

TITLE OF RESEARCH TOPIC: Evaluation of thermally accessible conformational states of proteins in solution**Summary:**

Proteins can undergo functionally relevant conformational transitions on a wide range of scales in time and space, ranging from displacements of side-chain rotamers by a few angstroms, to larger motions involving flexible stretches of amino acids, to broad subunit rotations involving molecular rearrangements of several tens of nanometers. At physiological temperatures, thermal fluctuations of a protein lead to the exploration of its conformations, which may be necessary for its function. Despite the low abundance and short lifetime of higher energy conformational states of proteins, it is becoming increasingly clear that these fleeting conformations can regulate fundamental biological processes. Our main goal is to identify the conformational dynamics of proteins on the picosecond to millisecond time scale under physiological conditions and to characterize the thermally accessible conformational states in atomic detail. The candidate will study proteins from different available in our group.

Research techniques used:

Mainly two experimental techniques, solution NMR spectroscopy at high magnetic fields (600 and 800 MHz) and two-dimensional (2D) femtosecond infrared spectroscopy, coupled with advanced molecular dynamics simulation methods on high-performance computing facilities will be used (all accessible in-house). Solution NMR spectroscopy can detect and characterize sparsely populated high-energy conformational states with population fractions near 1% at atomic resolution. While 2D femtosecond infrared spectroscopy is fast enough to temporally resolve virtually any process of biological importance.

The reason why the topic is innovative:

Any success in experimentally characterizing the dynamic equilibrium of protein conformational states, including the distribution of populations and the characterization of conformations that are 'invisible' to most biophysical methods, can provide presently unforeseen insights into protein function.

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