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QM/MM Nonadiabatic Decay Dynamics of 9H-Adenine in Aqueous Solution

Zhenggang Lan,^{*,[a]} You Lu,^[a] Eduardo Fabiano,^[b] and Walter Thiel^[a]

Dedicated to Professor Karl Kleinermanns on the occasion of his 60th birthday

The photoinduced nonadiabatic decay dynamics of 9H-adenine (hereafter, adenine) in aqueous solution were investigated by surface-hopping simulations within a quantum mechanical/molecular mechanical (QM/MM) framework. The QM subsystem (adenine) was treated at the semiempirical OM2/MRCI level, whereas the MM solvent (water) was described by the TIP3P force field model. Classical molecular dynamics (MD) simulations were used to generate snapshots with different solvent configurations and geometries. For a representative number of these snapshots, the energy minima of the lowest electronic

states and the most important conical intersections were located by QM/MM geometry optimization. Surface-hopping QM/MM MD simulations were performed for all selected snapshots to study the nonadiabatic dynamics after photoexcitation, including the two lowest excited singlet states, which are both populated in the initial photoexcitation due to strong vibronic coupling in the Franck–Condon region. The simulations yield ultrafast S_2 – S_1 decay within 40 fs and S_1 – S_0 internal conversion to the ground state within 410 fs, which is consistent with recent experimental results from time-resolved spectroscopy.

1. Introduction

In recent years, the nonadiabatic decay dynamics of 9H-adenine (hereafter, adenine) has been widely investigated because it represents the prototypical photoinduced process in DNA bases.^[1–5] The mechanism of the radiationless decay of isolated adenine in the gas phase is reasonably well understood.^[6–37] Experimentally, the excited-state lifetime of isolated adenine is extremely short.^[6–16,23] Time-resolved pump–probe experiments on gas-phase adenine indicated the existence of two decay components with different timescales (less than 200 fs and less than 1 ps).^[10–14,16] In theoretical studies, several conical intersections ($\pi\pi^*/n\pi^*$, $\pi\pi^*/\pi\sigma^*$, $n\pi^*/gs$, $\pi\pi^*/gs$, $\pi\sigma^*/gs$) were located that are relevant for the nonadiabatic decay of adenine.^[17–36] Minimum-energy reaction paths connecting the Franck–Condon (FC) region and different conical intersections were constructed to explore possible radiationless decay pathways.^[18–22,24–31,35,36] Furthermore, direct on-the-fly dynamic simulations were performed^[32–34,37] to assess the relative importance of different decay channels and to compare the corresponding decay times with those measured in time-resolved pump–probe experiments. On the basis of this work, it was possible to identify three main decay paths in gas-phase adenine. For excitation energies close to the center of the main absorption band (≈ 250 nm), there are two competing mechanisms that involve two distinctly different conical intersections, namely, $\pi\pi^* \rightarrow gs$ ^[19–22,26,28,29,32,34–36] and $\pi\pi^* \rightarrow n\pi^* \rightarrow gs$.^[10–14,19,20,24,25,30,33,34,36] According to our previous semiempirical OM2/MRCI surface-hopping study on gas-phase adenine, the $\pi\pi^* \rightarrow n\pi^*$ and partially also the $\pi\pi^* \rightarrow gs$ channels are responsible for the ultrafast decay component, whereas the $n\pi^* \rightarrow gs$ decay mainly contributes to the slower sub-picosecond decay.^[33] At different excitation energies (< 233 nm and ≈ 267 nm) there is also a $\pi\pi^* \rightarrow \pi\sigma^* \rightarrow gs$ channel,^[15,18,21,23,35,36]

which is accessed through a Rydberg-type $\pi\sigma^*$ excitation and leads to hydrogen dissociation.

Compared with detailed knowledge about radiationless decay dynamics in the gas phase, the photophysical behavior of adenine in solution or in a DNA environment is much less understood. Experimentally, the excited-state lifetime of adenine in solution was found to be even shorter than in the gas phase, with published values ranging from 180 to 670 fs.^[38–46] In these experimental studies, it was difficult to identify the dominant decay mechanisms or details of the dynamics. On the theoretical side, vertical excitation energies and conical intersections between low-lying electronic states were computed by using continuum solvation models^[47] and the reference interaction site model self-consistent field method.^[48] A sequential Monte Carlo/CASPT2 study on the photophysics of adenine in aqueous solution addressed the solvent effects on gas-phase minimum-energy paths in the two lowest excited states by using the simple point charge (SPC) model to describe the surrounding water molecules.^[49]

The simulation of the nonadiabatic dynamics in the condensed phase is a challenging task because of the need to realistically describe both the electronic structure of all relevant excited states under the influence of the environment and the

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dynamics of the entire system, including the environment. This will generally require an explicit representation of the environment. Continuum models, such as the polarizable continuum model (PCM)^[50–54] and the conductor-like screening model (COSMO)^[55,56] are expected to be less suitable, even in the seemingly isotropic case of a solvated molecule, since nonadiabatic transitions between different electronic states may cause ultrafast changes in the electronic density of the solute molecule, which in turn may trigger a strong anisotropic perturbation of the solvent. The resulting reorganization of the solvent may have a non-negligible influence on the time evolution of the system. Hybrid QM/MM schemes^[57,58] provide a convenient way to combine an accurate quantum description of the solute with an explicit and efficient atomistic model of the solvent environment at the force field level. In recent years, the QM/MM approach has been successfully used in combination with surface-hopping methods to study nonadiabatic dynamics in condensed-phase systems, both in solution and in biological environments.^[48,59–69] A purely QM surface-hopping simulation has recently been reported for microsolvated adenine, taking into account the first solvation shell (26 water molecules) and treating the entire system by the time-dependent density functional tight-binding (TD-DFTB) method.^[70]

Herein, we study the nonadiabatic dynamics of adenine in aqueous solution by surface-hopping QM/MM simulations. The electronic structure in the ground state and the excited states of adenine is described quantum mechanically by using the OM2/GUGA-Cl approach,^[71–75] while the solvent water molecules are represented by a classical force field model. The OM2/GUGA-Cl method provides a good compromise between computational cost and accuracy. It has been applied successfully in recent investigations of the gas-phase relaxation dynamics of isolated DNA bases.^[33,76,77] Herein, we characterize the relevant potential-energy surfaces and report the results of surface-hopping simulations for adenine in water. We analyze the effects of solvation on the photoinduced nonadiabatic dynamics of adenine, by comparing the results in the gas phase and in aqueous solution, and we also comment on accuracy issues.

