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The influence of protonation in protein-ligand docking

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With the use in Virtual Screening (*VS*) in experiments Protein-Ligand-Docking has gained more and more importance in pharmaceutical research over the past years. To model the interactions between the protein and a ligand empirical scoring functions are used in many programs. These scoring functions consist of different terms, which describe physical and chemical properties important for an attractive interaction between the protein and the ligand. Most scoring functions use hydrogen bonds and salt bridges as descriptors. For both the knowledge of the protein's and the ligand's protonation state is important but experimental methods like x-ray crystallography do not resolve the hydrogen atom positions in protein structures.

To estimate the influence of the ligand's protonation on the docking results with PLANTS [1] and Gold [2] different protonation states of each ligand of the ASTEX clean test set [3] were automatically generated using a combinatorial method. This method adds and removes single hydrogen atoms and considers ketone-enol tautomerism on the ligand side. The number of different protonation states ranged from 1 to 64 depending on the ligand's structure. For a small number of test cases, the different protein protonation states were also generated by applying the same method to the surface atoms of the binding pockets. Docking studies for all gernerated protonation states were made using PLANTS and Gold with standard settings.

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