

Hydrogen-Bonding-Induced Shifts of the Excitation Energies in Nucleic Acid Bases: An Interplay between Electrostatic and Electron Density Overlap Effects

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The UV/vis spectra measured in various environments are frequently used to deduce the atomistic level data concerning the environment of a chromophore in the condensed phase.¹ This approach is especially useful in studies of biological systems to investigate the local environment of nucleic acid bases,² structural transitions in membranes,³ protein–chromophore interactions,⁴ structural transitions in biopolymers,⁵ and the structure of biological membranes,⁶ for instance. The theoretical methods currently in use in the interpretation of the UV/vis spectra follow one of two general strategies. One applies the quantum mechanical level of description for the whole system (*a supermolecule*) comprising the chromophore and its neighbors. In the other,^{7–9} the wave function description is limited to the investigated molecule, whereas its environment is accounted for by means of an additional term in the potential (*embedding potential*). Unfortunately, the supermolecule strategy using high-level *ab initio* quantum mechanical description is applicable only to relatively small systems.^{10,11} The embedding strategy provides, therefore, an appealing alternative. The effect of nonspecific interactions between the chromophore and its polarizable environment can be accounted for accurately by means of a polarizable continuum-type of approach.⁹ Accounting for the specific interactions (hydrogen bonding, for instance) requires an atomic-level description of the environment.¹² Various methods within the *embedded molecule* approach have been proposed in the last three decades.¹³ They differ in the domain of applicability and in the extent of the use of the system-specific experimental data in the embedding potential.

Density functional theory (DFT) provides a general framework for describing embedded molecules. One of the consequences of the Hohenberg–Kohn theorems¹⁴ is that the ground-state electron density of an embedded molecule (ρ_I) can be derived from Kohn–Sham-like equations in which an orbital-free and density-dependent term ($V_{\text{emb}}^{\text{eff}}[\vec{r}, \rho_I, \rho_{\text{II}}]$) is added to represent the interactions of the embedded molecule with its environment:¹⁵

$$V_{\text{emb}}^{\text{eff}}[\vec{r}, \rho_I, \rho_{\text{II}}] = \sum_{A_{\text{II}}} - \frac{Z_{A_{\text{II}}}}{|\vec{r} - \vec{R}_{A_{\text{II}}}|} + \int \frac{\rho_{\text{II}}(\vec{r}')}{|\vec{r}' - \vec{r}|} d\vec{r}' + \frac{\delta E_{\text{xc}}[\rho_I + \rho_{\text{II}}]}{\delta \rho_I} - \frac{\delta E_{\text{xc}}[\rho_I]}{\delta \rho_I} + \frac{\delta T_s^{\text{nad}}[\rho_I, \rho_{\text{II}}]}{\delta \rho_I} \quad (1)$$

where $T_s^{\text{nad}}[\rho_I, \rho_{\text{II}}] = T_s[\rho_I + \rho_{\text{II}}] - T_s[\rho_I] - T_s[\rho_{\text{II}}]$, the functionals $E_{\text{xc}}[\rho]$ and $T_s[\rho]$ are defined in the Kohn–Sham¹⁶ formulation of DFT, and ρ_{II} is the electron density of the environment.

Practical applications of eq 1 rely on two key elements: (i) the overall accuracy of the applied approximations in the last three terms in eq 1¹⁷ and (ii) the adequacy of the electron density ρ_{II} representing the microscopic environment in eq 1. Due to the

representation of the kinetic energy of the whole system as a sum of orbital-dependent and electron-density-dependent contributions, the Kohn–Sham orbitals for the whole investigated system can be replaced by the localized *embedded orbitals*.^{15,19}

Recently, we extended the range of applicability of the *orbital-free embedding* potential by merging it with the *linear-response* formulation of DFT.²⁰ This generalization is especially useful for studying the electronic excitations that involve only the orbitals localized on the same molecule (intramolecular excitations). Therefore, opposite to the supermolecular calculations, the electronic excitations are restricted to the ones involving only the changes in the electron density of the nonfrozen partner in the dimer. Obviously, if the system comprises two monomers, they can switch their roles to obtain two sets of intramolecular excitation energies, one set for each monomer.

The present work reports on two key issues: (i) We demonstrate that the embedding and supermolecule strategies are numerically equivalent as far as the interaction-induced shifts of the intramolecular excitation energies are concerned even in the case where the investigated molecule interacts with its environment via hydrogen bonds. (ii) We determine the relative significance of various effects contributing to the shifts.

As the object of study, we have chosen the guanine–cytosine (G–C) and adenine–thymine (A–T) base pairs in their Watson–Crick arrangements. These complexes are representative for other systems where specific hydrogen bonding interactions affect the spectroscopic properties of the organic chromophore. The excited states of the nucleic bases are known to depend strongly on their microscopic environment.² For each symmetry of the transition, the energy of the lowest excitation was calculated. In the linear-response DFT formalism, a given excitation cannot be attributed to a single pair of occupied/unoccupied orbitals. Usually, several such pairs contribute with different weights. Therefore, the labels given in Table 1 can be used only as qualitative descriptors characterizing the dominating pair. For the excitations analyzed in this work, identification of the dominating pair is straightforward.

