Electronic coupling between Watson–Crick pairs for hole transfer and transport in desoxyribonucleic acid

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Electronic matrix elements for hole transfer between Watson–Crick pairs in desoxyribonucleic acid (DNA) of regular structure, calculated at the Hartree–Fock level, are compared with the corresponding intrastrand and interstrand matrix elements estimated for models comprised of just two nucleobases. The hole transfer matrix element of the GAG trimer duplex is calculated to be larger than that of the GTG duplex. ''Through-space'' interaction between two guanines in the trimer duplexes is comparable with the coupling through an intervening Watson–Crick pair. The gross features of bridge specificity and directional asymmetry of the electronic matrix elements for hole transfer between purine nucleobases in superstructures of dimer and trimer duplexes have been discussed on the basis of the quantum chemical calculations. These results have also been analyzed with a semiempirical superexchange model for the electronic coupling in DNA duplexes of donor (nuclobases)–acceptor, which incorporates adjacent base–base electronic couplings and empirical energy gaps corrected for solvation effects; this perturbation-theory-based model interpretation allows a theoretical evaluation of experimental observables, i.e., the absolute values of donor–acceptor electronic couplings, their distance dependence, and the reduction factors for the intrastrand hole hopping or trapping rates upon increasing the size of the nucleobases bridge. The quantum chemical results point towards some limitations of the perturbation-theory-based modeling. [DOI: 10.1063/1.1352035]

I. INTRODUCTION

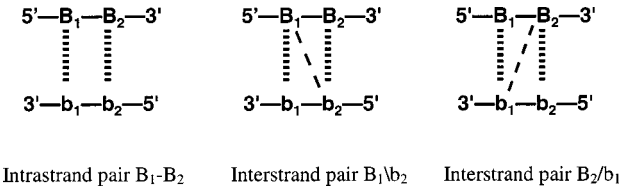
While the central primary biological function of desoxyribonucleic acid (DNA) involves information storage and transduction, its electrical properties are of considerable interest in the novel research areas of the dynamics, response, and function of nanostructures and biosensors. The majority of the experimental information on charge transfer and transport in DNA[1–12] pertains to the positive charge (hole) migration. In view of the hierarchy of the oxidation potentials of single nucleobases in solution[13,14] and of the ionization potentials of nucleobases in duplexes (G<A<C,T),[15] it is inferred that hole hopping occurs between guanine (G) bases. Furthermore, it has been shown experimentally that G^+ can be generated in DNA far away from an oxidant due to long-range hole transport.[1–9] Neighboring nucleobases affect the stability of guanine radical cations (G^+) in an essential fashion. Our calculations showed that the energetic stabilization of a nucleobase B^+ in 5′-XBY-3′ duplexes is considerably influenced by the subsequent base Y while the effect of the preceding base X is rather small.[15] Several experimental[3,8,10,11] and computational[15–17] studies corroborated that GG and GGG fragments act as hole traps in DNA.

The conceptual framework for quantifying charge migration in DNA rests on the theory of charge transfer, with the rates of the elementary processes being determined by the electronic coupling and the nuclear Franck–Condon factors.[18–23] In a previous study[24] we considered the rates for hole transfer and hopping in DNA by calculating electronic coupling matrix elements in model systems containing two nucleobases B_1 and B_2(B_1,B_2=A,G,C,T). All possible pairs of intrastrand combinations as well as several interstrand pairs were calculated. In the present work we extend that study on hole transfer matrix elements in DNA to systems which consist of two and three Watson–Crick pairs (WCP). We calculated hole transfer matrix elements between nucleobases with the lowest ionization potentials (G and A), which belong to the superstructures of two and three WCPs in DNA. These data for dimer and trimer duplexes establish a semiquantitative scheme for hole transfer and transport in DNA on the basis of the superexchange model.

II. METHOD

The calculations of electronic matrix elements for hole transfer between pairs of nucleobases in one strand (intrastrand coupling) and between two nucleobases belonging to complementary strands of a duplex (intrastrand coupling) in the regular DNA structure were described in our previous article.[24] We have also performed calculations of hole transfer matrix elements between the members of the Watson–Crick pairs G═C and A═T in the regular structure of DNA

using the two-state model[25] for charge transfer. In what follows, we shall denote intrastrand nucleobases $5'-B_1-B_2-3'$ as B_1-B_2; the base of the opposite strand complementary to B_i will be referred as b_i (see Scheme A)



Intrastrand pair B_1-B_2 Interstrand pair $B_1\backslash b_2$ Interstrand pair B_2/b_1

For brevity, we shall refer to the two different configurations of interstrand pairs $5'-B_1-b_2-5'$ and $3'-B_2-b_1-3'$ as $B_1\backslash b_2$ and B_2/b_1, respectively, where the backslash and the slash are chosen to represent the structural schemes $5'\rightarrow 5'$ and $3'\rightarrow 3'$, respectively. For the base sequence B_1B_2 the intrastrand base–base matrix element in the $5'-3'$ direction is denoted as $V(B_1\backslash B_2)$, while the interstrand matrix elements are denoted as $V(B_2/b_1)$ for the $5'-5'$ configuration and as $V(B_1\backslash b_2)$ for the $3'-3'$ configuration. The electronic coupling in a single WCP A═T or G═C will be denoted by $V(B_1{=}b_1)$.

