Charge sensing using point-functionalized carbon-nanotube transistors for single-molecule detection

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***Abstract*—We have demonstrated that carbon-nanotube field-effect transistors act as highly sensitive single-molecule detectors when point functionalized. The hybridization kinetics of two complementary strands of DNA are associated with two-level fluctuations in the conductance of the nanotube to which the DNA is bound. We have studied the temperature dependence of the nanotube conductance and shown that the transport mechanism is consistent with Frenkel Poole emission, in which negatively charged DNA modulates a tunnel barrier at the point functionalized defect site. These transistors represent an important potential sensing platform for label-free single-molecule diagnostics.**

Keywords - carbon nanotube sensor, single-molecule electronic detection

I. INTRODUCTION

Single-molecule techniques have become an important tool for studying biomolecular systems *in vivo* and *in vitro*. Single-molecule measurements probe microscopic behavior of folding, assembly and dynamics, which are not possible with ensemble measurements. Single-molecule sensors represent the ultimate limit of sensitivity and eliminate the need for amplification in many assay protocols. Most single-molecule techniques are based on fluorescence detection [1], requiring labeling of the molecules in question. Noise-limited detection bandwidths are limited by the relatively long time required to integrate collected photons in CCD or CMOS imaging detectors.

Nanoscale transistors in electronics applications are approaching single-molecule dimensions. In particular, transistors based on carbon nanotubes are an important emerging technology [2]. Carbon nanotube devices offer the possibility of covalently binding molecules directly to the device channel [3]. In this work, we explore the use of carbon nanotubes to create an electronic sensing platform for single-molecule detection. In particular, a point defect in the nanotube device is created by electrochemical oxidation. This defect controls electronic transport and is extremely sensitive to local charge densitiy. We show that a simple Frenkel-Poole emission model describes this transport behavior. In our case, probe DNA is covalently attached to the defect, and the binding of complementary DNA target molecules results in two-level fluctuations in the tube conductance. These transistors represent an important potential sensing platform for label-free single-molecule diagnostics.

II. CARBON NANOTUBE CHARGE-SENSING DEVICE

Chemical vapor deposition is used to grow carbon nanotubes approximately 1.4 nm in diameter on silicon wafers with a thin 300 nm grown silicon oxide layer. Photolithography is used to pattern titanium electrodes on top of the grown nanotubes to make source and drain contacts separated by about 2.5µm. Another fabrication step is used to make an on-chip platinum electrode, after which the chip is wire-bonded and assembled in a microfluidic setup using a polydimethylsiloxane (PDMS) mold as shown in Fig. 1.

In order to create the point defect in the carbon nanotube, we use a conductance-controlled electrochemical etching of the tube in 1 M sulfuric acid using the on-chip platinum electrode, followed by a 45 s exposure to 6.5 mM potassium permanganate to create a defect with a carboxylic acid functional group [3]. A typical conductance-based oxidation of the carbon nanotube is shown in Fig. 2. As the electrolytic gate voltage applied to the platinum electrode is changed below a threshold voltage (around -1V), the conductance shows a very slow decrease, followed by an abrupt jump. A Labview program detects this jump and immediately ramps up the platinum voltage in order to avoid further oxidation. While holding the potential constant, the device is now immersed in 6.5 mM potassium permanganate to create the carboxylic acid functional group.

In order to characterize the location of the defect, scanning gate microscopy (SGM) is used, which uses the biased tip of an atomic force microscope as a very localized gate. Fig. 3a shows an SGM image overlaid with a topography image of a pristine semiconducting nanotube device. The Schottky barriers at the

