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Applications Note

Structural bioinformatics

DockingPie: a consensus docking plugin for PyMOL

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Abstract

Motivation: The primary strategy for predicting the binding mode of small molecules to their receptors and for performing receptor-based virtual screening studies is protein–ligand docking, which is undoubtedly the most popular and successful approach in computer-aided drug discovery. The increased popularity of docking has resulted in the development of different docking algorithms and scoring functions. Nonetheless, it is unlikely that a single approach outperforms the others in terms of reproducibility and precision. In this ground, consensus docking techniques are taking hold.

Results: We have developed DockingPie, an open source PyMOL plugin for individual, as well as consensus docking analyses. Smina, AutoDock Vina, ADFR and RxDock are the four docking engines that DockingPie currently supports in an easy and extremely intuitive way, thanks to its integrated docking environment and its GUI, fully integrated within PyMOL.

Availability and implementation: https://github.com/paiardin/DockingPie.

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Supplementary information: Supplementary data are available at *Bioinformatics* online.

1 Introduction

The extensive usage and continuous improvement of molecular docking in structure-based drug design drives the development of many different search algorithms, scoring functions and protocols, which in turn are exploited in a high number of docking strategies (Dos Santos *et al.*, 2018). Because of this heterogeneity, setup of a docking analysis, that is, preparation of input files, setup of search space, parameters setting, visualization and analyses of the results, is often hampered by the need of different, non-integrated tools for accomplishing each individual step. To overcome such limits, several free, integrated Docking Environments (DoEs), along with their Graphical User Interfaces (GUIs), have been developed, for example, AutoDockTools (ADT) within the PMV graphical package (Morris *et al.*, 2009), PyMOL AutoDock plugin (Seeliger *et al.*, 2010), PyRx (Dallakyan *et al.*, 2015) and AMDock (Valdés-Tresanco *et al.*, 2020). Most of these tools implement the popular docking program AutoDock (Morris *et al.*, 2009) and/or AutoDock Vina (Eberhardt *et al.*, 2021). Methods that combine the results of different docking algorithms and Consensus Scoring (CS) are also available, for example, ConsDock (Paul *et al.*, 2002), VoteDock (Plewczynski *et al.*, 2011) and DockBox (Preto *et al.*, 2019). However, a major hurdle to the use of such consensus approaches is the lack of any DoEs or GUIs.

Such limitations prompted us to develop DockingPie, an open source PyMOL (Schrödinger, LLC) plugin for assisting molecular and consensus docking analyses. DockingPie currently implements four docking engines, that is, Smina (Koes *et al.*, 2013), AutoDock Vina (Eberhardt *et al.*, 2021), ADFR (Ravindranath *et al.*, 2015) and RxDock (Ruiz-Carmona *et al.*, 2014), in an easy and highly intuitive way, thanks to its DoE and GUI, and the full integration with the popular molecular viewer PyMOL (Fig. 1). Providing an easy interface to four docking programs, DockingPie is particularly suited as a platform to carry out consensus docking and scoring analyses. The CS protocols implemented in DockingPie are the so-called 'Rank by Rank' (Wang *et al.*, 2001), 'Average of Auto-Scaled Scores' (Oda *et al.*, 2006) and 'Z-Scores' (Liu *et al.*, 2012). If needed, a root mean square deviation (RMSD)-based filtering can be applied, as often used as an 'a priori' step in CS analyses (Ochoa *et al.*, 2021).

In conclusion, DockingPie offers a fully integrated DoE and GUI within PyMOL, providing support for handling multiple docking programs at once.

