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LETTERS

On the Long-Range Charge Transfer in DNA

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The sequence dependence of charge transport through stacked Watson–Crick base pairs was analyzed for coherent hole motion interrupted by a temporary charge localization on guanine bases. The relative rate of hole transfer to the GGG sequence has been expressed in terms of the frequency of jumps through adenine–thymine base pairs separating adjacent guanine sites. The obtained expression yields practically the same sequence dependence as measurements, without invoking adjustable parameters. For alternating adenine–thymine/guanine–cytosine sequences, our analysis predicts that the relative charge-transfer rate varies in inverse proportion to the sequence length at short distances, with change to the slow exponential decay at longer distances.

Charge transfer in DNA between donor and acceptor sites bridged by well-stacked base pairs is of considerable interest, particularly due to the relevance to DNA damage¹ and repair.² The observed long-range translocation of charge in this biologically important molecule^{3–8} (up to ca. 200 Å) was found to be in dramatic conflict with the conventional mechanism of unistep electron tunneling, which reduces the charge-transfer efficiency by almost a factor of 10 for every 2 Å extension of the DNA bridge.⁹ To resolve the contradiction, recent studies^{4,6,8,10–12} suggest that long-range charge transfer in DNA can be viewed as a series of short-range hops between energetically appropriate G bases. Here we present a quantitative analysis of this mechanistic picture with special reference to the experiments^{6,8} on the short-range and long-range ground-state transfer of “electronic” holes through DNA bridges of different lengths. We demonstrate that the efficiency of this process can be deduced accurately from the known arrangement and number of adenine–thymine (AT) and guanine–cytosine (GC) pairs on the bridge.

The system considered is identical to that used in experiments^{6,8} on the ground-state hole transfer in DNA. It consists of a guanine radical cation G^{•+} as hole donor and a GGG unit as acceptor, separated from the donor by a bridge of stacked AT and GC pairs (Figure 1). Earlier kinetic analysis, verified by experimental studies,⁶ has shown that the ratio of damage products formed due to the reactions of GGG^{•+} and G^{•+} with water defines the relative rate constant of ground-state hole transfer through the DNA bridge, $k_{\text{rel,CT}}$, used as a measure of the charge-transfer efficiency. Our calculations of this quantity are based on the combination of two limiting extremes for the mechanism of hole motion along the bridge. One extreme corresponds to the unistep superexchange mediated tunneling.^{13,14} This coherent mechanism yields a charge transfer rate depending exponentially on the length of the DNA bridge, R ,

$$k_{\text{CT}} = k_0 \exp(-\beta R) \quad (1)$$

where k_0 is a preexponential factor and β is a falloff parameter, expected (e.g., ref 9) to be of the order $\sim 1 \text{ Å}^{-1}$. The other mechanism involves incoherent hopping between adjacent bases (see Figure 1).

Following recent suggestions^{4,6,8,10–12} and current comment,¹⁵ we describe the motion of “electronic” holes along the DNA

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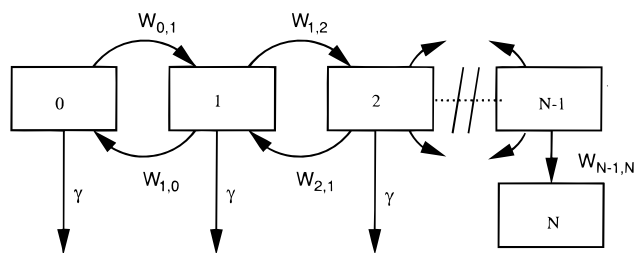


Figure 1. Schematic rate picture for charge transfer along the DNA bridge with AT and GC base pairs. The hopping rates W_{ij} ($i = 0, 1, \dots, N-1$; $j = 1, 2, \dots, N$) are shown by curved arrows. The irreversible decays are indicated by γ and by $W_{N-1,N}$.

bridge as a set of coherent hops between G sites. The preference is given to G bases, since they have the lowest oxidation potential of the four natural bases.¹⁶ The fast exponential decrease of the tunneling rate (1) makes the direct superexchange process much less effective than the multistep hopping process between the G bases, where the individual steps contribute to the overall rate according to eq 1. In this case the damage ratio can be calculated by integration of the master equation for the probability, $P_i(t)$, of finding a hole on the i th G site at time t ($i = 0, 1, \dots, N-1$). This equation has the form

$$\frac{dP_i(t)}{dt} = -\gamma P_i - W_{i,i+1}(P_i - P_{i+1})(1 - \delta_{i+1,N}) - W_{i,i-1}(P_i - P_{i-1})(1 - \delta_{i,0}) - W_{i,i+1}P_i\delta_{i,N-1} \quad (2)$$

