Simulating the Folding of Proteins
Executive Summary

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The computational modeling of protein structures is an active field of research that could provide valuable insight on the nature of proteins and allow for a comparatively quick method of determining the structures of unknown proteins at a much lower cost than that of performing laboratory experiments. Ab initio computational methods provide a promising means to predict the structure of a protein based on thermodynamic data and the sequence of amino acids making up the structure. To attempt to reduce computational time while approximating the manufacture of a polypeptide, a linear optimization technique was employed to reduce the free energy of the molecule, and the polypeptide was slowly constructed by optimizing a short chain of amino acids and then adding additional residues to the C-terminal end of the chain and re-optimizing the process. Additionally, a genetic algorithm was employed as an alternative optimization method. Both methods used the ECEPP/3 energy parameters, the GBr6 model of electrostatic solvation energy, and an approximation of the volume of the hydration shell around the polypeptide to determine the conformational energy of the polypeptides. The linear optimization technique was found to be an inferior method in terms of both computational efficiency and the accuracy of results, often giving unrealistic or poorly optimized outputs. On the other hand, the genetic algorithm performed admirably to find the global minimum of conformational free energy. However, it produced structures that exist at lower energy than the NMR measured structures, indicating inaccuracies within the energy parameters used. Further research should focus on determining the optimum energy parameters to enable the successfully optimized results to correspond with actual native structures as found in nature.