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Hole Trapping, Detrapping, and Hopping in DNA†

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In this paper we present a self-consistent kinetic-quantum mechanical analysis of chemical yield data for hole trapping/detrapping in $G^+(T-A)_mGGG$ duplexes (with free energy gaps Δ_t) and for hole hopping/trapping/detrapping in $G^+[(T)_mG]_n(T)_mGGG$ duplexes of DNA. Bridge specificity of hole trapping/detrapping by GGG traps was specified by superexchange electronic contributions, inferred from electronic coupling matrix elements between nearest-neighbor nucleobases and semiempirical energy gaps, and energetic contributions, which determine the nuclear Franck−Condon factors. Unistep hole-trapping yields are accounted for by a weak bridge length dependence for short ($N = 1, 2$) bridges, due to detrapping. Marked bridge specificity is manifested for short ($N = 1, 2$) bridges, being distinct for $(T)_N$ and for $[(A)_{m+1}(T)_{m'}]_n$ ($m, m' \geq 0$ and $N = n(m + m' + 1)$) bridges. For long ($N > 2$) bridges an exponential bridge size dependence of the trapping yields prevails. Multistep hole transport results in different reaction rates of G^+ (rate k_d) and of $(GGG)^+$ (rate k_{dt}) with water, i.e., $k_d/k_{dt} = 1.6$, which, in conjunction with the unistep trapping/detrapping data, results in the free energy gaps for hole trapping of $\Delta_t = 0.096$ eV in the $G^+(T)_NGGG$ duplexes and of $\Delta_t = 0.062$ eV in the $G^+[(A)_{m+1}(T)_{m'}]_nGGG$ duplexes.

1. Introduction

Interest in charge transfer and transport in DNA[1−10] stems from biological implications, e.g., radiation damage, protection and repair, and from the novel area of dynamics, response, and function of nanostructures and biosensors. The majority of the experimental information on charge transport in DNA involves positive charge (hole) migration. For resonance donor-bridge interactions, hole hopping occurs between guanine (G) bases. Experimental chemical yield data of Giese et al.,[11−15] Saito et al.,[16−19] Barton et al.,[20,21] and Schuster et al.[22−25] and time-resolved data of Lewis et al.[26−28] infer that intrastrand GG doublets and GGG triplets act as hole traps from G^+ in accord with computational results.[19,29,30]

Recent semiempirical calculations by Voityuk et al.[29] for the energetics of hole trapping yield stabilization energies of 0.3−0.13 eV for $(GGG)^+$ and for $(GG)^+$ relative to G^+, with the spread of the energetic values being due to effects of nearest neighbor bases and to directional asymmetry. These calculated energetic data are considerably lower than those calculated by Saito et al.,[19,30] and seem to be in semiquantitative agreement with experimental kinetic data of Lewis et al.[27,28] The rates of hole trapping and reversible detrapping in the systems

$$G^+AGGA \underset{k_{-tr}}{\overset{k_{tr}}{\rightleftharpoons}} G\,A(GG)^+A$$

and

$$G^+AGGGA \underset{k_{-tr}}{\overset{k_{tr}}{\rightleftharpoons}} GA(GGG)^+A$$

result in the free energy gaps $\Delta G_t = 0.053$ eV[27,28] between the states $GA(GG)^+A$ and G^+AGGA, and $\Delta G_t = 0.077$ eV[28] between $GA(GGG)^+A$ and G^+AGGGA, pointing toward the role of (GG) and (GGG) as shallow hole traps. Meggers et al.[13] provided extensive experimental information for the yields of hole trapping in a series of duplexes $G^+(T-A)_m$ GGG, which indicates that the relative yields for the reaction with water between the terminal (GGG) and the initial G (separated by the distance R) obey an approximate exponential distance dependence of the trapping rate ($\propto \exp(-\beta R)$, with $\beta = 0.9$ Å^{-1}), in qualitative agreement with unistep superexchange hole transfer for this elementary process.

The description of hole transport through G^+ "resting states" brought together multistep hopping and unistep superexchange, with the individual hopping rates between G bases in GXY...G (with X, Y = T or A) being superexchange mediated through the bridging (T−A) bases. Experimental evidence for long-range (distance scale 50 Å − 300 Å) hole transport via G bases induced by hole shift or injection, stems from chemical yield data and was reported by Barton et al.,[20,21] Giese and Michel-Beyerle,[14] and Schuster et al.[22−25] The moderately large distance scale for hole transport in DNA duplexes is limited by the parallel side reactions of the G^+ "resting sites" and of the $(GGG)^+$ hole traps with water,[11−15,20−25] which involves a major depletion channel for the hole charge carriers in DNA. Analytical kinetic models, based on the superexchange mediated hopping picture in conjunction with the water reaction of the G^+ radical cations, were applied[31−35] to account for the bridge size dependence of the chemical yields for long-range hole shift in the $G^+[(T)_mG]_n(T)_mGGG$ over the G^+...GGG distance scale of 10−40 Å ($n = 0−3$, $m = 2$) reported by Giese et al.[13,14]

The heuristic kinetic analysis of hole trapping in the $G^+(T-A)_nGGG$ duplexes,[13] and the previous kinetic analysis of hole hopping and trapping in the $G^+[(T)_mG]_n(T)_mGGG$ duplexes by Bixon et al.[32,33] and by Berlin, Burin, and Ratner[34,35] and by Siebbeles and Berlin[36,37] considered only exoergic hole

