The Role of Aromaticity, Hybridization, Electrostatics, and Covalency in Resonance-Assisted Hydrogen Bonds of Adenine–Thymine (AT) Base Pairs and Their Mimics

Invited for this issue’s cover are Dr. Célia Fonseca Guerra from the VU University of Amsterdam and her collaborators at the University of Girona. The cover picture shows H-bonds in the adenine–thymine Watson–Crick base pair. An essential part of these H-bonds is their covalent component arising from donor–acceptor interactions between N or O lone pairs and the N–H antibonding π* acceptor orbital. This charge-transfer interaction is represented by green figures walking on the pedestrian crossing, connecting the bases. This covalent component is the reason why H-bonds between DNA and/or unsaturated model bases are significantly stronger than those between analogous saturated bases. This contrasts sharply with the classical picture of predominantly electrostatic H-bonds which is not only incomplete in terms of a proper bonding mechanism, but also fails to explain the trend in stability. For more details, see the Full Paper on p. 318 ff.

What is the most significant result of this study?
Our quantum chemical bonding analyses shatter a textbook model. Up till now, the explanation for the enhanced strength of the H-bonds between two sp² hybridized monomers, such as adenine (A) and thymine (T) bases, has been attributed to a reinforcement by the π electrons, the so-called resonance-assisted hydrogen bonding (RAHB). But we prove RAHB is not the reason for this enhanced H-bond strength. Instead, our analyses identify that the main reason is the more stabilizing covalent component in such H-bonds which occur in the A–T DNA base pair. Besides getting the bonding mechanism right and explaining an experimentally observed trend, our work also highlights the value of molecular orbital (MO) theory in the realm of supramolecular chemistry.

What was the inspiration for this cover design?
It was an association of Salvador Dalí’s surrealist paintings with our finding that electronic orbitals hold together the “molecule of life”. I learned about many of these paintings during my research stays in Girona when I visited the Dali museum in nearby Figueres.

What other topics are you working on at the moment?
I am working on various quantum chemical studies about bonding mechanisms in different self-assembly processes in supramolecular chemistry. Self-assembly is based on weak interactions, such as halogen- and H-bonding, commonly conceived as caused exclusively by van der Waals forces and/or electrostatic attraction. However, the stabilization associated with the aggregation process and the directionality of the resulting bonds are often driven by the covalent part of these interactions. A detailed understanding of the nature and bonding mechanism of halogen- and H-bonds can consolidate the theoretical foundation of supramolecular chemistry and provide valuable design principles.