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Electron transport through 8-oxoG: NEGF/DFT study

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Abstract We present a first-principles study of the conductance of Guanine and 8-Oxoguanine (8-oxoG) attached to Au(111) electrodes. Cellular levels of 8-oxoG have been found in larger concentrations in cancer patients. The current through the structure was calculated using a DFT–NEGF formalism. We have compared flat and pyramidal electrode geometries and show that there is a measurable difference between the I–V characteristics of the pristine molecule and the 8-oxoG. For a flat electrode geometry, 8-oxoG produces a 2.57 (18.3) times increase in current than the corresponding counterpart at 3 V with a bond separation of 1.2 Å (2.4 Å). This can be attributed to molecular orbital energies shifting at the junction. Overall the flat geometry produces larger currents. We have also investigated the sensitivity of the current to the electrode molecule separation. For the flat geometry, the current dropped approximately 80% (97%) for 8-oxoG (pristine Guanine) with the doubling of the electrode separation.

Keywords DFT/NEGF · 8-Oxoguanine · Early disease detection · Cancer

1 Introduction

Deoxyribose nucleic acid (DNA) is one of the main types of nucleic acid, which in turn is composed of four nucleotides

which are the fundamental building blocks which contains a base, Adenine (A), Cytosine (C), Guanine (G) and Thymine (T), a molecule of sugar and phosphate group. The bases pair off to form a rung of the DNA ladder with A pairing with T and G pairing with C and are held together by weak hydrogen bonds. Ever since DNA showcased its ability to conduct current where it can be applied to the large area of study nanotechnology which joins many fields of study to improve performance of electronic devices. It has gathered much attention for its charge conducting properties. Measuring these properties is no easy task and requires highly sensitive instrumentation and many papers show contradicting evidence that have shown it to be conducting, insulating [1] semiconducting [2] and even superconducting [3]. This can be largely attributed to the varying experimental conditions such as conformational changes, the inter-nucleotide distance, water molecules, counter-ions and many other variables [4].

A typical experimental set-up for making electrical measurements involves placing DNA on a non-conductive surface and then attaching probes to either end allowing charge to flow through the DNA. In Braun et al. [1] developed a technique to instil electrical conductivity to DNA on two gold electric contacts, firstly a 12-base oligonucleotide with a thiol liker at the 3' end as gold has a natural affinity for Sulphur. This was then used as a template to deposit a 100-nm-wide silver wire, importantly the self-assembly properties of DNA show the potential as a template for deposition of metal atoms. Theoretical studies have also been conducted to understand the electronic properties of DNA and potential applications; Anantram et al. [5] have shown that the electronic properties offer a unique framework for the future of electronic devices, and by measuring the current through DNA it can be applied in the detection of disease.

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It is well understood that electron transport through a biological molecule is ultimately determined from the intrinsic chemical and electronic structure of the molecule, and thus, a unique conduction signature should be seen. Recent papers establish methods for electrical methods of disease detection, where base molecules modify the charge conducting properties of short DNA complexes [6]. Maintaining the integrity of the genetic code is a fundamental biological functions for transmitting the genetic information from cell to cell. While aerobic respiration is necessary, it also produces by-products, namely reactive oxygen species (ROS) for example superoxide, hydrogen peroxide and hydroxyl radicals. Being highly reactive they are detrimental to macromolecular cells and readily oxidize proteins, lipids and nucleic acids. There are multiple oxidative lesions that result in mutations or cell death, but none are studied as well as 8-Oxoguanine (8-oxoG) [7]. Undamaged DNA does not allow for incorrect Watson–Crick base pairs; however, the oxidation of the C-8 position on G allows for pairing with A or C with equal efficiency. The accumulation of 8-oxoG is found in both mitochondrial and nuclear DNA, and has been seen to contribute to ageing and human cancer. Studies have shown an increased accumulation of oxidized DNA in lung cancer compared to the surrounding healthy tissue [8].

To this end, we employ density functional theory (DFT) combined with non-equilibrium Green's functions (NEGF) to elucidate the effect of base oxidation on electron transport.

The NEGF approach is used in the TranSIESTA code [9] which allows for open-boundary systems where we consider ballistic transport only. In this study, the ultimate goal is to determine whether the electronic structure of a single oxidized base molecule provides a unique electron transport signature that could be used in early disease detection. We have calculated the transmission using a flat electrode geometry and modified the bond separation, and then repeated the calculations with pyramidal-shaped electrodes and noted a modification of the transmission. This is important on single molecule measurements as the geometry at the atomic level is uncontrollable.