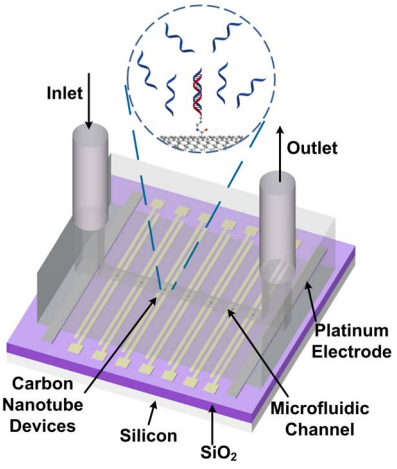

Figure 1. Microfluidic setup on top of carbon nanotube devices

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contacts (darker areas) can clearly be seen when the tip is biased with a -5 V bias. With the presence of a point defect, the sensitivity is then localized to a very small region around the center of the nanotube (Fig 3b). We further confirm this localization by a coupling reaction with gold-labeled streptavidin; a gold nanoparticle can be found around the region of highest sensitivity, indicating that the defect is both localized and chemically reactive (Fig 3c).

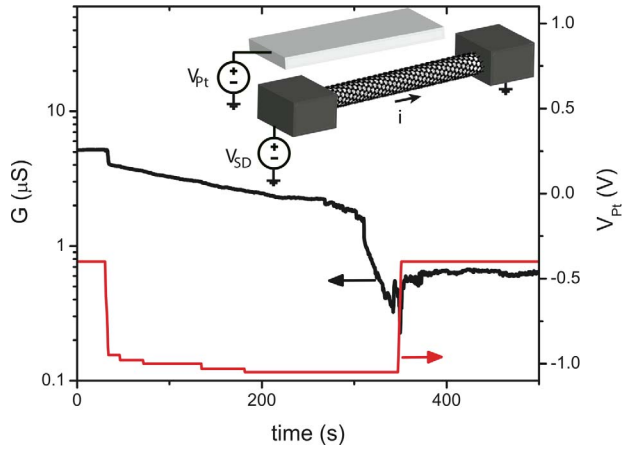

Figure 2. Conductance controlled real time oxidation of carbon nanotube

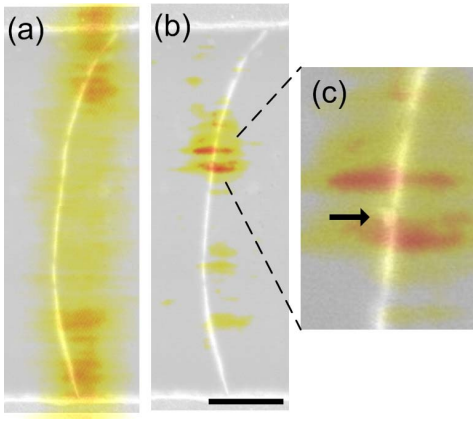

Figure 3. Combined SEM/SGM image before (a), after oxidation (b) and after coupling (c). Scale bar is 500nm.

III. DNA HYBRIDIZATION DYNAMICS

A 10-mer DNA probe with an amine group at the 5' end (NH_2-5'-GTGAGTTGTT-3') is attached to the freshly created defect in the nanotube by a standard amine to carboxylic acid coupling reaction assisted by 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) and sulpho-N-hydroxysuccinimide (sulpho-NHS). After thoroughly rinsing the device with deionized water, the conductance is monitored in phosphate buffered saline buffer (1X PBS). No particular features in the conductance are observed and the device is dominated by flicker (1/f) noise as shown in Fig. 4a. The histogram of the conductance is fit to a single Gaussian shown in Fig. 4b.

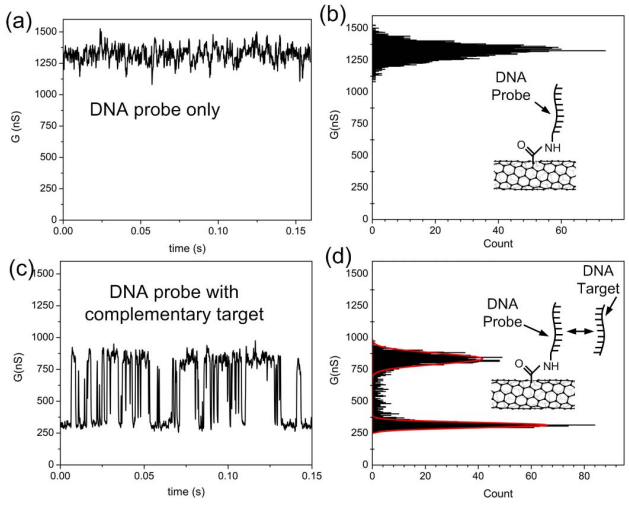

Figure 4. Real time conductance data of probe only (a) and with complementary target DNA (c) and conductance histograms (b,d)

