



The Conversation on Non-Covalent Interactions: an introduction

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We are pleased to present *Non-Covalent Interactions* as the topic of the first *Conversation* in *Journal of Molecular Modeling*. The theory of covalent bonding was the central topic within the quantum chemistry in the twentieth century. After the passing of more than two decades into the new century, it is becoming clear that non-covalent interactions will take the corresponding role of the twenty-first century. This change of focus is a logical consequence of the developments in theory and computational technology. In the early days of quantum chemistry, the efforts were focused on small molecules where the predictions of chemical reactivity and molecular properties were largely governed by the accuracy of the modeling of the covalent bond. However, as the size of molecular systems that are feasible to study gradually has increased, the high importance of non-covalent interactions has become increasingly evident. A typical example is that London dispersion, which was largely ignored in twentieth century quantum calculations, has been found to be of significant importance not only for intermolecular interactions but also for intramolecular interactions, findings that have to a great extent resulted from the introduction by Grimme and coworkers of dispersion in terms of force-field type corrections into molecular DFT calculations [1].

However, the major reasons for the increasing interest in non-covalent interactions are developments outside of the theoretical community. The instrumental role of non-covalent interactions in medical and biochemical processes has become increasingly apparent; computational drug design, as an example, is today mainly the task of modeling

non-covalent interactions. Similarly the emerging field of supramolecular chemistry has sparked a renewed interest for non-covalent interactions. Here the exclusive role of hydrogen bonding for building supramolecular structures has been challenged by a range of new interaction types bearing the names of the groups of elements involved, starting with halogen and followed by chalcogen, pnictogen, tetrel, icosagen, aerogen, and most recently by the regium bond, where regium refers to the coinage metals, copper, silver, and gold [2–4].

Although relatively new by name, the halogen bond as interaction has been known since the nineteenth century; the first halogen bonded complex was reported already in 1863 [5]. The theory of the halogen bond is an excellent example of how the conceptual understanding of non-covalent interactions has changed with time. The halogen bond was originally characterized as a charge transfer interaction by Mulliken in 1950 [6]. This remained the commonly accepted paradigm until 1993 when Brinck et al. recognized that the strength and directionality of the interactions between Lewis bases and organic halogen compounds can be explained from the anisotropy of the surface electrostatic potential on the halogen atom [7]. The electrostatic interpretation formulated as σ -hole bonding became commonly accepted in the beginning of this century [8], but has in recent years been increasingly challenged by scientists advocating the importance of charge transfer [9–11].

The vivid discussion on the physical origin of halogen bonding has been an inspiration for introducing *Conversations* to *Journal of Molecular Modeling*, and for choosing the theory of non-covalent interactions as one of the first topics. In this issue, a number of scientists have been invited to present their preferred methods for analysis and to discuss the bearing of the analysis on the physical understanding of non-covalent interactions. Each contribution ends with a question and answer section (Q&A) where questions from the authors of the other articles are answered. The intention behind the Q&A is to encourage discussion, and to highlight the differences and similarities of the different interpretations. The reader will note that consensus is rarely reached

This paper belongs to the Topical Collection Conversation on Non-Covalent Interactions.

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after the Q&A. Instead, we encourage the interested reader to draw his/her own conclusions, get involved in the discussion, and contribute to the *Conversation*.

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