1. Introduction

Interest in charge transfer and transport in DNA 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. and Barton et al. provided extensive experimental information for the yields of hole trapping in a series of duplexes G\textsuperscript{\textdagger}T−A\textsubscript{m}GGG and for hole hopping/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)\textsubscript{N} and for [(A)\textsubscript{m}+1(T)\textsubscript{m}G] (m, m′ ≥ 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\textsuperscript{\textdagger} (rate k\textsubscript{tr}) and of (GGG)\textsuperscript{\textdagger} (rate k\textsubscript{sh}) with water, i.e., k\textsubscript{sh}/k\textsubscript{tr} = 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\textsuperscript{\textdagger}(T)\textsubscript{N}GGG duplexes and of \( \Delta_t = 0.062 \) eV in the G\textsuperscript{\textdagger}[(A)\textsubscript{m}+1(T)\textsubscript{m}G]GGG duplexes.

In this paper we present a self-consistent kinetic-quantum mechanical analysis of chemical yield data for hole trapping/detrapping in G\textsuperscript{\textdagger}(T−A)\textsubscript{m}GGG duplexes (with free energy gaps \( \Delta_t \)) and for hole hopping/trapping/detrapping in G\textsuperscript{\textdagger}[(T)\textsubscript{N}G] (T)\textsubscript{m}GGG 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)\textsubscript{N} and for [(A)\textsubscript{m}+1(T)\textsubscript{m}G] (m, m′ ≥ 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\textsuperscript{\textdagger} (rate k\textsubscript{tr}) and of (GGG)\textsuperscript{\textdagger} (rate k\textsubscript{sh}) with water, i.e., k\textsubscript{sh}/k\textsubscript{tr} = 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\textsuperscript{\textdagger}(T)\textsubscript{N}GGG duplexes and of \( \Delta_t = 0.062 \) eV in the G\textsuperscript{\textdagger}[(A)\textsubscript{m}+1(T)\textsubscript{m}G]GGG duplexes.

The description of hole transport through G\textsuperscript{\textdagger} “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. and Schuster et al. and by Siebbeles and Berlin considered only exoergic hole transport through G...GGG distance scale of 10−40 Å (n = 0−3, m = 2) reported by Giese et al. The moderately large distance scale for hole transport in DNA duplexes is limited by the parallel side reactions of the G\textsuperscript{\textdagger} “resting sites” and of the (GGG)\textsuperscript{\textdagger} hole traps with water, and 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\textsuperscript{\textdagger} radical cations, were applied to account for the bridge size dependence of the chemical yields for long-range hole shift in the G\textsuperscript{\textdagger}[(T)\textsubscript{m}G] (T)\textsubscript{m}GGG over the G\textsuperscript{\textdagger}...GGG distance scale of 10−40 Å (n = 0−3, m = 2) reported by Giese et al.

The heuristic kinetic analysis of hole trapping in the G\textsuperscript{\textdagger}(T−A)\textsubscript{m}GGG duplexes and the previous kinetic analysis of hole hopping and trapping in the G\textsuperscript{\textdagger}[(T)\textsubscript{m}G] (T)\textsubscript{m}GGG duplexes by Bixon et al. and by Berlin, Burin, and Ratner and by Siebbeles and Berlin considered only exoergic hole transport through G...GGG distance scale of 10−40 Å (n = 0−3, m = 2) reported by Giese et al.
trapping processes. Thermally induced detrapping should be significant. Lewis et al. have provided time-resolved evidence for thermally induced detrapping from (GGG)+ 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 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+4(T–A)mGGG duplexes and (ii) multistep long-range hole hopping transport followed by hole trapping and detrapping in G+4(T)mGGG(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+4...GGG Duplexes

The hole trapping in the 5′–G+4(T–A)mGGG–3′ systems studied by Meggers et al. 13 will be described in terms of trapping by (GGG) (rate k₁), detrapping from (GGG)+ to G (rate k₋₁), and the reaction with water (rate k_d for G+ and k_dT for (GGG)+). The kinetic scheme is

\[ G^+(T–A)_mGGG &\xrightarrow{k_{k_1}}& G(T–A)_m(GGG)^+ \]

\[ k_d \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad k_{dT} \quad (1) \]

The rate constants for trapping (k₁) and detrapping (k₋₁) are related by the Boltzmann factor (with a free energy gap Δe)

\[ k₋₁/k₁=\exp(-\Delta e/k_BT) \quad (2) \]

