M. H. J., Timmins, P. A., and May, R. P. (2013) Small angle x-ray and neutron scattering from solutions of biological macromolecules, Oxford University Press. 358 pp.

SAXS for biological macromolecules provides

- overall particle shape;
- domain organization and quaternary structure;
- conformational changes (e.g. on ligand binding);
- complex formation;
- oligomerization behavior;
- influence of buffer conditions/temperature;
- assembly and folding states;
- flexibility of fragments or entire structures;
- solubility and interparticle interactions;
- temporal stability;

and much more



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