A: Kinetics, Dynamics, Photochemistry, and Excited States

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Modulating Excited Charge Transfer States of G-Quartet Self-Assemblies by Earth Alkaline Cations and Hydration

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Abstract

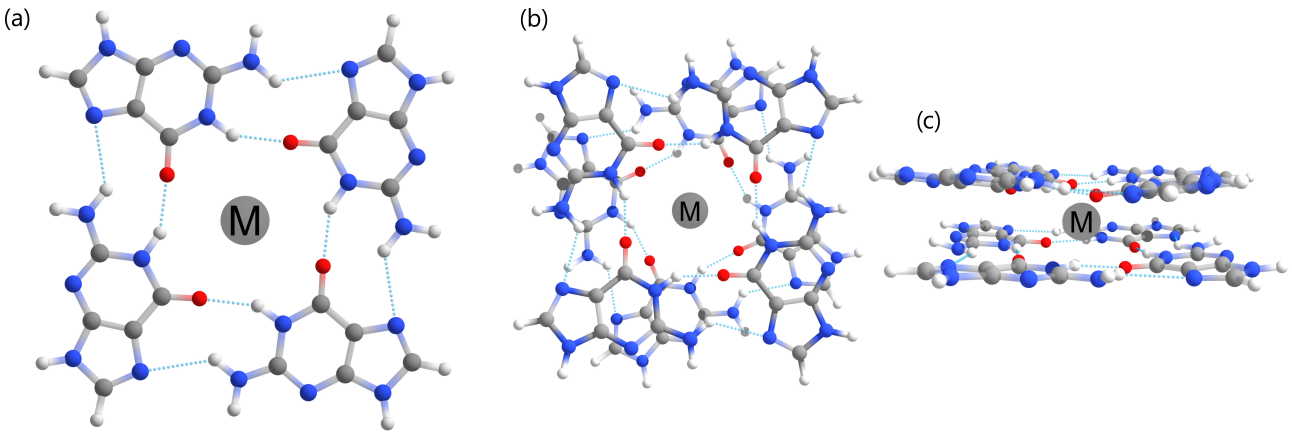
Guanine self-assemblies are promising supramolecular platforms for optoelectronic applications. The study [*J. Phys. Chem. C* **2012** *116* 14682–14689] reported that alkaline cations cannot modulate the electronic absorption spectrum of G-quadruplexes, although a cation effect is observable during electronic relaxation due to different mobility of Na^+ and K^+ cations. In this work, we theoretically examined whether divalent Mg^{2+} and Ca^{2+} cations and hydration might shift excited charge transfer states of a cation templated stacked G-quartets to the absorption red tail. Our results showed that earth alkaline cations blue-shifted $n\pi^*$ states and stabilized charge transfer $\pi\pi^*$ states relative to those of complexes with alkaline cations, although the number of charge separation states was not significantly modified. Earth alkaline cations were

not able to considerably increase the amount of charge transfer states below the L_b excitonic states. Hydration shifted charge transfer states of Na^+ coordinated G-octet to the absorption red tail, although this part of the spectrum was still dominated by monomer-like excitations. We found G-octet electron detachment states at low excitation energies in aqueous solution. These states were distributed over a broad range of excitation energies and could be responsible for oxidative damage observed upon UV irradiation of biological G-quadruplexes.

Introduction

Guanine (G) and its derivatives are able to self-assemble into ribbons and macrocycles formed by four monomers (quartets). In both structures monomers are connected by four hydrogen bonds formed between complementary Watson-Crick and Hoogsteen edges of neighboring units, but their relative stability depends on the experimental conditions.[1] Particularly, monovalent and divalent cations dictate the self-assembly of guanines into a cation templated G-quartet structure (see Figure 1). The stability of this supramolecular structure is determined by cooperative hydrogen bonding, the size of the cation and its hydration energy.[2–9]

Figure (1) (a) Structure of G-quartet coordinated with a metal cation. (b) Top and (c) side view of stacked G-quartet coordinated with a metal cation.



Stacking of G-quartets into columnar aggregates gives rise to G-quadruplexes in which cations are sandwiched between two G-quartets or between every other G-quartet pair as in the case of Sr^{2+} cation.[10] The latter binding mode likely occurs due to unfavorable electrostatic repulsion between double positive charges. Among monovalent cations, K^+ has the strongest ability to govern 5'-guanosine monophosphate self-assembly into G-quadruplexes followed by Na^+ and Rb^+.[11] Generally, divalent cations are known to be more effective in stabilization of G-quadruplexes than alkaline cations.[12,13] Kwan *et al.* found that divalent cation ability to promote formation of a guanosine derivative self-assembly follows the ordering of ionic radii found for monovalent alkaline cations ($Sr^{2+} >> Ba^{2+} > Ca^{2+}$).[14] G-quadruplexes are also found in guanine rich DNA and RNA sequences and have important biological functions.[15,16] It is possible to form superstructures called G-wires by polimerization of short biological G-quadruplex sequences by gel electrophoresis in the presence of K^+, Na^+ or Mg^{2+} cations.[17]

Self-assembly of functional building blocks into nanometer-sized structures is found to be a more efficient approach for optoelectronic applications than covalent syntheses.[18] Guanine absorbs light in the UV spectral region and it is not suitable for Solar radiation absorption. For photovoltaic applications, it might be functionalized with a dye molecule. Wasielewski and coworkers exploited G-quadruplex decorated with π-chromophores as a supramolecular platform for photochemical charge separation.[19–21] The core-shell columnar architecture of these systems favors photoinduced charge separation over long distance, which demonstrates that G-quadruplexes can serve as effective hole conduits in these assemblies. Pu *et al.* used Sr^{2+} templated G-quartet self-assembly of guanosine 5'-monophosphate intercalated with dye molecules as a light-harvesting antenna.[22] This nanostructure showed good light-harvesting properties both in solution and in the solid state indicating the potential for application as a photoelectric device.

Given the growing interest in G-quadruplex-based optoelectronic devices, it is necessary to examine how structural parameters modulate absorption and electronic relaxation

of these supramolecular structures. Previous experimental and theoretical studies examined biological G-quadruplexes and G-wires templated with Na^+ and K^+ cations.[23–38] These studies found that their photophysics depends on the number of stacked G-quartets, relative orientation between neighbouring G-quartets and a templating cation. Absorption spectra of G-quadruplexes are dominated by collective excitations[23] which include Frenkel excitons and charge transfer states.[32] Excitons are found to be more stongly coupled between stacked guanines than between hydrogen-bonded guanines.[31,32]

Although the G-quadruplex structure is necessary for promoting intramolecular energy transfer, the templating cations are also needed for the unusually efficient energy transfer reactions within the G-quadruplex.[25] Hua *et al.* studied absorption and emission spectra of a short DNA sequence containing G-quadruplexes templated with Na^+ and K^+ cations.[26] Two-dimensional NMR experiments could not detect any differences in the relative positions of guanine moieties indicating that the overall structure is not affected by the cation type. Also, the absorption spectra did not exhibit significant differences in either the shape or intensity. On the other hand, fluorescence spectra showed remarkable differences since they were dominated by emission from charge transfer and Frenkel excitons for Na^+ and K^+ templated structures, respectively. These findings were related to different mobility of Na^+ and K^+ cations in the central vacancies of G-quadruplexes. More mobile Na^+ cations stabilized charge transfer states during electronic relaxation, whereas this decay channel is obstructed by less mobile K^+ cation.

In this work, we examined to what extent the absorption spectra of G-quadruplexes templated with divalent cations differ to those of alkaline cations. Excited charge transfer states are sensitive to environment polarity and double positive charges of divalent cations might stabilize them to a grater extent than those of monovalent cations. It is particularly intriguing whether earth alkaline cations are able to shift charge transfer states below the first bright state since this might result in a more efficient photoinduced charge separation. We also studied the hydration effects on the excited state properties of G-quadruplexes.

To this end, we simulated electronic absorption spectra of stacked G-quartets (G-octet) templated with divalent earth alkaline cations Mg^{2+} and Ca^{2+} in the gas phase. As a reference, we also examined structures with monovalent alkaline cations Li^+, Na^+, K^+ as well as the structure without a cation. These systems represent a minimal model of G-quartet self-assemblies which is at the same time feasible for computational study. The lack of a sugar-phosphate backbone enables G-quartets to exhibit various close-energy conformers and hydrogen bonding patterns.[4] Hence, we computed the ground state nuclear ensemble by employing classical density functional theory-based molecular dynamics. Subsequently, the excited states and their properties were calculated using time-dependent density functional theory. The hydration effects on the excited states were examined by comparing the density of states of G-octets templated with sodium cation in the gas phase and in the microhydrated environment.

The paper is organized as follows. In the next section, we discuss various computational methods which were employed in this work. In the following section, we present and discuss results related to the relative arrangements of guanines in the G-octets as well as the cation and hydrogen bonding interactions with the carbonyl group. Also, we discuss the density of excited states, charge transfer character, absorption spectra and hydration effects. Finally, we draw conclusions from our study.

Methods

Density functional theory-based molecular dynamics simulations were performed with the CP2K program package.[39] We employed the BLYP functional[40,41] and Grimme's D3 correction for dispersion interaction.[42] The electron density was expanded using a mixed Gaussian and plane waves method[43] with a DZVP basis set for the localized functions, and a cutoff of 320 Ry for the plane waves. GTH pseudopotentials[44] were used to replace core electrons, whereas the valence electrons were correlated. The simulation was performed in a cubic box

with the edge size of 25 Å under the non-periodic conditions. The SCF convergence was set to 5.0×10^{-7} in atomic units. The nuclei were propagated on the Born-Oppenheimer surface of the electronic ground state using a time step of 0.5 fs. The CSVR thermostat[45] was employed in order to simulate a canonical ensemble at 300 K. The initial geometries for equlibriation were choosen to be anti/anti partial 5/6 ring structure (see Figure 1), which was reported to be the most common stacking geometry within the G-quadruplex core.[46] The structures were equilibriated for 2 ps and subsequently propagated for 14 ps in the NVT ensemble.

