Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad – 500 046

Seminar

Studying Multi-State Conformational Exchange in Proteins Using ^{15}N CEST NMR Experiments

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Chemical exchange between the different conformational states of proteins plays pivotal roles in fundamental biological processes such as folding, misfolding, aggregation, ligand binding, and enzyme catalysis. Nuclear Magnetic Resonance (NMR) is a vital tool for investigating these exchange processes, encompassing both major and minor protein states across diverse time scales, spanning microseconds to seconds. Notably, relaxation dispersion NMR techniques like CPMG, $R_{1\rho}$, CEST, and DEST are particularly useful to uncover sparsely populated conformational states. Chemical Exchange Saturation Transfer (CEST) NMR experiment, tailored to study the exchange processes on the order of 5 to 200 milliseconds, and capable of detecting minor-state populations as low as 0.5%, is playing a vital role in characterising the above-mentioned exchange processes. Here, we have used ^{15}N CEST experiments to probe multi-state exchange processes occurring between more than two conformational states. During my doctoral work I have investigated the folding mechanism of A39G and WT FF domains from human HYPA/FBP11, using the information hidden in the minor-state dips of ^{15}N CEST profiles and have detected a new minor state, I2, of the FF domain. This state eluded detection in conventional CPMG experiments employed for WT FF. We have demonstrated that ^{15}N CEST experiments can be used to study multi-state exchange processes occurring on approximately 100 milliseconds to 100 microseconds range even when dealing with minor-state populations as low as ~0.1%.

Monday, May 6th 2024

11:30 Hrs (Tea / Coffee 11:15 Hrs)

Auditorium, TIFR-H