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Effect of GC Base Pairs on Charge Transfer through DNA Hairpins: The Importance of Electrostatic Interactions

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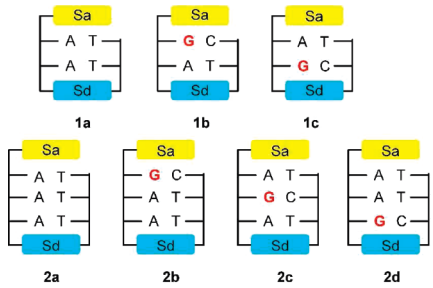
Over the past decade, the efficiency and mechanism of charge transfer in DNA have received a lot of attention from both experimentalists and theoreticians.[1−4] Apart from possible biological implications related to oxidative damage in DNA, it is a subject of considerable fundamental interest. DNA presents an excellent model for the study of charge separation in weakly coupled π-stacked systems because a variety of well-defined DNA molecules can be synthesized with full control over the base pair sequence in the stack. Among the best examples of such well-defined systems are the DNA hairpins synthesized and studied by Lewis and co-workers.[5,6] These hairpins consist of two complementary strands of nucleobases joined by a stilbene linker (Sd) as schematically indicated in Scheme 1. The hairpins are completed by a 'capping' stilbene (Sa) and have been shown to adopt a regular B-DNA structure. In a typical experiment Sa can be selectively photoexcited leading to Sa*. Subsequently, transfer of a positive charge can occur, resulting in a positively charged hole being trapped at the acceptor (Sd^+), while a negative charge stays behind on Sa^-.[7] The charge separation rate depends strongly on the length of the DNA segment and on the base pair sequence.[7,8]

Scheme 1. Structure of DNA Hairpins



Recently, we have theoretically studied charge transfer through DNA hairpins of the type in Scheme 1 containing only adenine:thymine (AT) base pairs. We have shown that the efficiency and distance dependence of the charge transfer rate are influenced by structural fluctuations and that the electrostatic interaction between Sa^- and the hole traveling through the DNA play an important role.[9]

In this communication we show that unexpected effects of including a guanine:cytosine (GC) base pair in the DNA segment of the hairpins[8] can be explained consistently by explicitly considering the electrostatic interaction between the positive and negative charges. Additionally, we argue that differences in the charge transfer integrals for different combinations of bases in the fixed B-DNA structure are of minor importance since the fluctuations are, in all cases considered here, of the same order of magnitude as the average value.

We have studied the forward hole transfer through the hairpins shown in Scheme 1 using a tight-binding model for charge transfer with effects of structural fluctuations taken into account according to the semiclassical TDSCF model.[9−11] The two important parameters in this model are the charge transfer integrals between neighboring bases and the site energies that determine the energy landscape for charge transfer. Both of these parameters have been shown to fluctuate considerably in time.[9,12,13] We have now calculated charge transfer integrals and site energies as a function of time for all combinations of bases and stilbene moieties that occur in the hairpins in Scheme 1. These data are included in the Supporting Information. The data show that for all combinations of bases the average charge transfer integral is close to zero, while the width of the distributions is 0.08 eV. The time scale of the fluctuations is of the time scale of 1 ps. This means that differences in charge transfer integrals for different neighboring bases are averaged out by structural fluctuations that are faster than the charge transfer process.[14]

Structural fluctuations also cause a considerable variation in the site energy; however, the width of the distributions of site energies (~0.18 eV; see Supporting Information) is much smaller than the differences in the average site energies that occur along the DNA stack. One of the origins for these differences is the electrostatic interaction between the positive charge moving along the stack and the negative charge that remains on the Sa hole donor. For a hairpin consisting of only AT base pairs, this results in a 'Coulomb well' from which the charge has to escape to form two free charges. The steepness of this Coulomb well depends considerably on the dielectric constant along the stack, which has been argued to be relatively low.[11] The average site energies for AT-only hairpins are indicated in Figures 1 and 2 for hairpins **1a** and **2a**. A consequence of this electrostatic interaction is that the barrier for charge transfer is not constant but increases with the length of the DNA segment, resulting in a nonexponential distance dependence of the charge transfer rate.[9]

The second origin of differences in site energies is in the inherent differences in the ionization potentials of the nucleobases. If GC base pairs are introduced in the AT DNA segment these GCs become localization sites for the charge since the ionization potential of G in the stack is ~0.5 eV lower than that of A. This results in hole transport by hopping between G's in DNA.[4,15,16] Recently, Lewis et al. have shown that the actual position of the G base strongly determines its effect on the hole transfer rate.[8]

To establish the reason for this position dependent effect of G on the charge transfer rate we have simulated charge transfer in