After exposure to 1 μM complementary DNA concentration at 28°C, the device shows two-level fluctuations as shown in Fig. 4c, which can also be clearly seen in the corresponding histogram in Fig. 4d. We have carefully analyzed the kinetics [4] and have developed a model in which the low-conductance state represents a device with DNA in the duplex form and the high-conductance state with only DNA probe attached.

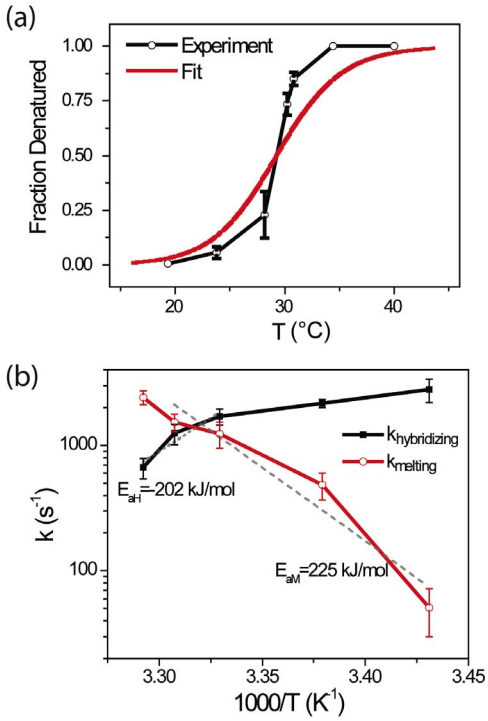

Figure 5. (a) Melting Curve and (b) Arrhenius plot

In addition to the two-level fluctuations, there is a small decrease in the overall conductance level with the addition of

target DNA, which we attribute to non-specific adsorption to the sidewall of the nanotube.

From this model, we can now extract the DNA melting curve (Fig 5a) by taking the ratio of the areas under the Gaussian fits to the histograms in Fig. 4d. The melting point measured with the nanotube conductance on a single DNA molecule is slightly lower (29.4°C) than the measurements in solution by UV-Vis spectroscopy (36.2°C not shown here). However, this observation is not unusual for surface-based hybridization and has also been observed for DNA linked to gold nanoparticles [5]. The fit uses the Langmuir isotherm $K=\alpha/(1-\alpha)C$ where C is the concentration of target DNA together with the thermodynamic relationship $-RT\ln(K)=\Delta H°-T\Delta S°$. We have also extracted the kinetics of both the high and low states, shown in the Arrhenius plot in Fig. 5b.

IV. Carbon Nanotube Transport Model

These studies have shown that transport in the carbon nanotube is very sensitive to the defect generated in the oxidation step as well as to local charge density in the vicinity of this defect. The exact nature of this defect-determined transport is unclear. In order to investigate this further, we have performed temperature-dependent transport studies both in a pristine and functionalized nanotube device in a vacuum cryostat after biological measurements.

Fig. 6 shows current-voltage (I-V) characteristics of a pristine device (Fig. 6a), which was exposed to both sulfuric acid and potassium permanganate without performing electrochemical oxidation compared to a point functionalized device with attached DNA probe (Fig. 6b) at different temperatures. The pristine device shows current saturation and the current decreases at higher temperatures. In contrast, the functionalized device shows a very different behavior. The high bias current is smaller by about a factor of 20 and the I-Vs are concave up, indicating the presence of a barrier. Also, the current increases with temperature.

