

Abstract Submitted
for the 4CF13 Meeting of
The American Physical Society

Role of native-state dynamics in thermophilic adaptation LUCAS SAWLE, KINGSHUK GHOSH, Univ of Denver — Thermophilic proteins denature at higher temperatures than mesophilic proteins. Among the many hypothesis related to thermophilic adaptation, reduced native state flexibility is one widely believed to be a signature of thermophilic proteins in comparison to their mesophilic homologues. While the majority of existing studies consist of investigating individual proteins, we instead focus on large-scale and detailed modeling of numerous proteins to infer the presence, if any, of general principles to thermophilic adaptation. We have curated and constructed the largest dataset of experimentally determined, monomeric, and non-complexed thermophilic-mesophilic homologue pairs. From this dataset of protein pairs, we performed comparative analysis of the native state fluctuations from molecular dynamics simulations at 300K in explicit solvent. From these dynamical fluctuations at short time scales (up to a cumulative of 300 ns for each protein), we calculated several quantities of interest: i) intra-residue fluctuations, ii) dipole moment fluctuation to calculate dielectric constant and iii) the entropy of the contact distribution. Here, we will present the selective role of these different metrics to distinguish thermophiles from mesophiles. Also, we will present our complementary approach based on thermodynamic analysis of the largest protein stability database, hinting at residual structure in the unfolded state to be an important factor in determining the enhanced stability of thermophiles.

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Date submitted: 19 Sep 2013

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