Computational Details

A model of adenine in aqueous solution was constructed by placing adenine (Figure 1) at the center of a pre-optimized TIP3P water sphere^[78] with a radius of 37 Å.

The system was then relaxed and equilibrated by running classical molecular dynamics (MD) simulations with a quartic boundary potential using the CHARMM program.^[79] Thereafter, all water molecules beyond a cutoff radius of 20 Å were deleted. The resulting structure was the starting point for a ground-state Born–Oppenheimer QM/MM MD simulation, during which all water molecules further than 16 Å from the center were kept fixed. A sample of 200 snapshots was extracted from this MD run to provide starting geometries for subsequent QM/MM excited-state calculations and surface-hopping dynamics.

Hybrid QM/MM calculations employed the development version of the ChemShell package^[80,81] by using a specifically adapted inter-

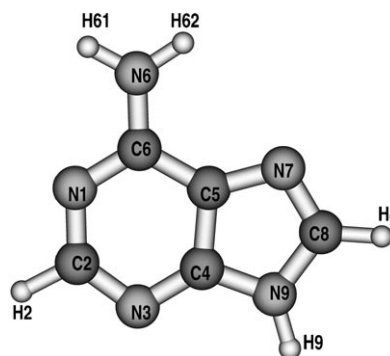


Figure 1. Molecular structure and atom numbering of 9H-adenine.

face to the MNDO code.^[82] The QM part (adenine) was described by the semiempirical orthogonalization model 2 (OM2) Hamiltonian^[71,72] using the restricted open-shell Hartree–Fock (ROHF) formalism in the self-consistent field (SCF) procedure. Excited states were calculated at the multireference configuration interaction (MRCI) level in the graphical unitary group approach (GUGA) formalism, with analytical evaluation of the OM2/MRCI gradients and nonadiabatic couplings.^[73–75] The active CI space consisted of 12 electrons in 10 orbitals, that is, the six highest occupied orbitals and the four lowest unoccupied orbitals. The MRCI treatment employed four reference configurations corresponding to the leading configurations of the four lowest singlet states of adenine: gs (closed-shell ground state), $n\pi^*$ ($n \rightarrow \pi^*$), L_a (HOMO–LUMO $\pi \rightarrow \pi^*$), and L_b ($\pi \rightarrow \pi^*$).^[18–22,27,28,31,33] The present OM2/MRCI calculations were thus carried out in exactly the same manner as in our previous study on gas-phase adenine.^[33] The MM part (solvent) was described by using the TIP3P water model.^[78] An electrostatic embedding approach was adopted to model the interactions between adenine and water: the MM charges were incorporated into the one-electron part of the QM Hamiltonian and the QM/MM electrostatic interactions were evaluated from the QM electrostatic potential and the MM partial charges. It should be noted that water is unpolarizable in the fixed-charge TIP3P representation and that dynamic solvent effects due to fast electronic rearrangements in the solvent molecules can thus not be captured in this model.

Geometry optimizations of energy minima and conical intersections were performed with the DL-FIND optimizer^[83] in ChemShell, using the Newton–Raphson and Lagrange–Newton algorithms, respectively. For an isolated gas-phase adenine molecule, the corresponding optimized geometries are well-defined and unique. In contrast, for adenine in aqueous solution, there are many of such geometries for each energy minimum or conical intersection because the solvent environment can adopt many different configurations. To investigate the influence of different solvent arrangements and to assess the fluctuations caused by different solvent configurations, geometry optimizations were carried out for a number of snapshots taken from the initial ground-state QM/MM MD run (see above). The following procedure was adopted: 1) 20 different snapshots were optimized to locate their S_0 ground-state minima. At each optimized geometry, the vertical excitation energies of the low-lying excited states were calculated. Thereafter, the average vertical excitation energy was determined for each state. 2) Starting from these optimized S_0 geometries, geometry optimizations were carried out for the S_1 minimum, the S_2 minimum, and the S_1 – S_2 conical intersection, assuming that these species can be reached directly from the FC geometry. 3) The S_0 – S_1 conical intersections were not accessible in this manner. They could be located,

however, by optimizations that started from the corresponding hopping geometries encountered during excited-state dynamics (see below). 4) The resulting geometries of the two S_0 – S_1 conical intersections were taken as the starting points for optimizations on the S_0 ground-state surface. These optimizations always led to the respective initial S_0 minimum and thus established a one-to-one correspondence for a given snapshot.

The surface-hopping MD method^[84–86] was implemented in a development version of the ChemShell package. This involved the integration of the surface-hopping dynamics module into the QM/MM framework and the adaptation of the ChemShell–MNDO interface. The present QM/MM implementation is analogous to the original MNDO implementation,^[86] with a few additional features: parts of the system can now be kept fixed during excited-state dynamics (to allow for a frozen outer solvent shell), and the nonadiabatic coupling terms can also be computed in the presence of the MM charges. For QM/MM simulations of the nonadiabatic dynamics of adenine in water, the nuclear degrees of freedom were propagated on classical trajectories for 1.2 ps with a time step of 0.2 fs, by using the velocity Verlet algorithm. The time evolution of the quantum amplitudes along these trajectories was calculated by using a unitary propagator and a time step 200 times smaller. The fewest switching algorithm^[85] was employed to compute the hopping probabilities. All simulations were performed in the adiabatic representation and final results were obtained by averaging over 90 trajectories. The selection of initial configurations was guided by the concept of obtaining an adequate approximate sampling of the center of the absorption band,^[87] which was achieved by applying the same procedure as in our previous gas-phase study of adenine,^[33] with the number of trajectories starting from a given snapshot and excited state determined from the corresponding oscillator strength. Further technical details about the surface-hopping calculations are documented in references [86] and [87].

2. Results

2.1. Potential Energy Surfaces

For adenine in water, the ground-state minimizations at the OM2/MRCI level led to snapshot geometries with planar aromatic rings and a slight pyrimidization of the amino group, see Figure 2, similar to that found at the *ab initio* level.^[47,48]

Table 1 lists OM2/MRCI results obtained at 10 such optimized snapshot geometries, for the vertical excitation energies, the oscillator strengths, and the weights of the leading configurations in the corresponding CI wavefunctions. The vertical excitation energies of the three lowest singlet excited states, S_1 , S_2 , and S_3 , lie between 4.45–4.69, 4.67–4.90, and 4.86–4.95 eV, respectively, and thus vary over a range of about 0.1–0.2 eV. In 9 out of 10 cases, the S_1 state is separated from the S_2 state by 0.22–0.32 eV, while the S_2 and S_3 states lie within 0.1 eV.

