Unexpected Dissociation Energetics of Na^{+} Counterion from GC Motifs in DNA Hole Migration

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Supporting information:

1. Molecular Dynamics Simulation Detail

To obtain the DNA configurations in which Na^{+} ions, the counterions, directly interact with individual base pair, molecular dynamics (MD) simulations were carried out on a designed DNA decamer with the sequence d(AGGAGACCAA) with W-C pairing to make the corresponding duplex, with use of the AMBER 8.0 suite1[S1] of programs and the parm99 force field.[S2] Each structure was neutralized with 18 Na^{+} ions and solvated with about 3000 TIP3P [S3] water molecules in a truncated octahedral box whose edges are approximately 10 Å in each direction from the closest decamer duplex. No salt was included. The SHAKE algorithm[S4] was employed to constrain all bonds involving hydrogens. After energy minimization to relax strains, the system was slowly heated from 0 to 300 K during 20 ps with harmonic restraints of 10.0 kcal/mol/Å^2 on the solute atoms, at constant volume. This was followed by another 300-ps MD run in which the restraints were gradually removed.[S5] After these equilibration procedures, 10 ns unrestrained molecular dynamics simulations were then carried out at constant pressure (1 atm) and temperature (300K) using the Particle Mesh Ewald algorithm[S6] and periodic boundary conditions.

The extended 10 ns long sampling was carried out to assess whether mobile Na^{+} counterions can penetrate into the DNA groove and bind to a given base pair during the MD trajectory. The MD trajectory analysis revealed that the mobile Na^{+} counterions are quite mobile. A Na^{+} counterion was observed to penetrate into the major groove of the decamer to combine directly with purine residue during the first 6 ns of MD simulation and, subsequently, this Na^{+} counterion slowly departed from the binding site. The DNA structures, including the presence or absence of Na^{+} counterions at particular locations, were saved every 0.5 ps during the simulations for further

minimizations of the Na^+-coupled configurations.

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S5. Auffinger, P.; Westhof, E. *J. Mol, Biol.* **2000**, *300*, 1113-1131.

S6. Darden, T.; York, D.; Pedersen, L. *J. Chem. Phys.* **1993**, *98*, 10089-10092.
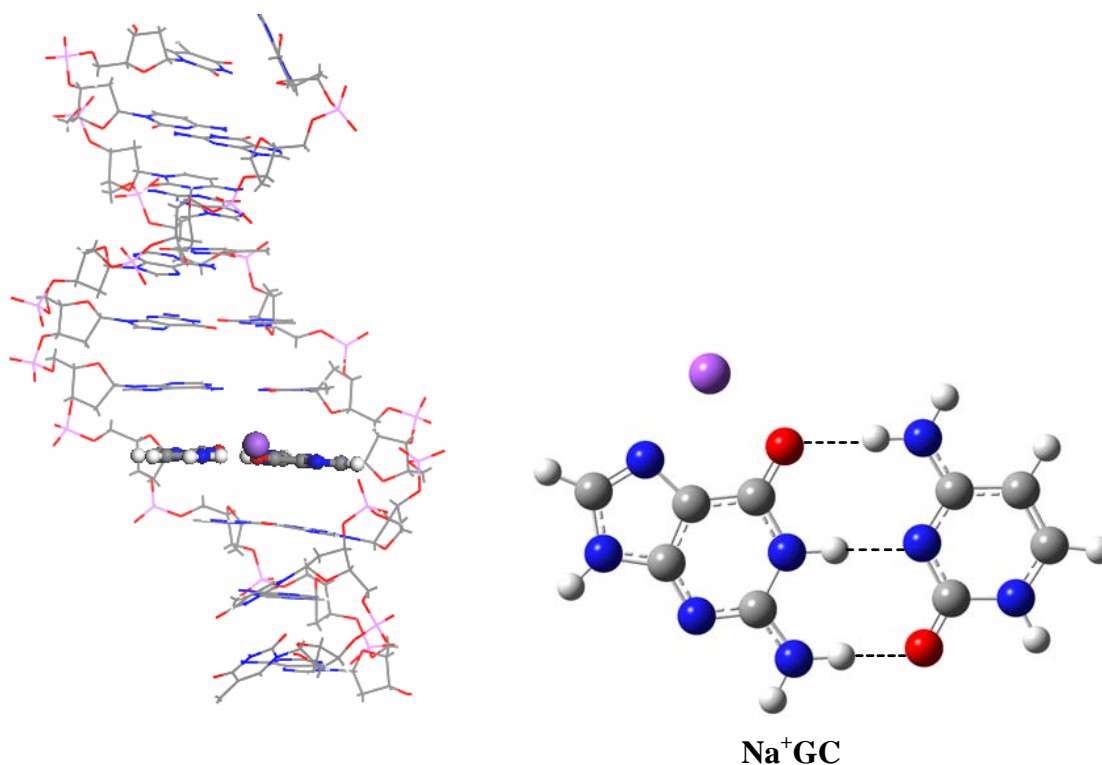
2. Relevant Figures

