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The power of simple hard-sphere models in protein structure prediction[1]

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There are several force-fields that are currently used to describe the potential energy of biological macromolecules such as proteins. These typically include many parameters, derived from a combination of statistical, experimental sources. These work on average to describe a protein, but the large number of parameters moves this description further away from a true physical understanding than is desirable. Our approach is to investigate to what extent simple hard sphere models can be used to model and predict the behavior of different aspects of protein structure. We present the results of specific calculations. The distributions of the side-chain dihedral angle chi1 of Val and Thr in proteins of known structure show distinctive features: Val side chains predominantly adopt dihedral angle, chi1, of 180, whereas Thr side chains typically adopt a dihedral angle, chi1, of 60 or 300. Several hypotheses have been proposed to explain these differences, including inter-residue steric clashes and hydrogen-bonding interactions. In contrast, we show that the observed side-chain dihedral angle distributions for both Val and Thr can be explained using only local steric interactions in a dipeptide mimetic. Our results emphasize the power of a simple physics-based approaches and their importance for future advances in protein engineering and design.

[1]In collaboration with Alice Zhou and Corey O'Hern, Yale University.