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Benchmark Studies on the Building Blocks of DNA. 2. Effect of Biological Environment on the Electronic Excitation Spectrum of Nucleobases

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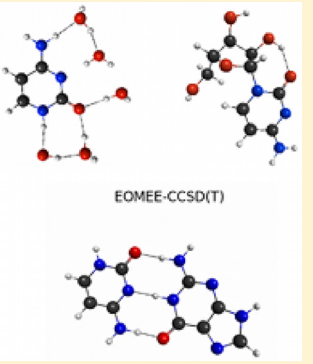
Supporting Information

ABSTRACT: In the first paper of this series (Szalay; et al. *J. Phys. Chem. A*, **2012**, *116*, 6702) we have investigated the excited states of nucleobases. It was shown that it is only the equation of motion excitation energy coupled-cluster (EOMEE-CC) methods, which can give a balanced description for all type of the transitions of these molecules; if the goal is to obtain accurate results with uncertainty of about 0.1 eV only, triples corrections in the form of, e.g., the EOMEE-CCSD(T) method needs to be included. In this second paper we extend this study to nucleobases in their biological environment, considering hydration, glycoside bond, and base pairing. EOMEE-CCSD and EOMEE-CCSD(T) methods are used with aug-cc-pVDZ basis. The effect of surrounding water was systematically investigated by considering one to five water molecules at different positions. It was found that hydration can modify the order of the excited states: in particular, nπ^* states get shifted above the neighboring $\pi\pi^*$ ones. The glycoside bond's effect is smaller as has been shown by calculations on cytidine and guanosine. Here the loss of planarity causes some intensity shift from $\pi\pi^*$ to nπ^* states. Finally, the guanine−cytosine (GC) Watson−Crick pair was studied; most of the states could be identified as local excitations on one of the bases, but there is also a low lying charge-transfer state. Significant discrepancy with earlier CASPT2 and TDDFT studies was found for the GC pair and triples effects seem to be essential for all of these systems.



INTRODUCTION

Without doubt, DNA is one of the most important molecules of life. Discovery of its structure by Watson and Crick[1] opened up the possibility of molecular level understanding of genetic expression, reproduction, and mutation. Fascinating properties of DNA (and also RNA) can be attributed to its building blocks and to the unique way these are connected. It seems, however, that not only ground state structure and properties are important to understand all features of DNA but also excited electronic states are involved in several processes. The basic building blocks, viz. the nucleobases, including chromophores, easily allowing electronic excitations to occur. The two, perhaps most important processes following excitation are the (i) relaxation of excited states[2−7] and (ii) charge transfer along the chain[8−18] (for a recent review, see ref 19; for recent theoretical reviews, see refs 20 and 21 and references therein). There is lot of evidence that DNA and RNA are very much protected against the harmful consequences of absorption of UV light: this property can be attributed both to the properties of the individual nucleobases[6,7] and also to their network.[4−6] Also, charge transfer through DNA/RNA chain involves excited and ionized states of the nucleobases, but the way they are connected is also an important ingredient.[3,20,22]

In our opinion, one cannot understand and quantitatively describe the properties of DNA/RNA unless we understand the properties of the building blocks and find the appropriate level of theory that is capable of providing the level of accuracy necessary for quantitative simulation. To that end, in this series of papers we systematically investigate the excited state properties of the building blocks of nucleic acids at a very high level of theory. The goal is to understand the basic processes and properties and their evaluation with the growing size of the system and to establish a benchmark set of results for future reference and development of approximate methods. According to the above arguments, these studies must be based on a high level of theory delivering unambiguous results.

The first paper of this series[23] presented systematic results on the vertical excitations of the nucleobases cytosine, guanine, adenine, and thymine. High level quantum chemical methods of coupled cluster (CC) type were used and the results were compared to other, lower level (CASPT2, CC2, TDDFT) calculations. It was found that it is only the equation-of-motion (EOM) CC methods that give consistent results for all four nucleobases and all possible excitation types. In particular, the method including triples correction, EOM-CCSD(T)[24] was found to give excitation energies with an error of not more than

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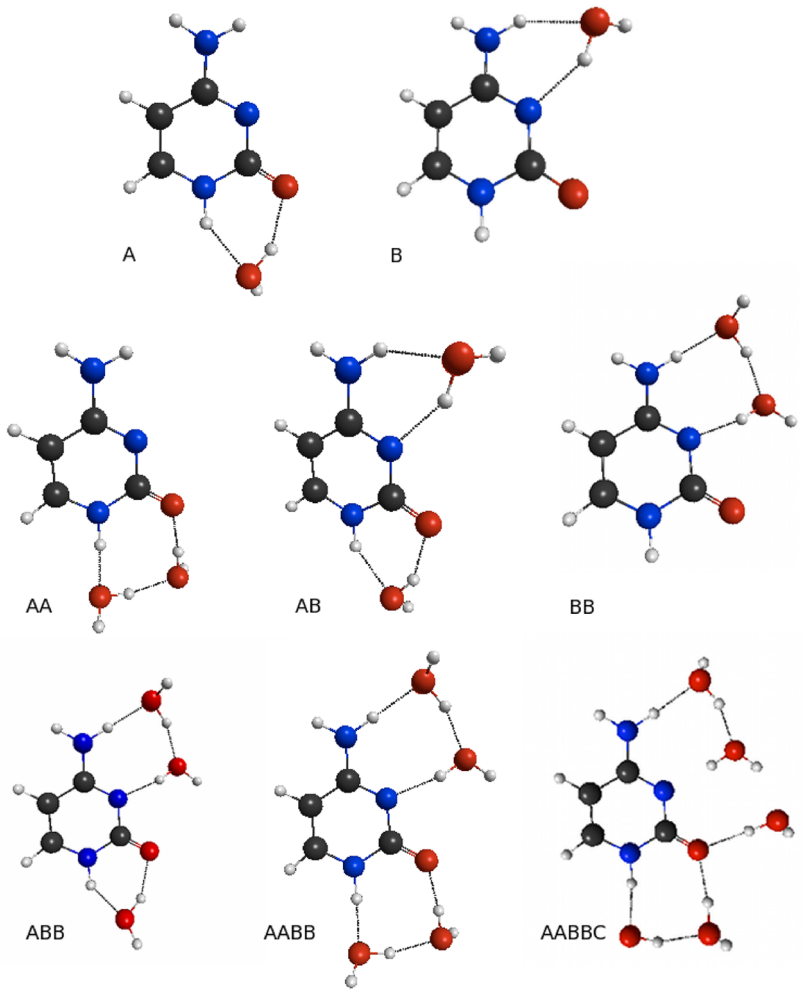

Figure 1. Structures of microhydrated cytosine clusters optimized at the MP2(fc)/aug-cc-pVDZ level.

