Systematic Study of the Influence of Base-Step Parameters on the Electronic Coupling between Base-Pair Dimers: Comparison of A-DNA and B-DNA Forms

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The electronic coupling is one of the key parameters governing electron hole transfer along DNA helices. In this study, we established the first comprehensive data base of electronic coupling elements, calculated at the *ab initio* level. The data set comprises *all* possible Watson−Crick base pair dimers, both in standard A-DNA and B-DNA geometries. We also quantified the sensitivity of the coupling elements with respect to geometry changes by varying each of the six standard base step parameters, which specify the relative orientation of neighboring base pairs. We compare the couplings in a systematic way by discussing variations in the coupling magnitude due to geometry or nucleotide sequence in the dimer, and we analyze how the structure affects the electronic coupling in terms of general and dimer-specific trends. Furthermore, we studied how the coupling changes when one introduces the chemically modified base 7-deazaguanine in the corresponding base-pair dimers. Finally, on the basis of the calculated coupling elements, we suggest a model duplex with an enhanced capacity for hole transfer.

Introduction

The strength of the electronic coupling between donor (D) and acceptor (A) sites is one of the rate-determining factors for hole transfer along organic conjugated π-stacks in general[1] and along DNA duplexes in particular.[2–4] Quantum mechanically calculated electronic coupling elements H_{DA} have been used to quantify the interaction between bases and base pairs in nucleic acids.[3d,5–10]

With electronic structure calculations, electronic coupling elements H_{DA} between stacked DNA bases have been shown to depend sensitively both on the nucleotide sequence[7a,10c,11] and on the degree of π-orbital overlap of donor and acceptor conjugated moieties.[6b,7b] These two types of sensitivity were registered also experimentally.[4a,10b,12] The extent of overlap between the nucleobases is critically affected by the global helical conformation of the DNA oligomer (A-, B-, or other form), but changes also due to the thermal dynamics of the macromolecule in solution. Thus, H_{DA} depends strongly on conformational fluctuations of a DNA stack of base pairs.[6b,c,7,8c,9g,10,11,13] All computational models applied predicted significant changes (up to several orders of magnitude) in hole transfer rates, just due to thermal fluctuations of bases in conventional B-DNA. In consequence, strategies were proposed where electronic coupling elements were calculated on ensembles of structure snapshots, extracted from molecular dynamics (MD) trajectories.[6b,d,8,14,15]

Differences of the electronic coupling between nucleobases stacked in A-DNA and B-DNA forms were rarely tackled. Some theoretical studies pointed out that the electronic coupling in the two conformations is dissimilar.[10c,11a,c,15] Different vibrational transition dipole moments have been estimated experimentally for A- and B-DNA duplexes.[16] As H_{DA} is directly related to electronic transition dipole moments, such differences can be expected also between electronic coupling elements.

A systematic set of electronic coupling elements for various conformations of DNA will aid in the design of DNA-based devices with enhanced hole transfer capacity.[17] Recently, DNA sequences with a predefined helical conformation have been synthesized using modified nucleotides.[18] Duplexes involving locked nucleic acid (LNA) monomers exhibit a propensity to hybridize as more rigid A-type helices, while those containing α^L-LNA nucleotides form predominantly B-type hybrids with DNA complementary strands.[19]

In the following, we present the first systematic study of electronic coupling elements of all possible DNA base pair dimers. We compared standard A-DNA and B-DNA forms. Additionally, we probed how perturbations of these regular structures affect the values of the couplings. For this purpose, we varied each of the six standard base step parameters[20] (BSPs). Three of them describe translational (rise, shift, slide) and three other rotational (twist, tilt, roll; Figure 1) degrees of freedom when each of two adjacent base pairs is considered as a rigid object. Hence, variation of these structural parameters affects the overlap and the electronic coupling between neighboring base pairs. Apart from their methodological value, these results form a database for assessing qualitatively the electronic coupling when one designs new DNA sequences for particularly efficient charge transfer.

Molecular Models and Computational Method

The models used throughout the study were dimers of Watson−Crick base pairs built from the four DNA bases guanine (G), adenine (A), cytosine (C), and thymine (T). The sugar-phosphate backbone was not included in the calculations as these parts of the system were shown to have only an insignificant effect on the coupling elements.[15,21] As before,[6,7,15,21] hydrogen atoms were used for capping the third bond of the N9/N1 atoms. The helical symmetry of DNA limits the number of different dimers to the 10 combinations listed in Figure 1. Throughout the text we will label dimers relying on the standard abbreviations for Watson−Crick base pairs and we will start

