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# High-accuracy QM in life sciences: From drug properties to binding

Most computational methods for biomolecular modeling rely on empirical parametrization, limiting their predictive power and applicability. This challenge is particularly pronounced for complex biomolecular targets such as RNA, metalloproteins, and targets for covalent binding, which often fall outside the applicability domain of standard force fields and require extensive parametrization efforts. In this talk, we introduce a new computational approach that enables the accurate calculation of interaction energies between fragments of ligands and fragments of the target's active site. This method builds upon the DLPNO-CCSD(T) framework, leveraging recent algorithmic advancements that enhance both accuracy and efficiency.[1, 2] By systematically decomposing the interaction energy, we provide detailed insights into the nature of ligand-target binding, identifying key interactions that drive molecular recognition. We demonstrate the power of this approach through applications to biomolecular systems, including protein-ligand and RNA-ligand interactions. By dissecting the energetic contributions of specific fragments and functional groups, we offer a deeper understanding of binding mechanisms, which can be directly applied to rational drug design and biomolecular engineering. Additionally, we discuss best practices for the method's application in real-world biochemical studies. This new fragment-based interaction energy analysis provides a valuable tool for deciphering complex biomolecular interactions, offering both high accuracy and practical applicability in drug discovery and structural biology.

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