

# Computational Design of Molecular Properties: Spotlight on Accuracy and Tuning

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**Abstract:** The Laboratory for Computational Molecular Design at ISIC devises original and accurate methodologies to establish, *in silico*, key structure–property relationships of large chemical systems with particular emphasis on those associated with  $\pi$ -conjugated framework. Herein, we discuss two specific focuses of our activities: i) the development of accurate formalisms based on Kohn–Sham density functional theory to achieve quantitative results for the energies and geometries of extended systems featuring weak interactions and ii) the introduction of schemes to probe and tune the effect of intra- and intermolecular charge transfer on molecular properties. The proposed methodologies are ideally designed to tackle and resolve some of today’s relevant aspects associated with the properties of  $\pi$ -conjugated molecules, such as identifying relationships resulting in high stacking capacities, proposing more stable alternative topologies to large acenes, and analyzing the course of reaction involving assemblies of  $\pi$ -conjugated molecules.

**Keywords:** Density functional theory · Molecular properties · Structure-property relationships



## 1. Introduction

The Laboratory for Computational Molecular Design was established in September 2007, headed by Sandoz Family Foundation Assistant Professor Clémence Corminboeuf.

The overarching laboratory objective is applying and developing computational-based techniques for establishing key structure-property relationships of extended systems and designing novel functional molecules and materials. Particular emphasis is placed on properties associated with  $\pi$ -conjugated frameworks featuring interactions which are ubiquitous in chemistry. The interactions of  $\pi$ -conjugated systems play, for instance, key roles in the field of organic electronics and gas storage materials. Additionally, such interactions are responsible for the stabilization of DNA, and the binding between proteins and drugs. In pursuit of our objectives, a two-pronged approach is used (Fig. 1). The first includes developing and benchmarking accurate Kohn–Sham density

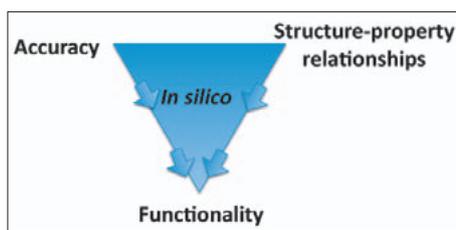


Fig. 1. Spotlight of LCMD’s research.

functional theory-based methodologies to achieve quantitative results for the energies and geometries of large-sized molecules. Secondly, we introduce schemes to probe and tune the effect of intra- and intermolecular charge transfer on molecular properties. The following gives a brief overview of two aspects of our current ongoing research.

## 2. Accuracy of Kohn–Sham Density Functional Theory

Density functional theory (DFT) now serves as the primary workhorse of many computational/theoretical chemistry groups due to its combination of accuracy and speed. Despite its widespread use, important shortcomings are known. For instance, DFT cannot accurately describe interactions between non-overlapping densities. This result is illustrated simply by the energy associated with the sandwich benzene dimer, which is established *via* both experiment<sup>[1]</sup> and high-level computation<sup>[2]</sup> to have an interaction energy of 1.7 kcal/mol, but is either unbound or

too weakly bound with standard density functionals.<sup>[3]</sup> Similar energetic problems are also seen for seemingly simple hydrocarbon compounds,<sup>[4]</sup> where DFT fails to reproduce the energy associated with intramolecular interactions.

As our laboratory is concerned with the accurate description of extended electronic systems and their associated properties, overcoming these errors is crucial. We demonstrated, in 2009, that inter- and intramolecular weak interactions could be corrected jointly by applying a dispersion correction tailored for weak intramolecular interactions.<sup>[5]</sup> This simple remedy consists in accounting for the missing interactions by adding *a posteriori* an attractive energy term summed over all atom pairs in the system. The damped atom pairwise additive London-dispersion expression is highly valuable for introducing weak long-range attraction in molecules and soft-matter, at minimal computational cost.<sup>[6]</sup> A significant shortcoming associated with fixed empirical dispersion coefficients (used in our earlier schemes<sup>[5,7]</sup>) is the lack of dependency on the electronic structure. The derivation of accurate atomic dispersion coefficients dependent on the molecular environment represents an attractive alternative. Thus our more recent scheme<sup>[8]</sup> derives system-dependent dispersion coefficients (Eqns (1) and (2)), computed according to Becke and Johnson’s exchange-hole dipole moment (XDM) formalism, based on the idea that the fluctuating dipole moments responsible for dispersion are related to the dipole arising from the exchange hole and its reference electron.<sup>[9]</sup>

