DEVELOPMENT AND APPLICATION OF COMPUTATIONAL METHODS FOR PROTEIN STRUCTURE PREDICTION

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The three-dimensional structure is obtained basically by Crystallography and X-ray Diffraction and Nuclear Magnetic Resonance. However, due to experimental limitations and the high costs involved with those techniques, determining the three dimensional structure of proteins is often insuperable challenges. 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 understanding of the factors that lead to a polypeptide folding to its native state sequence. In general, it is assumed that the native structure are found in the global minimum of energy and the information to achieve the bioactive structure is stored in amino acid sequence.

The objective of this work was the development of simulation methodologies based on Generalized Simulated Annealing (GSA) and the Molecular Dynamics (MD) in implicit solvent, for protein structure prediction.

In order to validate this study, we used a set of 65 models of proteins with lengths from 10 to 60 residues. We apply the GSA in the search for energy global minimum, and then MD to refine the structures.

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 with respect to 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.

Generally, our results showed that the optimization method with GSA, from extended conformation and with DM further refinement, is a promising strategy for studies of protein folding.

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