Na^+GC

Figure S-1. Averaged DNA structure (*left*) obtained from MD trajectory averaged over a 10-ps MD run when a Na^+ binds with a base.   **MD-Na^+GC** was obtained from MD simulations on the d(AGGAGACCAA).   The given Watson-Crick base pair bound with a Na^+ counterion is highlighted by ball and stick type in duplex, and also given in the top-view (*right*).   The Na^+ counterion penetrating into the major groove with direct interaction with a Watson-Crick pair is represented as a big purple ball.
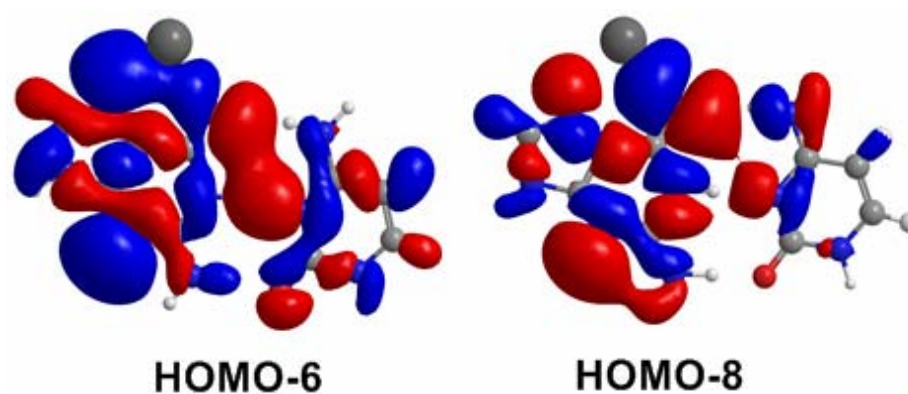
Figure S-2. The maps of two molecular orbitals (HOMO-6 and HOMO-8) for the Na^+G^+C complex. HOMO denotes the highest occupied molecular orbital.
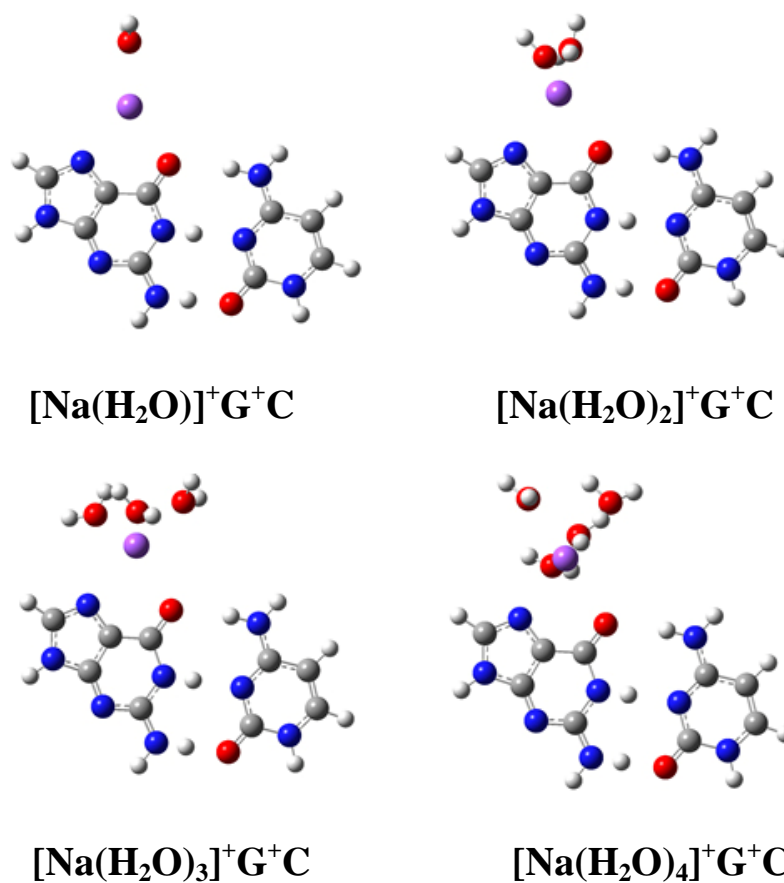

