Electronic Coupling for Charge Transfer and Transport in DNA

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We calculated electronic matrix elements for hole transfer between adjacent nucleobases in DNA. Calculations of the matrix elements for intrastrand and interstrand transfer were performed at the Hartree−Fock level employing the 6-31G* and 6-311G** basis sets. The matrix elements for intrastrand hole transfer, for which a wealth of experimental solution data is available, are almost independent of the basis set and exhibit an exponential interbase distance dependence, sensitivity to the donor−acceptor geometry, and dependence on $5' \rightarrow 3'$ direction base sequence. The calculated intrastrand hole transfer matrix elements between adjacent thymines, $v_+(T,T) = 0.16$ eV, is in good agreement with the experimental estimate, $v_+(T,T) = 0.18$ eV, inferred from hole hopping in $G^+(T)_mGGG$ ($m = 1-3$). The features of the nucleobase bridge specificity for superexchange-induced hole hopping between guanines in $G^+XY...G$ (X,Y = T or A) were elucidated, with the prediction of enhanced efficiency of thymine relative to adenine as mediator. Information on superexchange-mediated intrastrand and direct interstrand hole hopping between guanine bases was also inferred. Our results for interstrand, adjacent G^+G coupling predict the existence of zigzagging pathways for hole hopping, in line with experiment.

I. Introduction

Material scientists have only recently turned their attention to charge migration in DNA for the development of DNA-based molecular technologies, that is, functional nanoscale electronic devices and hybridization−conduction at metal surfaces in electrochemical or fluorescence diagnosis for chip technology.[1−9] Biological implications of charge transfer and transport in DNA may pertain to repair induced by charge transfer[10−13] and also to radiation damage followed by long-range charge transport, which leads to mutations.[14,15] The conceptual framework for the quantification of charge migration in DNA[9−40] rests on the theory of charge transfer,[41] with the rates for the elementary processes being determined by electronic coupling and nuclear Franck−Condon factors.[41−46] In this paper, we address the electronic couplings that determine hole (or electron) transfer and transport in DNA.

II. Short-Range Charge Transfer and Long-range Charge Transport

Two distinct mechanisms were advanced to account for a wealth of apparently contradictory experimental data[11−40] for charge migration in DNA:

(i) Two-center superexchange-mediated unistep charge transfer between the donor (D) and the acceptor (A),[32−37,43] which occurs for off-resonance donor-nucleotides $\{B_j\}$ bridge coupling.[42] This mechanism is characterized by an exponential D−A distance (R) dependence of the rate $k_{ET} \propto \exp(-\beta R)$ (with $\beta = 0.6-1.4$ Å^{-1} for DNA bridges), allowing only a short-range transfer, that is, ≤10 Å.

(ii) Multistep charge transport via hopping between the appropriate nucleobases of the bridge.[29,35,36,38−40,42−46] This is realized under the conditions of resonant donor-bridge coupling, giving rise to long-range (≥100 Å) charge transport.

There is no dichotomy between the two mechanisms. Rather, the prevalence of either form of charge transfer or transport is determined by the donor-bridge energetics, with the superexchange mechanism realized for a large positive bridge-donor energy gap ΔE, whereas the hopping mechanism prevails for negative ΔE. For the hopping mechanism (ii), the features of charge transport are controlled by the intrabridge energetics. These involve the relative energetics of the oxidized/reduced nucleobases for hole/electron hopping. The majority of the experimental information on charge separation, shift, and recombination of DNA in solution[11−36,47−52] pertains to hole (positive charge) transfer or transport. Hole hopping occurs between guanine (G) bases, that is, the nucleobases with the lowest oxidation potential in vitro.[53,54] This feature was inferred by Hush and Chueng in 1975 in their pioneering study[55] of the gas-phase vertical ionization potentials of the nucleobases. The role of G as the lowest-energy cation radical among the four nucleobases is manifested by gas-phase experimental[55] and calculated[56] ionization potentials, with the order of the ionization potentials being invariant with respect to base pairing and strand formation.[56] Thus, the G^+ radical cations constitute hole "resting states" among the nucleobases in DNA. Each elementary $G^+...G$ hopping step can be mediated by intervening T or A bases. On the other hand, the electron (negative charge) hopping is expected to proceed via reduction of both thymine (T) and cytosine (C) bases, whose reduction potentials (in vitro) are similar[53,54] and lower than those of G and A. As each base pair in the Watson−Crick duplex of DNA contains either T or C, nearest-neighbor electron hopping between adjacent bases can prevail.[44]