Given these small energy gaps, one may expect heavy mixing between the leading configurations and a strong variation of this mixing between different snapshots, which is indeed confirmed by inspection of the CI wavefunctions (see Table 1). In the first excited state (S_1), the $\pi\pi^*$ (HOMO–LUMO, L_a) configuration contributes most in 7 out of 10 cases, with weights in the CI wavefunction that are typically around 50% and always above 30%, while the contributions from the $\pi\pi^*$

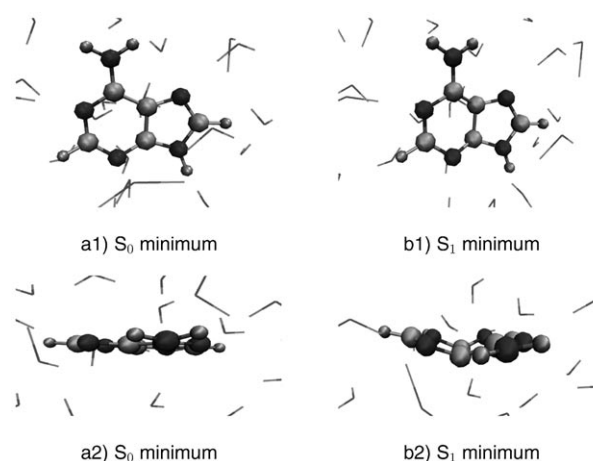


Figure 2. Typical molecular geometries of adenine in water at the a) S_0 and b) S_1 minima. Upper panel: top view; lower panel: side view.

(L_b) configuration are always smaller (but not negligible) and those from the $n\pi^*$ configuration vary substantially between different snapshots (highest in 3 cases, lowest in 6 cases). The $n\pi^*$ excitation dominates the second excited state (S_2) in 4 snapshots and the third excited state (S_3) in 3 snapshots, with weights of more than 50%, whereas these states are mostly of mixed L_a and L_b $\pi\pi^*$ character in the other cases. The $\pi\pi^*$ excitation to the L_a configuration carries most of the oscillator strength, and therefore, the transitions to S_1 and to either S_2 or S_3 are computed to be reasonably intense in the individual snapshots. In an overall assessment of the data in Table 1, it is clear that the lowest three singlet excited states of adenine in water are closely spaced and that their electronic character thus depends strongly on the solvent configuration at each individually optimized snapshot geometry. Hence, sampling over snapshots appears to be necessary to account for solvent fluctuations and to arrive at realistic theoretical predictions.

Experimentally, the absorption band maximum of adenine in aqueous solution is located at 4.77 eV (260 nm) compared with 4.92 eV (252 nm) in the gas phase,^[88,89] which corresponds to a redshift of 0.15 eV (8 nm). According to OM2/MRCI, the vertical excitation energies of gas-phase adenine are 4.58, 4.66, and 4.97 eV for the $n\pi^*$, L_a , and L_b states, respectively, with most of the oscillator strength being carried by the L_a transition.^[33] Although there is much mixing in the excited states of adenine in water (see above), the most pronounced L_a character is found in the S_1 state, which is on average redshifted by about 0.1 eV relative to the gas phase (see Table 1), in qualitative agreement with experiment. By the same token, the $n\pi^*$ transition is blueshifted by about 0.1–0.3 eV, whereas the changes for the L_b transition are small. For a more direct comparison with experiment, we have simulated the first absorption band of adenine in the gas phase (QM) and in aqueous solution (QM/MM) by selecting 200 snapshots from ground-state MD runs at 300 K and performing single-point OM2/MRCI calculations for the excitation energies and oscillator strengths of the three lowest singlet excited states, which were then used to generate theoretical spectra following established proce-

Table 1. Adenine in water: vertical excitation energies [eV], oscillator strengths, and weights [%] of the leading configurations in the OM2/MRCI wavefunctions of the lowest three singlet excited states for 10 selected snapshots, with oscillator strengths given in parentheses and weights in square brackets.

Snapshot	Excitation	S_1	S_2	S_3
1	$n \rightarrow \pi^*$	4.69 (0.099)	4.77 (0.057)	4.86 (0.157)
	$\pi \rightarrow \pi^* (L_a)$	[34]	[50]	[<1]
	$\pi \rightarrow \pi^* (L_b)$	[30]	[14]	[37]
2	$n \rightarrow \pi^*$	4.56 (0.102)	4.88 (0.055)	4.91 (0.165)
	$\pi \rightarrow \pi^* (L_a)$	[41]	[1]	[37]
	$\pi \rightarrow \pi^* (L_b)$	[37]	[11]	[32]
3	$n \rightarrow \pi^*$	4.58 (0.177)	4.90 (0.165)	4.91 (0.010)
	$\pi \rightarrow \pi^* (L_a)$	[8]	[52]	[22]
	$\pi \rightarrow \pi^* (L_b)$	[49]	[32]	[<1]
4	$n \rightarrow \pi^*$	4.58 (0.178)	4.89 (0.142)	4.91 (0.032)
	$\pi \rightarrow \pi^* (L_a)$	[26]	[38]	[2]
	$\pi \rightarrow \pi^* (L_b)$	[24]	[40]	[<1]
5	$n \rightarrow \pi^*$	4.57 (0.193)	4.87 (0.031)	4.92 (0.142)
	$\pi \rightarrow \pi^* (L_a)$	[8]	[71]	[<1]
	$\pi \rightarrow \pi^* (L_b)$	[50]	[5]	[26]
6	$n \rightarrow \pi^*$	4.61 (0.161)	4.89 (0.164)	4.95 (0.021)
	$\pi \rightarrow \pi^* (L_a)$	[24]	[<1]	[41]
	$\pi \rightarrow \pi^* (L_b)$	[1]	[18]	[62]
7	$n \rightarrow \pi^*$	4.64 (0.079)	4.79 (0.083)	4.89 (0.160)
	$\pi \rightarrow \pi^* (L_a)$	[44]	[34]	[4]
	$\pi \rightarrow \pi^* (L_b)$	[32]	[30]	[6]
8	$n \rightarrow \pi^*$	4.54 (0.164)	4.81 (0.020)	4.89 (0.178)
	$\pi \rightarrow \pi^* (L_a)$	[59]	[16]	[14]
	$\pi \rightarrow \pi^* (L_b)$	[28]	[18]	[36]
9	$n \rightarrow \pi^*$	4.45 (0.236)	4.67 (0.008)	4.89 (0.137)
	$\pi \rightarrow \pi^* (L_a)$	[1]	[34]	[23]
	$\pi \rightarrow \pi^* (L_b)$	[18]	[22]	[25]
10	$n \rightarrow \pi^*$	4.56 (0.189)	4.88 (0.082)	4.89 (0.088)
	$\pi \rightarrow \pi^* (L_a)$	[2]	[85]	[<1]
	$\pi \rightarrow \pi^* (L_b)$	[56]	[22]	[22]
	$n \rightarrow \pi^*$	4.56 (0.189)	4.88 (0.082)	4.89 (0.088)
	$\pi \rightarrow \pi^* (L_a)$	[8]	[64]	[5]
	$\pi \rightarrow \pi^* (L_b)$	[50]	[15]	[17]
	$n \rightarrow \pi^*$	4.56 (0.189)	4.88 (0.082)	4.89 (0.088)
	$\pi \rightarrow \pi^* (L_a)$	[25]	[4]	[35]
	$\pi \rightarrow \pi^* (L_b)$	[25]	[4]	[35]

