Long-Distance Charge Transport in DNA: The Hopping Mechanism

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ABSTRACT
Long-distance charge transport from a guanine radical cation ($G^{+\bullet}$) to a G-rich sequence is of biological importance. This reaction was studied by selective charge injection into a G, monitoring the charge transport to a GGG sequence by competing H_2O-trapping. The efficiency of the charge transport diminished dramatically with increasing number of A:T base pairs between $G^{+\bullet}$ and GGG. But in DNA strands where G's are located between the $G^{+\bullet}$ and GGG sequence, long-distance charge transport occurred by a multistep hopping mechanism.

I. Introduction

Deoxyribonucleic acid (DNA), which stores our genetic information, is a very stable polymeric biomolecule. Nevertheless, DNA damage can occur under the conditions of oxidative stress[1] and UV irradiation.[2a] A major target for oxidants is guanine (G), the base with the lowest ionization potential of the four DNA bases.[3] This leads, among other oxidation products, to 8-oxoguanine, which reveals a lower fidelity in the replication process and enhances the probability for adenine (A) incorporation into the complementary strand.[1] Thus, under conditions of oxidative stress, mutations from guanine-cytosine (G:C) base pairs into thymine-adenine (T:A) base pairs occur.

Under UV irradiation[2a] and in the presence of certain oxidants,[2b] the first step of the oxidation process is the formation of a guanine radical cation ($G^{+\bullet}$). Because GG and GGG sequences have lower ionization potentials than single G's,[4] the positive charge should migrate from the single $G^{+\bullet}$ to G clusters if long-distance electron transport through DNA is possible.[2,5,6] As a consequence, mutations will occur predominantly at G clusters. This is very dangerous, since several hot spot codons of p53 tumor suppressor genes as well as human ras proto-oncogenes contain GG sequences (Figure 1).[2] A mutation in these codons increases carcinogenesis.

The question of whether and how electrons migrate over long distances through DNA was raised over 30 years ago,[7] and is still a matter of controversial debate.[8] Different experiments in the 1990s have led to conclusions that DNA can function as a "π-way" over which electron-transfer reactions might be promoted efficiently,[9] as an insulator,[10] or both as wire and insulator.[11] The discussion is focused on the β-value of the Marcus−Levich−Jortner correlation (eq 1) that establishes an exponential rate decrease of the electron-transfer step with increasing distance. Depending

$$k \propto e^{-\beta \Delta r} \quad (1)$$

on the experiment, β-values between 1.4 and 0.1 $Å^{-1}$ have been reported for DNA double strands.[11−16] These differences in β-values demonstrate dramatic divergent effects of the distance on the electron-transfer rate.

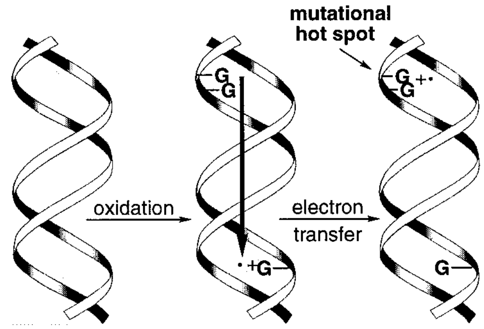

FIGURE 1. Oxidation of a single G and long-distance charge transport to a GG mutational hot spot.

Because of the biological implications, our interest was in determining the possibility of charge transfer from a single $G^{+\bullet}$ to a GGG cluster. To answer this question, we developed an assay which enabled site-selective oxidation of single G bases.

II. Charge Injection into a Single G

Our method of charge injection is based on the spontaneous heterolytic cleavage of the phosphate ester C,O-bond in a 4′-DNA radical, **2**.[16a] This reaction generates an enol ether radical cation in **3**, which triggers electron transfer through DNA from the nearest G. As a result, the radical cation in **3** is reduced to the enol ether unit in **4**, and the guanine radical cation ($G^{+\bullet}$) is formed (Figure 2).

