FlexS – Superposition

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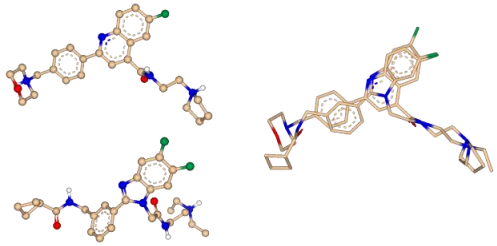
FlexS is a tool for predicting ligand superpositions. For a given pair of ligands, FlexS predicts the conformation and orientation of one of the ligands relative to the other one.

How does FlexS work?

FlexS is based on sophisticated physico-chemical models. In FlexS the reference-ligand is assumed to be rigid, thus, it should be given in a conformation which is similar to the bound state. The MIMUMBA torsion angle database is used for the creation of conformers, an interaction geometry database is used to exactly describe intermolecular interaction patterns. For scoring, the Böhm function (with minor adaptions necessary for docking) is applied.



Advantages

- Align molecules in 3D
- Prepare compounds for 3D QSAR analysis
- Find scaffolds and compound mimics
- Perform ligand-based virtual screening

What can I use FlexS for?

The two main applications of FlexS are ligand super-positioning (eg. for CoMFA/QSAR) and virtual screening. If you have a protein and a small molecule binding to it (so called reference-ligand) but no structure of the protein, you can take the reference structure as a negative fingerprint of the active site. Instead of calculating a docking, FlexS determines the similarity between the test and the reference structure by aligning them. In virtual screening, you have a reference-ligand and a set of compounds and you are interested in prioritizing the compounds for experimental testing. FlexS provides you with a ranked list by similarity in order to do so.

Interactive superpositioning

The superposition algorithm in FlexS requires only little manual intervention. Nevertheless, in some cases additional information about the ligands or even the superposition is known. You can integrate this knowledge into the computations with FlexS by carrying out single step manually. Thus, FlexS is designed for interactive work on ligand pairs as well as for ligand-based virtual screening.

Features of FlexS

On our ligand-ligand benchmark set of about 280 molecule pairs, FlexS takes less than 2 minutes per superpositioning prediction on the average. The computing time depends on the size of the ligands, and the degree of ligand symmetry and flexibility and lies in the range from a few seconds up to a few minutes. The conformational flexibility of the ligand is taken into account by considering both torsion angle flexibility as well as the conformational flexibility of ring systems. In the current version of FlexS, the reference ligand is rigid. The placement algorithm in FlexS is based on aligning interacting groups common between the molecules. This ensures that the search is limited to low-energy structures improving the quality of the results in a given amount of computing time.

Application scenarios

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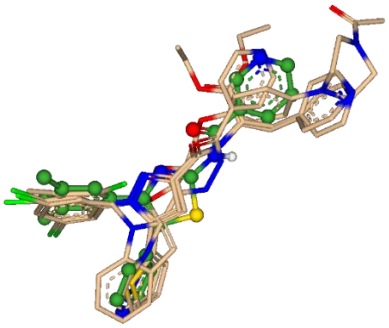

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Literature

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