Oral presentation

Extraction of quantitative information through a noncovalent interaction index (NCI) method based on extremely localized molecular orbitals

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In modern quantum chemistry and quantum crystallography, the Noncovalent Interaction (NCI) index [1, 2] has recently emerged as a prominent and useful tool for discerning noncovalent interactions within molecular systems. Initially, its application was merely confined to qualitative descriptions. However, recent advancements have expanded its capabilities to provide quantitative insights [3, 4]. This extension involves the consideration of integrals of powers of the electron density and necessitates a clear decomposition of the overall electron distribution into fragment contributions for the definition of the underlying integration region. This fragmentation was previously based only on approximate promolecular electron densities, which are overly simplistic due to their reliance on tabulated spherically averaged atomic electron density distributions.

To improve the quantum mechanical rigor of NCI-index analyses, we have recently proposed [5] to exploit electron densities obtained through the transfer of Extremely Localized Molecular Orbitals (ELMOs) from tailor-made libraries [6-8] or through the application of the novel Quantum Mechanics/Extremely Localized Molecular Orbital (QM/ELMO) embedding technique [9,10]. Both approaches cheaply offer fully quantum mechanical electron densities that always remain easily partitionable into subunit contributions. This characteristic makes the obtained electron distributions suitable for NCI integral calculations and for subsequent quantitative NCI analyses.

In this presentation, in addition to presenting the new quantitative versions of the NCI technique, the values of NCI integrals obtained through different approximations will be compared to interaction energies computed at a high quantum chemical level (notably at Coupled Cluster level). It will be shown that the NCI integrals based on ELMO electron densities always largely outperform the promolecular ones [5]. Moreover, it will be particularly described how the novel quantitative NCI-(QM/)ELMO approach proves to be valuable for characterizing and assessing the strength of interactions between ligand subunits and protein residues in protein-ligand complexes, also allowing to easily track the evolution of noncovalent interactions during Molecular Dynamics simulations [5].

Although there is room for further methodological enhancements, the newly proposed variants of the quantitative NCI approach relying on extremely localized molecular orbitals show high promise to study situations that will require rapid and reliable assessments of noncovalent interactions, such as in computational high-throughput screenings for drug discovery endeavours. Moreover, possible applications of the new ELMO-based quantitative NCI techniques to supramolecular chemistry and crystal engineering are also expected and will be discussed as interesting perspectives.

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