2 Method

The structure of the base molecule was first obtained using Avogadro molecular editor [10], and this molecule was then attached to the Au. The molecule was then relaxed using SIESTA [11] to obtain the most stable structures. For simplicity the sugar-phosphate backbone was disregarded. Figure 1a shows the central region of the system inserted between two Au(111) leads. The system is composed of 3 regions: left electrode, right electrode and a central scattering region where the molecule under investigation is surrounded by a fraction of the electrodes to screen out the perturbation of the scatter.

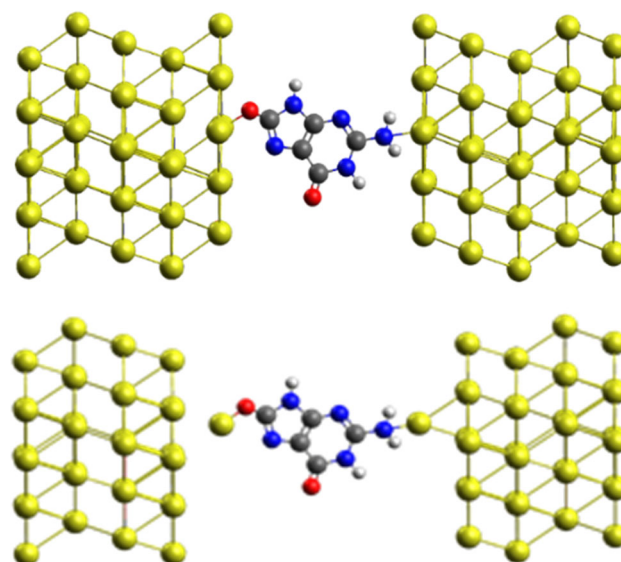


Fig. 1 Geometries of the central region of the junction sandwiched between Au(111) electrodes used for electronic transport calculations in TranSIESTA. The model consists of two layers of Au(111) from the electrode and the 8-oxoG molecule

The distance between the electrode and molecule is varied from 1.2 to 2.4 Å. The geometry of the electrode was modified to elucidate the interaction between the molecule and electrode as shown in Fig. 1b. In order to evaluate the conducting properties, the electronic states have to be properly characterized and DFT has been shown to accurately describe DNA bases. In all calculations, a double- ζ polarized basis set (DZP) was used as in previous studies [12]. Generalized gradient approximation (GGA) has previously produced satisfactory results [13,14] and has been used for the exchange-correlation energy functional using the PBE version [15]. The real-space mesh was set to a cut off of 200 Ry. The molecule was relaxed until forces were less than 0.01 eV/Å tolerance to obtain an optimized structure. The current through the system was calculated using Landauer's formula (Eq. 1). The transmission is obtained from the Green's function of the scattering region, which was calculated using TranSIESTA. In Eq. 1, $\mu^{L/R}$ denotes the electrochemical potentials of the source and drain electrodes and are shifted $V/2$ and $-V/2$, respectively; and $T(\varepsilon)$ is the transmission probability of the electrons with energy ε . f_L and f_r are the Fermi distribution function in the source and drain. T is the temperature and was 300 K.

$$I = \frac{e}{h} \int_{-\infty}^{\infty} d\varepsilon (f_L(\varepsilon) - f_r(\varepsilon)) T(\varepsilon) \quad (1)$$

$$f_{L/R}(\varepsilon) = \frac{1}{e^{\frac{\varepsilon - \mu^{L/R}}{kT}} + 1} \quad (2)$$