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III. Coupling Matrix Elements Determine Transfer and Hopping Rates

To quantify the elementary processes of charge transfer/transport[41−46] in DNA, we consider charge migration in a system $DB_1B_2...B_NA$, where B_j ($j = 1, ..., N$) are the N nucleobases of the bridge, which may belong either to a single strand or to the two strands of a DNA duplex, D is the ground or electronically excited donor, and A is the acceptor. The diabatic electronic states are denoted by (valence bond) wave functions describing localized states:

$$|D\rangle = |DB_1B_2...B_NA\rangle \tag{1a}$$

$$|A^{\pm}\rangle = |D^{\mp}B_1B_2...B_NA^{\pm}\rangle \tag{1b}$$

$$|B_j^{\pm}\rangle = |D^{\mp}B_1B_2...B_j^{\pm}...B_NA\rangle; \quad (n = 1, ..., N) \tag{1c}$$

The superscripts + and − refer to hole and electron transfer, respectively. Superexchange charge transfer between D and A is characterized by the unistep rate[41,42,57]

$$k_{CT} = (2\pi/\hbar)|v_{\pm}(D,A) + V_{DA}|^2 F_{CT} \tag{2}$$

where F_{CT} is the D−A Franck−Condon nuclear factor. The electronic coupling for charge transfer consists of a first-order donor−acceptor coupling element matrix $v_{\pm}(D,A) = \langle D|H|A^{\pm}\rangle$ and the traditional second-order term[41,42]

$$V_{DA} = v_{\pm}(D,B_1)v_{\pm}(B_N,A)\frac{1}{\Delta E_{DB_1}}\prod_{j=1}^{N-1}\left[\frac{v_{\pm}(B_j,B_{j+1})}{\Delta E_{DB_{j+1}}}\right] \tag{3}$$

The energy differences $\Delta E_{DB_{j+1}}$ are effective energy gaps, which correspond to weighted averages (by the Franck−Condon factors between B_{j+1} and B_{j+1}^+) over the vibrational states of each bridge base. The individual donor-base, base-base and base-acceptor coupling matrix elements for hole (+) or electron (−) transfer, which determine V_{DA}, eq 3, are

$$v_{\pm}(D,B_1) = \langle D|H|B_1^{\pm}\rangle \tag{4a}$$

$$v_{\pm}(B_N,A) = \langle B_N^{\pm}|H|A^{\pm}\rangle \tag{4b}$$

$$v_{\pm}(B_j,B_{j+1}) = \langle B_j^{\pm}|H|B_{j+1}^{\pm}\rangle \tag{4c}$$

with H being the system's Hamiltonian. The electronic coupling matrix elements, eq 4c, correspond to direct electron or hole exchange between adjacent bases, that is, B_j, $B_{j+1} \equiv$ G, A, C, and T. The electronic coupling through a duplex stack of nucleobases is expected to involve both intrastrand and interstrand pathways.[41−43] The issue of parallel and possibly interfering pathways for the superexchange coupling between D and A is not addressed here, although eq 3 can be readily extended to incorporate such contributions.