0.1 eV and this conclusion was also supported by comparison with experimental observations in the case of cytosine.[25] Other methods (CC2, CASPT2, and TDDFT) resulted in much larger, and what is even more problematic, less systematic error, sometimes influencing even the order of the excited states.[23]

In this paper we study how the environment influences the excited states of the nucleobases. The effect of hydration will be described by considering cytosine and explicit water molecules around it. The influence of the glycoside bond will be studied in cytidine and guanosine. Finally, the effect of neighboring nucleobases in the Watson−Crick pairs will be investigated on the guanine−cytosine pair. In all of these studies we succeeded in using the same high level of theory as in paper 1[23] on the nucleobases, i.e., EOM-CCSD and EOM-CCSD(T).

Our study is clearly not the first one on these systems. However, because of the demanding computations, most previous studies used approximate methods. Hydrated nucleobases have been investigated at the TDDFT,[26−32] CASPT2,[33−36] DFT/MRCI,[37] MCQDP,[38] CIS,[39] and MRCI[40] levels. There is also a study at the EOM-CC level on cytosine in solution restricted to the two lowest excited states[41] and a more detailed analysis of hydrated uracil again at the EOM-CC level.[30] As for modeling of hydration, both explicit[37,39,40] and implicit[28−35,38−41] water models, or even combinations thereof have been used (see in particular the very recent paper by Domingo et al.[36]). In the present paper various numbers of explicit water molecules will be placed around cytosine, allowing the systematic study of the change of transition energies with respect to the increasing number and changing positions of the waters.

To our knowledge, there is only one theoretical paper on the excited states of nucleotides, a semiempirical molecular dynamic simulation by Alexandrova et al.[42] Experimentally, nucleotides, including cytidine and guanosine, have been studied by fluorescent lifetime measurements.[43−46] The lowest excitation energies (maximum of the absorption band) are known from early circular dichroism spectra for both cytidine[47] and guanosine.[48]

The excitation energy of Watson−Crick pairs have been studied by theoretical methods more often than nucleosides. In particular, in a series of papers Shukla and Leszczynski studied adenine−thymine (AT)[49] and adenine−uracil[50] pairs by CIS methods. Sobolewski and Domcke[51] performed CASSCF and CASPT2 calculations on the guanine−cytosine (GC) pair. Recently, Shukla and Leszczynski[32] compared CC2 and the TDDFT with several functionals on both GC and AT pairs. Finally, we mention two molecular dynamics calculations: Groenhof et al.[52] used the CASSCF method, and Alexandrova et al.[42] used semiempirical methods to study the relaxation mechanism after excitation. All of these calculations give rather contradictory results on the ordering of the excited states. We hope to resolve this discrepancy by our calculations.

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Table 1. Change of the Excitation Energies (eV) of Cytosine by Interaction with Water (Structure B) Calculated at the EOMEE-CCSD and EOMEE-CCSD(T) Levels with Frozen Cores[a]

transition		cytosine		cytosine−water (B)[b]		
type	assignment	CCSD	CCSD(T)	Δ_{CCSD}	$\Delta_{CCSD(T)}$	$\Delta\Delta$[c]
1($\pi\pi^*$)	$\pi \rightarrow \pi^*$	4.94	4.74	−0.06	−0.07	0.01
1(nπ^*)	$n_N \rightarrow \pi^*$	5.46	5.25	0.20	0.18	0.02
1(πR)	$\pi \rightarrow$ R	5.56	5.49	0.08	0.07	0.01
2($\pi\pi^*$)	$\pi_{-1} \rightarrow \pi^*$	5.86	5.62	−0.17	−0.17	0.00
2(πR)	$\pi_{-1} \rightarrow$ R	6.04[d]	5.91	0.00	−0.03	0.03
2(nπ^*)	$n_O \rightarrow 2\pi^*$	6.06[d]	5.96	0.12	0.15	−0.03
3(πR)	$\pi \rightarrow$ R	6.19	6.08	0.18	0.18	0.00
3(nπ^*)	$n_O \rightarrow \pi^*$	6.34	5.90	−0.05	−0.06	0.01
3($\pi\pi^*$)	$\pi \rightarrow 2\pi^*$	6.50	6.35	−0.03	−0.03	0.00
4(πR)	$\pi \rightarrow$ R	6.51	6.43	0.10	0.10	0.00
1(nR)	n_O,$n_N \rightarrow$ R	6.70	6.57	0.10	0.11	−0.01
4($\pi\pi^*$)	$\pi_{-1} \rightarrow 2\pi^*$	6.88	6.69	−0.11	−0.13	−0.02

[a]MP2(fc)/aug-cc-pVDZ geometry, aug-cc-pVDZ basis. [b]Change of excitation energy with respect to isolated cytosine. [c]Difference of the triple shift between monomer and hydrated molecule. [d]These two states are strongly mixed.

The paper is organized as follows. In the Methodology we briefly describe the methodology used in paper 1[23] and in this study. In the Discussion we first discuss hydrated cytosine, then cytidine and guanosine, and finally the guanine−cytidine Watson−Crick pair. The Conclusions summarizes our results.

METHODOLOGY

Methodology similar to that in paper 1[23] has been used, for more details see that paper. In short, structures of the microhydrated cytosines, as well as cytidine and guanosine, have been obtained at the MP2/aug-cc-pVDZ level with or without core correlation as specified later. These calculations have been performed by the PQS[53] and ACES III[54] programs using redundant internal coordinates.[55,56]

The vertical excitation energies at the optimized structures were obtained by the EOMEE-CCSD and EOMEE-CCSD(T) methods using the appropriate modules in ACES III.[57] The aug-cc-pVDZ basis was used in all of these calculations, with the core electrons frozen. In all cases the twelve lowest-energy states have been determined.

Transition moments were calculated at the EOMEE-CCSD level using both the left and right eigenvectors.[58] Assignment of the excitations has been performed by using natural orbitals of the density differences or by identifying dominant excitations and the form of the corresponding orbitals. When the assignments in the tables are described, as in paper 1,[23] π, n, and R will be used to denote π, lone pair, and Rydberg orbitals, respectively; virtual orbitals are designated by *, a preceding number referring to its sequential number; for occupied orbitals, the sequential number with respect to the corresponding HOMO is given as subscript, but for lone pairs, if appropriate, the subscript designates the type of atom (O or N) they belong to.