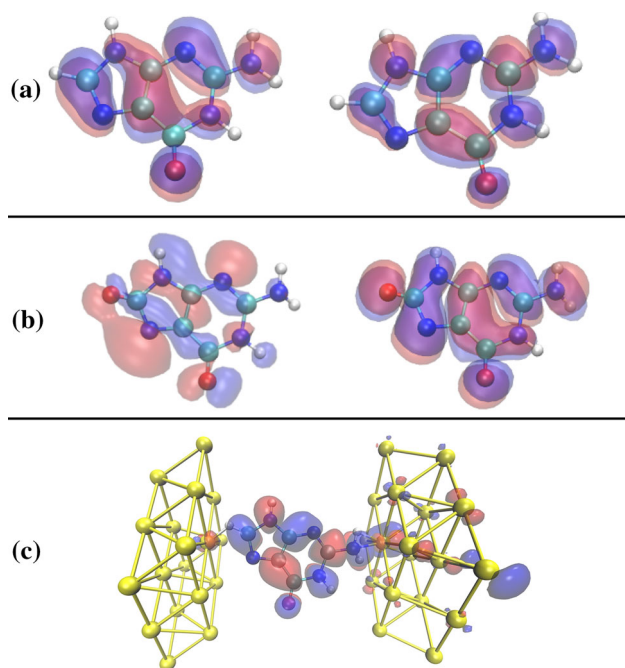


Fig. 2 HOMO (*left*) and LUMO (*right*) of **a** Guanine, **b** 8-oxoG, **c** transmission eigenchannel of Guanine at the energy of the HOMO. Calculated using SIESTA and the GGA functional. *Red* and *blue* indicate the positive and negative values of the wave function, respectively (Color figure online)

3 Results and discussion

We have obtained the spatial distribution and energy levels of the molecular orbitals of the HOMO–LUMO by geometry optimization; this provides the necessary foundation to evaluate the mechanism for conduction. Figure 2 shows the spatial distribution of the HOMO and LUMO of G and 8-oxoG. The pi and pi* character of the Guanine molecule is clearly shown in Fig. 2a and matches the existing results of Kilina et al. [16]. With the addition of an oxygen molecule the wavefunction takes on a vastly different electronic structure. The calculation of the transmission eigenchannel at the energy of the HOMO shows a small hybridization between G and Au electrode, shown in Fig. 2c and the electron density located on the electrode is less than 10% for that orbital. Figure 3 shows the energy levels of the orbitals near the Fermi level for G and 8-oxoG, which matches those obtained in a similar study utilizing DFT based simulations to explore the effect of DNA base sequence on conductivity [17].

The I–V characteristic of the molecule with flat electrodes is shown in Fig. 4a. This was calculated using Eq. 1 where the transmission probability is integrated as a function of energy. The current through 8-oxoG was 2.57 larger than a single G molecule at 3 V with a bond separation of 1.2 Å. The bond separation was increased to 2.4 Å and the current at 3 V through 8-oxoG was 18.3 times larger than G. This result can be explained by the behaviour of the transmission

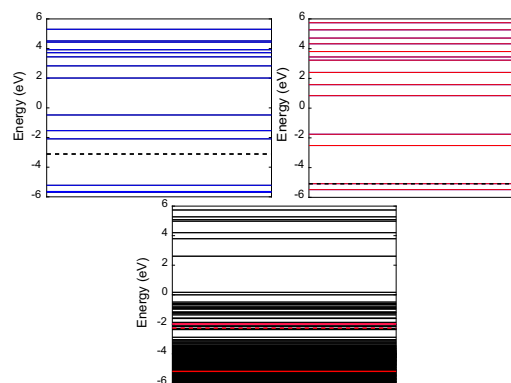


Fig. 3 Energy levels of the orbitals (*top left*) Guanine $E_f = -3.1118$ eV (*top right*) 8-oxoG $E_f = -4.99$ eV and (*bottom*) G + Electrode $E_f = -2.29$, HOMO and LUMO of G are shown in *red*, and *dashed line* indicates E_f (Color figure online)

coefficients around the energy window of the transport. Figure 4b and c shows the calculated transmission calculated from TranSIESTA for G and 8-oxoG, respectively, while varying the Au-molecule separation from 1.2 to 2.4 Å. Comparing the transmission in Fig. 4b with c, it can be seen that the HOMO–LUMO gap has moved up in energy making the transmission larger for 8-oxoG as compared to the pristine molecule in the energy window (Fermi source, Fermi drain).

These results are presented more clearly in Fig. 4d in which the current spectra are shown. As the molecule–electrode separation increases, the current through G is reduced by 97.8% and 8-oxoG is reduced by 84.24%. 8-oxoG with a separation of 2.4 Å exhibits higher current at lower voltages; this is due to the molecular orbital energies within the junction shifting with respect to the electrode Fermi level resulting in the transmission peak at 0 V in Fig. 4c, this is clearly shown in Fig. 4d which shows the current spectra at 0.1 V, the states in 8-oxoG begin to dominate at low bias voltages, this counterintuitive rise in current has been demonstrated previously [18–21] where the molecular orbitals move into resonance.

