FlexX – Docking

BioSolveIT
expect actives!

FlexX is our modern, ultra-high-speed docking approach to predict the binding mode of ligands at a target binding site. Screen whole compound libraries within minutes to identify promising binders.

How does FlexX work?

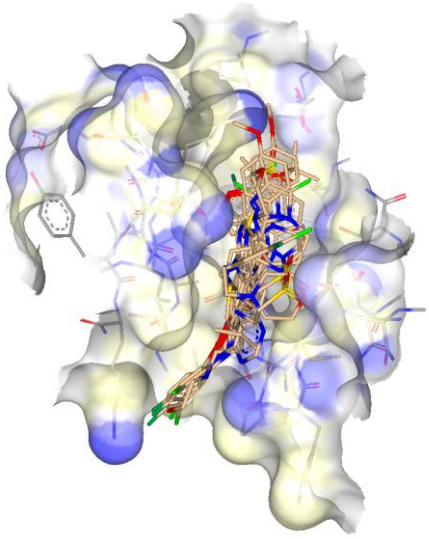
The FlexX docking functionality in SeeSAR places a ligand into a binding site. It is based on an incremental construction algorithm. Ligands are split into so-called fragments; An initial fragment (or combinations thereof) is placed into multiple places in the pocket – and scored using a simple yet very fast pre-scoring scheme. From the *n* solutions placed, the ligand is further built up, fragment by fragment, and the interim solutions are scored against each other. The best scored survive the process, and those are delivered to the user.

Advantages

- Docking for non-experts: No more receptor preparation – simply dock!
- Accurate binding mode prediction
- Dock gigantic libraries by using ultra-high-speed docking (< 1 s/ligand)

Virtual screening

FlexX4 sets new records in virtual HTS. It runs in parallel and automatically uses all cores of your computer – thread-safe. You can screen a library of ~1,000 compounds in less than an hour on a laptop with 8 cores. FlexX-based docking led in many application studies to superior enrichment ratios. Therefore, you effectively find active compounds in large libraries. It uses ligand-based or protein-based pharmacophore constraints not only as a post-filter but as guidance to find in a vast solution space the ones which obey the constraints.



Accurate binding mode prediction

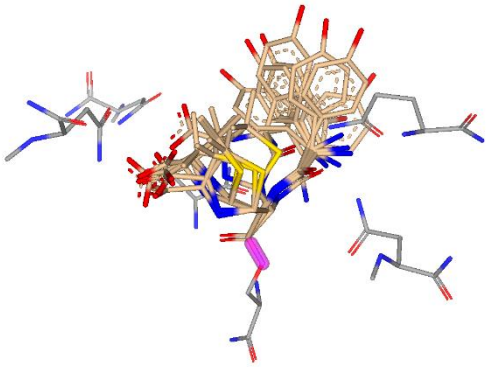
For a protein with known three-dimensional structure and a small ligand molecule, FlexX4 accurately predicts the geometry of the protein-ligand complex within a few seconds. It has been validated, benchmarked, and successfully used thousands of times as more than 10.000 citations of the original scientific publication (Rarey 1996) impressively demonstrate.

Template-based docking

Congeneric compound series can easily be docked. FlexX can superimpose a part of a ligand to dock onto a known crystal structure of a ligand. Template-based docking is performed by determining the Maximum Common Substructure (MCS) between the template and the compound-to-dock. Based on the MCS multiple overlays are generated to preserve the binding mode of the common core. The template needs to have at least 5 heavy atoms. Template-based docking represent an interesting method to accelerate virtual screening campaigns: By providing a reference molecules are sampled faster which reduced computational to a fraction.

Covalent docking

FlexX supports covalent docking and covers a broad array of scenarios: In general, all covalent warheads and targeted residues are supported. The flexibility allows the investigation of even rarely used functional groups and amino acids to generate sophisticated predictions of the ligands' binding modes.



Literature

Rarey, M.; Kramer, B.; Lengauer, T.; Klebe, G. A Fast Flexible Docking Method Using an Incremental Construction Algorithm. *J. Mol. Biol.* **1996**, *261* (3), 470–489.
https://doi.org/10.1006/jmbi.1996.0477.

Warren, G. L.; Andrews, C. W.; Capelli, A. M.; Clarke, B.; LaLonde, J.; Lambert, M. H.; Lindvall, M.; Nevins, N.; Semus, S. F.; Senger, S.; Tedesco, G.; Wall, I. D.; Woolven, J. M.; Peishoff, C. E.; Head, M. S. A Critical Assessment of Docking Programs and Scoring Functions. *J. Med. Chem.* **2006**, *49* (20), 5912–5931.
https://doi.org/10.1021/jm050362n.

Gastreich, M.; Lilienthal, M.; Briem, H.; Claussen, H. Ultrafast de Novo Docking Combining Pharmacophores and Combinatorics. *J. Comput. Aided. Mol. Des.* **2006**, *20* (12), 717–734.
https://doi.org/10.1007/s10822-006-9091-x.

Kubinyi, H. Success Stories of Computer-Aided Design. Computer Applications in Pharmaceutical Research and Development, **2006**, 377-424.
https://doi.org/10.1002/0470037237.ch16