To demonstrate the applicability of ACES III, we finally report some typical timings of our calculations. These refer to calculations with 512 processors on an Cray XE6, although some of the calculations have been performed with 1024 or even more processors. All twelve transition energies of any of the nucleobases at the EOM-CCSD(T) level could be obtained in a couple of hours. All twelve excited states of cytidine, which has already 94 valence electrons, could be obtained within a week. The largest calculations we performed were on guanosine with 108 valence electrons and 577 basis functions. The CCSD calculations for all 12 states took less than 3 days, and the CCSD(T) calculations required little bit more than 1 day per root, i.e., about 2 weeks for all states. Note that triples calculations can easily be divided into smaller jobs, namely two jobs for each state ($\alpha\alpha\alpha$ and $\alpha\alpha\beta$ contributions), and all such calculations are feasible even considering restricted job length at the computer centers.

DISCUSSION

Microhydrated Cytosine. On the basis of earlier results by Fogarasi,[59,60] various numbers of water (one to five) molecules have been placed at different positions around cytosine. Reference 59 suggests three possible bonding positions for waters: the one designated as *A* is at the N1H site where the water can bind to the NH (H-donor) and to the neighboring carbonyl (H-acceptor). The second, designated as position *B*, is at the NH_2 group (H-donor) and the lone pair of the neighboring N3 nitrogen (H-acceptor). Finally, a third position (*C*) can be defined between these two using both the carbonyl oxygen and the ring nitrogen (N3) as H-acceptors. In this paper the structures will be designated accordingly: structure A means one water at position *A*, B means one water at position *B*, AA stands for a structure with two waters at position *A*, AB one water at both positions *A* and *B*, etc. The largest complex studied here had five water molecules (AABBC). The optimized structures (MP2/aug-cc-pVDZ) are shown in Figure 1, with their Cartesian coordinates and relative energies given in the Supporting Information.

In the case of the monohydrated cytosine molecule the most favorable position is site *A* but structure B is also only 0.6−0.8 kcal/mol higher in energy.[59] Note that in nucleosides the situation is different because the sugar replaces the donor hydrogen at N1, and therefore, only the carbonyl H-acceptor is present at position *A*. On the other hand, position *C* is not favored, and the energy of structure C is several kcal/mol higher;[59] therefore, it is expected that this position will be occupied only if the other positions are closed, i.e., in the case of more water molecules. See ref 59 for more detail on the energetics of the ground state monohydrated structures.

In the dihydrates, the second water can again attach itself to different sites. As the table in the Supporting Information shows, structure AA is the most stable followed by AB and BB, but the energies of these structures are within a range of about

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1 kcal/mol. In the case of three waters, AAB is the most stable form followed by ABB (energy difference of 0.6 kcal/mol). In the present study only ABB is included because, as will be seen later, excitation energies are much more influenced at position *B* than at *A*.

On the basis of the above experience, we have optimized only one tetrahydrated structure (AABB). The fifth water bounds to the carbonyl oxygen resulting in structure AABBC for the pentahydrated complex. Although not included in the excitation energy calculations, we note that a structure with six waters could also be identified that is similar to AABBC except an additional water binds to the NH_2, the latter acting as H-donor.

Discussing the excitation energies, we start with a methodological question on the effect of triples. In paper 1[23] it was found that triples effects on the excitation energy can be as large as 0.1−0.3 eV; therefore, inclusion thereof is substantial to get reliable results, in particular, for correct ordering of the states. To test triples effects on the monohydrated complex, structure B was chosen as an example because (i) position *B* is open for hydration also in nucleosides and (ii) water at position *B* influences excitation energies much more (see below). In Table 1 the change of excitation energies caused by a water at position *B* is listed as calculated at the EOMEE-CCSD and EOMEE-CCSD(T) levels. The table shows clearly that the change of excitation energies due to the water is not negligible (up to 0.2 eV), but the effects are almost identical at both computational levels: the double difference does not exceed 0.03 eV. This small energy difference is probably not negligible when the hydration energy is investigated (it corresponds to almost 1 kcal/mol), but much smaller than the expected uncertainty of the excitation energy. Therefore, it appears to be sufficient to investigate hydration effects on the excitation energy at the CCSD level. Keep in mind, however, that the triples effects are the same order of magnitude as the energy change due to hydration; therefore, triples effects can modify the ordering of the states of hydrated molecules. According to Table 1, the excitation energy of the complex at the CCSD(T) level can, however, be accurately approximated by correcting the CCSD excitation energy with the triples contribution calculated for the isolated molecule.

For each of the eight cytosine−water structures (Figure 1) the 12 lowest excitation energies were calculated at the EOM-CCSD/aug-cc-pVDZ level (core electrons frozen), and the states have been assigned using the EOM vectors and the orbitals. In Table 2 these excitation energies are compared with the corresponding ones of isolated cytosine, and Figure 2 shows the changes for the valence states graphically. Starting the discussion with the most intense $\pi\pi^*$ type transitions, one observes that the excitation energies change relatively little; the energy difference between the isolated cytosine and the pentahydrated AABBC complex is only +0.15, −0.14, −0.18, and −0.17 eV for the first four $\pi\pi^*$ states, respectively. Except for the first state, the energy decreases slightly. By investigating the results more closely (see in particular Figure 2), one can observe a somewhat different effect of the water at different positions. In the case of the first $\pi\pi^*$ transition ($\pi \rightarrow \pi^*$ excitation) the first water slightly lowers the excitation energy, which starts to grow when the hydration shell gets saturated. Quite a large effect of the fifth water can be seen; note that this fifth water binds at position *C*. For the second $\pi\pi^*$ transition ($\pi_{-1} \rightarrow \pi^*$ excitation) one can observe an oscillatory behavior: water at position *A* has negligible effect, whereas at *B* it decreases the excitation energy. The opposite effect is shown