2 Overview of DockingPie features

The main DockingPie's features are the following: (i) simplified installation and configuration of the external tools (Vina, Smina, ADFR, RxDock, ADTs and Openbabel) through the 'configuration' tab (Morris *et al.*, 2009; O'Boyle *et al.*, 2011); (ii) preparation of input files: protonation, handling of non-standard residues and water molecules, setting of active torsions, setup of search space and generation of grid maps, which are interactively visualized in PyMOL; (iii) inspection of the results: interactive tabular formats and docked conformations shown in PyMOL; (iv) RMSD with reference ligands, RMSD versus Score scatter plots and (v) consensus docking analysis:

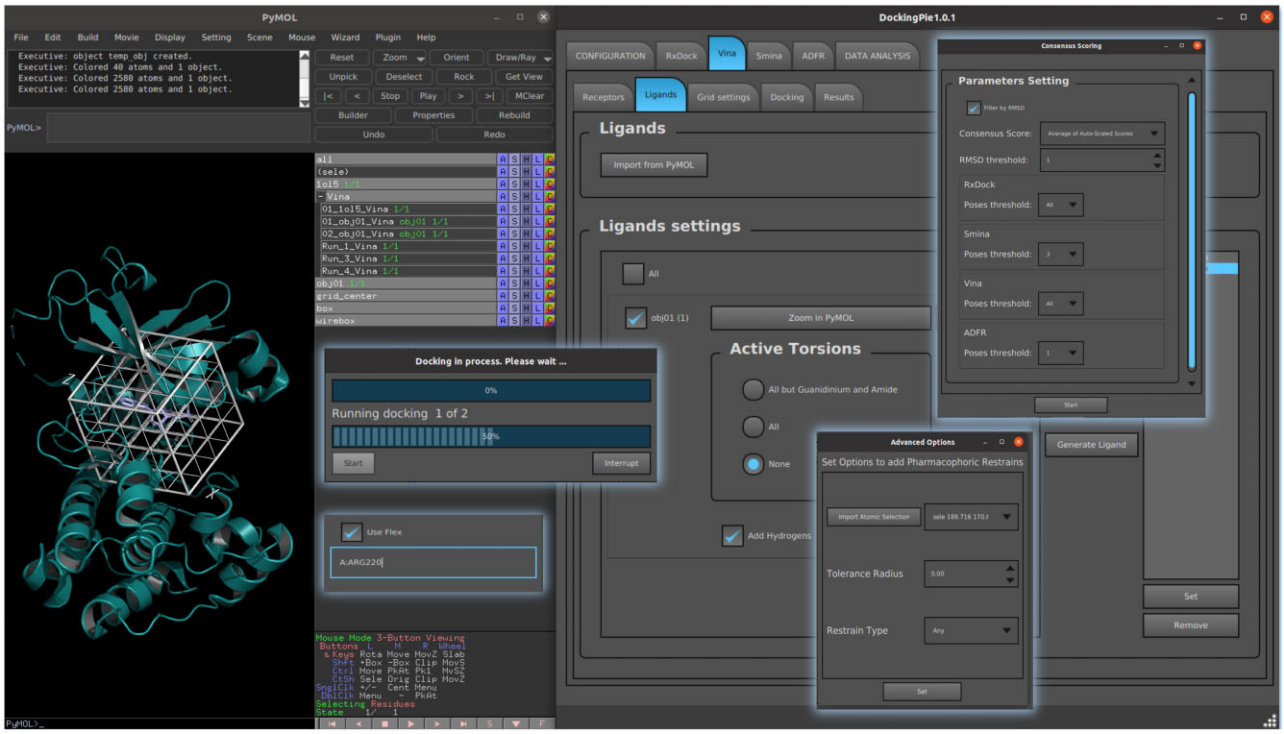

Fig. 1. Overview of DockingPie and its integration within PyMOL. Some of the analyses that is possible to carry out with DockingPie are shown

the results of different docking programs can be rescored according to one of the available consensus protocols and interactively visualized in PyMOL.

3 Implementation

DockingPie is implemented in PyMOL as a freely available plugin. It has been written in Python 3 and it is compatible with PyMOL version 2.3 (or higher). DockingPie has been successfully tested on different versions of Windows, MacOS and Ubuntu Linux. Its usage on Windows is limited to Vina and ADFR, since Smina and RxDock are currently not supported on this OS. In-depth information about DockingPie installation, configuration and functions, as well as step-by-step video tutorials, can be found in its User's Guide (Supplementary Material).

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Conflict of Interest: none declared.

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