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Section 7: Protein Simulation 1

The two readings introduce methods for understanding the molecular composition of proteins. The first, by Karplus and McCammon, is a review paper describing the essentials of molecular dynamics. The second, by Regan et al., studies conformational constraints on protein structure. While the first is dynamic and the second static, both papers demonstrate the value of modeling the nature of biomolecules.

Karplus and McCammon begin by describing molecular dynamics, along with its history and significance. Although simulation of biomolecules over time have only been in use for 25 years, great advancements has been made in understanding internal motions in biomolecular function. These have helped elucidate the role of various dynamical factors (such as hinge bending, flexibility, and configurational entropy) in important biological functions (such as solvation, ligand binding, bilayer formation, and catalytic activity). Together, these factors provide the detail necessary to understand essential aspects of protein function. Today, simulations can last more than 10-7 seconds, and can study much larger systems (up to 106 atoms in size). Karplus and McCammon argue that the next stage of molecular dynamics will bring simulation to the cellular level, including complex activities and simplified normal mode models. The authors conclude with the hope that computational advancements will pave the way more detailed investigations of protein function.

The paper by Zhou, O' Hern, and Regan examines 86,299 residues in 850 proteins from the Dunbrack database to demonstrate the effect of the backbone angle (tau) on the distribution of allowed phi/psi combinations. They confirm that the allowed dihedral angles are sterically dependent on tau, which is roughly normally distributed between 100 and 120 degrees (95%). This varies by residue type, where the character of the amino acid may affect allowed angles. Regan et al. find that larger values of tau relieve N-N clashes and increase the allowed bridge regions on the Ramachandran plot. This confirms the original predictions by Ramachandran et al. The conclusion of this work allows for simplifications to be made in the study and modeling of dihedral angles in peptides, by considering only inter-atomic separations and not additional interactions.

- Martin Karplus and J. Andrew McCammon. (2002) Molecular dynamics simulations of biomolecules. Nature Structural Biology,9, 646-52. PMID: 12198485.PDF
- Zhou, AQ, O'Hern, CS, Regan, L (2011). Revisiting the Ramachandran plot from a new angle. Protein Sci., 20, 7:1166-71 PDF