Electronic absorption spectrum was simulated within the semi-classical approximation in which it is proportional to an ensemble average of vertical electronic excitations:

$$A(\omega) \sim \langle \sum_n f_{n,0}\ g(\omega - \omega_{n,0}) \rangle, \tag{1}$$

where $f_{n,0}$ and $\omega_{n,0}$ are the oscillator strength and frequency of the electronic transition to the n-th electronic state, respectively, and g is a line-broadening function with the Gaussian shape

$$g(\omega) = \sqrt{\frac{2}{\pi\delta^2}} exp(-2\omega^2/\delta^2). \tag{2}$$

We used a large broadening value $\delta = 0.2$ eV, which enables us to remove statistical noise. The nuclear distribution in the ground electronic state was prepared by molecular dynamics simulation. The density of transition was determined by taking the equation 1 and substitution $f_{n,0} = 1$. Excited electronic states were computed by employing linear response time-dependent density functional theory with long-range corrected CAM-B3LYP functional[47] and split valence 6-31G(d) basis set. We calculated 32 excited electronic states at 10 sampled configuration separated by 1 ps for each G-octet. The excited states calculations were carried out by using Gaussian software package.[48] Analysis of the excited states was conducted using TheoDORE program,[49] which evaluates the one-electron transition density matrix[50,51] and natural transition orbitals (NTOs).[52,53] Excited states of multichromophoric G-octet sys-

tems might be monomer-like excited states, delocalized Frenkel excitons and charge transfer states. Charge transfer states involve transitions between orbitals localized on different guanines. Charge separation states are a subset of charge transfer states in which there is a net charge transfer from one group of guanines to the other. In this work, we only consider charge separation states arising from excitations from one to the other G-quartet. In order to distinguish between locally excited and charge transfer states we used a CT descriptor implemented in the TheoDORE program, which gives a fraction of the charge transferred between guanines - a value of 1 for the pure charge transfer state and 0 for locally excited state. Point from which the locally excited state turns into the charge transfer state has to be chosen arbitrary and in this work we chose a threshold value of 0.5. Charge separation states were determined by analyzing a CT_{net} descriptor and two fragments, each consisted of one G-quartet. We also used a threshold value of 0.5 for assigning charge separation character. Delocalization of electronic transitions (the number of guanines which participate in the excitation) was computed by employing DEL descriptor in the TheoDORE program. This descriptor provided a real value from one up to the number of guanine fragments (eight). The computed values were rounded to the nearest integer.

The configurations of microsolvated cluster used to elucidate the hydration effect were generated by the following procedure. The ten previously selected structures of Na^+ coordinated G-octet were selected for molecular dynamics simulations in aqueous solution. Each structure was placed in the center of the orthorhombic box and solvated by water molecules using AmberTools20.[54,55] Edges of the box were expanded to a distance of 10 Å away in all directions from the solute, resulting in a box size of around 40, 40 and 31 Å along the x, y and z directions, respectively. The box was filled with 1150 TIP3P[56] water molecules on average. We added one Cl^- ion to maintain system electrostatically neutral. The G-octet was described using generalized AMBER force field (GAFF)[57] while Na^+ and Cl^- were described using TIP3P model. The energy of the system was initially minimized by 1000 steps. After minimization, we carried out a 1 ns long classical NVT molecular dynamics run by using

NAMD program.[58] The temperature was kept constant at 298 K by means of Langevin dynamics method.[59] During the minimization and dynamics, coordinates of G-octet and Na^+ cation were kept fixed to preserve DFT-MD geometries. This was necessary since GAFF does not preserve the G-octet structure. The time step for integrating classical equations of motion was 1 fs. 12 Å cutoff with smooth switching function starting at 10 Å was used to describe van der Waals forces, whereas electrostatic forces were treated via particle mesh Ewald method.[60] A microsolvated cluster was created by taking the G-octet structure with 57 closest water molecules from the last configuration of the molecular dynamics run.

Results and Discussion

The Ground State Properties

The lack of sugar-phosphate backbone in stacked G-quartets gives larger flexibility in relative arrangements of guanine moieties than those in biological G-quadruplexes. These arrangements determine dipolar coupling among guanines, which influences the absorption lineshape. A theoretical study[61] found that the coordination number of Li^+ cation in optimized stacked G-quartets differs from other alkaline cations as Li^+ is positioned in the middle of one G-quartet and it coordinates only four oxygens. This was attributed to small ionic radius which prevents coordination of all oxygen atoms.[61] In our molecular dynamics simulations, we observed that Li^+ might interact with both G-quartets. Its most probable coordination numbers were four and five. We also noticed that Mg^{2+} strongly interacted with six oxygen atoms of which three belong to one G-quartet. Na^+, K^+ and Ca^{+2} cations were found to be coordinated with eight oxygen atoms, so that oxygen atoms formed square antiprismatic molecular geometry.

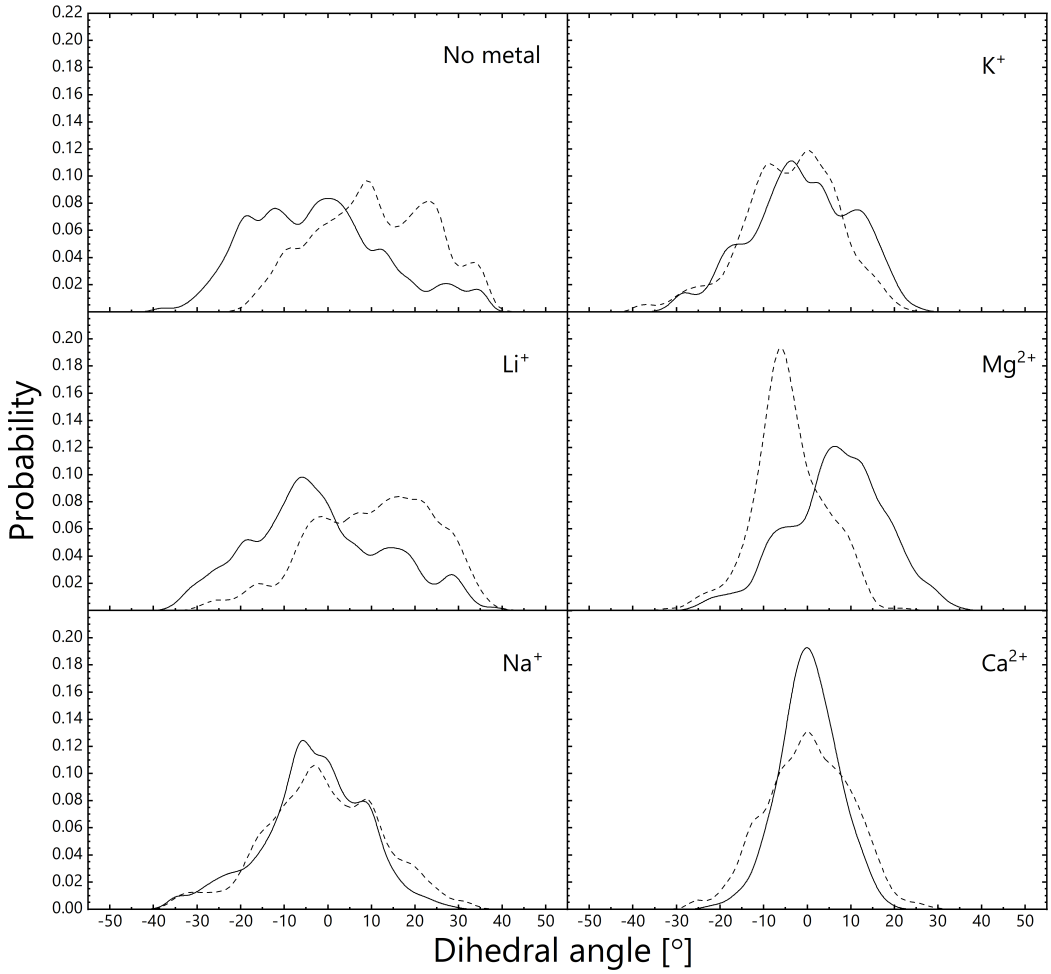
Having discussed the coordination of the cations, let us proceed to relative orientation of guanines in the G-octets. The probability distribution of dihedral angles defined between the carbonyl oxygen atoms is presented in Figure 2. It reflects a deviation of G-quartet from

planarity (dihedral angle equals to zero degrees). The structures with Na^+, K^+ and Ca^{+2} exhibit planar G-quartets, Ca^{+2} having the least deviations. The G-octets coordinated with Li^+, Mg^{2+} cations and without a cation have G-quartets which are nonplanar. The broad probability distributions of these systems indicate that they possess shallow potential energy surface along the dihedral angle. Pronounced asymmetry of the distributions for G-quartets with Li^+, Mg^{2+} cations is due to flexibility of non-coordinated guanines.

Azargun et al. failed to produce 9-ethylguanine octet coordinated with Li^+ cation in the gas phase, although other alkaline cations easily formed the complexes.[62] We believe that the instability of Li^+ coordinated G-octets originates from the inability of Li^+ cation to coordinate all oxygen atoms and subsequent the lack of G-quartet rigidity which is crucial for G-quartet stacking. In the case of Mg^{2+} cation, the stability might be even more reduced since it was previously shown that G-quartets with earth alkaline cations only exist because of strong cation-guanine attraction[9] and this cation also does not coordinate all oxygen atoms. We will show below that the earth alkaline cations even reduce the strengths of the inner hydrogen bonds in the G-octets relative to those of G-octets coordinated with alkaline cations.

