

# Importance of Metastable Conformational States in Proteins: From Function to Drug Discovery

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## Abstract

Structural biology of proteins is dominated by a native structure centric view. However, biomolecular functions are intimately connected to protein motion/dynamics. For example, recent examples of “dynamic allostery” have established that a static structural view is not enough.<sup>1,2</sup> Moreover, low lying excited states or metastable states of protein conformation seem to play an important role in the function of proteins. In this talk, we shall discuss several such examples based on large scale classical molecular dynamics (MD) simulations. We demonstrate that a “population shift” of highly coordinated hydrogen bonds and salt bridges might lead to the allosteric modulation in several proteins.<sup>1,2</sup> We shall also present our new ideas on indentifying allosteric hotspots on protein surface to modulate therapeutically important protein-protein interactions (PPI).<sup>3</sup>

## References:

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