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Does Stacking Restrain the Photodynamics of Individual Nucleobases?

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Nonadiabatic photodynamical simulations of 4-aminopyrimidine (4-APy) used as a model for adenine were performed by embedding it between two stacking methyl-guanine (mGua) molecules to determine the effect of spatial restrictions on the ultrafast photo-deactivation mechanism of this nucleobase. During the dynamics the formation of a significant fraction of intrastrand hydrogen bonding from 4-APy to mGua above and below is observed. These findings show that this type of hydrogen bond may play an important role for the photodynamics within one DNA strand and that it should be of interest even in irregular segments of double stranded nucleic acids structures. The relaxation mechanism of internal conversion to the ground state is dominated by ring puckering, and an overall elongation of the lifetime by ~20% as compared to the isolated 4-APy is computed.

Ultrafast relaxation of excited states of naturally occurring nucleobases on the time scale of a few picoseconds is a well-known phenomenon.[1−4] Computational studies performed by means of static[5−8] and nonadiabatic dynamics simulations[9−12] helped to reveal the excited-state time evolution of nucleobases as isolated species. It is generally accepted that isolated nucleobases relax into the ground state through nonadiabatic transitions via conical intersections characterized by strongly ring-puckered structures. Experimental observations[13−15] supported by theoretical calculations[16−18] indicate that in DNA excimers and/or excitons can be formed affecting the resulting excited-state lifetime strongly. Additionally, localization of the excitation on a single base, which is expected to resemble the behavior of the isolated base, has been reported as well.[14]

The theoretical treatment of the photodynamics of DNA, especially explicit nonadiabatic simulations, is quite involved, and corresponding investigations are only at the beginning.[19−21] In this contribution we focus in a first step on steric effects which adjoining nucleobases will have on an embedded base and its possibilities to reach conical intersections. These calculations are performed in the framework of on-the-fly surface hopping dynamics simulations which provide a detailed picture of the occurring photophysical processes. A combined quantum mechanical/molecular mechanical (QM/MM)[22−24] approach is used in which 4-APy is embedded between two methyl-guanine molecules (see Figure 1). The methyl groups were used to terminate the N-glycosidic bond in Gua. In these calculations the electronic excitation is confined to 4-APy, which is treated quantum mechanically, whereas the mGua mol-ecules are treated at the MM level. Although this approach does not account for the electronic reactivity of 4-APy with adjacent nucleobases, it provides information on their possible sterical constraints during the excited state decay. Based on previous experience with dynamics simulations on isolated 4-APy[25−27] this molecule has been chosen because it is flexible enough to allow investigating restrictions to puckering at C_2 and C_4 atoms, relevant for purine bases, and at the C_6 atom, relevant for pyrimidine bases (for numbering scheme, see Figure 2).

The stacking model of mGua−4-APy−mGua was obtained by replacing adenine with 4-APy in the Gua−Ade−Gua sequence cut out from a B-DNA dodecamer crystal structure (PDBID: 196D).[28] These results are compared to those obtained from photodynamics simulation of isolated 4-APy[27] performed with identical procedures for creating initial conditions as used in the present study.
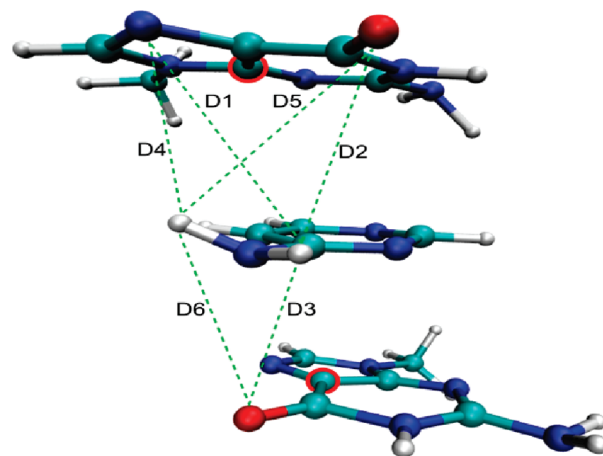

Figure 1. Starting structure of mGua−4-APy−mGua for dynamics calculations. Distances D1−D6 were used to analyze possible hydrogen bonds forming through the dynamics simulation. The atoms constrained by harmonic potential function are highlighted by red circles.