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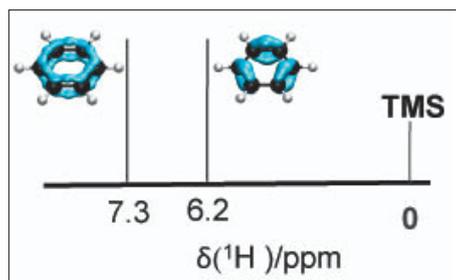


Fig. 4. NMR  $\delta(^1\text{H})$  chemical shifts for benzene (left) and 1,3,5-cyclohexatriene (1b). The iso-surfaces represent the localized orbital locators of benzene and 1,3,5-cyclohexatriene. Chemical shifts are computed at the (BLW)-PW91/IGLO-III level. (See ref. [15] for more details).

to demonstrate experimentally can be generalized to other pericyclic reactions (e.g. Cope).<sup>[21]</sup>

Multiple efforts to extend and validate the robustness and the fields of applicability of the current formalism are underway. In addition, special emphasis is placed on the combination<sup>[14]</sup> and applications of both schemes (i.e. dDsC and BLW-based methods), which are ideally designed to tackle and resolve some of today's relevant aspects associated with the properties of  $\pi$ -conjugated molecules (e.g. identifying relationships resulting in high stacking capacities, proposing more stable alternative topologies to large acenes, analyzing the course of reaction involving assemblies of  $\pi$ -conjugated molecules).

Other aspects of LCMD's research, not elaborated herein, include the derivation and quantification of chemical concepts using computational means,<sup>[4g,22]</sup> and the analysis of tools for the prompt characterization of potential energy surfaces.<sup>[23]</sup>

#### 4. Conclusions and Outlooks

To summarize, LCMD has recently delivered accurate and innovative methodologies that allow theory and computation to obtain fundamental insights into structure–property relationships of extended systems especially those carrying a  $\pi$ -conjugated framework. Our simple GGA-based model for computing density-dependent dispersion coefficients has led to the inclusion of the missing dispersion interactions into standard density functional at low computational cost. Our resulting density-dependent correction, dDsC, that has proven to be highly accurate for describing various intermolecular complexes and reaction energies, is now used routinely in our laboratory and implemented in several quantum chemistry codes. The computation of the molecular properties of resonance structures have also been shown

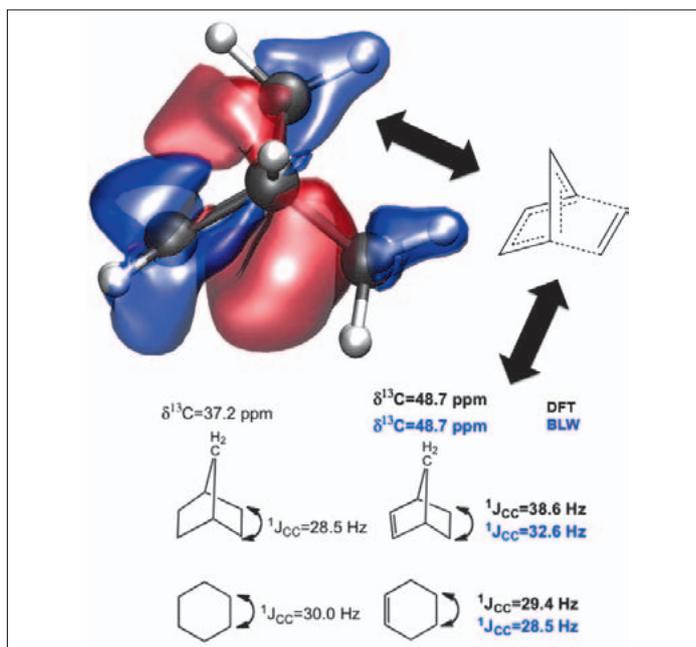


Fig. 5. Electron density difference,  $\delta(^{13}\text{C})$  chemical shifts and  $^1\text{J}$  coupling constants of norbornene and localized norbornene (see ref. [17] for details).

to offer a unique strategy for establishing relevant guidelines inaccessible otherwise. Relying on these schemes, our current research efforts should result in the design of  $\pi$ -conjugated molecular systems optimized with respect to their properties.

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