In this kinetic scheme, the G triplet 5′–G1G2G3–3′ 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 (G₀) by the G₁G2G3 triplet in the G₀–(T–A)mG₁G₂G₃ duplex is

\[ G₀ \xleftarrow{k_{k_1}} G₁ \xrightarrow{k_{k_1}^{(1)}} G₂ \xrightarrow{k_{k_1}^{(2)}} G₃ \]

\[ k_d \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad k_{dT(1)} \quad k_{dT(2)} \quad k_{dT(3)} \quad (1a) \]

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(G₁G₂G₃) = 0. The right side portrays the energetics of hole states in the triplet G 5′G₁G₂G₃–3′ duplexes, with the dashed area for BG₁G₂G₃ representing the energy spread for B = T and A, and exhibiting the energetic ordering δ(G₂G₃T) > δ(G₂G₃A) > E(G₁G₂G₃) = E(G₁G₂G₃). The energies of the single guanine hole sites BG₀/T and G₀/A on the left side show the energy spread for B = T and A. The energies for hole trapping are G₁BG₂G₃T = G₀BG₁G₂G₃, with B = A or T obeying the ordering Δe(G₁G₂G₃) < Δe(G₀G₃T).

The hole transfer rates k₁(i) and k₀(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 k₋₁(i) ~ (0.1)k₁(i) (i = 1, 2), so that k₋₁k₁ ≪ k₁(i) k₀(i) (i = 1, 2). Accordingly, the fast hole exchange within the guanine triplet G₁G₂G₃ results in thermal equilibration between the three hole sites, with the thermal populations of G₁, G₂, and G₃ 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′–G₁G₂G₃–3′ 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(G₁) ≈ E(G₂) < E(G₃). This conclusion is consistent with the experimental results of Yoshioha et al. 17 who showed that hole trapping in 5′–GGG–3′ occurs mainly on the first two G₁ and G₂ 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 AG₁G₂G₃ and TG₁G₂G₃ are close, while the energy of G₁G₂G₃A is lower than that of G₁G₂G₃T (Figure 1). On the basis of the experimental 17 and theoretical 29 results (Figure 1) results, we take the oxidation potentials of G₁ and G₂ to be equal, while
that of G1 is higher by the (free) energy \( \delta \). The energy difference \( \delta \) depends on the subsequent base to G1.

Making contact with the kinetic scheme (1) and writing [GGG]\(^+\) for the initial trap concentration, we obtain for the concentration of G1\(^+\)

\[
[G1^+] = \frac{[2 + \exp(-\delta/k_BT)]^{-1}}{[GGG]^+} \tag{3}
\]

The back reaction from G1\(^+\), GG to the hole donor G is characterized by the rate \( k_{a} \) which gives

\[
k_{at}[G1^+] = k_{a}(2 + \exp(-\delta/k_BT))^{-1} [GGG]^+ = k_{-a}[GGG]^+ \tag{4}
\]

so that the effective detrapping rate is

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

while the hole trapping rate by G1 is

\[
k_{a} = k_{a}\exp(\Delta/k_BT) \tag{6}
\]

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

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

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

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

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

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

Provided that the individual chemical rates \( k_{at(i)} \) are weakly site dependent, i.e., \( k_{at(1)} = k_{at(2)} = k_{at(3)} = \langle k_{at(0)} \rangle \), then \( k_{a} = \langle k_{at(0)} \rangle \) is independent of \( \delta \).

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

\[
\phi_i = \frac{1}{a(1 + b^{-1})} \tag{10}
\]

where

\[
a = k_d/k_i \tag{11}
\]

\[
b = [(k_d/k_{-d})(k_a/k_i)] = \exp(\Delta/k_BT)(k_d/k_l) \tag{12}
\]

where \( k_d/k_{-d} = \exp(\Delta/k_BT) \) in eq 11, according to eq 2, \( \phi_i \) for a G\(^+\)B\(_1\)B\(_2\)...B\(_N\)GGG 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 \( k_a \) are assumed to be invariant with respect to the nature of the bridge, \( \phi_i \) for every bridge is expected to exhibit a bridge specificity originating from \( k_i \) and from \( k_d/k_{-d} \) (or \( \Delta_e \)), as well as from a specific bridge size dependence of \( k_i \). The bridge specificity of \( k_i \) is thus manifested by the hole transfer rate\(^{66}\)