In competition with this electron-transfer step (**5** → **7** in Figure 3), the radical cation (**5** in Figure 3) is trapped by H_2O, which leads via radicals **8** and **10** to the stable products **9** and **11**. Careful HPLC analyses showed that the yield of 5′-phosphate **6** is equal to the combined yields of **7** + **9** + **11**, the products of electron transfer (**7**) and water addition (**9** + **11**) to the radical cation **5**.[17] Thus, we observed a quantitative product balance. Because the reactions of radical cation **5** are irreversible and of first order (electron transfer) or pseudo-first order (trapping reaction by H_2O), the ratio of the products **7**/(**9** + **11**) is equal to the relative rate of the electron-transfer reaction step **5** → **7**.[18]

We have measured these relative electron-transfer rates in several double-stranded 20mers that contained one 4′-acylated thymidine unit, as in **1**.[17,18] Photolytic generation of the radical cation **3** occurred in 70−90% yield, which triggered the electron transfer from the

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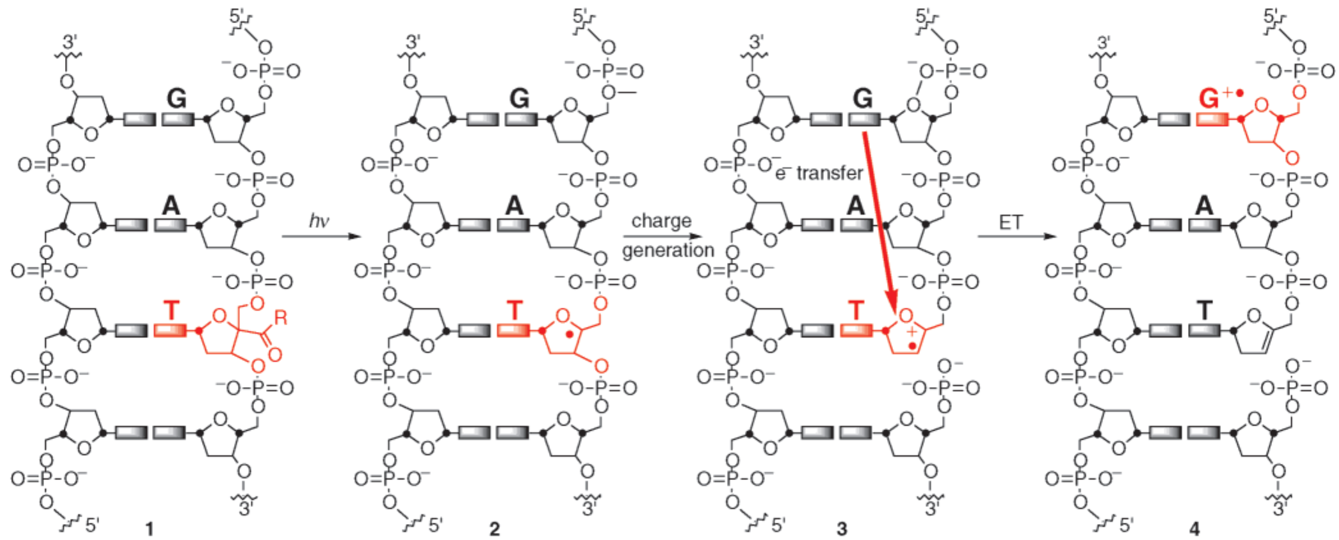

FIGURE 2. Photolytic generation of the 4′-DNA radical **2** from **1**: charge generation by heterolytic cleavage (**2** → **3**), and electron transfer (ET) through DNA (**3** → **4**). This assay is used for site-selective charge injection into a single G.

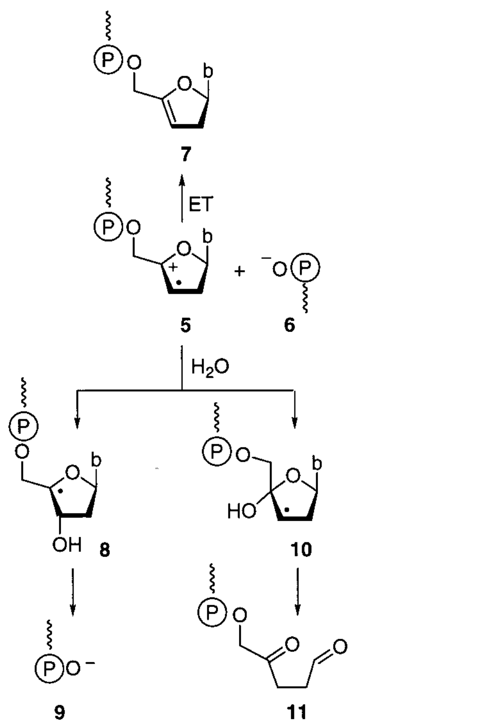

FIGURE 3. Competition between electron transfer (ET) and H_2O-trapping of the sugar radical cation **5** that is formed together with the 5′-phosphate **6** during the spontaneous cleavage of a 4′-DNA radical.