The mechanism of unistep, superexchange-mediated hole transfer is also applicable for hole hopping between G bases in the system GXY...G where X,Y = T or A are off-resonance mediators. For hole transport via G groups, the intrastrand hopping steps can occur along a single strand of the duplex

$$\begin{matrix} G^+ & & G & & G & \\ | & (T-A)_m & | & (T-A)_{m'} & | & ... \\ C & & C & & C & \end{matrix} \tag{5}$$

where each (T−A) corresponds either to a

$$\begin{matrix} T & & A \\ | & \text{or an} & | \\ A & & T \end{matrix}$$

Watson−Crick pair. Such a situation for hopping in the duplex

$$\begin{matrix} G^+ & & G & \\ | & \begin{pmatrix} T \\ | \\ A \end{pmatrix}_n & | & \begin{pmatrix} T \\ | \\ A \end{pmatrix}_n & | & ...; \quad n = 1-3 \\ C & & C & & C & \end{matrix} \tag{6}$$

was realized in the experiments of Giese et al.[35,36,44] Charge hopping through a duplex stack may involve intrastrand as well as interstrand individual hopping steps ("zigzagging"),[42] occurring between G bases on different strands, which belong to neighboring Watson−Crick pairs. For example, in the duplex

$$\begin{matrix} G_1^+ & & G_2 & & C & & C & & G_5 & \\ | & (T-A)_m & | & \ddots & | & (T-A)_{m'} & | & \ddots & | & \cdots \\ C & & C & & G_3 & & G_4 & & C & \end{matrix} \tag{7}$$

the pairs G_2, G_3 and G_4, G_5 correspond to interstrand coupling, whereas intrastrand coupling occurs for the pairs G_1, G_2 and G_3, G_4.

For intrastrand G−G hole hopping between nearest-neighbor G bases separated by T bases in the duplex (6), the individual hopping rates k are determined by superexchange interactions

$$k = (2\pi/\hbar)\left|v_+^{(\alpha\alpha)}(G,G) + \frac{v_+^{(\alpha\alpha)}(G,T)[v_+^{(\alpha\alpha)}(T,T)]^{(m-1)}v_+^{(\alpha\alpha)}(T,G)}{\Delta E^m}\right|^2 F \tag{8}$$

where ΔE is the G^+TG-GT^+ energy gap ($\Delta E \cong 0.6$ eV),[53,54] F is the nuclear Franck−Condon factor, and the label ($\alpha\alpha$) denotes intrastrand electronic coupling between adjacent nucleobases. In a recent quantum chemical model study on isolated base pair fragments in regular structure, which excludes solvation effects, the energy gap $\Delta E(G^+,T)$ was estimated as 1.2 eV.[56] Similar expressions for k can be written for intrastrand hole hopping in the duplex (5) mediated by A bases.

The nearest-neighbor interstrand electronic coupling in (7) is expected to be considerably lower than the intrastrand coupling between adjacent bases, in view of the larger interbase distance in the former case. Accordingly, the most effective interstrand hole coupling and hopping involves adjacent G−G pairs on different strands. For interstrand G−G hole hopping in the duplex (7), the individual hopping rates are

$$k = (2\pi/\hbar)|v_+^{(\alpha\beta)}(G,G)|^2 F' \tag{9}$$

where the label ($\alpha\beta$) denotes interstrand electronic coupling, eq 4c, between adjacent G bases while F' is the Franck−Condon factor for this process. Analogous expressions can be written for interstrand electron hopping rates between adjacent T and C nucleobases.

The hole and electron hopping rates, eqs 8 and 9, as well as the superexchange rate, eqs 2 and 3, are determined by the electronic coupling matrix elements between adjacent nucleobases. Calculations of the pair coupling matrix elements for electron and hole transfer were reported by Bauer and Dee in 1974,[19] using techniques for approximate evaluation of intermolecular electronic interactions in molecular crystals.[58,59] Extended Hückel calculations of donor−acceptor electronic coupling in DNA were conducted by Beratan et al.[43] In this

paper, we report on the calculation of matrix elements v_+ for all pairs of nucleotide bases using a two-state model (see below). Thereby, one uses the ground and charge transfer states of the supermolecular donor−acceptor system (adiabatic states) to evaluate off-diagonal Hamiltonian matrix elements corresponding to diabatic localized donor and acceptor states. From our results for the transfer matrix elements, we shall infer their dependence on the nature of the base, on the donor−acceptor separation and relative geometry, and on the distinction between intrastrand and interstrand coupling.