The 4-APy (QM part) was calculated at the state-averaged complete active space self-consistent field (SA-CASSCF) level of theory. A state averaging procedure with three states (SA-3) was used throughout the calculations. The active space was composed of two lone pair orbitals localized on nitrogen atoms of the pyrimidine ring and three π orbitals and three π^* orbitals, i.e., 10 electrons in 8 orbitals (CAS(10,8)). The molecular orbitals were expanded in the 6-31G* basis set.[29,30] Analytic energy gradients and nonadiabatic coupling vectors required for the dynamics were computed as described in refs 31−34 using the COLUMBUS program system.[35−37]

During the dynamics the empirical Parm99 potential[38] was used for the guanine molecules. Atomic point charges were determined with the ChelpG[39] method employing the HF/6-31G* level using the Gaussian program package.[40] The potential of the ChelpG charges was included in the Hamiltonian of the QM system within the framework of an electrostatic embedding scheme. Nonbonded interactions between the QM and MM parts were taken into account by the OPLS force field.[41,42] Distances between guanines were constrained by restricting the motion of the two atoms highlighted by red circles in Figure 1 by a harmonic potential. Its parameters are given by a force constant of 500 kcal/Å² and the minimum distance of 7.2 Å corresponding to the distance between these two atoms in the B-DNA dodecamer crystal structure.

The nuclear dynamics was treated integrating Newton's equations with a 0.5 fs time step. The surface hopping probabilities between electronic states were calculated by means of the Tully's fewest switches algorithm.[43] The initial conditions were created using a Wigner distribution for the quantum mechanical oscillator in the ground state for geometries and velocities (see ref 44). The settings for the surface hopping method are the same as described in ref 45. The dynamics was performed with the program system NEWTON-X[24] extended by a module including the QM/MM approach.[23]

During the dynamics the structures of 4-APy were analyzed and characterized by adopting the Cremer−Pople parameters[46] and the Boeyens classification scheme.[47] Possible hydrogen bonds formed within one chain were monitored during the dynamics simulation (labeled as D1−D6) and are shown in Figure 1.
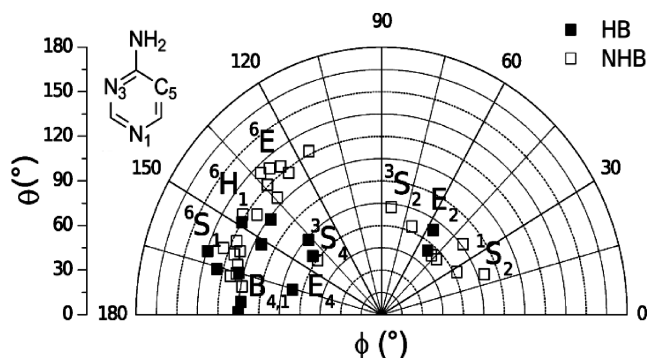
Figure 2. Cremer−Pople characterization of the structures at the hopping of 4-APy. HB and NHB stand for structures with and without hydrogen bonds formed between 4-APy and guanine, respectively.

Surface hopping dynamics simulations were performed for 45 trajectories and a maximum simulation period of 3 ps. The dynamics started in the $S_1(\pi\pi^*)$ state with initial energies of 5.15 ± 0.75 eV. During the time period of the simulation 13% of trajectories did not return to the ground state. Fitting of the evolution of the average occupation of the S_1 state by a single exponential decay function gives a lifetime of 1540 fs, slightly longer than that of isolated 4-APy computed as 1293 fs.

The structures of conical intersections occurring at the hopping during the dynamics are shown in Figure 2. They can be characterized according to their twisted bonds by defining three regions (for definition and representative structures, see Figure 3): (i) twist around N_1C_6 and C_5C_6 bonds with the puckering of N_1 and C_6 atoms (region A); (ii) twist around N_3C_4 bond, puckered at N_3 and C_4 atoms (region B); and (iii) twist around N_1C_2 and C_2N_3 bonds with the puckering at N_1 and C_2 as well as N_3 atoms (region C). As shown in Figure 2, 65% of trajectories decay in region A ($^6H_1$, $^6S_1$, and ^6E), ~11% of trajectories decay in region B with
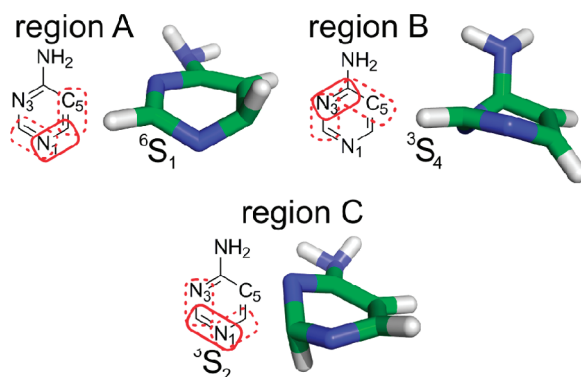
Figure 3. Classification of structures at conical intersections found in the dynamics simulations. The schemes show the bonds involved in the formation of conical intersections. Solid lines indicate the main twisting; dotted lines indicate auxiliary twisting (nitrogens in blue, carbons in green, and hydrogens in white).

