

# Ion Selectivity at the Internal Cavity Site of G-Quadruplexes: a Quantum-Chemical Approach

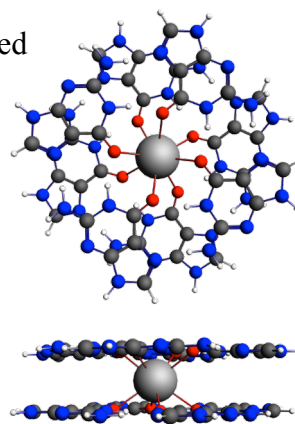
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In the telomeric part of the chromosome, which is crucial for the protection of the genetic code,<sup>1</sup> quadruplexes occur which are composed of stacked guanine quartets. The guanine bases in the latter are essentially coplanar and interact through hydrogen bonds. The quadruplexes are furthermore stabilized by the presence of monovalent ions, such as  $K^+$  and  $Na^+$ , in between the layers of quartets with a preference for  $K^+$  under physiological conditions (see Figure).<sup>2</sup>

We report quantum-chemical calculations based on dispersion-corrected density functional theory (DFT-D)<sup>3</sup> of bi-layered G-quadruplex (GQ) structures interacting in turn with  $K^+$ ,  $Na^+$ ,  $Rb^+$ ,  $Li^+$  or  $Cs^+$  at the channel coordination site. The model includes bi-layered GQs provided with sugar-phosphate backbone, interacting in turn with  $Li^+$ ,  $Na^+$ ,  $K^+$ , and  $Rb^+$ . The computational studies were performed for the conditions in the gas phase and in water described with an implicit solvent model. The simulations in water reproduced the consolidated experimental channel site cation affinity sequence<sup>4</sup>  $K^+ > Na^+ > Li^+$ .



With our quantitative Kohn-Sham molecular orbital (MO) and corresponding energy decomposition analyses (EDA), we have been able to understand the cooperativity of the hydrogen bonds.<sup>5,6</sup> In this study, we analyzed the interaction of the alkali cation with the guanine bases and explain the experimental order of affinity in guanine quadruplexes.

## References

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