

Insights from Theory into Structure and Stability of Guanine Quadruplexes

Célia Fonseca Guerra^{a,b}

a, Vrije Universiteit, De Boelelaan 1083, Amsterdam, The Netherlands,

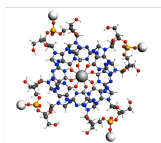
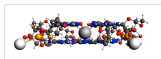
b, Leiden University, Einsteinweg 55, Leiden, The Netherlands.

* c.fonsecaguerra@vu.nl



Abstract

Guanine-rich sequences of DNA, which occur at crucial regulatory hotspots of the human genome, such as telomeres, can 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 DFT computations on these large biological systems are presented and quantitative Kohn-Sham molecular orbital (MO) theory together with the corresponding energy decomposition analyses are applied to elucidate the bonding mechanism in molecular recognition.[1-4] We show that the cooperative reinforcement between hydrogen bonds in guanine quartets is not caused by π -electronic resonance assistance, but originates from the charge separation that goes with donor-acceptor orbital interactions in the σ -electron system.[1-4].



Furthermore, the quantum chemical computations on these supramolecular systems reproduce the experimental order of affinity of the guanine quadruplexes for the cations Li^+ , Na^+ , K^+ , Rb^+ , Cs^+ . The strongest binding is computed between the potassium cation and the quadruplex as it occurs in nature. We reveal that (and how) desolvation and the size of the alkali metal cation both matter for the order of affinity.[1,6]

Reference and notes

- [1] F. Zaccaria, G. Paragi, C. Fonseca Guerra, *Phys. Chem. Chem. Phys.* 2016, 18, 20895-20904.
- [2] L.P. Wolters, N. W. G. Smits, C. Fonseca Guerra, *Phys. Chem. Chem. Phys.* 2015, 17, 1585-1592.
- [3] F. Zaccaria, C. Fonseca Guerra, submitted.