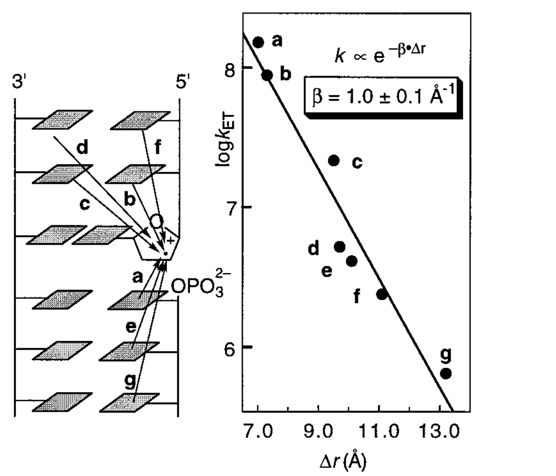

FIGURE 4. Electron transfer (depicted as arrows) from the nearest guanine to the sugar radical cation in seven different strands. The diagram shows the exponential distance dependence (Δr) of the electron-transfer rate (k_{ET}).

nearest G through DNA. The product ratio **7**/(**9** + **11**) depends on the distance of the nearest G in the oligonucleotide, and a plot according to eq 1 revealed a β-value of 1.0 ± 0.1 $Å^{-1}$ (Figure 4).

Analogous experiments with single strands showed a completely different influence of the base sequence on the electron-transfer rate: the number of T nucleotides between the radical cation and the G has only a weak influence on the rate.[17] There are nearly no rate differences in strands where G is separated by two, three, or four T's from the radical cation site (Figure 5). We explained these results on the basis of the flexibility of single strands that can adopt conformations in which the distance between the charge donor and the charge acceptor can be small, even if they are separated by several T units. Recent experiments by Kan and Schuster[19] led to the same conclusion. The results demonstrate how important it is to exclude reactive single strands in double-strand experiments.

The ionization potential of the electron donor also influences the rate. Thus, if guanine was substituted by 8-oxoguanine, which has a 0.5 V lower ionization potential,[20] the rate of the electron transfer was increased by a factor of 4 in our assay.[17] Nevertheless, the β-value remained unchanged within the experimental error.

III. Charge Transfer between $G^{+\bullet}$ and GGG

The method of charge injection described above offers the possibility for a site-selective formation of a single

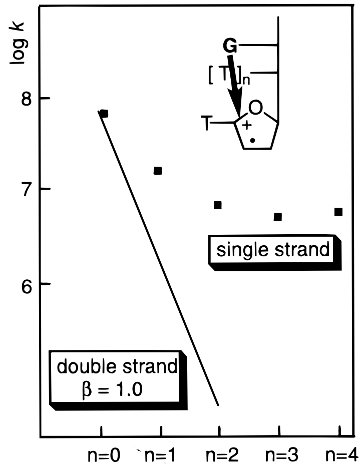

FIGURE 5. Influence of the number (*n*) of intervening thymines (T) between the sugar radical cation and the nearest guanine (G). The straight line is the distance dependence in double strands (see Figure 4). The squares are the results for single strands.

$G^{+\bullet}$. To study the biologically important question of whether this $G^{+\bullet}$ stimulates electron transfer from a G-rich sequence through DNA, we developed the assay shown in Figure 6.[16b]

Photolysis of double strand **12** generated $G^{+\bullet}$ in **14** by electron transfer to the enol ether radical cation in **13**. For analytical reasons, the charge was transferred to the complementary strand (**14** → **15**) that was radiolabeled at the 5′-end. For $G^{+\bullet}$ in **15**, a competition exits between two first- or pseudo-first-order reactions: electron transfer (**15** → **16**) and water addition (trapping of $G^{+\bullet}$ with H_2O). The H_2O reaction of $G^{+\bullet}$ leads to an oxidatively modified guanine that can be cleaved off selectively by base treatment.[21] The relative rate (k_{rel}) of the electron transfer from $G^{+\bullet}$ to the GGG sequence (**15** → **16**) is given by the ratio of the cleavage products at the GGG unit and the single G base in the radiolabeled strand that can be analyzed by gel electrophoresis.[16b] Figure 7 shows the results for double strands **17**–**20**, where the distances between the $G^{+\bullet}$ and the GGG units increase from 7 to 17 Å.

