Effect of proton transfer on the electronic coupling in DNA

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Abstract

The effects of single and double proton transfer within Watson–Crick base pairs on donor–acceptor electronic couplings, \( V_{da} \), in DNA are studied on the bases of quantum chemical calculations. Four dimers [AT,AT], [GC,GC], [GC,AT] and [GC,TA] are considered. Three techniques – the generalized Mulliken–Hush scheme, the fragment charge method and the diabatic states method – are employed to estimate \( V_{da} \) for hole transfer between base pairs. We show that both single- and double proton transfer (PT) reactions may substantially affect the electronic coupling in DNA. The electronic coupling in [AT,AT] is predicted to be most sensitive to PT. Single PT within the first base pair in the dimer leads to increase in the hole transfer efficiency by a factor of 4, while proton transfer within the second pair should substantially, by 2.7 times, decrease the rate of charge transfer. Thus, directional asymmetry of the PT effects on the electronic coupling is predicted. The changes in the \( V_{da} \) matrix elements correlate with the topological properties of orbitals of donor and acceptor and can be qualitatively rationalized in terms of resonance structures of donor and acceptor. Atomic pair contributions to the \( V_{da} \) matrix elements are also analyzed.

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1. Introduction

Charge transfer (CT) in DNA is currently the subject of intense experimental and theoretical research (see [1] and references therein). Investigations of charge migration in DNA are relevant for understanding the oxidative damage and mutations of DNA [2,3] as well as for elaboration of nanoelectronic devices [4–6]. The majority of experimental information on charge transport in DNA pertains to the movement of a radical-cation state (an electron hole) through \( \pi \) stacks [7–10]. Theoretical aspects of charge transfer in DNA have recently been considered by Bixon and Jortner [11,12] and Berlin et al. [13,14]. In these studies one supposed that the motion of a positive charge occurs as a series of hops between guanine sites. An alternatively mechanism, phonon-assisted polaron hopping is considered by Conwell [15] and Shuster [16]. In this case hole transport in DNA has been treated theoretically within the adiabatic model which assumes that the excess positive charge is extended over several bases in the stack. However, recently it has been demonstrated that charge delocalization in DNA is essentially suppressed by polar environment, and hole states are localized on individual guanines even in sequences consisting only of GC pairs [17]. This result does not support the suggestion of Basko and Conwell [18] that the hole charge spread over five or more neighboring base pairs, leading to polaron formation in DNA stacks.

When the hole charge is confined to individual base pairs, the electronic coupling between pertinent sites, \( V_{da} \), is a parameter that mainly determines how the charge transfer (CT) rate depends on the nature and mutual position of the donor and acceptor moieties [19,20]. The matrix element has been shown to be very sensitive to conformational changes of DNA fragments: thermal structural
fluctuations can change its magnitude by an order of magnitude [21–23]. The importance of stacking dynamics was demonstrated in experimental studies [10]. Comparing electronic couplings of purine nucleobases to those calculated for Watson–Crick pairs one finds a remarkable effect of pyrimidine nucleobases on the electronic coupling matrix elements of hole transfer in DNA [24]. Detailed charge partitioning analysis showed that the electronic coupling is notably affected by electrostatic and exchange interactions between the nucleobases within a base pair. Because even inter-base hydrogen bonds influence $V_{ds}$ one can expect that proton transfer within the base pair may considerably modulate the donor–acceptor coupling [24].

Hydrogen bonds occurring in the adenine–thymine, AT, and guanine–cytosine, GC, base pairs (Fig. 1) play key role in genetic molecular recognition and structure determination of nucleic acid base pairs [25]. Hydrogen bonding interactions between complementary nucleobases are also suspected for being responsible for the exceptional photo-stability of DNA since recent reports [26,27] have suggested that light-triggered motion of a proton in one of the hydrogen bonds of an isolated base pair initiates non-radiative decay to the electronic ground state. This hypothesis is, however, questioned in the recent report by Kohler et al. [28] who demonstrated, using transient absorption spectroscopy, that π-stack rather than base pairing determines the fate of electronically excited states in single- and double stranded oligonucleotides. It is well known that each base pair may be converted to its minor, but often reasonably stable enol–imine tautomer by a double proton transfer (prototropic tautomerism). The rare imino/enol tautomers of Watson–Crick pairs are thought to be responsible for genetic instabilities [25]. When a proton of the N–H···O hydrogen bond in an AT or GC base pair moves from N to O, the reverse motion of a proton in another H-bond is likely to be induced, and therefore, both nucleobases remain electrically neutral. Thus, the coupled proton transfer in two H-bonds occurs. Proton transfer (PT) within base pairs has attracted much attention. Florian and Leszczynski carried out ab initio calculations of several tautomers of GC [29] involving the canonical pair, tautomers formed from this pair by simultaneous transfer of two protons, and ion pairs produced by single proton transfer between the nucleobases. The relative stabilities and dissociation energies of the base pairs were determined at the MP2/6-31G**//HF/6-31G* level. The computations indicated that the electron correlation is important for reliable estimation of the relative energy of tautomers. It was