Electronic coupling matrix elements for hole transfer between the nucleobases of the lowest ionization potential, i.e., the purine bases G and A, were calculated for all possible combination of GC and AT pairs. The structures of the models were constructed with the program SCHNARP[26] using the step parameters of regular B–DNA (rise: 3.38 Å, twist 36°) as well as experimental idealized atomic coordinates of the nucleobases.[27,28] The system $[(B_1b_1),(B_2b_2)]$ shown in Scheme A gives rise to four configurations of two nucleobases (previously represented by two-base couplings[24]). Ten different dimer duplexes denoted as $[(B_1b_1),(B_2b_2)]$ (see Scheme A) were considered with the sequences given in the direction $5'\rightarrow 3'$: [(GC), (GC)], [(GC), (CG)], [(CG), (GC)], [(AT), (AT)], [(AT), (TA)], [(TA), (AT)], [(GC), (AT)], [(GC), (TA)], [(AT), (GC)], [(AT), (CG)].

For instance, the structures [(GC), (AT)] and [(TA), (CG)] are equivalent and so are the structures [(CG), (CG)] and [(GC), (GC)] (see Scheme A). The electronic coupling matrix elements between purine bases in a duplex are denoted by $V[(B_1b_1),(B_2b_2)]$.

Apart from these ten dimers, we also considered the two trimer duplexes GAG≡[(GC), (AT), (GC)] and GTG≡[(GC), (TA), (GC)] and the complex G_G. The last system consisting of two GC pairs was generated by removing the central AT pair from the trimer GAG. This configuration may also be obtained from two GC pairs using step parameters of 6.76 Å and 72° for rise and twist, respectively. Calculations on G_G allow to estimate the role of through-space guanine–guanine interaction in the trimers GAG and GTG.

The common two-state model of electron transfer was applied.[25] The electronic coupling matrix elements for equivalent donors and acceptors, i.e., within the structures [(GC), (CG)], [(CG), (GC)], [(AT), (TA)], and [(TA), (AT)], were estimated as half of the splitting Δ of the adiabatic states.[25] Other pairs of regular structure are not equivalent. In those cases, the minimum splitting between two adiabatic states had to be found. For this purpose, an external electric field was applied[24,29] to bring donor and acceptor states into resonance. This procedure of estimating the coupling matrix element does not provide the sign (phase) of the coupling matrix element.

TABLE I. Electronic coupling matrix elements (in eV) for hole-transfer between two nucleobases in the regular structure of DNA calculated using HF/6-31G*.

	Intrastrand[a]		Interstrand	
Base pair	$5'-B1-B2-3'$	$3'-B1-B2-5'$	$B_1\backslash b_2$	B_2/b_1
GG	0.084	0.084	0.019	0.043
AA	0.030	0.030	0.034	0.062
CC	0.041	0.041	0.0007	0.002
TT	0.158	0.158	0.003	0.001
GA	0.089	0.049	0.021	0.004
GC	0.110	0.042	0.010	0.025
GT	0.137	0.085	0.009	0.013
AC	0.061	0.029	0.001	0.013
AT	0.105	0.086	0.016	0.007
CT	0.100	0.076	0.001	0.003

[a]From Ref. 24.

Invoking Koopmans' approximation, the energy splitting $\Delta = E_2 - E_1$ between two adiabatic states of the cationic system can be estimated as the difference of the one-electron energies of the HOMO (highest occupied molecular orbital) and the subsequently lower-lying orbital HOMO-1 of the corresponding closed-shell neutral system, $\Delta \approx \varepsilon_{\mathrm{HOMO}-1} - \varepsilon_{\mathrm{HOMO}}$. We have adopted this Hartree–Fock based approach as such results have been found to agree very well with those of the more accurate complete active space–state interaction method (CASSI).[30]

The Hartree–Fock self-consistent field calculations of the present work have been carried out with the program GAUSSIAN98 using the standard basis set 6-31G*.[31] For several calculations, more extended basis sets 6-311+G* and 6-311++G** including diffuse functions were employed.

III. RESULTS AND DISCUSSION

For the sake of completeness we present in Table I the electronic coupling matrix elements for hole transfer between nearest-neighbor nucleobases for the interstrand coupling (reported in Ref. 24) and for the interstrand coupling (partially reported earlier).[24] We have also calculated the base–base hole coupling within Watson–Crick pairs (GC) and (AT), which were found to be $V(G{=}C) = 0.050$ eV and $V(A{=}T) = 0.034$ eV.

