UNDERSTANDING THE EFFECT OF PRESSURE AND TEMPERATURE ON HYDROPHOBIC INTERACTIONS

Caitlin E. Scott, [1,2] Sapna Sarupria,[1] Shekhar Garde[1]

1. Department of Chemical and Biological Engineering, Rensselaer Polytechnic Institute, Troy, NY
2. Department of Chemistry, Mount Holyoke College, South Hadley, MA

Proteins are large, complex macromolecules made of chains of amino acids. These residues can be charged or neutral. The neutral or hydrophobic amino acids form a hydrophobic core of the protein. A similar tendency is seen for non-polar molecules to aggregate in water. This tendency to aggregate is driven by water-mediated interactions, called hydrophobic interactions.[1] Two ways a protein can unfold are by thermal denaturation or pressure denaturation.[2] While must studies focus on one variable over a small range, this project will focus on the effects of pressure and temperature that span most of the liquid water phase.

In an effort to investigate hydrophobic interactions, the interactions of methane in water were modeled. Using GROMACS[3,4] (version 3.2.1) computer software, molecular dynamics (MD) simulations were performed to find the radial distribution function, $g(r)$, for methane molecules. With this information, the potential of mean force $(W(r))$ can be determined since $W(r) = -kT \ln(g(r))$, where k is Boltzmann's constant and T is temperature. Three $W(r)$ features corresponding to different methane configurations are particularly interesting, including the contact minimum (CM), the desolvation barrier (BARR), and the solvent-separated minimum (SSM). These configurations can be related to different protein structures. The CM resembles the folded protein because the hydrophobic residues are in contact in the core. The SSM relates to the water-swollen globule, or the denatured protein. The difference between the energy values tells the strength of the hydrophobic interactions for the folding process.

In addition, using the first and second derivatives of $W(r)$ and fitting equations, several thermodynamic properties can be determined, including the entropy, the specific heat capacity, the volume, and the compressibility. From the hydrophobic interactions, our results suggest that hydrophobic interactions may play an important role in the pressure denaturation process. In addition, ionic interactions are involved in protein folding.[5] For future work, we plan to perform a similar analysis for ion systems under similar pressure-temperature conditions.

---

[1] Dill, K.A. *Biochemistry*, **1990**, *29* (31), 7133.

[2] Bridgeman, P. W. *J. Biol. Chem.* **1914,** *19*, 511.

[3] Berendsen, H. J. C. v. d. S., D. *Comput. Phys. Commun.* **1995**, *91*, 43.

[4] Lindahl, E. H., B.; van der Spoel, D. *J. Mol. Model* **2001**, *7*, 306.

[5]