Table 2. Excitation Energies (eV), Oscillator Strengths (au), and Transition Types[a] of Cytosine and Its Various Water Complexes (EOM-CCSD(fc)/aug-cc-pVDZ Results)[b]

	cytosine	cytosine + water																	
		A		B		AA		BB		AB		ABB		AABB		AABBC			
type																			
1($\pi\pi^*$)	4.94	0.049	4.85	0.065	4.88	0.066	4.88	0.079	4.93	0.068	4.93	0.077	4.98	0.086	5.00	0.092	5.09	0.104	
1($n\pi^*$)	5.46	0.002	5.42	0.004	5.66	0.001	5.45	0.003	5.75	0.006	5.77	0.002	5.86	0.005	5.90	0.003	5.93	0.014	
1(πR)	5.56	0.004	5.79	0.017	5.64	0.005	5.81	0.014	5.66	0.004	5.85	0.006	5.87	0.005	5.89	0.005	6.01	0.003	
2($\pi\pi^*$)	5.86	0.142	5.83	0.130	5.69	0.171	5.85	0.125	5.64	0.182	5.72	0.169	5.68	0.200	5.71	0.181	5.72	0.184	
2(πR)	6.04[c]	0.003	6.18	0.011	6.18	0.002	6.21	0.001	6.18	0.002	6.26	0.010	6.27	0.011	6.29	0.016	6.43	0.013	
2($n\pi^*$)	6.06[c]	0.006	6.15	0.000	6.04	0.000	6.18	0.014	6.12	0.000	6.28	0.002	6.36	0.005	6.41	0.000	6.64	0.044	
3(πR)	6.19	0.006	6.44	0.090	6.37	0.015	6.49	0.065	6.42	0.014	6.59	0.003	6.65	0.011	6.66	0.031	6.83	0.004	
3($n\pi^*$)	6.34	0.000	6.40	0.003	6.29	0.000	6.47	0.001	6.39	0.000	6.53	0.000	6.63	0.007	6.71	0.002	7.07	0.007	
3($\pi\pi^*$)	6.50	0.412	6.34	0.414	6.47	0.416	6.31	0.459	6.47	0.377	6.39	0.358	6.38	0.314	6.35	0.286	6.32	0.267	
4(πR)	6.51	0.005	6.62	0.004	6.61	0.002	6.59	0.003	6.63	0.008	6.67	0.049	6.70	0.097	6.69	0.008	6.87	0.003	
1(nR)	6.70	0.026			6.80	0.022			6.85	0.026									
5(πR)	6.82	0.000									7.09	0.006	7.08	0.006	7.10	0.003			
4($\pi\pi^*$)	6.88	0.180	6.81	0.192	6.77	0.224	6.80	0.229	6.69	0.249	6.72	0.297	6.64	0.299	6.63	0.367	6.61	0.557	
4($n\pi^*$)			6.87	0.047			6.83	0.017									6.94	0.008	

[a]For orbital based assignment compared with Table 1. [b]Oscillator strength from right-hand vector only. [c]These two states are strongly mixed.

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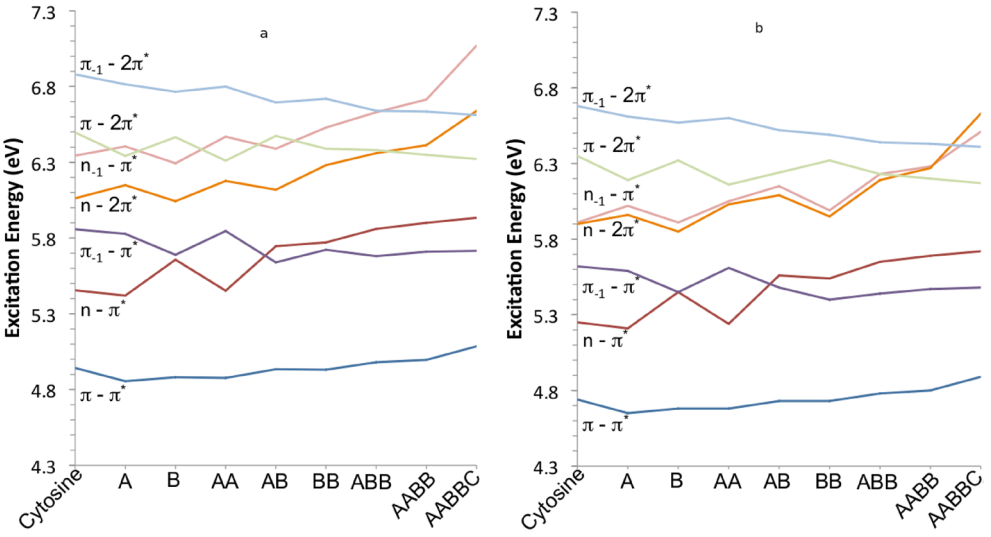

Figure 2. Change of cytosine's excitation energy with microhydration. Only valence states are given. (a) EOM-CCSD results. (b) EOM-CCSD results corrected by triples contribution. See text for more detail.

for the third $\pi\pi^*$ transition ($\pi \rightarrow 2\pi^*$ excitation): the effect at position *B* is negligible, whereas it is −0.16 and −0.19 eV for structures A and AA, respectively. Finally, in the case of the fourth $\pi\pi^*$ transition ($\pi_{-1} \rightarrow 2\pi^*$ excitation) water at both positions lowers the excitation energy. As of the intensity of the $\pi\pi^*$ type transitions (note that these are dominating the excitation spectrum), one can observe substantial changes of the oscillator strength (Table 2). The relative intensities of the first four $\pi\pi^*$ transitions change considerably; the first two transitions gain some intensity, whereas the third becomes less intense. A very large effect (a factor of 3!) is observed, on the other hand, for the fourth state at 6.6−6.8 eV with five waters, but the factor is 2-fold already for the AABB (four waters) structure. The positions do not seem to be important, the more waters are around, the larger the intensity is. Apparently, the microhydrated complex becomes more and more polarizable.

In contrast, the excitation energy of the $n\pi^*$ transitions increases considerably, differences of 0.5 eV or more can be observed for the first three $n\pi^*$ states when the isolated cytosine and the AABBC complex are compared. The corresponding curves in Figure 2 are far from being monotonic, the change of excitation energy depends strongly on the position of the waters. For example, in the case of the transition characterized by excitation from the highest n orbital localized on the N3 nitrogen (first $n\pi^*$ transition), the water at position *B* has a substantially larger effect than at position *A*. On the other hand, transitions involving the second highest lone pair orbital (n_O, localized mostly on the carbonyl oxygen) water at position *A* increases the excitation energy. Having already five water molecules in the hydration shell (AABBC complex) the excitation energy is already higher by 0.73 eV: this is not surprising because in this case, by occupying also position *C*, already two waters donate proton to the carbonyl oxygen, which has lost an electron in the excitation process. The $n\pi^*$ type excitations have very low intensity, which changes very little due to hydration; it is only the pentahydrated AABBC complex where notable gain of oscillator strength can be observed. This can be most probably attributed to the fact that the planarity of cytosine, which is mainly preserved up to four water molecules, cannot be maintained in the AABBC complex and there is a possibility of interaction between the $n\pi^*$ and $\pi\pi^*$ transitions.