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trapping processes. Thermally induced detrapping should be significant. Lewis et al. have provided time-resolved evidence for thermally induced detrapping from $(GG)^+$ [27,28] and for $(GGG)^+$.[28] Thermally induced processes for charge injection, hopping, and detrapping[27,28,38] are expected to contribute to the kinetics of charge transport in DNA. Another interesting process in this context is charge injection from a donor to the bridge for a positive energy gap, which gives rise to thermally induced hopping.[33,38] Theoretical studies of the "transition" from superexchange to multistep hopping for small positive energy gaps were presented by Friesner et al.,[39,40] by Mukamel et al.,[41−43] and by Nitzan et al.,[44,45] while we have advanced a kinetic-quantum mechanical analysis of thermally induced hopping[38] to account for the possible hole transport through adenine nucleobases in DNA. In this paper we extend our previous kinetic scheme[32,33] providing an analysis of hole trapping and hopping in DNA duplexes studied by Giese et al.[13,14] to include thermally induced processes. We shall provide a kinetic-quantum mechanical self-consistent analysis of two classes of processes: (i) unistep hole trapping and detrapping in $G^+(T-A)_mGGG$ duplexes and (ii) multistep long-range hole hopping transport followed by hole trapping and detrapping in $G^+[(T)_mG]_n(T)_mGGG$ duplexes. To make contact with experimental reality, chemical yields will be calculated. We shall transcend previous "coarse graining" approaches,[32−35] which neglected the bridge specificity of hole trapping dynamics. Bridge specificity of hole trapping will be specified in terms of electronic contributions due to superexchange coupling and energetic contributions via nuclear Franck−Condon factors. Theoretical input information for energetics of hole states[29] and for electronic coupling matrix elements between nearest-neighbor nucleobases[46,47] will provide guidelines for the establishment of electronic and nuclear contributions to bridge-specificity, which determines the energetics and kinetics of hole trapping via GGG in DNA.

2. Unistep Hole Trapping in G⁺...GGG Duplexes

The hole trapping in the $5' - G^+(T - A)_nGGG - 3'$ systems studied by Meggers et al.[13] will be described in terms of trapping by (GGG) (rate k_t), detrapping from $(GGG)^+$ to G (rate k_{-t}), and the reaction with water (rate k_d for G^+ and k_{dt} for $(GGG)^+$). The kinetic scheme is

$$\begin{array}{ccc} G^+(T-A)_m GGG & \underset{k_{-t}}{\overset{k_t}{\rightleftarrows}} & G(T-A)_m (GGG)^+ \\ k_d \downarrow & & \downarrow k_{dt} \end{array} \qquad (1)$$

The rate constants for trapping (k_t) and detrapping (k_{-t}) are related by the Boltzmann factor (with a free energy gap Δ_t)

$$k_{-t}/k_t = \exp(-\Delta_t/k_BT) \qquad (2)$$

In this kinetic scheme, the G triplet $5'-G_1G_2G_3-3'$ was treated as a single entity for hole trapping and detrapping.

A more detailed scheme for hole trapping/detrapping from and to the single guanine (G_0) by the $G_1G_2G_3$ triplet in the G_0-$(T-A)_mG_1G_2G_3$ duplex is

$$\begin{array}{ccccccc} G_0 & \underset{k_{bt}}{\overset{k_t}{\rightleftarrows}} & G_1 & \underset{k_{-G}^{(1)}}{\overset{k_G^{(1)}}{\rightleftarrows}} & G_2 & \underset{k_{-G}^{(2)}}{\overset{k_G^{(2)}}{\rightleftarrows}} & G_3 \\ k_d \downarrow & & \downarrow k_{dt(1)} & & \downarrow k_{dt(2)} & & \downarrow k_{dt(3)} \end{array} \qquad (1a)$$

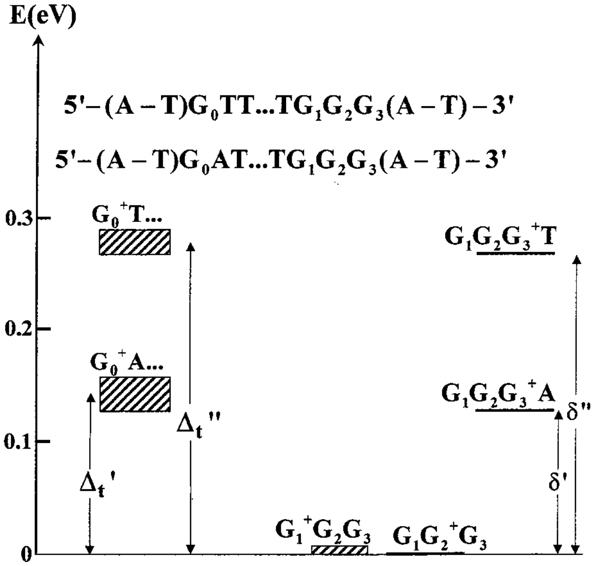


Figure 1. Energetics of the guanine hole sites in DNA duplexes, as obtained by semiempirical quantum mechanical calculations of Voityuk, Jortner, Bixon, and Rösch (ref 29). The reference energy is $E(G_1G_2^+G_3) = 0$. The right side portrays the energetics of hole states in the triplet G $5'-G_1G_2G_3-3'$ duplexes, with the dashed area for $BG_1^+G_2G_3$ representing the energy spread for B = T and A, and exhibiting the energetic ordering $\delta''(G_2G_3^+T) > \delta'(G_2G_3{}^+A) > E(G_1G_2^+G_3) \simeq E(G_1^+G_2G_3)$. The energies of the single guanine hole sites BG_0^+T and G_0^+A on the left side show the energy spread for B = T and A. The energies for hole trapping are $G_0^+BG_1G_2G_3 \rightarrow G_0BG_1^+G_2G_3$, with B = A or T obeying the ordering $\Delta_t'(G_0^+AG_1) < \Delta_t''(G_0^+TG_1)$.