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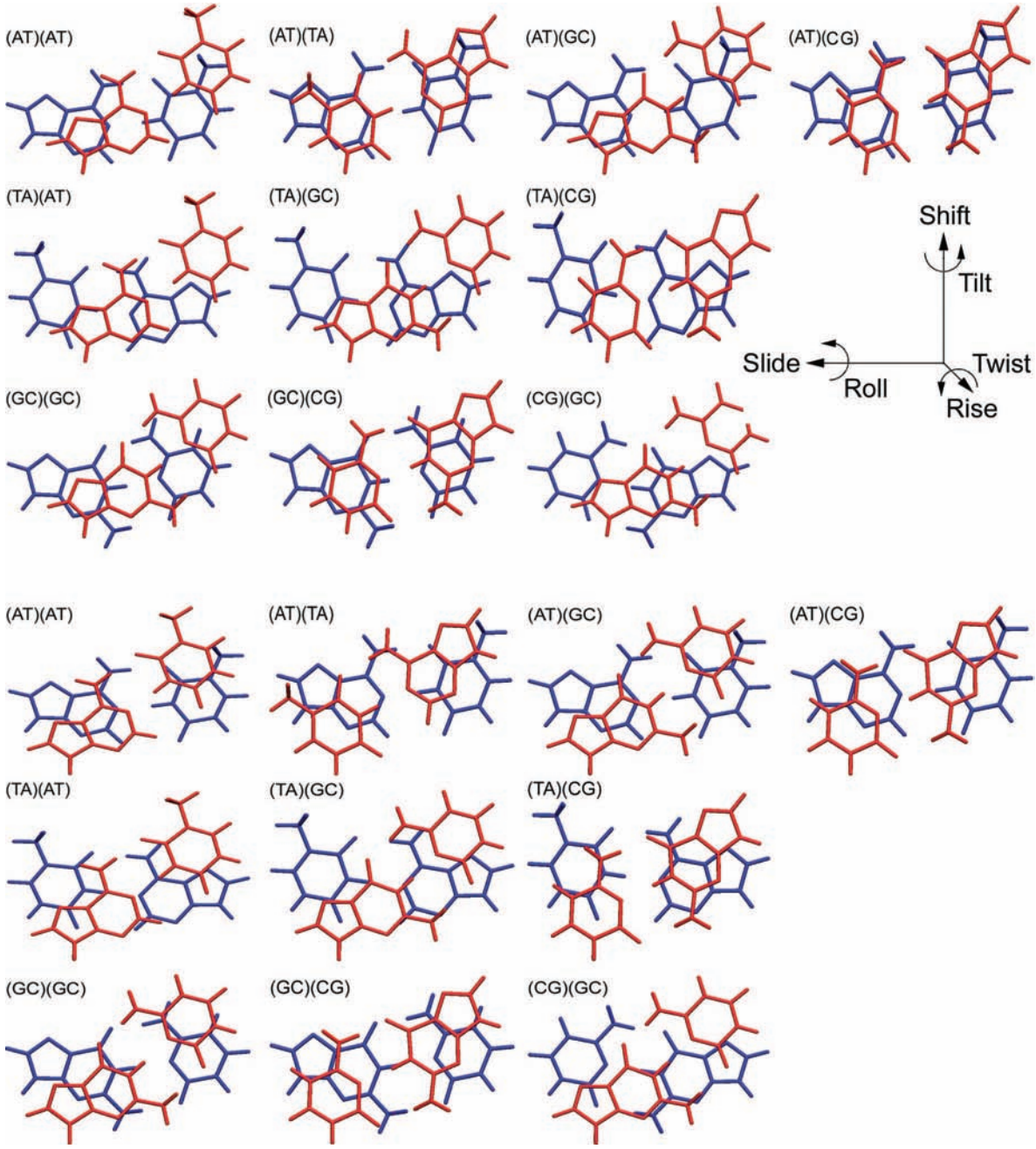

Figure 1. Sketches of the studied base pair dimers in standard A-DNA (upper panel) and B-DNA (lower panel) geometry. Base pairs in blue correspond to those mentioned first in the label of each dimer. The coordinate system of the base step parameters is also shown. Arrowheads indicate positive signs of the parameters.

from the 5′-base of the first base pair; for example, the dimer $^{3'AC-5'}_{5'-TG-3'}$ will be denoted as (TA)(GC).

Molecular geometries of the four bases were optimized at the B3LYP/6-31G* level[22] to establish construction blocks for setting up the base pair dimers. First, reference dimers were built with geometries that correspond to standard A-DNA[23] and B-DNA[24] structures. These models were constructed with the program 3DNA[20b] from standard base pair and base step parameters (Table 1).[23,24] Then, perturbed structures of each reference were created by increasing or decreasing exactly one of the BSPs by a certain amount (Figure 1), keeping the remaining five BSPs at their reference values. In this way, a total number of 320 perturbed structures were generated. The variations of the base step parameters (Table 1) were chosen to correspond to their standard deviations as obtained from a statistical analysis of a substantial set of X-ray structures of A-DNA and B-DNA duplexes.[25] Because the range of slide, rise, and tilt is rather large, dimers with intermediate variations of these three parameters were calculated, too.

We estimated the electronic coupling element H_{DA} between the base pairs of each dimer with the help of the fragment charge difference (FCD) method.[6d] Invoking a two-state model, the coupling matrix element between donor and acceptor states is

$$H_{DA} = (E_2 - E_1)|\Delta q_{12}|\left[(\Delta q_{11} - \Delta q_{22})^2 + 4\Delta q_{12}^2\right]^{-1/2} \quad (1)$$

Here, Δq_{11} and Δq_{22} are the differences between the charges of donor and acceptor in the corresponding adiabatic states, Δq_{12} is the off-diagonal term (see below), and E_2—E_1 is the adiabatic energy splitting between donor and acceptor states. We estimated E_2—E_1 within Koopmans' approximation as difference between the two highest occupied molecular orbitals (HOMO and

TABLE 1: Base Pair and Base Step Parameters of Conventional A-DNA[23] and B-DNA[24] Used for Building the Reference Structures of the Base Pair Dimers[a]

base-pair parameter	A-DNA	B-DNA	base-step parameter	A-DNA	B-DNA	variation
shear	0.00(A-T)	0.00(A-T)	shift	0.00	0.00	±0.5
	−0.15(G-C)	−0.15(G-C)				
stretch	−0.10(A-T)	−0.10(A-T)	slide	−1.70	0.00	±0.5
	−0.20(G-C)	−0.20(G-C)				±1.0
stagger	0.00	0.00	rise	3.28	3.38	±0.25
						±0.5
buckle	0.00(A-T)	0.00	tilt	0.00	0.00	±2.0
	−0.20(G-C)					±5.0
propeller	11.75	−1.25	roll	11.00	0.00	±5.0
opening	−5.80(A-T)	−2.70(A-T)	twist	31.00	36.00	±5.0
	−5.30(G-C)	−1.60(G-C)				

[a] Also listed are the variations of each base step parameter applied when perturbing these reference structures (see text). Distances in Å, angles in degree.

