MAR15-2015-021052

Abstract for an Invited Paper
for the MAR15 Meeting of
the American Physical Society

**Hard-Sphere Models for Predicting Side Chain Conformations of Proteins**

LYNNE REGAN, Yale University

We now have Angstrom-level resolution of the atomic positions for thousands of protein crystal structures. From these structures, we can determine the probability distributions of the side-chain dihedral angles for each type of amino acid. However, we lack a predictive understanding of these distrbutions, for example, are the shapes of the distributions determined primarily by steric or electrostatic interactions and are they dominated by local interactions within an amino acid or by longer-ranged interactions? Similarly, we do not have a fundamental understanding of what interactions determine the energy barriers that control transitions between either main-chain or side-chain amino acid conformations. To address these questions, we performed all-atom molecular dynamics simulations using a simple model of dipeptides that includes steric interactions plus stereochemical constraints We show that transitions between different backbone or side-chain conformations are strongly coupled to local bond-angle fluctuations. Moreover, the effects are causal, not merely correlative: By fixing the range of the local bond angles sampled, we influence the frequency of transitions in a predictable fashion. These results emphasize the somewhat under-appreciated importance of steric interactions and stereochemical constraints in determining many aspects of protein structure.

In collaboration with Corey O'Hern Diego Caballero, Jennifer Gaines, Alejandro Virrueta and Alice Zhou.