A. Electronic coupling between Watson–Crick pairs

Each of our models consists of two WCPs and contains two purine bases (G or A) and two pyrimidine bases (C or T). According to the calculations, the two highest-lying orbitals HOMO and HOMO−1 of each duplex are mainly localized on purine nucleobases. Of course, this finding is not unexpected since the ionization potentials of the nucleobases increase in the order: G<A<C≈T.[15] Thus, the two highest occupied MOs are localized on the purines, whereas the two

TABLE II. Matrix elements V for hole transfer in DNA. Comparison between V values for two Watson–Crick pairs with the corresponding nucleobases pair, and the superexchange model (all in eV).

Two Watson–Crick pairs	V [WCP][a]	Corresponding purine pair[b]	$V(B_1:B_2)$[c]	Superexchange model[d] V_S
[(GC), (GC)], [(CG), (CG)]	0.093	G–G	0.084	0.085
[(GC), (CG)]	0.022	G\G	0.019	0.026
[(CG), (GC)]	0.078	G/G	0.043	0.046
[(AT), (AT)], [(TA), (TA)]	0.026	A–A	0.030	0.029
[(AT), (TA)]	0.055	A\A	0.034	0.043
[(TA), (AT)]	0.050	A/A	0.062	0.055
[(GC), (AT)], [(TA), (CG)]	0.122	G–A	0.089	0.090
[(AT), (GC)], [(CG), (TA)]	0.025	A–G	0.049	0.043
[(GC), (TA)], [(AT), (CG)]	0.026	G\A, A\G	0.021	0.029
[(TA), (GC)], [(CG), (AT)]	0.027	G/A, A/G	0.004	0.009

[a]Matrix elements calculated for hole transfer between two WCPs.

[b]The orientation of two purine nucleobases B_1,B_2 are denoted as: B_1–B_2 for intrastrand configuration, B_1/B_2 and $B_1\backslash B_2$ for the two different configurations of the interstrand pairs (see text).

[c]Coupling matrix element between two nucleobases B_1 and B_2 calculated from a two-base model (Table I) for the configuration indicated in the preceding column. The configuration is indicated generically as B_1:B_2.

[d]$V_s = V(B_1:B_2) + \delta V$, where δV is the superexchange second-order correction, evaluated from Eqs. (1)–(3). The sign of δV was chosen to yield best agreement between the calculation for the WCP and for the superexchange model.

occupied MOs following at energies, HOMO−2 and HOMO−3, are localized on pyrimidine nucleobases.

The resulting coupling matrix elements for hole transfer between purine bases within all dimer duplexes are collected in Table II. For comparison, the matrix elements for purine–purine two-base couplings (both intra- and interstrand configuration) are also presented. Formally, the two-base systems can be generated from the corresponding duplexes by dropping the two pyrimidine bases; the atomic coordinates of the purine bases remain unchanged. Our methodology for the analysis of the coupling between WCPs rests on the comparison to the direct coupling between the corresponding bases and on the consideration of a superexchange correction to the coupling between WCPs.

First, let us consider the systems with two identical Watson–Crick pairs where the purine bases belong to the same strand. The matrix elements for [(GC), (GC)] and [(AT), (AT)] are calculated at 0.093 and 0.026 eV, respectively. These values are close (within 10%) to the hole-transfer matrix elements calculated for the intrastrand interactions G–G and A–A which were estimated as 0.084 and 0.030 eV, respectively (Table II). The proximity of the numerical results for the coupling between these two WCPs and the intrastrand base–base interactions can be readily rationalized by expressing the coupling between WCPs in terms of direct coupling and a superexchange correction. Thus for the coupling within the systems [(GC), (GC)] and [(AT), (AT)] we obtain the superexchange model result

$$V_s[(\mathrm{Bb}),(\mathrm{Bb})] = V(B-B) + V(B=b)\{V(b/B) + V(b\backslash B)\}/\Delta E_{\mathrm{Bb}}, \quad (1)$$

where B, b=G,C or B, b=A,T, and ΔE_{Bb} is the energy gap for hole transfer from B to b. Different approaches may be used for estimating this energy gap: (i) experimental redox potentials for nucleobases in a polar solvent (see below), (ii) results of semiempirical calculations on DNA fragments[15] that account for the stacking interaction between nucleobases, and (iii) one electron energies from the present self-consistent field (SCF) calculations. The data of our semiempirical calculations[15] will be used throughout the article unless explicitly mentioned otherwise. According to that estimate, $\Delta E_{\mathrm{GC}} = 1.6\,\mathrm{eV}$ and $\Delta E_{\mathrm{AT}} = 0.8\,\mathrm{eV}$. The superexchange correction contains the matrix element $V(\mathrm{B=b})$ for the (GC) pair: this coupling matrix element is quite large. The superexchange corrections determined by the small interstrand coupling (Table II) contribute only 1%–3% in Eq. (1). We assert that hole transfer within the dimer duplexes [(GC), (GC)] and [(AT), (AT)] is dominated by direct intrastrand coupling, i.e. G–G for [(GC), (GC)] and A–A for [(AT), (AT)].