Fig. 1. Relevant single- and double proton-transfer reactions in GC and AT base-pairs.
demonstrated that one ion pair and one neutral pair resulted from single- and double PT within GC are energetically accessible [29]. All, stable at the B3LYP/6-31G** level tautomers of the AT and GC Watson–Crick pairs have been recently reported by Hayashi and Mukamel [30].

The situation can essentially change when canonical base pairs are involved in electron transfer. It has been recognized that charge migration in DNA can be accompanied by proton transfer. Sevilla et al. [31] demonstrated that both proton transfer from G to the cytosine radical anion (C−) forming neutral hydrogenated cytosine radical (CH) and PT from the guanine radical cation (G+) to C forming neutral dehydrogenated guanine radical (G(–H)) slow electron and hole transfer rates in DNA. Hole transfer to a nucleobase will change its pKₐ-values and thereby can enforce rapid deprotonation of the base due to proton transfer between the nucleobase and surroundings. For instance, a guanine radical cation formed after charge transfer between the nucleobase and surroundings. For instance, a guanine radical cation formed after charge transfer to G exhibits a pKₐ value of 3.9 [32] and, therefore, can lose the positive charge by donating a proton. As a result, inter-strand proton transfer may interrupt the migration of the hole in DNA due to the conversion of the radical cation to the corresponding neutral radical state. The interrelation between CT and PT in DNA has been experimentally demonstrated by Giese and Wessely [33]. When the proton-transfer and hole-transfer events are separated, the first reaction step is energetically unfavorable; because of that a concerted process, proton-coupled electron transfer (PCET), often occurs. Thorp and co-workers observed a deuterium kinetic isotope effect for the electron transfer in several DNA systems and suggested that PCET occurs in DNA [34]. A general theoretical approach for treatment of proton-coupled electron transfer reactions is described by Hammes-Schiffer [35]. In particular, it was shown that PCET strongly affects the CT efficiency [36].

As was demonstrated by Bertran et al. [37] and Li et al. [38], among several types of single and double PT that might occur in the radical cations of Watson–Crick pairs (WCPs), just one single proton transfer (SPT) and one double PT (DPT) reactions are feasible for each WCP (see Fig. 1). While the SPT thermodynamic barriers for the GC and AT cations are quite low (1.2 kcal/mol at the B3LYP level), the DPT barriers are remarkably higher, in the range of 6–10 kcal/mol. No stationary point corresponding to the DPT structure was found – for GC [37]. Therefore, only four PT reactions (one single and one double PT for AT and GC pairs each) are considered in the paper.

While the donor–acceptor electronic coupling mediated by DNA n-stacks have been computationally studied in several papers [21–24,39–42], not much is known about the effect of inter-base PT on V₃₃. In this work, we consider the sensitivity of the matrix element between neighboring base pairs to single and double proton transfer within the pairs.

2. Details of calculations

The coupling between proton and hole transfer were studied in four WCP dimers: [AT,AT], [GC,GC], [GC,AT] and [GC,TA]. A stack of two Watson–Crick base pairs, for instance, GC and TA, in the order 5′ → 3′ is denoted here as [GC,TA]. The letter “s” and “d” before a base pair stands for single and double proton transfer, respectively. Thus, [sGC,AT] denotes that single PT within the GC base pair took place in the stack [GC,AT], whereas [GC,dAT] indicates a structure resulting from double proton transfer within the AT pair of the same stack.

To model structural changes caused by PT just the position of protons involved in PT has been optimized in the base pairs. The corresponding geometries of base pairs resulted from SPT were obtained using the constrained optimization of radical cations. The proton positions resulting from DPT reactions were generated within the optimization of the WCPs in which two protons were exchanged between the proton donor and acceptor sites involved in hydrogen bonds. The optimization was carried out at the Hartree–Fock level employing the 6-31G* [43] basis set. The optimized proton positions were used to generate WCP dimers of regular structure (the base step parameters – rise = 3.38 Å and twist = 36°) with the program SCHNARP [44]. Our models of the PT transformed WCP dimers can be treated only as a first approximation to the geometry changes due to the proton transfer process. Of course, the movement of proton(s) must finally lead to the relaxation of local DNA geometry adjacent to the base pair where proton transfer takes place. However, we believe that constrained geometry optimization carried out in the present work comprises the most important changes in the electronic structure of the system considered and, therefore, are able to describe the main portion of variation in V₃₃, due to PT.