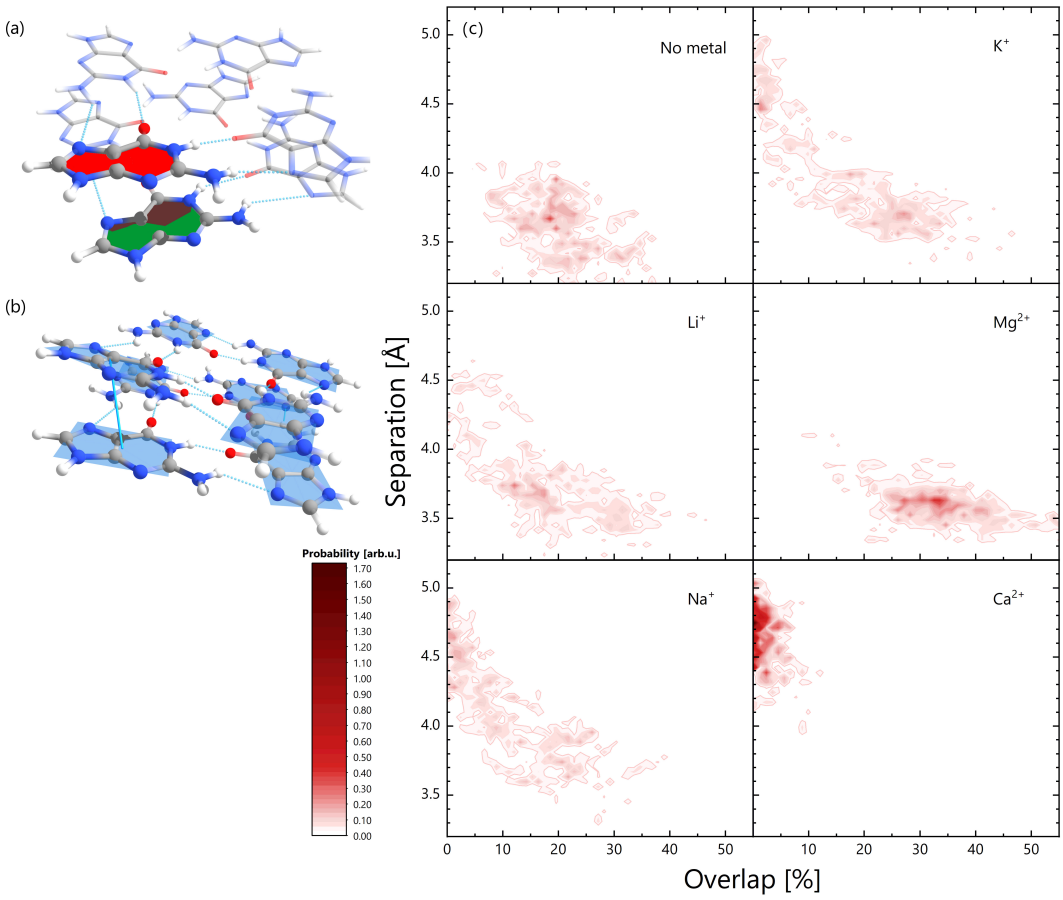
G-quartet arrangements which have a high degree of 5/6-ring overlap in G-quadruplexes exhibit exceptional electron hole transfer rates and charge transfer properties.[29,32] In order to examine to what extent cations modify guanine stacking in the G-octets, we studied the following two coordinates: (1) guanine overlap coordinate - defined as an average overlap between the surfaces enclosed with purine ring atoms obtained by projecting a ring of one quartet on its counterpart, expressed in percents, (2) guanine separation coordinate - defined as a minimal distance between geometrical centers of purine rings in one quartet and their analogues in the other quartet. The probability distribution of these coordinates is given in Figure 3. It can be noticed that G-octets with alkaline cations have similar distributions, although the average base separation coordinate is smaller for Li^+ templating structure than for the other two structures. In these cases, the guanine overlap coordinates takes values

Figure (2) Probability distributions of the dihedral angles between the carbonyl oxygen atoms for each G-quartet (full and dashed lines).



from 0 to 40 %, with larger values indicating smaller separation. The structure without a metal cation preserves guanine overlap better than the structures with alkaline cations. The highest guanine overlap is found for the Mg^{2+} templating G-octet with an average value of 35 %. On the other hand, Ca^{2+} cation disrupts base overlap since it does not allow small separations between the bases. These data might indicate that the Mg^{2+} containing G-octet would have a higher degree of exciton delocalization in comparison to other G-octets. Yet, we will later show that this is not the case since nonplanar G-quartets in the presence of Mg^{2+} cation prevents exciton delocalization.

Figure (3) (a) Schematic display of overlap between the surfaces enclosed with purine ring atoms within a guanine dimer (brown surface). (b) Guanine separation coordinate. (c) Probability distribution of guanine separation and overlap coordinates.



The carbonyl group plays an important role in low-lying electronic excitations of G-octets since these transitions originate from non-bonding n and bonding π orbitals localized on this group. The electron density of carbonyl is perturbed by inner hydrogen bonds and oxygen-cation interaction. Although the later interaction is dominated by electrostatics[6,9] it also has partially covalent nature. Selected geometrical parameters related to these interactions are collected in the Table 1. Similarly as for the guanine overlap-separation probability distribution, we find that G-octets with alkaline cations have comparable geometrical parameters. The inner hydrogen bonds of alkaline cation coordinated G-octets amount to $1.82 - 1.84$ Å, whereas their angles are in the range of $160 - 165$ degrees. In the case of

earth alkaline cations, the hydrogen bond length is found to be longer. This implies that G-octets in complexes with earth alkaline cations have weaker inner hydrogen bonds relative to the alkaline analogues. Particularly, the Mg^{2+} coordinated structure has a 0.23 Å longer inner hydrogen bond than the one in the G-octet without the cation. On the other hand, earth alkaline cations make the oxygen-cation distance even shorter than the alkaline cations, which is favorable for electrostatic interaction between lone pairs of the oxygens and cation. This interaction results in elongation of the oxygen lone pair toward the metal cation and subsequent stabilization of the oxygen n orbital. Hence, the excitations form the oxygen n orbitals will have higher energies in G-octets with earth alkaline than with alkaline cations.

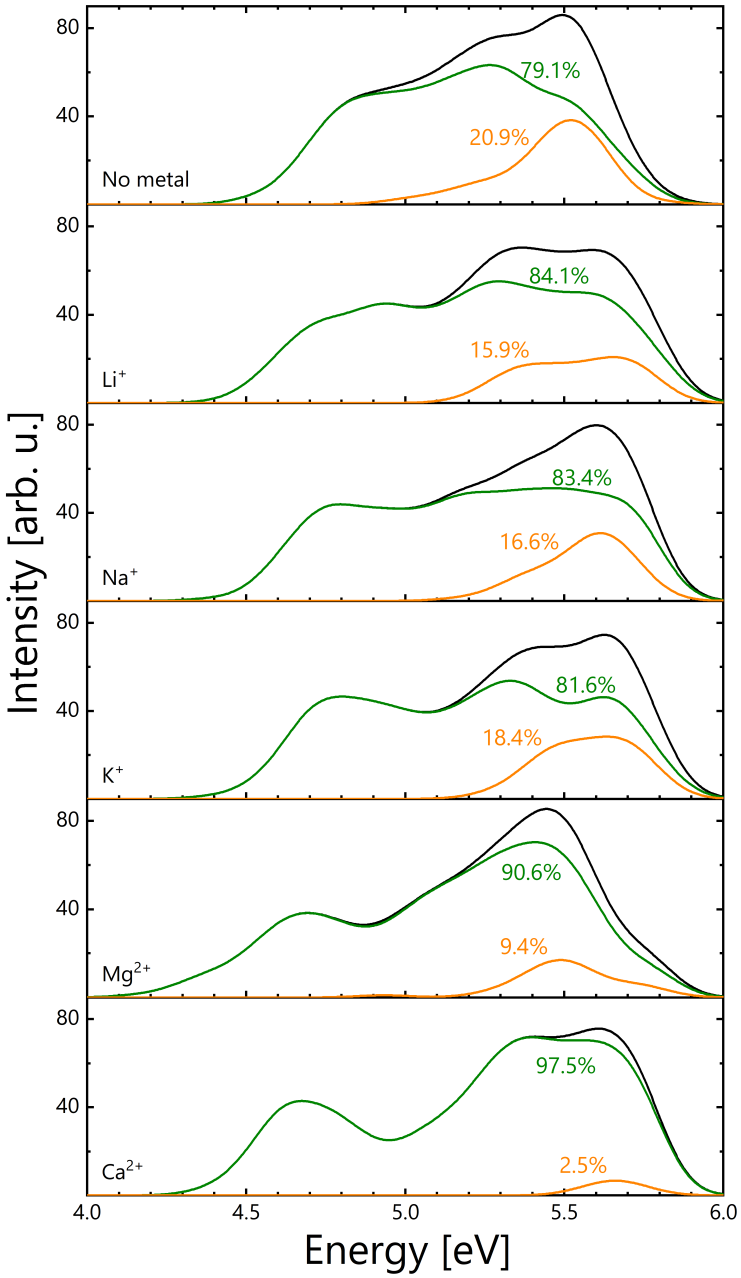
Table (1) Selected distances (in Å) and an angle (in degrees): $O\cdots M^{+/2+}$ is the oxygen-cation distance (in the case without cation, it is the distance between geometrical center of eight oxygen atoms and oxygen atoms), $\delta[WC_{LP}\cdots O]$ is the distance between a Wannier center of the oxygen lone pair (directed toward the cation) and oxygen nucleus relative to the value for the G-octet without a cation, N-H$\cdots$O is the inner hydrogen bond length, N-H-O is the inner hydrogen bond angle.

Cation	$O\cdots M^{+/2+}$	$\delta[WC_{LP}\cdots O]$	N-H$\cdots$O	N-H-O
No metal	3.51	0.000	1.96	153
Li^+	2.96	0.011	1.84	160
Na^+	2.77	0.009	1.82	163
K^+	2.93	0.007	1.84	165
Mg^{2+}	2.63	0.028	2.19	146
Ca^{2+}	2.60	0.024	1.88	158

Density of Excited States

Assigning the diabatic character of excited electronic states from each configuration in a nuclear ensemble is a difficult task. A recently proposed procedure for automatic spectral assignment [63] is not applicable due to large discrepancies between the selected reference geometry and other geometries in the ensemble that result from G-octets' pronounced flexibility. Yet, we were able to assign $n\pi^*$ and $\pi\pi^*$ transitions by visual inspection of natural transition orbitals.