\[
k_i = (2\pi\hbar)V_{super}^2 F(\Delta_e) \tag{12}
\]

where \( V_{super} \) is the superexchange electronic matrix element for G\(^+\)...GGG coupling across the B\(_1\)B\(_2\)...BN bridge and \( F(\Delta_e) \) is the nuclear Franck–Condon factor, which depends on the G\(^+\)...GGG (effective) energy gap \( \Delta_e \). We thus infer that both parameters \( a \) and \( b \), eq 11, depend on the parameters \( V_{super} \) and \( \Delta_e \) for each bridge. The energetic data (Figure 1) imply that \( \Delta_e \) is markedly affected by the nature of the nucelbase preceding the hole donor G\(^+\), being different for G\(^+\)A... and for G\(^+\)T...

brides. 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 \( \Delta_e \) 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 \( \Delta_e \) are equal:

Class(1): G\(^+\)(T)\(_N\)GGG  \( (N = 1 - 4) \)

Class(2): G\(^+\)([A]\(_m\)+1(T)\(_n\)k)GGG

\( (m,m' = 0,1; n = 1,2; \quad N = n(m+m' + 1) = 1 - 4) \)

For each of the duplexes in classes (1) or (2), the squared electronic coupling matrix element \( |V_{super}|^2 \), which determines \( k_i \) according to eq 12, is different. In Table 1 we present the superexchange matrix elements for the G\(^+\)B\(_1\)B\(_2\)...BN GGG duplexes presented in Figure 2 and related systems, which were calculated from the second-order expression\(^{56-48}\)

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

where \( V(G,B_j) \), \( V(B,N,G) \), and \( V(B_j,B_{j+1}) \) are the electronic matrix elements between nearest-neighbor nucleobases, which
were obtained by Voityuk et al.46,47 by quantum mechanical calculations. \( \Delta E(G,B) \) are the off-resonance energy gaps for hole transfer. The calculated energy gaps for six-base duplexes29 include some features of base-base interactions but do not include solvation effects. The energy gaps are taken from a semiempirical analysis38,46,47 as \( \Delta E(G,T) = 0.60 \text{ eV} \) and \( \Delta E(G,A) = 0.22 \text{ eV}. \)

The bridge specificity of \( \phi_t \) cannot be solely attributed to the dependence of \( k_t \) on the electronic contribution \( |V_{\text{super}}|^2 \), and nuclear Franck-Condon effects have as well to be incorporated. A cursory examination of Table 1 indicates that as \( |V_{\text{super}}(TT)|^2/|V_{\text{super}}(AT)|^2 = 0.7 \), 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 that13,14 \( \phi_t(G^+TTGGG)/\phi_t(G^+ATGGG) \approx 3 \). This marked difference is attributed to composite effects in opposite directions, i.e., the reduction of \( |V_{\text{super}}| \) for the TT relative to the AT bridges, together with a marked increase of \( \Delta \lambda \) between classes (1) and (2), which results in the enhancement of \( k_t \) and of \( \exp(\Delta/\kappa T) \) 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

\[
k_t = k_t(GTTGGG)r^{(N-2)} \quad \text{(class(1))} (14a) \\
k_t = k_t(GATGGG)r^{(N-2)} \quad \text{(class(2))} (14b)
\]

where the reduction factor upon the addition of an extra (T\(^-\)A) base pair is \( r = 0.07 \) 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 \( \lambda \),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 \( \lambda \) values invariant to the bridge result.50

Parameters \( a \) and \( b \), eq 11, exhibit an exponential bridge length (N) dependence of the form

\[
a(N) = a(N=2)r^{(N-2)} \\
b(N) = b(N = 2)r^{(N-2)} (15)
\]

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

Class(1): \( a(N = 2) = 0.08, b(N = 2) = 2.5, r = 0.07 \) (16a)
Class(2): \( a(N = 2) = 0.13, b(N = 2) = 1.0, r = 0.07 \) (16b)

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

Class(1):

\[
\phi_t^{(N)} = \frac{12.5(0.07)^{(N-2)}}{1 + 0.4(0.07)^{(N-2)}}
\]

Class(2):

\[
\phi_t^{(N)} = \frac{7.5(0.07)^{(N-2)}}{1 + (0.07)^{(N-2)}} (17)
\]

