

Accepted Manuscript

Evaluation of the novel algorithm of flexible ligand docking with moveable target-protein atoms

Alexey V. Sulimov, Dmitry A. Zheltkov, Igor V. Oferkin, Danil C. Kutov, Ekaterina V. Katkova, Eugene E. Tyrtysnikov, Vladimir B. Sulimov

PII: S2001-0370(16)30104-0
DOI: doi:[10.1016/j.csbj.2017.02.004](https://doi.org/10.1016/j.csbj.2017.02.004)
Reference: CSBJ 177

To appear in: *Computational and Structural Biotechnology Journal*

Received date: 1 December 2016
Accepted date: 28 February 2017

Please cite this article as: Sulimov Alexey V., Zheltkov Dmitry A., Oferkin Igor V., Kutov Danil C., Katkova Ekaterina V., Tyrtysnikov Eugene E., Sulimov Vladimir B., Evaluation of the novel algorithm of flexible ligand docking with moveable target-protein atoms, *Computational and Structural Biotechnology Journal* (2017), doi:[10.1016/j.csbj.2017.02.004](https://doi.org/10.1016/j.csbj.2017.02.004)

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Evaluation of the novel algorithm of flexible ligand docking with moveable target-protein atoms

Alexey V. Sulimov^{a,b}, Dmitry A. Zheltkov^c, Igor V. Oferkin^a, Danil C. Kutov^{a,b}, Ekaterina V. Katkova^{a,b}, Eugene E. Tyrtshnikov^{c,d}, Vladimir B. Sulimov^{a,b,*}

^a Dimonta, Ltd, Nagornaya Street 15, bldg 8, Moscow 117186, Russia

^b Research Computer Center, Moscow State University, Leninskie Gory 1, bldg 4, Moscow 119992, Russia

^c Faculty of Computational Mathematics and Cybernetics of Lomonosov Moscow State University, Leninskie Gory 1, bldg 52, Moscow 119992, Russia

^d Institute of Numerical Mathematics of Russian Academy of Sciences, Gubkin str., 8, Moscow, 119333, Russia

Corresponding Author

* Telephone: +7 (916) 5123418. Email: vladimir.sulimov@gmail.com

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*

Download English Version:

<https://daneshyari.com/en/article/8408388>

Download Persian Version:

<https://daneshyari.com/article/8408388>

[Daneshyari.com](https://daneshyari.com)