We have repeated the calculations by modifying the geometry of the electrode so that a single Au atom sits between the electrode and molecule, and we have called this new geometry pyramidal. Figure 5a shows the I–V characteristics of the pyramidal electrode compared with flat electrode. At 3 V bias the current is larger through both molecules for the flat electrode case. At low bias we observe an early onset current for the pyramid electrode case through 8-oxoG, and this can be observed in Fig. 5b which exhibits a peak in the transmission around 0 eV; the current is 57% smaller with the addition of a single Au atom in the electrode at 3 V. This effect has been observed in other studies which have attributed this decrease in current to being analogous to an increase in bond length

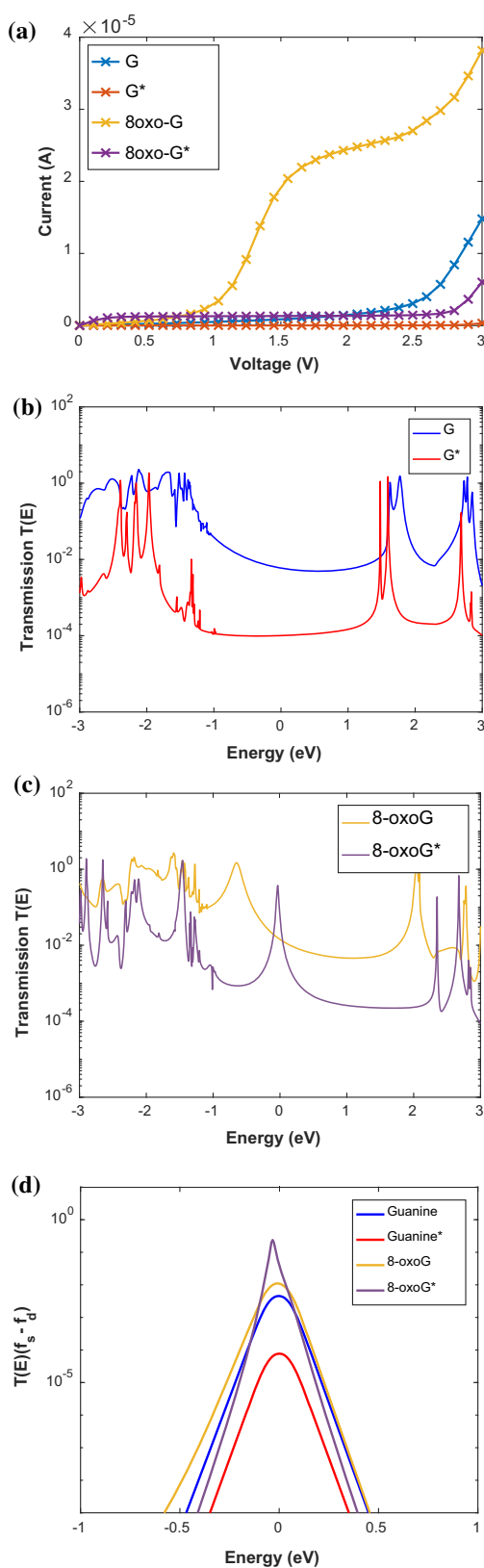


Fig. 4 **a** I–V characteristics and transmission spectra obtained from TranSIESTA, **b** Guanine and **c** 8-oxoG, **d** current spectra. Separation between molecule and contact 1.2 Å. Asterisk denotes electrode–molecule separation = 2.4 Å