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 \( N = 1 \), \( \phi_t = b(N = 2)a(N = 2) \), while for \( N = 2 \), \( \phi_t \) is somewhat smaller \( b(N = 2)a(N = 2)(1 + b(N = 2)) \). For large values of \( N \), the exponential bridge length dependence \( \phi_t(N) = [k(N = 2)r^2]^2 \exp[-N \ln(1/r)] \) 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 \( \log \phi_t \) 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 \( \phi_t \) vs \( N \) plots inferred from a heuristic analysis of experimental data 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 results13,14 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, \( |V_{\text{super}}|^2 \), energetics (\( \Delta \lambda \)), and nuclear Franck-Condon factors. Of considerable interest is the prediction \( \phi_t(GAGGG)/\phi_t(GTGGG) = 0.25 \), while for larger values of \( N \) we predict that \( \phi_t((TT)_N)/(\phi_t((AT))_N) = 0.60 \), with \( \phi_t((AT))_N \) 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

\[
\alpha(N/\beta(N)) = (k_d/k_b)\exp(\Delta/\kappa T) (18)
\]

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 \( k_d/k_b \) 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 \( G^+(TTG)_n TTGGG \) duplexes were experimentally studied by Giese et al.14 (for \( n \)
Figure 3. Analysis of the chemical yields \( \phi \) 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).

\[ \phi = Y(P_t) / \sum_{j=1}^{N} Y(P_j) \]  

Alternatively, the ratio of the yields of \( P_1 \) and \( P_1 \) was measured\(^{13,14}\) and is given by

\[ \phi' = Y(P_1) / Y(P_1) \]  

We calculated \( \phi \) and \( \phi' \) 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.

Figure 4. Analysis of the relative chemical yields \( \phi' \), 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).

detrapping, and hopping through two T bases, together with the chemical reaction rates of \( G^+ \)

\[ k_{d/k} = 0.08 \]

\[ k_{d/k} = 0.05 \]

\[ k_{d/k} = 2 - 1 \]

\[ k_{d/k} = 0.1 - 0.02 \]  

The range of the rates ratio \( k_{d/k} \) and \( k_{d/k} \) 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.,

\[ k_{d/k} = 1.6 \]  

A qualitatively similar conclusion was reached by Giese and Spichy\(^ {15}\) who have inferred on the basis of a kinetic analysis (excluding hole detrapping) that \( k_{d/k} = 3.7 \).

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 \( k_{d/k} \) 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)) \( k_{d/k} = 48 \), so that \( \Delta_s = 0.096 \) eV, while for the (AT) bridge (and for other bridges of class (2)) \( k_{d/k} = 12 \), and \( \Delta_s = 0.062 \) eV. The values of \( \Delta_s \) 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 \( \Delta_s \) imply that GGG acts as a shallow hole trap, where the back trapping can be quite substantial. These (effective) free energy gaps of \( \Delta_s \) can be well fit (Figures 1, 3, and 4) by the four kinetic parameters for hole trapping, involving several side reactions, e.g., deprotonation and reactions with water) with the rates \( k_d \) (for all \( G_j^+ \)) and \( k_{at} \) (for \( (GGG)^+ \)).

This scheme corresponds to the initial formation of \( G_j^+ \) 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 \( G_j^+ \) is reversible, with the trapping \( (k) \) and detrapping \( (k_{d}) \) 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 1a (with \( G_0 \) replaced by \( G_N \)) and eqs 3–8. The hole hopping between the \( G_j^+ \) \( (j = \ldots, N) \) groups, trapping, and detrapping via \( (GGG)^+ \) competes with the chemical side reactions of \( G^+ \) and \( (GGG)^+ \) (including several side reactions, e.g., deprotonation and reactions with water) with the rates \( k_d \) (for all \( G_j^+ \)) and \( k_{at} \) (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 \( P_j \) \( (j = \ldots, N) \) in terms of

\[ \phi = Y(P_t) / \sum_{j=1}^{N} Y(P_j) \]  

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

\[ G_1 \xrightleftharpoons[k_d]{k} G_2 \xrightleftharpoons[k_d]{k} G_3 \ldots \xrightleftharpoons[k_d]{k} G_N \xrightleftharpoons[k_{d/t}]{k} GGG \]  

\[ k_d \quad k_d \quad k_d \quad k_d \quad k_d \quad k_{at} \]  

\[ P_1 \quad P_2 \quad P_3 \quad P_N \quad P_t \]  

(19)