where W_{ij} is the jump rate from i th to j th sites; γ is the rate constant for the reaction of $G^{+\bullet}$ and water, and δ_{mn} is the Kronecker symbol. Since at $t = 0$ a hole was site-selectively generated on the G site with $i = 0$, the initial condition is given by $P_0(t = 0) = 1$, $P_{i \neq 0}(t = 0) = 0$. The measured damage ratios^{6,8} $k_{\text{rel,CT}}$ and $k_{\text{tot,CT}}$ are determined¹⁷ by the ratio of the hole current to the GGG structure unit (given by $I_N = \int_0^\infty dt W_{N-1,N} P_{N-1}(t)$, which irreversibly traps the hole,⁶ so that $W_{N,N-1} = 0$) and the processes of the $G^{+\bullet}$ reaction with water at the end G site only ($i_{\text{end}} = \int_0^\infty dt \gamma P_0(t)$, $k_{\text{rel,CT}} = I_N/i_{\text{end}}$) or for the whole set of G sites ($i_{\text{tot}} = \int_0^\infty dt \gamma (P_0(t) + \dots + P_{N-1}(t))$, $k_{\text{rel,CT}} = I_N/i_{\text{tot}}$). We suggested that there are no differences between the isolated G sites, so that the hopping is reversible within the bridge ($W_{i,i+1} = W_{i+1,i}$, $i < N-1$).

Equation 2 can be used to interpret the sequence-dependent charge transfer in DNA, if information about the jump rates for each step of hopping motion is available. The necessary information is provided by recent theoretical and experimental studies of hole transfer from $G^{+\bullet}$ to GGG through one, and two AT base pairs.^{6,8,18} As has been found, the transfer rate decreases by about a factor of 0.3 for each intervening AT base pair linked directly to the previous pair⁸ (like AA) or about the order of magnitude for cross linked pairs⁶ (like $\begin{smallmatrix} \text{TT} \\ \text{TA} \end{smallmatrix}$). This permits the use of eq 2 to predict the relative transfer rate in the DNA bridge with arbitrarily complicated sequences of AT and GC pairs (Table 1). As follows from eq 2, the values of relative transfer rates for the irregular bridges **IV–VI** are determined by the rates for the homogeneous sequences **I**, **II**, and **III** given by the ratio of the corresponding transfer rate and the $G^{+\bullet}$ reaction rate W/γ . The direct use of experimental values^{6,8} of these ratios in eq 2 gives the relative hole transfer rate through the DNA bridges **IV–VIII** without fitting parameters. Bridge **IX** has been described making use of eq 1 based on the results for bridges **I** and **II**. Theoretical results obtained (Table 1) are seen to be in agreement with observations^{6,8} within the experimental error.

In Figure 2 the data of ref 6 are shown together with the theoretical predictions obtained according to the rules formulated above. The non-monotonic charge-transfer rate dependence on the bridge length is described satisfactorily within the hopping model.

The analysis performed above is easily applicable to other important aspects of charge transfer in DNA. In particular, eq 2 can be exploited for specifying the dependence of the relative ground-state charge-transfer rate on the bridge length R . The solution of eq 2 shows (see Table 1) that the sequence effect strongly suppresses the length dependence of $k_{\text{rel,CT}}$ for irregular bridges with AT and GC base pairs. This becomes evident from the fact that $k_{\text{rel,CT}}$ are almost equal for bridges composed of sequences **IV** and **VIII** with lengths $R = 17$ and 54 \AA , respectively. Therefore, experiments with irregular DNA bridges of distinct lengths do not provide unambiguous results. Our theoretical analysis, however, enables us to clarify the situations where measurements on the distance dependence do make sense. One case involves experiments with the bridges consisting of homogeneous AT sequences. These systems are known to exhibit exponential distance dependence.^{6,19} Alternative measurements⁸ explore regular bridges composed of alternating AT and GC base pairs. For the latter case, all jump rates in eq 2 are equal, i.e., $W_{0,1} = W_{1,2} = \dots = W$. In this case the steady-state analytical solution of eq 2 yields

$$k_{\text{rel,CT}} = \frac{W}{\gamma} \frac{\sinh(\lambda)}{\sinh(N\lambda)}, \quad k_{\text{tot,CT}} = \frac{W}{\gamma} \frac{2 \sinh(\lambda) \sinh(\lambda/2)}{\cosh(\lambda(N+1/2)) - \cosh(\lambda/2)} \quad (3)$$

$$\lambda = \ln \left(1 + \frac{\gamma}{W} + \sqrt{\frac{\gamma}{W} + \frac{\gamma^2}{4W^2}} \right) \approx \sqrt{\gamma/W}$$

The approximate expression for the decrement λ is given for the experimental case of hopping rate fast with respect to the reaction rate. Then for a sufficiently short bridge containing N repeating chains with $N < W/\gamma$ the dependence of the relative transfer rates on the bridge is given by the power laws $k_{\text{rel,CT}} \sim 1/N$ and $k_{\text{tot,CT}} \sim 1/(N(N+1))$. In the opposite case of a long bridge eq 3 leads to exponential decrease of both rates as $k \sim \exp(-\sqrt{W/\gamma}N)$. The bridges, investigated in ref 8 are examples of regular alternating bridges. The agreement of the experimental length dependence and the predictions of eq 3 for the relative charge-transfer rate $k_{\text{tot,CT}}$ is demonstrated in Table 1 for sequences **II**, **VI**, and **VII**. As follows from eq 2 (see bridge **II** in the table) $W/\gamma \approx 8.9$. Accordingly, decay length for the transfer rate is around 9 base pairs. This length is more than an order of magnitude greater than the decay length β in the superexchange law (1).