Figure (4) Density of states (black line) decomposed on the $\pi\pi^*$ (green line) and $n\pi^*$ (orange line) contributions.

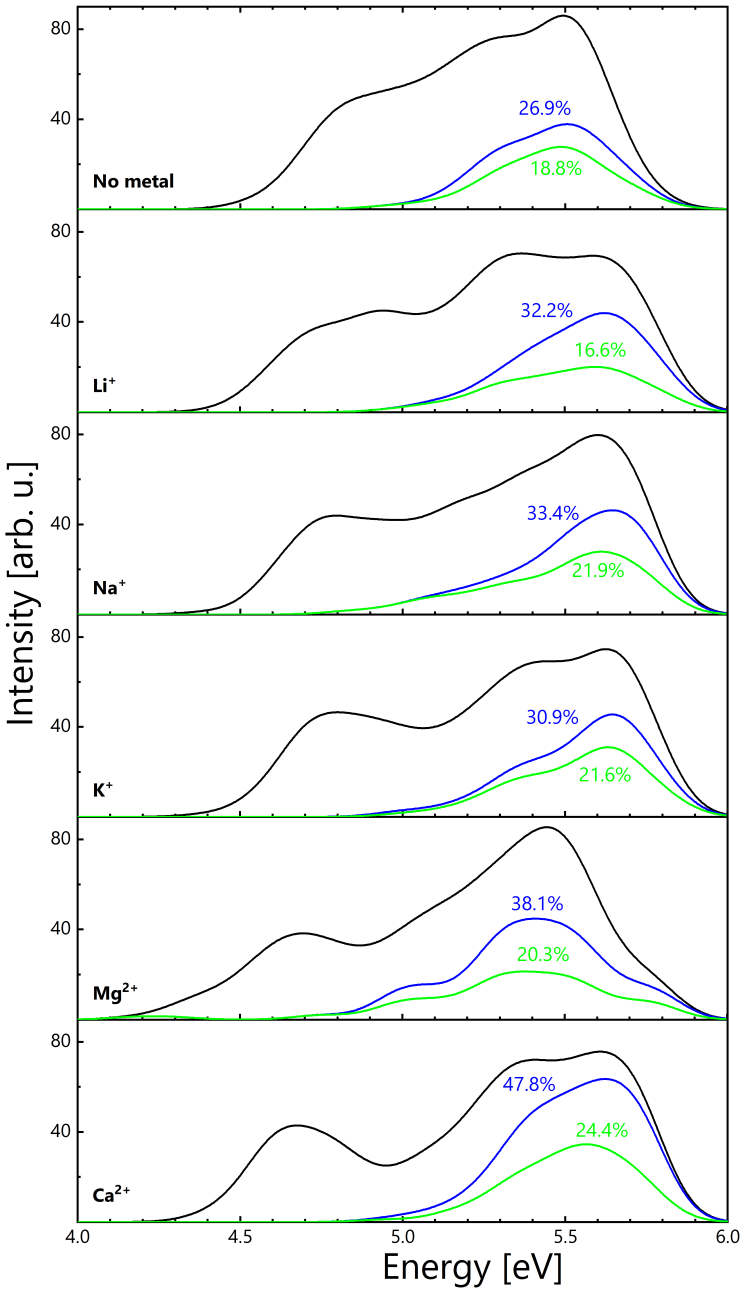


The density of states for examined G-octets are given in Figure 4. There is a correlation between the ground state properties of the G-octets and those densities. As we already discussed, the ground state properties of the G-octets with alkaline cations are similar. The same is valid for their densities of states. The situation is somewhat different with earth alkaline cations. This is in line with a finding of Jissy *et al.* who showed that electronic properties of a G-quartet are more sensitive to cation radii in the case of earth alkaline cations than for alkaline cations.[4] Note that the density of states for the Mg^{2+} coordinated G-octet exhibits a long tail at the low-energy side likely due to insufficient sampling in the nuclear ensemble.

In all analyzed systems, most of the first 32 computed excited states belong to $\pi\pi^*$ excitations. The first two $\pi\pi^*$ states of guanine are well-known L_a and L_b states. By using the semi-classical approximation, Sapunar *et al.* estimated their energies to be 4.57 and 5.22 eV in the gas phase at ADC(2)/aug-cc-pVDZ level of theory.[63] From the shoulder of the $\pi\pi^*$ density of states, we find that L_a states are positioned at 4.40 eV in the empty G-octet. The presence of the alkaline and earth alkaline cations red-shifts these states by 0.15 and $0.20 - 0.25$ eV, respectively. The energy of the L_b states amounts to 5.25 eV in the empty G-octet. The complexation of G-octet with alkaline and earth alkaline cations, blue-shifts the L_b states by $0.05 - 0.10$ and 0.10 eV, respectively. Interestingly, the L_a and L_b states in aqueous solution[63] have the opposite energy shift relative to those due to the cation complexation in G-quadruplexes. The L_a and L_b states are followed with two close-energy groups of $\pi\pi^*$ states[63] which are difficult to resolve in our density of states.

$n\pi^*$ transitions are found above the L_a states. Their ratio in the first 32 states decreases from 21 % in the empty G-octet to $16-18$ % in G-octets coordinated with alkaline cations and 9 and 2 % for Mg^{2+} and Ca^{2+} coordinated complexes, respectively. This is a consequence of the stabilization of the oxygens' n orbitals due to hydrogen bonding and interaction with a cation which results in higher excitation energies of $n\pi^*$ states. These states are shifted above the first 32 states and at the same time higher $\pi\pi^*$ states are lowered to their

Figure (5) Density of states (black line), and its charge transfer (blue line) and charge separation (green line) contributions.



positions. In order to understand the origin of the later effect, we examined charge transfer and charge separation characters of the excited states. Their contributions to the density of states is displayed in Figure 5. Only $\pi\pi^*$ states above the L_a states exhibit significant charge transfer character. Their contribution for energies below 5 eV is less than 1 %. The exception is the Mg^{2+} coordinated G-octet which has approximately 4 % of charge transfer states. The contribution of charge transfer states to density of states of empty G-octet is 27 %. It increases to $31-33$ % for the G-octets with alkaline cations, which again confirms that Franck-Condon states of these G-octets have very similar properties. An even larger increase is found in the systems coordinated with earth alkaline cations, with 38 and 48 % for Mg^{2+} and Ca^{2+}, respectively. Stabilization of these $\pi\pi^*$ charge transfer states is due to the cation electrostatic field. Contrary to charge transfer states, the total number of charge separation states does not considerably depend on the cation type. The largest number of charge transfer states is observed in the G-octet coordinated with Ca^{2+} cation - only 2% more than the G-octets with Na^+ and K^+ cations. Thus, it is not possible to employ earth alkaline cations to significantly modulate charge separation in the vertical electronic excitation spectrum. Besides, this finding reveals that additional charge transfer states due to a cation coordination do not have net transfer of charge but are formed from the mutual charge relocations between guanines.

Charge transfer states are typically characterized with low oscillatory strengths. Let us now discuss the absorption spectra and their charge transfer contribution (Figure 6). The absorption spectrum consists of two peaks due to the L_a and L_b transitions. These two peaks converge into a single broad peak with a shoulder in the case of the empty G-octet. On the other hand, the gap between them is larger for earth alkaline than for alkaline cations. UV light absorbing charge transfer states are positioned at somewhat higher energies than the maximum of the L_b band. The contribution of these states to absorption of the empty G-octet is 10 %. Alkaline cations have negligible effects on the charge transfer states absorption, whereas earth alkaline cations increase this contribution by 50 %. These results

demonstrate that photoabsorption leads to a more pronounced population of charge transfer states of earth alkaline complexes compared to their alkaline analogues. Decompositions of the absorption spectra according to excited state delocalization are given in Figure S1 in the SI. The absorption is dominated by excited states delocalized on two guanines. The contribution of states delocalized on three guanines is larger than those of monomer-like states. The later states contribute at most to the absorption in the red tail, similarly as in single-stranded polyadenine.[64] We find that that delocalization does not considerably vary with the cation type. This implies that intramolecular energy transfer occurring upon photoexcitation of these systems has similar initial dynamics.

Hydration Effects

Charge transfer states in aqueous solution exhibit strong solvatochromism due to dipole electric field caused by the hydration shell. Yin *et al.* found that the lowest charge transfer state of stacked adenine in water is red-shifted by $0.7 - 1.0$ eV relative to the value in the gas phase.[65] The charge transfer state is found to be positioned below bright states in the absorption red tail. Motivated by this finding, we studied hydration effects on charge transfer states of G-octets templated with Na^+ cation.

Figure 7 displays absorption spectra, density of states and their decomposition for the system in the gas phase and aqueous solution. Both charge transfer and charge separation states are considerably stabilized in water relative to the gas phase. They appear in the absorption red tail but their density is lower than monomer-like states. In the blue part of the spectrum, charge transfer density of states also increases, whereas $n\pi^*$ states are blue-shifted. It is interesting that delocalization of excited states in water is larger than in the gas phase. Particularly, there are two times less monomer-like states and three times more states that are delocalized on three guanines.

Beside charge transfer states localized on the G-octet, we also found charge transfer states which include electron transfer for the G-octet to water molecules. These electron

detachment states have a very broad distribution that begins at 4.4 eV. Their contribution to the total density of states amounts to 7.5 %, which points to their probable population upon photoexcitation. In Figure 7, we also provide natural transition orbitals for one such transition. This is a long-range electron transfer, i. e. an electron is transferred from a guanine to water molecules that are not in its vicinity.

Note that unlike other nucleobases, guanine is very weakly soluble in water. It has to be functionalized with hydrophilic moieties, such as sugar-phosphate group in order to become more soluble. Yet, it is not clear to what extent these moieties screen guanines from water electric field. Nogueira *et al.* showed that charge transfer states of single-stranded polyadenine in aqueous solution are not located in the red side of the absorption spectrum.[64] They argued that the sugar-phosphate backbone prevent water molecules to interact directly with nucleobases and thus small cluster models with hydrated nucleobases do not appropriately describe hydration of biological self-assemblies.