HOMO-1) of the closed-shell neutral base-pair dimer. The fragment charge differences $\Delta q_{mn} = q_{mn}(D) - q_{mn}(A)$ were defined from Mulliken-type expressions:[6d]

$$q_{mn}(F) = \frac{1}{2}\left[\sum_{i\in F} C_{i,\mathrm{HOMO}+1-m}\sum_{j=1}^{M} C_{j,\mathrm{HOMO}+1-n}S_{ij} + \sum_{i\in F} C_{i,\mathrm{HOMO}+1-n}\sum_{j=1}^{M} C_{j,\mathrm{HOMO}+1-m}S_{ij}\right] \quad (2)$$

Here, the generic fragment designator F is either D or A, the state indices m, n take the values 1 or 2, M is the number of atomic functions in the basis set, C_i, C_j are coefficients of the corresponding molecular orbitals, and S_{ij} are overlap integrals.

The FCD method was shown to be quite robust for describing the electronic coupling between base pairs with different degree of overlap.[6d,26] Results for various dimers were very similar to those obtained with the generalized Mulliken−Hush method.[6d,27] An advantage of the FCD method is that it describes in a qualitatively correct manner the diabatic electronic coupling between donor and acceptor moieties, using only information from their neutral adiabatic states. Moreover, this can be done within a fairly large range of D−A energy separations.

All calculations were carried out within the two-state model. This strategy had been shown to provide adequate estimates of the relative magnitude of H_{DA} although the values may not be quantitatively precise.[11b,28] As the foremost aim of the present study was to obtain a complete data set in a systematic fashion, the two-state model was considered as an acceptable compromise between accuracy and computational efficiency. Energies and wave functions of each dimer were calculated at the RHF/6-31G* level[22] and subsequently used in an FCD estimate of H_{DA}.

Results and Discussion

We will discuss the obtained results from two perspectives. We will analyze (*i*) the influence of the *type* of dimers on the magnitude of the coupling, and (*ii*) the effect of the *geometry* of dimers on the coupling strength.

Electronic Coupling Elements of A-DNA and B-DNA Dimers at Standard Geometry. Table 2 collects the values of the FCD coupling elements calculated for the base pair dimers at standard A-DNA and B-DNA geometries. The calculated coupling elements indeed change with the helical conformation of the duplex as characterized by the base step parameters set of the dimers. The largest difference of H_{DA} between A-DNA and B-DNA was calculated for the dimers (TA)(AT), 0.179 eV; (TA)(GC), 0.099 eV; and (AT)(TA), 0.036 eV. In general, the coupling elements calculated for the B-DNA dimers are more uniform; their magnitudes vary between 0.02 and 0.08 eV. In contrast, H_{DA} values of A-DNA dimers span a broader range, from 0.001 to 0.23 eV. The most substantial coupling elements among the A-DNA dimers are for (TA)(AT) at 0.231 eV, followed by (TA)(GC) at 0.124 eV; these are also the only two values above 0.1 eV. The largest H_{DA} value of dimers with standard B-DNA structure is 0.074 eV for (CG)(GC). Dimers containing only G-C base pairs have similar H_{DA} values in the two reference structures. As observed previously, for both helical types the electronic coupling in the homodimer (GC)(GC) is stronger than that in (AT)(AT).[10c,11a]

TABLE 2: Electronic Coupling Elements H_{DA} (in eV) from FCD Calculations on Each Dimer in Standard A-DNA or B-DNA Geometry (Figure 1)[a]

	A-DNA		B-DNA	
dimer	H_{DA}	H_{DA}^{deaza}	H_{DA}	H_{DA}^{deaza}
(AT)(AT)	0.008		0.022	
(AT)(TA)	0.001		0.037	
(AT)(GC)	0.040	0.089	0.043	0.070
(AT)(CG)	0.007	0.007	0.020	0.012
(TA)(AT)	0.231		0.052	
(TA)(GC)	0.124	0.100	0.025	0.017
(TA)(CG)	0.044	0.041	0.060	0.031
(GC)(GC)	0.058	0.115	0.063	0.086
(GC)(CG)	0.010	0.008	0.022	0.009
(CG)(GC)	0.074	0.055	0.074	0.056

[a] The values of dimers containing 7-deazaguanine instead of guanine H_{DA}^{deaza} are also shown.

As is well-known,[6e] a substantial overlap between the purine bases in a dimer is one of the important factors for effective electronic coupling. Guanine and adenine are more easily ionized[29] than the two pyrimidines and therefore they are mostly involved in hole transport along the π-stack of DNA; their overlap notably affects the magnitude of coupling matrix elements.[6e,7b] As can be seen from Table 2, Supporting Information Tables S1, S2, and Figure 1, in the dimers (AT)(AT), (AT)(TA), (AT)(CG), and (GC)(CG) in A-DNA as well as (AT)(CG) and (GC)(CG) in B-DNA, the overlap between the two purine bases is negligible, resulting in small H_{DA} values. For an effective electronic coupling, however, not only the degree but also the type of interaction, e.g., bonding or non-bonding, between the frontier molecular orbitals (MOs) of the bases seems to be essential; see the discussion below. In Supporting Information, Tables S3 and S4, we collected the overlap values between donor and acceptor fragments which

correlate well with the calculated coupling elements of the corresponding dimers (Supporting Information, Figure S1), in accordance with previous analyses.[6e,7b]

Within the two-state model used in this study, the coupling strength will be determined essentially by the two highest occupied molecular orbitals, HOMO and HOMO−1. Analysis of these orbitals of the dimers shows (Supporting Information, Figure S2) that in all cases these two orbitals are dominated by contributions from the HOMO of the two purines. Only in two dimers of A-DNA form is there minor admixture of pyrimidine MOs due to a combination of negligible purine−purine and very efficient purine−pyrimidine interaction. In these two cases, MOs of adenine and thymine mix.

