Comparing Apples and Oranges – How Reliable are Molecular Docking Tools?

Vigneshwaran Namasivayam, Robert Günther*

Institute of Biochemistry, Faculty of Biosciences, Pharmacy und Psychology, Leipzig University, Leipzig, Germany

*E-mail: robguent@uni-leipzig.de

The development a novel drug is a time consuming and expensive process. Besides the identification of the target, a significant amount of time and money is required to screen large libraries of compounds for drug candidates. Computational methods, namely molecular docking techniques, play, thus, an important role in the drug discovery process. Employing these techniques, scientists hope to identify novel drug candidates by screening chemical libraries in silico.

A number of different molecular docking approaches have emerged in the last two decades. As all of these methods employ different algorithms and methods to create and evaluate the proposed protein-ligand complexes, a direct comparison is difficult. Moreover, some programs might be particularly more suited for docking on certain classes of proteins, e.g., kinases or proteases.

In this presentation, we will introduce a novel measure to compare the reliability of docking methods: the Docking Reliability (DR). This measure can be regarded as a standard deviation of all predicted protein-ligand poses of a data set with respect to the experimentally determined structures. In contrast to the commonly used average rmsd value, it considers wrongly predicted poses of a data set more stringent.

Based on a highly diversified data set comprising 100 protein-ligand complexes from the Protein Data Bank, numerous well-established docking programs will be compared. The resulting DR values will help the scientist to determine that particular docking program, which delivers the most reliable results with respect to the target under investigation.

Acknowledgement. The author acknowledges support of this work by the Deutsche Forschungsgemeinschaft (SFB 610).