The rate of the charge-transfer step decreased by about a factor of 10 per each intervening A:T base pair.[16b,22] Thus, the amount of charge (ϵ) trapped by the H_2O reaction at the GGG unit decreased from 97% at 7 Å to 3% at 17 Å (Figure 7). At distances longer than 17 Å, a charge transfer from $G^{+\bullet}$ to a GGG sequence could not be detected by our assay. Recently, Saito et al.[23] observed similar effects in an assay where the charge was injected from a photoexcited benzophenone system. The distance influence on the charge transfer led to a β-value of 0.7 ± 0.1 Å^{-1} which is in very good accord with experiments of Lewis and Wasielewski *et al.*[12] where the electron transfer was triggered by a photoexcited stilbene (Figure 8).

IV. Hopping Mechanism

In our assay the efficiency of the charge transfer (ϵ)—that is, the amount of charge trapped by the H_2O reaction at the GGG unit—decreased from 97% at 7 Å to 3% at 17 Å (Figure 7).[16b] In experiments with strands having five and more A:T base pairs between $G^{+\bullet}$ and the GGG unit, a charge transfer could no longer be detected.[16b,23] Nevertheless, we observed a very efficient long-distance charge transport (70%) in double strand **21**, although the charge donor $G^{+\bullet}$ and the charge acceptor GGG are separated from each other by 15 base pairs (54 Å) (Figure 9).[16b] This was a surprising result and showed that it is not the distance alone that determines the efficiency of the long-range charge transport; the sequence also has to play a decisive role.

DNA **21** contains 8 G's between the first $G^{+\bullet}$ and the GGG unit. We assume that these intervening G's can be oxidized by the $G^{+\bullet}$; thus, they act as relay stations for the charge on the way to the GGG unit.[16b] As a result, the charge transport from the first $G^{+\bullet}$ to the GGG occurs not

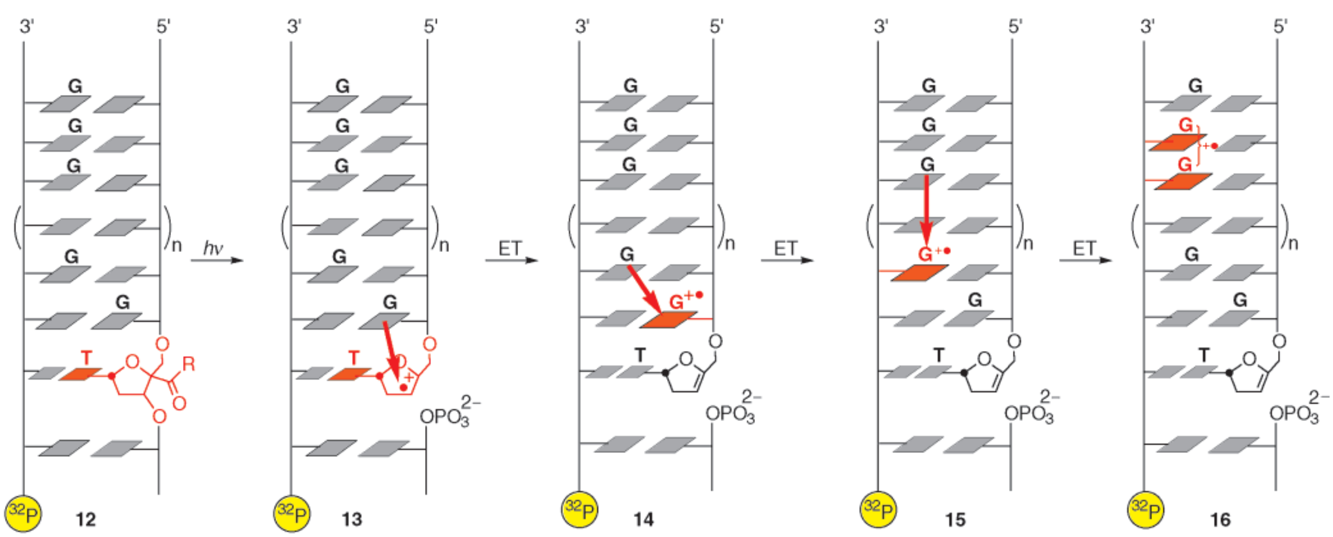

FIGURE 6. Charge injection into a single G (**12** → **14**), charge transport to the complementary, radiolabeled strand (**14** → **15**), and charge transport from a single $G^{+\bullet}$ to a GGG sequence (**15** → **16**). This assay is used to determine the relative rates and efficiencies of the charge transport from a single $G^{+\bullet}$ to a GGG sequence.

