

# Charge transfer mechanism in a PolydGpdCp Fiber and in wet DNA

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## Abstract

Recently there has been great interest in the conducting properties of DNA because of their potential applications to nanotechnology and their role in protecting the molecule from oxidative damage. Unfortunately, experiments have provided very contradictory results. Using state of the art ab-initio simulation we investigated the hole localization and transfer in both a laboratory realizable polydGpCp wet Z-DNA molecule and in a fully solvated B-DNA

*Key words:* Density functional calculations; DNA damage; electron transfer; molecular dynamics; nucleobases

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## 1. Introduction

Charge transfer in DNA is currently the subject of intense theoretical and experimental investigation [1]. This is due both to a possible use of DNA as a conducting wire [2] and to the role of conductivity in oxidatively generated damage and possibly in repairing mechanisms. [1,3] Unfortunately the experiments conducted so far have provided contradictory results, with conductivities that cover the entire range from metallic to insulator. [4–7] Such experiments are technically difficult since they require handling of single molecules or small bundles of DNA and fine control of their contact to the metallic leads and to the supporting surfaces. Despite experimental difficulties, a general consensus has been reached. [1,8] In particular, experiments on chemically modified or photosensitizer intercalated DNA have demonstrated that wet DNA and DNA bundles can carry charge. [1,9,10] On the other hand, long DNA helices deposited on mica surfaces or in

dry conditions were found to be insulators or wide-bandgap semiconductors. [8]

As discussed in Ref. [11], charge transport in duplex DNA can occur via a coherent single step transport from donor to acceptor (superexchange limit) or multistep charge hopping. [12]

Both mechanisms have been observed in wet DNA experiments, where the charge is injected site-selectively by introducing some modification into the DNA and a charge sink is created by the introduction of a modified base or of a GGG sequence. [13,1]

On the basis of experimental and theoretical evidence different localization and transport mechanisms have been proposed: a change in the tilt angle of the bases, a rearrangement of the solvation shell, a fluctuation in the position of counterions and a change in the protonation state of G.

The importance of the polarization of the solvent shell has been shown to play a fundamental role in the charge transfer, at least in poly(A:T). [14] The ion-gated charge hopping mechanism was proposed from first-principles simulations that showed a correlation between the charge localization and the position of the counterion, and it was supported by indirect experimental evidence. [15]

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The proton-coupled charge transfer mechanism received most attention and different groups found experimental and theoretical supporting evidence. [16,?,18] In this scenario the charge hopping is linked to the proton transfer from G to C. In this paper we will give a summary of the evidence that we obtained on the proton-coupled hole localization by performing large-scale density functional theory (DFT) calculations on a fiber Z-DNA and DFT/MM calculations on B-DNA in water solution.

## 2. Method

The first system studied is a fully hydrated double strand self-complementary DNA (polyd(**GpCp**)) [19]. This is an infinitely repeated biopolymer, which in the unit cell contains twelve guanine:cytosine (**G:C**) pairs in the Z conformation. The atomic and electronic structures of this system have been thoroughly characterized via first-principles optimizations [20] while the oxidation of the guanine radical cation, a parasitic event with respect to hole migration, was studied with QM/MM calculations [21]. The simulation cell contains 12 base pairs, 654 heavy atoms and 540 hydrogen atoms (6 water molecules and 1 Na<sup>+</sup> counterion per nucleotide). Periodic boundary conditions were used throughout.

The second system is a fully solvated 38-base pair B-DNA. The chosen sequence is the same as that used in the experiments of Giese et al. [22] The structure was equilibrated at room temperature for 10 ns in a box  $38 \times 41 \times 154 \text{ \AA}^3$  with 5902 water molecules and Na<sup>+</sup> counterions, for a total of 20265 atoms, using the Amber99 force field. [23]

Quantum (QM) and QM/MM calculations were performed within DFT. [24,25] In the case of the B-DNA we performed different QM/MM molecular dynamics simulations starting from uncorrelated structures extracted from the MM run. The quantum subsystem was taken to be the central segment d(5'GTGG-3'). The QM subsystem included the sugar-phosphate backbone and was terminated with 4 capping hydrogens.

The present-day exchange and correlation functionals used in DFT have a well-known drawback in describing radical states due to the incomplete cancellation of the electron self interaction, which artificially favors charge delocalization. [26]

Thus, in the case of delocalized states we checked the robustness of our results by repeating our calcu-

lations with the self-energy corrections introduced in Ref.[27], where adjustable parameters were fitted to reproduce the distribution of the spin density of a guanine pair stacked at 3.5 and at 9 Å obtained with a correlated (MP2) ab-initio calculation.

## 3. Results

The full quantum calculations on the polyd(GpCp) fiber have shown that the hole can indeed be localized by a proton transfer from G to C. [18] This result was confirmed on the B-DNA in solution, where we observed the charge transfer from a GGG to a G site upon deprotonation of the latter. [28] To do that we performed a metadynamics simulation. Our goal was to understand how a hole, which is initially localized on the stacked GGG triplet, reversibly hops to a different isolated G, separated from the GGG by an AT bridge. We start adding energy to the  $H_1$  of the isolated guanine that initially has no radicalic character. As the reaction proceeds, the proton is transferred from this G base to the nearby paired C base and, simultaneously, the  $H_4$  proton belonging to C is transferred to G. This double proton exchange makes the final state energetically more favorable than a single proton transfer ( $G_{-H} : C - H^+$ ). Soon after the proton transfer the hole is transferred from the GGG triplet to the *isolated G* (Fig 3).

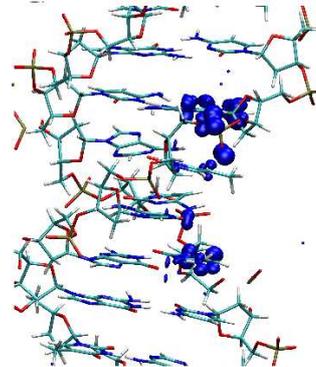


Fig. 1. Details of the three-dimensional structure of the B-DNA 38-mer and of the spin density isosurface (in blue) associated with the radical cation state during the hole transfer from GGG to the isolated G.

## 4. Summary

Our calculations provided an important insight into the details of the mechanism that are not

directly accessible to experimental probes. We observed directly the proton-coupled charge transfer, a mechanism already proposed on the basis of multiple H/D isotope effects studies on the charge mobility [17,16] and indirectly shown by us on a fiber Z-DNA. [18] Moreover we found a new and unexpected role for the tautomers of G and C generated by double proton transfer.

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