The hole transfer rates $k_G^{(i)}$ and $k_{-G}^{(i)}$ ($i = 1, 2$) between the nearest-neighbor guanine bases are determined by the G−G interbase electronic matrix elements for hole transfer,[44,45] which are considerably larger than the superexchange mediated rates, which determine the hole trapping/detrapping rates. For a $(T-A)_m$ bridge we expect that[13,44,45] $k_t \sim (0.1)^m k_G^{(i)}$ ($i = 1, 2$), so that $k_t, k_{-t} \ll k_G^{(i)}, k_{-G}^{(i)}$ ($i = 1, 2$). Accordingly, the fast hole exchange within the guanine triplet $G_1G_2G_3$ results in thermal equilibration between the three hole sites, with the thermal populations of G_1^+, G_2^+, and G_3^+ in (GGG) being determined by their relative energies. A similar assumption of "fast relaxation" in GGG was invoked by Berlin, Burin, and Ratner.[35] The energetics of these three guanine hole sites in the $5'-G_1G_2G_3-3'$ duplex was inferred from the semiempirical calculations by Voityuk et al.[29] summarized in Figure 1. Although the absolute values of the energies cannot be adopted with confidence (in view of their small values), we infer that the relative values of these energies of the hole states (Figure 1) are $E(G_1^+) \simeq E(G_2^+) < E(G_3^+)$. This conclusion is consistent with the experimental results of Yoshioka et al.,[17] who showed that hole trapping in $5'-GGG-3'$ occurs mainly on the first two G_1 and G_2 sites. We also note the bridge selectivity and the directionality of the energetics,[29] where in triads $5'-XG^+Y-3'$ (X,Y = A, G, C, T) the stabilization energy of G^+ is considerably influenced by the subsequent base Y, while the effects of the preceding base X is small. Thus the energies of $AG_1^+G_2G_3$ and $TG_1^+G_2G_3$ are close, while the energy of $G_1G_2G_3^+A$ is lower than that of $G_1G_2G_3^+T$ (Figure 1). On the basis of the experimental[17] and theoretical[17,29] (Figure 1) results, we take the oxidation potentials of G_1 and G_2 to be equal, while that of G_3 is higher by the (free) energy δ. The energy difference δ depends on the subsequent base to G_3.

Making contact with the kinetic scheme (1) and writing $[GGG^+]$ for the initial trap concentration, we obtain for the concentration of G_1^+

$$[G_1^+] = [2 + \exp(-\delta/k_BT)]^{-1}\,[GGG^+] \tag{3}$$

The back reaction from G_1^+GG to the hole donor G is characterized by the rate k_{bt} which gives

$$k_{bt}[G_1^+] = k_{bt}(2 + \exp(-\delta/k_BT))^{-1}\,[GGG^+] = k_{-t}[GGG^+] \tag{4}$$

so that the effective detrapping rate is

$$k_{-t} = k_{bt}/[2 + \exp(-\delta/k_BT)] \tag{5}$$

while the hole trapping rate by G_1 is

$$k_t = k_{bt}\exp(\Delta/k_BT) \tag{6}$$

The ratio between the trapping and detrapping rate constants, eqs 5 and 6, is

$$\frac{k_{-t}}{k_t} = \exp(-\Delta/k_BT)[2 + \exp(-\delta/k_BT)]^{-1} \tag{7}$$

which can be expressed in terms of an effective (free) energy gap, Δ_t, eq 2, where

$$\Delta_t = \Delta + k_BT\ln[2 + \exp(-\delta/k_BT)] \tag{8}$$

The effective reaction rate with water in eq 1 is given in terms of the individual reaction rates of eq la by

$$k_{dt} = \frac{[k_{dt(1)} + k_{dt(2)} + k_{dt(3)}\exp(-\delta/k_BT)]}{[2 + \exp(-\delta/k_BT)]} \tag{9}$$

Provided that the individual chemical rates $k_{dt(j)}$ are weakly site dependent, i.e., $k_{dt(1)} = k_{dt(2)} = k_{dt(3)} = \langle k_{dt(j)}\rangle$, then $k_{dt} = \langle k_{dt(j)}\rangle$ is independent of δ.

Following the kinetic analysis of Appendix A, the ratio $\phi_t = Y(GGG^+)/Y(G^+)$ of the yields at the final GGG^+ and the initial G^+, eq A5, can be expressed in the form

$$\phi_t = \frac{1}{a(1 + b^{-1})} \tag{10}$$

where

$$a = k_d/k_t$$

$$b = [(k_t/k_{-t})(k_{dt}/k_t)] = \exp(\Delta_t/k_BT)(k_{dt}/k_t) \tag{11}$$

where $k_t/k_{-t} = \exp(\Delta_t/k_BT)$ in eq 11, according to eq 2. ϕ_t for a $G^+B_1B_2...B_NGGG$ duplex with a bridge containing N bases (where the bridge elements are $B_1, B_2... = T, A$) is determined by the parameters a and b, eq 11. While the chemical reaction rates k_d and k_{dt} are assumed to be invariant with respect to the nature of the bridge, ϕ_t for every bridge is expected to exhibit a bridge specificity originating from k_t and from k_t/k_{-t} (or Δ_t), as well as from a specific bridge size dependence of k_t. The bridge specificity of k_t is thus manifested by the hole transfer rate[46]