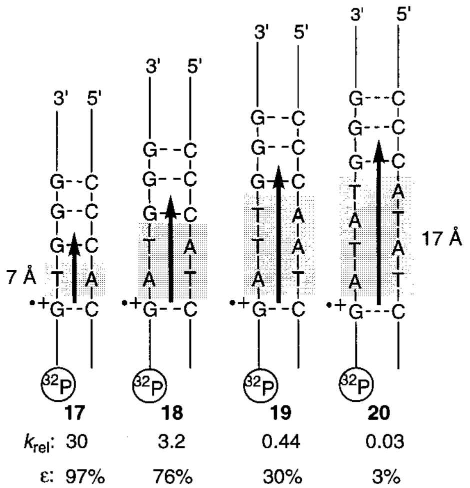

FIGURE 7. Relative rates (k_{rel}) and efficiencies (ϵ, amount of charge detected at the GGG unit) for the charge hopping from $G^{+\bullet}$ to the GGG sequence in double strands **17**−**20**.

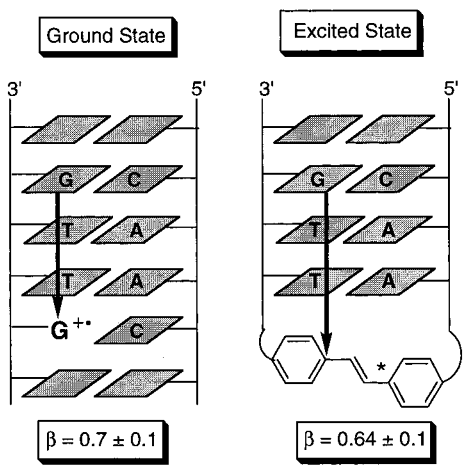

FIGURE 8. Assays for the determination of β-values in the ground state[16b] and the photoexcited state.[12]

in one step but in a multistep reaction. Jortner et al.[24] have characterized such a situation by correlation (2), where a

$$\ln E \propto -\ln N \tag{2}$$

charge migrates by a random walk (linear diffusion) through DNA. In eq 2, E is the efficiency of the charge transport expressed as the ratio between the trapped GGG sequence and the single G's. The number of the equidistant hopping steps is N.

We proved correlation (2) in experiments with four different double strands, where the number (N) of the electron-transfer steps, each of them over a distance of 10 Å, increased from 1 to 4.[25]

Equation 1 gives the distance dependence of each single step, and eq 2 describes the overall charge transport via several steps. Whereas the rate of each charge-transfer step depends exponentially on the distance (eq 1), the efficiency of the overall, long-distance charge transport of the multistep reaction has an algebraic dependence on the number of steps (eq 2). Therefore, the multistep hopping process reduces dramatically the influence of the

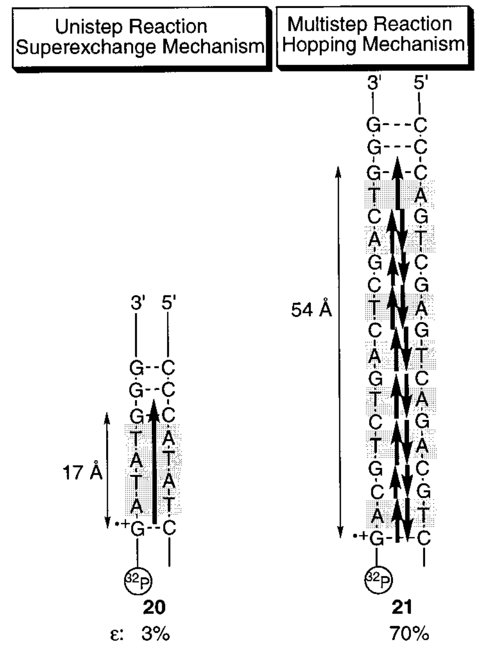

FIGURE 9. Efficiencies (ϵ, amount of charge detected at the GGG unit) of the charge transfer in a unistep and a multistep reaction over 17 and 54 Å, respectively.

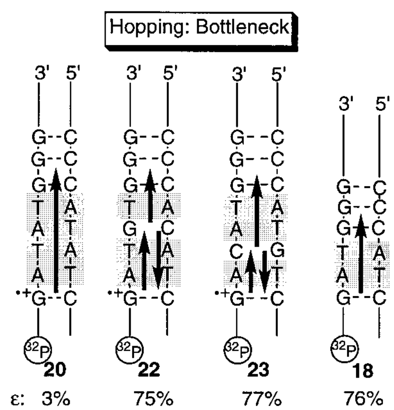

FIGURE 10. Sequence influence on the efficiency (ϵ, amount of charge detected at the GGG unit) of the charge transport over 17 Å in strands **20**−**23**.

distance on the overall transport efficiency.[26] Actually, in mixed DNA double strands, the efficiency of the long-distance charge transport is determined by the longest hopping step. Such a "bottleneck" situation could be demonstrated by exchanging A:T pairs by G:C pairs in strand **20** or by exchanging G:C pairs by A:T pairs in **21**.[16b] This AT−GC exchange led to systems **22**−**24**, which contained intervening A:T sequences of different lengths. The data of Figures 10 and 11 show that the efficiencies of the long-distance charge transport in **22**−**24** are nearly the same as those through the "bottleneck" sequences (the longest individual step between two G's).

