SINGLE-MOLECULE DNA CONDUCTANCE IN WATER SOLUTIONS: ROLE OF EXPLICIT WATER–COUNTERION SHEATH AND CHEMICAL MODIFICATION OF NUCLEOBASES

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Dependence of charge transmission through several conventional and extended DNA duplexes on the explicit presence of their water–counterion surrounding has been theoretically studied. We show here that: (a) the latter does not form specific charge transmission channels in addition to those available in DNA duplexes themselves; (b) chemically modifying DNA bases to extend their π-electronic systems does not significantly alter time-averaged charge transmission probability through DNA duplexes.

Keywords: DNA; counterion; hydration; charge transfer; chart transport.

1. Introduction

Unravelling detailed physical–chemical mechanisms of DNA charge transfer/transport is one of the hotly debated issues in the modern nanobioscience, and much research has been conducted in this field (for the comprehensive reviews, see, for example, Refs. 1–3). Despite numerous experimental studies, there is still no universal agreement on DNA conductance properties, with suggestions ranging from insulator to superconductor. The pertinent theoretical work also delivers disparate results and experiences lack of predictive force in general, frequently suffering from the blatant naivety of the DNA models involved. This is why, further systematic studies on this topic, using reliably approved methods and approaches, are absolutely necessary.
One of the points, where some consensus has already been achieved, is that DNA duplexes are as a rule more conductive than single-stranded DNAs (see, for example, Refs. 4–7), so that the present work deals with the former molecules. Another point of convergence is that electric properties of DNA duplexes are appreciably dependent on the experimental conditions. Many of the relevant experiments are carried out either in water solutions or in humid atmosphere, therefore it is of crucial importance to learn in detail what is the role of water and counterions in DNA charge transfer/transport.

Water is very well known as the agent regulating DNA duplex structures, in that it controls order–disorder and all other DNA conformational transitions. Thus, it is tempting to assume that it plays mostly an indirect role in DNA electric properties. Specifically, one physically appealing proposal could be to treat DNA water–counterion surrounding as a continuous dissipative bath environment capable of creating new electronic states within the band gap and thus promoting DNA conductance. Further, due to the charge transfer through DNA base pair stacks, the hydration shell may be rearranged together with the DNA conformation, thus facilitating the electron/hole propagation.

On the other hand, the role of DNA hydration has also been considered at the atomistic level using various methods of quantum chemistry, sometimes in combination with classical molecular dynamics simulations and/or simplistic tight-binding models (for the most recent treatises see, for example, Refs. 11 and 12). The main findings here consist in detecting some DNA band gap narrowing and even formation of impurity levels caused by the very presence of explicit water–counterion shells around the biopolymers under study. There was even a proposal to place the LUMO (lowest unoccupied molecular orbital) of the DNA–water–counterion system near that of the Na$^+$ counterions. Whereas the band gap narrowing due to the explicit presence of DNA hydration shell is quite plausible and has been shown in numerous works by Ladik et al. to be independent of the AO (atomic orbital) basis set employed, the result of the paper Ref. 15 is most probably just an AO basis set artefact (the pitfalls of the alkali cation quantum chemistry are long known, see, for example, the review Ref. 16). As concerns the problem of impurity levels due to DNA hydration shells, a serious caution should be made, since earlier systematical studies have shown that the onset of such impurity levels might also be dependent on the AO basis set used.

With all this in mind, the following question arises: Could DNA water–counterion hydration shell play a direct role in DNA charge transfer/transport processes, that is, be capable of providing specific electron/hole transmission channels, in addition to the approved ones formed by the overlapping $\pi$-orbitals in DNA base-pair stacks? Asking such a question is absolutely justified, especially in view of the experimental results published in Ref. 24. The latter work has measured radiation-induced conductivity on aligned fibre samples of hydrated DNA and found evidence for highly mobile charge carriers within such samples. However, the lack of conductivity anisotropy and the second-order nature of the decay enabled the authors
of Ref. 24 to argue against the conventional one-dimensional conduction mechanism via “π-way” (with the charge transport confined to the DNA base-pair core). Instead, Ref. 24 suggests that there ought to be rapid migration of charge carriers in the “outer mantle” of hydrated DNA. Thus, the present communication is an attempt to systematically resolve the posed question, and our final answer rules out any possibility of charge transfer/transport through the DNA outer mantle.

2. Methods

Here we have considered four compounds: two DNA oligomer duplexes with homogeneous base pair sequences \((dA)_{14}-(dT)_{14}\) and \((dG)_{14}-(dC)_{14}\) — from here on, they will be referred to as DADT and DGDC, respectively, as well as their counterparts containing the so-called “extended” DNA base residues (BABT and BCBG, respectively), where both purines and pyrimidines contain an additional conjugated aromatic ring (cf. Fig. 1 to observe the structural differences between the conventional and extended bases). Due to the latter “extension,” the corresponding duplexes turn out to have much larger diameter than their conventional counterparts (see Fig. 2 for the comparison). The synthesis and experimental characterization of such “extended” DNA duplexes has been pioneered by Kool et al. (see, for example, Ref. 25 and the references therein), and systematic quantum-chemical studies have also been carried out on them (see, for example, Refs. 26 and 27 and the references therein). As the works\(^{26,27}\) argue that the extended DNA ought to exhibit appreciably higher conductivity than their natural counterparts, we decided to investigate the roles of two factors — namely, the presence of explicit DNA counterion-hydration shells and the chemical modification of the DNA bases — in changing conductive properties of the biopolymer in question.