The two frontier occupied orbitals of all dimers always have higher energies than the HOMOs of the isolated bases. Therefore, interactions within the base pair and between neighboring base pairs facilitate the formation of holes compared to their generation in isolated bases, in agreement with experimental observations.[12b]

Depending on the structure of the dimer, however, HOMO and HOMO−1 are either localized on one purine base or represent a linear combination of the two purine HOMOs, i.e., they are delocalized over the dimer. (TA)(AT), (GC)(CG), and (CG)(GC) in both helical types, (AT)(GC) and (TA)(GC) in A-DNA form, and (AT)(TA) in B-DNA form belong to that latter group. There, the bonding combination (in the sense of interbase overlap between π-orbitals) of the two purine HOMOs becomes the HOMO−1 orbital and the antibonding combination gives rise to the HOMO of the dimer. All these dimers are characterized by large H_{DA} values, both due to substantial ΔE values resulting from the linear combination and to a large value of Δq_{12} (eq 1). The only exception is (GC)(CG), where the G-G interaction is not strong enough because of large distances of pertinent atomic centers between the two base pairs.

The dimers with frontier MOs localized on a single purine base can be further divided into two subgroups. In the systems (AT)(CG) of both conformations and (AT)(TA) in A-DNA form, there is no purine−purine interaction, hence no mixing takes place. These three dimers exhibit the smallest overlap (0.001) between the two base pairs (Supporting Information, Tables S3, S4). In consequence, the calculated coupling elements for these structures are very small. In the remaining dimers, namely, (AT)(AT), (TA)(CG), and (GC)(GC) in both forms, and (AT)(GC) and (TA)(GC) in B-DNA conformation, the two frontier orbitals are again localized on the corresponding purine bases despite appreciable purine-purine stacking. In these cases, the orientation of the two molecules is such that one moiety with a large HOMO contribution is stacked on top of a moiety that exhibits a node of the other HOMO or that the two orbitals interact repulsively. Thus, the linear combination between the two HOMOs does not stabilize the system; the frontier MOs of the dimer remain localized. These dimers exhibit electronic couplings of intermediate magnitude resulting from a fairly large ΔE (eq 1).

The fact that (AT)(TA) frontier orbitals can be delocalized over more than one base pair and that thymine does not participate in hole transport along (AT)(AT) and (AT)(TA) fragments of B-DNA have also been observed in a previous theoretical study.[10b]

Response of the Electronic Coupling to the Nucleotide Sequence. Among the systems modeled, the structure sensitivity of the dimer coupling H_{DA} to the BSP considered depends on the particular combination of nucleotides (Figure 2). The coupling also varies with the geometry of the dimer as a detailed analysis of H_{DA} deviations from the reference values shows. According to the maximum variation of the coupling (Table 3), the sensitivity of the dimers towards structural change decreases in the following order: (TA)(AT) > (TA)(GC) > (CG)(GC) > (GC)(GC) > (TA)(CG) > (AT)(GC) > (AT)(AT) > (AT)(TA) > (GC)(CG) > (AT)(CG) in A-DNA form; (CG)(GC) > (AT)(AT) > (GC)(GC) > (TA)(CG) > (AT)(GC) > (TA)(AT) > (AT)(TA) > (TA)(GC) > (GC)(CG) > (AT)(CG) in B-DNA form. These arrangements match in general the order in which the electronic coupling of the reference structures decreases. On the other hand, if one takes the maximum variation as a fraction of the reference value, then the relative change of the electronic coupling of most dimers is rather constant, about 1.6 times the value of the reference.

Within a certain helical type, the sensitivity of the coupling to a change Δ in a base step parameter depends (besides on the amount of Δ) on the nucleotide sequence of the dimer. Nevertheless, some general trends can be observed and on that basis the dimers can be classified into groups. According to the changes of H_{DA} caused by a variation of tilt, twist, and shift, the dimers can be divided into two groups, irrespective of the helical conformation. (AT)(AT), (AT)(GC), (TA)(CG), and (GC)(GC) form a group where the coupling is significantly affected by these three parameters while the sensitivity toward the remaining three parameters is not so systematic. The coupling magnitude in the remaining six dimers is practically not altered when tilt or twist change; the effect of shift is either small for both conformations or is expressed in only one of the forms. This dissimilar behavior of the two groups of dimers is due to the fact that changing shift, tilt, or twist affects mainly the overlap between the bases that belong to the same strand. The first group described above consists only of dimers, in which the two purine bases are in the same strand, whereas in all dimers of the second group, the interaction between the purines is between strands, rendering the coupling fairly insensitive to a variation of shift, tilt or twist.

If one compares the influence of BSPs on the coupling of a specific dimer, but uses either A-DNA or B-DNA helical conformation, it is evident that this effect also depends on the nucleotide sequence.

The amount by which H_{DA} changes with the variation of the three translations will be discussed next. In general, the most notable change of coupling elements is due to rise in A-DNA form (max. deviation ~0.4 eV). In particular, rise influences most significantly the coupling of the A-DNA dimers (TA)(AT), (TA)(GC), and (CG)(GC) and of the B-DNA dimers (CG)(GC), (GC)(GC), (TA)(CG), and (AT)(GC), which have the largest coupling in both reference structures. This finding confirms the known strong correlation between rise and strength of the coupling.[6b,c,7b] The A-DNA dimers (TA)(AT), (TA)(GC), and (CG)(GC) are most sensitive to slide. In B-DNA form, the strength of the perturbation due to slide is similar among all dimers that are affected at all. The effect of shift is largest for (TA)(CG) and (GC)(GC) in A-DNA form, while in B-DNA the base step parameter affects most strongly the dimers (AT)(AT), (TA)(CG), (AT)(GC), and (GC)(GC) (Figure 2, Supporting Information, Tables S1, S2).