The preceding discussion shows that the superexchange model in combination with electron coupling matrix elements of two-base models is rather successful. Yet, a critical remark on this procedure of interpreting our quantum chemical results of complex models by Eq. (1) is appropriate. It relates to the fact that all our quantum chemical results for the coupling matrix elements are derived from energy splittings and thus yield only absolute values. For estimating electron transfer rates this is not a restriction since rates depend on the square of the coupling matrix element between initial and final states only. On the other hand, application of Eq. (1) [or of Eqs. (2) and (3), see below] requires knowledge of the relative signs of the various two-base coupling elements which we have chosen such that the superexchange model results fit best with the quantum chemical results of the complex models. Therefore, our choice of signs rests on the assumption that the superexchange-based perturbation analysis is valid, and thus agreement with individual quantum chemical results cannot be taken as a confirmation of such analysis. However, the overall success of our approach lends support to our strategy.

Exchange of nucleobases within the first pair, [(GC),(GC)]→[(CG),(GC)], or the second pair, [(GC),(GC)]→[(GC),(CG)], leads to two new systems,

where the guanine moieties belong to distinct strands. Therefore, the first-order contribution to matrix elements of the two systems is determined by the direct interstrand interaction between the guanine units. Again, we express the coupling for the systems [(GC), (CG)] and [(CG), (GC)] in terms of direct and superexchange interactions,

$$V_S[(\mathrm{Bb}),(\mathrm{bB})] = V(\mathrm{B/B}) + 2V(\mathrm{B{=}b})V(\mathrm{B{-}b})/\Delta E_{\mathrm{Bb}}, \tag{2a}$$

$$V_S[(\mathrm{bB}),(\mathrm{Bb})] = V(\mathrm{B\backslash B}) + 2V(\mathrm{B{=}b})V(\mathrm{B{-}b})/\Delta E_{\mathrm{Bb}}, \tag{2b}$$

where B, b=G,C and the energy gaps ΔE_{Bb} were obtained previously.[15] From Eq. (2) we infer that the superexchange correction terms now involve moderately large intrastrand base–base coupling, with these corrections amounting to 10%-30% (Table II). The coupling between these WCPs exhibits a configurational asymmetry, with quite different values of 0.022 eV for [(GC), (CG)] and 0.078 eV for [(CG), (GC)] (Table II). Let us compare these results to those calculated for the superexchange model (Table II). For [(GC), (CG)] Eq. (2) gives a direct interstrand contribution of 0.019 eV and a value of 0.026 eV with the superexchange correction, compared with the result of 0.022 for the WC pair calculation. The value of 0.078 eV for [(CG), (GC)] is higher than the direct interstrand G/G contribution of 0.043 eV and the superexchange corrected contribution, Eq. (2), of 0.046 eV (Table II). From the comparison of the electronic coupling in [(GC), (CG)] and [(CG), (GC)] we infer that the matrix elements of related systems are very sensitive to the order of a WCP in the model. The guanine–guanine interstrand coupling depends crucially on the mutual orientation of these bases, i.e., G\G or G/G, in DNA. To check whether the computational results are reasonably stable with respect to the basis set used we repeated the calculation on [(GC), (CG)] using the very flexible basis set 6-311++G** which contains diffuse exponents and polarization functions also on hydrogen atoms. The calculated matrix element of 0.025 eV is similar to the value of 0.022 eV obtained within the standard 6-31G* basis set, yet the computational effort differs by a factor of 40.

Next, we compare the electronic coupling matrix elements for the structures [(AT), (TA)] and [(TA), (AT)] where the adenine bases belong to opposite DNA strands with the results of two-base models for the orientations A\A and A/A (Table II). These two couplings can be expressed in terms of Eqs. (2a) and (2b) with B,b=A,T. For the systems [(AT), (TA)] and [(TA), (AT)] the direct contribution to the interaction involves the interstrand A\A and A/A couplings, respectively, whose magnitude is larger than that for the intrastrand A–A pair coupling (Table I). On the other hand, the superexchange correction terms [(AT), (TA)] and [(TA), (AT)] (Table II), which involve the contribution of intrastrand couplings, are quite large (10%–30%). Bearing in mind that we do not calculate the sign of the coupling matrix elements (both between WCP and between bases), we assert that for [(AT), (TA)] a positive superexchange correction (with $\Delta E_{\mathrm{AT}} = 0.8\,\mathrm{eV}$) applies in Eq. (2), resulting in a calculated coupling of 0.043 eV, while for [(TA), (AT)], a negative superexchange correction in Eq. (2) results in a calculated coupling of 0.055 eV. Then, the results corrected by the superexchange term are in reasonable agreement with the calculated couplings for the full model of two WCPs. While the A/A and A\A base couplings differ markedly, the coupling strengths for [(AT), (TA)] and for [(TA), (AT)] are rather similar due to large canceling contributions of the superexchange interactions.