IV. Methodology

The electronic coupling matrix elements for hole transfer were calculated for all possible base pairs in DNA within one strand (intrastrand coupling) and for several selected pairs where nucleobases belong to complementary strands of a duplex (interstrand coupling). Mutual positions of nucleobases in the DNA strand may be defined by using the following six base-step parameters. The three translations, slide, shift, and rise, are defined as components of the relative displacement of two bases and the three rotation angles, tilt, role, and twist (for more detail, see ref 60). An accurate building protocol was fully considered.[61] Experimental idealized atomic coordinates of the four bases (adenine, cytosine, guanine, and thymine) taken from high-resolution X-ray and neutron studies were used for generating the structures.[62] The mutual positions of the nucleobases in the models studied correspond to a regular DNA structure with a rise of 3.38 Å and a twist of 36°. In addition, four one-strand *symmetrical* structures GG, AA, TT, and CC with a twist of 0° were considered. The geometries of the various B-DNA fragments were constructed with the program SCHNArP.[61]

A two-state model for electron transfer was applied. The electronic coupling matrix elements for symmetry-equivalent donor and acceptor (within symmetrical structures XX, X = G, A, T, and C) were estimated as one-half of the adiabatic state splitting Δ.[63] Note that the donor and acceptor within XY pairs of regular structure are not equivalent. To induce the charge transfer, the donor and acceptor states have to be brought in resonance. In hole transfer reactions, such a resonance occurs due to thermal fluctuations of the polar environment.[64] These fluctuations were modeled by applying a homogeneous electric field in the direction from the donor to the acceptor.[65−67] The field strength was adjusted to obtain minimum splitting; this situation is equivalent to that where donor and acceptor diabatic states are in resonance. Thus, for all XY pairs of regular structure, the minimum splitting between two adiabatic states had to be found.

In turn, the splitting Δ may be obtained as the difference between the energies of two adiabatic states, $\Delta = E_2 - E_1$, of the ionic system. According to Koopmans' theorem (KT), one-electron energies of the occupied orbitals of a system as determined in a Hartree−Fock self-consistent field (HF−SCF) calculation provide ionization energies in the frozen MO approximation. Therefore, the parameter Δ may be estimated within HF−KT by the splitting of one-electron energies of the HOMO (highest occupied molecular orbital) and HOMO-1 of the corresponding closed-shell neutral system. This procedure provides the absolute values of the matrix elements. It is widely used for calculating electron coupling matrix elements.[63] Comparison of Δ values calculated using HF−KT and the CASSI (complete active space−state interaction) method with the same basis set are in very good agreement.[68] In preliminary calculations (see also below), we found that the value of Δ for hole transfer depends only weakly on the basis set, as distinct from results for electron transfer where the energies of more diffuse, unoccupied orbitals are employed.

TABLE 1: Matrix Elements $v_+^{(\alpha\alpha)}(X,X^+)$ for Intrastrand Hole Transfer in Symmetric Nucleobase Pairs XX^+ (in eV)[a]

rise	2.88 Å		3.38 Å		3.88 Å	
XX^+	6-31G*	6-311G**	6-31G*	6-311G**	6-31G*	6-311G**
GG	0.928	0.928	0.426	0.429	0.187	0.191
AA	0.861	0.860	0.446	0.449	0.198	0.201
TT	1.019	1.022	0.471	0.471	0.198	0.214
CC	0.641	0.640	0.364	0.369	0.157	0.165

[a] Calculations were performed for a twist of 0° at various values of the rise parameter, using the standard basis set 6-31G* and the extended basis set 6-311G**.