Recently, Markovitsi and coworkers reported that photoionization of biological G-quadruplexes occurs at much lower energies than for guanine mononucleotide.[37,66] This process is found to be operative in a very broad excitation energy range. Since the cation effect was noticed,[37] these authors argued that photoionization of G-quadruplexes does not proceed vertically but occurs in a series of steps which start from the population of G-quadruplex charge-transfer states. The similarity between properties of electron detachment states observed in our simulation and experimentally detected photoionization states of biological G-quadruplexes[37,66] led us to tentatively propose that G-quadruplex oxidative damage upon UV light absorption might also take place in a single step.

Conclusions

In this work, the cation and hydration effects on low-energy excited states of G-quartet self-assemblies in the Franck-Condon region were studied. We employed a minimal model

consisting of two stacked G-quartets coordinated with alkaline Li^+, Na^+, K^+ and earth alkaline Mg^{2+}, Ca^{2+} cations. The lack of a sugar-phosphate backbone in these systems resulted in larger conformational flexibility of guanine molecules. Generally, all alkaline cation coordinated G-octets had similar ground state properties. The exception was lower coordination number of Li^+ cation, which enabled larger distortions of G-quartets. Also, the complex with Na^+ cation had somewhat shorter oxygen-cation distance and stronger inner hydrogen bonds than the complexes with other alkaline cations. On the other hand, the G-octets coordinated with earth alkaline cations exhibited larger variations in guanine arrangements and the inner hydrogen bond strength. Interestingly, it was found that stacked guanine molecules in the Mg^{2+} containing G-octet experience more pronounced overlap than in any other G-octet.

G-octets coordinated with divalent earth alkaline cations had slightly different excited state properties than their alkaline counterparts. Apart from the larger L_a-L_b gaps, the presence of earth alkaline cations blue-shifted $n\pi^*$ states and stabilized charge transfer $\pi\pi^*$ states. Yet, the number of states which resulted in charge separation between G-quartets was not considerably modified upon cation exchange. The ratio of charge transfer states lower than 5 eV was below 1 % in all G-octets except for the Mg^{2+} coordinated one, which had approximately 4 %. Therefore, earth alkaline cations are not able to increase the density of charge transfer states in the absorption red tail. The present study unraveled a complex relation between the properties of the metal cation and the electronic absorption spectra of G-quadruplexes that might be exploited in the design of novel nanostructures with adjustable optical properties. In this respect, it would be interesting to study the effects that may arise from the coordination with trivalent lanthanide metal ions[67] or two divalent cations coordinated between consecutive G-quartets.

Hydration shifted charge transfer states to the absorption red tail. However, this spectral range was dominated by monomer-like excitations as in the gas phase. We found a broad density of states related to electron transfer from G-octet to water molecules. These

electron detachment states might also be present in biological G-quadruplexes, although sugar-phosphate backbone screens guanines from water electric field. We tentatively proposed that these states are responsible for oxidative damage of G-quadruplexes[37,66] upon UV photoexcitation.

Acknowledgement

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Supporting Information Available

Decomposition of absorption spectra according to excited state delocalization. This material is available free of charge via the Internet at http://pubs.acs.org/.

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Graphical TOC Entry

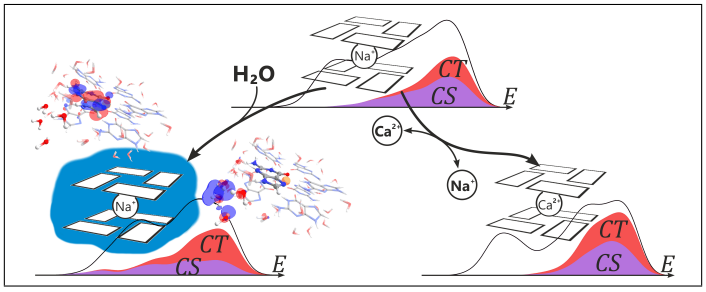


Figure (6) Computed absorption convoluted and stick spectra (black lines), their CT contributions (red lines) and density of states (gray shaded area).

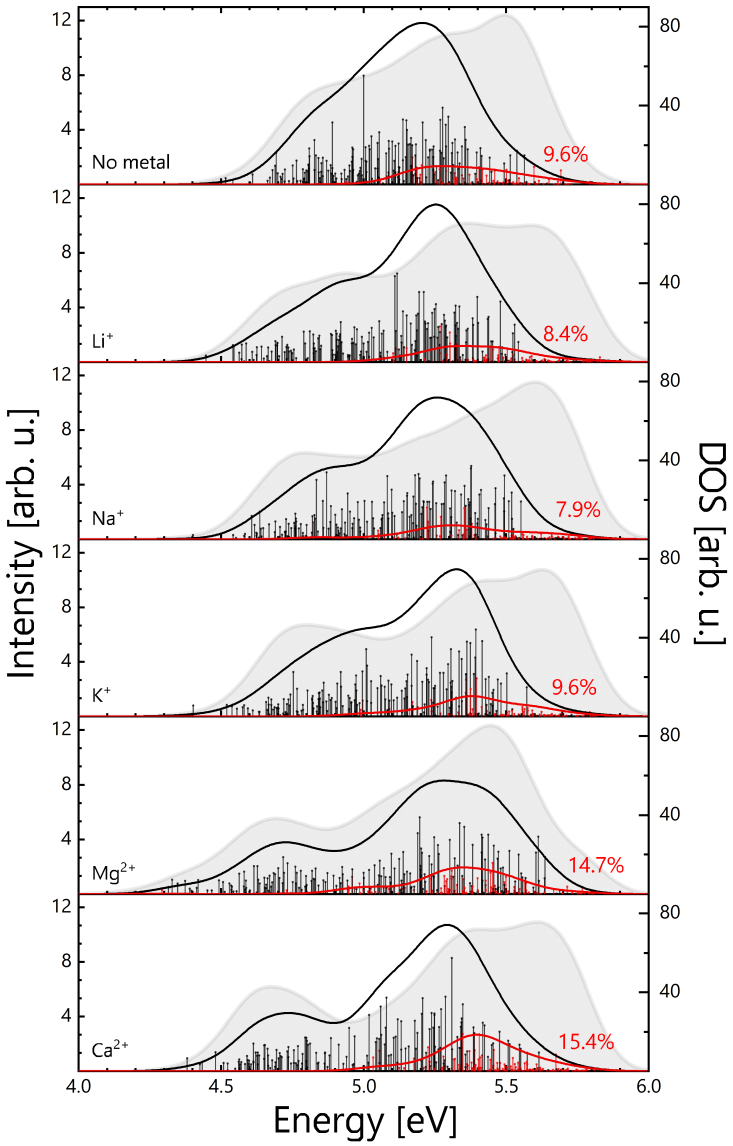
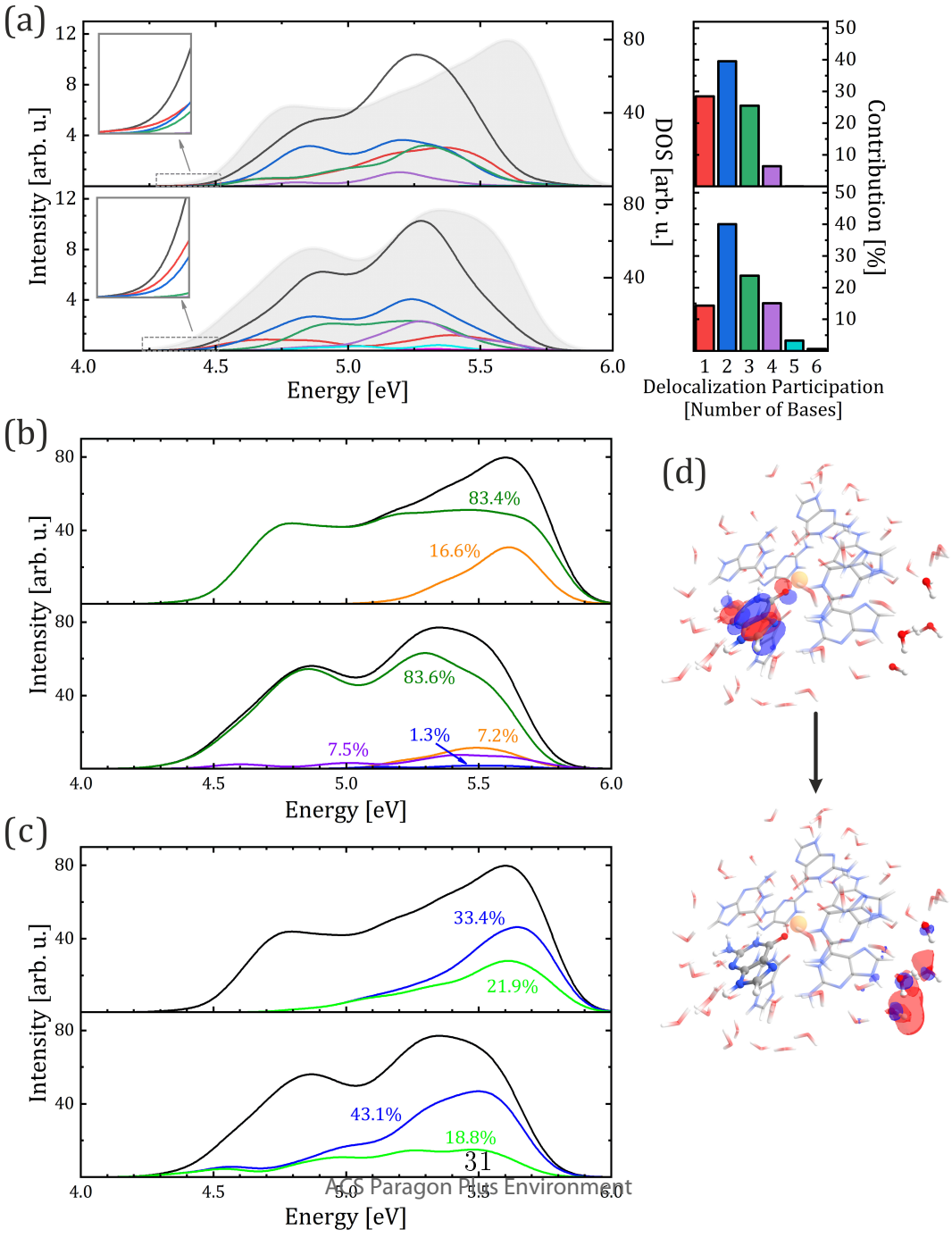
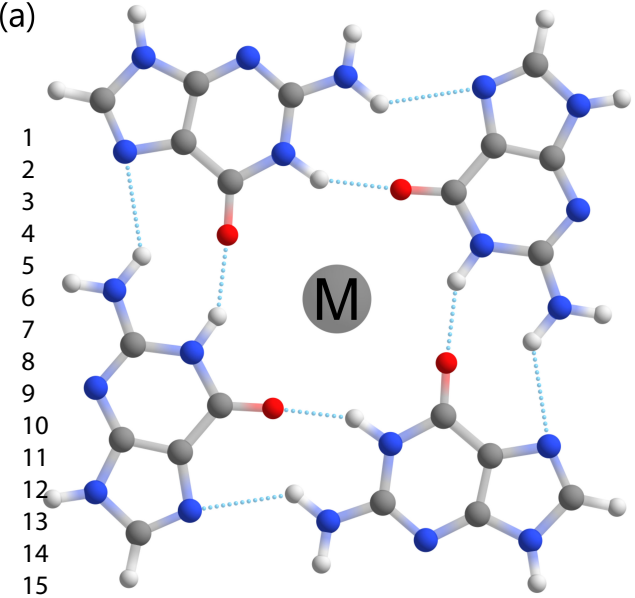
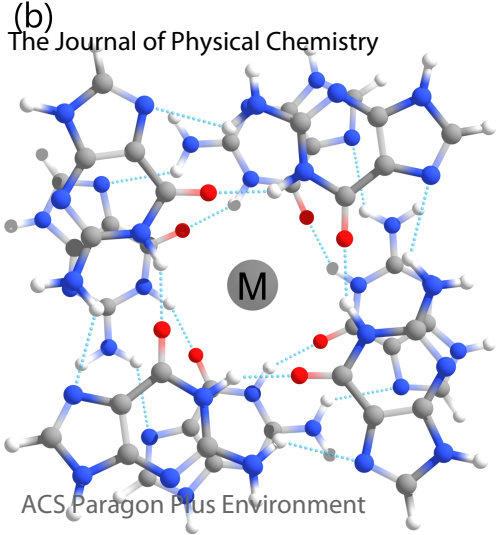
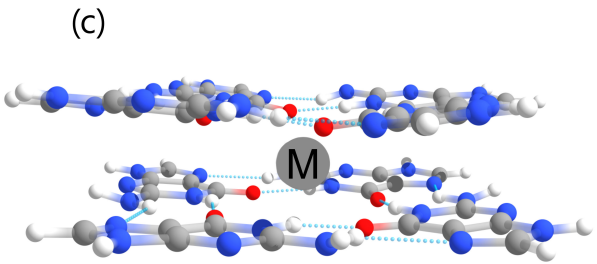


