Effects of intra base-pairs flexibility on hole transfer coupling in DNA

Anna Sadowska-Aleksiejew a, Janusz Rak a,*, Alexander A. Voityuk b, *

a University of Gdańsk, Faculty of Chemistry, Sobieskiego 18, 80-952 Gdańsk, Poland
b Institució Catalana de Recerca i Estudis Avançats (ICREA), Institute of Computational Chemistry, Universitat de Girona, Campus de Montilivi, E-17071 Girona, Spain

Received 21 July 2006; in final form 31 July 2006
Available online 15 August 2006

Abstract

Based on Hartree–Fock calculations we consider how changes in base-pair parameters affect the electronic coupling matrix element in DNA. The range of the parameters was determined using the statistical analysis of crystallographic data for DNA sequences. The electronic coupling is found to be very sensitive to intra base-pair deformations and its fluctuations can result in essential (several orders of magnitude) variation of the charge transfer rate. We conclude that structural distortions of nucleobase pairs significantly influence the electronic coupling in DNA π-stacks and have to be accounted for by modeling of the hole transfer process and interpreting experimental findings.

© 2006 Elsevier B.V. All rights reserved.

1. Introduction

Many recent experimental and theoretical studies have been devoted to charge transfer in DNA [1–11]. It has been well established that radical cation states of guanine (G+1) are key intermediates in the hole transfer. When the hole donor and acceptor GC pairs are separated by a short (AT)n bridge (n ≤ 3) the coherent charge transfer process proceeds through superexchange tunneling. A sequence of such tunneling steps, G-hopping, make it possible the long-range charge transport through DNA over distances of ~100 Å [1–4]. The rate of each tunneling step is proportional to the square of the electronic coupling, Vda, between the donor and acceptor sites [12,13], and therefore, this parameter plays a fundamental role in the charge transfer mediated by DNA.

Recently it has been demonstrated that proton transfer within GC and AT base pairs leads to essential changes in the coupling [14]. On the basis of quantum-mechanical calculations it was also established that electronic coupling is extremely sensitive to mutual position of neighboring base pairs and thermal fluctuations of the DNA structure considerably affect the efficiency of the charge transfer [15,16]. The effects of structural dynamics on hole transfer through a DNA π-stack have recently been considered [17,18]. Based on generalized spin–boson Hamiltonian, Jang and Newton developed a theory of electron transfer with torsionally induced non-Condon effects [19].

All models of charge transfer in DNA treat each base pair (BP) as a rigid planar unit. However, many crystallographic data for DNA oligomers (see for instance Ref. [20]) demonstrate that base pairs are often not planar but essentially distorted due to propeller-twisting about the long base-pair axis. Further evidences which came from crystal database analysis [21] and molecular dynamics simulations [22] suggest that the magnitude of intra-BP distortions is quite comparable to that of inter-base-pair fluctuations. In particular, the harmonic force constants associated with the intra-BP parameters shear and stagger amount to ca. 8 and 4–6 kcal/(mol Å2) [22], respectively, whereas the value of the force constant for the rise parameter, which describes inter-BP distance in a stack, is found to be about 18 kcal/(mol Å2) [21]. Similarly, when comparing the force constants corresponding to rotational parameters one finds...
that intra-BP deformations should be more feasible than perturbations of the helical structure [21,22]. Recently, it has been found that intra-BP distortions may considerably affect the energetics of the charge transfer in DNA [23]. However, still there have been no estimation of how structural distortions of BPs influence the electronic coupling of neighboring pairs in the π-stack.

The Letter reports the results of quantum-mechanical calculations on the electronic couplings in dimers containing structurally distorted base pairs.

2. Methods

The relationship between intra-BP parameters and electronic couplings was studied in two dimers [GC,AT] and [GC,TA]. The atomic coordinates of the dimers were generated using the program X3DNA [24]. As the base-step parameters we employed the values corresponding to the regular B-DNA (rise = 3.38 Å, twist = 36°, other 4 parameters, shift, slide, roll, and tilt, are assumed to be zero). The reference geometries of GC and AT pairs were optimized at the RI-MP2/TZVPP level [25]. The corresponding intra-BP parameters are listed in Table 1.

The BP distortion effects were studied in a systematic manner. First, we analyzed base pair parameters in seven double-stranded B-DNA dodecamers [26]. The statistical evaluation is presented in Table 1. Then, the standard deviations (SD) found for each parameters were used as increments for intra-BP parameters.

The two-state model of the Generalized Mulliken–Hush method [27,28], was employed to derive electronic couplings. The energy difference and the dipole moment matrix were estimated within Koopmans’ approximation and the Hartree–Fock calculations. Recently, it has been shown that the electronic couplings for hole transfer in DNA calculated in this way are in good agreement with CAS-PT2 and CASSCF estimates [29].

