B-DNA and G-DNA Structure and Stability: insight from quantum chemical computations

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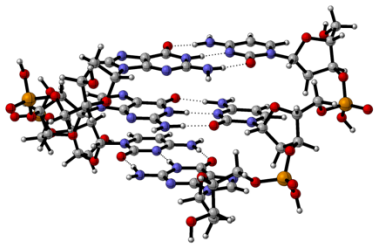
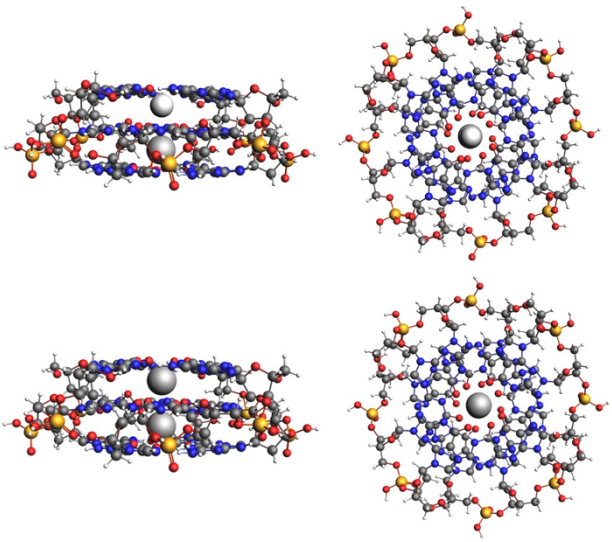
DNA can fold into different structures. In this presentation, quantum chemical studies on large segments of B-DNA and G-DNA will be presented.



The influence of the nucleotide composition and order on the stability of double-stranded DNA triplets will be presented. We have studied 32 duplexes, covering all possible nucleotide sequences with Watson-Crick base pairing. The formation energy of the duplex from two complementary strands can be decomposed into the deformation, (de)solvation, and the interaction between the complementary strands. Our analyses reveal enhanced stabilities for B-DNA duplexes possessing a higher GC base pair content, and that the stability depends on the order in which the nucleotides occur. Explanations for this will be shown. [1,2]



In the second part of the presentation, the focus will be on the G-DNA, guanine-rich sequences of DNA, which occur at crucial regulatory hotspots of the human genome, such as telomeres, and fold up into a four-stranded type of structure. Understanding of the stability and bonding of these quadruplexes is traditionally obtained in an indirect way via experiments. In this presentation, dispersion-corrected Density Functional Theory computations on these large biological systems are presented. We show that the cooperative reinforcement between hydrogen bonds in guanine quartets originates from the charge separation that goes with donor–acceptor orbital interactions in the electronic system and expresses the need for a quantum chemical approximation. Furthermore, the experimental order of affinity of the guanine quadruplexes for the cations Li^+, Na^+, K^+, Rb^+, Cs^+ is reproduced by our computations on these large biological systems. We reveal also how pollution metals can interfere with these DNA superstructures upon coordination and how they could induce genomic instability.[3-7]

[1] G. Barone, C. Fonseca Guerra, F. M. Bickelhaupt, ChemistryOpen **2013**, *2*, 186.
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[3] C. Nieuwland, F. Zaccaria, C. Fonseca Guerra, *Phys. Chem. Chem. Phys.* **2020**, *22*, 21108.
[4] F. Zaccaria, C. Fonseca Guerra, *Chem. Eur. J.* **2018**, *24*, 16315.
[5] F. Zaccaria, G. Paragi, C. Fonseca Guerra, *Phys. Chem. Chem. Phys.* **2016**, *18*, 20895.
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