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Stable and reproducible electronic conduction through DNA molecular junctions

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This letter presents the observation of stable and reproducible electronic conduction through double stranded (ds) DNA molecules in a nominally dry state. Stable conduction was realized by immobilizing 15 base-pair guanine:cytosine rich dsDNA within gold nanogap junctions, stabilizing the dsDNA with a polycation, and characterizing in nitrogen. In air, the current levels decrease with successive voltage scans likely due to oxidation of the guanine bases under bias. In nitrogen, reproducible current-voltage traces are observed and the current levels at specific bias points are stable with time. The stability allows comprehensive electrical studies and could enable conductance-based DNA sensors. © *2009 American Institute of Physics*. [DOI: 10.1063/1.3186056]

Electronic transport studies of biofunctionalized devices are important to biotechnology and nanoelectronics.[1,2] Prior experiments provide evidence of electronic transport through DNA molecules and show significant conduction for short double stranded (ds) DNA molecules, i.e., shorter than 40 nm in length.[3–8] Sequence-specific trends in conductance have been observed both in solution[4] and in a nominally dry state[8] and suggest a qualitative explanation for electronic transport through DNA molecules.[9] Although studies in liquid are most biologically relevant, they prohibit low temperature measurements, which would elucidate the transport mechanisms, and may include contributions due to ions in solution. Quantitative studies of conductivity of DNA in a relatively dry state and the effect of environment during electrical measurements would provide information for the development of DNA based devices compatible with conventional electronics and could provide label-free sensing approaches with direct electrical readout.

Several challenges must be addressed to enable studies of electronic conduction in DNA, including engineering a suitable and stable contact structure for biomolecules, defining a chemical method to stabilize the DNA double strands in a relatively dry state without mobile counter ions, and providing a suitable environment for preventing damage to the DNA bases. Recently, techniques have been developed for fabricating nanogaps at room temperature[10] and stabilizing the DNA double strands within a nanogap using a polycation[8] (spermidine, Sp^{+3}). The resulting Au/dsDNA/Au device structure provides stable DNA junctions and allows electrical transport measurements through dsDNAs in a relatively dry state. These devices have been utilized to study sequence-specific conductance in series of 15 base-pair (bp) dsDNA.[8]

In this work, we demonstrate a procedure for observing reproducible electronic conduction through short (≈5 nm) dsDNAs in a relatively dry state, utilizing nanogap junctions,[8] and polycation stabilization. Stable and reproducible current-voltage (*I-V*) characteristics were recorded through the DNA junctions functionalized with 15 bp G:C-rich dsDNA strands, when measured under N_2-environment, in contrast to decreasing in conductance with successive voltage scans under ambient. The latter is believed to be due to the oxidation of G-bases. N_2-atmosphere prevents this oxidation, protects the DNA double strands from degradation, and ensures reproducible electrical conduction. At constant voltages, steady current levels over time were observed through the junctions.

Molecular scale gaps between Au contacts were formed by room temperature electromigration breaking of Au microwires evaporated on oxidized silicon substrates coated with an adhesion layer of (three-mercaptopropyl)trimethoxysilane, procured from Aldrich and Co., USA. Detailed experimental procedures for Au layer deposition[11] and nanogap formation and characterization[10] have been described previously. Figure 1(a) shows a confocal microscope, LEXT (Olympus, USA), image of a nanogap

