7. STRUCTURAL BIOINFORMATICS & PROTEOMICS

ZOLTÁN GÁSPÁRI, Associate Professor; ANNAMÁRIA F. ÁNGYÁN, Postdoctoral researcher
Graduate students: DÁNIEL DUDOLA, ANNAMÁRIA KISS-TÓTH, ANETT KORAI, BERTALAN KOVÁCS

The two main projects in the laboratory are

- Generation and analysis of dynamic protein conformational ensembles
- Experimental investigations of selected proteins of the postsynaptic density

Proteins are the most versatile biomolecules responsible for a number of tasks on living organisms. Their efficiency is conventionally attributed to their geometric and physicochemical complementarity with their partners that can be e.g. other proteins, nucleic acids or small molecules like drugs. However, proteins are not static entities but display dynamics on time scales spanning 14 orders of magnitude. In the last decade, the exact mode of action is linked to internal dynamics and its changes for an increasing number of proteins. In spite of this, atomic-level descriptions of experimentally determined internal protein motions are not routinely generated and used for explaining biological phenomena. Our aim is to use and further develop an approach that synergistically puts together conventional molecular dynamics calculations and restraints determined with experimental techniques, primarily NMR spectroscopy. The calculations result in an ensemble of conformations that reflect the internal dynamics of the molecule on a given time scale and are in agreement with experiments. Such ensembles can be used to investigate the role of dynamics in partner molecule binding, catalysis and regulation and are expected to lead to a deeper understanding of the nature of intra- and intermolecular interactions. Molecules studied at the moment include the antifungal protein PAF with potential therapeutic value, a DNA polymerase involved in DNA repair the small prolyl isomerase parvulin and selected domains of proteins of the postsynaptic density.

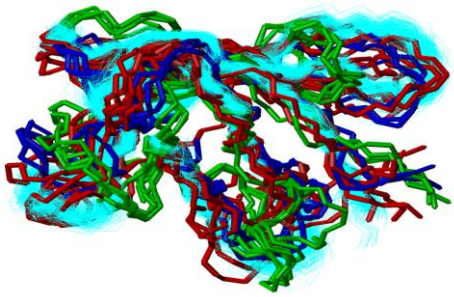

Fig. 1 *Structural ensembles of different conformational states of the antifungal protein PAF. Cyan: native-state observable ensemble representing ps-ns timescale dynamics, blue: conformers characteristic at 265 K, red: conformers characteristic at 344 K, green: normally "invisible" conformers in exchange with the observable state at 273 K*

In 2015 we have completed the setup of a novel biotechnology laboratory where we aim to initiate experimental investigation of selected proteins of the postsynaptic density. We are particularly interested in the detailed organization of the interaction network between these proteins.

Fig. 2 *Views of the interior of the recently equipeed biotechnology laboratory at PPCU FIT.*

REFERENCES

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