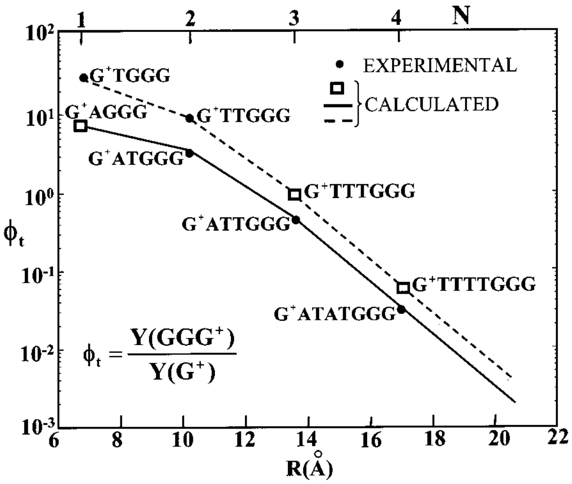


Figure 2. Analysis of the relative chemical yields ϕ_t, eqs 10 and 11, for unistep hole trapping/detrapping. The solid curve represents the calculated data for $(T)_N$ bridges (class (1)), with the parameters given by eq 16a. The dashed curve corresponds to the calculated data for $[(A)_{m+1},(T)_{m'}]_n$, ($m, m' \geq 0$, $N = n(m + m' + 1)$) bridges (class (2)), with the parameters given by eq 16b. The experimental data (●) of Giese et al. (refs 13, 14) are marked. Predictions for bridge-specific yields (□) are also presented.

$$k_t = (2\pi/\hbar)|V_{super}|^2F(\Delta_t) \tag{12}$$

where V_{super} is the superexchange electronic matrix element for $G^+...GGG$ coupling across the $B_1B_2...B_N$ bridge and $F(\Delta_t)$ is the nuclear Franck−Condon factor, which depends on the $G^+...GGG$ (effective) energy gap Δ_t. We thus infer that both parameters a and b, eq 11, depend on the parameters V_{super} and Δ_t for each bridge. The energetic data (Figure 1) imply that Δ_t is markedly affected by the nature of the nucleobase preceding the hole donor G^+, being different for $G^+A...$ and for $G^+T...$ bridges. We do not think that the numerical results from the semiempirical calculations[29] are accurate enough, but assert that they give the order of the Δ_t values.

In Figure 2 we present the available experimental results[13,14] for unistep hole trapping in two classes of bridges, for each of which we expect that the parameters Δ_t are equal:

Class(1): $G^+(T)_NGGG \quad (N = 1-4)$

Class(2): $G^+[(A)_{m+1}(T)_{m'}]_nGGG$
$(m,m' = 0,1;\ n = 1,2, \text{ and } N = n(m+m' + 1) = 1-4)$

For each of the duplexes in classes (1) or (2), the squared electronic coupling matrix element $|V_{super}|^2$, which determines k_t according to eq 12, is different. In Table 1 we present the superexchange matrix elements for the $G^+B_1B_2...B_N$ GGG duplexes presented in Figure 2 and related systems, which were calculated from the second-order expression[46−48]

$$V_{super} = [V(G,B_1)V(B_N,G)/\Delta E(G,B_1)]\prod_{j=1}^{N-1}V(B_j,B_{j+1})/\Delta E(G,B_{j+1}) \tag{13}$$

where $V(G,B_1)$, $V(B_N,G)$, and $V(B_j,B_{j+1})$ are the electronic matrix elements between nearest-neighbor nucleobases, which

TABLE 1: Superexchange Electronic Contribution $|V_{super}|^2$ to the Trapping Rate k_t, eq 12, in the 5′−GB$_1$B$_2$...B$_N$GGG−3′ Duplex[a]

DUPLEX	$\|V_{super}\|^2$ (eV)^2
GTG	3.76×10^{-4}
GAG	3.92×10^{-4}
GTTG	2.61×10^{-5}
GAAG	7.28×10^{-6}
GATG	3.62×10^{-5}
GTTTG	1.80×10^{-6}
GATTG	2.51×10^{-6}
GTTTTG	1.25×10^{-7}
GATATG	1.69×10^{-7}

[a] V_{super} were calculated from eq 13 with the pair elements from quantum mechanical calculations[46,47] and the semiempirical energy gaps being ΔE(GT) = 0.60 eV[47,38] and ΔE(GA) = 0.22 eV.[38]

were obtained by Voityuk et al.[46,47] by quantum mechanical calculations. $\Delta E(G,B_j)$ are the off-resonance energy gaps for hole transfer. The calculated energy gaps for six-base duplexes[29] include some features of base−base interactions but do not include solvation effects. The energy gaps are taken from a semiempirical analysis[38,46,47] as $\Delta E(G,T) = 0.60$ eV and $\Delta E(G,A) = 0.22$ eV.

The bridge specificity of ϕ_t cannot be solely attributed to the dependence of k_t on the electronic contribution $|V_{super}|^2$, and nuclear Franck−Condon effects have as well to be incorporated. A cursory examination of Table 1 indicates that as $|V_{super}(TT)|^2/|V_{super}(AT)|^2 = 0.7$, the electronic contribution lowers k_t for the TT bridge relative to the AT bridge. In contrast, the experimental results of Giese et al. reveal that[13,14] $\phi_t(G^+TTGGG)/\phi_t(G^+ATGGG) \simeq 3$. This marked difference is attributed to composite effects in opposite directions, i.e., the reduction of $|V_{super}|$ for the TT relative to the AT bridges, together with a marked increase of Δ_t between classes (1) and (2), which results in the enhancement of k_t and of $\exp(\Delta_t/k_BT)$ for class (1) duplexes.

