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Evaluation of Automated Docking Programs for Screening and Structure-Based Inhibitor Design.
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A structural-based approach to drug design and screening has become increasingly important as the number of protein-ligand complexes available in the Protein Data Bank (PDB) continues to increase rapidly. The quality of the results from virtual screening is directly related to the ability of a particular software program to position the ligands into a targeted binding site (called a targeted receptor molecule) with accuracy and precision. Because of the different algorithms used by various docking programs combined with the inherent differences in shape of a binding pocket for ligand-bound proteins, a particular program may be appropriate for one targeted binding site, while another docking program may not. In order to better understand and reconcile these differences, four docking programs are evaluated in this comparative study: AutoDock3, DOCK5, Surflex, and GOLD. Differences between the algorithms of these programs are presented utilizing single-ligand docking and database screening. Testing the programs against the target receptor site with known inhibitors already evaluated through “actual” not “virtual” screening provides the most effective method to select the appropriate program for each individual binding site. An automated approach to evaluating docking programs for use with available structures in the PDB is presented.