TABLE 2: Matrix Elements for Intrastrand Hole Transfer $v_+^{(\alpha\alpha)}(X,Y)$ between Nucleobase Pairs 5′-XY^+-3′ in DNA (in eV)[a]

DNA base pair	$v_+^{(\alpha\alpha)}(X,Y)$	DNA base pair	$v_+^{(\alpha\alpha)}(X,Y)$
GG	0.084	TG	0.085
GA	0.089	TA	0.086
GT	0.137	TT	0.158
GC	0.110	TC	0.076
AG	0.049	CG	0.042
AA	0.030	CA	0.029
AT	0.105	CT	0.100
AC	0.061	CC	0.041

[a] Calculations performed using the HF/61-31G* basis set at the standard geometry (rise = 3.38 Å and twist = 36°).

Table 1 lists results of HF−SCF calculations[69] on the matrix elements for hole transfer in symmetrical base pairs XX. This parallel geometry (twist = 0°) is not thermally accessible but is presented for the sake of general methodology. The calculations were carried out using two basis sets: a standard basis 6-31G* and an extended basis set 6-311G**,[69] the latter being a triple-ζ basis set with d polarization functions on heavy atoms (C,N,O) and p polarization functions on hydrogen atoms. Comparing the results given in Table 1, we conclude that the matrix elements for hole transfer in the range $R_{XX} = 2.88-3.88$ Å are almost independent of the basis sets used. Therefore, we applied HF/6-31G* calculations to the hole transfer matrix elements, which are summarized in Table 2. As the matrix elements for hole transfer depend on the "tails" of the electronic wave functions, further checks were performed to establish the stability of the numerical results with respect to the choice of the basis set at large interbase distances. This situation is important for interstrand hole transfer between nucleobases on different strands that belong to neighboring Watson−Crick pairs where the average center-to-center distance is ca. 7 Å and the edge-to-edge distance is 3.5 Å. The data presented in Table 3 reveal deviations of less than 15% for interstrand hole transfer matrix elements calculated with the standard 6-31G* basis and the extended basis 6-311G**. To examine this issue further, we used large basis sets with diffuse functions. Using the basis sets[69] 6-311+G* and 6-311++G** for the regular pair AA resulted in interstrand hole transfer matrix elements of 0.036 and 0.035 eV, respectively, which are within 20% of the results (Table 3) obtained with the standard basis set.

In contrast to hole transfer, the matrix elements for intrastrand electron transfer in symmetric pairs XX^- were found to be very sensitive to the basis set employed, that is, exhibiting a change by a numerical factor of about 2 between results obtained with the basis sets 6-31G* and 6-311G** at fixed R_{XX}. It has already been pointed out[68] that the matrix elements for electron transfer

TABLE 3: Matrix Elements for Interstrand Hole Transfer $v_+^{(\alpha\beta)}$(X,Y) between Nucleobase Pairs in the Configuration 5′-XY-5′ in DNA[a]

	$v_+^{(\alpha\beta)}$(X,Y), eV	
DNA base pair	6-31G*	6-311G**
GG	0.0193	0.0188
AA	0.0347	0.0307
TT	0.0032	0.0037
CC	0.0007	0.0007
GA	0.0211	0.0185
AG	0.0213	0.0237
AT	0.0163	0.0189
TA	0.0163	0.0200

[a] Calculations performed using the standard basis set 6-31G* and the extended basis set 6-311G** at the standard geometry (rise = 3.38 Å and twist = 36°).

in the ethylene dimer are very dependent on the basis set due to the diffuse character of the π^* orbital.

According to the statistical evaluation based on experimental crystal structures of oligonucleotides, the DNA base-step parameters and thus the relative orientation of neighboring bases can vary significantly.[60] Our computations show (see below) that the values of the matrix elements are sensitive to the mutual position of the nucleobases. Thus, depending on the time scale of the dynamic processes involved, molecular dynamics or Monte Carlo simulations have to be applied for an accurate evaluation of the hole transfer kinetics.