The generalized Mulliken–Hush (GMH) method [45,46], the fragment charge (FC) scheme [47] and the diabatic state (DS) method [20] were employed to derive electronic couplings in the WCP dimers. These approaches provide reliable estimates of V₃₃ even though the donor and acceptor electronic levels are off resonance. The GMH and FC methods imply transformations of adiabatic states to diabatic states localized on donor and acceptor, with subsequent evaluation of the coupling matrix element V₃₃. In the DS scheme, the electronic coupling V₃₃ between diabatic states of donor and acceptor, ψ₃ and ψ₃, is calculated as:

\[
V₃₃ = \frac{H₃₃ - S₃₃(H₃₃ + H₃₃)/2}{1 - S₃₃²}.
\]

The wave functions ψ₃ and ψ₃ are calculated for separated donor and acceptor. In one-electron approximation, these states can be represented as Hartree–Fock orbitals. For hole transfer through DNA stack, ψ₃ and ψ₃ can be approximated with HOMO of neutral base pairs. The integrals H₃₃ and the overlap integrals S₃₃ are calculated using
the corresponding matrix elements computed in AO basis for the whole system.

In the present study, we estimate coupling matrix elements using three different schemes on the basis of the HF/6-31G* calculations. It has been shown that this level of theory is sufficient to produce reliable estimates of $V_{da}$ for hole transfer in DNA stacks [21,24]. Already 10 years ago, Rodriguez-Monge and Larsson [48] have proven that Hartree–Fock based approach yields results in close agreement with those of more accurate treatment including electron correlation. Also, it was demonstrated that the couplings for hole transfer in DNA calculated within Koopmans’ theorem are in good agreement with the experimental estimates [40,49].

All HF calculations were performed with Gaussian 98 [43] using the 6-31G* basis set. ChemCraft was used for the visualization of molecular orbitals [50].

3. Results and discussion

Due to their low ionization potentials, purines are the most probable sites in DNA where electron holes are localized. The formation of a radical cation changes the acidic properties of the nucleobases and can be associated with proton transfer from purine to pyrimidine bases. PT reactions within the cationic Watson–Crick base pairs were studied by Bertran et al. [37] and Sevilla and co-workers [38]. In particular they found that the structures formed after single PT are less stable than the corresponding Watson–Crick configurations of GC and AT base pairs by only 1.2 kcal/mol. The single PT in the GC radical cation occurs from N1–H of guanine to N3 of cytosine while the N6 center of adenine and O4 atom of thymine are involved in PT within the AT radical cation (see Fig. 1). Transfer of the first proton may be followed by the subsequent PT (in the opposite direction) leading to double PT structures. The most probable second proton transfer concerns the N4 site of cytosine and the O6 site of guanine in GC, whereas for AT the only possibility involves the movement of proton from the N3 atom of cytosine to the N1 site of adenine (see Fig. 1). These DPT processes lead to the formation of so-called rare base pairs. Bertran et al. [37], found that the formation of these species is less likely than the occurrence of SPT structures. According to their B3LYP/6-31G** calculations, the rare configurations of GC and AT cations are found to be less stable than the Watson–Crick configurations by 10.5 and 6.4 kcal/mol, respectively. While other types of proton transfer reactions within AT and GC can be thought of, they are, however, thermodynamically strongly disfavored. Therefore, we will consider electronic couplings in systems where one of two base pairs undergoes single or double PT.

Ten different dimers can be identified in double-stranded DNA. Since hole transfer occurs between purine bases there are intra-strand and inter-strand couplings. In this paper we will examine three dimers with intra-strand purine bases [AT,AT], [GC,GC], [GC,AT] as well as the [GC,TA] dimer with inter-strand G and A bases.

3.1. Effect of single proton transfer on hole transfer matrix elements

Table 1 lists matrix elements calculated using the FC, GMH and DS methods in the intact dimers and related systems formed as a result of PT. All methods give similar estimates for the matrix elements indicating the reliability of the calculated $V_{da}$ values.

