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

Seminar

Extending CEST NMR experiments to study protein conformational dynamics occurring over the ~10^{-4} to ~10^{0} seconds timescale

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Protein conformational dynamics is crucial for their functions like catalysis, ligand binding etc. in addition to folding / misfolding and aggregation. NMR spectroscopy is particularly powerful for studying such dynamics as it allows monitoring of the process at the atomic level. Chemical Exchange Saturation Transfer (CEST) NMR experiments developed over the past decade are now routinely employed to study biomolecular dynamics occurring over the 10^{-3} to 10^{-1} s timescales. In this talk, I will discuss our efforts towards extending the range of applicability of CEST NMR experiments to study conformational dynamics accessing timescales of 10^{-4} to 10^{0} seconds. For the folding/unfolding transition occurring on 10^{-4} seconds timescale in the peripheral subunit binding domain (PSBD), it is showed that experimentally derived constraints on the fitting parameters aid in determination of precise exchange rates and minor-state populations in the fast-exchange regime. For slower processes (~10^{-1} s), the choice of the fields is crucial to determine accurate exchange parameters. We demonstrate that when the exchange rate between the major and minor conformers is comparable to the transverse relaxation rates, it is important to account for the transverse relaxation rates while choosing the fields. The above analysis also showed that exchange between visible states can be quantified using CEST data recorded at a single field. Finally, applications of CEST to understand the conformational dynamics of the cavity mutant (L99A) of T4 Lysozyme via urea m-values will also be presented.

Wednesday, Sep 18th 2024

16:00 Hrs (Tea / Coffee 15:45 Hrs)

Seminar Hall, TIFR-H