The different behavior of the $\pi\pi^*$ and $n\pi^*$ transitions toward hydration affects the relative ordering of the states (see the crossing lines in Figure 2). In particular, the $2(\pi\pi^*)$ transition becomes the second excited state in the larger complexes having lower energy than the $1(n\pi^*)$ transition. Because in the photodynamics calculations on free cytosine[61] the lowest $n\pi^*$ transition plays an important role, the present results, indicating a change of the ordering of states and increased gap between the first $\pi\pi^*$ and $n\pi^*$ transitions, might have pronounced consequence on the conclusion of these studies. In this respect, the triples effects are again not negligible, because, as discussed above, these are of the same magnitude as the effect of hydration; they therefore might influence the ordering of the states. However, as we have seen above, triples effects are much the same in free cytosine as in the hydrated form. Thus, the EOMEE-CCSD(T) excitation energies of the complexes can be approximated by adding the triples corrections obtained for cytosine to the CCSD excitation energies. Figure 2 also shows these corrected excitation energies for the valence transitions. A full set of excitation energies is given in the Supporting Information. Comparing the two panels in Figure 2, one can observe some change in relative energies: the gap between the $2(\pi\pi^*)$ and $1(n\pi^*)$ transitions is further increased and both of the next two $n\pi^*$ excitations become higher in energy than the $3(\pi\pi^*)$ and $4(\pi\pi^*)$ transitions, when five waters are around the cytosine molecule.

The present results clearly show that the effect of water needs to be considered when the dynamics properties are investigated. Concerning the question whether implicite bulk-water models are capable of describing these effects, we refer to the recent paper by Domingo et al.[36] who compared the simulated spectra of cytosine tautomers obtained with different models. They have found that inclusion of some explicit water molecules in addition to the polarizable continuum model (PCM) causes blue shifts of ∼0.2 eV. This suggests that PCM alone does not cover all the effects and an explicit consideration of the first hydration shell, bound strongly by hydrogen bonds, is needed.

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Nucleosides: Effect of the Attached Sugar. In DNA/RNA the nucleobases are substituted by a sugar (ribose) at the N1 position, forming the nucleosides. On the way to understanding the excited state properties of DNA/RNA, the effect of the sugar needs first to be investigated. In this study we include cytidine and guanosine.

The structure of cytidine has also been optimized at the MP2(fc)/aug-cc-pVDZ level using the CID-6175[62] structure from PubChem[63] as starting guess. This structure corresponds to the most stable syn conformer of cytidine (see textbooks, for example ref 64). The resulting structure is given in Figure 3,

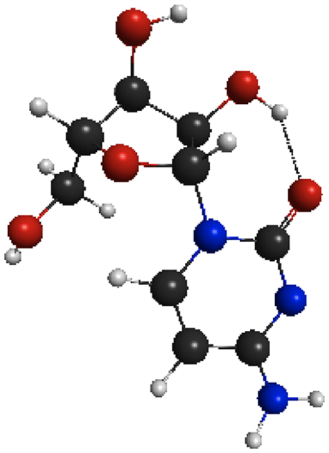

Figure 3. MP2(fc)/aug-cc-pVDZ optimized structure of cytidine.

and Cartesian coordinates are listed in the Supporting Information. Comparing the optimized and the PubChem structures, one can observe that these are quite similar, but in the optimized structure there is a rotation around the glycoside bond[64] (108° vs 89°) allowing a more efficient hydrogen bond between the carbonyl group of cytosine and the OH group of the sugar.

Excitation energies of cytidine obtained at the frozen-core EOM-CCSD/aug-cc-pVDZ and EOM-CCSD(T)/aug-cc-pVDZ levels using the optimized structure are given in Table 3 and compared to the excitation energies of the parent cytosine. For the first four transitions there is a definite analogy: these transitions can be assigned as 1($\pi\pi^*$), 1(nπ^*), 1(πR), and 2($\pi\pi^*$), respectively, in both cytidine and cytosine. Excitation energies do not change much: the energy of the $\pi\pi^*$ type transition decreases by a maximum of 0.1 eV, that of the first nπ^* transition changes little, and the largest shift is observed for the Rydberg transition (increase by about 0.2 eV). Considering intensities, this quantity grows considerably in the case of the first $\pi\pi^*$ transition, whereas there is no significant change for the others, including the bright 2($\pi\pi^*$) one.

A strong interaction of several transitions is observed at higher energies. There are three transitions of cytosine between 6 and 6.5 eV having orbital 2π^* as target of the excitation. These are a strongly mixed pair of $\pi_{-1} \rightarrow$ R and $n_O \rightarrow 2\pi^*$ excitations (A'') at 6.04 and 6.06 eV and the bright $\pi \rightarrow 2\pi^*$ excitation (A') at 6.50 eV. In the presence of the sugar, the strict planarity constraint is lifted and these transitions, due to the involvement of the same orbital as target, can interact, resulting in substantial intensity borrowing by the dark transitions. On the other hand the $\pi \rightarrow 2\pi^*$ excitation (6.50 eV) has its hole orbital common with the two $\pi \rightarrow$ R excitations (at 6.51 and 6.82 eV) which again leads to intensity borrowing. Note that the sum of the oscillator strengths of these five transitions is only a little higher than that of the corresponding transitions in cytosine. This process, however, changes the spectrum in comparison to the parent cytosine above 6 eV: substantial intensity should be observed at 6.1−6.2 eV, whereas the intense cytosine band at 6.5 eV would split up with significantly smaller intensities of the new lines. Note that the 3(πR) transition of cytosine (6.19 eV) is not involved in this mixing which we can not explain.

Closer analysis shows that the H-bond to the sugar might be partly also responsible for this mixing, the 2(πR) transition (state 5) of cytidine (6.14 eV) is the only one showing electron density loss also on the sugar (atom C2′ according to the numbering in, e.g., ref 64). The next Rydberg transition, 3(πR), has again higher energy by more than 0.2 eV, which might be attributed to the fact that the Rydberg orbitals overlap with some of the sugar's orbitals.

