FlexSPS: A Monte Carlo update for protein refinement from I-TASSER models

Roosevelt Alves da Silva

Universidade Federal de Goiás

Comparative modeling is the main technique used in the protein structure prediction. 3D models are resolved based in the sequence alignment between the target and templates extracted from experimental protein structures in order to use the structural information of the aligned regions (from template) to construct a structural model for the target protein. Significant progress has been made in order to achieve high resolution models. The I-TASSER program has been extensively used by the community and it has been ranked as the best methodology for the protein structure prediction. However, this tool still requires improvements in order to increase the resolution of the predicted models, particularly avoiding the presence of steric clashes, unfavorable torsion angles, and unphysical bond length and bond angles. In this work, we have developed a tool for this purpose. The initial challenge was ensure improvement to the molProbity score and TMScore. Based on this initial goal, we have developed a tool called FlexSPS (Flexible Sampling for Protein Structure) that it allows sampling a large set of conformations around the predicted structure from I-Tasser. FlexSPS is a Monte Carlo program that modifies locally the protein conformations with the help of the *replica exchange method* around solutions from Amber forcefield and a ramachandran potential used to represent the protein. Our preliminary results indicate a substantial improvement in molProbity score and parameters related to the quality of the structures. However, changes in the force field will be needed to provide an increase in TMScore values. FlexSPS has been developed with the purpose of its application to the refinement of protein structures, protein-protein molecular docking, mutagenesis and loop predictions. The main application with this integrated tool will be the search for new drugs.

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