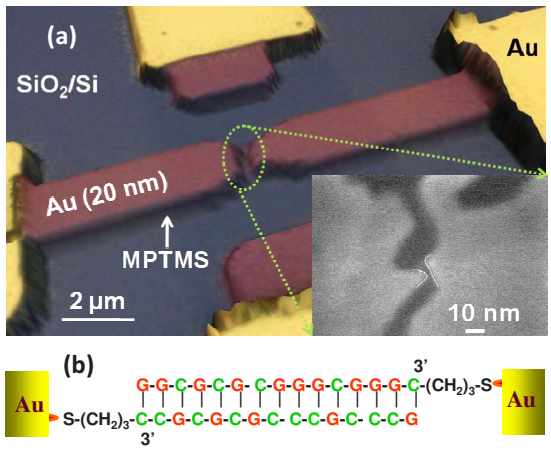

FIG. 1. (Color online) Optical image of a nanogap break junction using a confocal microscope, LEXT (Olympus, USA). Inset shows the FESEM image of a representative nanogap formed through electromigration induced break junction at room temperature that shows a sub-5-nm gap length over 5–10 nm width at the junction region. (b) Schematic of the *M*/dsDNA/*M* structures of the dithiol derivatized dsDNA used in the current work.

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junction. A field emission scanning electron microscope (FESEM) image of a representative nanogap with a sub-~5-nm gap length is shown in the inset of Fig. 1(a). Compared to electromigration techniques employing metallic adhesion layers[6,7] or free-standing structures,[3] the current procedure provides sub-5-nm gaps with a high yield (~25% for gap length of 1–2 nm and >40% for gap length of ~5 nm, as estimated from conductance values) eliminates leakage conduction paths through the adhesion layers and minimizes the possibility of inherent cantilever effects. This technique provides a stable contact structure for localizing organic/biomolecules and allows electrical measurements through single/few molecular entities[8,10,12] at room temperature.

The 15 bp G:C rich single-stranded oligonucleotides, thiolated at their $-3'$ ends with $-(CH_2)_3-SH$ spacers [Fig. 1(b)], were procured from Integrated DNA Technology (Coralville, IA) and were high-pressure liquid chromatography (HPLC) purified and matrix assisted laser desorption/ionization (MALDI) analyzed. All the chemicals (K_2HPO_4, KH_2PO_4, NaCl, ethanol, and spermidine) used in this study were at least American Chemical Society (ACS) grade (Sigma-Aldrich, St. Louis, MO), and the water was prepared with a Millipore ultraviolet-ozone (UVO) purification system (Bedford, MA). The thermodynamically stable dsDNA strand shown in Fig. 1(b) was prepared from fully complementary single-stranded DNAs in a phosphate buffer solution (PBS) and immobilized between isolated pairs of gold (Au) nanoelectrodes. Finally, the devices were exposed to spermidine in PBS solution. The samples were rinsed with water, which was then replaced slowly with ethanol to ensure stable hybridization. The samples were dried by blowing nitrogen (N_2) prior to electrical characterization. Figure 1(b) presents the schematic of the test device consisting of the G:C rich dsDNA molecule within the nanogap. *I-V* measurements through the Au/dsDNA/Au junctions were carried out using a Keithley semiconductor analyzer connected to a microprobe station (MMR Technology, USA), with the chamber at ambient or N_2 purged.

The various binding forces stabilizing the DNA double helix include radial base-base interaction through hydrogen bonding between the base pairs [a binding energy (BE) as high as 16 kcal/mole for G:C pairs and 14 kcal/mol for A:T pairs with a variation of ±5 kcal/mol depending on the hydrogen interaction to the protein residues],[13] stacking interactions through bonding between successive base pairs (BE ranges from −14.6 kcal/mol for G:C pairs to −3.8 kcal/mole for A:T pairs),[14] and the contributions from the sugar-phosphate conformation (negligible compared to the above forces).[15] These binding forces are opposed by electrostatic repulsive forces between negatively charged phosphate groups (one charge per sugar-phosphate link) along the backbones. In equilibrium, counterions are required to stabilize the double helix by neutralizing the negative backbone charges and weakening the repulsive forces. An increase in salt concentration reduces the magnitude of the strand-strand electrostatic repulsive energy (a factor of ~2 going from 1 to 10 mM).[15,16] In a nominally dry state the absence of counter ions increases the repulsive forces, enhancing the probability of denaturing the strands. A simple calculation for repulsive force between two charges without local screening [$F_R = q^2/(\varepsilon_0 \varepsilon_r d)$, where "$q$" is the electronic charge, "ε_0" and "ε_r" are the permittivity of free space and dielectric constant of the medium, and "d" is the distance between the charges] indicates that the repulsive force between strands within a dsDNA ($d \sim 2$ nm and $\varepsilon_r = 2$ for organic molecule) is ~4.5 eV/base-pair (~110 Kcal/mol). The current technique exposes the DNA functionalized junctions to the polycation spermidine (Sp^{+3}) solution before drying. The excess positive charges of Sp^{+3} molecules bind with the negative backbone charges, reducing the electrostatic repulsion and preventing denaturing of the dsDNA strands.