Table 3. Excitation Energies (eV) of the Lowest 12 Transitions of Cytosine and Cytidine Calculated by EOM-CC Methods (Frozen-Core and aug-cc-pVDZ Basis)

transition		cytosine			cytidine					
type	assignment	CCSD		CCSD(T)	CCSD		CCSD(T)	Δ_{CCSD}[a]	$\Delta_{CCSD(T)}$[a]	$\Delta\Delta$[b]
1($\pi\pi^*$)	$\pi \rightarrow \pi^*$	4.94	0.049	4.74	4.84	0.129	4.63	−0.10	−0.11	0.01
1(nπ^*)	$n_N \rightarrow \pi^*$	5.46	0.002	5.25	5.49	0.006	5.29	0.03	0.04	−0.01
1(πR)	$\pi \rightarrow$ R	5.56	0.004	5.49	5.77	0.009	5.67	0.21	0.18	0.03
2($\pi\pi^*$)	$\pi_{-1} \rightarrow \pi^*$	5.86	0.142	5.62	5.81	0.142	5.58	−0.05	−0.04	−0.01
2(πR)	$\pi_{-1} \rightarrow$ R	6.04[c]	0.003	5.91	6.14[d]	0.115	5.99	0.10	0.08	0.02
2(nπ^*)	$n_O \rightarrow 2\pi^*$	6.06[c]	0.006	5.96	6.16[d]	0.051	6.02	0.10	0.06	0.04
3($\pi\pi^*$)	$\pi \rightarrow 2\pi^*$	6.50	0.412	6.35	6.24[d]	0.191	6.12	0.05	0.04	0.01
3(πR)	$\pi \rightarrow$ R	6.19	0.006	6.08	6.46	0.011	6.34	0.27	0.28	−0.01
3(nπ^*)	$n_O \rightarrow \pi^*$	6.34	0.000	5.90	6.47	0.008	6.05	0.13	0.15	−0.02
4(πR)	$\pi \rightarrow$ R	6.51	0.005	6.43	6.55[e]	0.107	6.42	0.04	−0.01	0.05
5(πR)	$\pi \rightarrow$ R	6.82	0.000	6.73	6.67[e]	0.101	6.54	−0.15	−0.19	0.04
1(nR)	$n_O, n_N \rightarrow$ R	6.70	0.026	6.57						
4($\pi\pi^*$)	$\pi_{-1} \rightarrow 2\pi^*$	6.88	0.180	6.68	6.82	0.174		−0.06		

[a]Relative excitation energy with respect to cytosine. [b]Difference of the triples shift between monomer and hydrated molecule. [c]These two states are strongly mixed, essentially a mixture of the two designations. [d]These three states are mixed combinations of the corresponding cytosine states causing intensity borrowing from the third state. [e]There is also a component $\pi \rightarrow 2\pi^*$, which introduces oscillator strength in both of these sates.

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Finally, the 4($\pi\pi^*$) transition ($\pi_{-1} \rightarrow 2\pi^*$) is less affected by the glycosidic bond, both the excitation energy and the intensity change only slightly.

Triples effects are again additive, the double difference (last column in Table 3) shows a maximum change of 0.05 eV. It seems, therefore, that the effect of sugar on the excitation energies can be well described at the CCSD level and excitation energies corresponding to the CCSD(T) method can be approximated by correcting the CCSD energies by the triples corrections obtained for isolated cytosine. Note, however, that the triples effects might change the order of the states, as in the case of the 1(πR) and 2($\pi\pi^*$) transitions; therefore, it can be very important to answer some questions.

For guanosine, the CID-6802 structure[65] from PubChem[63] turned out to be wrong: the guanine part of the structure is a tautomer having the hydrogen on the N3 nitrogen instead of N1. This is a very high-lying tautomer usually not considered among the studied tautomers.[66] According to our MP2/aug-cc-pVDZ calculations the energy difference is about 15 kcal/mol. Note also that this tautomer of guanine would not form a proper Watson–Crick pair. We have checked the PubChem database[63] and found that most structures involving guanine have this wrong structure.

Therefore, we replaced guanine in CID-6802 by the canonical form and performed geometry optimization at the MP2/aug-cc-pvDZ level. The resulting structure is depicted in Figure 4 and the coordinates can be found in the Supporting Information.

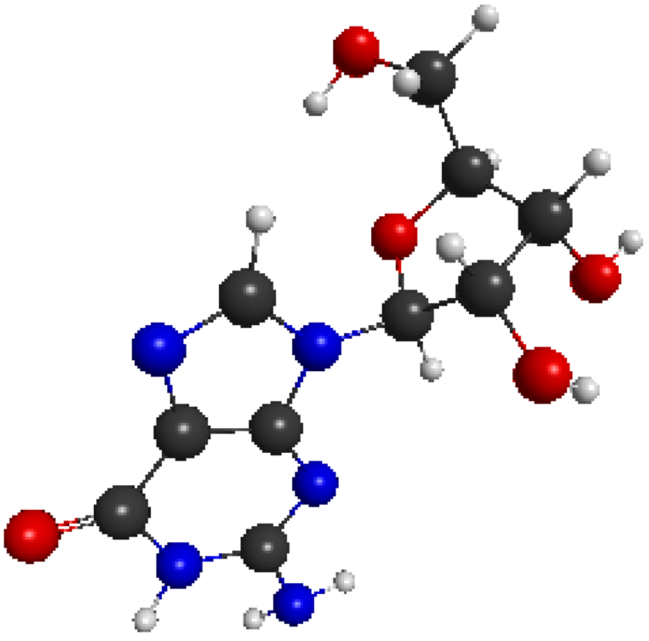

Figure 4. MP2/aug-cc-pVDZ optimized structure of guanosine.

Excitation energies of guanosine calculated at the frozen-core EOM-CCSD/aug-cc-pVDZ and EOM-CCSD(T)/aug-cc-pVDZ levels compared to the parent guanine are given in Table 4. The general conclusion is similar to that obtained for cytidine: energies of the Rydberg transitions grow the most, whereas $\pi\pi^*$ excitation energies decrease. On the other hand we find that the energy of the nπ^* transitions also decrease a little bit. As a consequence, unlike in the case of cytosine, we find changes in the ordering of the states. It is now the 1($\pi\pi^*$) transition that is the lowest in energy and also the 2(πR) transition gets shifted above the 2($\pi\pi^*$) and 1(nπ^*) transitions. We do not observe strong interaction between transitions except for the small intensity borrowing of the 1(nπ^*) transition from the 2($\pi\pi^*$) transition. Also, there is a considerable oscillator strength for 2(πR). These do not change the spectrum much because both of these states are close in energy to an intense band.

As of the triples effects, these again seem to be additive, the double difference being quite small (0.01–0.02 eV).

Guanine–Cytosine Watson–Crick Pair. In the structure of DNA the nucleobases are connected pairwise, these are the famous Watson–Crick pairs. The monomers are connected by hydrogen bonds and only specific pairs are possible. To investigate the effect of the neighboring bases on the excitation energy, in this paper we have chosen the guanine–cytosine (GC) pair.

The structure of the GC Watson–Crick pair has also been optimized at the MP2/aug-cc-pVDZ level. This structure is depicted in Figure 5, with the coordinates given in the Supporting Information. The excitation energies of the first twelve transitions have been obtained at the EOM-CCSD and EOM-CCSD(T) levels using aug-cc-pVDZ basis sets. Table 5 lists the results of these calculations and also compares to the corresponding transitions of the monomers.