We have already seen that the strength of the electronic coupling for hole transfer can depend crucially on the ordering of two pairs in DNA, e.g., [(GC), (CG)] and [(CG), (GC)] (Table II). As a further example, we consider hole transfer between G and A in the systems [(GC), (AT)] and [(AT), (GC)], where the purine bases belong to the same strand. We express again the coupling for [(GC), (AT)] and [(AT), (GC)] in terms of direct and superexchange interactions

$$\begin{aligned} V_S[(\mathrm{B_1,b_1}),(\mathrm{B_2b_2})] = {} & V[\mathrm{B_1{-}B_2}] \\ & + V(\mathrm{B_1{=}b_1})V(\mathrm{b_1\backslash B_2})/\Delta E_{\mathrm{B_1b_1}} \\ & + V(\mathrm{B_2{=}b_2})V(\mathrm{B_1/b_2})/\Delta E_{\mathrm{B_2b_2}}, \end{aligned} \tag{3}$$

where B_1, b_1=G, C and B_2, b_2=A, T, or B_1, b_1=A, T and B_2, b_2=G, C, while $\Delta E_{\mathrm{B_1b_1}}$ and $\Delta E_{\mathrm{B_2b_2}}$ represent the appropriate energy gaps. The direct couplings G–A or A–G, as well as the perturbative results from Eq. (3), i.e., 0.090 eV for [(GC), (AT)] and 0.043 eV for [(AT), (GC)] (Table II), exhibit the same trend of large directional asymmetry as the calculated couplings between WCP. Finally, for the system [(GC), (T,A)] we find a large superexchange correction (30%) for the direct interstrand G/A coupling, with the perturbation expansion resulting in a coupling of 0.029 eV, in good agreement with the calculation (0.026 eV) of the coupling between WCPs (Table II). The perturbative superexchange correction is problematic for the system [(TA), (GC)], where the direct coupling between the two purine bases is very small ($4\times10^{-3}\,\mathrm{eV}$) and the superexchange correction gives 30% of the coupling between the WCP.

From these results and analysis of the matrix elements for hole transfer between neighboring WCP we conclude the following.

(1) The purine–purine electronic coupling provides the dominant contribution to the hole transfer matrix elements, irrespective whether the nucleobases belong to the same or to opposite strands.

(2) Superexchange corrections are large (10%–30%) for interstrand hole transfer between purines within dimer duplexes, where the superexchange corrections are determined by the (large) intrastrand couplings. For intrastrand hole transfer between the purines, superexchange corrections are small (1%–3%), as the correction is determined by the (mostly small) interstrand couplings.

(3) The couplings exhibit a marked base order specificity, which can be traced to the specificity of the coupling between the purines. While the electronic coupling between (GC) pairs with the guanines being located on the same strand is significantly larger than the matrix elements for complexes, where the guanines are located on different

TABLE III. Electronic coupling matrix elements (in cm^{-1}) for hole transfer between guanine bases in GAG and GTG trimer duplexes.

Duplex	Calculation on complete model	Superexchange V_S[a]	Direct and superexchange V'_S[b]
GAG	163	121	158(+), 84(−)
GTG	48	91	54(−), 128(+)

[a]Equation (4).
[b]Equation (5).

strands. The opposite trend is found for (AT) pairs. This distinction can be rationalized in terms of the extraordinary large interstrand A/A and A\A couplings.

(4) Hole transfer can exhibit a pronounced directional asymmetry. For instance, the coupling matrix in [(GC), (AT)] is about five times larger than that of [(AT), (GC)]; in both systems G and A are in the same strand with the orientations $5'-GA-3'$ and $3'-AG-5'$, respectively. On the other hand, very similar electronic couplings are found for the systems [(GC), (TA)] and [(CG), (AT)] with distinct interstrand orientation of G and A.

(5) The matrix elements for hole transfer between WCPs can be evaluated in most cases (except for [(TA), (GC)]) from the perturbative superexchange expressions, Eqs. (1)–(3), with an accuracy of 40%. This implies an uncertainty of about a numerical factor of 2 in the corresponding rates. This conclusion is significant for the transferability of the information obtained for the electronic matrix elements between nucleobases to estimate the electronic couplings for hole transfer (hopping) between guanines in large systems.