Thus, for sufficiently long bridges the hopping mechanism of charge transfer along DNA bridges with regular base pair sequences exhibits exponential distance dependence similar to the distance dependence expected for the mechanism of unistep superexchange-mediated tunneling, cf. Equation 1. The falloff parameters for these two mechanisms are, however, distinct. While the falloff parameter β in eq 1 is a measure of electronic coupling between donor and acceptor sites, the falloff parameter $(\gamma/W)^{1/2} \sim 0.1 \text{ \AA}^{-1}$ for the distance dependence of $k_{\text{rel,CT}}$ reflects the ability of the hole to react with water during the hopping motion along the bridge.

In the above analysis we have followed the experimental literature in defining the yield ratio of $\text{GGG}^{+\bullet}$ decay to $G^{+\bullet}$ decay as relative rate constants, $k_{\text{rel,CT}}$, $k_{\text{tot,CT}}$. These are the actual

TABLE 1: Relative Hole Transfer Rates through DNA Bridges^a

	bridge	relative transfer rates			
		$k_{\text{rel,CT}}$		$k_{\text{tot,CT}}$	
		expt	theor	expt	theor
I	T	30 ± 6^6			
	A				
II	TT	8.9 ± 1.9^8			
	AA				
III	TA	3.2 ± 0.6^6			
	AT				
IV	TGTA	3.4 ± 0.7^6	2.8 ± 0.6	3.0 ± 0.7^6	2.6 ± 0.6
	ACAT				
V	TACA	3.8 ± 0.8^6	2.8 ± 0.6		1.4 ± 0.6
	ATGT				
VI	TTGTT		4.2 ± 0.9	2.8 ± 0.4^8	2.8 ± 0.6
	AACAA				
VII	TTGTTGTTGTT		1.7 ± 0.7	0.9 ± 0.1^8	0.8 ± 0.3
	AACAACAACAA				
VIII	TCAGCTCAGTCTGCA	3.4 ± 0.7^6	3.15 ± 0.8		0.7 ± 0.2
	AGTCGAGTCAGACGT				
IX	TATA	0.03 ± 0.015^6	0.036 ± 0.02		
	ATAT				

^a Theoretical predictions concerning the relative hole transfer rates, were based on experimental data of refs 6 and 8 for bridges I, II, and III. Theoretical λ values were obtained from eq 2. Errors are experimental.

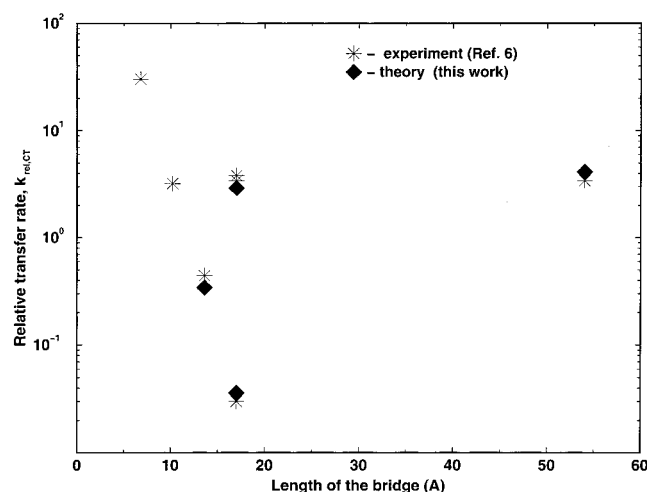


Figure 2. Theoretical fit of the distance dependence for the relative charge-transfer rate observed in ref 6.

measured results for ground-state hole transfer. The hopping model is demonstrated to have the strong predictive power. It can describe the charge transfer through arbitrarily complicated DNA bridges, containing isolated G bases. The relative charge-transfer rates $k_{\text{rel,CT}}$ and $k_{\text{tot,CT}}$ decrease with the length of the bridge according to a power law for the short bridges and change to exponential decrease for long bridges. However the exponential falloff is much slower than for the superexchange mechanism. The same conclusion follows from recent important papers^{20,21} which also suggest²⁰ and analyze²¹ a hopping-like model for hole transfer in DNA. These papers do not, however, consider both sequence and length dependencies as is done here.

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