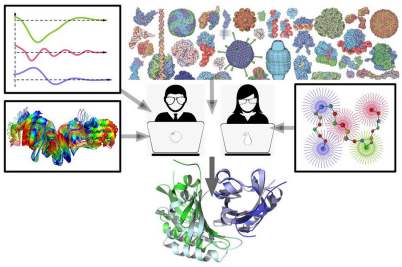

Contribution ID: **5** Type: **Poster**

Usage of the chemical-crosslink experiment data in a protein structure modeling

Prediction of protein structures is one of the most important problems of current structural bioinformatics. Many proteins in living organisms form multimeric structures or are involved in the complexes with other biomacromolecules, such as other proteins or small ligands. Prediction of protein structure in the monomeric state is already very challenging and therefore the structures of their complexes are even more tricky to determine. There are several experimental techniques whose results can assist in protein structure prediction. For example, chemical crosslinking/mass spectrometry (XL-MS) and small-angle X-ray scattering (SAXS) experiments provide solution data describing approximated shape of molecular system. Such data can be used as a potential term and be included in the energy function in molecular simulations or as a scoring function. Big advantages of SAXS and XL/MS, comparing to the crystallography and NMR measurements, are that they are not that demanding in terms of time, money and sample specificity requirements. This study presents our progress in integrating the XL/MS data in protein structure determination by the probability estimation and rigid-body docking.

In our approach, we integrated information from crosslink experiments to a combination of a statistical potentials derived based on the distance distributions from reference 1 (residue-specific XL, big-X) or based on the calculated actual distance distributions of Cα atoms in experimental structures for restraints provided by previous CASP experiments (CASP11-13, residue-non-specific XL, small-x)2. Depending on the distribution, the data were fitted either using a single Gaussian or a sum of two Gaussians. The function parameters were obtained by a scaled Levenberg-Marquardt fitting algorithm of the specific distance distributions of each XL type. We made a Boltzmann-like hypothesis and considered that there is a pseudo-potential associated with each of the XL constraints, whose value is given by the logarithm of the probability of a certain Cα-Cα distance. Finally, we combined these potentials with a rigid-body docking methods and can conclude that XL-MS data is very useful in the prediction of protein complexes, if the number of false distance restraints is not very high.

Leitner A, Joachimiak LA, Unverdorben P, et al. Chemical cross- linking/mass spectrometry targeting acidic residues in proteins and protein complexes. P Natl Acad Sci U S A. 2014;111(26):9455-9460.

Kryshtafovych, A, Schwede, T, Topf, M, Fidelis, K, Moult, J. Critical assessment of methods of protein structure prediction (CASP)—Round XIII. Proteins. 2019; 87: 1011– 1020.

Primary authors: Dr KARCZYNSKA, Agnieszka (Univ. Grenoble Alpes, Inria, CNRS, Grenoble INP, LJK, 38000 Grenoble, France); GRUDININ, Sergei

Presenter: Dr KARCZYNSKA, Agnieszka (Univ. Grenoble Alpes, Inria, CNRS, Grenoble INP, LJK, 38000 Grenoble, France)