To account for the bridge length dependence (N) we infer from the data of Table 1 that the trapping rates can be represented by

$$k_t = k_t(\mathrm{GTTGGG})r^{(N-2)} \qquad (\mathrm{class(1)}) \tag{14a}$$

$$k_t = k_t(\mathrm{GATGGG})r^{(N-2)} \qquad (\mathrm{class(2)}) \tag{14b}$$

where the reduction factor upon the addition of an extra (T−A) base pair is $r \simeq 0.07$ for both class (1) and class (2) duplexes. Rates k_t(TT) and k_t(AT) represent the trapping rates for the TT and AT bridges, i.e., for $N = 2$ in classes (1) and (2), respectively. Equations 14a and 14b manifest an exponential bridge dependence of $k_t \propto \exp[-N \ln(1/r)]$ originating from the electronic coupling. We did not include any changes of the medium reorganization energy λ,[49] as the medium polarization effects do not seem to be accounted for in terms of a continuous dielectric medium. From the experimental point of view, a detailed analysis of the energy gap dependence of hole injection in DNA results in λ values invariant to the bridge result.[50] Parameters a and b, eq 11, exhibit an exponential bridge length (N) dependence of the form

$$\begin{aligned} a(N) &= a(N{=}2)/r^{(N-2)} \\ b(N) &= b(N = 2)/r^{(N-2)} \end{aligned} \tag{15}$$

In Figure 2 we present the results of model calculations of ϕ_t vs N for classes (1) and (2), with the parameters

$$\mathrm{Class(1)}:\ a(N = 2) = 0.08,\ b(N = 2) = 2.5,\ r = 0.07 \tag{16a}$$

$$\mathrm{Class(2)}:\ a(N = 2) = 0.13,\ b(N = 2) = 1.0,\ r = 0.07 \tag{16b}$$

These numerical parameters predict the following numerical relations for the chemical yields

$$\begin{aligned} \mathrm{Class(1)}: &\quad \phi_t^{(N)} = \frac{12.5(0.07)^{(N-2)}}{1 + 0.4(0.07)^{(N-2)}} \\ \mathrm{Class(2)}: &\quad \phi_t^{(N)} = \frac{7.5(0.07)^{(N-2)}}{1 + (0.07)^{(N-2)}} \end{aligned} \tag{17}$$

From the model calculations based on eqs 11, 16, and 17, we infer on the bridge specificity and the (identical) bridge length dependence of the chemical yields, which are presented in Figure 2. From these model calculations we find that for $N = 1$, $\phi_t \simeq b(N = 2)/a(N = 2)$, while for $N = 2$, ϕ_t is somewhat smaller $(b(N = 2)/(a(N = 2)[1 + b(N = 2)]))$. For large values of $N > 2$, the exponential bridge length dependence $\phi_t(N) = [k(N = 2)/r^2] \exp[-N \ln(1/r)]$ is expected to prevail (Figure 2), with an identical exponential dependence for classes (1) and (2). Indeed, for lower values of N (i.e., $N = 1$ and 2), the plot of log ϕ_t vs N exhibits marked deviations from the exponential dependence $\phi_t \propto k_t \propto \exp(-\beta N)$ (Figure 2), and this exponential dependence is manifested only for high N (Figure 2). Thus, the phenomenological linear log ϕ_t vs N plots inferred from a heuristic analysis of experimental data[14] have to be regarded with some caution, as the relation $\phi_t \propto k_t$ has to be modified to account for back transfer, which exhibits a marked contribution for lower values of N, and bridge specificity effects (for a fixed value of N) have to be incorporated.

In addition to the good fit of the experimental results[13,14] for classes (1) and (2) (Figure 2), our analysis, based on eq 17, provides predictions for bridge specificity of the chemical yields for unistep trapping, marked in Figure 2. These predictions rest on the consideration of the cumulative effects of the electronic couplings, $|V_{super}|^2$, energetics (Δ_t), and nuclear Franck−Condon factors. Of considerable interest is the prediction $\phi_t(\mathrm{GAGGG})/\phi_t(\mathrm{GTGGG}) = 0.25$, while for larger values of N we predict that $\phi_t((\mathrm{T})_N)/\phi_t((\mathrm{AT})_{N/2}) = 0.60$, with $\phi_t((\mathrm{AT})_{N/2})$ exhibiting an exponential N dependence (Figure 2). The confrontation of these predictions with experimental reality will be of interest.

From this rather elaborate analysis of the unistep hole trapping, we have used two parameters for each class of duplexes, eqs 11 and 14, whose ratio, given by

$$a(N)/b(N) = (k_d/k_{dt})\exp(-\Delta_t/k_BT) \tag{18}$$

is independent of N but dependent of the composition of the bridge. To extract information on the energetics and kinetics of hole trapping by GGG in these duplexes, an independent estimate of the ratio k_d/k_{dt} should be obtained. Such information is accessible from the analysis of multistep hole hopping in well characterized duplexes, which we shall now consider.

3. Multiple Hole Transport

The relative chemical yields for the $G^+(TTG)_mTTGGG$ duplexes were experimentally studied by Giese et al.[14] (for n

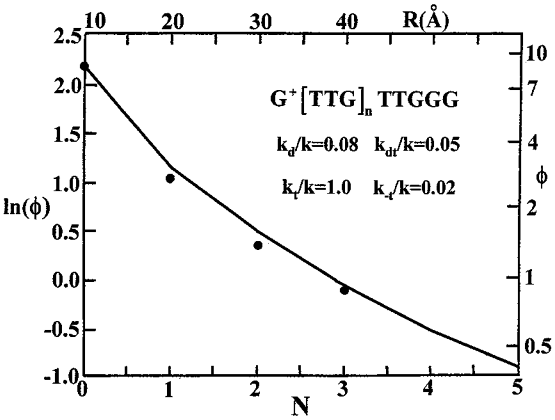
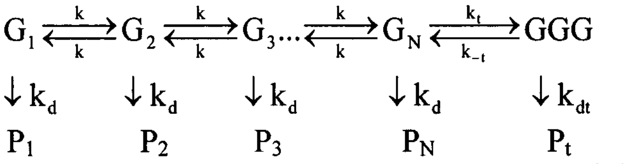


Figure 3. Analysis of the chemical yields ϕ for hole trapping, eq 20, with the kinetic parameters marked on the figure. The experimental data (●) are taken from Giese et al. (refs 13, 14).