Although the absolute value of $V_{da}$ in the [AT,AT] system is one of the smallest (only 26–28 meV; see Table 1) among the 10 possible complexes in DNA [24], it turned out to be the most sensitive towards single proton transfer (Table 1). The PT reaction within the second AT pair essentially increases the matrix element while noticeable decrease in the coupling is found when PT occurs in the first base pair (Table 1). Since the hole transfer efficiency is proportional to the square of $V_{da}$ [19], single PT in the second base pair should increase the rate of electron transfer by about 4 times and decrease it by factor 2.7 while occurring in the first pair. The $V_{da}$ values clearly demonstrate the directional dependence of the donor–acceptor coupling. The effect of directional asymmetry for hole transfer has been predicted on the basis of calculated $V_{da}$ between neighboring nucleobases [39] and base pairs [40] and subsequently detected by O’Neill and Barton [51]. It is worth noting that the $V_{da}$ matrix element changes even its sign when PT proceeds in the first pair. Among the systems examined this is the only instance showing the change of $V_{da}$ sign due to proton transfer.

<table>
<thead>
<tr>
<th>System</th>
<th>FCM</th>
<th>GMH</th>
<th>DS</th>
</tr>
</thead>
<tbody>
<tr>
<td>[AT,AT]</td>
<td>26</td>
<td>26</td>
<td>28</td>
</tr>
<tr>
<td>[sAT,AT]</td>
<td>−16</td>
<td>−16</td>
<td>−15</td>
</tr>
<tr>
<td>[dAT,AT]</td>
<td>−14</td>
<td>−14</td>
<td>−13</td>
</tr>
<tr>
<td>[AT,sAT]</td>
<td>52</td>
<td>49</td>
<td>44</td>
</tr>
<tr>
<td>[AT,dAT]</td>
<td>56</td>
<td>56</td>
<td>61</td>
</tr>
<tr>
<td>[GC,GC]</td>
<td>94</td>
<td>93</td>
<td>107</td>
</tr>
<tr>
<td>[sGC,GC]</td>
<td>103</td>
<td>100</td>
<td>116</td>
</tr>
<tr>
<td>[dGC,GC]</td>
<td>123</td>
<td>122</td>
<td>109</td>
</tr>
<tr>
<td>[GC,dGC]</td>
<td>93</td>
<td>91</td>
<td>100</td>
</tr>
<tr>
<td>[GC,AT]</td>
<td>73</td>
<td>73</td>
<td>73</td>
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<tr>
<td>[sGC,AT]</td>
<td>121</td>
<td>122</td>
<td>122</td>
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<tr>
<td>[dGC,AT]</td>
<td>136</td>
<td>129</td>
<td>130</td>
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<tr>
<td>[GC,sAT]</td>
<td>167</td>
<td>165</td>
<td>166</td>
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<tr>
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<tr>
<td>[GC,TA]</td>
<td>143</td>
<td>144</td>
<td>146</td>
</tr>
<tr>
<td>[sGC,TA]</td>
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<td>−26</td>
<td>−26</td>
</tr>
<tr>
<td>[dGC,TA]</td>
<td>−22</td>
<td>−21</td>
<td>−24</td>
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<td>[GC,sTA]</td>
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<td>−10</td>
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<tr>
<td>[GC,dTA]</td>
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<tr>
<td>[GC,dTA]</td>
<td>−35</td>
<td>−35</td>
<td>−30</td>
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</table>
As seen from Table 1, the [GC,GC] dimer exhibits one of the largest coupling, of about 100 meV. Unlike [AT,AT], single proton transfer causes here only minor changes in the electronic coupling. As in [AT,AT], SPT proceeding in the first and second base pairs of [GC,GC] exerts opposite effects. Namely, when PT occurs in the lower base pair of [GC,GC] it increases the matrix element by about 10 meV. On the other hand, PT in the second GC leads to decreasing $V_{da}$. However, due to relatively strong coupling in the reference system, these variations in the matrix element have no essential effect on the charge transfer efficiency.

In the [GC,AT], the purine bases are on the same strand. Different from the [GC,GC] and [AT,AT] dimers, single proton transfer both in the first and second base pairs of [GC,AT] increase the $V_{da}$ value (see Table 1). Respectively, the matrix element becomes stronger by 10 and 20 meV. Thus, the effect of PT is more apparent for AT and less evident for GC in line with the $V_{da}$ changes calculated for the [AT,AT] and [GC,GC] dimers. Also, the position of the base pair that undergoes PT affects the coupling.

