

Protein Folding by Generalized Simulated Annealing and Molecular Dynamics Methods

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Protein 3D structures are obtained basically by X-ray Crystallography and Nuclear Magnetic Resonance. However, due to experimental limitations and the high costs involved in those techniques, determining these structures is often a demanding challenge. This has led to an enormous and growing gap between the number of known sequences and determined structures. In this sense, theoretical and computational studies have made possible to increase the comprehension of the factors that lead to a polypeptide folding into its native 3D state. In general, it is assumed that the native structures are found in the global free energy minimum and the information to achieve it is stored in amino acid sequence. The objective of this work was to develop a simulation methodology based on Generalized Simulated Annealing (GSA) and Molecular Dynamics (MD) in implicit solvent, for protein structure prediction. In order to validate this study, we used a set of 65 protein models with lengths ranging from 10 to 60 residues. We applied the GSA in the search for a conformation into energy folding funnel, and then MD to refine the models. The results show that the proposed protocol is able to find models very close to the native structures determined experimentally. For about 57% of the sequences analyzed, we found models with less than 3.0Å of deviation from the experimental structure, which is considered a high quality prediction. Furthermore, over 70% of the generated models showed deviations below 4.0Å, and 87% less than 5.0Å, which are considered good results in the literature. In general, our results showed that the optimization method with GSA, from extended conformation combined with further MD refinement, is a promising strategy to find native states.

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