Figure S-3. The optimized structures of the $[Na(H_2O)_n]^+G^+C$ (n=1, 2, 3, 4) complexes, obtained at the B3LYP/6-311++G** level.
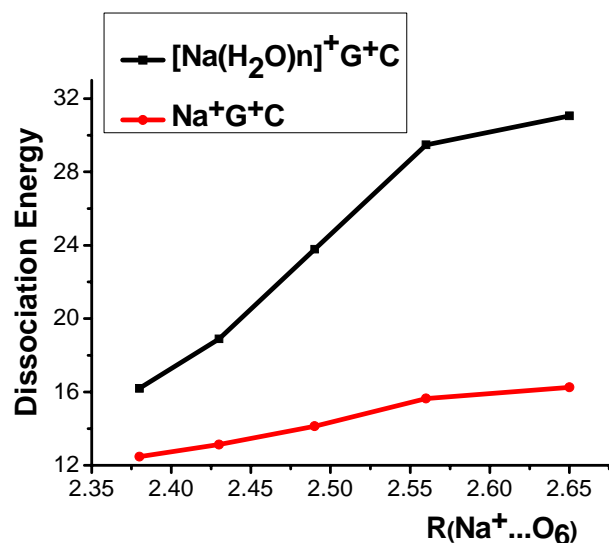
Figure S-4. Effects of $R_{Na+\cdots O6}$ (the distance between Na^+ and O_6) on ΔE_1, the dissociation energies of the Na^+-N_7/O_6 bonds in all considered complexes: Na^+G^+C and its corresponding hydrates $[Na(H_2O)_n]^+G^+C$ (n=1, 2, 3, 4), and ΔE_2, the vertical dissociation energies of the Na^+-N_7/O_6 bonds in Na^+G^+C, viz. $[Na(H_2O)_n]^+G^+C$ for n=0 (no water molecules attached). All data for this figure is given in Table S-5.
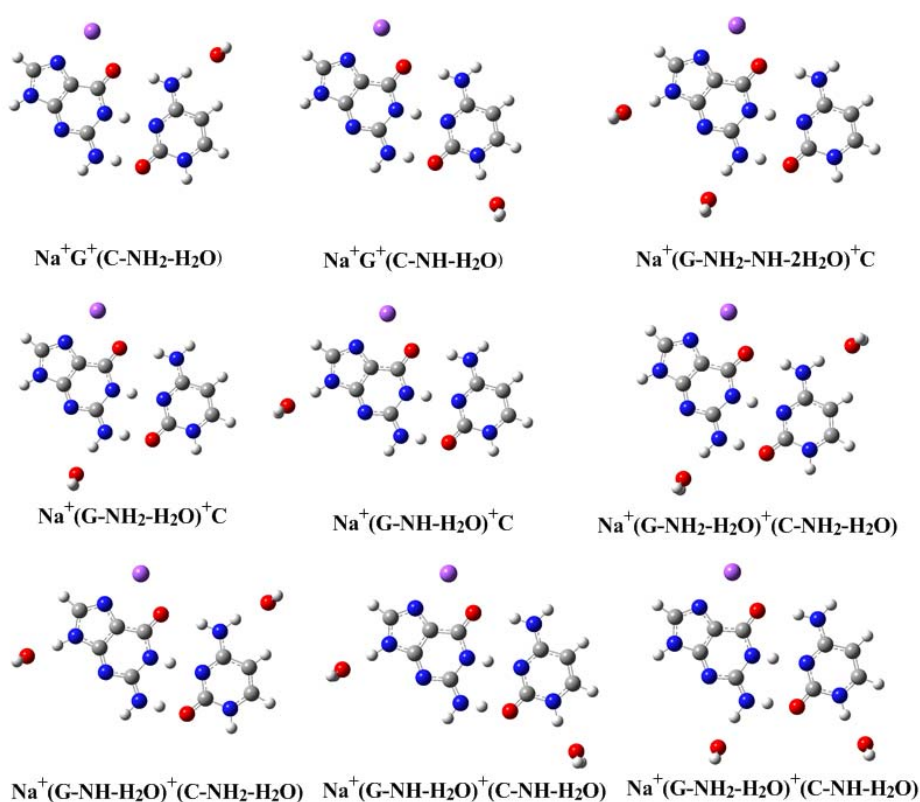