Among the three rotational degrees of freedom, the smallest deviation from the coupling with respect to the A-DNA reference structures is caused by roll (~0.1 eV) whereas twist and roll have the largest perturbative effect on B-DNA dimers. For (CG)(GC), (TA)(CG), and (GC)(GC) in B-DNA form, the coupling is most affected by roll. Twist has the largest effect on (GC)(GC) and (AT)(GC) in A-DNA form and on (TA)(CG)

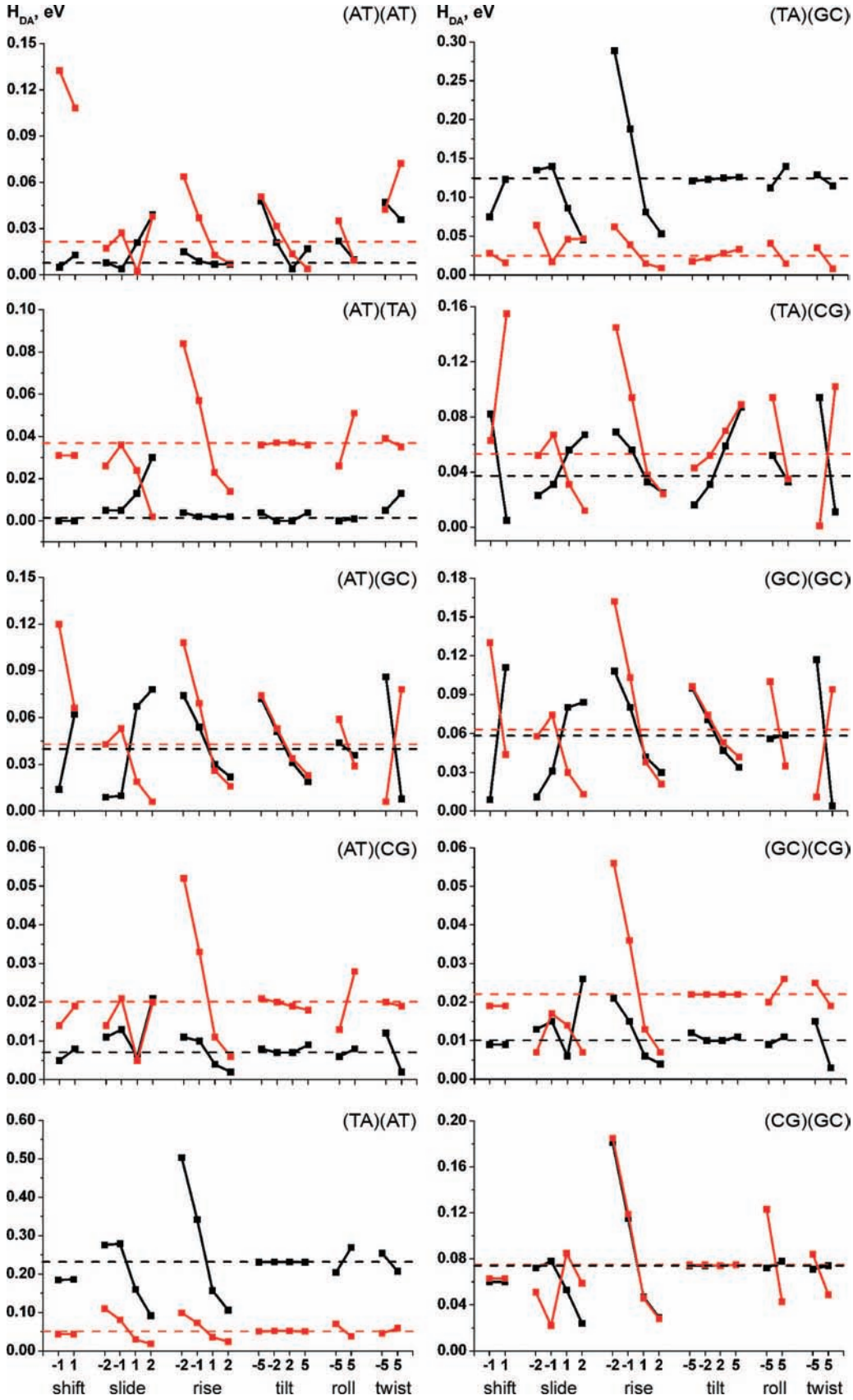

Figure 2. FCD coupling elements of all perturbed dimers starting from A-DNA (black) or B-DNA (red) initial geometry as function of the relative variation of the six base step parameters with respect to the reference structure. Dashed lines mark the corresponding reference values. Relative displacements are in units of 0.5 Å (shift and slide), 0.25 Å (rise), and 1° (angles).

and (GC)(GC) in B-DNA form. Tilt affects most strongly the dimers (AT)(GC), (TA)(CG), and (GC)(GC), for both helix types (Figure 2, Tables S1, S2).

Thus far, we noted some trends in the variation of the electronic coupling upon changes of nucleotide composition; variations in shift, tilt, and twist allowed us to classify the dimers

TABLE 3: Maximum Absolute Change of the Coupling Element (in eV) in the Various Base Pair Dimers Due to Structural Perturbations by Variation of the Base-Step Parameters

dimer	A-DNA	B-DNA
(AT)(AT)	0.040	0.110
(AT)(TA)	0.029	0.047
(AT)(GC)	0.046	0.077
(AT)(CG)	0.014	0.032
(TA)(AT)	0.272	0.058
(TA)(GC)	0.165	0.039
(TA)(CG)	0.050	0.095
(GC)(GC)	0.059	0.099
(GC)(CG)	0.016	0.034
(CG)(GC)	0.107	0.111

into various groups. Next, we will analyze the H_{DA} values by taking into account the specific characteristics of particular dimers.

Response of the Electronic Coupling to Individual Base Step Parameters. Figures 3 and 4 show how each of the six base step parameters affects the electronic coupling H_{DA} in the systems under study. Such replotting of the data already shown in Figure 2 highlights the effect of the various BSPs.

Figure 3 demonstrates that among the three translational degrees of freedom only rise has an unequivocal qualitative effect, irrespective of the type of dimer or the helical conformation. As expected, smaller values of rise always induce stronger coupling and vice versa, because a reduced distance between the planes of the two base pairs uniformly enhances the overlap of all interacting atomic centers without changing the type of interaction. The influence of slide and shift is less uniform. The dimers (AT)(CG) and (GC)(CG) are practically insensitive to these two parameters in both conformations because the variation of these translations does not appreciably affect G-A or G-G interaction between the strands. The effect of slide on the remaining systems seems to be specific to the dimers, depending both on the nature of the dimer and the helical conformation. In A-DNA form, at least the coupling values vary systematically for a given dimer when going from negative to positive values of slide. For most of the dimers in A-DNA form, values of slide that are more negative than −2.2 Å no longer have an essential effect on the coupling (Figure 3); dimer (GC)(GC) is the only exception to this trend.

