

## Nanochemistry and biotechnology

### A theoretical study of cation movement in G-quadruplex DNA nanostructure

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Specific guanine-rich DNA sequences can form G-quadruplex (G4) structures consisting of the stacks of planar guanine quartets linked by non-canonical systems of hydrogen bonds. These structures present e.g. in telomeres and promoter regions of some genes play a crucial biological role and are promising targets for modern anticancer therapy. G4 assemblies are stabilized by Na<sup>+</sup> or K<sup>+</sup> ions coordinating the guanine bases and localized in the central quadruplex channel between guanine quartets. The movement of these cations within G-quadruplex nanostructures may be a key factor in such processes as G4 folding/defolding and ligand intercalation.

In this work we have studied by quantum chemical methods the possibility of movement of Na<sup>+</sup> cations in model G4 structure Tel22 (22-mer oligonucleotide AGGG(TTAGGG)<sub>3</sub>, a fragment of human telomeric DNA, Protein Data Bank code 143D). We have used MOPAC2016 software package and applied semi-empirical method PM7 with COSMO solvent model. The side view of the optimized Tel22 structure is shown in the figure. This nanosystem contains 3 coplanar guanine quartets coordinated by 2 sodium cations (presented as spheres); arrows A-C indicate the studied directions of ion movement. In all cases one Na<sup>+</sup> cation was moved along the selected line, while the second one was kept fixed.

We have found that the energetic barrier for the upper sodium ion to pass through the quadruplex channel in direction A is 12.90 kcal/mol. At the same time, the barriers for the second cation to exit the quadruplex along its channel (B) or between the hydrophobic guanine quartets (C) are as high as 29.42 and 44.47 kcal/mol, respectively. The computation data suggest that the ion path through the central channel in direction A is most probable. However, even in this case the energetic barrier is high. Thus, it is hardly possible that cations can freely move within G4 nanosystem or even leave it, i.e. it should be quite difficult to remove the quadruplex-stabilizing metal ions from G4 assemblies. This is in full agreement with experimental data on high stability of K(Na)-quadruplex DNA.