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Title (English) New scoring-functions for docking smaller molecules to proteins: Evaluation on ligands containing nitrogenous base -moieties		
Title (Swedish)		
Abstract <p>Molecular modeling approaches aimed at prediction of the spatial structure of a ligand-receptor complex, given the 3D-model of the latter, are referred to as molecular docking. They are widely used in both the fundamental studies of molecular mechanisms of protein functioning and in drug design. In this work, new methods to improve the efficiency of scoring the putative protein-ligand complexes in molecular docking are presented. A promising method – consensus docking, which has been previously successfully used in scoring the interactions of adenine-containing ligands with proteins is now adapted for another important class of nitrogenous base -ligands – cytosine-containing compounds.</p> <p>Based on statistical analysis of 3D-structures of a representative set of 50 complexes of cytosine-containing ligands with different proteins an array of new scores is proposed which capture and model concepts of physical phenomena that drive the recognition of cytosine by protein-receptors – such as hydrogen bonds, aromatic stacking interactions and hydrophobic/hydrophilic interactions.</p> <p>The proposed scores implement the concept of molecular hydrophobicity potential to model the hydrophobic/hydrophilic properties of molecules. Also, statistical modeling through a knowledge-based potential is used to implicitly describe the above-mentioned intermolecular interactions. The new scores were validated on a set of docking conformers for the studied 50 complexes that were generated using two popular docking programs, GOLD and Glide. Most of our scores combining multiple scoring methods were demonstrated to have an excellent potential for scoring the targeted type of molecular complexes.</p>		
Keywords Molecular docking, protein, ligand, scoring function, nitrogenous base, cytosine, hydrogen bond, stacking, hydrophobic, hydrophilic, MHP, empirical, knowledge-based, backbone, motif, GOLD, Glide		
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