Meeting: 1003, Atlanta, Georgia, SS 7A, AMS Special Session on Beyond the Spherical Cow: Mathematical Sciences Research to Support Computational Biology

1003-92-1634 **Richard Friesner*** (rich@chem.columbia.edu). *Protein Folding: Computational Challenges and Solutions.*

We will discuss the problem of predicting the high resolution structure of a protein sequence via a combination of knowledge based and physical chemistry based methods. Approximate, low resolution initial guesses for the structure can be generated via bioinformatics type approaches involving sequence similarity, threading techniques, profile-profile alignments, etc. High resolution refinement of local regions (side chains, loops, and loop-helix-loop regions, for example) can be achieved using accurate molecular mechanics potential functions, a continuum solvation model, and hierarchical conformational sampling algorithms that employ fast screening and clustering methods to reduce an exponeitally large search space to examination of a relatively small number of candidate conformations with the full detailed energy model. Bridging the gap between approximate structures and local refinement methods with an acceptable level of computational effort is at present an unsolved problem that will likely require novel mathematical approaches, highly efficient implementation, and very large scale supercomputing power. A brief discussion of what makes this problem hard, and possible avenues of solution, will be presented. (Received October 05, 2004)