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 1a (with \( G_0 \) replaced by \( G_N \)) and eqs 3–8. The hole hopping between the \( G_j^+ \) \( (j = \ldots, N) \) groups, trapping, and detrapping via \( (GGG)^+ \) competes with the chemical side reactions of \( G^+ \) and \( (GGG)^+ \) (including several side reactions, e.g., deprotonation and reactions with water) with the rates \( k_d \) (for all \( G_j^+ \)) and \( k_{at} \) (for \( (GGG)^+ \)).
are lower than the calculated energetic results summarized in Figure 1. This is not surprising, as the calculated results refer to model duplexes in a vacuum and do not incorporate solvation effects. The energy gap \( \Delta(G^+\text{AGGG}) = 0.062 \text{ eV} \) inferred from our analysis is close to the free energy gap \( \Delta G_i = 0.077 \pm 0.005 \text{ eV} \) evaluated by Lewis et al.\(^\text{28}\) for hole trapping in the G\(^+\)AGGGA duplex. It is gratifying that the experimental results for the chemical yields\(^\text{13,14}\) presented herein and for the time-resolved rates\(^\text{29}\) for the G\(^+\)AGGG duplexes provide good internal agreement. Time-resolved data for the energy gaps in the G\(^+\)TGGG duplex, for which our analysis provides \( \Delta_t = 0.096 \text{ eV} \), will be of considerable interest in the context of bridge specificity of the energetics of hole trapping.

The ratio of \( k_+ / k_\text{ref} = 0.021 \) for (T)\(_n\) bridges obtained from the foregoing analysis is consistent with the lower limit of the rate ratios \( k_\text{T} / k_1 = 1 \) and \( k_\text{TT} / k_1 = 0.02 \), i.e., \( k_- / k_\text{ref} = 0.02 \) 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 \( k_\text{T} / k_1 = 2 \) 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 \( \lambda \) is the reorganization energy) \( k_\text{T} < k_1 \) and rough estimates for TT bridges would then indicate that \( k_\text{T} / k_1 \sim 7 \). This apparent discrepancy may be due to large intramolecular distortions with the (GGG)\(^+\) trap.

Finally, we move toward some speculative grounds, attempting to attain further insight into the contribution of the (bridge specific) energy gap \( \Delta_t \) to the Franck-Condon factor \( F(\Delta_t) \), eq \( 12 \). The trapping rate \( k_\text{T} \) can be estimated for the “normal” charge transfer Marcus region when \( \Delta_t < \lambda \), where \( \lambda \) is the thermal reorganization energy. Then a rough estimate gives\(^\text{38}\) \( k_\text{T} \approx |V_{\text{super}}|^2 / C \exp(\Delta_t/2k_\text{B}T) \), 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

\[
k_\text{T} = C |V_{\text{super}}|^2 (k_\text{ref} / k_-)^{1/2}
\]

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

\[
k_\text{T}(\text{TT}) / k_\text{T}(\text{AT}) = |V_{\text{super}}(\text{TT})|^2 / |V_{\text{super}}(\text{AT})|^2 \exp[(\Delta_t(\text{TT}) - \Delta_t(\text{AT})) / 2k_\text{B}T] \quad \text{(25)}
\]

