

Electronic Supplementary Information

Charge–Dipole Interactions in G-Quadruplex Thrombin-Binding Aptamer

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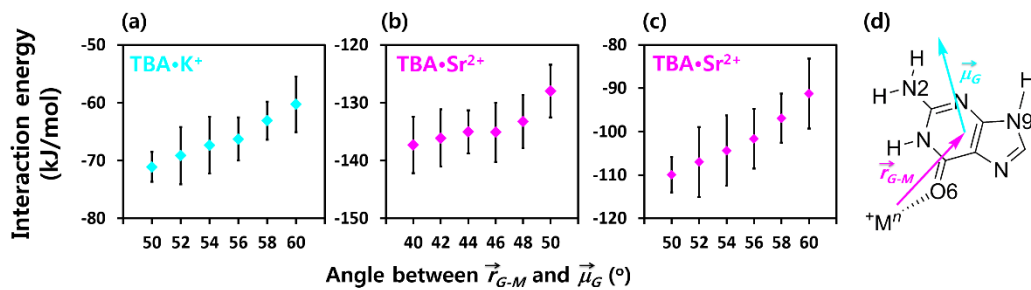


Figure S1. The interaction energy between guanine and the metal ion (K^+ or Sr^{2+}) as a function of the angle between \vec{r}_{G-M} and $\vec{\mu}_G$ in the 1:1 guanine–metal complex. In (a) and (b), the interaction energy was calculated with DFT on sampled structures from MD simulations. Meanwhile, in (c), the interaction energy between guanine and Sr^{2+} was computed on sampled structures of the $TBA \cdot K^+$ complex by replacing K^+ with Sr^{2+} .

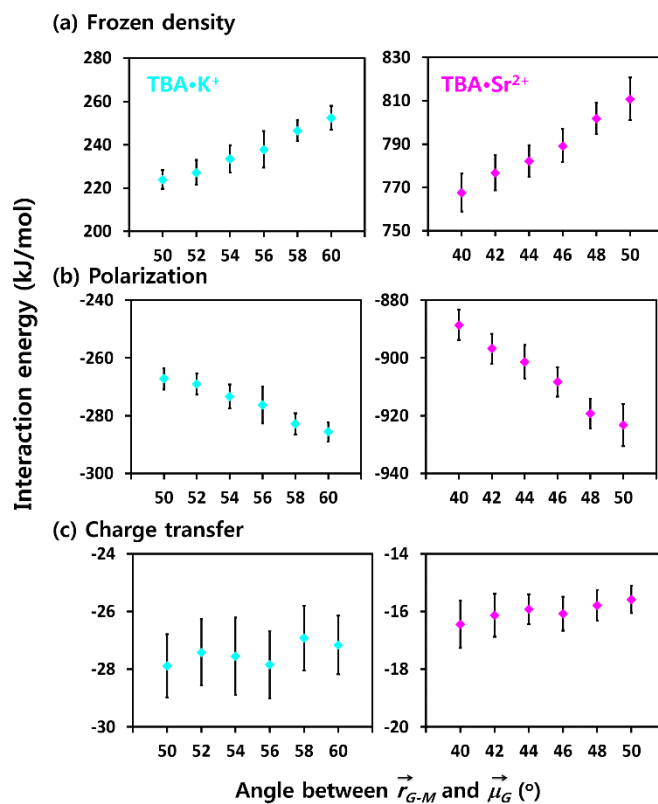


Figure S2. Three energy components in the interaction energy. As described in the Computational Details section, (a) the interaction between frozen electron densities and (b) the polarization energy due complexation and (c) the stabilization energy due to charge transfer are separately considered and displayed.

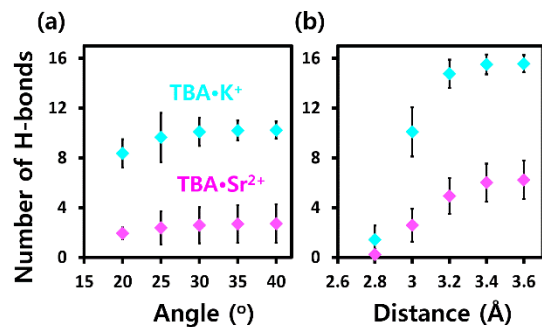


Figure S3. The number of hydrogen bonds (H-bonds) as a function of the angle and distance criteria for counting hydrogen bonds in G-tetrads of the TBA·K⁺ (cyan) and TBA·Sr²⁺ (magenta) complexes. (a) The criterion for the donor–acceptor–hydrogen bond angle is varied from 20° to 40° at the distance criterion of 3.6 Å; (b) the criterion for the donor–acceptor bond distance is varied from 2.8 Å to 3.6 Å at the angle criterion of 30°.

