Poster Presentation

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Stock-based detection of biological assemblies in PISA software

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PISA (Protein Interfaces, Surfaces and Assemblies) software from CCP4 remains a popular computational tool for the prediction of biological assemblies (complexes) from macromolecular crystallography data [1]. The method is based on the estimation of the dissociation free energy of predicted complexes, and reaches 90-95% correct results for the current content of the PDB. It was found that the probability of getting wrong predictions grows exponentially with the decrease in the dissociation free energy, reaching over 50% for complexes bound as weakly as few kcal/mol [2]. Among few reasons for this behaviour [2] is the fact that oligomeric state of weakly bound complexes is expected to vary in dependence of chemical environment, in particular, protein concentration. It has been noticed in multiple use cases, that a considerable share of disagreements between predicted and measured oligomeric states belongs to situations where the relation between experimental conditions and protein's working environment in the cell is unclear. We report further advance in PISA software, which allows a researcher to model concentration dependence of predicted oligomeric states, and by this to improve interpretation of both experiments and computations in the biologically interesting case of weakly bound macromolecular associations. The new PISA is based on the concept of assembly stock, which represents an equilibrated set of of all complexes, compatible with crystal packing. Graphical representation of concentration (or newly introduced aggregation index) profiles of stock's components allows a user to quickly identify the most probable oligomeric state. This is vastly superior over the previous way of analysis, based on the interpretation of bare figures for dissociation free energies. Other developments include advanced graphical interface and multi-parametric interaction radar, which indicates the likelihood for interface to represent a biologically-relevant interaction.

[1] *E. Krissinel, K. Henrick, J Mol Biol 2007, 372, 774-797,* ***[2]*** *E. Krissinel, J Comp Chem 2009, 31, 133-143*

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