$= 0-4$) and were analyzed by us[32,33] and by Berlin et al.[34-37] This previous analysis requires some extension and modification to account for thermally induced backtrapping, as well as for the distinct reaction rate of the oxidized trap (GGG)$^+$ with water. The kinetic scheme is



(19)

This scheme corresponds to the initial formation of G_1^+ by hole shift from a cation, followed by the reversible (superexchange mediated) hole hopping with a rate k between nearest-neighbor G bases, which are separated by two T bases. The hole trapping from G_N^+ is reversible, with the trapping (k_t) and detrapping (k_{-t}) rates being related by detailed balance, eq 2. As in the analysis of the unistep hole trapping/detrapping in section 2, the analysis based on hole equilibration within the GGG triplet trap is given by eq la (with G_0 replaced by G_N) and by eqs 3−8. The hole hopping between the G_j^+ ($j = 1,...,N$) groups, trapping, and detrapping via (GGG)$^+$ competes with the chemical side reactions of G$^+$ and (GGG)$^+$ (involving several side reactions, e.g., deprotonation and reactions with water) with the rates k_d (for all G_j^+) and k_{dt} (for (GGG)$^+$).

The kinetic analysis of the reaction scheme, eq 19, is presented in Appendix A. The relative chemical yield data can be expressed in terms of the ratio of the yields of the product P_t to all the other products P_j ($j = 1,...,N$) in terms of

$$\phi = Y(P_t)/\sum_{j=1}^{N} Y(P_j) \tag{20}$$

Alternatively, the ratio of the yields of P_t and P_1 was measured[13,14] and is given by

$$\phi' = Y(P_t)/Y(P_1) \tag{21}$$

We calculated ϕ and ϕ' in Appendix B. The experimental chemical yield ratios of Giese et al.[13,14] can be well fit (Figures 3 and 4) by the four kinetic parameters for hole trapping, detrapping, and hopping through two T bases, together with the chemical reaction rates of G$^+$

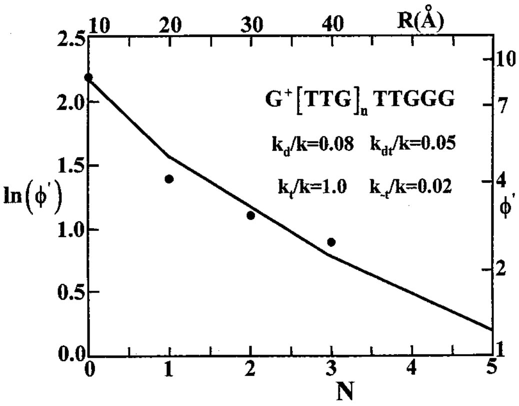


Figure 4. Analysis of the relative chemical yields ϕ', eq 21, with the kinetic parameters being identical to those of Figure 3. The experimental data (●) are taken from Giese et al. (refs 13, 14).

$$\begin{aligned} k_d/k &= 0.08 \\ k_{dt}/k &= 0.05 \\ k_t/k &= 2-1 \\ k_{-t}/k &= 0.1-0.02 \end{aligned} \tag{22}$$

The range of the rates ratio k_t/k and k_{-t}/k provides a reasonable fitting of the experimental yield data.[14] An interesting conclusion emerging from this analysis is that the reaction rates of G$^+$ and of (GGG)$^+$ with water are somewhat different, i.e.,

$$k_d/k_{dt} = 1.6 \tag{23}$$

A qualitatively similar conclusion was reached by Giese and Spichty[15] who have inferred on the basis of a kinetic analysis (excluding hole detrapping) that $k_d/k_t = 3.7$.

4. Discussion

The kinetic data obtained from the analysis of multistep hole hopping, eqs 22 and 23, and unistep hole trapping, eqs 15, 16, and 18, can now be combined to provide a self-consistent picture of the bridge specificity of hole trapping/detrapping energetics and kinetics. From eq 16 we conclude that $a/b = 30$ for the (TT) and other (T)$_N$ bridges of class (1) and $a/b = 7.7$ for (AT) and other bridges of class (2). Assuming that the ratio k_d/k_{dt} is independent of the nature of the nucleobase adjacent to G$^+$, and making use of eqs 8 and 23, we can evaluate ratios of trapping/detrapping rates. For the (TT) bridge (and for other bridges of class (1)) $k_t/k_{-t} = 48$, so that $\Delta_t = 0.096$ eV, while for the (AT) bridge (and for other bridges of class (2)) $k_t/k_{-t} = 12$, and $\Delta_t = 0.062$ eV. The values of Δ_t for these processes of hole trapping/detrapping by hole shift, which do not involve Coulomb barriers,[31] are expected to be independent of the length of the bridge, for both classes (1) and (2) of the duplexes. The relatively low bridge specific values of Δ_t imply that GGG acts as a shallow hole trap, where the back trapping can be quite substantial. These (effective) free energy gaps of $\Delta_t = 0.096$ eV for (T)$_N$ ($N = 1, 2$) bridges and of $\Delta_t = 0.062$ eV for $[A_{m+1}T_{m'}]_n$ ($m, m' \geq 0$; $N = n(m + m' + 1) = 1-4$), i.e., A, AT, ATT, and ATAT bridges. The free energy gaps exhibit the same ordering as the energy gaps Δ_t' (G$^+$AGGG), and Δ_t'' (G$^+$TGGG), which were obtained from semiempirical calculations (Figure 1), i.e., Δ_t(G$^+$AGGG) < Δ_t(G$^+$TGGG). However, the free energy Δ_t data inferred from the experimental analysis are lower than the calculated energetic results[29] summarized in Figure 1. This is not surprising, as the calculated results[29] refer to model duplexes in a vacuum and do not incorporate solvation effects. The energy gap $\Delta_t(\mathrm{G^+AGGG}) = 0.062$ eV inferred from our analysis is close to the free energy gap $\Delta G_t = 0.077 \pm 0.005$ eV evaluated by Lewis et al.[28] for hole trapping in the $\mathrm{G^+AGGGA}$ duplex. It is gratifying that the experimental results for the chemical yields[13,14] presented herein and for the time-resolved rates[28] for the $\mathrm{G^+AGGG}$ duplexes provide good internal agreement. Time-resolved data for the energy gaps in the $\mathrm{G^+TGGG}$ duplex, for which our analysis provides $\Delta_t = 0.096$ eV, will be of considerable interest in the context of bridge specificity of the energetics of hole trapping.

