DockThor: A Brazilian Receptor-Ligand Docking Program

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Receptor-ligand docking methodologies are important tools for structure-based rational drug design studies. These methods aim to predict the experimental binding mode and affinity of a small molecule within the binding site of the receptor target of interest. The DockThor program, developed by the Brazilian group GMMSB/LNCC, uses a grid based methodology and was implemented to deal with highly flexible ligands using a multiple-solution steady state genetic algorithm[1]. The scoring function is based on the MMFF94S force field[2]. Dockthor performance was evaluated through a comparative analysis of redocking experiments with Glide, GOLD and Autodock Vina docking programs. This study was carried out using a high quality test set of 115 protein-ligand complexes (including 75 selected by Astex Therapeutics Ltd). Dockthor obtained a very good comparative performance and also obtained an excellent results for highly flexible HIV-1 protease ligands. A Web Server (http://www.dockthor.lncc.br) was also developed to enable and facilitate the use of the program by the academic community using the computational facilities provided by the Brazilian high performance platform (SINAPAD, https://www.lncc.br/sinapad/). The DockThor Server implements the major steps of the ligand and protein preparation. It is possible to set the residues protonation states and also consider cofactors molecules during the docking experiments. Cross-docking studies, development of empirical free energy functions to predict protein-ligand binding affinities and future developments associated with the DockThor project will be also presented.

1- Camila Silva de Magalhães, Diogo A. Marinho Hélio José Correa Barbosa, Laurent Emmanuel Dardenne, Information Sciences, 289, 206-224, 2014

2- Thomas A. Halgren Merck molecular force field. I. Basis, form, scope, parameterization, and performance of MMFF94 Journal of Computational Chemistryv. 17 (5-6)p. 490-519, 1996.