This hopping model was supported by the kinetic analysis of Jortner and Bixon et al.,[27] who treated the hopping process as a sequential reaction which is characterized by the rates of the electron-transfer steps and the trapping steps. Another breakthrough is the absolute rate measurements of Lewis and Wasielewski et al.,[28] who

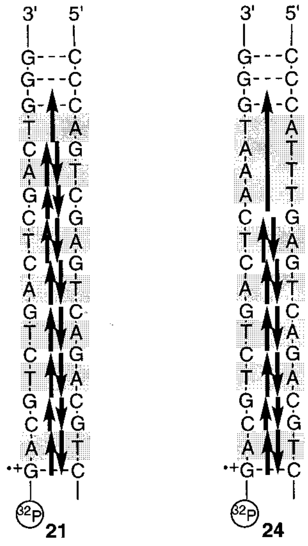

FIGURE 11. Sequence influence on the efficiency (ϵ, amount of charge detected at the GGG unit) of the charge transport over 54 Å in **21** and **24**, respectively.

could show that the rate of the charge hopping between a single $G^{+\bullet}$ and a GG that were separated from each other by one A:T base pair is about 5×10^7 s^{-1}.

V. Refinement of the Model

The hopping model described above is based on a limited number of experiments. It is highly likely that further experiments will refine this model. Saito *et al.*[6] have demonstrated that the redox potential of a G:C pair depends on the neighboring nucleotides. Thus, equally distant hopping steps between nearest G's should be slightly different for different sequences.[22] Schuster et al.[29] have pointed out that the dynamic behavior of the DNA prevents a localization of the charge on the G's alone but distributes it over certain sequences, and they described the long-distance charge transport through DNA as a phonon-assisted polaron hopping process.

Another aspect of this hopping process is the depletion of the charge, which might hamper the charge transport. Steenken[30] has shown that oxidation of guanine increases the acidity of G. This could lead, even in a DNA double strand, to deprotonation and formation of the neutral guanosyl radical that stops charge transfer because it has a lower oxidation potential than the guanine radical cation.

VI. Conclusion

Very long-distance charge transport through DNA is possible even if the β-value of the Marcus–Levich–Jortner correlation (eq 1) is large. In these systems, the charge migrates through DNA by a hopping process. Each hopping step depends strongly upon the hopping distance. Nevertheless, very long-distance charge transport is possible because the total distance is split up and the largest step becomes rate determining.[31]

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References

(1) Halliwell, B.; Gutteridge, J. M. C. *Free Radicals in Biology and Medicine*: Oxford University Press: Oxford, 1999.

(2) (a) Sies, H.; Schulz, W. A.; Steenken, S. Adjacent Guanines as Preferred Sites for Strand Breaks in Plasmid DNA Irradiated with 193 nm and 248 nm UV laser light. *Photochem. Photobiol. B* **1996**, *32*, 97–102. (b) Wolf, P.; Jones, G. D. D.; Candeias, L. P.; O'Neil, P. Introduction of Strand Breaks in Polynucleotides and DNA by Sulfate Radical Anion: Role of Electron Loss Centres as Precursors of Strand Breakage. *Int. J. Radiat. Biol.* **1993**, *64*, 7–18.

(3) (a) Seidel, C. A. M.; Schulz, A.; Sauer, M. H. M. Nucleobase-Specific Quenching of Fluorescent Dyes. 1. Nucleobase One-Electron Redox Potentials and Their Correlation with Static and Dynamic Quenching Efficiencies. *J. Phys. Chem.* **1996**, *100*, 5541–5553. (b) Steenken, S.; Jovanovic, S. V. How Easily Oxidizable is DNA? One-Electron Reduction Potentials of Adenosine and Guanosine Radicals in Aqueous Solution. *J. Am. Chem. Soc.* **1997**, *119*, 617–618.

