

Solution X-ray Scattering of Biological Macromolecules

Is it More Than Just Looking Behind the Beamstop?

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Knowledge of the size and shape of a biological macromolecule is one of the key stages of getting the picture of its functioning. There are a variety of techniques available that provide information at various degrees of reliability and detail. Protein crystallography and multidimensional NMR in solution are the main experimental methods that provide models of biological macromolecules on atomic scale. Three dimensional image reconstructions from electron micrographs is a valuable tool applied routinely in structural biology, particularly for examining large, mostly highly symmetrical molecular assemblies. Small-angle X-ray scattering (or solution X-ray scattering) is an additional promising method to investigate the structure of biological macromolecules in solution. Owing to its dependence on geometric shape, scattering data are sensitive to domain orientations and therefore to conformational changes and/or flexibility as well as to molecular associations in solution. The technique is often most powerful when used as a complementary tool with other structural techniques and may gain in interest due to the major challenges in the post-genome era.

Recent developments of shape restoration from scattering profiles allow the extraction of more meaningful biological information (contrary to only calculating Guinier radii or distance distribution functions). This talk will concentrate on the use of the scattering technique by combining data interpretation with results from other techniques (CD, EXAFS, NMR, PX and computational tools) so as to enhance the structural information. Examples for the following aspects will be included:

Study of multisubunit proteins (or protein complexes) of which only fragments (or subunits) have been successfully determined at atomic scale (by NMR or PX). Positioning and arrangement of these fragments within the overall boundary are feasible in analogy to recent strategies in electron microscopy.

Even the low-resolution shape of biomolecules in the absence of any atomic information can be of significant interest. The presence or absence of substrate or cofactors can play an important role in functionally important structural transitions. Alterations of form are often achieved through “lock-and-key” interactions of signalling and receptor molecules.

In conjunction with secondary structure analysis, the scattering technique can contribute meaningfully to an understanding of protein stability by providing structural information instigated by mutational studies.

With regards to structure prediction a molecular shape along with a well defined scattering profile of a protein with unknown structure offers significant experimental constraints which may be used to distinguish among alternative structural models

either predicted by computational efforts or by comparison with known structures in the database.