V. Coupling Matrix Elements

Table 1 shows the calculated matrix elements for symmetric hole transfer between parallel stacked identical nucleobases with rise values (distance between planes of bases) ranging from 2.88 to 3.88 Å and a twist of 0°. The distance dependence of v_+(X,X) (X = G, T, C, A) is exponential of the form $\exp(-bR_{XX})$ with $b = 1.58$ Å^{-1}. This large exponential parameter b differs from the parameter β that determines the exponential donor−acceptor distance dependence for the unistep donor−acceptor hopping rate, eqs 2 and 3,[42] or for the approximately exponential G...G distance dependence of the hole hopping rate, eq 8. Taking each matrix element between adjacent groups within a linear chain in the form A $\exp(-bR_0)$, where R_0 is the average nearest-neighbor distance and the values of b are taken to be equal, then the matrix element in eq 3 assumes the form $V_{DA} = B \exp(-\beta R)$ where $B = v_+(D,B_1)v_+(B_N,A)/\Delta E$, $R = (N-1)R_0$ is the length of the bridge, and $\beta = b - \ln(A/\Delta E)/R_0$.

From the results of Tables 1 and 2, we infer that the transfer matrix elements vary with the base and are very sensitive to the donor−acceptor geometry, in particular to the rise value. For instance, an increase of the rise value by 0.3 Å, which corresponds to the standard deviation for this base-step parameter (due to thermal motion of DNA),[60] will increase this matrix element by a numerical factor of 1.6 and its contribution to the intrastrand hopping rate, eq 8, by a substantial numerical factor of 2.6. The calculated transfer matrix elements v_+ for intrastrand hole transfer between pairs of nucleotides are presented in Table 2 for the regular (average) structure (rise = 3.38 Å, twist = 36°). The coupling matrix elements change considerably with the twist angle (not shown in Table 2), demonstrating their sensitivity to the relative geometry of the nucleobases. By convention, the base sequence XY is written in the 5′ → 3′ direction. Because the mutual position of bases X and Y in the pairs XY and YX is different, the matrix elements are distinct. The matrix elements for hole transfer calculated in the present work are all smaller by numerical factors of 3−10 than the data of Dee and Bauer,[19] who evaluated matrix elements from intermolecular transfer integrals involving charge-molecule and charge-dipole interactions.[58]

To obtain information on interstrand coupling and hopping pathways (zigzagging), we calculated the matrix elements $v_+^{(\alpha\beta)}$(X,Y) for intrastrand hole transfer between nucleobases on different strands, which belong to neighboring Watson−Crick pairs and are in the 5′-X-Y-5′ configuration (Table 3). The comparison between the intrastrand (Table 2) and the interstrand (Table 3) matrix elements for hole transfer (as expressed in terms of the ratio, γ, of their absolute values) manifests a strong dependence on the geometry and the nature of the base pair. For the pair AA, $\gamma = 1$; for GG, GA, AG, AT, and TA, $\gamma = 2-5$; whereas for TT and CC, $\gamma = 40-60$. These results reflect the sensitivity of the electronic couplings to the relative geometry of nucleobases at relatively large distances. Two important conclusions emerge from these results regarding the mechanisms of interstrand zigzagging.[42] First, interstrand direct hole hopping between adjacent G groups is facilitated by the relatively large values of $v_+^{(\alpha\beta)}$(G,G) = 0.019 eV. It should be borne in mind that for intrastrand hole transport via G bases, these "resting states" are usually separated by mediating T or A groups, and the rate of hole hopping occurs via G...G superexchange interactions, according to eq 8. On the other hand, interstrand hole hopping can occur via adjacent G bases on different strands, as shown in eq 7, and the hole hopping is determined by the direct G−G interaction $v_+^{(\alpha\beta)}$(G,G), according to eq 9. Second, interstrand superexchange-mediated hole hopping may be feasible. This can occur between G bases separated by one or two A bases, being induced by the relatively large GA and AA interstrand coupling matrix elements. These conclusions seem to be consistent with the observations of Kelley and Barton[13] and of Schuster et al.[40] of interstrand hole hopping, either by direct G^+G coupling or via G^+AAG superexchange.

