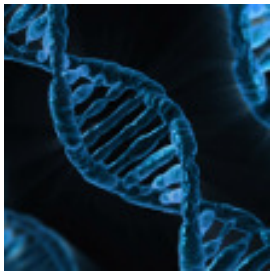

Contribution ID : **45** Type : **Oral presentation**

Contributed talk 3 - Efficient Prediction of Macromolecular Flexibility and its Applications to Small-Angle Scattering

Monday, 4 June 2018 17:05 (20)

Large macromolecular machines, such as proteins and their complexes, are typically very flexible at physiological conditions. Computationally, this flexibility can be approximated with just a few collective molecular motions, computed e.g. using the Normal Mode Analysis (NMA). NMA determines low-frequency motions at a very low cost and these are particularly interesting to the structural biology community.

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. 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 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]. Pepsi-SAXS is a novel and very efficient method that calculates 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. Recently, we designed a computational scheme that uses the NOLB modes as a low-dimensional representation of the protein motion subspace and optimises protein structures guided by the SAXS and SANS profiles. Overall, this scheme allows to significantly improve the goodness of fit to experimental profiles in a very reasonable computational time.

[1] https://team.inria.fr/nano-d/software/nolb-normal-modes/
[2] https://team.inria.fr/nano-d/software/pepsi-saxs/
[3] https://team.inria.fr/nano-d/software/pepsi-sans/

Primary author(s) : GRUDININ, Sergei (Inria / CNRS)

Presenter(s) : GRUDININ, Sergei (Inria / CNRS)

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