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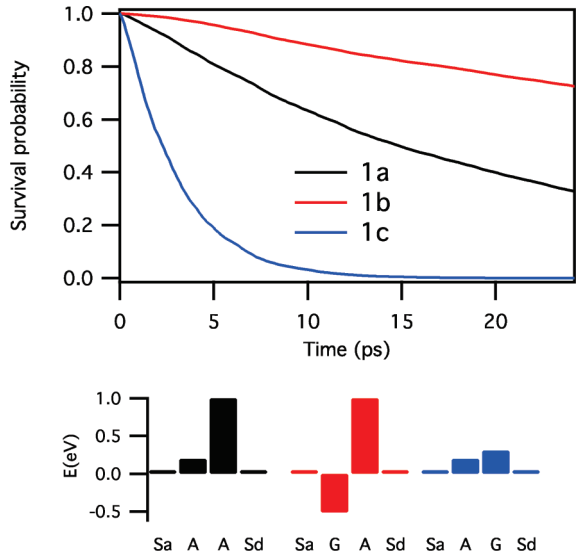

Figure 1. Top: survival probability as a function of time for DNA hairpins consisting of two base pairs. Bottom: energy landscapes for charge transfer (average values of the fluctuating site energy).

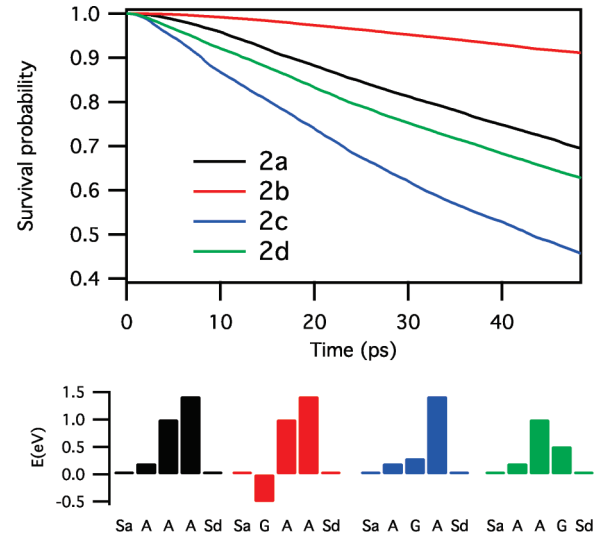

Figure 2. Top: survival probability as a function of time for DNA hairpins consisting of three base pairs. Bottom: energy landscapes for charge transfer (average values of the fluctuating site energy).

the hairpins in Scheme 1. In these simulations a charge is initially generated on the hole donor Sa and it decays infinitely fast at the acceptor Sd. The charge transfer rate is then characterized by the survival probability, i.e. the probability that the hole has not disappeared at the acceptor yet. In hairpins **1** that consist of two base pairs there are two possible positions to replace AT by GC. The survival probability as a function of time for these hairpins (**1b** and **1c**) is compared to those for the all-A hairpin (**1a**) in Figure 1. If G is located next to Sa (**1b**) the charge transfer is significantly slower than that for **1a**, whereas a G next to Sd increases the charge transfer rate. This is consistent with the experimental data. These results can be understood by considering the energy landscapes for charge. These energy landscapes include effects due the electrostatic interaction, and the ionization potential difference between A and G are shown in the bottom part of Figure 1. If G is present next to Sa in hairpin **1b**, a trapping site next to Sa^- is formed and separation of this contact ion pair is much slower than that in **1a**. When G is located next to Sd in **1c**, the energy landscape becomes rather flat and the charge transfer rate is higher than that in **1a**.

A similar effect of the introduction of a G is observed in hairpins **2** that contain three base pairs. The simulated results for these hairpins are shown in Figure 2. As in **1b**, if a G is present next to Sa in hairpin **2b** the charge is trapped in the Coulomb well and transfer is considerably slower than that for **2a**. If the middle A is replaced by G as in **2c**, the total height of the barrier does not change but it becomes more narrow than that in **2a**. This results in faster tunneling through this barrier and hence a higher charge transfer rate. Finally, in **2d** where G is next to Sd, the barrier for charge transfer is equally wide as in **2a** but it is lower, leading to a somewhat higher rate.

These results are consistent with the experimental data by Lewis, although the rates cannot always be directly compared due to different charge separation yields.[8] The arrival rate may be influenced by the recombination reaction of a hole in the DNA and the electron on Sa, leading to a higher 'apparent' charge transfer rate combined with a lower charge separation yield.

In conclusion, we have shown that the strong dependence of the position of a single GC base pair in an AT-containing DNA hairpin can be consistently explained if the electrostatic interaction between the hole in DNA and the negative charge on the hole donor is taken into account. This indicates that electrostatic interactions of the separated electron−hole pair play an important role in the kinetics of charge transfer through these hairpins.

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Supporting Information Available: Full data on time dependence and distribution of charge transfer integrals and site energies. Calculated charge transfer rates. Description of computational methodology. This material is available free of charge via the Internet at http://pubs.acs.org.

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