Flexible Receptor Molecular Docking – Performance of Molecular Docking Methods on Physiologically Important Protein Targets

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Knowledge about the molecular details of protein-ligand recognition is crucial for understanding many biochemical processes. Computational molecular docking tools are frequently used to predict the geometries of protein-ligand complexes. However, to increase the computational efficiency of the methods, in most docking approaches the receptor geometry is treated either rigid or semi-rigid. Although this is a valid approximation in many cases, often full flexibility of the receptor during docking is needed for a realistic prediction of the geometry of the protein-ligand complex.

Recently, we developed a docking program, DynaDock [1], which treats the whole protein-ligand complex fully flexible. It is based on a specially tailored simulation method, Optimized Potential Molecular Dynamics (OPMD), and allows for a very efficient refinement of protein-ligand poses.

We evaluated the methods' performance for protein-ligand complexes which show conformational changes in the protein backbone upon ligand binding. For this purpose cross-docking studies were performed on different physiologically important protein targets. The results show that with our docking approach we are able to treat conformational changes in the backbone of the receptors binding site upon ligand binding correctly. This is not possible with most other docking programs, which are based on the use of side chain rotamers for the treatment of binding site flexibility, like AutoDock [2].

[1] I. Antes, *Proteins: Struct. Funct. Bioinf.*, **2010**, *78 (5)*, 1084-1104
[2] G. M. Morris, R. Huey, W. LindStrom, M. F. Sanner, R. K.Blew, D. S. Goodsell, A. J. Olson, *J. Comput. Chem.*, **2009**, *30 (16)*, 2785-2791.