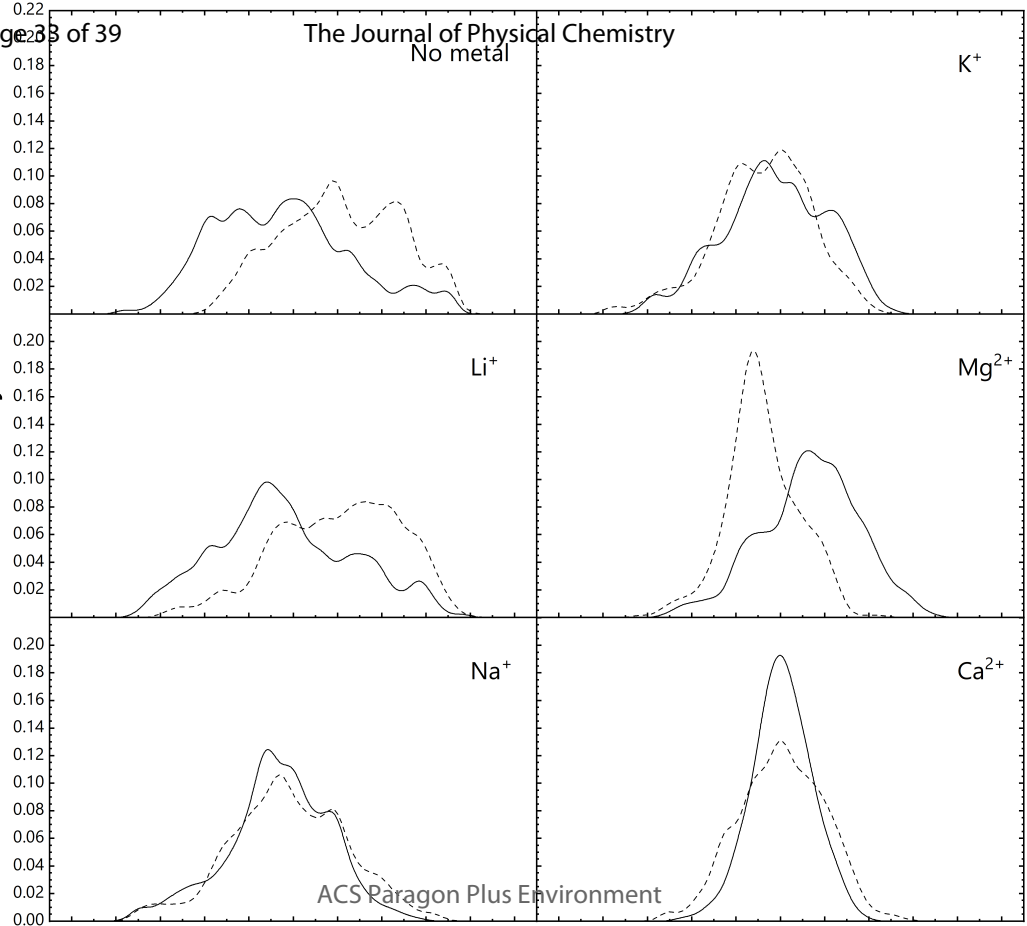
Figure (7) Excited state properties of of the G-octet templating with Na^+ cation in the gas phase (upper plots) and aqueous solution (lower plots): a) Left: decomposition of absorption spectra (black lines) according to excited state delocalization: $DEL = 1$ (red lines), $DEL = 2$ (blue lines), $DEL = 3$ (green lines), $DEL = 4$ (purple lines), $DEL = 5$ (cyan lines), $DEL = 6$ (yellow lines). The insets show the decomposition of the absorption red tail. Density of states is represented by gray shaded area. Right: histograms of DEL contributions to the spectrum (the same coloring code as in the spectrum plots). b) Density of states (black line) decomposed on the $\pi\pi^*$ (green line) and $n\pi^*$ (orange line) states, charge transfer states between the G-octet and water (purple line) and transitions localized on water molecules (blue line). c) Density of states (black line), and its charge transfer (blue line) and charge separation (green line) states localized on the G-octet. d) Natural transition orbitals involved in a selected charge transfer from the G-octet to water molecules.