Only four dimers in A-DNA form are appreciably affected by shift, namely (AT)(GC), (TA)(GC), (TA)(CG), and (GC)(GC). In these systems, the coupling correlates with the variation of the parameter. For instance, a negative shift in (GC)(GC) leads to a decrease of H_{DA} while a positive shift strengthens the coupling. In the other four dimers, namely (AT)(AT), (AT)(GC), (TA)(CG), and (GC)(GC) (in B-DNA form), the coupling is sensitive (always increasing) to at least one of the variations of shift (Figure 3, Supporting Information, Tables S1, S2).

The influence of the rotational degrees of freedom is in general more uniform for the two types of helices (Figure 4). Again, in both conformations, the coupling of the two dimers (AT)(CG) and (GC)(CG) hardly changes with the three rotations, similar to the absence of response towards translational perturbation, in agreement with the range of H_{DA} being the narrowest as discussed above. Combined with the small magnitude of the coupling, this singles out these two dimers as building blocks with the worst coupling for hole transfer among the models studied.

The effect of roll on H_{DA} of the remaining dimers is most systematic among all rotations (Figure 4). Practically none of the A-DNA couplings is affected by a variation of roll, probably due to the already substantial reference value and the overall shape of the A-DNA helix, in which the bases are more displaced along the long axis of the base pair than in B-DNA. Thus, rotation about this axis does not change appreciably the pattern of interaction between the molecules. In B-DNA form, the coupling elements of all eight dimers anticorrelate with the change of roll. Twist affects four dimers, (AT)(AT), (AT)(GC), (TA)(CG), and (GC)(GC), in a noticeable fashion, and it does so for changes from both helical reference structures. Thus, twist is the only degree of freedom among the six BSPs, whose influence on the electronic coupling does not depend on the type of the helix. In the affected dimers, there is again an anticorrelation between the coupling and the amount of twist, similar to findings for roll.

The three parameters slide, rise, and tilt are those that entail more substantial overall variations from the reference. Thus, results for intermediate values are of interest to judge approximately the quality of the variation. In all dimers where the coupling depends notably on the tilt, namely (AT)(AT), (AT)(GC), (TA)(CG), and (GC)(GC), this dependence is linear (Figure 2). The same holds for rise of all models. In contrast, the coupling depends on slide in a non-linear fashion because this parameter changes both intra- and interstrand interactions between the base pairs.

As an example, we discuss the dimer (TA)(CG) in more detail. In this system, the coupling varies linearly with the change of slide from the A-DNA reference geometry: the more negative the value of slide, the weaker the coupling. This structural change reduces the overlap between the five-atom ring of adenine and the six-atom ring of guanine without simultaneously introducing new patterns of overlap. In contrast, starting from the B-DNA reference geometry, for slide values of 1.0, 0.5, and −0.5 Å the predominant overlap occurs between the six-atom rings of the two purines, while for a slide of −1.0 Å mostly the five-atom ring of adenine and the six-atom ring of guanine interact. As already mentioned, changing the type of overlap in this fashion alters the coupling, which allows one to rationalize the change of the trend of H_{DA} for the B-DNA conformation of this dimer. In none of the (TA)(CG) configurations discussed is there any notable overlap of the pyrimidine with the purines or among the two pyrimidine moieties.[6e]

The dimer (AT)(TA) provides an example for how the interstrand interaction changes with a variation of slide. In the reference A-DNA structure, the two adenines do not interact; H_{DA} almost vanishes. In B-DNA, the two amino groups of adenines interact, which results in a coupling element of ∼0.04 eV. When making the slide less negative in the A-DNA dimer, two effects take place. First, the two adenine bases approach each other, and the distance between their amino N centers decreases from 4.72 Å at a slide of −2.7 Å to 3.59 Å at a slide of −0.7 Å. Second, the intrastrand overlap between adenine and thymine increases from 0.0001 to 0.0005. Both effects combined increase the coupling, but the overall effect is more pronounced in configurations where the amino N centers are less than 4.0 Å apart. The same factors govern the change of H_{DA} when starting from the B-DNA reference geometry; in this case, the two amino N centers approach each other on going from negative to positive values of slide (their distance changes from 3.77 Å at slide −2.70 Å to 3.45 Å at slide −0.7 Å), but at the same time the overlap between adenine and thymine of the same strand decreases, from 0.0012 to 0.00005. The structure with a slide of −0.5 Å features the best combination of A-T