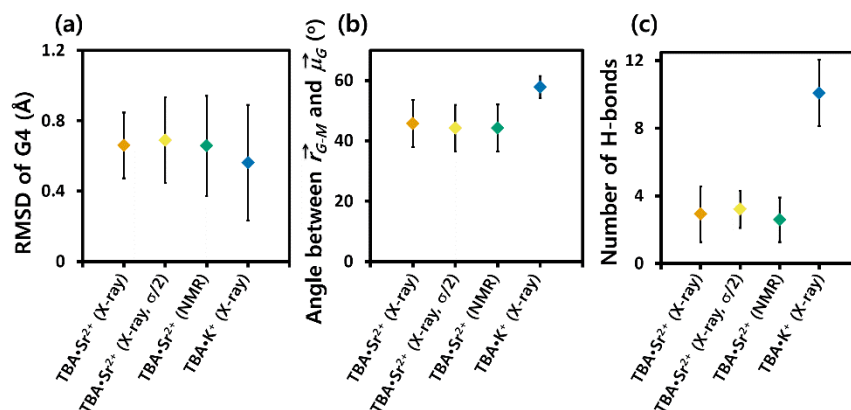


Figure S4. Effects of initial structures and parameters for the MD simulation on G-tetrads of the TBA·Sr²⁺ complex: (a) the root-mean-square displacement (RMSD) of all atoms in G-tetrads in the left, (b) the angle between \vec{r}_{G-M} and $\vec{\mu}_G$ in the middle, and (c) the number of hydrogen bonds in the right. TBA·Sr²⁺ (X-ray), the structure substituting K⁺ with Sr²⁺ in the X-ray structure of the TBA·K⁺ complex; TBA·Sr²⁺ ($\sigma/2$), the structure reducing the LJ interaction distance σ by half in the NMR structure of the TBA·Sr²⁺ complex; TBA·Sr²⁺ (NMR), the NMR structure of the TBA·Sr²⁺ complex; TBA·K⁺ (X-ray), the X-ray structure of the TBA·K⁺ complex.

Table S1. Angle between \vec{r}_{G-M} and $\vec{\mu}_G$ ($^\circ$), number of hydrogen bonds, and interaction energy between guanine and the metal ion for TBA·K⁺ and TBA·Sr²⁺ complexes. From MD simulations of 50 ns, we analyzed the MD trajectories in the first and last 5 ns. Average values are listed with the standard deviation in parenthesis.

Time period (ns) ^a	Angle between \vec{r}_{G-M} and $\vec{\mu}_G$ ($^\circ$)		Number of hydrogen bonds		Interaction energy (kJ/mol)	
	TBA·K ⁺	TBA·Sr ²⁺	TBA·K ⁺	TBA·Sr ²⁺	TBA·K ⁺	TBA·Sr ²⁺
0–5	57.8 (3.5)	44.2 (7.8)	10.1 (2.2)	2.6 (1.4)	–62.6 (7.6)	–113.9 (12.6)
45–50	58.2 (3.7)	43.0 (9.5)	10.4 (1.9)	1.9 (1.4)	–62.1 (7.9)	–119.8 (15.9)

^a For each complex, all five MD trajectories were used for the first 5-ns analysis, whereas a single trajectory was used for the last 5-ns analysis.

Table S2. Structural analysis on TBA·M³⁺ and TBA·Gd³⁺ complexes. As explained in the main text, the force field parameter of M³⁺ was prepared by modifying the charge of K⁺, whereas that of Gd³⁺ was adopted from the OPLS force field. Average values are listed with the standard deviation in parenthesis.

	Angle between \vec{r}_{G-M} and $\vec{\mu}_G$ ($^\circ$)	Number of hydrogen bonds
TBA·M ³⁺	41.4 (9.9)	1.6 (1.4)
TBA·Gd ³⁺	41.4 (9.4)	1.9 (1.8)