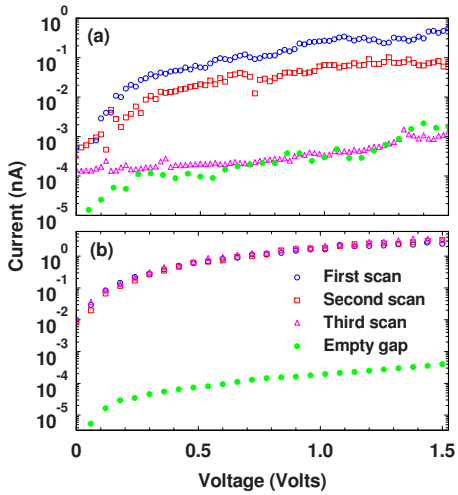

FIG. 2. (Color online) Successive *I-V* scans through a 15 bp GC-rich dsDNA functionalized Au/dsDNA/Au molecular junction. (a) At ambient, the conduction level decreases with successive scans and finally falls to the empty-gap current. (b) In N_2-atmosphere, successive scans shows reproducible conduction levels through the dsDNA molecular junctions.

The current levels of the "empty" nanogaps were measured before DNA immobilization. In both ambient and N_2 atmospheres, a $\sim 10^2-10^4$ increase in current level is observed through a given nanogap after DNA immobilization. This increase in conductivity is observed through the junctions with gap dimensions (determined by FESEM imaging) comparable to the dsDNA length of ~5.4 nm but not in devices with longer gaps, indicating that the increase in conductance was due to dsDNA molecules bridging the nanogap. Junctions with 8–10 nm gaps do not show increases in conductivity following DNA functionalization, indicating negligible contributions due to ionic conduction through residual salt (counterion effect) or Na^+-ions. This suggests successful bridging of the dsDNA molecules in the nanogaps and conduction via electronic processes in the respective DNA double strands.

Figure 2(a) shows the measured *I-V* characteristics of a representative Au/dsDNA/Au junction [as sketched in Fig. 1(b)] at ambient along with the empty-gap current of the same device. For the Au/dsDNA/Au junction, curves are presented for the first three consecutive measurements. The current level drops in successive scans and reaches a level comparable to that of the empty-gap current by the third scan. Comparable current degradation was also observed in junctions containing various other 15 base-pair strands[8] when measured over this voltage range, although current degradation was not noticeable for junctions scanned within the bias voltage of 0.3V. To understand the effect of atmosphere on the degradation of DNA conductivity, the same measurements were performed in a N_2 environment. Figure 2(b) shows the first three *I-V* measurement scans for a represen-

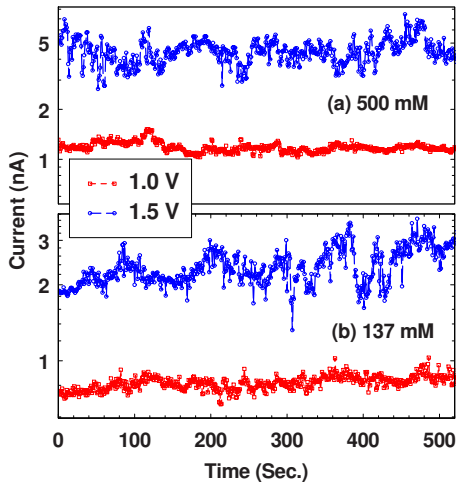

FIG. 3. (Color online) Current as a function of time through Au/dsDNA/Au junctions at 1.0 and 1.5 V when experiments are performed in N_2-atmosphere. Reproducible and stable electronic conduction through the junctions formed at salt concentrations of (a) 500 and (b) 137 mM for DNA immobilization.

tative Au/dsDNA/Au junction in N_2-atmosphere along with the empty-gap current for the same junction. In this case, the successive scans show stable current levels throughout the voltage range.