VI. Discussion and Conclusions

From these results we infer the following.

1. Matrix Elements for Intrastrand Hole Transfer. The results of the calculations are in good agreement with available recent estimates[44,45] of matrix elements for G+...GGG hole trapping, induced by a hole shift in structurally unmodified DNA.[34,35] The experimental data for intrastrand hole trapping yields in the strand $G^+(T)_mGGG$ exhibit a reduction factor of $r = 0.1$ per each T nucleobase.[34,35] This reduction factor for each extra TA base pair in the bridge is $r = (v_+^{\alpha\alpha}(T,T)/\Delta E)^2 = 0.1$,[44,45] with $\Delta E = 0.6$ eV[53] resulting in $v_+^{(\alpha\alpha)}(T,T) = 0.18$ eV.[44,45] This value is within 10% of the calculated matrix element at the equilibrium geometry $v_+^{(\alpha\alpha)}(T,T) = 0.158$ eV (Table 2). Configurational fluctuations[60] may affect the value of the calculated matrix elements.

2. Features of Superexchange-Induced Hole Hopping. Most of the processes of intrastrand hole hopping are expected to occur via elementary superexchange steps between G bases separated by T or A bases. The superexchange matrix elements in the duplex (6) are of the form $v_+^{(\alpha\alpha)}(G,T)[v_+^{(\alpha\alpha)}(T,T)]^{(m-1)}v_+^{(\alpha\alpha)}(T,G)/\Delta E^m$ which, on the basis of the data of Table 2 and $\Delta E = 0.6$ eV,[53] assume the low values of 1.9×10^{-2} eV for $m = 1$, 5.1×10^{-3} eV for $m = 2$, and 1.4×10^{-3} eV for $m = 3$. These superexchange matrix elements are considerably lower than the nearest-neighbor intrastrand G−G coupling $v_+^{(\alpha\alpha)}(G,G) = 0.084$ eV, which induces hole transport in the GGGGG...

strand. Charge transport in the duplex 5′-GGG....-3′-CCC...-5′ was recently studied.[9] Provided that hole transport occurs in this duplex via nearest-neighbor hopping (small polaron) motion, the ratio of the hopping rates between superexchange-mediated hopping in $G(T)_mG$ and direct exchange-induced hole hopping in the GGGG... strand will be, according to eqs 8 and 9 and the data of Table 2, about 5.3×10^{-2} for $m = 1$, 3.7×10^{-3} for $m = 2$, and 2.8×10^{-4} for $m = 3$. Of course, these estimates are valid provided that hopping, rather than band transport, prevails in the GGGGG... system. These estimates demonstrate the dominance of direct nearest-neighbor exchange over superexchange-induced hopping.

3. Bridge Specificity for Superexchange-Induced Intrastrand Hole Hopping in $G^+XYZ...G$ Strands. On the basis of the matrix elements of Table 2, we infer that the rates for hole hopping in $G^+(T)_mG$ is faster than in $G^+(A)_mG$ (for a fixed value of m). The hopping rate in the strand G^+TTG is faster than for the systems G^+TAG and G^+ATG, the ratio of the rates being $\rho(GTAG/GTTG) = 0.10$ and $\rho(GATG/GTTG) = 0.19$. The difference in the relative ratios reflects on the different mutual positions of the T and A bases across the 5′-3′ direction. The experimental data of Giese et al.[35,36] indicate that the yield for hole hopping in GTTG is higher than in GATG, in accord with our prediction. However, according to Giese, these experiments for the two systems were conducted under different conditions and further experimental work is required.[70] From the foregoing analysis, we conclude that T constitutes the most effective mediator for G^+...G hole hopping. A bridge $(T)_m$ is more effective than $(A)_m$ or any combination of m T and A nucleobases. The prediction of the enhanced efficiency of the nucleobases T relative to A for G^+...G is in accord with the experimental data of Giese et al.[35,36]