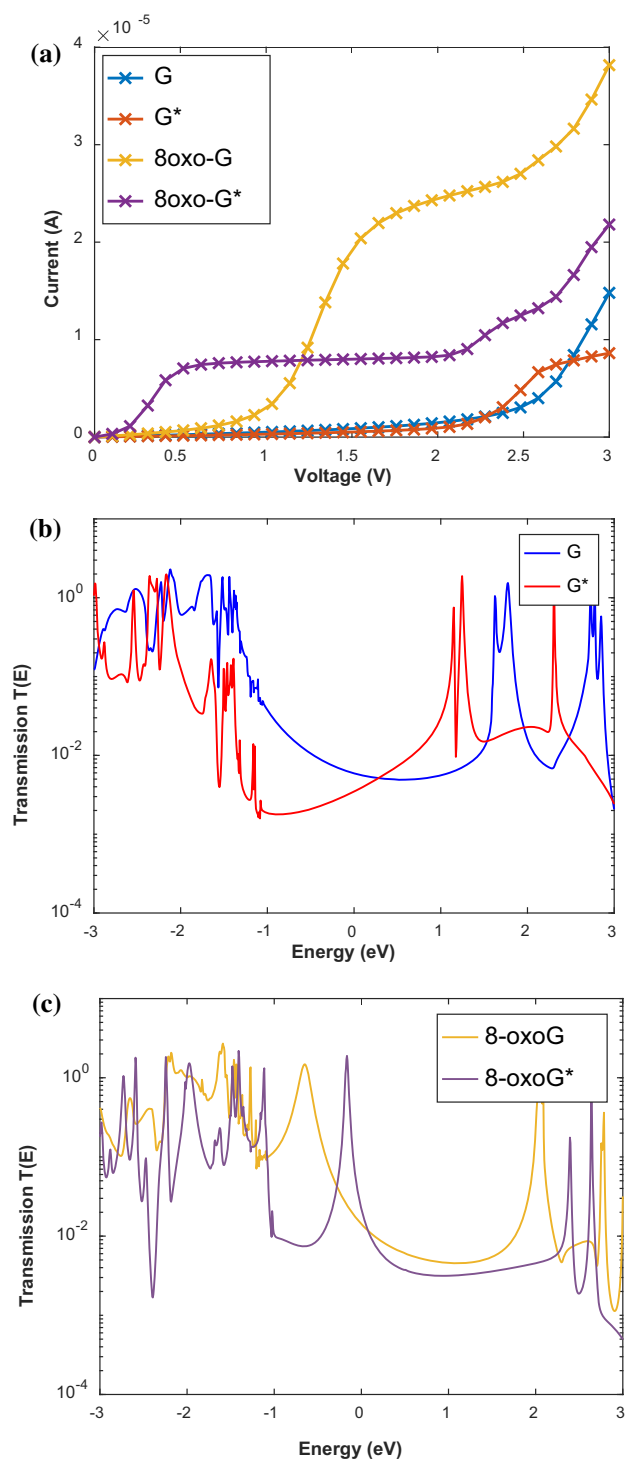


Fig. 5 **a** I–V characteristics and transmission spectra obtained from TranSIESTA, **b** Guanine and **c** 8-oxoG. Separation between molecule and contact 1.2 Å in all cases. Asterisk denotes modified geometry of electrode

due to the addition of a single Au atom at the electrode surface [13, 14].

Figure 5c shows the transmission for Guanine for the two electrode geometries mentioned previously, and the

flat(pyramid) electrode is blue(red). At low bias the flat electrode case has a slightly larger current. At a voltage of 2.2 V the window between the quasi-fermi levels is sufficiently large to introduce the peak in transmission at 1.1 eV for G*, ergo higher current occurs between 2.3 and 2.7 V. Further increases in bias introduce a peak in G transmission and the current begins to rise, at 3 V the pyramidal case current is 58% of the flat electrode case.

We also increased the bond separation of the pyramidal electrode; the current was very low as the single Au atom on the contact surface was already effectively increasing the bond length.

4 Conclusion

In this study, first principles (DFT) and non-equilibrium Green function formalism have been deployed to calculate current–voltage characteristic of a DNA base sandwiched between two gold electrodes. Guanine and its oxidized counterpart have been selected due to their excellent conductance properties. Different electrode geometries and electrode molecule separation have been investigated. The structure of the contact surface was Au(111). In general, our results show that at large bias, 8-oxoG has a substantially larger current than G. We found that the current through 8-oxoG with a pyramidal electrode was 57% smaller than with the flat electrode. Similarly, the current through G with pyramidal electrode was 58% than the flat case. This indicated that the flat electrode was more desirable to be used as a sensor. In order to explore the sensitivity of the current to the molecule electrode separation, the distance has been doubled. For the flat electrode the current through 8-oxoG is reduced by 84.24% when the separation is doubled. However, for the pristine molecule the reduction is current is larger and equal to 97.8%. The current through 8-oxoG compared to G with a flat electrode was larger for both separation distances, 2.57 times and 18.3 times at 1.2 and 2.4 Å, respectively. The enhancement of current due to the oxidation of G can be potentially used by the design of sensors for early cancer detection. However, this current is quite sensitive to the electrode–molecule distance, and therefore, further work should be required to study the statistical distribution of bonding distances and molecule orientation close to the electrode. In the future we plan to extend this result to investigate DNA of several base pairs in length.

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