Figure S-5. The optimized structures of the $Na^+[G$-$R(H_2O)_n]^+[C$-$R(H_2O)_n]$ (R=NH$_2$, NH; n=0, 1, 2) complexes, the hydrates of Na^+G^+C, obtained at the B3LYP/6-311++G** level.

(a)

(b)

(c)
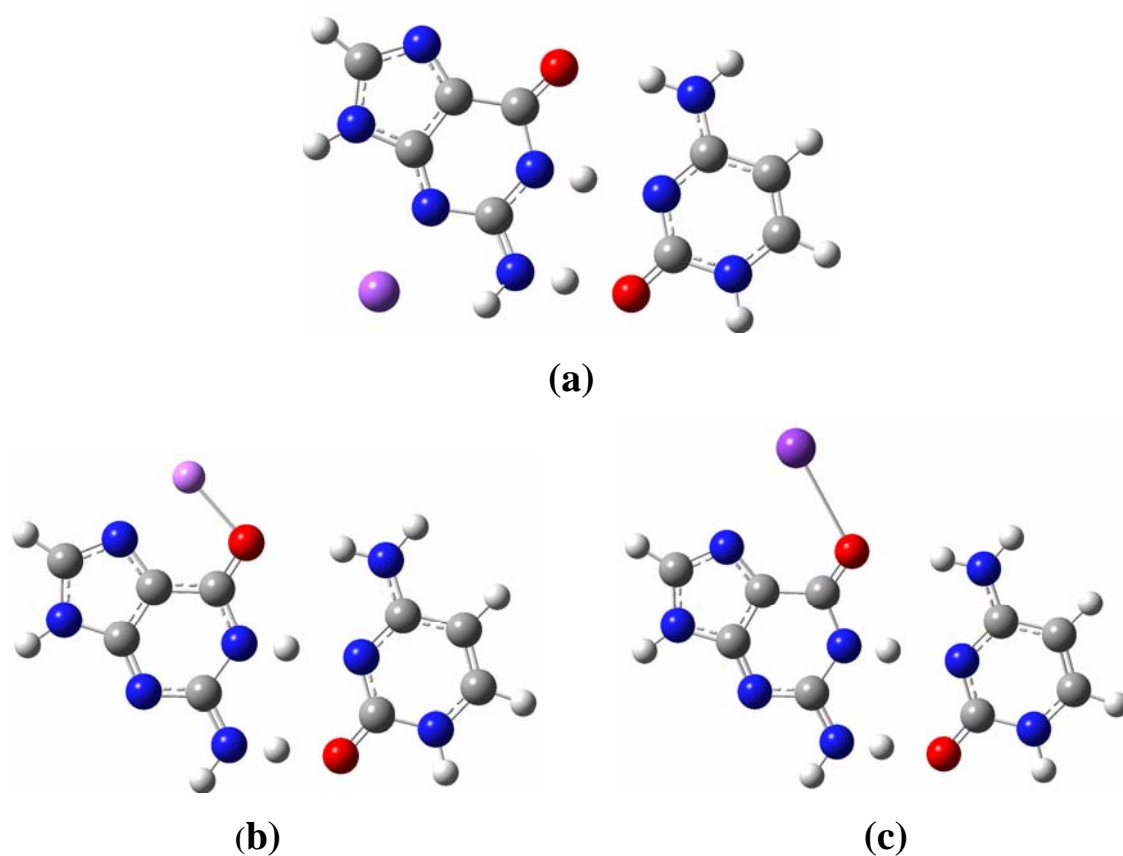
Figure S-6. The optimized structures: (a) Na$^+$G$^+$C-min, (b) Li$^+$G$^+$C, and (c) K$^+$G$^+$C, obtained at the B3LYP/6-311++G** level.   The complex Na$^+$G$^+$C-min denotes the hole-trapped one when Na$^+$ resides in the minor groove of the DNA duplex, while Li$^+$G$^+$C and K$^+$G$^+$C are the corresponding hole-trapped those when Li$^+$, or K$^+$ resides in the major groove of the DNA duplex.