The ratio of $k_{-t}/k_t = 0.021$ for $(\mathrm{T})_m$ bridges obtained from the foregoing analysis is consistent with the lower limit of the rate ratios $k_t/k = 1$ and $k_{-t}/k = 0.02$, i.e., $k_{-t}/k_t = 0.02$ for the independent analysis of hole hopping via TT bridges, eq 22, and is presented in Figures 3 and 4. Thus, in this respect the analysis of unistep and multistep processes is self-consistent. We are somewhat concerned about the $k_t/k = 1-2$ result inferred from the analysis of hole hopping, eq 22. We would expect that for an exothermic charge-transfer process in the normal region (i.e., $\Delta_t < \lambda$, where λ is the reorganization energy) $k_t/k > 1$ and rough estimates for TT bridges would then indicate that $k_t/k \sim 7$. This apparent discrepancy may be due to large intramolecular distortions with the $(\mathrm{GGG})^+$ trap.

Finally, we move toward some speculative grounds, attempting to attain further insight into the contribution of the (bridge specific) energy gap Δ_t to the Franck−Condon factor $F(\Delta_t)$, eq 12. The trapping rate k_t can be estimated for the "normal" charge transfer Marcus region when $\Delta_t \ll \lambda$, where λ is the medium reorganization energy. Then a rough estimate gives[38] $k_t \approx |\mathrm{V_{super}}|^2\ C \exp(\Delta_t/2k_\mathrm{B}T)$, where the parameter C contains numerical constants, together with the contributions of medium modes and of high-frequency modes. Making use of eq 2 we can write

$$k_t = C|\mathrm{V_{super}}|^2(k_t/k_{-t})^{1/2}$$

$$k_{-t} = C|\mathrm{V_{super}}|^2(k_t/k_{-t})^{-1/2} \qquad (24)$$

where the ratio (k_t/k_{-t}), eq 2, was obtained from our analysis. Turning to the bridge specificity of k_t, we infer that for the $N = 2$ bridges of classes (1) and (2), we get

$$k_t(\mathrm{TT})/k_t(\mathrm{AT}) = \frac{|\mathrm{V_{super}(TT)}|^2}{|\mathrm{V_{super}(AT)}|^2} \exp[(\Delta_t(\mathrm{TT}) - \Delta_t(\mathrm{AT}))/2k_\mathrm{B}T] \qquad (25)$$

Making use of the quantum mechanical data of Table 1 we have the contribution of the electronic matrix elements $|\mathrm{V_{super}(TT)}|^2/|\mathrm{V_{super}(AT)}|^2 = 0.72$, while the contribution of the nuclear Franck−Condon factors is $\exp[[\Delta_t(\mathrm{TT})-\Delta_t(\mathrm{AT})]/2k_\mathrm{B}T] = 2$, so that $k_t(\mathrm{TT})/k_t(\mathrm{AT}) = 1.44$. This result demonstrates again the cumulative effects of electronic and nuclear terms to the kinetics of charge transport in DNA.

From the foregoing analysis we conclude that hole trapping/detrapping and hopping requires an analysis which avoids "coarse gaining" assumptions previously used.[32,33] Theoretical information from quantum mechanical calculations of energetics and electronic coupling matrix elements is of considerable importance as guidelines for the theory of the kinetics of charge separation in DNA. The semiempirical calculations of energetics, although not providing absolute values due to the lack of a complete account of solvation effects, provide important guidelines for specificity of the energetics which govern the trapping/detrapping processes. The electronic coupling matrix elements allow the estimates of superexchange coupling, which was calculated using semiempirical energy gaps.[38,46,47] The results provide input information on (small) electronic bridge specificity effects and on the bridge length dependence of the trapping/detrapping and hopping rates.