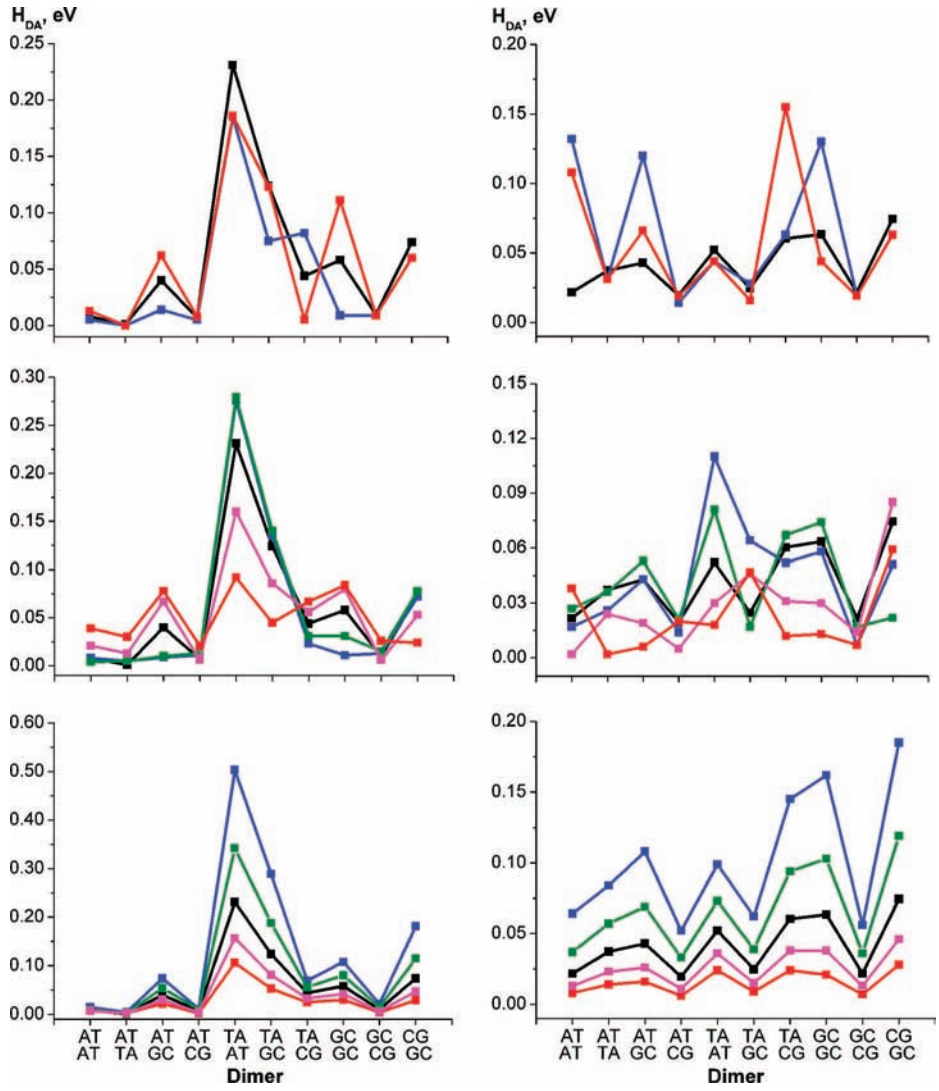

Figure 3. Influence of shift (upper panels), slide (middle panels), and rise (lower panels) on the calculated coupling elements of the perturbed dimers starting from A-DNA (left panels) or B-DNA (right panels) reference geometries. Color coding: blue, full decrement; green, half-size decrement; black, reference; magenta, half-size increment; and red, full increment of the BSP parameters.

overlap and N−N distance and therefore has the largest coupling among all four systems.

Specific results of the present comprehensive study agree well with values available from theoretical and experimental investigations of specific systems. The observation that twist affects more the coupling in (GC)(GC) than in (AT)(AT) dimers is in line with the findings of a previous model study of such homoduplexes.[10c] The change of H_{DA} with roll and twist reported in a former investigation[10b] of (AT)(TA) resembles that found here. Just as in an earlier study[7b] on the dimers (AT)(AT) and (TA)(CG) in B-DNA, we also found the coupling to be most sensitive to variations of shift. Our data also lead to the conclusion that a computational model beyond the tight-binding approximation is required if the sensitivity of the coupling towards changes of BSPs is to be properly represented. Previously, such a simple computational approach[11a] failed to diagnose any response of the coupling to changes of twist and even of rise.

Coupling Elements of Dimers Containing a Modified Nucleobase. Obviously, one may use the results obtained so far to construct a duplex with an expected high capacity for hole transfer by assembling a sequence of dimers with large coupling elements. However, if one tries to do this using the calculated matrix elements for the reference geometry, one can not avoid building sequences where a dimer with a large coupling is always followed by another dimer having a negligible coupling. This holds for both helical conformations. As the hole transfer rate decays exponentially with the distance between donor and acceptor,[3,30a] even one intervening small coupling will lead to a significantly decreased overall efficiency of hole transfer.

One may increase the electronic coupling in dimers with weak coupling by chemical modification of at least one of the bases involved. 7-Deazaguanine (D) has been used extensively in experimental studies of hole transfer along DNA[4b,30] because it is more easily oxidized than guanine[30] and it readily replaces that base in Watson−Crick base pairs. In this spirit, we calculated the coupling elements of all guanine-containing dimers for both helical conformations, but with 7-deazaguanine instead of guanine in the G-C base pairs (Table 2). These data show that substitution of guanine with its modified analogue indeed has an effect on the calculated coupling. The amount of influence is different for dimers in A-DNA and B-DNA form, but the trends of the changes are similar.

The three smallest couplings of the A-DNA dimers remain essentially unaffected by this (formal) substitution. Among the

