Abstract Submitted
for the MAR14 Meeting of
The American Physical Society

Computational stability ranking of mutated hydrophobic cores in staphylococcal nuclease and T4 lysozyme using hard-sphere and stereochemical constraints ALEJANDRO VIRRUETA, ALICE ZHOU, COREY O'HERN, LYNNE REGAN, Yale University — Molecular dynamics methods have significantly advanced the understanding of protein folding and stability. However, current force-fields cannot accurately calculate and rank the stability of modified or *de novo* proteins. One possible reason is that current force-fields use knowledge-based corrections that improve dihedral angle sampling, but do not satisfy the stereochemical constraints for amino acids. I propose the use of simple hard-sphere models for amino acids with stereochemical constraints taken from high-resolution protein crystal structures. This model can enable a correct consideration of the entropy of side-chain rotations, and may be sufficient to predict the effects of single residue mutations in the hydrophobic cores of staphylococcal nuclease and T4 lysozyme on stability changes. I will computationally count the total number of allowed side-chain conformations Ω and calculate the associated entropy, $S = k_B \ln(\Omega)$, before and after each mutation. I will then rank the stability of the mutated cores based on my computed entropy changes, and compare my results with structural and thermodynamic data published by the Stites and Matthews groups. If successful, this project will provide a novel framework for the evaluation of entropic protein stabilities, and serve as a possible tool for computational protein design.

Alejandro Virrueta
Yale University

Date submitted: 15 Nov 2013 Electronic form version 1.4