NCI, a full story : theory, implementations and applications

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Atoms in Molecules (AIM) theory [1] is routinely used to assess hydrogen bond formation, however its stringent criteria controversially exclude some systems that otherwise appear to exhibit weak hydrogen bonds.
NCI [2,3] is a new tool based on the density and its derivatives that provides a rapid and rich representation of van der Waals interactions (green), hydrogen bonds (blue), and steric clashes (red) as low-gradient-low-density isosurfaces (see Figure 1). More generally, a view of non-bonded interactions emerges as continuous surfaces rather than close contacts between atom pairs, providing insight into the multiple small contribution to macromolecular interaction.
This regional approach to interactions overcomes the known caveats of analyzing electron density critical points in AIM, which are too restrictive because of their locality. Firstly, we show that NCI is able to provide a chemically intuitive description of hydrogen bonding for a series of 1,n-alkanediols that experimentally demonstrate hydrogen bonds of varying strength, where AIM fails. [4]

Since understanding non-convalent interactions requires an inherent quantification for their comparison, we have introduced the definition of NCI volumes The connexion between integrals and energetics is reviewed for benchmark systems, showing that this simple approach can lead to GGA-quality energies while scaling with the number of atoms involved in the interaction (not the total number of atoms). Given the inherent interest of these local approaches to big systems, we have also incorporated an adaptive grid which allows the quantification of NCI properties in big systems where wavefunctions are not available in a fast, parallelizable and efficient manner. This type of implementation can for example be used to analyse the evolution of classical MD trajectories. We show that the approach is able to reveal non-equilibrated runs and highlight the main interactions in equilibrated ones.

In order to render it more accessible, this latest version of the code [5] has been implemented in the free web server NCIweb [6], which allows the fully automatized analysis of non-covalent interactions of large PDB files in a matter of minutes, providing a powerful resource to the biochemistry community.

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