A Benchmark Study of the “Soft Docking” Module of MIAX, Using a Set of Unbound Proteins

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Keywords: MIAX, protein-protein interaction, soft docking

1 Introduction

Molecular recognition is involved in all biological processes. Detailed energetic and structural knowledge of interactions between biomolecules is fundamental to understand the complex regulatory and metabolic pathways that occur in living organisms and also to design drugs for blocking or modifying these interactions. Theoretical prediction of protein-protein complexes is becoming critically important in structural biology. A large number of protein structures have been experimentally determined and deposited in the Protein Data Bank (PDB), however, only a small fraction of numerous protein-protein complexes has been experimentally characterized so far. In this study, unbound protein pairs with corresponding complexes structures, which have been experimentally determined and deposited in the protein data bank, are used to test and verify a new protein-protein interaction module in MIAX [1,2,3,4,5] that we have termed “soft docking module in MIAX”. The algorithm underlying this module consists in softening the surface of the proteins regardless of the type of amino acid side chains, in order to allow smooth interpenetrations among interacting partners and reduce the number of candidate protein complexes output by the system.

2 Method and Results

In recent years we have been involved in the development of the system MIAX for macromolecular interaction in living organisms. MIAX is endowed of rigid and flexible docking modules that perform outstandingly in cases where the interacting subunits undergo limited conformational change at interaction. A later development in the system to treat unbound molecules that undergo pervasive conformational change at interaction has improved the performance of the system. In the present article we have carried out an exhaustive test of this module, and we reveal some of the new characteristics of the system. To benchmark this new module in MIAX, 48 pairs of unbound protein molecules were docked and superimposed with their corresponding complexes. Homology analysis showed that all the receptor and ligand structures used in the present study have very low homology, less than 20%. We also conducted an analysis of the type of complexes. The classification of complexes showed that these 48 complexes belong to different binding modes, indicating that the structures we chose from PDB to perform our benchmarking study possessed a high degree of diversity, enough to assure a valid statistical evaluation of the soft docking module of the MIAX program. After the soft docking was performed we computed the root mean square deviations
(RMSD) between the best decoys output by MIAX and the corresponding complexes. As shown in Figure 1, PDB:1PTS is a homodimer, both complex and unbound structures are available in PDB. Figure 1 also shows that the docked structure perfectly coincides with the experimental one PDB:1PTS and RMSD is 1.0Å. Statistical study of RMSDs shows that 94% docking results are in the range of good docking with RMSDs smaller than 10 Å; and 67% docking results are in the range of very good docking with RMSDs smaller than 6 Å Figure 2.

3 Discussion
The present benchmark study shows that our new methodology is effective for the prediction of protein-protein interactions. Most of the structures are within X ray resolution, while those structures that have been predicted only approximately show change of conformation of the subunits at interaction. The results are similarly good with the target structures proposed by several rounds of the CAPRI [6] experiment, which will be treated in this presentation.

References