MS03 - Combining methods in macromolecular structure determination, including special conditions MX

Chairs: Dr. Martin Walsh, Dr. Victor Lamzin

MS03-P01

BioSAXS at ESRF: The solution scattering Beamline BM29

Martha Brennich[1], Pernot Petra[2], Mark Tully[2]

1. EMBL Grenoble, Grenoble, France
2. ESRF, Grenoble, France

email: brennich@embl.fr

Small angle X-ray scattering (SAXS) is ideally suited to study the structure and structural changes of biological macromolecules in solution. The last decade has seen a surge of technological and conceptual development in small angle scattering that increased the importance of SAXS in the toolkit of structural biology. At the ESRF, the BioSAXS beamline BM29 is dedicated to solution scattering and optimized for routine measurements of biological macromolecules [1]. It aims at facilitating SAS for non-experts by providing easy and rapid access as well as reducing the effort to collect and assess data.

BM29 primarily offers two data collection modes: BioSAXS with a robotic liquid handling sample changer (SC) and BioSAXS with online size-exclusion chromatography (SEC). Both modes are highly automated and switching between modes is instantaneous. In both modes, primary data processing from azimuthal integration to determination of SAS invariants is completely automated and provides immediate feedback. The electronic logbook ISPyB collects all data and associates relevant meta-data. It assists the users in designing their experiments, in associating data with meta-data and in the primary assessment of data quality.

Here the experimental setups available on BM29 will be described together with the various examples of the BioSAXS data obtained. Recent examples of BM29 research, including the integration of microfluidics systems and online ion-exchange chromatography as well as the possibilities for new experiments in BioSAXS.

References:

[1] P. Pernot et al., J. Syn. Rad. 20 (2013) 660-664.

Keywords: SAXS, complementary techniques, instrumentation

MS03-P02

Flexible Fitting of Macromolecular Structures into Small-Angle Scattering (SAXS and SANS) Profiles

Sergei Grudinin[1], Alexandre Hoffmann[1], Anne Martel[2], Sylvain Prévost[2]

1. Univ. Grenoble Alpes, Inria, CNRS, Grenoble INP, LJK, Grenoble, France
2. Institut Laue-Langevin, Grenoble, France

email: sergei.grudinin@inria.fr

Large macromolecular machines, such as proteins and their complexes, are typically very flexible at physiological conditions, and this flexibility is important for their structure and function. Computationally, this flexibility can be approximated with just a few collective coordinates, which can be computed e.g. using the Normal Mode Analysis (NMA). NMA determines low-frequency motions at a very low computational cost and these are particularly interesting to the structural biology community because they are commonly assumed to give insight into protein function and dynamics.

We have recently introduced a new conceptually simple and computationally efficient method for *nonlinear* normal mode analysis called NOLB [1]. Overall, the NOLB method produces structures with a better local geometry compared to the standard techniques, especially at large deformation amplitudes, and it also predicts better structural transitions between conformational states of macromolecules. Finally, the NOLB method is scalable and robust, it typically runs at interactive time rates, and can be applied to very large molecular systems, such as ribosomes.

NMA can be combined with other computational techniques for various applications. I will specifically highlight our very recent flexible fitting methods for small-angle X-ray (SAXS) and neutron (SANS) profiles. This was made possible thanks to our SAXS and SANS packages called Pepsi-SAXS [2], and Pepsi-SANS [3], respectively. Pepsi-SAXS is a novel and very efficient method that computes SAXS profiles from atomistic models. It is based on the multipole expansion scheme and is significantly faster with the same level of precision compared to CRYSOL, FoXS and other methods. Similarly, Pepsi-SANS is our novel approach for computing SANS profiles. Recently, we designed a computational scheme that uses the NOLB nonlinear modes as a low-dimensional representation of the protein motion subspace and optimizes protein structures guided by the SAXS and SANS profiles. Overall, this scheme allows to significantly improve the goodness of fit to experimental profiles, has a very reasonable computational time, and produces plausible structural structural atomistic-level predictions.

References:

[1] Hoffmann, A. & Grudinin, S. (2017). J. Chem. Theory Comput. 13, 2123 – 2134. For more information https://team.inria.fr/nano-d/software/nolb-normal-modes/

[2] Grudinin, S. et al. (2017). Acta Cryst. D, D73, 449 – 464. For more information https://team.inria.fr/nano-d/software/pepsi-saxs/

[3] Grudinin, S. et al. (2018). In preparation. For more information https://team.inria.fr/nano-d/software/pepsi-sans/

Keywords: SAXS,SANS,NMA