dures.^[90] This yields band maxima of 4.73 and 4.67 eV in the gas phase and in aqueous solution, that is, 0.19 and 0.10 eV below the experimental values, respectively. The computed redshift of 0.06 eV is in the right direction, but smaller than that observed experimentally (0.15 eV, see above).

A detailed comparison of the present results with previous ab initio calculations^[47,48] is not possible because the latter disregarded the fluctuations arising from different solvent configurations. However, concerning the ordering of the excited states, there is qualitative agreement: the ab initio calculations also predicted that the $n\pi^*$ state is the lowest excited singlet state of adenine in the gas phase, but not in water where it is above at least one of the $\pi\pi^*$ states.^[47,48]

Geometry optimizations on the S_1 surface were attempted for all 20 snapshots that had been optimized in the ground state. Starting from the corresponding S_0 minima, these opti-

mizations reached an excited-state minimum in five cases (25%). These minima are characterized by moderate ring distortions and out-of-plane displacements of the C4 and C5 atoms (for a typical example see Figure 2, right panel). Compared with the ground state, the C2–N3 and C5–C6 bonds are lengthened by around 0.03 and 0.06 Å, whereas the N3–C4 and C5–N7 bonds are shortened by around 0.01 and 0.04 Å, respectively, in agreement with ab initio results.^[47] These minima lie 3.6–4.2 eV above the corresponding S_0 minima and 2.2–2.4 eV above the S_0 ground-state energy at these geometries (see Table 2). The computed oscillator strengths for emis-

Table 2. Adenine in water: relative energies [eV] of the lowest singlet states at the optimized geometry of the S_1 minimum, for the snapshots where this minimum could be located (see text). For a given snapshot, the energy of the corresponding S_0 minimum is set to zero.

	Snapshot				
	1	2	3	4	5
S_0	1.93	1.48	1.40	1.46	1.34
S_1	4.18	3.68	3.60	3.87	3.77
S_2	5.49	4.93	4.86	4.97	4.75
S_3	5.56	5.09	5.21	5.33	5.25

sion are rather low (between 0.026 and 0.031), so that these S_1 minima are best viewed as dark $n\pi^*$ states. In previous ab initio CASSCF calculations for adenine in water, the lowest $n\pi^*$ minimum was found 4.31 eV above the S_0 minimum.^[48] The remaining OM2/MRCI optimizations on the S_1 surface (15 cases, 75%) led to a S_0 – S_1 conical intersection with a strong out-of-plane distortion of the amino group (see below).

It was not possible to locate any S_2 minimum by geometry optimizations on the S_2 surface. Starting from the available S_0 minima, all optimizations ended up at an S_1 – S_2 conical intersection (CI₁₂) very close to the FC region that is characterized by small ring distortions and a slight pyramidalization of the amino group (for a typical example, see Figure 3, left panel). It lies at 4.47–5.17 eV (see Table 3) and has $n\pi^*/L_a$ character. At

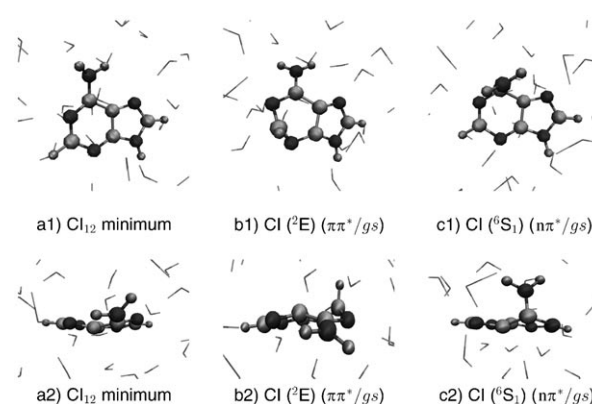


Figure 3. Typical molecular geometries of adenine in water at the a) CI₁₂, b) 2E , and c) 6S_1 conical intersections. Upper panel: top view; lower panel: side view.

Table 3. Adenine in water: relative energies [eV] of the Cl_{12} conical intersection for five selected snapshots. In each case, the energy of the corresponding S_0 minimum is set to zero.

	Snapshot				
	1	2	3	4	5
energy [eV]	4.93	4.47	4.89	4.57	5.17

the OM2/MRCI level, there is another S_1 – S_2 conical intersection with L_a/L_b character and small out-of-plane distortions (at C4, C5, and H2), similar to the one identified in a CASSCF study of adenine in water,^[48] however, this conical intersection plays no role in the deexcitation dynamics (see below).

Consistent with previous ab initio studies,^[48] two S_0 – S_1 conical intersections could be located for each of the snapshots. The first one is of L_a /gs character and lies 3.95–4.33 eV above the corresponding S_0 minimum (and hence in each case below the lowest vertical excitation energy at the S_0 minimum). The optimized geometries of this conical intersection are quite similar in all five snapshots. There is a moderate out-of-plane displacement of the C4 and C5 atoms, a small pyramidalization of the amino group, and a strong out-of-plane displacement of the C2 and H2 atoms: the C2–H2 bond is almost perpendicular to the ring, with dihedral angles $|\chi(N1C2N3C4)|$ ranging from 77.9 to 80.7° and $|\chi(H2C2N3C4)|$ from 81.5 to 85.9° (see Figure 3 central panel and Table 4). This type of conical intersection has been assigned^[32] as 2E for adenine in the gas phase according to the Cremer–Pople–Boeyens classification.^[91,92]

Table 4. Adenine in water: relative energies [eV] and characteristic internal coordinates of the 2E conical intersection for 5 selected snapshots. In each case, the energy of the corresponding S_0 minimum is set to zero.

