MAS17-2017-000019

Abstract for an Invited Paper
for the MAS17 Meeting of
the American Physical Society

Entropy in Protein Function[1]

JOSHUA WAND, Univ of Pennsylvania

Biological processes are most often controlled using molecular recognition by proteins. The physical origin of high affinity interactions involving proteins continues to be the subject of intense investigation. Conformational entropy represents perhaps the last piece of the thermodynamic puzzle that governs protein structure, stability, dynamics and function. The importance of internal conformational entropy in proteins has been debated for decades but has resisted experimental quantification. Recently we have developed and validated an NMR-based approach that uses a dynamical proxy to determine changes in conformational entropy. This approach, which we term the "entropy meter," requires few assumptions, is empirically calibrated, and is apparently robust and universal. It can now be shown that proteins retain considerable conformational entropy in their native functional states and that this entropy can play a decisive role in the thermodynamics of molecular recognition. Changes conformational entropy of a protein upon binding a high affinity ligand are system specific and can vary from strongly inhibiting to even strongly promoting binding. Thus one cannot understand how proteins work without considering conformational entropy. This approach also allows for the refinement of empirical coefficients that relate changes in accessible surface area to changes in the entropy of water and the determination of the loss of rotational-translational entropy in high affinity protein complexes.

[1]Supported by the NIH and the Mathers Foundation