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# EuCompChem2025 – Snezhana Bakalova – Oral Conformations of Model G-quadruplexes

Conformations of Model G-quadruplexes Snezhana M. Bakalova, Jose Kaneti Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences Acad. G. Bonchev str., Block 9, 1113 Sofia, Bulgaria snezhana.bakallova@orgchm.bas.bg Our simplest model of a G-quadruplex consists of two guanine Hoogsteen-bonded quartets, stacked onto each other and neglects the connecting pentose—phosphate links of DNA or RNA. Amid the two quartets resides a K+, or Na+. The two alkali cations coordinate guanine oxygen atoms in a square antiprism. [1] Thermochemical DFT calculations show this structure is stabilized by more than 100 kcal.mol-1 with respect to isolated component molecules. The great complex stabilization, and its remarkable hydrophobicity, explain the exceptional self-association of guanine-rich strands of RNA or DNA into the noncanonical quadruplex secondary structure. Divalent and higher valence cations might in principle participate in the formation of G-quadruplexes as well. However, our calculations show that even the closest to alkali cations, Mg2+, does not produce the approximate square planar arrangement of G-quartets around the cation. The structure of the putative magnesium quadruplex is computed to have a saddle form instead of square planar.

Our hypothesis is that divalent and transition metal cations, building nonplanar guanine quartet complexes, are not capable of functions served by K+ and Na+ and possibly unwind secondary structures of DNA and RNA. [2] The roles of planar G-quadruplexes are possibly due to the additional stacking mode of interactions with potential ligands, facilitated by the planar guanine quartets, instead of just binding to hydrophilic grooves of canonical NA. This research has been funded by the Bulgarian National Research Fund via grant KP-06-N59/1 of 15.11.2021, and sponsored by grant D01-325/01.12.2023 and Consortium Petascale Supercomputer-Bulgaria and EuroHPC supercomputer.

[1] J. Kaneti, M. Georgieva,... S. M. Bakalova, BBA Gen. Subjects. 2020, 1865, 129773. [2] J. Kaneti, N. Kircheva, S. Angelova, S. M. Bakalova, submitted.

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