	Snapshot				
	1	2	3	4	5
energy [eV]	4.33	3.95	4.11	3.96	4.12
$\chi(H2-C2-C5)$ [°]	109.6	107.7	106.6	106.2	106.5
$\chi(H2-C2-N3-C4)$ [°]	84.1	81.5	–85.9	82.1	83.1
$\chi(N1-C2-N3-C4)$ [°]	–80.7	–80.1	77.9	–79.1	–78.4

The second S_0 – S_1 conical intersection is labeled as 6S_1 .^[32] It is characterized in all snapshots by a pronounced out-of-plane distortion of the C6 atom and the amino group, such that the C6–N6 bond is almost perpendicular to the ring, with dihedral angles $|\chi(N1C5C6N6)|$ between 123.8 and 129.3° and $|\chi(C2N1C6N6)|$ between 73.6 and 81.8° (see Figure 3 right panel and Table 5). The OM2/MRCI wavefunction indicates strong configurational mixing at this 6S_1 conical intersection, but it is still possible to assign a predominant $n\pi^*$ /gs character. The 6S_1 energy varies rather strongly (3.38–4.33 eV relative to the ground-state energy of the respective snapshot, see Table 5) such that it lies above the 2E energy in two cases, and below in three cases (see Table 4).

Generally speaking, the types and geometries found for the conical intersections of adenine in water are quite similar to

Table 5. Adenine in water: relative energies [eV] and characteristic internal coordinates of the 6S_1 conical intersection for 5 selected snapshots. In each case, the energy of the corresponding S_0 minimum is set to zero.

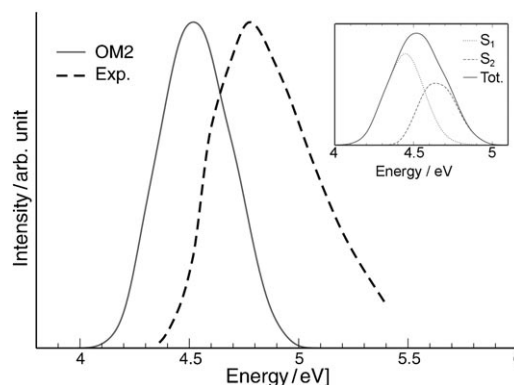
	Snapshot				
	1	2	3	4	5
energy [eV]	4.28	4.26	4.33	3.73	3.38
$\chi(N3-C6-N6)$ [°]	103.4	100.6	101.3	99.0	100.5
$\chi(C2-N1-C6-N6)$ [°]	–81.8	75.1	–78.3	–73.6	75.9
$\chi(N1-C5-C6-N6)$ [°]	125.7	–129.3	127.7	126.1	–123.8

those in the gas phase. This is true not only for comparisons with OM2/MRCI gas-phase results,^[33] but also with regard to ab initio studies.^[19–22,24–28,31,32] The qualitative topology of the computed potential-energy surfaces thus seems to be rather robust when going from the gas phase to aqueous solution. On the other hand, the OM2/MRCI relative energies show larger variations that indicate a significant influence of the solvent environment. One common feature for all five snapshots is that the energies of the 2E and 6S_1 conical intersections are always below the lowest vertical excitation energy at the S_0 minimum. It is thus energetically possible that they can be quickly reached after vertical excitation, provided that a direct downhill path exists. The geometry optimizations on the S_1 potential-energy surface indicate that this is indeed the case, since they directly accessed the 6S_1 conical intersection for most of the snapshots (75%).

2.2. Nonadiabatic Dynamics

The selection of the initial configurations for the surface-hopping trajectories was governed by the idea to simulate photoexcitation near the center of the absorption band of solvated adenine (263 nm). The resulting simulated absorption band is shown in Figure 4 and compared with the experimental spectrum.^[42]

Apart from a redshift of 0.25 eV, the curve calculated at the OM2/MRCI level agrees very well with the experimental one, indicating that the sampling procedure was adequate. The OM2/MRCI calculations show that the absorption band con-

**Figure 4.** Simulated and experimental absorption bands of solvated adenine. The inset shows the contributions of the S_1 and S_2 states to the total absorption band. The experimental data are taken from reference [42].

tains significant contributions from both the S_1 and S_2 states (see inset of Figure 4), which are close in energy and show significant configurational mixing in the FC region. Consequently, initial sampling yields 51 trajectories (57%) starting on the S_1 potential-energy surface and 39 (43%) starting on the S_2 potential-energy surface.

The average occupation of the adiabatic states as a function of time is illustrated in Figure 5. In the early stage of the dynamics, the strong electronic mixing causes an ultrafast $S_2 \rightarrow S_1$

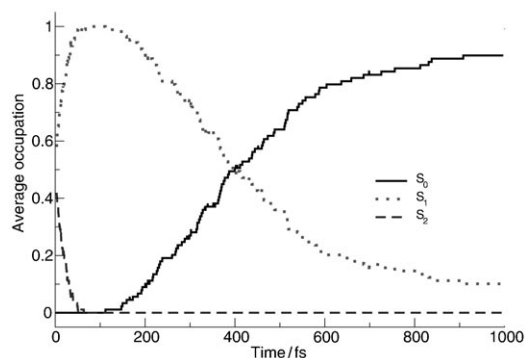


Figure 5. Time-dependent average occupation of the low-lying adiabatic states of solvated adenine.

population transfer with a time constant of 40 fs. After 80 fs, no more trajectories are evolving on the S_2 potential-energy surface and the average occupation of the S_1 state reaches its maximum. After around 100 fs, the decay of the S_1 population starts and internal conversion to the S_0 state occurs with a time constant of 410 fs.

