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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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 in 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. I will present insights in the folding mechanism of the A39G and WT FF domains from human HYPA/FBP11, obtained using the information hidden in the minor-state dips of ^{15}N CEST profiles. Using CEST experiments, we detected a new folding intermediate, I2 that had eluded detection by CPMG experiments. Our results demonstrate 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%.

Thursday, Oct 5th 2023

4:00 PM (Tea / Coffee 3.45 PM)

Auditorium, TIFR-H