Ab initio electron propagator calculations of transverse conduction through DNA nucleotide bases in 1-nm nanopore corroborate third generation sequencing

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ABSTRACT

Background: The conduction properties of DNA molecule, particularly its transverse conductance (electron transfer through nucleotide bridges), represent a point of interest for DNA chemistry community, especially for DNA sequencing. However, there is no fully developed first-principles theory for molecular conductance and current that allows one to analyze the transverse flow of electrical charge through a nucleotide base.
Methods: We theoretically investigate the transverse electron transport through all four DNA nucleotide bases by implementing an unbiased ab initio theoretical approach, namely, the electron propagator theory.
Results: The electrical conductance and current through DNA nucleobases (guanine [G], cytosine [C], adenine [A] and thymine [T]) inserted into a model 1-nm Ag–Ag nanogap are calculated. The magnitudes of the calculated conductance and current are ordered in the following hierarchies: $g_A > g_G > g_C > g_T$ and $I_G > I_A > I_T > I_C$ correspondingly. The new distinguishing parameter for the nucleobase identification is proposed, namely, the onset bias magnitude. Nucleobases exhibit the following hierarchy with respect to this parameter: $V_{onset}(A) < V_{onset}(T) < V_{onset}(G) < V_{onset}(C)$.
Conclusions: The difference in current magnitudes and onset voltages implies the possibility of nucleobases electrical identification by virtue of DNA translocation through an electrode-equipped nanopore.
General significance: The results represent interest for the theorists and practitioners in the field of third generation sequencing techniques as well as in the field of DNA chemistry.

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1. Introduction

Nowadays the conduction properties of DNA molecule are of high interest for mankind. The particular interest is directed at the DNA transverse conduction, i.e. the electron transfer through the nucleotides in the direction transverse to the longitudinal axis of the double helix. A large amount of research on DNA transverse conduction is driven by the needs of the third generation sequencing techniques for the whole-genome analysis that can significantly reduce the cost of DNA sequencing process [1]. The third generation sequencing techniques are based on the measurements of the transverse electric currents through nucleotides as the single-stranded DNA chain is being translocated through a nanopore [2,3]. These techniques would allow us to operate on single DNA molecules without amplification and enable orders-of-magnitude longer base-read-lengths.

In this paper we theoretically investigate the transverse electron transport through all four DNA nucleotide bases by implementing an unbiased ab initio theoretical approach, namely, the electron propagator theory (many-body theory based on Green–Keldysh functions formalism) [4–9]. The calculation of electrical conductance and *I-V* characteristics of nucleobase junctions (nucleotide bases sandwiched between model Ag electrodes 1 nm apart) is accomplished by means of the genuine theoretical scheme [10–16].

The idea of implementing nanopores for DNA sequencing was proposed in 2000 [22], while in 2005 Lee and Thundat proposed to use the transverse electron tunneling across a DNA molecule as means of the single nucleotides identification [23]. The nucleotide identification by means of DNA translocation through a nanopore looks especially promising in the light of the recent advancements in the low-cost fabrication of 1 nm to 3 nm nanopores [21].

The basic fact that renders the proposed identification methods operational is the unique electrical signature of each nucleobase. The ratio of current values for different nucleotides gives a measure of the difference in their electrical signatures. The detection of all four DNA bases [18,19] and the sequencing of several DNA oligomers [17] have

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been recently accomplished by means of transverse tunneling current measurements. The magnitudes of measured currents range from tens of pA [17,19,20] to hundreds of pA [17], while the conductance values range from $10-30\,p\Omega^{-1}$ [19] to $40-90$ $p\Omega^{-1}$ [17].

The theoretical calculations (including those presented in this work) support the experimentally obtained difference in transverse electrical conductance of four nucleotide bases. Recent reports of theoretical results include density-functional-theory (DFT) studies of nucleotides located between graphene electrodes [24,25] and Green functions calculations of current through nucleotides located between gold electrodes [26–28].

Notwithstanding the pioneering character of the theoretical research on nucleotides transverse conductance reported so far, it lacks the detailed analysis of the charge transfer through nucleotide bases. Namely, the published theoretical papers in this field lack the fully developed first-principles theory for molecular conductance and current that allow to analyze how electrical current through a nucleotide base is affected by the alteration of molecular orbital energies due to bias applied. These are the aspects that the present work addresses. In addition, to the best of our knowledge, no author has investigated the transverse conduction through the isolated nucleotide bases (detached from the sugar). The present work investigates this topic for the first time.

2. Materials and methods

Our theoretical scheme for calculating the conductance and current through DNA nucleotide base junctions is based on Landauer conduction formalism coupled to the theoretical approach to solving the Dyson–Schwinger equation [29–31] proposed by Dahnovsky et al. [10–12].

The Landauer formula for the electrical conduction of molecular junction is the starter [32,33]:

$$g(\omega) = \frac{2e^2}{h} \overline{T}(\omega) \tag{1}$$

where ω is the energy of the electron incoming from the electrode to the molecule and $\overline{T}(\omega)$ is the transmission coefficient that in the framework of Green–Keldysh functions formalism [4,32] is expressed as:

$$\overline{T} = Tr\left\{\mathbf{\Gamma}^R \mathbf{G}^r \mathbf{\Gamma}^L \mathbf{G}^a\right\}, \tag{2}$$

where $\mathbf{\Gamma}^L$ and $\mathbf{\Gamma}^R$ are the coupling (linewidth) matrices describing the interaction between the molecule and the respectively left (with no bias) and right (under bias) electrodes, and $\mathbf{G}^r$ and $\mathbf{G}^a$ are the retarded and advanced Green function matrices of the molecular junction (describing a propagation of electron through the junction).

