

# The temptation of high-throughput docking: Possible strategies and the development of required tools

Peter Block, Christof Gerlach, Gerhard Klebe

Department of Pharmaceutical Chemistry, Marbacher Weg 6, 35032 Marburg  
Germany

*peter.block@staff.uni-marbug.de*

Recent improvements in both software and hardware principally allows to use docking in high-throughput mode as tool for virtual screening without prior application of sophisticated pharmacophore filters. Due to computational demand, ligand docking is usually applied as final step in virtual screening. As it is no longer the methodological bottleneck, it now can be used to generate ensembles of binding conformers which have to be post-processed with respect to sophisticated pharmacophore models and robust scoring schemes. This puts increasing demand on the reliability of the latter tools and affords efficient protocols for analyzing protein-ligand interaction geometries to filter vast amounts of docking solutions for various molecules to retrieve reliably the most promising candidates in automated fashion.

As a test example, we used the binding of Fusicocin, a fungal phytotoxin stabilizing the interaction between the C-terminus of the plant plasma membrane  $H^+$ -ATPase and 14-3-3 proteins. This stabilization leads to permanent activation of the proton pump resulting in wilting of the plant. Recently, the crystal structure of the ternary complex between a plant 14-3-3 protein, Fusicocin, and a pentapeptide representing the C-terminus of the  $H^+$ -ATPase has been solved[1]. We selected the Fusicocin binding site as target for our high-throughput docking attempt to screen for potential new ligands stabilizing the protein-protein interaction.

We used FlexX 2.0[2] as docking tool, tested on i386 and amd64 architectures. The results were analyzed with the Oracle-based Docking Database (DDB)[3]. Scoring functions newly developed in our group have been applied to rank the obtained data.

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## References

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