3. Relevant Tables

Table S-1: The dissociation energies (ΔEs) of Na^+-N_7/O_6 bond and Watson-Crick H-bond (WC HB) in these complexes Na^+GC, Na^+G^+C, and $Na^+G(-H^+)C_p$ at the B3LYP/6-311++G** level (Method 1), and those dissociation energies of Na^+G^+C were also calculated at the MP2/6-311++G**//MP2/6-31+G* level (Method 2) and M05-2X/6-311++G** level (Method 3) for comparison.

Complexes			Na^+GC	Na^+G^+C	$Na^+G(-H^+)C_p$
Method 1	ΔE [a]	Na^+-N_7/O_6 bond	62.30	-15.49	-6.38
		WC HB	30.70	53.56	-16.32
	ΔE_{bsse} [b]	Na^+-N_7/O_6 bond	61.51	-16.18	-7.15
		WC HB	29.57	52.32	-18.14
Method 2	ΔE [a]	Na^+-N_7/O_6 bond		-18.03	
		WC HB		51.96	
	ΔE_{bsse} [b]	Na^+-N_7/O_6 bond		-19.35	
		WC HB		47.64	
Method 3	ΔE [a]	Na^+-N_7/O_6 bond		-15.20	

Notes：ΔE^a are the dissociation energies, $\Delta E_{bsse}{}^b$ are the BSSE-corrected ones.　All of the dissociation energies are in kcal/mol.

Table S-2: AIM parameters ρ (the electron density) and Lap (the Laplacian of electron density) for the Na^+GC and Na^+G^+C complexes.　ρ and Lap are in atomic units.

Chemical bond	Na^+GC		Na^+G^+C	
	ρ	Lap	ρ	Lap
Na^+....N_7	0.0225	0.1330	0.0161	0.0869
Na^+....O_6	0.0245	0.1500	0.0184	0.1050
O_6....H-N	0.0251	0.0790	0.0152	0.0508
N_1-H....N	0.0366	0.0971	0.0479	0.1140
N_2-H....O	0.0374	0.1230	0.0761	0.2058

Table S-3: The dissociation energies (ΔEs) of the Na$^+$G$^+$C-min, Li$^+$G$^+$C, and K$^+$G$^+$C complexes according to the dissociation mode, M$^+$G$^+$C$\rightarrow$ G$^+$C + M$^+$ (M$^+$= Li$^+$, Na$^+$ or K$^+$). The Na$^+$G$^+$C-min complex denotes the hole-trapped one when Na$^+$ resides in the minor groove of the DNA duplex, while Li$^+$G$^+$C and K$^+$G$^+$C are the hole-trapped those when Li$^+$, or K$^+$ resides in the major groove of the DNA duplex, respectively.

complexes	B3LYP/6-311++G**	
	ΔE	ΔE_{BSSE}[a]
Na$^+$G$^+$C-min	-44.33	-44.89
Li$^+$G$^+$C	-3.12	-3.69
K$^+$G$^+$C	-24.39	-24.64

[a] the dissociation energies corrected with basis set superposition error (BSSE). All the dissociation energies are in kcal/mol.

Table S-4: $R_{Na+\ldots O6}$ (the distance between Na$^+$ and O_6), attraction (interaction between Na$^+$ and GC in Na$^+$GC), added electrostatic repulsion (the increased electrostatic repulsion upon one-electron oxidation).