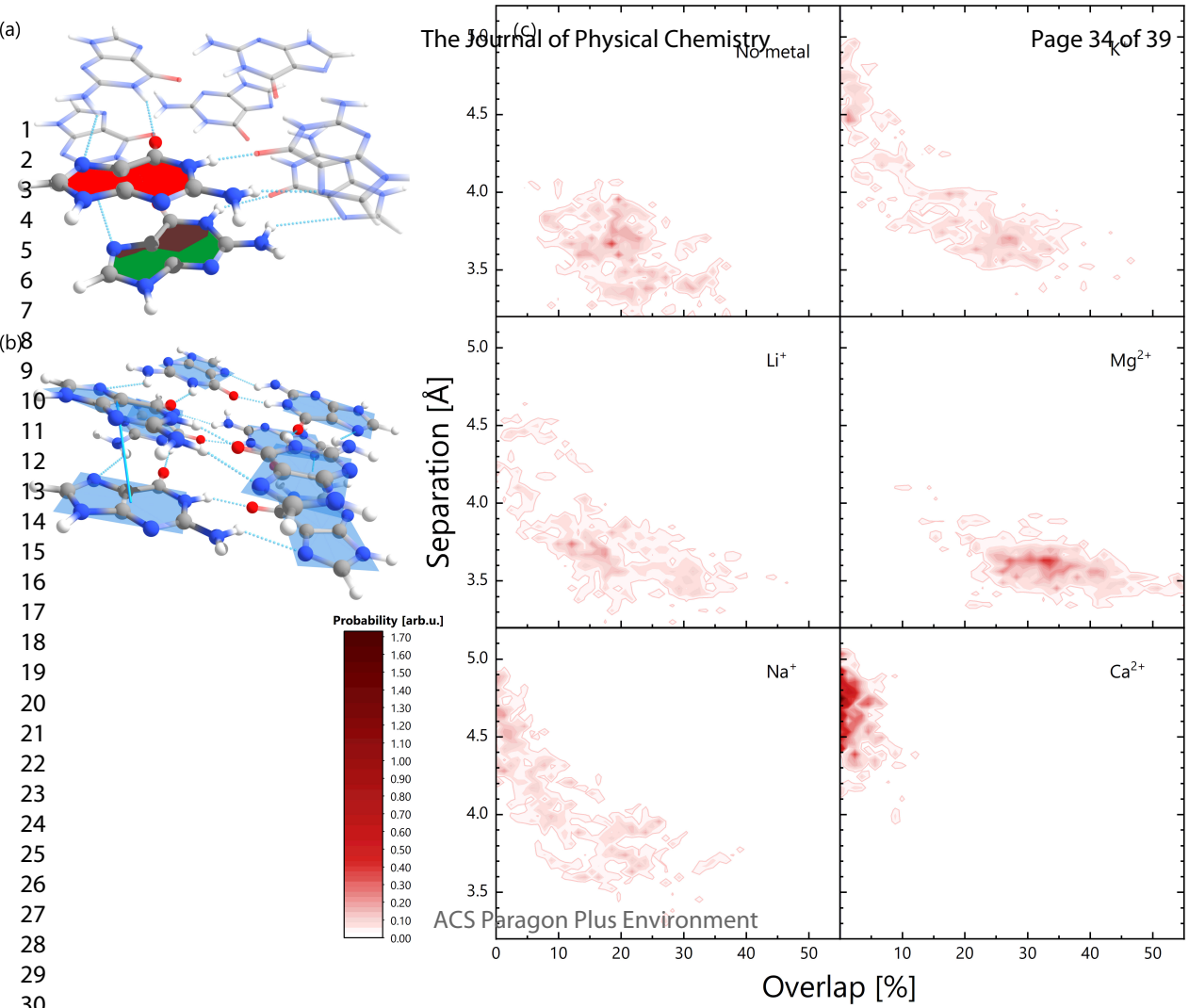











(a)
(b)
(c)
No metal
K+
Li+
Mg2+
Na+
Ca2+
Separation [Å]
Overlap [%]
Probability [arb.u.]
1.70
1.60
1.50
1.40
1.30
1.20
1.10
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
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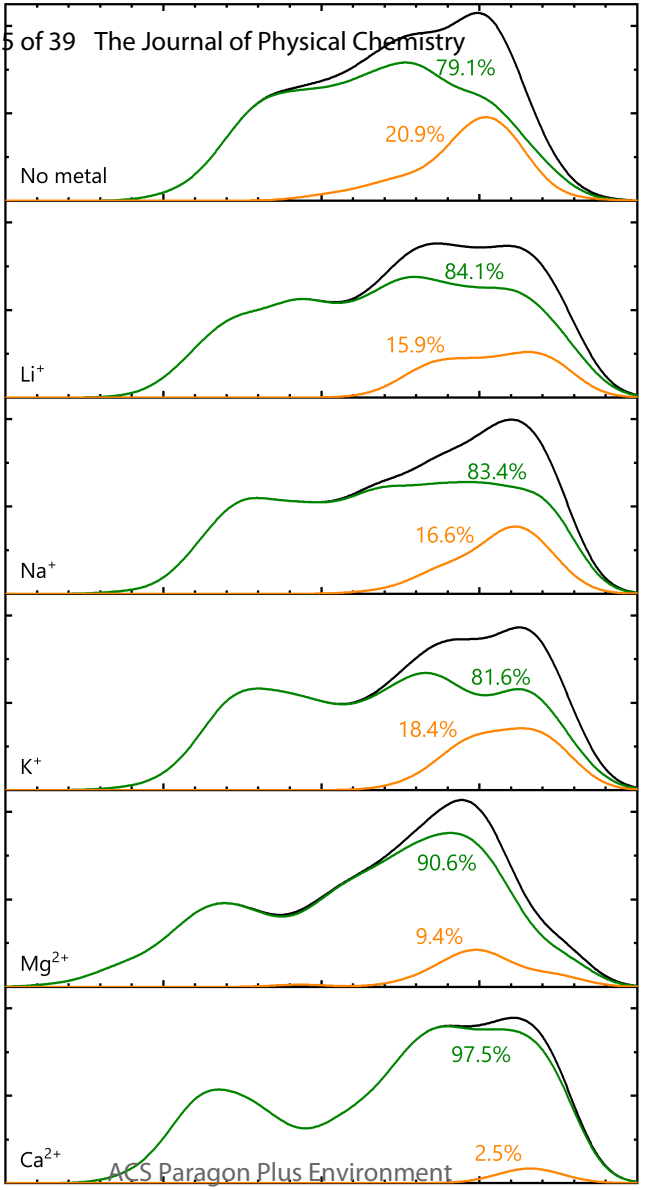
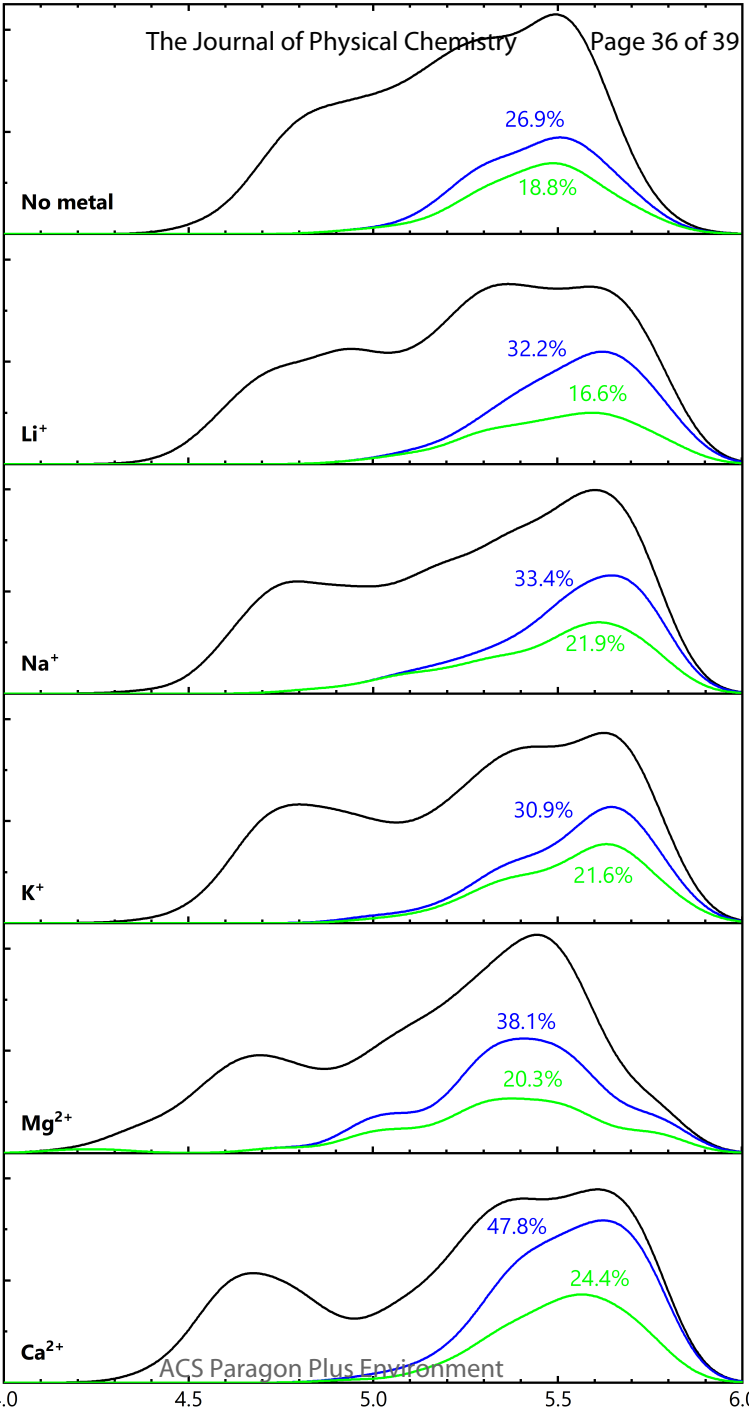
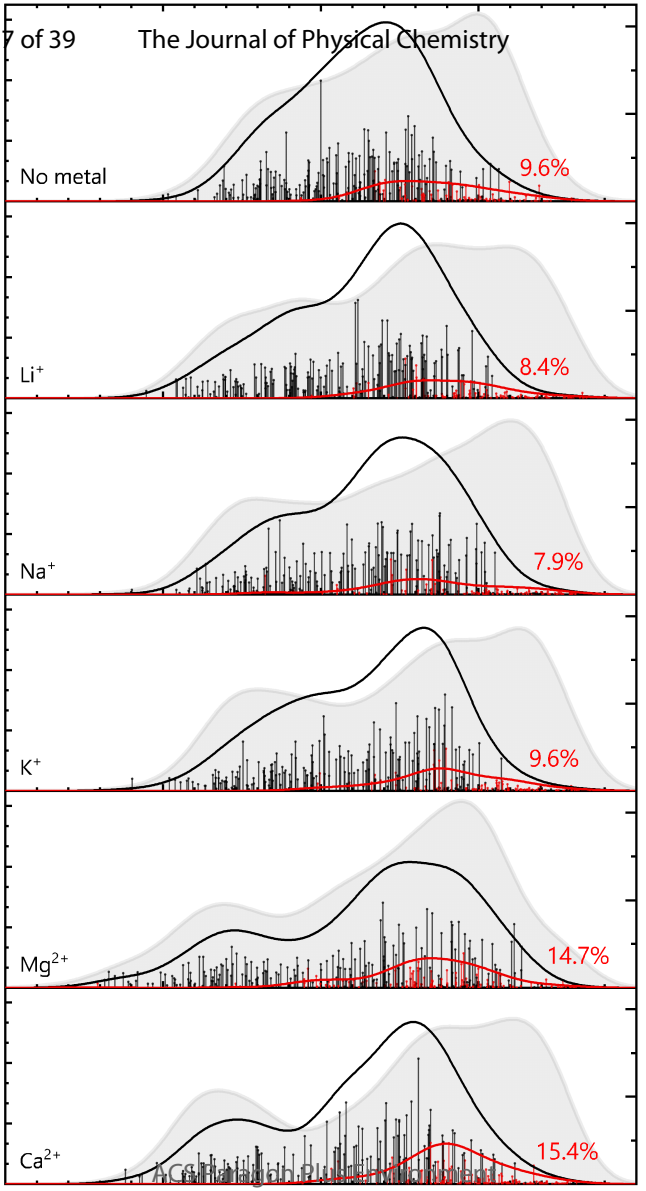
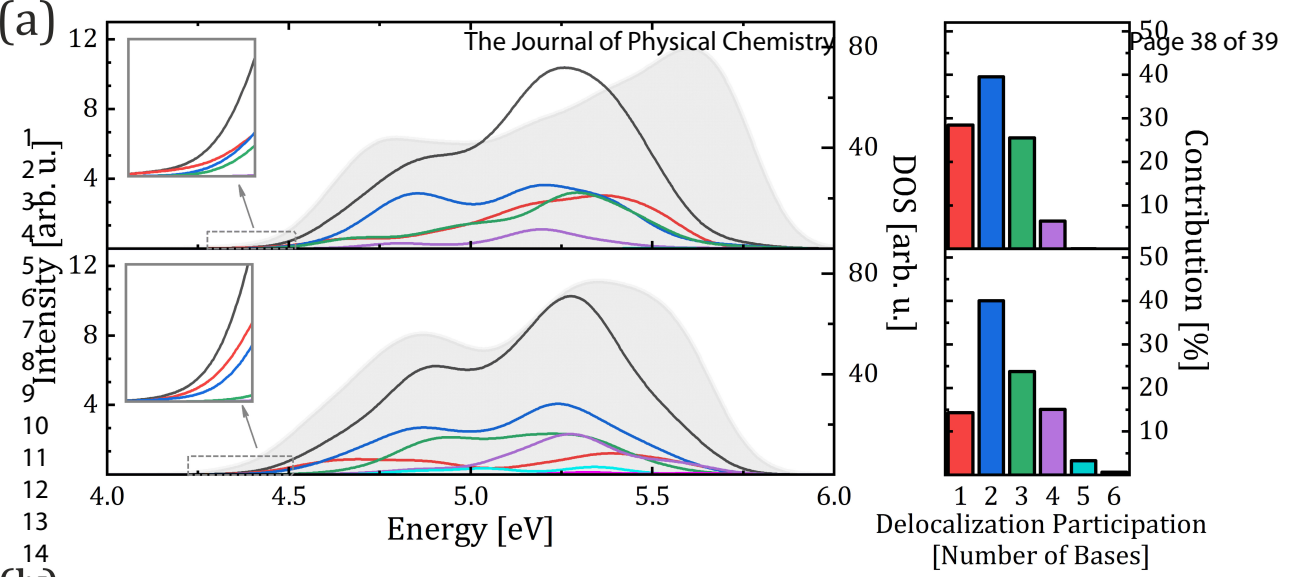
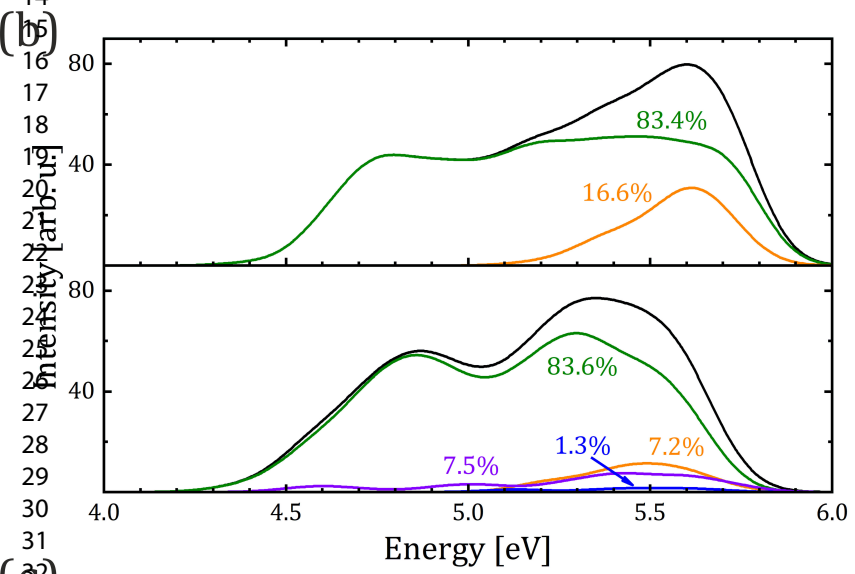
0.00
ACS Paragon Plus Environment

