

Molecular Evaluation using Comparative Molecular Interaction Profile Analysis system

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Abstract

Creating a new molecular description factor based on the results of computational docking study will add new dimensions in molecular evaluation. We propose a new molecular description factor analysis system named Comparative Molecular Interaction Profile Analysis system (CoMIPA) in which the AutoDock program is used for docking evaluation of small molecule compound-protein complexes. Interaction energies are calculated, and the data sets obtained are named interaction profiles (IPFs). Using IPF as a scoring indicator, the system could be a powerful tool to cluster the interacting properties between small molecules and bio macromolecules such as ligand-receptor bindings. The system can use computational molecular docking results to explain biological events such as adverse drug reactions and possibly other unforeseen interactions caused by environmental hormones. We believe that the system has the potential to be a major stepping-stone for bridging computational science and biology.

1. Introduction

In this paper, we introduce a system named

Comparative Molecular Interaction Profile Analysis system (CoMIPA) that utilize virtual docking study for comprehensive analysis of molecular interactions. The docking engine uses AutoDock 3.0, which is widely used for docking evaluation of small molecule compound/protein complexes. By using pre-made grid maps for each receptor, the system can evaluate the possibility of these interactions faster. We propose that the new concept of profiling be called interaction profiles (IPFs), which is a dataset of interaction energies. Conventionally, physical and chemical properties such as molecular weight, volume, and electric charge have been used to characterize small molecules. We propose a new description factor, IPF which is valuable for directly comparing different molecular interactions.

2. Materials and Methods

Comparative Molecular Interaction Profile Analysis system (CoMIPA) is an application aimed to evaluate the molecular interactions between a small molecule compound and multiple proteins by docking analysis. The docking engine of CoMIPA

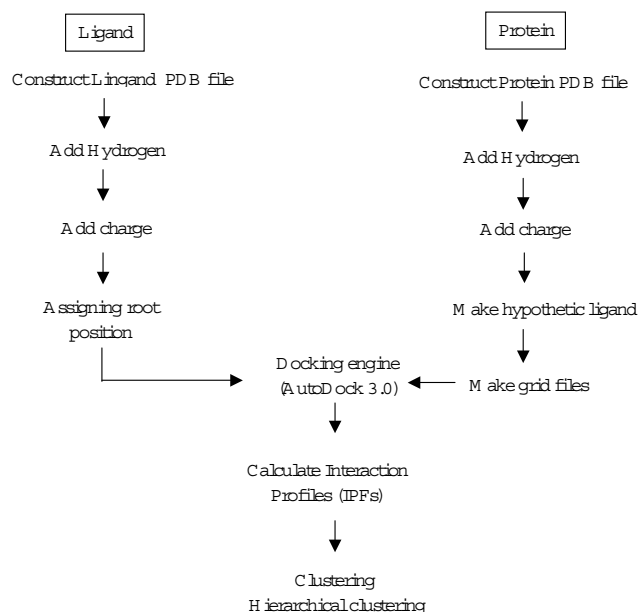


Figure 1. Outline of CoMIPA

consists of the AutoDock 3.0 program by script processing. AutoDock 3.0 is a molecule docking evaluation program that consists of three main components, AutoGrid, AutoTools and AutoDock 3.0¹. The results are displayed using a color-coded graphic representation with the freely available applications CLUSTER and TREEVIEW by M. B. Eisen et al.². We have reported the use of this system for another subject³ (Figure 1).

3. Result and discussion

We evaluated the interaction energy between one small molecule and 67 receptors in the receptor database using Comparative Molecular Interaction Profile Analysis system (CoMIPA). Gibbs free energy of docking (kcal/mol) against each receptor was calculated and the results were displayed online by using Web browsers.

For example, as multi-dimensional analysis of IPFs, we tried hierarchical clustering based on

coefficient of correlations between ligands and receptors. Using IPF as a scoring indicator, the system could be a powerful tool to cluster the interacting properties between small molecules and biomacromolecules such as ligand-receptor bindings.

In summary, we have developed a new system for biomolecular docking evaluation, named Comparative Molecular Interaction Profile Analysis system (CoMIPA). By using IPF, the system can use computational molecular docking results to explain biological events such as adverse drug reactions and possibly other unforeseen interactions caused by environmental hormones. We believe that the system has the potential to be a major stepping-stone for bridging computational science and biology.

4. References

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