HF calculations were performed with GAUSSIAN 98 using the 6-31G* basis set [30].

3. Results and discussion

In the following we shall demonstrate that variations in intra-BP parameters have profound impact on the electronic coupling for hole transfer in DNA. The reference geometries of the [GC,AT] and [GC,TA] systems are displayed in Fig. 1. The intra-BP parameters are defined in Fig. 2.

3.1. [GC,AT] system

Among all possible BP dimers, the [GC,AT] stack should be most efficient hole transfer mediator as indicated by the comparison of the corresponding electronic couplings [5]. The variation of the \( V_{da} \) matrix element with the intra BP parameters is presented in Table 2. These data suggest that changes in the base pair parameters may lead to substantial alteration in \( V_{da} \), and in consequence, to substantial modulation of the rate of elementary G-hopping steps (the rate is proportional to the square of \( V_{da} \)). The squared ratio (\( R \)) of the matrix elements in the distorted and reference structures indicates that the electronic coupling is very sensitive to a variation of shear and propeller twist in GC (Fig. 3a) and opening in AT pairs (Fig. 3b). The rate of hole transfer decreases by a factor of 250 by deformation of GC along the shear mode (\( R^2 = 0.004 \), Fig. 3a). However, the considerably smaller effect is found for the corresponding distortion of AT (\( R^2 = 3.5 \), Fig. 3b). Electronic coupling is also strongly sensitive to changes in rotational parameters. The decrease in the opening
parameter of AT should slow down the hole transfer by 2 orders of magnitude \( (R^2 = 0.01; \text{ Fig. 3b}) \) while 15-fold change in the rate is expected when changing the propeller twist in GC \( (R^2 = 0.07, \text{ Fig. 3a}) \).

When comparing the \( V_{\text{da}} \) values calculated for distorted structures two factors should be accounted for: (1) the stiffness of a particular deformation mode which is reflected in the standard deviation and thereby determines the increment of the parameter; (2) the influence of the corresponding deformation on the overlap of donor and acceptor orbitals which determines the coupling matrix element \([6,16]\).

3.2. [GC,TA] system

The dimer [GC,TA] of regular structure is characterized by one of the smallest \( V_{\text{da}} \) elements \([5]\). The calculated electronic couplings are listed in Table 2 and \( R^2 \) values.
As seen from Fig. 4, distortion of BPs in this complex leads to much smaller effects as compared to the [GC,AT] dimer. Inspection of $V_{da}$ values (Table 2) indicates that the electronic coupling is most sensitive to variation of the parameters stagger and propeller twist. The maximum change of the hole transfer ($R^2 = 0.2$; see Fig. 4b) is found for the stagger deformations in TA. On contrary, the electronic coupling is calculated to be almost insensitive to stretch in TA (Table 2 and Fig. 4b).

In the dimer, the inter-strand G–A interaction determines the electronic coupling. The $V_{da}$ magnitude depends on the overlap between the donor and acceptor diabatic wave functions. Analysis of the orbital overlap in [GC,AT] and [GC,TA] complexes showed that in the inter-strand [GC,TA] dimer there exists only one leading orbital interaction—between the oxygen atom of guanine and the nitrogen of amino group in adenine [6]. Thus, the structural distortions in [GC,TA] are related to the change in the orbital overlap just in one region. By contrast, the overlapping pattern in the [GC,AT] with the intra-strand G–A interaction is more complicated and includes the interaction of several orbital lobes [6]. This is the reason why relatively small deformations in the [GC,AT] complex are followed by distinctive changes in the overlap and the electronic coupling.

4. Conclusions

We have analyzed the impact of base pair distortion on the electronic coupling for hole transfer between neighboring BPs. The present study demonstrates that the intra-BP degrees of freedom should be taken into account when modeling the influence of DNA dynamics on hole transfer. The results can be summarized as follows:

- Changes in base pair parameters within the range observed in the crystallographic structures exert profound effects on the electronic coupling. In the most spectacular example, deformation of GC along the shear mode in [GC,AT] leads to change in the hole transfer rate by a factor of 250.
- Both translational and rotational parameters influence the electronic coupling in the π-stacks. The most essential effects are associated with a variation of shear and propeller twist in the GC and opening in AT pair for systems with the intra-strand G–A interaction. The inter-strand electronic coupling is found to be less sensitive to deformations of the base pairs.

Acknowledgements

The authors would like to thank Dr. Iwona Dąbkowska for providing them with the RI-MP2/TZVPP optimized geometries of the AT and GC base pairs. This work was supported by the Polish State Committee for Scientific Research (KBN) via International Co-operation Program, Grant Dec.127/02/E-335/S/2006 (J.R.) and the Spanish Ministerio de Educación y Ciencia, Project No. CTQ2005-04563 (A.A.V.). The calculations were performed at the Academic Computer Center in Gdańsk (TASK).

References