Because of the strongly mixed character of the electronic states involved in the nonadiabatic dynamics of solvated adenine, it is difficult to make clear assignments of these processes within the adiabatic representation used in the simulations. Nevertheless, some information about the character of these states and the different decay paths followed can be inferred from an analysis of the S_0 – S_1 conical intersections that are accessed during the decay dynamics. These intersections, 2E (L_a /gs) and 6S_1 ($n\pi^*$ /gs), are characterized by strong ring puckering at the atoms C2 and C6, which induces large out-of-plane displacements of the H2 atom and the amino group, respectively. They can be easily identified by monitoring the dihedral angles $|\chi(N1C2N3C4)|$ and $|\chi(N1C5C6N6)|$. The values of these two dihedral angles at the hopping points are shown in Figure 6 for all trajectories computed in the gas phase^[33] and in water.

It is evident from Figure 6 that there are two distinct decay paths. The vast majority of the trajectories (95%) decay to the ground state through the 6S_1 conical intersection, indicating that the S_1 state acquires a predominant $n\pi^*$ character far from the FC (and Cl_{12}) region. In a few trajectories (5%), the S_1 state is apparently of $\pi\pi^*$ character and decays via the 2E conical intersection. We also note that the decay route of a trajectory is independent of whether it started in the S_1 or S_2 state, suggesting that the system leaves the FC (and Cl_{12}) region

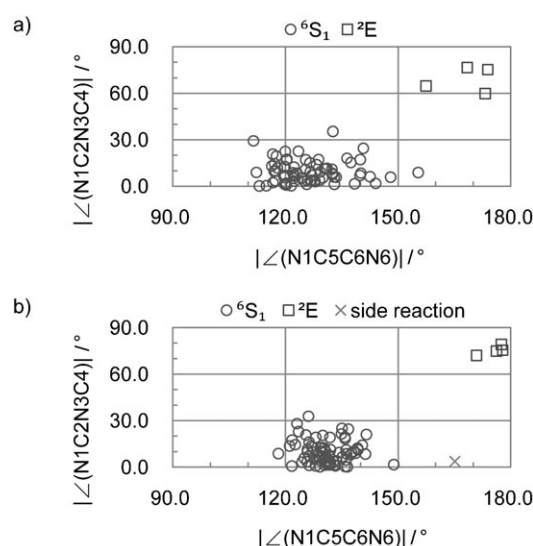


Figure 6. Dihedral angles $|\chi(N1C5C6N6)|$ and $|\chi(N1C2N3C4)|$ that characterize the 2E and 6S_1 conical intersections at the $S_1 \rightarrow S_2$ hopping events: a) adenine in vacuo;^[33] b) adenine in water (this work).

with no memory of its previous dynamics, which is lost because of the strong nonadiabatic interactions. A similar observation was also made for adenine and aminopyrimidine in the gas phase.^[33,93]

Simulation of the nonadiabatic dynamics of solvated adenine yields two decay constants, corresponding to the ultrafast decay of the S_2 state (40 fs) and to the slower decay of the S_1 state (410 fs). The ultrafast decay reflects the strong nonadiabatic coupling experienced by the excited states in the FC region. The S_1 decay time results from two distinct relaxation paths. The main contribution comes from trajectories passing through the 6S_1 conical intersection, where hopping occurs from 200 to 600 fs after the beginning of the dynamics. The overall decay time is then slightly reduced by a small contribution from the trajectories that return to the ground state via the 2E conical intersection within 180 fs.

The present QM(OM2/MRCI)/MM surface-hopping results for solvated adenine (1111 MM water molecules) are qualitatively consistent with the QM(TD-DFTB) surface-hopping simulations for microsolvated adenine (16 QM water molecules), which also gives a two-step nonradiative decay involving the ultrafast relaxation of the initially excited S_2 state with a lifetime of 16 fs and the subsequent transition to the ground state within 200 fs.^[70]

A direct comparison of the experimentally measured decay times with those obtained from our simulations is not straightforward because the surface-hopping calculations have been performed in the adiabatic representation, whereas experiments essentially probe the global decay behavior. Nevertheless, we note that the computed decay time for the S_1 state is consistent with available experimental data.^[38–44,46] It compares particularly well with the decay constant obtained from recent fluorescence up-conversion experiments, which led to a lifetime of 300–500 fs for excitations around the center of the absorption band of solvated adenine.^[44] Experimental time con-

stants have not yet been reported for the ultrafast decay of the S_2 state (computed: $\tau \approx 40$ fs).

3. Discussion

3.1. Solvent Effects

In this section, we compare the present results for adenine in water with those obtained previously in the gas phase.^[33] The optimized ground-state geometry of adenine is completely planar in the gas phase, whereas there is a slight pyramidalization of the amino group in water. For the computed vertical excitation energies, solvation causes a redshift of about 0.1 eV for the $\pi\pi^*$ L_a state and a blueshift of 0.1–0.3 eV for the $n\pi^*$ state, in good agreement with CASSCF calculations^[48] and experimental data.^[88,89] As a consequence of these shifts, the two lowest excited states of solvated adenine are strongly mixed in the FC region, so that two transitions contribute to the absorption band (see inset of Figure 4). This is in contrast to the gas phase where the absorption band is essentially due to excitations into the S_2 ($\pi\pi^*$ L_a) state, according to the OM2/MRCI calculations.^[33]

In our standard procedure, excited-state geometry optimizations start from an optimized ground-state structure. In the gas phase, this leads to an S_1 ($n\pi^*$) minimum of adenine with rather small ring distortions.^[33] In water, the optimizations on the S_1 surface either directly reach the 6S_1 conical intersection (see above) or yield an S_1 minimum with notable ring distortions at the C4 and C5 atoms. On the other hand, an S_2 minimum cannot be located in this manner, neither in the gas phase nor in water, because geometry optimizations always directly lead to an S_1 – S_2 conical intersection of $n\pi^*/L_a$ character. Finally, there are two S_0 – S_1 conical intersections, namely, 2E and 6S_1 , that connect the ground state with the L_a and $n\pi^*$ states, respectively; these are found both in the gas phase and in water, with very similar structures.

As already mentioned, the OM2/MRCI electronic structure of the two lowest excited states of adenine is different in the gas phase and in aqueous solution, which might also suggest different nonadiabatic dynamics. According to the gas-phase OM2/MRCI results, the initial excitation populates almost exclusively the bright S_2 ($\pi\pi^*$) state and the deexcitation proceeds mainly through a two-step $\pi\pi^* \rightarrow n\pi^* \rightarrow \text{gs}$ pathway. In water, due to strong mixing, the bright L_a transition populates both the S_1 and S_2 states with almost the same probability; the 2E and 6S_1 conical intersections lie close to each other energetically and one might thus expect that these two decay paths are of similar importance. However, the OM2/MRCI surface-hopping simulations show that this is not the case: the deexcitation dynamics in solution is similar to that in the gas phase, since the $\pi\pi^* \rightarrow n\pi^* \rightarrow \text{gs}$ decay path is again clearly favored, even more so than in the gas phase.