Each of the above compounds has been placed into an explicit water–Na\(^+\) surrounding to perform a 1 ns MD simulations in the NVT ensemble with periodic boundary conditions using the conventional MD thermostat at room temperature. Thiol linkers similar to those normally used in experiments (like \(-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{SH}\), for example) have not been attached to terminal groups of the DNA duplexes, so that the \(-\text{SH}\) groups were directly connecting the terminal 3’-OH-groups and the gold electrodes. The simulations were carried out with the AMBER simulation package,\(^{28,29}\) and DNA was parameterized according to the AMBER-99 force field with the BS0 corrections.\(^{30,31}\)

For every duplex, and each MD-snapshot thereof, DNA charge transmission spectrum around the Fermi level at zero bias has been estimated using the Kubo technique.\(^{32-37}\) Restriction to zero-bias data is justified by the observation that application of bias voltages higher than 0.4–0.5 V causes parasitic chemical reactions which destroy the thiol linkers.\(^{6,35}\) The applied electric fields were thus not high enough to have a significant influence on either the electronic structure or the observed transmission spectra. To describe our computational technique in brief, we use the extended Hückel level of approximation for the electronic structures
Fig. 1. Molecular structures of nucleotide pairs in (a) the extended (BABT) and conventional (DADT) adenosine–thymidine, as well as (b) extended (DCDG) and conventional (BCBG) cytidine–guanosine homooligonucleotide duplexes. The difference between the BA, BG and DA, DG, respectively, consists in the additional aromatic ring inserted between the pyrimidine and imidazole rings of the conventional purine bases, whereas both in BT and BC an additional aromatic ring is conjugated with the C5=C6 bond of the conventional thymidine (DT) and cytidine (DC) rings and also takes over the chemical connection to deoxyribose, instead of the conventional N1–C1′ glycosidic bond.

of both DNA and golden electrodes, with defining the interface between the DNA device and ideal electrodes as three Au atoms adopting the pertinent triangular form and conditionally belonging to the molecular device. The Kubo technique employs the Green-function-based formulation of the conventional Kubo–Greenwood linear
Fig. 2. Molecular structures of (a) the extended (BABT) and conventional (DADT) adenosine–thymidine, as well as (b) extended (DCDG) and conventional (BCBG) cytidine–guanosine oligonucleotide duplexes. The extension of the both bases renders the corresponding duplexes much wider and less compact than the conventional ones.

response theory without vertex corrections owing to optical and acoustic phonon scattering. The transmission spectra obtained were averaged over the MD-snapshots to include the conformational fluctuation effects (250 MD snapshots have been used for each molecule in the transmission spectra averaging procedure). The self-energy of the long DNA polymer has been iteratively estimated using Dyson equation and the conventional decimation scheme, whereas the starting point for this iteration, the self-energy of the semi-infinite ideal electrodes, has been analytically calculated in the tight-binding approximation with the transversal mode basis.
Two stages of the above computations have been carried out for every duplex under study: (a) in the absence of all the explicit environment (water molecules and counterions) and (b) in its presence.

3. Results and Discussion

Figure 3 presents our results concerning the influence of explicit DNA water–counterion environment on the charge transfer/transport through these biopolymer duplexes. We see practically no difference between the probabilities of charge transmission through “naked” BABT, BCBG, DADT, DCDG and their explicitly hydrated–sodiated counterparts. This is indicative of that no stationary charge transfer/transport “channels” (which could in principle arise from some overlapping lone pair orbitals of water molecules and survive the conventional time averaging along the MD trajectory) are formed in the water–counterion sheath of the DNA duplexes involved. This is why any calculated charge transmission ought to be ascribed to DNA duplexes themselves. At least for the DADT duplex, this ought to be a non-trivial result, because it is well known that the homogeneous dA–dT-sequences have a so-called “hydration water backbone,” which comprises a chain of well-ordered water molecules in the minor groove of the duplex, which is completely absent in other DNA base sequences. This “water backbone” turns out to be rather rigid, and its presence helps to stabilizel B-DNA conformation of the homogeneous dA–dT-sequences (see, for example, Refs. 38, 39 and the references therein). Still, our results show that even such a rigidity is obviously not enough for the formation of specific transmissive channels.