B. The trimer duplexes GAG and GTG

Our calculations on the trimer duplexes GAG and GTG yield hole transfer matrix elements between the guanines of 0.020 and 0.006 eV, respectively. It is instructive to express these coupling matrix elements for the trimer duplexes by superexchange expressions based on the two-nucleobase model. The leading superexchange contributions are

$$V_S(\mathrm{GTG}) = V(\mathrm{G–T})V(\mathrm{T–G})/\Delta E_{\mathrm{GT}}, \tag{4a}$$

$$V_S(\mathrm{GAG}) = V(\mathrm{G–A})V(\mathrm{A–G})/\Delta E_{\mathrm{GA}}, \tag{4b}$$

where the intrastrand couplings $V(B_1–B_2)$ are taken from Table I and the energy gaps are $\Delta E_{\mathrm{GT}} = E(\mathrm{GT^+G}) - E(\mathrm{XG^+A}) = 1.0\,\mathrm{eV}$ and $\Delta E_{\mathrm{GA}} = E(\mathrm{GA^+G}) - E(\mathrm{XG^+A}) = 0.30\,\mathrm{eV}$, as estimated using our energy data for trimer duplexes.[15] Additional superexchange corrections to Eqs. (4a) and (4b) involving interstrand couplings [e.g., $V(\mathrm{G/T})V(\mathrm{T\backslash G})/\Delta E_{\mathrm{GT}}$ to Eq. (4b)] are small ($\sim 1\ cm^{-1}$) and can be safely neglected. In Table III we compare the superexchange results, which are confronted with the direct calculations of the coupling matrix elements, where the agreement is within a numerical factor of 2. One source of the discrepancy involves the contribution of the direct G–G ''through-space'' coupling interaction which we will consider next. Comparing the matrix elements for GAG and GTG one immediately concludes that the intervening Watson–Crick pair determines the efficiency of the hole transfer between guanines. Yet, there remains the interesting question concerning the role of through-space interaction between the guanines in these trimers. To this end, we calculated the duplex G_G, obtained by removing the intermediate AT pair from the complexes GAG or GTG. The resulting ''through-space'' electronic coupling is calculated to $V(\mathrm{G\_G}) = 0.0046\,\mathrm{eV}$. This result is somewhat smaller than the matrix elements computed for the trimer GTG, and comparable to the matrix elements for GAG. Again, this value is rather stable with respect to the basis set used; with the flexible basis set 6-311+G* the G_G coupling is calculated to 0.0050 eV. In any case, the contributions of the through-space G_G coupling in the trimer duplexes considered here is substantial and this direct coupling has to be incorporated in the superexchange expressions. Thus, Eqs. (4a) and (4b) have now to be modified to read

$$V'_S(\mathrm{GTG}) = V(\mathrm{G\_G}) + V_s(\mathrm{GTG}), \tag{5a}$$

$$V'_S(\mathrm{GAG}) = V(\mathrm{G\_G}) + V_s(\mathrm{GAG}). \tag{5b}$$

The relative signs of the direct $V(\mathrm{G\_G})$ and of the superexchange contributions are not determined from our calculations. In Table III we presented the estimates of V'_S, Eqs. (5a) and (5b), when the direct and superexchange contributions are of the same sign [denoted by (+)] and of opposite signs [denoted by (−)]. It appears that good agreement can be accomplished between the complete calculation for the duplex trimer and the direct plus superexchange coupling scheme, Eq. (5), with an appropriate (but admittedly arbitrary) choice of the relative signs of the two contributions in Eq. (5).

From these data and analysis we conclude that:

(1) The difference between the coupling matrix elements of the trimer duplexes GAG and GTG originates from cumulative contributions to the superexchange terms comprising (i) the base–base intrastrand interactions, which are considerably larger for the GTG duplex $[V(\mathrm{G–T})V(\mathrm{T–G}) = 1.2 \times 10^{-2}\,\mathrm{eV}^2$, while $V(\mathrm{G–A})V(\mathrm{A–G}) = 4.4 \times 10^{-3}\,\mathrm{eV}^2]$, and (ii) the energy gaps, which are considerably lower for GAG ($\Delta E_{\mathrm{GA}} \approx 0.3\,\mathrm{eV}$ and $\Delta E_{\mathrm{GT}} \approx 1.0\,\mathrm{eV}$), which increase $V_s(\mathrm{GAG})$ relative to $V_s(\mathrm{GTG})$.

(2) The mutually compensating contributions (i) and (ii) [see point (1) above] manifest the influence of the intervening pair (i.e., the ''through-pair'' interaction) on the matrix element; concurrently, the ''through-space'' interaction of the guanines in the trimer duplexes is significant.

(3) The ''through-space'' G_G interaction ($37\ cm^{-1}$ at $R_{\mathrm{GG}} = 6.76\,\text{Å}$) is large. It appears that for hole transfer in DNA, in contrast to that for charge transfer in proteins,[3] the ''through-space'' electronic coupling is important. This value of $V(\mathrm{G\_G})$, together with the intrastrand nearest-neighbor value of $677\ cm^{-1}$ at $R_{\mathrm{GG}} = 3.38\,\text{Å}$, implies that this matrix element for GG coupling (at the DNA regular configuration) decreases exponentially, i.e., $V(\mathrm{G–G}) \propto \exp(-bR_{\mathrm{GG}})$ with $b = 0.86\,\text{Å}^{-1}$. This value of b is considerably lower than the value of $b = 1.58\,\text{Å}^{-1}$ inferred in our study[24] for parallel nucleobases, over a small R range, possibly reflecting the angular dependence of the electronic coupling matrix elements.