Using the expressions of the retarded and advanced Green matrices of molecular junction, $\mathbf{G}^r$ and $\mathbf{G}^a$ [10], the Landauer Formula (1) yields the zero-bias conductance of a metal–molecule–metal junction [12]:

$$g(\omega) = \frac{2e^2}{h} \sum_k \frac{a_k^2 \gamma_1(k)\gamma_2(k)c_{12}^2}{(\omega-\varepsilon_k)^2 + \frac{a_k^2}{4}(c_{11}\gamma_1(k) + c_{22}\gamma_2(k))^2}, \tag{3}$$

where ω is the energy of an electron being injected from the electrode to the molecule (usually assumed to coincide with the Fermi energy of the electrode); k is the order number of Dyson molecular orbital; ε_k and a_k are Dyson orbital pole (electron binding energy) and Dyson pole strength of the corresponding Dyson orbital; $\gamma_1(k)$ and $\gamma_2(k)$ are the coupling constants showing the smearing of the k-th molecular orbital level; c_{11}, c_{22} and c_{12} are the partial contributions of the k-the Dyson molecular orbital into the overall molecular conductance through the left, right and both electrodes, respectively. All quantities needed to calculate electrical conductance of molecular junction by means of

Formula (3) (except for the energy of incoming electron) are taken from the output of any quantum chemistry computational software able to run OVGF (EPT) calculations (e.g., GAUSSIAN 09 [34]).

In the multi-terminal atom approximation (when the coupling occurs through many terminal atomic orbitals) [11] the zero-bias conductance becomes [12],

$$g(\omega) = \frac{2e^2}{h} \sum_k \frac{a_k^2 \gamma^L(k)\gamma^R(k)}{(\omega-\varepsilon_k)^2 + \frac{a_k^2}{4}(\gamma^L(k) + \gamma^R(k))^2}, \tag{4}$$

where the *global coupling matrices* for the left and right electrodes are given by:

$$\gamma^L(k) = \sum_{i=1}^{n_L} <i\big|k>^2 \gamma_i^L(k), \quad \gamma^R(k) = \sum_{i=1}^{n_R} <i\big|k>^2 \gamma_i^R(k) \;. \tag{5}$$

The index i denotes the order number of atomic orbital of the terminal atom(s) of the electrode with corresponding linewidth, γ_i. n_L is the number of left terminal atomic orbitals and n_R is the number of right terminal atomic orbitals. The k-th Dyson orbital matrix element, $<i|k>$, reflects the partial contribution into the total conduction through the junction from the overlap between the i-th terminal atomic orbital and the k-th Dyson molecular orbital.

Our theoretical approach is also used for calculating the electrical current through a junction, expressed in terms of Dyson orbital poles, ε_k, pole strengths, a_k, the global coupling matrices, $\gamma^{L,R}(k)$, and the Fermi-functions of the electrodes, $f_{L,R}(\varepsilon_k)$ [10,11]:

$$J = \frac{e}{\hbar} \sum_k \frac{\gamma^L(k)\gamma^R(k)a_k[f_L(\varepsilon_k)-f_R(\varepsilon_k)]}{|\gamma^L(k) + \gamma^R(k)|} \;. \tag{6}$$

The analysis of the Fermi functions term, $[f_L(\varepsilon_k)-f_R(\varepsilon_k)]$, allows one to see the major role played by the alignment of Fermi levels of the electrodes with the closest molecular orbitals (HOMO and LUMO) in electron transport through the molecular junction: (a) it determines which molecular orbitals participate in electron transport — namely, those orbitals whose energies approach the kT-region (thermal excitation energy range) of the right or left electrode's Fermi level and enter the "window" between two Fermi levels; (b) it allows one to predict the voltage magnitudes at which current turns on and turns off. The magnitude of *onset voltage* (voltage at which current starts to flow) is determined by the alignment of energies of occupied/unoccupied molecular orbitals and the Fermi level of the right/left electrode. Current starts either when the energy of occupied molecular orbital enters the kT-region of the right (unbiased) electrode's Fermi level or when the energy of unoccupied molecular orbital enters the kT-region of the left (biased) electrode's Fermi level.

3. Results

The above scheme is used to calculate conductance and *I-V* characteristics of the four nucleobases inserted into the Ag–Ag nanogap. For this purpose we employ four simulation models represented on Figs. 1–4).
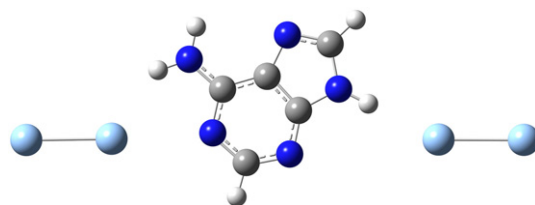

Fig. 1. Adenine molecular junction.