4. Difference between Intrastrand Hole and Electron Transport. Hole hopping between G...G bases is induced in most cases by superexchange interactions induced by the intervening T or A groups. On the other hand, electron hopping is expected to occur by direct exchange between C and T groups. Direct electron coupling is expected to exceed the hole superexchange coupling terms because of the more diffuse nature of the anionic states.[68] We expect that nearest-neighbor electron hopping induced by direct exchange between the T and/or C nucleobases present in each Watson−Crick pair, that is, T−T, T−C, and C−C, will dominate over G^+...G hole hopping via superexchange.[36,44]

5. The Interstrand Zigzagging Picture. A comparison of matrix elements for intrastrand and interstrand hole hopping (Tables 2 and 3) provides compelling evidence for the zigzagging model.[42] The interstrand G^+G electronic coupling is sufficiently large to induce hole hopping between the two strands of the duplex. The intrastrand $G^+(T)_mG$ or $G^+(A)_mG$ hole hopping states will occur sequentially with the interstrand G^+G hopping. The ratio of the rates for direct G^+G interstrand hopping (Table 3) and for $G^+(T)_mG$ superexchange intrastrand hopping (estimated from Table 2) is ~1 for $m = 1$, ~15 for $m = 2$, and ~200 for $m = 3$. Accordingly, direct interstrand G^+G exchange does dominate over $G^+(T)_mG$ intrastrand superexchange.

6. Role of Configurational Fluctuations in Structurally Floppy Systems. These effects are of considerable importance for charge hopping and transfer in DNA, which exhibits marked structural nonrigidity. We have seen the manifestation of the fluctuations in the rise base-step parameter, which appreciably modifies the coupling matrix elements and the rates. How do these configurational fluctuations affect hole or electron transfer and transport dynamics? Two limiting cases can be readily distinguished. Slow configurational relaxation on the time scale of charge hopping results in structural heterogeneity, whereas fast configurational relaxation on the time scale of charge hopping probes the statistical average. The combination of molecular dynamics or Monte Carlo techniques to explore the potential energy landscape of a DNA duplex, in conjunction with electron transfer theory, will be useful for analyzing those two limiting cases. Most interesting is the situation when configurational relaxation occurs on the time scale of charge hopping, which requires a new conceptual framework.

The electronic coupling matrix elements presented herein provide central input information for the quantification of the elementary rates of hole transfer and transport in DNA, which correspond to either unistep donor−acceptor hole transfer or intrastrand/interstrand hole hopping between G bases. The second component that determines the elementary rates involves the nuclear Franck−Condon factors (F_{CT}, F, and F' in eqs 2, 8, and 9). For the interesting case of long-range hole transport in DNA, the general dynamic picture has to consider the elementary rates for hole injection from the donor to the bridge, hole hopping in the DNA bridge, and hole trapping. Experimental time-resolved data for hole injection[31−33,37] and for hole trapping[34−36] are emerging, whereas no temporal information on hole hopping is currently available. The chemical yield data of Giese et al.[34−36] were analyzed[44−46] to evaluate the ratio of the hopping and the trapping rates.

The theory has to be extended in several directions. First, electronic matrix elements have to be calculated for hole injection from (capped,[31,32] intercolated,[22−29] or substituted[37,71]) donors to a nearest neighbor nucleobase. Second, electronic matrix elements for hole trapping by chemically substituted nucleobases[71] have to be calculated. Third, nuclear Franck−Condon factors have to be evaluated by the combination of experimental information on medium reorganization energy (λ),[44,47] the strengths of vibronic coupling with high-frequency modes (S),[42] and energetics.[56] The first step in this direction was undertaken for the estimate of hole hopping rates.[44] Fourth, the theory of charge transfer and hopping rates in DNA focused on idealized structures has to be extended (see section 6 above) to account for the effects of configurational fluctuations in nonrigid systems on charge transfer and transport dynamics.

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