Most of the transitions can be classified as excitations localized on either cytosine or guanine and these closely correspond to the transitions of the monomers. Thus, the lowest transition of the GC pair corresponds to 1($\pi\pi^*$) excitation in guanine, the second one to the same excitation in cytosine, etc. Except for the lowest transition of cytosine, the excitation energy of the $\pi\pi^*$ transitions decreases in the pair by 0.2–0.3 eV, whereas the former increases by 0.1 eV. Note that the same effect of the microhydration of cytosine has been observed above: for the largest cluster, i.e., five water molecules, where the same H-bond sites are occupied as in the GC pair, the energy of the 1($\pi\pi^*$) transition increased by 0.15 eV, whereas those of the other $\pi\pi^*$ transitions decreased by 0.2–0.3 eV. The important consequence of the exceptional behavior observed for the 1($\pi\pi^*$) transition of cytosine is that the first two transitions of the GC pair (corresponding to guanine and cytosine, respectively) are in opposite order than in the monomers.

Two nπ^* transitions could be identified in GC, one corresponding to an excitation on cytosine, the other on guanine. As in the case of microhydration, the excitation energy is much larger in the GC pair than in the monomers, an increase of up to 0.6 eV could be observed. Obviously, this can be explained by the involvement of those lone pairs in the hydrogen bonds that characterize these excitations in both cases. The changes of intensities of these dark states are negligible, even smaller than that observed for the micro-hydrated complexes and considerably smaller than in the nucleosides. One can explain this finding by noting that GC stays planar thus the nπ^* and $\pi\pi^*$ states cannot interact.

Much smaller effect of the dimerization is observed for the Rydberg transitions than in the case of microhydration. We do not have any qualitative explanation for this. Note in passing that the higher Rydberg transitions strongly couple and cannot be assigned clearly to monomer states anymore which is not surprising considering the large spatial extent of the Rydberg states.

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Table 4. Excitation Energies of the Lowest 12 Transitions of Guanine and Guanosine Calculated by EOM-CC Methods (Frozen-Core and aug-cc-pVDZ Basis)

transition		guanine			guanosine					
type	assignment	CCSD		CCSD(T)	CCSD		CCSD(T)	Δ_{CCSD}[a]	$\Delta_{CCSD(T)}$[a]	$\Delta\Delta$[b]
1(πR)	$\pi \rightarrow$ R	4.92	0.003	4.81	5.16	0.034	5.03	0.24	0.22	0.02
1($\pi\pi^*$)	$\pi \rightarrow \pi^*$	5.11	0.114	4.93	5.05	0.125	4.87	−0.06	−0.06	0.00
2(πR)	$\pi \rightarrow$ R	5.32	0.005	5.23	5.90	0.006	5.80	0.58	0.57	0.01
2($\pi\pi^*$)	$\pi \rightarrow 2\pi^*$	5.61	0.297	5.43	5.54	0.246	5.36	−0.07	−0.07	0.00
1(nπ^*)	$n_O \rightarrow \pi^*$	5.65	0.000	5.51	5.56	0.092	5.40	−0.09	−0.11	0.02
3(πR)	$\pi \rightarrow$ R	5.85	0.001	5.76	5.99	0.001	5.88	0.14	0.12	0.02
4(πR)	$\pi \rightarrow$ R	6.01	0.001	5.94	6.17	0.015	6.04	0.16	0.10	0.06
5(πR)	$\pi \rightarrow$ R	6.29	0.001	6.22	6.34	0.004	6.20	0.05	−0.02	0.07
6(πR)	$\pi \rightarrow$ R(π)	6.32	0.010	6.24	6.23	0.001	6.10	−0.09	−0.14	0.05
3($\pi\pi^*$)	$\pi \rightarrow 3\pi^*$	6.49	0.025	6.31	6.39[c]	0.033	6.22	−0.10	−0.09	−0.01
2(nπ^*)	$n_N \rightarrow 2\pi^*$	6.62	0.003	6.46	6.41	0.016	6.24	−0.21	−0.22	0.01
7(πR)	$\pi \rightarrow$ R	6.68	0.005	6.60	6.68	0.006	6.50	0.00	−0.10	0.10

[a]Relative excitation energy with respect to guanine. [b]Difference of the triples shift between monomer and hydrated molecule. [c]Includes strong Rydberg component.

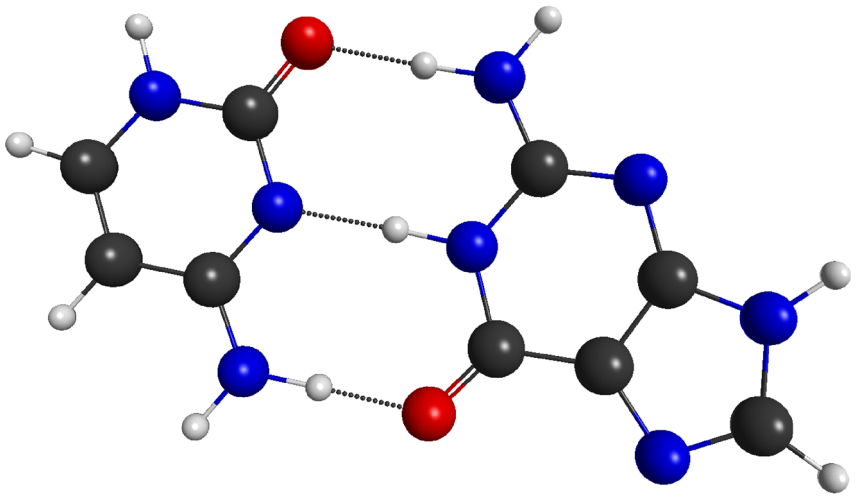

Figure 5. MP2/aug-cc-pVDZ optimized structure of guanine−cytosine Watson−Crick pair.