Unlike systems considered above, the donor and acceptor sites in [GC,TA] are on the opposite strands, and therefore, the inter-strand coupling between the guanine and adenine bases is relevant for hole transfer. The coupling in the reference system is calculated to be 27 meV. The FC, GMH and DS schemes provide similar estimates of $V_{da}$ in [sGC,TA], 22, 21 and 24 meV, respectively (see Table 1). Thus, some decrease in the hole transfer efficiency due to SPT in the GC pair is expected. More considerable effect was found for PT proceeding in the AT base pair. In this case, $V_{da}$ increases to 40 meV (Table 1).

### 3.2. Effect of double proton transfer

Single proton transfers in radical-cation base pairs can be followed by a PT reaction in the opposite direction resulting in the double-proton transfer structures dGC$^+$ and dAT$^+$. In these species, less stable (rare) tautomers of nucleobases form hydrogen-bonded pairs (see Fig. 1). However, the resulting DPT structures are not thermodynamically stable. As already noted, dGC$^+$ is not even a minimum on the potential energy surface and the energy corresponding to the dGC$^+$ geometry is 10.5 kcal/mol higher as compared with GC$^+$ [37]. Similarly, the dAT$^+$ cation was found to be less stable than AT$^+$ by ca. 6.5 kcal/mol [37]. However, the situation may change due to environmental effects. So, we also calculated the changes of the electronic coupling in dimers containing dGC$^+$ and dAT$^+$ pairs.

Our estimates of $V_{da}$ listed in Table 1 show that the effects of single and double PT are qualitatively very similar for all dimers. In [AT,AT], DPT within the first base pair is accompanied by the essential decrease of the electronic coupling while the formation of [AT,dAT] leads to the considerable increase of the matrix element (see Table 1). In consequence, similarly to the SPT effects, the hole transfer efficiency should substantially decrease in [dAT,AT] and increased by ~5 times in [AT,dAT] as compared to [AT,AT]. In the [GC,GC] dimer, the changes of $V_{da}$ due to DPT, are more evident than the SPT effects (see Table 1). Note that the FC and GMH schemes predict very similar $V_{da}$ values in [sGC,GC] and [dGC,GC], while the corresponding magnitudes calculated with the DS method deviate by about 15%. Regardless of the base pair involved in DPT, the coupling in [GC,AT] becomes stronger in line with the SPT results. This effect is found to be more evident than in the case of SPT. In the [GC,TA], the electronic coupling becomes weaker when DPT occurs within the GC pair. The effect is essentially bigger than in the case of SPT. The coupling is found to be stronger in the [GC,dTA] as compared with the reference system [GC,TA] though the effect is smaller than in [GC,sTA].

### 3.3. Analysis of the orbital interaction

As shown above, the electronic coupling can increase or decrease depending on the position of the pair in which PT occurs. It appears to be quite difficult to predict the changes in the matrix element changes without doing appropriate calculations. Comparing the PT effects calculated for [AT,AT] and [GC,GC], we can predict qualitatively the corresponding changes in $V_{da}$ for the dimer [GC,AT] (see Section 3 above), but not for [GC,TA]). Thus, a question arises: What are main electronic interactions which determine the coupling matrix element in DNA π-stacks? Below we provide an analysis of the orbital interaction in the system [AT,AT] with the aim to explain the calculated effects of SPT. Despite the fact that the complex is formed by two identical pairs, the variation of the electronic coupling depends on the position of the AT pair in which PT occurs.

Two diabatic states which are involved in hole transfer can be represented by a linear combination of HOMO and HOMO-1 orbitals of the corresponding neutral system (Koopmans’ approximation). The magnitude of $V_{da}$ depends on the overlap between the wave function of hole donor and acceptor. Thus, one can rationalize the $V_{da}$ changes caused by proton transfer in terms of the overlap between the corresponding orbitals. Such an analysis can be carried out if the diabatic states are brought into resonance, and therefore, HOMO and HOMO-1 (see Fig. 2) represent ± combinations of the diabatic states of donor and acceptor [21,24]. This resonance may be achieved by applying external electric field that minimizes the energy splitting of the two hole states [21,24,39].

Single proton transfer in the neutral AT base pair formally leaves a negative charge at the N6 atom of adenine; recall that electronic states of the neutral system are employed for estimating the electronic coupling for hole transfer. As a result of SPT, the π-density increases mainly at the N6 and N3 atoms of adenine (see the resonance structures shown in Fig. 3). On contrary, the π-density at
the C6 atom decreases since now it is involved in one double bond with N6 rather than in two partially double bonds in the canonical structure of adenine. Moreover, the C2–N3 bond partially loses its double bond character and the C4–C5 double bond becomes more localized (see III in Fig. 3).