(4) Sugiyama, H.; Saito, I. Theoretical Studies of GC–Specific Photocleavage of DNA via Electron Transfer: Significant Lowering of Ionization Potential and 5′-Localization of HOMO of Stacked G Bases in B-Form DNA. *J. Am. Chem. Soc.* **1996**, *118*, 7063–7068.

(5) Thus, G-clusters are not only ionized preferentially but they also collect the positive charge from oxidation events at other DNA sites.[6]

(6) Saito, I.; Nakamura, T.; Nakatani, K.; Yoshioka, Y.; Yamaguchi, K.; Sugiyama, H. Mapping of the Hot Spots for DNA Damage by One-Electron Oxidation: Efficacy of GG Doublets and GGG Triplets as a Trap in Long-Range Hole Migration. *J. Am. Chem. Soc.* **1998**, *120*, 12686–12687.

(7) Eley, D. D.; Spivey, D. I. Nucleic Acid in the Dry State. *Trans. Faraday Soc.* **1962**, *58*, 411–415.

(8) For recent commentaries, see: (a) Diederichsen, U. Charge Transfer in DNA: A Controversy. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2317–2319. (b) Wilson, E. K. DNA's Conductance Still Confounds. *Chem. Eng. News* **1998**, *76* (30), 51–54. (c) Wilson, E. K. DNA Conductance Convergence? *Chem. Eng. News* **1999**, *77*, (34), 43–48. (d) Wu, C. The Incredible Shrinking Laboratory. *Science News* **1999**, *156*, 104–106. (e) Ratner, M. Photochemistry—Electronic Motion in DNA. *Nature* **1999**, *397*, 480–481. (f) Grinstaff, M. W. How Do Charges Travel through DNA?—An Update on a Current Debate. *Angew. Chem., Int. Ed.* **1999**, *38*, 3629–3635.

(9) (a) Murphy, C. J.; Arkin, M. R.; Jenkins, Y.; Ghatlia, N. D.; Bossmann, S. H.; Turro, N. J.; Barton, J. K. Long-Range Photo-induced, Electron Transfer through a DNA Helix. *Science* **1993**, *262*, 1025–1029. (b) Turro, N. J.; Barton, J. K. Paradigms, Supermolecules, Electron Transfer and Chemistry at a Distance. What's the Problem? The Science or the Paradigm? *J. Biol. Inorg. Chem.* **1998**, *3*, 201–209.

(10) Debije, M. G.; Milano, M. T.; Bernhard, W. A. DNA Responds to Ionizing Radiation as an Insulator, not as a "Molecular Wire". *Angew. Chem., Int. Ed.* **1999**, *38*, 2752–2756.

(11) Kelley, S. A., Barton, J. K. Electron Transfer between Bases in Double Helical DNA. *Science* **1999**, *283*, 375–381.

(12) Lewis, F. D.; Wu, T.; Zhang, Y.; Letsinger, R. L.; Greenfield, S. R.; Wasielewski, M. R. Distance-Dependent Electron Transfer in DNA Hairpins. *Science* **1997**, *277*, 673–676.

(13) Meade, T. J.; Kayyem, J. F. Electron-Transfer through DNA—Site-Specific Modification of Duplex DNA with Ruthenium Donor and Acceptors *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 352–354.

(14) Brun, A. M.; Harriman, A. Dynamics of Electron-Transfer between Intercalated Polycyclic Molecules—Effect of Interspersed Bases. *J. Am. Chem. Soc.* **1992**, *114*, 3656–3660.

(15) Fukui, K.; Tanaka, K. Distance Dependence of Photoinduced Electron Transfer in DNA. *Angew. Chem., Int. Ed.* **1998**, *37*, 158–161.

(16) (a) Meggers, E.; Kusch, D.; Spichty, M.; Wille, U.; Giese, B. Electron Transfer through DNA in the Course of Radical-Induced Strand Cleavage. *Angew. Chem., Int. Ed.* **1998**, *37*, 460–462. (b) Meggers, E.; Michel-Beyerle, M. E.; Giese, B. Sequence Dependent Long-Range Hole Transport in DNA. *J. Am. Chem. Soc.* **1998**, *120*, 12950–12955.