Making use of the quantum mechanical data of Table 1 we have the contribution of the electronic matrix elements \( |V_{\text{super}}(\text{TT})|^2 / |V_{\text{super}}(\text{AT})|^2 = 0.72 \), while the contribution of the nuclear Franck-Condon factors is \( \exp[(\Delta_t(\text{TT}) - \Delta_t(\text{AT})) / 2k_\text{B}T] = 2 \), so that \( k_\text{T}(\text{TT}) / k_\text{T}(\text{AT}) = 1.44 \). 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.\(^\text{32,33}\) 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.\(^\text{38,46,47}\) 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”.\(^\text{1–38}\) Our analysis focused on hole trapping in GT\(_4\), (A)n...G(T–A)n...GG... duplexes \( (n = 1–4) \) and on hole hopping in GT\(_4\), (T–A)n...GG... duplexes. For short \( (n \leq 4) \) \( (T–A)n \) mediating bridges, hole superexchange between guanine prevails, and our previous\(^\text{32,33}\) 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 \( (T–A)n \) \( (n = 1–4) \) bridges, the individual hopping/trapping steps are super exchange mediated and long-range hole transport can be realized over a distance scale of \( 50–300 \text{ Å} \).\(^\text{13,14,32–38}\) We have shown\(^\text{38}\) 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 G\(^+\)(T–A)n...GG... duplexes \( (n > 4) \) through long \( (A)n \) duplexes. Furthermore, for TIH via long \( (T–A)n \) \( (n > 4) \) duplexes, interstrand zigzagging between the A bases in the two strands can occur, with the \( (A)n \) 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 \( (G^n+)...(G) \) and \( (G)\,...(G^n+) \) 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.\(^\text{21}\) who reported hole transfer in long (GGG\(^+\))(A)n(GGG\(^+\)) \( (n = 4–10) \) duplexes and of Schuster et al.\(^\text{22–25}\) who observed hole transfer between GG groups separated by AAATT segments. The efficiency of TIH via long \( (A)n \) bridges is determined by the relative rate of the competing side reaction of \( (G)_n^+ \) with water and by the \( G^+A \) energy gap. Indeed, the relative reaction rates of \( G^+ \) and \( GGG^+ \) inferred herein from Giese’s data \( k_d / k_\text{ref} = k_d / k_0 = 0.08 \) (for \( m = 2 \) bridge) and \( k_d / k_\text{ref} \approx 1.6 \), seem to be too high to warrant an effective TIH via the A chain for which the energy gap is 0.22 eV.\(^\text{36}\) It appears that under the experimental conditions of Barton et al.\(^\text{20,21}\) and of Schuster et al.\(^\text{22–25}\) the \( G^+ \), \( (G)^+ \) or \( (GGG)^+ \) water reaction seems to be sufficiently slow not to overwhelm the TIH. There is a distinct possibility that we have to distinguish between \( (GGG)_n^+ \) long-range transport induced by hopping/trapping superexchange steps through “short” \( (T–A)n \) \( (n < 4) \) bridges considered herein and very long-range transport induced by TIH via \( (A)n \) chains in long \( (GGG)_n^+ \) \( (T–A)n \) \( (GGG)^+ \) duplexes.

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Appendix A

Kinetic Analysis of Unistep Hole Trapping in G$^+(T^-A)_m$

GGG Duplexes. The kinetic matrix of the rate constants for
the kinetic scheme (1) is

\[
K = \begin{pmatrix}
-k + k_d \\
k_t \\
-k + k_d
\end{pmatrix}
\]

(A1)

where \(a(t)\) is the concentration of the initial state 
\(G^+(T^-A)_m \text{GGG} \) and \(b(t)\) is the concentration of the final state
\(G(T^-A)_m \text{GGG}^+\). The kinetic equation is then

\[
\frac{dv}{dt} = Kv
\]

(A2)

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

\[
Y(G^+) = k_d \int_0^\infty a(t)dt = k_d \left[ \int_0^\infty e^{Kt}dt \right]_{1,1} = k_d K^{-1}_{1,1}
\]

(1)

\[
Y(\text{GGG}^+) = k_d \int_0^\infty b(t)dt = k_d \left[ \int_0^\infty e^{Kt}dt \right]_{2,2} = k_d K^{-1}_{2,2}
\]

(A3)

These are given by

\[
Y(G^+) = \frac{k_d (k_{-1} + k_d)}{k_{d,1} + k_{-1,1} + k_{d,1}}
\]

(A4a)

(2)

\[
Y(\text{GGG}^+) = \frac{k_d k_{-1}}{k_{d,1} + k_{-1,1} + k_{d,1}}
\]

(A4b)

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

\[
\phi = \frac{Y(\text{GGG}^+)}{Y(G^+)} = \frac{k_t}{k_d (1 + k_{-1,1})}
\]

(A5)

Appendix B

Kinetic Analysis of Multistep Hole Hopping in

G$^+(T\text{TGG})_n TTGGG$ Duplexes. The kinetic analysis of
the reaction scheme, eq 19, \(a(t)dt = A a(t)\), where \(A\) is the kinetic matrix and \(a(t)\) the vector of the normalized concentrations of
\(G^+(j = 1,...,N)\) and \(\text{GGG}^+\) (with the initial conditions
\(a(0) = 1\) and \(d_{ref}(t=0) = 0\)) follows the treatment previously
given by us. The yields in eqs 20 and 21 can be expressed by

\[
Y(P_j) = k_d \left[ \int dt \exp\{A t\} \right]_{j,1} = k_d A_{j,1}
\]

(B1)

where obtained by the inversion of the kinetic matrix.

References and Notes