$R_{Na+\ldots O6}$	Attraction	Added electrostatic repulsion
(angstroms)	kcal/mol	
2.38	-65.06	77.53
2.68	-61.64	75.51
2.98	-56.86	73.35
3.28	-51.57	70.96
3.58	-46.05	68.24
3.88	-40.63	65.32
4.18	-35.51	62.32
4.48	-30.86	59.33
4.78	-26.77	56.46
5.08	-23.25	53.77
5.38	-20.25	51.28
5.68	-17.73	48.98
5.98	-15.62	46.89
6.28	-13.84	44.97
6.58	-12.35	43.21

Table S-5: ΔE_1, the dissociation energies (ΔEs) of the Na^+-N_7/O_6 bond in these complexes: Na^+G^+C and its corresponding hydrates $[Na(H_2O)_n]^+G^+C$ (n=1, 2, 3, 4); ΔE_2, the vertical dissociation energies of the Na^+-N_7/O_6 bond in Na^+G^+C, viz. $[Na(H_2O)_n]^+G^+C$ (n=0, no water molecules). Both ΔE_1 and ΔE_2 are obtained at the B3LYP/6-311++G** level. $R_{Na+\ldots O6}$ denotes the distance between Na^+ and O_6.

Complexes	ΔE_1	$\Delta E_{1(BSSE)}$[a]	ΔE_2	$R_{Na+\ldots O6}$
Na^+G^+C	-15.49	-16.19	-12.47	2.38
$[Na(H_2O)]^+G^+C$	-18.08	-18.89	-13.14	2.43
$[Na(H_2O)_2]^+G^+C$	-22.92	-23.78	-14.14	2.49
$[Na(H_2O)_3]^+G^+C$	-28.59	-29.48	-15.64	2.56
$[Na(H_2O)_4]^+G^+C$	-30.04	-31.06	-16.25	2.65

[a] the dissociation energies corrected with the basis set superposition error (BSSE). All of the dissociation energies are in kcal/mol.

Table S-6: ΔE, the dissociation energies (ΔEs) of the Na^+-N_7/O_6 bonds in these complexes: Na^+G^+C and its corresponding hydrates $Na^+[G-R(H_2O)_n]^+[C-R(H_2O)_n]$ (R=NH$_2$, NH; n=1, 2) as shown in **Fig. S-5**; R denotes the groups with which water molecules interact. ΔE_s are obtained at the B3LYP/6-311++G** level. $R_{Na+\ldots O6}$ denotes the distance between Na^+ and O_6.

Complexes	ΔE	$\Delta E_{(BSSE)}$[a]
Na^+G^+C	-15.49	-16.19
$Na^+(G-NH_2-H_2O)^+C$	-12.43	-13.15
$Na^+(G-NH-H_2O)^+C$	-11.74	-12.46
$Na^+G^+(C-NH_2-H_2O)$	-10.93	-11.64
$Na^+G^+(C-NH-H_2O)$	-10.10	-10.81
$Na^+(G-NH_2-NH-2H_2O)^+C$	-7.94	-8.65
$Na^+(G-NH_2-H_2O)^+(C-NH_2-H_2O)$	-7.12	-7.84
$Na^+(G-NH_2-H_2O)^+(C-NH-H_2O)$	-7.61	-8.36
$Na^+(G-NH-H_2O)^+(C-NH-H_2O)$	-6.79	-7.51
$Na^+(G-NH-H_2O)^+(C-NH_2-H_2O)$	-5.66	-6.40

[a] the dissociation energies corrected with the basis set superposition error (BSSE). All of the dissociation energies are in kcal/mol.

Table S-7: Various of dissociation energies (ΔEs-PCM) using the polarizable continuum (PCM) self-consistent reaction field method when Na^+ is separated from the complex Na^+G^+C in the gas phase and ten solvents with different dielectric constants ranging from the gas phase ($\varepsilon=1$) to water ($\varepsilon=78.39$), RE denotes the released energies in dissociation of Na^+ from the Na^+G^+C complex, and ε denotes dielectric constants.

solvent	ε	ΔE-PCM	RE(-ΔE)
gas phase	1.00	-15.49	15.49
ether	4.22	-6.57	6.57
chlorobenzene	5.62	-6.06	6.06
aniline	6.89	-5.40	5.40
quinoline	9.03	-5.35	5.35
acetone	20.7	-3.37	3.37
ethanol	24.55	-3.03	3.03
methanol	32.63	-2.56	2.56
DMSO	46.70	-2.85	2.85
water	78.39	-1.66	1.66