(17) Meggers, E.; Dussy, A.; Schäfer, T.; Giese, B. Electron Transfer in DNA from Guanine and 8-Oxoguanine to a Radical Cation of the Carbohydrate Backbone. *Chem. Eur. J.* **2000**, *6*, 485–492.
(18) Because the absolute rate of the competing H_2O addition to the radical cation **5** was measured to be 10^8 $M^{-1}s^{-1}$, we could also deduce the absolute electron-transfer (ET) rates from the relative ET rates.[17]
(19) Kan, Y.; Schuster, G. B. Long-Range Guanine Damage in Single-Stranded DNA: Charge Transport through a Duplex Bridge and in a Single-Stranded Overhang. *J. Am. Chem. Soc.* **1999**, *121*, 10857–10864.
(20) (a) Yanagawa, Y.; Ogawa, Y.; Ueno, M. Redox Ribonucleosides—Isolation and Characterization of 5-Hydroxyuridine, 8-Hydroxyguanosine, and 8-Hydroxyadenosine from Torula Yeast RNA. *J. Biol. Chem.* **1992**, *267*, 13320–13326. (b) Prat, F.; Houk, K. N.; Foote, C. S. Effect of Guanine Stacking on the Oxidation of 8-Oxoguanine in B-DNA. *J. Am. Chem. Soc.* **1998**, *120*, 845–846. (c) Bernstein, R.; Prat, F.; Foote, C. S. On the Mechanism of DNA Cleavage by Fullerenes Investigated in Model Systems: Electron Transfer from Guanosine and 8-Oxo-Guanosine Derivatives to C60. *J. Am. Chem. Soc.* **1999**, *121*, 464–465.
(21) The structure of the oxidized guanine, formed in our assay after charge transfer and H_2O-trapping, is not known yet. Therefore, we treated in some cases the strands after the experiments with K_2IrCl_6 before piperidine treatment. This did not change the ratio of the cleavage products.[16b]
(22) In experiments with two A:T base pairs between $G^{+\bullet}$ and GGG (double strand **18**) the sequence was varied: $G^{+\bullet}$NNGGG, NN = AA, AT, TA, TT. This variation changed the ratio of the trapping products by less than a factor of 2. Thus, the orientation of the two A:T base pairs has only a small effect on the charge-transfer step. Similar experiments with longer AT sequences are under way.
(23) Nakatani, K.; Dahno, C.; Saito, I. Chemistry of Sequence-Dependent Remote Guanosine Oxidation: Photoreaction of Duplex DNA Containing Cyanobenzophenone-Substituted Uridine. *J. Am. Chem. Soc.* **1999**, *121*, 10854–10855.
(24) Jortner, J.; Bixon, M.; Langenbacher, T.; Michel-Beyerle, M. E. Charge Transfer and Transport in DNA. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 12759–12765.
(25) Giese, B.; Wessely, S.; Spormann, M.; Lindemann, U.; Meggers, E.; Michel-Beyerle, M. E. On the Mechanism of Long-Range Electron Transfer through DNA. *Angew. Chem., Int. Ed.* **1999**, *38*, 996–998.
(26) Our experiments do not exclude the possibility that, under certain conditions, the β-value of a modified or an unmodified DNA double strand might be small. We have just shown that very long-range charge transport is possible even if the β-value of each step is large.
(27) Bixon, M.; Giese, B.; Wessely, S.; Langenbacher, T.; Michel-Beyerle, M. E.; Jortner, J. Long-Range Charge Hopping in DNA. *Proc. Natl. Acad. Sci. U.S.A.* **1999**, *96*, 11713–11716.
(28) I am very grateful to F. D. Lewis and M. R. Wasielewski for giving me the information before publication.
(29) Henderson, P. T.; Jones, D.; Hampikian, G.; Kan, Y.; Schuster, G. B. Long-Distance Charge Transport in Duplex DNA: The Phonon-Assisted Polaron-Like Hopping Mechanism. *Proc. Natl. Acad. Sci. U.S.A.* **1999**, *96*, 8353–8358.
(30) (a) Steenken, S. Electron-Transfer-Induced Acidity Basicity and Reactivity Changes of Purine and Pyrimidine-Bases—Consequences of Redox Processes for DNA-Base Pairs. *Free Rad. Res. Commun.* **1992**, *16*, 349–379. (b) Steenken S. Electron Transfer in DNA? Competition by Ultra-Fast Proton Transfer? *Biol. Chem.* **1997**, *378*, 1293–1297.
(31) In a recent publication, Lewis and Wasielewski described the situation with the following words: "Thus, efficient long-distance electron transfer may be achieved in DNA without the need for a new paradigm." Lewis, F. D.; Wu, T.; Liu, X.; Letsinger, R. L.; Greenfield, S. R.; Miller, S. E.; Wasielewski, M. R. Dynamics of Photoinduced Charge Separation and Charge Recombination in Synthetic DNA Hairpins with Stilbenedicarboxamide Linkers. *J. Am. Chem. Soc.* **2000**, *122*, 2889–2902.

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