Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad - 500107

Colloquium

Using protein side-chain dynamics to characterize protein function and allosteric enzymatic regulation

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Side chains cover protein surfaces and are fundamental to processes as diverse as substrate recognition, protein folding and enzyme catalysis and regulation.

In the first part of the presentation, an approach anchored in Methyl-TROSY NMR spectroscopy is presented to obtain site-specific insight into the enzymatic regulation of the Histone Deacetylase 8 (HDAC8). Multi-quantum Methyl Carr-Purcell Meiboom-Gill (CPMG) experiments show that HDAC8 exchanges on the millisecond time-scale between an active and an inactive state that differ in a regulatory region located 28 Å from the active site. A phosphorylation mimicking mutation as well as other mutations stabilise the inactive state of HDAC8. A new pulse sequence to obtain intra-residue methyl-methyl correlations in large proteins and thus to aid methyl chemical shift assignments will also be presented.

Subsequently, a general set of ^{13}C-detected NMR methods to characterise functional side-chains in proteins will be presented. These methods allow, amongst others, to elucidate the interactions and dynamics of the guanidinium group of arginine side chains. Specifically, a new multi-quantum chemical exchange saturation transfer (MQ-CEST) method will be shown. This method allows a quantification of the interactions formed by arginine side chains in proteins, such as salt-bridges.

Tuesday, Feb 18th 2020

11:30 AM (Tea/Coffee at 11:00 AM)

Auditorium, TIFR-H