Tata Institute of Fundamental Research
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Internal Seminar

The Small FF domain folds via multiple paths and multiple intermediates

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Proteins sample different conformational states which are critical for function. However, their detection with traditional biophysical techniques has remained a challenge due to their low populations and short lifetimes. Here, we have used CEST NMR experiments to study the folding of the 71 residue A39G FF domain (PNAS 118.46, 2021). We show that by inspecting the broadening of the minor state dip in CEST profiles, one can detect even more sparsely populated states (~0.1%). Our analysis of CEST profiles that exploits the minor state line widths shows that A39G FF exchanges between the unfolded and the folded state via two paths involving two intermediates (I1 and I2). The I1 chemical shifts correlate well with the shifts of the intermediate detected for WT FF using CPMG experiments (Korzhnev et al. Science 2010). The chemical shifts of I2 are more native-like except for residues 50-60. In addition to discussing the folding mechanism of the FF domain, I will also present the CEST derived structure of the I2 state. Moreover, to get more insight into this folding pathway we have also estimated the m-values of all the conformational and transition states using CEST NMR experiment.

Thursday, Dec 21st 2023

11:30 AM

Seminar Hall