out-of-plane NH_2 group deformation ($^3S_4$ and E_4), and ~24% of trajectories decay in region C ($^3S_2$, E_2, and $^1S_2$). Dynamics studies of isolated 4-APy[27] show that approximately 63, 20, and 17% of trajectories decay in the regions A, B, and C, respectively. Comparison between these two systems reveals the same relaxation mechanism of isolated and stacked 4-APy.
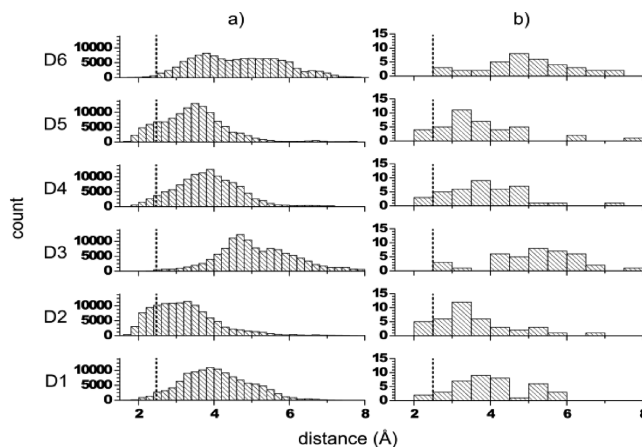
Figure 4. Histograms of the distances D1−D6 (see Figure 1) of possible hydrogen bonds collected for the entire trajectories (a) and in $S_1 \rightarrow S_0$ hopping structures (b). The vertical dashed line denotes a distance of 2.5 Å. Distances below this value were considered as hydrogen bonds.

The occurrence of hydrogen bond (HB) formation with the stacked mGua molecules is monitored in Figure 4. The HBs are mainly formed by the interaction of H atoms belonging to the NH_2 group with the O atom of the carbonyl group on mGua (D2 and D5) and to a smaller extent also with the N atom of the imidazole ring of mGua (D1 and D4). The HBs are formed relatively frequently during the whole simulation period (panel a of Figure 4) and also at the hopping event (panel b of Figure 4). A fraction of 36% of trajectories decays via conical intersections with HB structures. This effect can be explained by retaining the molecule in a more puckered structure increasing the hopping probability.

The statistical distribution of the hopping time for the trajectories which decay via HB and non-HB conical intersections is given in Figure 5. Among the trajectories with HB structures at the hopping, almost 60% decay within 1 ps, while only 30% of trajectories with non-HB structures decay during this time period indicating a faster decay of trajectories relaxing via HB conical intersections.
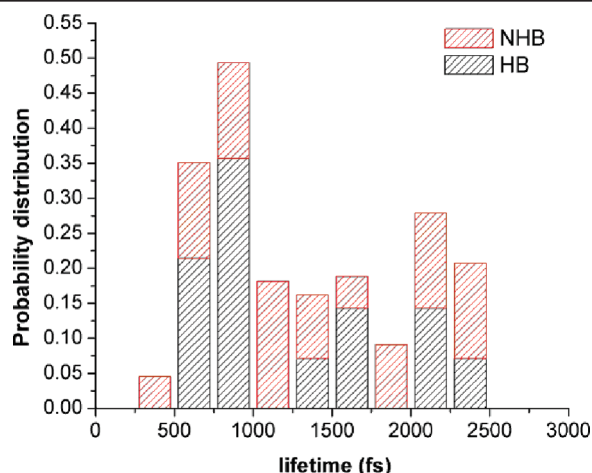
Figure 5. Histograms of hopping times at conical intersections characterized by hydrogen bonded and non-hydrogen bonded structures.

In conclusion, photodynamical simulations of 4-APy embedded between guanine molecules show that the stacking conformation does not substantially restrain the strong out-of-plane deformations which lead nucleobases to conical intersections. The same relaxation mechanisms as reported for isolated 4-APy are observed in mGua−4-APy−mGua, and only a relatively small overall increase of the lifetime is found. However, a new feature observed during the simulations, the dynamical formation and disappearance of hydrogen bonds between stacked bases, may have important implications for the photorelaxation of nucleic acids. In the present case these dynamical hydrogen bonds contribute to a faster decay component via a specific region of conical intersections in which the out-of-plane motion of the NH_2 group was enhanced.

Supporting Information Available: The full refs 37 and 40, Cartesian coordinates, and total energies of the initial structure for the dynamics. This material is available free of charge via the Internet at http://pubs.acs.org.

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