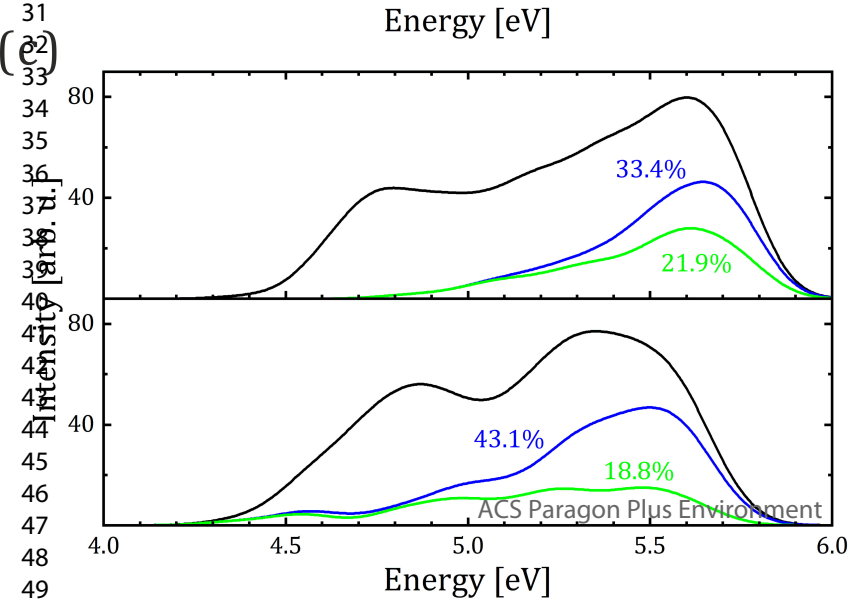


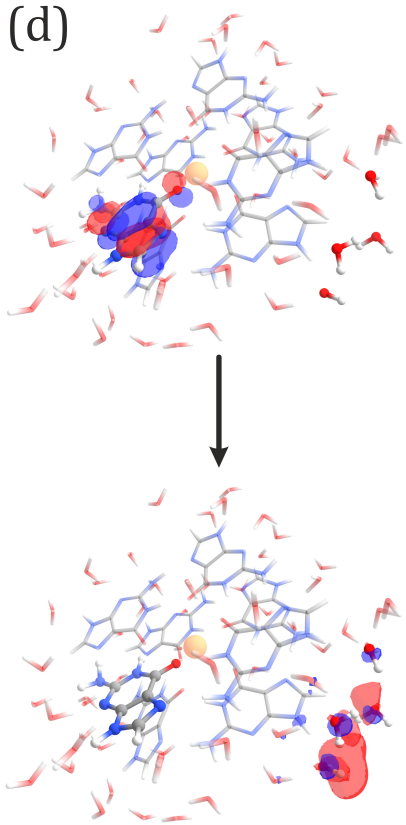


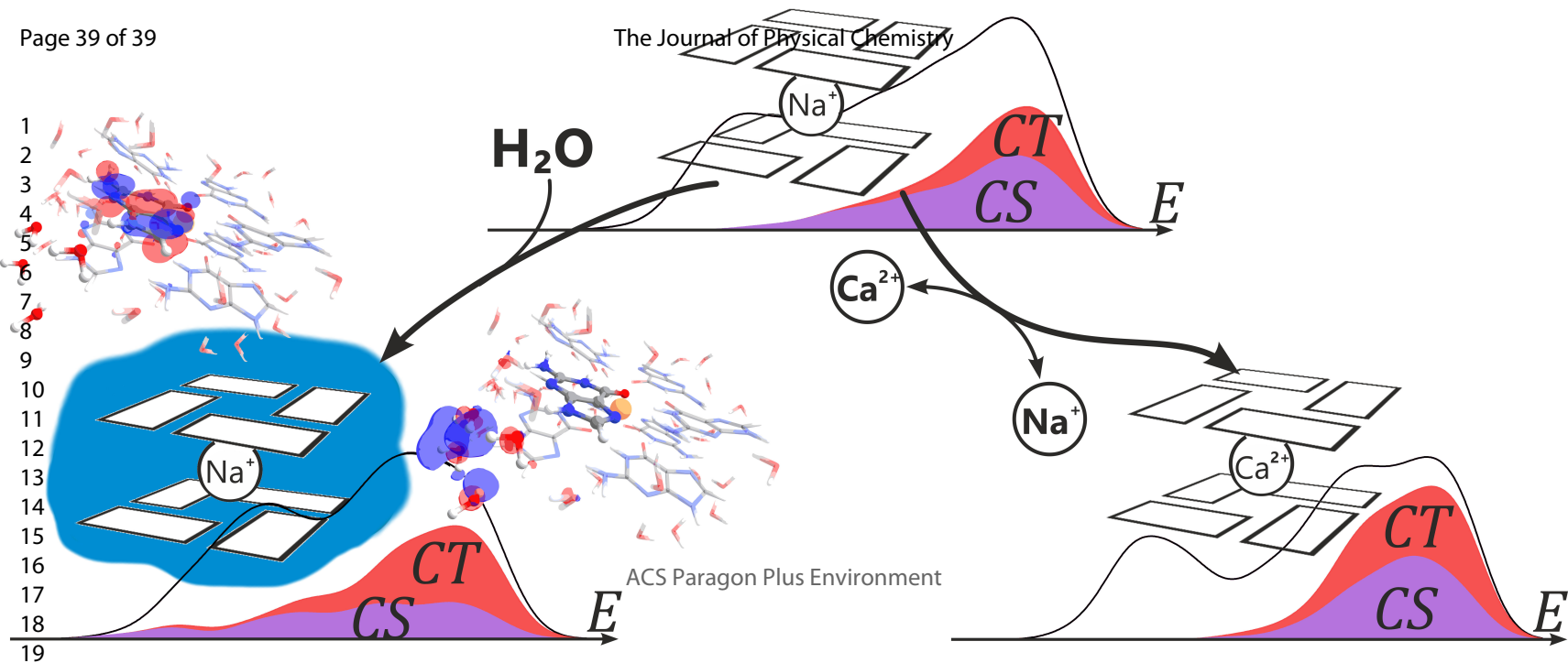








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Na+
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CS
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Ca2+
Na+
Na+
CT
CS
E
Ca2+
CT
CS
E