Reg. No: 2015/18/A/ST4/00270; Principal Investigator: prof. dr hab. Wiktor Adam Koźmiński

Nuclear Magnetic Resonance (NMR) spectroscopy is widely used technique for investigation of molecular properties based on the interaction of external magnetic field with nuclear magnetic moments. The key advantage of NMR is the ability to describe at the atomic level not only the molecular structure, but at the same time, their dynamics and interactions. The range of applications vary from small molecules to complex biomolecules like proteins and nucleic acids, and from the solutions to solid state. Therefore, NMR spectroscopy is considered as one of basic tools in contemporary chemistry and molecular biology.

The first aim of the project is the development of new methods of NMR spectroscopy for the investigation of proteins in solution. The realization of the project will require the development, the implementation, and the optimization of new techniques (pulse sequences), as well as improvement of existing methods. The progress in the field of experimental methods will be associated with, performed in parallel, development of processing algorithms and software necessary for acquisition and interpretation of NMR data sets. The planned research work refers to the fundamental problems of NMR spectroscopy, like sensitivity, signal sampling, and effective reconstruction of the spectra. The proposed solutions will improve spectra quality by increase of sensitivity, resolution, and reduction of artefacts arising due to employment of non-uniform sampling (NUS). On the other hand, the new approaches for the determination of the physical quantities as for example cross-correlated relaxation (CCR) rates, are proposed.

The second part of the project, is focused on the application of new methods of NMR spectroscopy for the investigation of intrinsically disordered proteins (IDP). Contrary to globular protein, IDPs lack the defined tertiary structure, and are abundantly present in complex living organisms. They play many important functions including signaling. Due to dynamically disordered structure, NMR spectra of IDPs feature low signal dispersion which frequently causes signal overlap. The solution of this problem is possible by the application of high- (more than 4) dimensional NMR spectroscopy. The molecular structure of IDPs can be described as a structural propensity or a residual structure. The aim of the project is the development and the application of the methodology of determination of the structural propensity in IDP molecules employing CCR experiments. The experiments will be performed at ambient as well at high pressure (up to 3 kbar) conditions. This will enable to observe the structural changes revealed during folding-unfolding processes. The new information regarding IDPs are crucial for the understanding of mechanisms of many diseases, like cancer and many neurodegenerative diseases.

The main motivation of the whole project is the new insight, at the atomic level, into a behavior and properties of protein molecules. This knowledge is essential for a better understanding of processes occurring in living organisms, and in the future it should enable the development of new treatment therapies and prevention of diseases that afflict the humanity.