Table 5. Excitation Energies (eV) and Oscillator Strengths of the Lowest Transitions of Cytosine, Guanine, and Their Watson−Crick Pair Calculated by EOM-CC Methods (Frozen-Core and aug-cc-pVDZ Basis)

transition		CCSD						CCSD(T)		
type	assignment	cytosine		guanine		GC pair		monomers	GC pair	$\Delta\Delta$[b]
1($\pi\pi^*$)	$G\pi \rightarrow \pi^*$			5.11	0.114	4.89	0.077	4.93	4.67	0.04
2($\pi\pi^*$)	$C\pi \rightarrow \pi^*$	4.94	0.049			5.07	0.097	4.74	4.86	0.01
3($\pi\pi^*$)	$G\pi \rightarrow 2\pi^*$			5.61	0.297	5.45	0.447	5.43	5.27	0.00
4($\pi\pi^*$)	$C\pi_{-1} \rightarrow \pi^*$	5.86	0.142			5.55	0.174	5.62	5.30	0.01
1(nπ^*)	$Cn_N \rightarrow \pi^*$	5.46	0.002			5.79	0.002	5.25	5.57	0.01
2(nπ^*)	$Gn_O \rightarrow \pi^*$			5.65	0.000	5.91	0.000	5.51	5.73	0.04
1(πR)	$G\pi \rightarrow$ R			4.92	0.003	4.92	0.000	4.81	4.84	−0.03
2(πR)	$G\pi \rightarrow$ R			5.32	0.005	5.37	0.006	5.23	5.27	0.01
3(πR)	$G\pi \rightarrow$ R			5.85	0.001	5.66	0.003	5.76	5.55	0.02
4(πR)	$G\pi \rightarrow$ R			6.01	0.001	5.76[a]	0.000	5.94		
5(πR)	$C\pi \rightarrow$ R	5.56	0.004			5.86[a]	0.002	5.49	5.76	0.03
5($\pi\pi^*$)	CT $G \rightarrow C$					5.68	0.004		5.40	

[a]The natural orbitals corresponding to the hole have substantial contribution on both cytosine and guanine. [b]Difference of the shift due to triples between monomer and GC pair.

A charge-transfer (CT) transition could be identified at 5.68 eV, which can be characterized as an excitation from guanine's highest occupied π orbital to cytosine's lowest virtual π^* orbital. This assignment can be explained by the lower ionization energy of guanine than that of cytosine (see ref 39 and references therein). The CT transition is the fifth lowest

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valence transition of the GC pair in our calculations, and—although its transition moment is small—it is very close in energy to some bright states. Moreover, compared to the monomers' excitation energies, this transition is lower in energy than the 3($\pi\pi^*$) excitations of the monomers; it is therefore easily reachable. Thus, when charge transfer in a DNS chain is considered, besides charge transfer between stacked pairs, CT along Watson−Crick pairs needs also be considered. This will be investigated in future studies.

The absolute value of triples effects is the same as found for the monomers,[23] i.e., a decrease of 0.1−0.3 eV. This effect seems to be very systematic, the difference in monomers and the Watson−Crick pair does not exceed 0.04 eV. Note, however, that in this case an incremental procedure, like for the microhydrated systems, cannot be used because the effect for the CT states cannot be approximated from monomer calculations. The effect for the triple excitation is substantial, one of the largest (−0.28 eV).

Comparing to earlier calculations, we find serious discrepancy between our results and those in the literature. CASPT2 calculations by Sobolewski and Domcke[51] predict a $\pi\pi^*$ excitation on the guanine component as the lowest transition followed by the analogous transition on cytosine, whereas a CT transition was found as the third one. The excitation energies are, however, very low, all three states being below 5 eV. Note that in ref 51 the excitation energies of the free nucleobases seem also to be underestimated. Shukla and Leszczynski in their recent work[32] compared several density functionals in the TDDFT framework. All functionals, except the ones with long-range corrections give the CT state as the lowest, a clear artifact on the basis of our present results. The long-range corrected functionals give the CT transition as the third one, being very close in energy with the next $\pi\pi^*$ transitions. In this respect, this result is similar to ours. However, the $\pi\pi^*$ excitation energies are too high whereas that of the CT state is by 0.3 lower than CCSD(T) one. It was noticed by Shukla and Leszczynski[32] that the excitation energies of the individual nucleobases are much more reliable with B3LYP than with the long-range corrected functionals. Therefore, it seems that none of the functionals investigated in ref 32 is capable of describing base pairs. Finally, in ref 32 also the CC2 excitation energies are given. Again, CT is the third transition, following the first pair of $\pi\pi^*$ states. Interestingly, nπ^* excitation energies of the base pair are too high on the CC2 level in contrast to that we have observed for the individual bases.[23] Note also that, according to Table 5 of ref 32, the transitions obtained by the CC2 method can not be assigned uniquely to transitions of the monomers as in the case of the EOM-CC calculations.

CONCLUSIONS

We have applied high level ab initio methods, EOM-CCSD and EOM-CCSD(T) to calculate the vertical transition energies of nucleobases considering their biological environment, viz. hydration, glycoside bond, and base pairing.

Hydration was modeled by placing one to five water molecules around cytosine. It was found that the waters usually slightly lower the excitation energy of $\pi\pi^*$ transitions but increase it substantially in the case of nπ^* transitions. In the latter case, the position of the water is important and correlates with the excited lone pair characteristics for the given excitation. The largest increase was 0.73 eV for the 3(nπ^*) transition. Triples effects are also important, the magnitude being the same as that of the hydration. Therefore, to get the correct order of the excited states, inclusion of triples effects is absolutely necessary. Fortunately, the value of the triples correction is about the same as in free cytosine; therefore, the correction can be transferred from the free cytosine.

The glycoside bond seems to have only a minor effect on the transition energies. The change for valence states do not exceed 0.1 eV; a somewhat larger effect on the nR transition can, however, lead to change of the orders of excited states. Thus, for example, the lowest energy transition is 1(πR) in the case of guanine, but it is 1($\pi\pi^*$) in the case of guanosine at the EOM-CCSD(T) level. Triples effects can again be transferred from the free nucleobases.

Finally, we have found substantial effect on the transition energies due to base pairing. The states can nicely be classified as excitations on the monomers cytosine or guanine, and charge-transfer (CT) transition. An exciton-like mixed transition could be only observed for Rydberg transitions. Notably, the lowest transition of GC pair can be assigned to a $\pi\pi^*$ transition on the cytosine followed by one on guanine, which is the opposite order found in the case of the free nucleobases. The CT state is the eighth excited state (fifth $\pi\pi^*$ state, no nπ^* state is below it) but has only very low oscillator strength. Comparing with earlier calculations on CASSCF, CASPT2, and CC2 and different TDDFT levels, we could point out that none of these methods is able to reproduce the order of the transitions, nor the correct excitation energies.

This study will be extended by calculations of stacked pairs in the forthcoming paper where we will show that, there too, the high level calculations are necessary to get reliable results.

It is clear that EOM-CCSD or more so, EOM-CCSD(T) are too expensive to study larger fragments of DNA/RNA. Therefore, there is a need to obtain appropriate approximate method(s) and the results presented here can serve for benchmark to calibrate these lower level (cheaper) methods.

ASSOCIATED CONTENT

Supporting Information

Cartesian coordinates of cytosine, hydrated cytosine, cytidine, guanosine, the guanine−cytosine Watson−Crick pair, as well as energetics of the hydrated cytosine complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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