The Influence of Mismatches on Long-Distance Charge Transport through DNA**

Bernd Giese* and Stefan Wessely

Studies by Barton et al.,[1] Schuster,[2] and our group[3] have shown that double-stranded deoxyribonucleic acids (DNA) are able to transport a positive charge over long distances (>50 Å).[4] We have described this long-range charge transport as a multistep reaction, in which the positive charge migrates by reversible tunneling reaction steps between neighboring guanine bases (G).[3, 5] Thus, guanines lying between the charge donor and the charge acceptor serve as relay stations for the positive charge (hopping mechanism).[6] Since guanines play a central role in this hopping mechanism, mismatches of the guanine:cytosine (G:C) base pair should influence dramatically the efficiency of the charge transport. Indeed, we have now observed a strong decrease of the charge transport in DNA double strands, in which a mismatch was introduced at a G:C base pair. The studies were performed with double strands **1** that contained a 4′-acylated nucleotide (Scheme 1).

Scheme 1. Generation of a guanine radical cation $G^{\bullet+}$ in the ^{32}P-labeled strand **3** by photolysis of the acyl-substituted strand **1**.

Norrish-I photocleavage of **1** and subsequent heterolysis generated radical cation **2** that selectively oxidized a neighboring guanine to its radical cation ($G^{\bullet+}$).[7] For analytical reasons we used double strands in which the charge was transferred to a G of the ^{32}P-labeled complementary strand (**2** → **3**). This $G^{\bullet+}$ initiates the charge transport through DNA towards the GGG sequence, a thermodynamic sink for the positive charge.[8] At the positions where the guanine radical cation was trapped by H_2O, treatment with piperidine led to DNA cleavage products P_G that were separated and quantified by gel electrophoresis (Figure 1).[5]

The kinetic analysis[9] of the charge transport from the donor $G_1^{\bullet+}$ over the bridge to the acceptor GGG in double strand **4**[10] (Figure 1) showed that tunneling steps of 10 Å

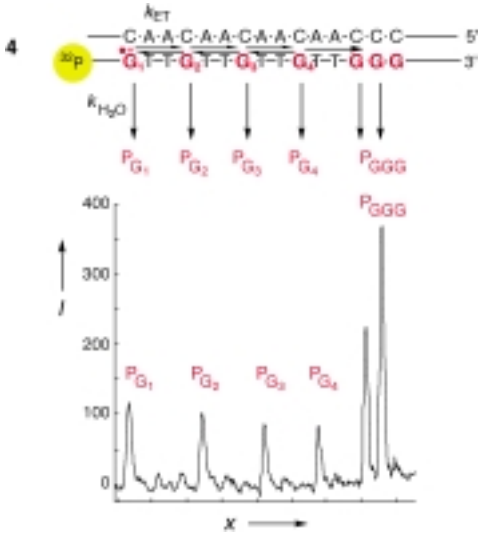

Figure 1. Charge transport from charge donor $G_1^{\bullet+}$ to charge acceptor GGG in the 54-mer **4**, from which only the decisive sequence segment is depicted.[9] Bottom: A histogram of the cleavage products P_G and P_{GGG}, which were separated by gel electrophoresis (x = position).

between the guanines (k_{ET}) are considerably faster than the H_2O-trapping of the charge (k_{H_2O}). Therefore, the positive charge in double strand **4** should be distributed over the single guanines G_1 to G_4 before it is trapped by H_2O. This is indeed the case as the appearance of cleavage products P_G in Figure 1 shows. The intensities P_{G_i}/P_{G_1} slowly decrease from G_1 over G_2 and G_3 to G_4 from 1.0 over 0.83 and 0.66 to 0.57 This slow decrease of the H_2O-trapping products with increasing distance from the charge injection site must not be interpreted as a weak distance dependence of the charge transfer rate k_{ET} described in the Marcus–Levich–Jortner Equation (a).[11]

$$\ln k_{ET} \propto -\beta \Delta r \qquad \text{(a)}$$

For the decrease of product yields, competition between the charge transfer (k_{ET}) and the H_2O-trapping reactions (k_{H_2O}) is decisive. Since in DNA strand **4** the charge transfer between the single guanines is considerably faster than the H_2O-trapping reaction,[9] the charge decreases only slowly during its migration through the DNA strands.[12] This reversible tunneling between the relay stations[13] of DNA **4** can be compared with a multistep chemical reaction in which the intermediates interconvert faster into each other than they react irreversibly yielding the products. Such a reaction is well described by the Curtin–Hammett principle that takes into account the rate of the reversible steps (k_{ET}), the equilibrium constants (ionization potentials of the relay stations), and the irreversible reactions leading to the products (k_{H_2O}).[14] In the extreme case, the yields of products P_G are nearly independent of the position of the DNA relay stations. Of course, this cannot be explained by a disappearance of the distance influence on the charge transfer rate (k_{ET}).