(4) The electronic coupling matrix elements in the trimer duplexes originate from a delicate balance between the couplings and energetic components of the superexchange term and between the superexchange ''through-pair'' and direct ''through-space'' interactions. In particular, our ignorance of the relative signs of these ''through-pair'' and ''through-space'' contributions implies that reliable estimates of the hole transfer matrix elements (in the idealized duplex in the gas phase) should rest on a complete calculation for the superstructure of the trimer duplex, while the superexchange contribution will result only in a semiquantitative estimate (see Table III) of these electronic coupling terms.

IV. CONCLUDING REMARKS

Electronic coupling matrix elements for hole transfer in DNA were estimated on the basis of self-consistent field (HF/6-31G*) calculations for all intrastrand and interstrand nucleobases pairs,[24] for the two nucleobases within the Watson–Crick pairs (GC) and (AT), for all dimer duplexes, and for the trimer duplexes GAG and GTG. The electronic coupling matrix elements obtained for the duplexes were analyzed in terms of direct and superexchange interactions between individual nucleobases. The intrinsic limitations of the superexchange scheme for the evaluation of hole transfer matrix elements, which determine the hole hopping rates between G nucleobases in GB_1B_2...G structures of DNA, pertain to the following issues, which call for further theoretical work.

(1) The electronic matrix elements for hole transfer between individual nucleobases and in duplex dimers and trimers depend crucially on the long-distance spatial ''tails'' of the electronic wave functions. Our tests (Ref. 24 and the present work) of the weak dependence of the electronic coupling between pairs of nucleobase on the size of the basis set inspire confidence in the accuracy of the electronic wave functions used herein.

(2) Contributions of the direct exchange interaction were found important for trimer duplexes. It is an open question whether this direct electronic coupling term is of importance for large duplexes.

(3) The calculations were performed for duplexes in the gas phase. Solvation energy and counterion effects on coupling matrix elements and on energy gaps as well as the effects of structural fluctuations of oligomer duplexes may be important.

Nevertheless, the analysis of electronic couplings in duplex dimers and trimers in terms of base–base interactions is significant for establishing propensity rules for the electronic couplings, i.e., bridge specificity and directional asymmetry. Furthermore, complete calculations of the electronic couplings for large DNA structures of a size exceeding a trimer duplex are not feasible yet. A semiempirical superexchange model based on the neglect of direct G_G couplings, together with superexchange contributions using base–base couplings and empirical energy gaps corrected for solvation effects, may be attractive for a semiquantitative evaluation of electronic coupling matrix elements in large DNA duplexes. The semiempirical superexchange model can be applied for the confrontation between the theoretical information on the electronic coupling matrix elements reported herein and the sparse experimental data on the hole electronic coupling which emerge from rates for hole injection, hopping, and trapping.[8,9,21,22] For an elementary hole transfer process in the DNA duplex

$$d^+B_1B_2B_3...B_Na \xrightarrow{k} dB_1B_2B_3...B_Na^+, \tag{6}$$

where d is the hole donor, a is the acceptor, and $B_1,B_2...B_N$ are the intervening nucleobases of the bridge, the semiempirical superexchange electronic coupling matrix is[18]

$$V=v(d,B_1)v(B_N,a) \times\{\Delta E_{dB_1}\}^{-1}\prod_{j=1}^{N-1} V(B_j,B_{j+1})/\Delta E_{dB_j}. \tag{7}$$

Here $v(d,B_1)$ and $v(B_N,a)$ are the nearest-neighbor electronic coupling matrix elements between the donor and the first bridge nucleobase B_1 and between the last bridge nucleobase and the acceptor. When d and a correspond to guanines[8,9,21,22] the electronic matrix elements reported herein are applicable, e.g., for hole transfer in $G(T)_mG$ or $G(A)_mG$ duplexes. Otherwise, further work is required to calculate the appropriate coupling matrix elements v for (hairpinned, intercalated, or substituted) donors and acceptors. In Eq. (7) $V(B_{jj+1})$ represents the matrix elements for hole transfer between adjacent nearest-neighbor nucleobases (Table I), while $\Delta E_{dB_j}=E(d^+,B_j)-E(d,B_j^+)$ represent the appropriate energy gaps. The hole transfer rate for reaction (6) is $k=(2\pi/\hbar)|V|^2F$, where F is the nuclear Franck–Condon factor, which is inferred from charge transfer theory.[19–23,32] Three sources of experimental information for the superexchange electronic couplings are available.

