[L11] Empirical scoring functions for affinity prediction of protein-ligand complexes

Lukas P. Pason and Christoph A. Sotriffer

Institute of Pharmacy and Food Chemistry, University of Würzburg, Am Hubland, D - 97074 Würzburg, Germany

The ability to rapidly assess the quality of a protein-ligand complex in terms of its affinity is of fundamental importance for various methods of computer-aided drug design. While simple filtering or matching criteria may be sufficient in fast docking methods or at early stages of virtual screening, estimates of the actual free energy of binding are required whenever refined docking solutions, ligand rankings or support for the optimization of hit compounds are required. If rigorous free energy calculations based on molecular simulations are impractical, such affinity estimates are provided by scoring functions. The class of empirical scoring functions aims to provide them via a regression-based approach. Using experimental structures and affinity data of protein-ligand complexes and descriptors suitable to capture the essential features of the interaction, these functions are trained with classical linear regression techniques or machine learning methods. The latter have led to considerable improvements in terms of prediction accuracy for large generic data sets. Nevertheless, many limitations are not yet resolved and pose significant challenges for future developments.