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ABSTRACT

We present the novel docking algorithm based on the Tensor Train decomposition and the TT-Cross global optimization applied to the docking problem with flexible ligand and moveable protein atoms. The energy of the protein-ligand complex is calculated in the frame of MMFF94 force field in vacuum. The conformation space of the system coordinates is formed by translations and rotations of the ligand as a whole, by the ligand torsions and also by Cartesian coordinates of selected target-protein atoms. Mobility of protein and ligand atoms is taken into account in the docking process simultaneously and equally. The algorithm is realized in the novel parallel docking SOL-P program and results of its performance for a set of 30 protein-ligand complexes are presented. Dependence of docking positioning quality is investigated as a function of the docking algorithm parameters as well as the number of moveable protein atoms, and it is shown that mobility of protein atoms improves docking positioning quality. The program is able to perform docking of a flexible ligand into the active site of the target protein with several dozen of protein moveable atoms: up to 160 degrees of freedom. For example, the docking time of the native ligand (7 torsions) into the target protein (PDB ID 3CEN) with 26 moveable protein atoms is 1 212 CPU*hour at the Lomonosov supercomputer.

Keywords: *docking, tensor train, protein-ligand complex, protein moveable atoms, flexible ligand, drug design*