In comparing our data with the earlier theoretical findings, we may notice that the absence of specific charge transmission channels corroborates with the previously invoked indirect role of water molecules during the DNA charge transfer/transport. Indeed, there was a proposal that orientational relaxation of the water surrounding contributes to the drag force facilitating charge propagation along DNA duplexes. More recently, the authors of Ref. 40 also concluded, on the basis of systematic DFT+MD+tight-binding simulations, that the most efficient conduction channel in DNA should be delocalized π-orbitals owing to the base-pair stacking, and not deoxyribose, phosphate or water orbitals. According to another most recent DFT+MD+tight-binding comprehensive investigation, the potential energy of the charge transported through DNA is determined in equal measure by the water–counterion environment and the DNA base composition/sequence, with the environment inducing a partial localization of the charge to be transferred (thus hindering the charge transmission to some extent). Finally, Ref. 12 advocates a rather strong interaction of the nucleobases with surrounding water molecules, which give rise to “breaking of some of the π-bonds and appearance of unbound π-electrons,” thus allegedly enhancing DNA charge transport and even favorably changing DNA magnetic properties at room temperature to a noticeable extent. This result seems to be doubtful, because the first ionization energy of DNA is
Fig. 3. Plots of charge transmission probability vs. energy for ‘dry’ and ‘wet’ oligonucleotide duplexes under study: (a) BABT, (b) BCBG, (c) DADT, (d) DCDG. From here on, the zero on the energy axis denotes the Fermi level, which is chosen to be at the halfway in energy between the HOMO and LUMO of the “DNA–Au-electrodes” complexes. Therefore, the negative energy region corresponds to DNA valence bands, whereas DNA conduction bands are situated at the positive energies. The energy window in our study extends from $-1 \text{ eV}$ to $1 \text{ eV}$, because the roughness of the extended Hückel approximation does not allow to reliably explore higher/lower orbital energies.
between 4–5 eV,\textsuperscript{41} whereas the energy of O–H···O, O–H···N or N–H···O hydrogen bonds with a water molecule as H-donor/acceptor is well known to be of maximum 4–5 kcal/mol (that is, around 0.2 eV). Even the whole free energy of DNA hydration would, most probably, not be enough to overcome the potential barrier of DNA
ionization. Indeed, although the first hydration shell of ordered DNA duplex consists of some 10–20 water molecules, only a couple of them can have direct access to the nucleobases, because the latter are usually situated in the hydrophobic core of DNA duplexes (see, for example, Ref. 42 and the references therein). Therefore, it is not clear how such a strong water–nucleobase coupling, like that invoked in Ref. 12, could arise under the normal conditions.

Another interesting result of our study is shown in Figs. 4 and 5. Specifically, we observe that there is no significant difference between the charge transmission propensities of the conventional and extended DNA duplexes. Here we rely solely upon the qualitative appearance of the DNA charge transmission spectra, and are not performing any further numerical estimates due to simplicity of our DNA-electrode junction model. Still, one may notice that the extended DNA duplexes are even somewhat less conductive than their conventional counterparts (see Figs. 4 and 5). In effect, this is contrary to the expectations based upon the systematical theoretical studies using the conventional quantum-chemical tools.26, 27 These works have expressed some hope that a mere extension of the π-electronic system of the DNA base-pair stack in the direction transversal to the double-helical axis ought to render the DNA fundamental gap narrower — and thus promote DNA conductive properties. Similarly, our earlier work43 would favor such a standpoint by noting that the extended DNA base pairs would exhibit much more powerful electrostatic screening of the excessive charges (electrons/holes), also facilitating their mobility. On the other hand, our direct transmission computations on DNA in different conformations36 show that not only the presence of conjugated aromatic rings, but rather their orientation with respect to each other in the DNA base-pair stack (as well as their disposition with respect to the DNA double-helical axis) is vitally important for the proper charge transfer/transport. With this in mind, we observe in Fig. 2 that the extended DNA duplexes are possessed of a much less compact structure than their conventional counterparts, which, most probably, results in somewhat worse conductive properties of the former as compared to the latter.

The above results are extremely important for the rational design of DNA-based molecular wires, because they demonstrate that synthetic modification of DNA bases should be carried out not only to decrease their individual fundamental gaps and polarizabilities, but also not to destroy the compact B-DNA-like conformation. Going this way might help increase DNA charge transmission probability.

4. Conclusions

By and large, using our novel method of direct computation of the charge transfer probability at atomistic level, we have demonstrated that (a) DNA water–counterion environment does not form specific charge transmission channels in addition to those available in DNA duplexes themselves; (b) chemically modifying DNA bases to extend their π-electronic systems does not significantly alter time-averaged charge transmission probability through DNA duplexes. These findings are of help for
Fig. 4. Charge transmission probability vs. energy plots for ‘dry’ oligonucleotide duplexes: (a) BABT vs. DADT, (b) DCDG vs. BCBG.
Fig. 5. Charge transmission probability vs. energy plots for ‘wet’ oligonucleotide duplexes:
(a) BABT vs. DADT, (b) DCDG vs. BCBG.
physically–chemically correct modeling of DNA charge transfer/transport phenomena and the rational design of DNA-based molecular wires.

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