Finally, we allude to charge transport in DNA, triggering "chemistry at a distance".[1−38] Our analysis focused on hole trapping in ...$\mathrm{G(T{-}A)_nGGG}$... duplexes ($n = 1-4$) and on hole hopping in $\mathrm{GT_nG}$ ($n = 2$) duplexes. For short ($n \leq 4$) $(\mathrm{T{-}A})_n$ mediating bridges, hole superexchange between guanine prevails, and our previous[32,33] and present analysis rests on this notion. Thus in duplexes where guanine hole carriers and GGG or GG hole shallow traps are separated by relatively short $(\mathrm{T{-}A})_n$ ($n = 1-4$) bridges, the individual hopping/trapping steps are super exchange mediated and long-range hole tranport can be realized over a distance scale of 50−300 Å.[13,14,32−38] We have shown[38] that superexchange mediated charge transfer through long bridges becomes ineffective with increasing the bridge length, and a thermally induced hopping (TIH) process can take over. The TIH involves thermally activated donor-bridge charge injection followed by intrabridge charge hopping. Adenines can participate in bridging for TIH in DNA. Provided that parallel side reactions with water are ineffective, the hole TIH can proceed in $\mathrm{G^+(T{-}A)_nGGG}$ duplexes ($n > 4$) through long $(\mathrm{A})_n$ duplexes. Furthermore, for TIH via long $(\mathrm{T{-}A})_n$ ($n > 4$) duplexes, interstrand zigzagging between the A bases in the two strands can occur, with the $(\mathrm{A})_n$ acting as an effective "chain" for hole transport, irrespective of the base ordering within the duplex. As every (T−A) Watson−Crick pair mediating between $(\mathrm{G^+})_n$...$(\mathrm{G})_n$ and $(\mathrm{G})_n$...$(\mathrm{G^+})_n$ is then involved in the TIH, bridge sequence specificity for this mechanism is eroded. This pattern of TIH is distinct from the bridge specificity for the superexchange mediating hopping/trapping steps analyzed herein. The proposed TIH mechanism is in accord with the experimental results of Barton et al.[21] who reported hole transfer in long $(\mathrm{GGG})^+(\mathrm{A})_n(\mathrm{GGG})$ ($n = 4-10$) duplexes and of Schuster et al.[22−25] who observed hole transfer between GG groups separated by AAATT segments. The efficiency of TIH via long $(\mathrm{A})_n$ bridges is determined by the relative rate of the competing side reaction of $(\mathrm{G})_n^+$ with water and by the $\mathrm{G^+A}$ energy gap. Indeed, the relative reaction rates of $\mathrm{G^+}$ and $\mathrm{GGG^+}$ inferred herein from Giese's data $k_d/k_t \simeq k_d/k \simeq 0.08$ (for an $m = 2$ bridge) and $k_d/k_{dt} \simeq 1.6$, seem to be too high to warrant an effective TIH via the A chain for which the energy gap is 0.22 eV.[36] It appears that under the experimental conditions of Barton et al.[20,21] and of Schuster et al.,[22−25] the $\mathrm{G^+}$, $(\mathrm{GG})^+$ or $(\mathrm{GGG})^+$ water reaction seems to be sufficiently slow not to overwhelm the TIH. There is a distinct possibility that we have to distinguish between $(\mathrm{GGG})_m^+$ long-range transport induced by hopping/trapping superexchange steps through "short" $(\mathrm{T{-}A})_n$ ($n < 4$) bridges considered herein and very long-range transport induced by TIH via $(\mathrm{A})_n$ chains in long $(\mathrm{GGG})_m^+$-$(\mathrm{T} - \mathrm{A}_n)$ $(\mathrm{GGG})_m^+$ duplexes.

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Appendix A

Kinetic Analysis of Unistep Hole Trapping in $\mathbf{G^+(T-A)_{\mathit{m}}GGG}$ Duplexes. The kinetic matrix of the rate constants for the kinetic scheme (1) is

$$\mathbf{K} = \begin{pmatrix} -(k+k_d) & k_{-t} \\ k_t & -(k_{-t}+k_{dt}) \end{pmatrix} \quad (A1)$$

Denoting the vector of the time-dependent concentration of the species

$$\mathbf{v} = \begin{pmatrix} a(t) \\ b(t) \end{pmatrix}$$

where a(t) is the concentration of the initial state $G^+(T-A)_nGGG$ and b(t) is the concentration of the final state $G(T-A)_n(GGG)^+$. The kinetic equation is then

$$\frac{d\mathbf{v}}{dt} = \mathbf{Kv} \quad (A2)$$

with the initial condition $a(t=0) = 1$. The yields for the water reaction with species G^+ and GGG^+, denoted by $Y(G^+)$ and $Y(GGG^+)$ respectively, are

$$Y(G^+) = k_d\int_0^\infty a(t)dt = k_d[\int_0^\infty \exp\{\mathbf{K}t\}dt]_{1,1} = k_d(K^{-1})_{1.1}$$

$$Y(GGG^+) = k_{dt}\int_0^\infty b(t)dt = k_{dt}[\int_0^\infty \exp\{\mathbf{K}t\}dt]_{2,1} = k_{dt}(K^{-1})_{2,l} \quad (A3)$$

These are given by

$$Y(G^+) = \frac{k_d(k_{-t} + k_{dt})}{k_t k_{dt} + k_{-t}k_d + k_d k_{dt}} \quad (A4a)$$

$$Y(GGG^+) = \frac{k_{dt}k_t}{k_t k_{dt} + k_{-t}k_d + k_d k_{dt}} \quad (A4b)$$

and the ratio of the chemical yields for the final GGG^+ and initial G^+ in unistep trapping is

$$\phi_t = Y(GGG^+)/Y(G^+) = \frac{k_t}{k_d(1 + k_{-t}/k_{dt})} \quad (A5)$$

Appendix B

Kinetic Analysis of Multistep Hole Hopping in $\mathbf{G^+(TTG)_{\mathit{n}}TTGGG}$ Duplexes. The kinetic analysis of the reaction scheme, eq 19, $d\mathbf{a}(t)/dt = \mathbf{A}\,\mathbf{a}(t)$, where $\mathbf{A}$ is the kinetic matrix and $\mathbf{a}(t)$ the vector of the normalized concentrations of G_j^+ ($j = 1,...,N$) and $(GGG)^+$ (with the initial conditions $a_1(t=0) = 1$ and $a_{j\neq l}(t=0) = 0$) follows the treatment previously given by us.[33] The yields in eqs 20 and 21 can be expressed by

$$Y(P_j) = k_d[\int dt \exp\{\mathbf{A}t\}]_{j,1} = k_d A^{-1}_{j,l}$$

$$Y(P_t) = k_{dt}[\int dt \exp\{\mathbf{A}t\}]_{(N+1),1} = k_{dt} A^{-1}_{(N+1),1} \quad (B1)$$

which are obtained by the inversion of the kinetic matrix.

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