In ambient, possible explanations for the drop in current levels with successive voltage scans include (i) degradation of the device structure, e.g., due to high electric fields, (ii) degradation of the S–Au contacts, (iii) denaturing of the DNA double strand by oxidative damage of the hydrogen bonding between the purin-pyridine base pairs, or (iv) oxidation of G-sites. Since stable measurements are observed in N_2 and since Au does not readily oxidize, degradation of the Au electrodes is not expected to be significant. Thiol–Au bonding has been utilized in molecular-electronic devices, and significantly larger currents per molecule have been observed without significant degradation.[17,18] Therefore, it is unlikely that the S–Au bond is rapidly degrading. The spermidine is thought to form a shielding layer over the DNA backbone, protecting the helical structure from humidity and counterion effects as well as electrostatically stabilizing the dsDNA. DNA junctions formed without spermidine do not show enhanced conductance compared to the respective empty gaps, under either ambient or N_2, presumably due to the relative instability of the double strand in the absence of polycation stabilization. Since the G-site is the most easily oxidized among the four DNA bases, as demonstrated in electron transfer experiments,[19,20] the dominant degradation mechanism is believed to be oxidation of the G-sites. Under bias, local Joule heating occurs within the DNA strand, which enhances the probability of the oxidation process and associated degradation of conductance. While comparable self-heating likely occurs in N_2, the absence of oxygen results in less oxidization.

To better understand the time-dependent properties of the spermidine-stabilized Au/dsDNA/Au junctions in N_2, the current was measured versus time for specific voltage biases, as shown in Fig. 3. Figures 3(a) and 3(b) depict representative devices in which the DNA was immobilized in PBS with salt (NaCl) concentrations of 500 or 137 mM, respectively. In \ the observation of consistent current levels over a 500 s time interval indicates the relative stability of the dsDNA junction. Fluctuations in the current level with time are observed, which are more pronounced at $V=1.5$ V than at $V=1.0$ V. The increase at higher driving voltage may arise due to the local heating through the DNA junctions or unstable S–Au contact at higher current density. The conductance of DNA junctions decreases at elevated temperatures,[7] which has been attributed to denaturing of the dsDNA stands. Therefore, it is likely that local heating effects are responsible for the observed current fluctuations. This supports the hypothesis of reduced G-sites oxidation in N_2. FESEM images of these two junctions show that the regions with a gap distance of ≤ 5 nm extend over widths (W) of 25 and 35 nm for the samples prepared with 137 and 500 mM salt concentrations, respectively. The nearly twofold difference in current is attributed primarily to the $\sim 80\%$ increase in DNA surface coverage for the 500 mM concentration compared to that for 137 mM, as measured using a fluorescence technique, and the associated larger average number of molecules bridging the gap.[8] Since the backbone charges are screened more effectively by the higher ion concentration, the increased coverage is attributed to reduced electrostatic repulsion.

In conclusion, stable and reproducible electronic conduction through double strands of dithiol derivatized DNA has been measured in nanogap junctions. The use of polycation stabilization and N_2 ambient provides a suitable condition for achieving stable electronic properties in a nominally dry state. Successive voltage scans show decreases in current level with successive measurements in ambient, which is attributed to oxidative damage of the G-sites. Measurements in N_2-atmosphere yield stable and repeatable current characteristics, which are of interest for studies of conduction mechanisms as well as for dsDNA-based biosensors.

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