This can be attributed to the topology of the S_1 surface of adenine in water: inside the FC region, the N6 atom normally has a larger S_1 gradient component perpendicular to the ring than H2, as can be seen from the norm of these gradient components plotted in Figure 7 for all trajectories. The S_1 gradient

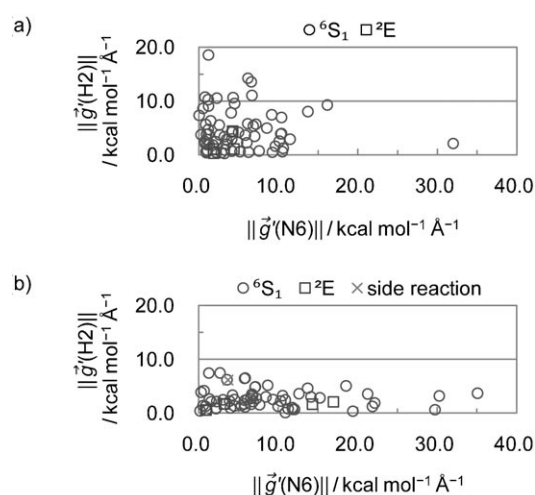


Figure 7. Norms of S_1 gradient components perpendicular to the (N1C5C6) and (N1C2N3) planes ($\|\vec{g}'\|$) at atoms N6 and H2, respectively, evaluated for each trajectory at the initial FC geometry. a) Adenine in vacuo (ref. [33]) and b) adenine in water (this work).

thus drives adenine towards geometries with an out-of-plane amino group, rather than H2, with diminishing $\pi\pi^*$ and increasing $n\pi^*$ character. As a consequence, the approach to the 6S_1 ($n\pi^*/\text{gs}$) conical intersection with an out-of-plane amino group is dynamically favored over the out-of-plane motion of the H2 atom that would lead to the 2E ($\pi\pi^*/\text{gs}$) conical intersection. When comparing with the situation in the gas phase (see Figure 7a) it is clear that, in the FC region, adenine has a larger out-of-plane gradient norm at N6 in water and hence a more pronounced tendency for the out-of-plane motion of the amino group towards the dominant 6S_1 ($n\pi^*/\text{gs}$) conical intersection. This explains the somewhat faster decay dynamics of adenine in water than in the gas phase. Furthermore, in the FC region, the S_1 gradient at N6 in water generally points towards the side of adenine with the most favorable hydrogen-bonding interactions between N6 and nearby solvent water molecules, and large S_1 gradient norms at N6 tend to be associated with short such hydrogen bonds—at the FC geometry, about 50% of the snapshots have $\text{N6}\cdots\text{H}$ hydrogen-bonds of 2.1 Å or less. Hence, hydrogen bonding appears to accelerate the decay of adenine in water through the 6S_1 ($n\pi^*/\text{gs}$) conical intersection.

We recall in this context that 75% of the geometry optimizations on the S_1 surface reach the 6S_1 conical intersection, indicating the existence of a direct path connecting the FC region and this intersection. Figure 8 shows an example for such a path that has been followed during one of the energy minimizations on the S_1 surface. Clearly the availability of such barrierless pathways is consistent with the predominance of trajectories heading towards the 6S_1 conical intersection.

3.2. Accuracy Issues

In this section we offer some cautionary comments on the accuracy and reliability of excited-state calculations in general and of our semiempirical OM2/MRCI approach in particular.

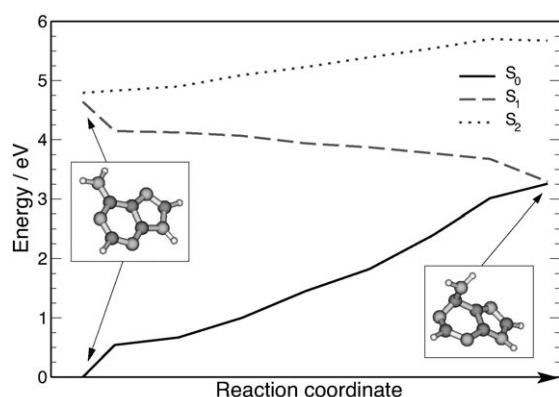


Figure 8. Adenine in water: energy profile of the S_0 , S_1 , and S_2 states along a path connecting the FC region and the 6S_1 conical intersection (see text). The reaction coordinate corresponds to the out-of-plane displacement of the amino group.

We have recently performed extensive benchmarks on electronically excited states,^[94–99] which covered 28 medium-sized organic chromophores and a total of 223 excitations. It is clear from this work that it is extremely difficult, even for rather small molecules, to obtain accurate (converged) ab initio results for electronically excited states. For larger molecules, such as adenine, state-of-the-art ab initio studies usually employ state-averaged CASSCF calculations (with a suitable active space and a moderate basis set) and then include dynamic correlation by perturbation theory (CASPT2) or by an MRCI treatment. The uncertainties of such an approach can be assessed, for example, by comparisons with the theoretical best estimates for vertical excitation energies of 104 singlet excited states that have been derived in our benchmarks.^[94,99] The corresponding mean absolute deviations (MAD) are very large for the CASSCF results as a result of neglecting dynamic correlation; they are 0.33 eV for CASPT2 results from the literature and 0.10 eV for our own MS-CASPT2/TZVP results (see ref. [94] for detailed data), and an extension of the basis set from TZVP to aug-cc-pVTZ leads to mean absolute changes in the CASPT2 energies of 0.16 eV.^[99] Given this situation, one can hardly expect an a priori accuracy of better than 0.2 eV in state-of-the-art CASPT2 (or other ab initio) calculations on molecules of the size of adenine. The semiempirical OM2/MRCI approach applied presently is several orders of magnitude faster than CASPT2 and it is thus not surprising that it is generally less accurate, with a MAD value of 0.50 eV in our singlet benchmark set.^[98] It is thus important to gauge its reliability for any given target molecule. This was done in our initial investigation on the excited-state dynamics of gas-phase adenine^[33] by demonstrating that the OM2/MRCI excitation energies and optimized geometries were in reasonable agreement with those from the high-level calculations then available.

