A Semi-Empirical Energy Decomposition Analysis for large (Bio)Molecular Systems

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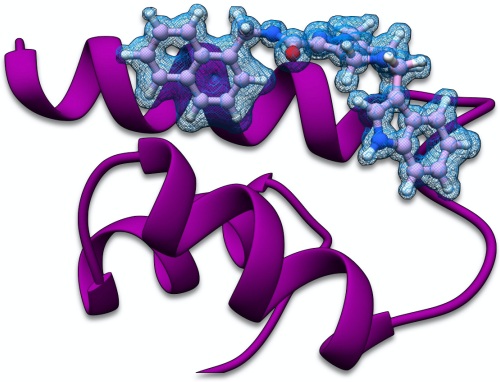

Quantum Chemical Energy Decomposition Analysis (EDA) is a valuable tool that permits understanding of the physical basis that leads to the formation of non-covalent interactions. Many algorithms have been proposed, which bring out several views over what is the physical basis that leads to binding. [1-10] Most of them are by construction compatible with Hartree-Fock or density functional methods, thus the system size that may be included in the calculations is quite limited. Treating systems of biological interest is unthinkable without severe truncation of the molecules. Nevertheless, EDA algorithms would be beneficial for the drug discovery communities in their efforts to develop better inhibitors: a more systematic view over the effects of certain structural modifications on the protein-ligand interactions.

Here we present a new Energy Decomposition Analysis fully compatible with semi-empirical quantum chemistry (NDDO and Tight Binding based). Due to the reduced computational cost of the underlying quantum mechanical methods, our new algorithm may be applied to large chemical systems, *e.g.*, of biological interest, using modest computational resources (a personal computer). We furthermore make our EDA algorithm atom specific. [10,11] Due to this construction, powerful interaction maps are constructed, which bring a deeper understanding of the role played by certain atoms/functional groups for the interactions with the biological target. The new semi-empirical EDA [12] will be available from our in-house semi-empirical package, ULYSSES. [13]

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