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## **AB-INITIO METHODS FOR MEMBRANE PROTEIN STRUCTURE RECOVERY FROM SMALL-ANGLE NEUTRON SCATTERING DATA**

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The study of membrane protein structure by high resolution techniques has proven to be quite challenging and only recently with the development of modern cryo-electron microscopy methods, associated difficulties seem to become partially addressed. Different approaches have been developed for solubilizing membrane proteins while at the same time keeping them folded and active involving the use of detergents that shield the hydrophobic transmembrane surface of the protein which otherwise leads to the aggregation of the protein in solution.

Success in keeping membrane proteins stable in solution permits the use of small-angle scattering (SAS) for the investigation of the protein/detergent complexes. However till today only a limited number of published works have attempted the use of SAS for related studies mainly due to the lack of theoretical tools for the treatment of scattering data for these particular systems.

Recently we have presented an ab-initio method [Biophys. J. 113, 2373] based on multi-contrast SANS for the determination of the low-resolution structure of detergent-solubilized membrane proteins. It has been shown that two contrast SANS measurements appear to provide enough information for obtaining reliable shape reconstructions. In this contribution we aim to review the methodological aspects of this approach, showcase aspects of its application in a range of different protein / detergent systems and also discuss its complementarity to other methods.

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