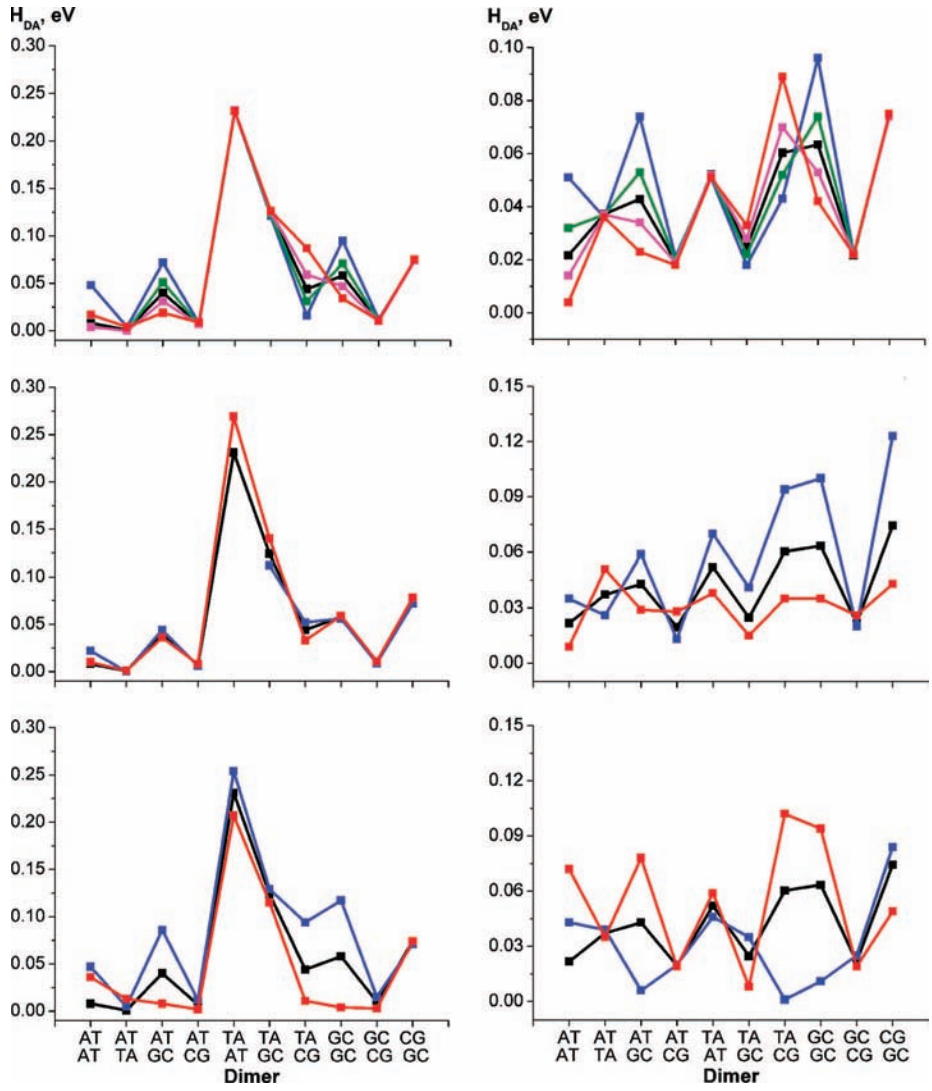

Figure 4. Influence of tilt (upper panels), roll (middle panels), and twist (lower panels) on the calculated coupling elements of the perturbed dimers starting from A-DNA (left panels) or B-DNA (right panels) reference geometry. Color coding: blue, full decrement; green, half-size decrement; black, reference; magenta, half-size increment; and red, full increment of the BSP parameters.

remaining four dimers of A-DNA form, the couplings of (TA)(GC) and (CG)(GC) decrease upon the change while the couplings of (AT)(GC) and (GC)(GC) increase. In contrast, the replacement mainly weakens the coupling of the dimers in B-form. However, the coupling in (AT)(GC) and (GC)(GC) becomes larger, as it also happens for the same dimers in A-DNA form. These findings indicate that changes induced by substitution of G by D depend exclusively on the chemical composition of the dimer, but not on the helical conformation.

With respect to the sensitivity upon variation of base step parameters (Supporting Information, Figure S3), the dimers containing 7-deazaguanine do not show new features. Trends are preserved, but the curves are often shifted from those of the standard, guanine.

As important consequence of the increased coupling magnitude of the two dimers (AT)(GC) and (GC)(GC), we note that introduction of 7-deazaguanine allows one to construct a model DNA duplex which contains a sequence of dimers with substantial electronic coupling among the base pairs. From the calculated values at the reference geometries, the best sequence would be an A-DNA type oligomer with the nucleotide sequence 5′-CT(ADD)$_n$CD-3′. That sequence in B-DNA geometry also promises a high potential capacity for hole transfer.

Summary and Conclusions

We calculated electronic coupling elements H_{DA} for all dimers of DNA Watson−Crick base pairs, and we explored for the first time in a systematic fashion the sensitivity of these couplings in response to variations of each of the six base step parameters. To test the influence of the helical conformation of the duplex on H_{DA}, we used dimers that reflect the local structure of either A-DNA or B-DNA. With these initial reference geometries, we explored the structure sensitivity of H_{DA}. We also studied the effect of a chemical modification by formally replacing guanine with 7-deazaguanine. In total, the current study comprised *ab initio* calculations of 499 coupling elements.

Detailed analysis confirmed that the electronic coupling is sensitive both to the nucleotide sequence within a dimer and to the relative position of the base pairs, as demonstrated by separate variation of each BSP. We were able to classify the dimers into two groups according to the response of their coupling to changes of shift, tilt, and twist. The effect of rise was found to be systematic for all dimers, both in A-DNA and B-DNA form, reflecting its regular effect on the π overlap between the base pairs. Response to slide and roll turned out to be dimer-specific. The difference of the electronic coupling

between the two helical types was expressed already in the ideal reference structures. Twist was found to be the only structural characteristic among the six BSPs, for which the influence of the coupling did not depend on the helix conformation.

Substitution of guanine by its 7-deaza analogue affected the coupling exclusively in a dimer-specific way. On the basis of the calculated values for H_{DA} of modified and non-modified dimers, we suggested a model duplex with potentially high capacity for hole transfer. This is just one example how the data base of coupling elements presented here may be exploited when designing experiments or further computational studies on the charge transport in DNA oligomers.

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Supporting Information Available: Calculated H_{DA} values of all base pair dimers in A-DNA or B-DNA form for different values of the base step parameters (Tables S1, S2); values of the HOMO/HOMO−1 overlap between donor and acceptor moieties in A-DNA and B-DNA form dimers (Tables S3, S4); correlation plot of FCD coupling element versus fragment overlap for all dimers (Figure S1); shapes of HOMO and HOMO−1 as obtained from RHF/6-31G* calculations for all dimers in the reference A-DNA and B-DNA geometry (Figure S2); sensitivity towards variation of the base step parameters of electronic coupling elements H_{DA} estimated for dimers containing 7-deazaguanine (Figure S3). This material is available free of charge via the Internet at http://pubs.acs.org.

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