Comparative Structural and Energetic Analysis of Receptor-Ligand Interactions

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To analyze interactions between biologically important molecules, two methods, Protein Interaction Property Similarity Analysis (PIPSA) [1-3] and COMparative BINding Energy (COMBINE) analysis [4-6], were developed in our group:

PIPSA compares the interaction properties of structurally homologous proteins and quantifies the similarities and dissimilarities between them. E.g., it can be used to examine correlations between electrostatic and biological properties to identify specific molecular recognition features for targeting in structure-based drug design.

COMBINE analysis permits the derivation of 3D quantitative structure-activity relationships (QSAR) using structures of receptor-ligand complexes and experimentally determined binding affinities. The principal idea of COMBINE analysis is that the binding free energy is correlated with a subset of weighted interaction energy terms for a training set of receptor-ligand complexes. After statistical analysis, a target-specific scoring function can be derived to predict the binding affinity of new receptor-ligand complexes and to highlight important interactions for binding specificity.

This talk will give a brief introduction to both methods and will show applications in drug discovery.

[1] Wade *et al.* (2001) Int. J. Quant. Chem. 83, 122-127. [2] Blomberg *et al.* (1999) Proteins 37, 379-387. [3] Henrich *et al.* (2008) ChemMedChem 3, 413-417. [4] Ortiz *et al.* (1995) J. Med. Chem. 38, 2681-2691. [5] Wade *et al.*. (2004) DDT: Technologies 1, 241-246. [6] Wade *et al.* (1998) Perspectives in Drug Discovery & Design 11, 19-34.