Poster Presentation
Inter-Disciplinary Exploration in Chemistry (I-DEC 2018)

"Intrinsic conformational preferences and solvation of protein backbone in aqueous solution of pure/mixture of denaturants: A molecular dynamics simulation study"

Rasenjit Ghosh Dastidar and Rajesh K Murarka*
Department of Chemistry, IISER Bhopal
Bhauri, Bhopal Bypass Road, Bhopal – 462066, Madhya Pradesh, INDIA
(E-mail: rasenjit@iiserb.ac.in, rkm@iiserb.ac.in)

Abstract:

Urea and guanidinium chloride are the most commonly used chemical denaturants to understand the equilibrium between the native and unfolded state of a protein. The comprehensive understanding of the molecular mechanisms by which both of the denaturants unfolds a protein is still unclear. Interestingly, recent studies further suggest that their aqueous mixture tend to stabilize the collapsed denatured state rather than the unfolded state of a protein. The driving forces for the collapse/unfolded state originate from a fine interplay among protein backbone and side chains in which the conformations and hydrogen bonding of the backbone plays the central role. In this work, we aim to elucidate the molecular mechanism of the formation and stability of the collapsed conformation using a protein backbone model and explore its conformational free energy landscape in the denaturant solutions. We have performed molecular dynamics and metadynamics simulations of Gly_{16} (prototype of protein backbone) peptide in aqueous solutions of pure as well as mixture of denaturants. Further, we have also calculated solvation free energy of the conformations of Gly_{16} identified from the free energy landscape using thermodynamic integration method. The thermodynamic decomposition of solvation free energy (ΔG^{sol}) into enthalpic (ΔH^{sol}) and entropic (ΔS^{sol}) components reveals the nature of solvation of Gly_{16} in the denaturant solutions.

References and Notes:

1. Zhen Xia, Payel Das, Eugene I. Shakhnovich, and Ruhong Zhou; *J. Am. Chem. Soc.* 2012, **134**, 18266-18274.
2. Justin A. Drake and B. Montgomery Pettit; *Biophys. J.* 2018, **114**, 2799-2810.