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JMOLSDOCK: A JAVA-BASED GUI FOR MOLSDOCK

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ABSTRACT:

Summary: MOLSDOCK is a FORTRAN based command-line-only protein-ligand docking algorithm, developed in our laboratory. In spite of having advantages over other docking algorithms, in terms of its exhaustiveness in search, MOLSDOCK could not reach the scientific community and the student community, as MOLSDOCK demanded expertise in programming using command line interface. Therefore, to make the algorithm more accessible to the scientific community, we have developed JMOLSDOCK, a Java-based Graphical User Interface (GUI) for MOLSDOCK. JMOLSDOCK has been developed using Jmol: an open-source Java viewer for chemical structures in 3D. JMOLSDOCK also has Fpocket, an open source protein cavity detection algorithm to find the active site in the receptor protein automatically.

Availability: Source code and binary of JMOLSDOCK are freely available for download at https://bitbucket.org/cascb/jmolsdock/downloads

1. INTRODUCTION

MOLSDOCK is a 'rigid receptor flexible ligand' protein-ligand docking method that uses mutually orthogonal Latin squares (MOLS) (Vengadesan and Gautham, 2003) to simultaneously sample both the 'docking space' and the conformational space of the ligand (Arun Prasad and Gautham, 2008). In MOLSDOCK, inputs have to be supplied using command line text editing. To make this docking tool more accessible to the wider scientific community, we have developed a Java-based GUI. The software package, including the GUI and the FORTRAN code is renamed JMOLSDOCK. The GUI has been developed using Jmol: an open-source Java viewer for chemical structures in 3D. http://www.jmol.org/.

2. DESCRIPTION OF JMOLSDOCK

JMOLSDOCK is equipped with the Jmol viewer, a Molecule Builder, MOLSDOCK

– a docking tool, and MOLS – a conformation search tool for peptides. The Molecule Builder may be used to create drug candidates for docking.

2.1 Prerequisites

JMOLSDOCK requires Java 7. Fpocket 2.0 (Le Guilloux *et al.*, 2009), available at http://fpocket.sourceforge.net/, is used for protein cavity detection in JMOLSDOCK. Open Babel (O'Boyle *et al.*, 2011), is used for file format conversions and energy calculations inside the docking tool. Fpocket 2.0 and Open Babel 2.2.0 are shipped, and may be installed, along with JMOLSDOCK. In case the basic docking algorithm, i.e. MOLSDOCK, which is written in FORTRAN, needs recompilation, it must be carried out using 'Intel® Fortran Composer XE for Linux (http://software.intel.com/en-us/non-commercial-software-development). JMOLSDOCK is developed for Linux.

2.2 MOLSDOCK Docking algorithm

A conformational search and ranking of potential solutions are essential ingredients of a successful docking tool (Halperin *et al.*, 2002). MOLSDOCK has a search algorithm to sample the conformational space of the ligand and to arrive at the optimal structure and "pose" of the drug candidate in the docking region of the receptor. MOLSDOCK uses the MOLS search algorithm, which is explained in detail elsewhere (Vengadesan and Gautham, 2004, 2003; Vengadesan *et al.*, 2004). The MOLS technique has already been used for various types of molecular structure explorations (Vengadesan and Gautham, 2004, 2003;Arunachalam *et al.*, 2006; Kanagasabai *et al.*, 2007). A detailed description of the MOLSDOCK method, used for docking, is given by Viji et al., 2009.

2.3 MOLSDOCK tool

The inputs to the MOLSDOCK tool include the project name, the output directory, the ligand specifications, including structure, the receptor specifications and structure, the number of structures to be generated, and specifications of the binding site (Fig. 1).

The ligand, which could be any organic chemical compound, is specified in MDL Molfile (.mol) format. If such a description is not already available, the Molecule Builder in JMOLSDOCK may be used. The receptor, usually a protein, to which the ligand is to be docked, is specified in .pdb format.

Usually in molecular docking, except the protein and the ligand, no additional data are given. However, if the binding site is known, for example from an experimentally determined structure of a protein-ligand complex, the manual button can be used, and the binding site can be defined by the coordinates of the centre of a box and its dimensions. If the binding site on the receptor protein is not known the auto option can be used; Fpocket (Le Guilloux et al., 2009) is then used to select the best binding pocket.

2.4 MOLS tool

MOLS, the conformational search algorithm for peptides developed in our laboratory, is also part of JMOLSDOCK. This tool takes an amino acid sequence as an input and generates for it a specified number of low energy structures. The sequence is specified using the single-letter amino acid code. Other options include controls to restrict the flexibility to the backbone alone, or to search over the entire conformational space of the molecule. There is also a 'rotamer' search option, in which the side chain dihedral angles are sampled from values given in a rotamer library (Tuffery *et al.*, 1997). Further options allow the generated structures to be minimized using conjugate gradient minimization, to be clustered using K-means or Hierarchical clustering algorithms. Two options are provided for energy calculations – the AMBER94 force field (Cornell *et al.*, 1995) and ECEPP/3 force field (Nemethy *et al.*, 1992).

3. OUTLOOK

JMOLSDOCK is a Java-based GUI developed using Jmol for MOLSDOCK, a docking tool and MOLS, a conformational search tool. The built-in molecule builder of JMOLSDOCK may be used to create chemical compounds to be used for docking. The MOLS conformational search tool may be used to identify low energy peptide structures. The current version of JMOLSDOCK performs 'rigid receptor – flexible ligand' docking. Future versions will incorporate receptor flexibility as well.

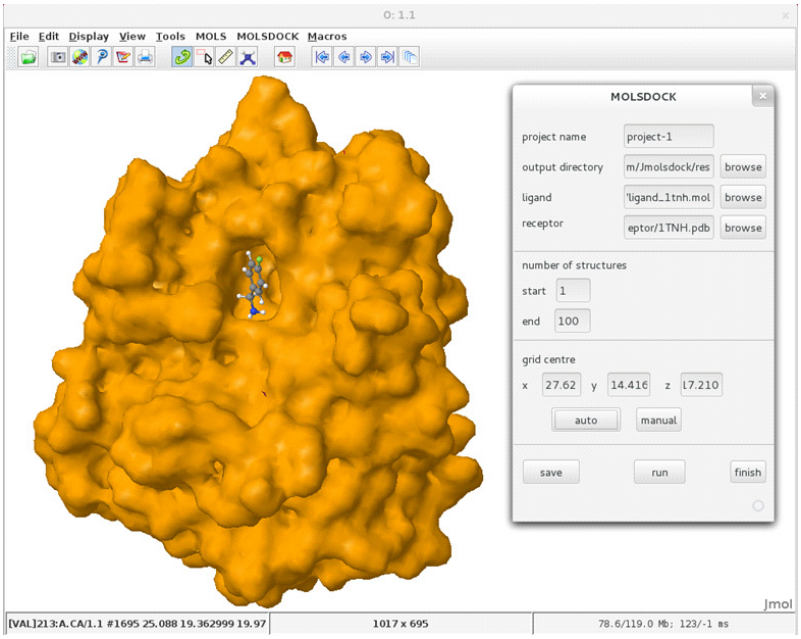

Fig. 1. JMOLSDOCK with MOLSDOCK input dialog box.

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