The supermolecule and embedding approaches lead to very similar numerical results (see Table 1). The complexation-induced shifts vary from from -0.18 to $+0.69$ eV, whereas discrepancies between the excitation energies derived from the supermolecule and embedding calculations do not exceed 0.05 eV. The very good agreement between *excitation energies* derived from the embedding and supermolecule calculations provides the first numerical evidence that the approximation to the nonadditive kinetic energy bifunctional ($T_s[\rho_I, \rho_{\text{II}}]$)²² (developed, tested, and applied so far to study ground-state properties) is also adequate in the linear-response formulation of DFT to study *excited states*. The intermolecular hydrogen bonding affects the excitation energy depending on the type of excitation. The largest positive shift amounting to 0.68 eV occurs

Table 1. Lowest Excited States in the Nucleic Base Pairs (A–T and G–C) and in the Isolated Bases^a

base	transition		excitation energy [eV]		
	symmetry	qualitative description	free base	base in the dimer supermolecule	embedding
T	A'	$\pi \rightarrow \pi^*$	4.71	4.64	4.66 (4.69)
T	A''	$n \rightarrow \pi^*$	4.19	4.29	4.31 (4.33)
		O(T)···H–N(A)			
A	A'	$\pi \rightarrow \pi^*$	4.73	4.69	4.68 (4.66)
A	A''	$\sigma \rightarrow \pi^*$	4.31	4.46	4.52 (4.43)
		N–H(T)···O=C(A)			
		N(T)···H–N(A)			
C	A'	$\pi \rightarrow \pi^*$	4.20	4.52	4.51 (4.42)
C	A''	$n \rightarrow \pi^*$	3.71	4.38	4.39 (4.23)
		C=O(C)···H–N(G)			
		C=O(C)···H–N(G)			
G	A'	$\pi \rightarrow \pi^*$	4.70	4.53	4.57 (4.64)
G	A''	$\pi \rightarrow \sigma^*$	3.89	4.12	4.17 (4.16)
		C=O(G)···H–N(C)			

^a Results of embedding calculations with nonpolarized environment are given in parentheses.

for the A'' transition in cytosine. The dominant contribution to this excitation arises from the $n \rightarrow \pi^*$ component where n is the lone pair of O in the CO group in cytosine. This group participates in the O···H–N intermolecular hydrogen bond. The orbitals localized on the same hydrogen bond are also involved in the A' excitation, which has $\pi \rightarrow \pi^*$ character. As in the previous case, the shift amounting to 0.32 eV is also quite large. A similar blue-shift of this excitation energy (0.23 eV) from CIS calculations was reported.¹¹ The magnitudes of other shifts are smaller. The A' transitions in adenine and thymine, which have $\pi \rightarrow \pi^*$ character are hardly affected by dimerization. A small red-shift amounting to –0.05 eV in both cases is comparable to the corresponding CIS shifts amounting to 0.00 eV and –0.04 eV for thymine and adenine, respectively.¹¹ The $\pi \rightarrow \pi^*$ transition in guanine is quite strongly affected by dimerization ($\Delta\epsilon = -0.17$ eV). Opposite to other excitations analyzed in this work where the involved unoccupied orbitals are typically smeared over the whole monomer, this excitation involves the unoccupied orbital, which is localized on the C=O group participating in the O···H–N intermolecular hydrogen bond.

The results discussed so far were obtained using the polarized electron density of the environment (i.e., derived from the minimization of the total energy bi-functional ref 18). Each base considered is a polar molecule that changes its electron density distribution upon the formation of the dimer. Table 1 collects also the excitation energies calculated using the gas-phase (i.e., not-polarized) electron density of the partner molecule as ρ_{II} in eq 1. The effect of the dimerization-induced electronic polarization of the environment on the shift is usually small. It affects, however, the magnitudes of the largest shifts corresponding to such transitions where the involved orbitals are localized on hydrogen bond donor groups. The largest effect of the environment induction occurs for the $n \rightarrow \pi^*$ transition involving the lone pair of oxygen in cytosine ($\Delta\epsilon = 0.67$ eV or 0.50 eV for the relaxed and frozen guanine, respectively).

According to our previous analyses of ground-state properties,^{22,23} inclusion of the term representing the repulsive kinetic-energy-dependent contribution to the embedding potential (the last term in eq 1) is indispensable if the two systems are hydrogen bonded. It prevents the subsystems from overpolarizing in variational calculations. Indeed, the shifts calculated using the electrostatic-only embedding (i.e., an embedding potential with all nonelectrostatic terms switched off in eq 1) depend very strongly on the basis

sets. (Moreover, they are meaningless if the basis set contains diffused functions.)

As far as the intermolecular orbital interactions are concerned, we note that the embedded orbitals (both occupied and unoccupied) were localized on the monomers in our calculations. Orbitals with mixed contributions from two different monomers were not constructed. The fact that the differences between the excitation energies derived from the embedding and supermolecule calculations do not exceed 0.05 eV indicates therefore that intermolecular orbital effects contribute negligibly to the analyzed shifts.

The analysis of the shifts in the complexes studied allows us to conclude that they are determined by two principal effects: the intermolecular electrostatic interactions and the repulsive overlap-dependent interactions represented in the applied formulation of density functional theory as the nonadditive kinetic energy component of the embedding potential. The last component originates from the Pauli exclusion principle, which results in the inequality $T_s^{\text{nad}}[\rho_I, \rho_{II}] \neq 0$ for overlapping electron densities.

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Supporting Information Available: Details of the computer implementation of the applied formalisms and of the calculations. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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