Assembly of Protein Tertiary Structures From Secondary Structures Using Optimized Potentials

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Abstract: Prediction of the three dimensional structure of proteins from their sequences of aminoacids is one of the most fundamental challenges in computational molecular biology due to a high number of degrees of freedom and the diversity of the interactions involved. We present a simulated annealing based method for the prediction of the tertiary structures of proteins given an a priori knowledge of the secondary structure associated with each amino acid in the sequence. Our model follows the LINUS model of Srinivasan and Rose, in which the backbone is represented in a detailed fashion whereas the sidechains and pairwise interactions are modeled in a simplified way. A perception based technique is used to optimize the interaction potentials for a training set of three proteins given a condition that the native state is the lowest energy conformation. For these proteins, our procedure is able to reproduce the tertiary structures to below 3Å in root mean square deviation (rmsd) from the experimentally determined native structures. We present the results of tests on twelve other proteins. For half of these, the lowest energy decoy has a rmsd from the native state below 6Å and in 9 out of 12 cases, we obtain decoys whose rmsd from the native states are also well below 5Å. These stimulating results suggest that our potentials can be adequate for a large number of proteins.

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