Assessing the role of Conformational Heterogeneity in Structure-Function Paradigm of Proteins

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Abstract:

Identification of multiple conformations across the energy landscape, and the characterization of the heterogenous native state is of significant interest considering their unparalleled contribution to protein's structure-dynamics-stability-function paradigm. Multidimensional protein NMR spectroscopy is a unique tool that can detect the dynamic interconversion of the multiple conformations and can provide fine details regarding the role of conformational heterogeneity of proteins at atomic level. Currently our research is focused on understanding the role of conformational heterogeneity of proteins arising due to monomer-dimer equilibrium (homo and heterodimers) and structural transitions due to protonation/deprotonation of His side chain networks that are involved in regulating the ligand binding, catalytic activity, conformational switching and pH dependent stability etc. A brief overview of various conformational transitions observed through an array of NMR, biophysical and computational approaches using protein systems associated to host immune system (chemokines), and peptidoglycan degrading enzymes (endolysins) will be presented.