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Exemplifying use of high accuracy quantum chemistry methods for protein ligand interaction

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Understanding the nature of protein–ligand interaction on an atomistic level is highly instructive to assess safety and efficacy of small molecule drugs as well as agrochemicals. The binding of drugs to their biomolecular targets involves complex patterns of noncovalent interactions between the ligand and the residues in the protein's binding pocket. Here we show two use cases of a generally applicable, parameter-free, computational method, that allows identification, quantification, and analysis of the key ligand–residue interactions responsible for molecular recognition. Ultimately, we use Local Energy Decomposition analysis coupled cluster DLPNO-CCSD(T) level of theory, which can be considered the "gold-standard" for electronic structure calculations. In two case studies we exemplify these methods for (i) rationalizing sensitivity and selectivity of nicotinic acetylcholin agonists and (ii) for deriving a binding mode hypothesis for an important CYP51 inhibitor. By inference, the method is applicable to any kind of host/guest interactions with potential applications in industrial biocatalysis and protein engineering.

Biography

After a PhD in theoretical chemistry from University Cologne (Prof. G. Hohlneicher) including some time as a visiting researcher at Lund University (Prof. B. Roos), followed by a PostDoc with Prof. W. Thiel at Zürich University, MEB joined Bayer AG as a computational chemist in 1999. Since 2005, he build up and managed computational science groups across different European research sites in Bayer's Crop Science Division. Since 2019, MEB is a distinguished science fellow at Bayer and focusses on scientific activities. Since 2008 he lectures computational methods for drug discovery at Technical University Dortmund.