To update these comparisons,^[33] we now consider the results from three recent ab initio studies of gas-phase adenine,^[32,35,36] which report geometry optimizations and reaction path calculations performed at the following levels: CASPT2//CASSCF-(16,12)/6-31G*,^[32] CASPT2//CASSCF(16,12)/6-31 + G*,^[35] and

MRCI//CASSCF(8,8)/6-31 + G*.^[36] These studies (as well as previous ones and OM2/MRCI) agree on some general qualitative features, for example, the presence of three closely spaced excited states around 5 eV ($n\pi^*$, $\pi\pi^*$ L_a , and $\pi\pi^*$ L_b), the existence of several competing nonradiative decay channels, and the type of distorted geometries at the corresponding conical intersections, especially for the low-energy 6S_1 and 2E species. However, there are significant differences in the computed energies and consequently also in the favored decay mechanisms. For example, relative to the ground-state S_0 minimum, the 6S_1 conical intersection is reported at 4.33,^[32] 4.86,^[35] and 3.74 eV,^[36] covering a wide range of more than 1 eV (OM2/MRCI: 4.08 eV). Likewise, the 2E conical intersection is located at 3.98^[32] and 3.50 eV^[36] (OM2/MRCI: 4.11 eV, not reported in ref. [35]). Ab initio MRCIS excited-state dynamics simulations indicate a two-step nonadiabatic relaxation in gas-phase adenine consisting of an ultrashort deactivation to S_1 and a longer subpicosecond exponential decay to the S_0 ground state,^[32] fairly analogous to the OM2/MRCI excited-state dynamics^[33] except that the second step mainly proceeds by the 2E channel (MRCIS) rather than the 6S_1 channel (OM2/MRCI). One of the recent ab initio pathway calculations^[36] arrives at a similar mechanistic scenario with several participating excited states, whereas another one^[35] proposes a different interpretation of the observed biexponential decay that involves only the bright L_a state, with ultrafast initial relaxation to an energy plateau followed by a slower direct conversion to the ground state. Furthermore, the computed energy profiles along linearly interpolated internal coordinate (LIIC) pathways between the initially generated FC geometry and the relevant conical intersections differ in that some are barrierless (as in OM2/MRCI), while others are associated with small or sizable barriers. For example, in their comprehensive CASPT2 study of conical intersections, Barbatti and Lischka find a “practically barrierless” LIIC path to the 2E conical intersection, and the same applies to the 6S_1 channel (see their Figure 3).^[32] Hassan et al. report a two-step $n\pi^*$ pathway with an ultrafast conversion from the initially populated L_a to the $n\pi^*$ state and a subsequent “downhill” LIIC path on the $n\pi^*$ surface to the 6S_1 conical intersection, while the direct $\pi\pi^*$ pathway goes through a minimum and then over a transition state (with a barrier of 0.21 eV) on the route toward the 2E conical intersection.^[36] In contrast, Conti et al.^[35] located the 6S_1 conical intersection at a much higher energy (0.42 eV above the $n\pi^*$ minimum) than the two other recent ab initio studies,^[32,36] and therefore, they ruled out the 6S_1 channel and favored the direct $\pi\pi^*$ pathway. Generally speaking, it is clear that the topology of the underlying potential-energy surfaces will largely govern the excited-state dynamics, and thus, also the preferred nonadiabatic decay mechanisms. In this sense, one should generally view the results from dynamics simulations with some caution, be it in the gas phase^[32–34] or in solution (this work), while recognizing that they offer much more detailed insight into photoinduced processes than static explorations of potential-energy surfaces.

In summary, it seems fair to state that the best available ab initio studies on gas-phase adenine agree on general qualitative features of the excited-state potential-energy surfaces, but

there are still substantial discrepancies with regard to quantitative aspects and the characterization of the decay mechanisms. Our OM2/MRCI results are generally within the range of the published *ab initio* results; they are more consistent with some of them than with others. Given this situation, it seems justified to exploit the computational efficiency of OM2/MRCI for investigating the excited-state dynamics of adenine. This allows us to perform an extensive sampling of phase space by running many trajectories with sufficiently long simulation times, so that dynamical aspects are well treated, both at the QM and QM/MM levels. OM2/MRCI simulations are thus expected to be realistic enough to provide useful insight into the effects of the environment.

4. Conclusions

We have reported a QM/MM study of the nonadiabatic dynamics of adenine in aqueous solution, with the QM part (adenine) treated at the OM2/MRCI level and the MM part (solvent) described by the TIP3P water model. For a number of snapshots from an initial ground-state MD simulation, the relevant potential-energy surfaces were characterized by locating energy minima and conical intersections. The optimized geometries turned out to be quite similar to those in the gas phase, especially in the case of the conical intersections, whereas the relative energies showed larger fluctuations that reflect different arrangements of the solvent molecules around the adenine.

Due to the strong vibronic coupling in the FC region, both the S_1 and S_2 states could be populated by photoexcitation. Surface-hopping QM/MM dynamics simulations predicted an ultrafast S_2 – S_1 decay with a time constant of less than 40 fs, whereas the S_1 – S_0 conversion to the ground state was computed to be somewhat slower, with a time constant of 410 fs that agreed well with the available experimental data. Most trajectories (>90%) returned to the ground state via the 6S_1 ($n\pi^*/gs$) conical intersection, while only a few (<10%) passed through the 2E ($\pi\pi^*/gs$) conical intersection. The topology of the S_1 surface favored paths leading towards 6S_1 because the necessary out-of-plane motion of the amino group was induced by large corresponding S_1 gradient components in the FC region. These out-of-plane gradient components generally tended to be larger for adenine in water than in vacuo, which led to faster S_1 decay in water. Overall, however, the nonadiabatic dynamics of adenine was found to be similar in the gas phase and in water, with regard to the crucial conical intersections and the dominant relaxation paths, irrespective of the solvent-induced changes in the electronic structure of the two lowest singlet excited states.

We believe that the present surface-hopping QM/MM approach provides a realistic description of the photoinduced nonradiative relaxation of adenine in aqueous solution. The use of the semiempirical OM2/GUGA-CI method for the QM part was essential to make this study feasible in terms of computational costs, considering that around 100 trajectories (6000 time steps each) had to be calculated for each snapshot. Clearly, this efficient approach can also be employed in analogous surface-hopping studies of other complex systems, for

example, DNA bases in a biological environment. Applications of this kind are in progress.

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Keywords: adenine • computational chemistry • gas-phase reactions • photochemistry • semiempirical calculations

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