A. Absolute values of the electronic couplings

From the analysis of the temperature dependence of charge transfer rates between intercalated donor and acceptor on the basis of the Marcus theory, Harriman[33] estimated a value of $V=4\ cm^{-1}$ for d and a separated by three AT base pairs. Using our semiempirical procedure, based on Eq. (7), together with the base–base matrix elements (Table I) and the *gas phase* energy gaps,[15] we estimate rather similar electronic matrix elements for the systems (i) $5'-G(T)_mG-3'$ and (ii) $5'-G(A)_mG-3'$, i.e., $V=91$, 10, and 1.2 cm^{-1} for (i) with $m=1$, 2, 3, and 120, 8, 0.6 cm^{-1} for (ii) with $m=1,2,3$, respectively (see Table III). These estimates of V, Eq. (7), are based on gas-phase energy gaps.[15] It is instructive to note that the nucleobase bridge specificity in the duplexes $G(X)_mG$ (X=T,A) is small, due to a delicate balancing between nearest-neighbor matrix elements for $m=1-3$ and gas phase energy gaps. Assuming that the nearest-neighbor matrix elements $V(B_j,B_{j\pm1})$ between adjacent nucleobases are solvent-independent, a major solvent effect will be manifested by the energy gaps. For the systems $G(T)_mG$ the relevant energy gaps in Eq. (7) are reduced from $\Delta E_{GT}=1.3$ eV in the gas-phase to $\Delta E_{GT}^{(S)}\approx 0.6$ eV, evaluated from the difference between the redox potentials of single nucleobases in solution.[13,14] Using this value in the ''solvent adjusted'' electronic couplings $V^{(S)}\sim V\cdot(1.3/0.6)^m$. This

very crude estimate for $G(T)_mG$ results in $V^{(S)} \sim 197$, 47, 12 cm^{-1} for $m=1$, 2, 3. The latter value ($m=3$) is in qualitative agreement with Harriman's estimate[33] of the electronic coupling of 4 cm^{-1} for intercalated *d* and *a* with $m=3$. A more elaborate comparison requires the evaluation of donor-nucleobase electronic matrix elements in the systems studied by Harriman.[33]

B. Distance dependence of the electronic coupling

More significant is the distance dependence of the solvent adopted electronic couplings estimated in Sec. IV A for the system $G(T)_mG$ ($m=1-3$). $V^{(S)}$ can be well-fit by the exponential dependence $V^{(S)}(R)=A\exp(-bR)$, where R is the center-to-center G...G distance. This fit gives $b=0.42\,Å^{-1}$. Accordingly, the charge transfer rate in this system is estimated to be of the form $k \propto \exp(-\beta R)$, where $\beta=2b=0.84\,Å^{-1}$. This value of β is in reasonably good agreement with the experimental value of $\beta=0.7\,Å^{-1}$ for charge trapping in the systems[8,9] $G(T-A)_mGGG$ and with the values of $\beta=0.7\pm0.1\,Å^{-1}$ and $\beta=0.9\pm0.1\,Å^{-1}$ obtained for charge separation and recombination, respectively, in the systems $d(A)_mG$ with photoexcited stilbene as hole donor *d*.[34]

C. Reduction factors *r* for the rates of intrastrand hole hopping or trapping upon addition of a nucleobase

As information on the electronic coupling matrix elements for extrinsic (hairpinned, intercalated, or substituted) hole donors are not yet available, one can consider the quantitative information on the reduction of the hole hopping, trapping, or recombination rates upon the increase of the size of the bridge of nucleobases. Provided that the electronic couplings obey the empirical exponential distance dependence discussed in Sec. IV B, the reduction factor can be expressed in the form $r=\exp(-bR_{BB})$, where R_{BB} is the nearest-neighbor interbase distance in the bridge. The reduction factor of the hole superexchange rate in systems $5'-G(T)_mG-3'$ per addition of an additional T base is $r_T=[V(T-T)/\Delta E_{GT}]^2$. Using the energy gap value[15] $\Delta E_{GT}=1.3\,eV$ together with the value $V(T-T)=0.16\,eV$ for the electronic coupling (Table I), one obtains $r_T=0.015$, i.e., the reduction of the rate by a numerical factor of 70 per bridge nucleobase. Using the energy gap $\Delta E_{GT}^{(S)} \approx 0.6\,eV$ estimated on the basis of experimental redox potentials of the nucleobases in solution results in $r_T=7\times10^{-2}$, i.e., a reduction of the rate by a factor of 15. Similarly, for the system $5'-G(A)_mG-3'$ the reduction factor upon the addition of an additional A base is $r_A=[V(A-A)/\Delta E_{GA}]^2$, where the gas phase energy gap $\Delta E_{GA}=0.35\,eV$ together with $V(A-A)=0.030\,eV$ results in the low value of $r_A=8\times10^{-3}$. The reduction of the effective energy gap due to solvation effects may increase this value of r_A. The experimental results of Giese *et al.* and of Lewis *et al.* seem to imply that the reduction factors are $r_T \approx r_A \approx 0.03-0.1$, i.e. a reduction of the hole hopping rate by a factor of 10–30 upon addition on one (AT) pair.[8,9,21,22,23,34] Thus far, no experimental evidence for the specificity of T vs A in mediating intrastrand hole hopping was recorded.

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