In the [AT,AT] complex, overlapping regions are (N3,C2:C4,C5), (C6,C5:N6) and (C4:N7) (see Fig. 2); atoms before colon refers to the first (lower) base pair, and atoms after colon to the second pair. When SPT proceeds within the upper base pair, increase in the C4,C5:N6 interaction is expected as a negative charge localizes at N6, and therefore, the electron coupling becomes stronger. This qualitative analysis can be justified using values of contributions from atomic pairs of donor and acceptor to the electronic coupling calculated within the DS scheme (see Table 2). In the intact [AT,AT] dimer, the interaction (C5:N6) (between C5 of the first adenine base and N6 of the second one) is calculated to be 79 meV. Similarly, (C6:N6) is 57 meV. These contributions increase substantially, to 98 and 72 meV, respectively (see Table 2), when single PT proceeds in the second base pair. Thus, the data confirm the conclusion based on the qualitative orbital analysis.

Single PT in the lower base pair exerts an opposite effect on the electronic coupling. Namely, the (C6:N6) interaction becomes weaker due to the decreasing π-density at the C6 atom (see the resonance structures in Fig. 3).

Fig. 2. HOMO-1 orbital of the [AT,AT] dimer in resonance for hole transfer. Arrows indicate overlapping regions between purine orbitals. Projection on the left shows the leading overlap region, view on the right demonstrates the minor overlap. Contour values at 0.015 Bohr−3/2.

Fig. 3. Resonance structures important for stabilization of the adenine anion, a hypothetical product of SPT within the AT base pair when Koopmans’ approximation is employed in calculating the electronic coupling (see the text for details).
between matrix elements were estimated for several stacks using the electronic coupling of hole transfer in DNA. The

4. Summary

C4,C5:N6 overlapping regions are mainly responsible for Fig. 2). Thus, the changes in the N3,C2:C4,C5 and N6:N6 increases with the electron density at N6 (see

According to Table 2, this interaction decreases from 57 meV in the original dimer to 19 meV in [sAT,AT]. Furthermore, lowering of the N3–C2 bond order of the first adenine base should also decrease the matrix element. Indeed, the calculated (C2:C4) and (C2:C5) contributions decrease from −38 and −65 meV in [AT,AT] to −29 and −49 meV in [sAT,AT]. Then, the antibonding interaction N6:N6 increases with the electron density at N6 (see Fig. 2). Thus, the changes in the N3,C2:C4,C5 and C4,C5:N6 overlapping regions are mainly responsible for the PT effects in the [AT,AT] dimer.

4. Summary

In this paper, we studied the effect of proton transfer on the electronic coupling of hole transfer in DNA. The matrix elements were estimated for several stacks using the FCM, GHM and DS methods. Good agreement between $V_{da}$ obtained using three different methods indicates the reliability of the calculated values. The results of our computational study lead to the following conclusions:

(i) Both single and double proton transfer reactions within base pairs may substantially influence the electronic coupling in DNA interfering thus with the hole transfer process.

(ii) The most essential effect of PT on the $V_{da}$ magnitude was calculated for the [AT,AT] dimer. The absolute value of the coupling in [AT,sAT] is twice that in the reference system. In contrast, PT within the first pair in [AT,AT] decreases the coupling by a factor of 1.6. Thus, essential directional asymmetry of the PT effects is predicted.

(iii) Single- and double PT in the first base pair increase the electronic coupling in the [GC,G] and [GC,A] complexes and decrease it in the [AT,AT] and [GC,T] dimers. The proton transfer reactions within the second base pair decrease $V_{da}$ in [GC,G] and increase the matrix element in [AT,AT], [GC,A] and [GC,T]. Double proton transfer leads to somewhat bigger changes in the electronic coupling than SPT.

(iv) The changes in the $V_{da}$ matrix elements caused by PT correlate with the topological properties of the donor and acceptor orbitals and can be qualitatively rationalized in terms of their overlap.

We stress that a more complete account of structural changes of the base pairs due to proton and electron transfer should be considered for a detailed description of the PT effects on electronic couplings. However, we believe that the trends found in the present work will remain unchanged when taking into account the structural and environment effects. We plan to improve the present models by carrying out a combined QM/MM optimization of the representative fragments of double-stranded DNA where proton transfer took place in a single base pair.

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