Further evidence that the charge in our assay is centered predominantly at the guanines was provided by experiments with DNA double strands containing mismatches. Thus, the efficiency of the charge transport from the donor $G_1^{\bullet+}$ to the acceptor GGG in oligomers **5**–**7** dropped from 68% for the

[*] Prof. Dr. B. Giese, Dipl.-Chem. S. Wessely
Department of Chemistry, University of Basel
St. Johanns-Ring 19, 4056 Basel (Switzerland)
Fax: (+41) 61-267-1105
E-mail: bernd.giese@unibas.ch

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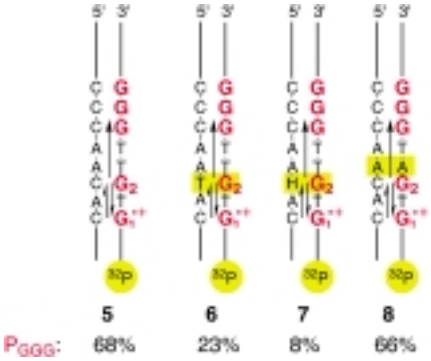
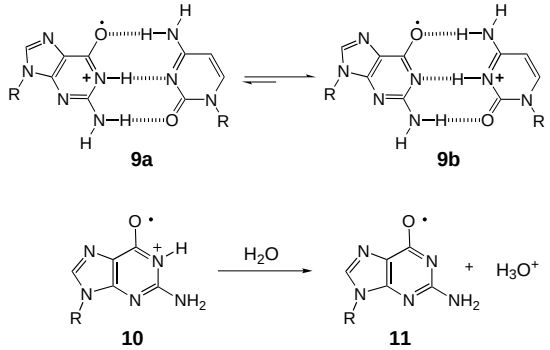
mismatch-free double strand **5** to 23 % (**6**) and 8 % (**7**), when a T or the abasic monomer H[15], respectively, was introduced opposite to G_2 (Scheme 2).[16] On the other hand, the



Scheme 2. Charge transport from the charge donor $G_1^{\bullet+}$ through double strands **5**–**8** towards the charge acceptor GGG. The efficiency of the charge transport was measured by the yield of the cleavage products P_{GGG} at the GGG sequence.[12] As double strands 31-mers having G_2 in the middle of the strand were used.

efficiency of the charge transport remained almost unchanged when a mismatch at adenine (A) was introduced by an A in the complementary strand (**8**).

We assume that these effects are induced by a weakening of the hydrogen bonds in the mismatched guanine radical cations $G_2^{\bullet+}$ (Scheme 2). Steenken[17] has shown that $G^{\bullet+}$ has a pK_a of 3.9. In a mismatch-free DNA the positive charge is distributed over both bases (**9a** ⇄ **9b**) of the G:C base pair **9**. If the hydrogen bonds are weakened, however, the probability of proton transfer to the surrounding water increases (**10** → **11**) and this retards the charge transport through DNA (Scheme 3).[18]



Scheme 3. Transfer of a proton from the guanine radical cation $G^{\bullet+}$ to the paired cytosine (**9a** ⇄ **9b**) and to the surrounding water (**10** → **11**).

Thus, proton transfer from a $G^{\bullet+}$ to water could explain why mismatches of G:C pairs strongly diminish the efficiency of the charge transfer to the GGG acceptor (strands **6**, **7**).[19] This interpretation is supported by another experiment in which we have generated a $G^{\bullet+}$ at the end of a double strand. This $G^{\bullet+}$ was unable to inject a positive charge into DNA because the base pair at the end of the double strand is so exposed to the surrounding water that a fast deprotonation of $G^{\bullet+}$ (**10** → **11**) occurs and the charge transport is suppressed.

Conclusion: A positive charge injected into DNA, is spread over the relay stations that are positioned between the charge donor and the charge acceptor. A slow decrease in the intensity of the H_2O-trapping products is not an indication for a weak distance dependence of the charge transfer rates (k_{ET}). It is the rate ratio between H_2O-trapping (k_{H_2O}) and charge transfer (k_{ET}) that plays the decisive role. Mismatched guanines suppress the charge transfer because of proton transfer from $G^{\bullet+}$ to the surrounding water.

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