The temperature dependence of point functionalized carbon nanotubes has been studied previously [6]. The best fit is found using the Frenkel-Poole emission model in which the current is given by

$$I = AV\exp^{\frac{q}{kT}\left(a\sqrt{V}-\Phi_B\right)} \quad (1)$$

where A and a are positive constants, q is the electron charge, k is the Boltzmann constant, T is temperature, V is the voltage and Φ_B is the barrier height. The I-V in Fig. 6b has been normalized and plotted in Fig. 7a. All waveforms exhibit the same slope and roughly the same values of the barrier heights. As the temperature is increased, there seems to be a slight increase in the barrier height. The height of the barrier is around 30 meV as shown in Fig. 7b.

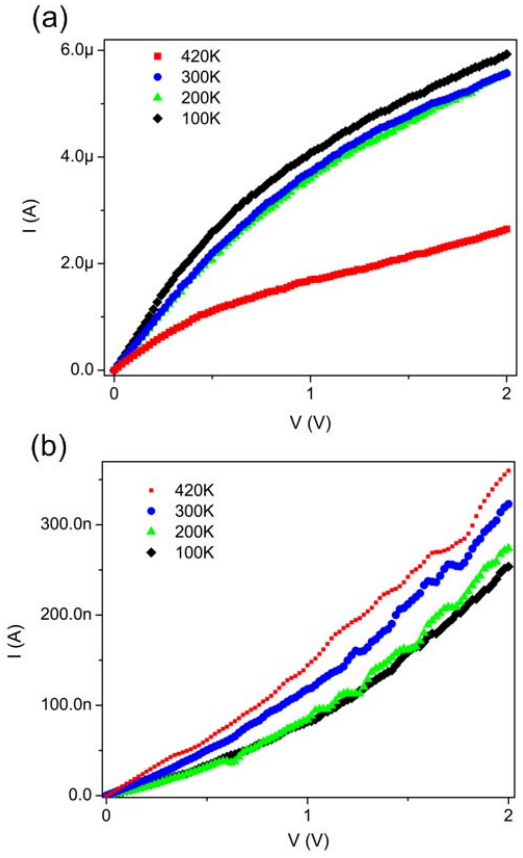

Figure 6. I-V curve for prisine device (a) and DNA probe point functionalized device (b)

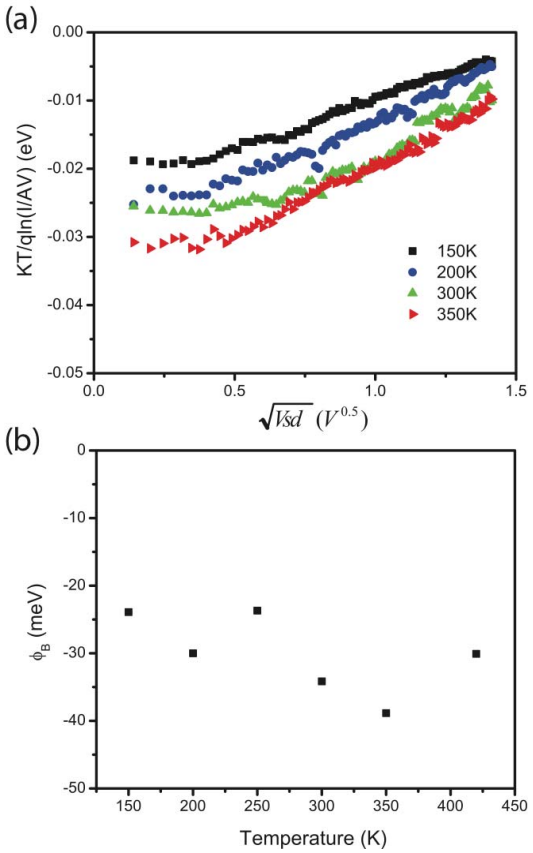

Figure 7. (a) Normalized current vs square root of voltage and (b) extracted barrier heights

In Frenkel-Poole emission, electrons in the conduction band are trapped in a localized state and then released by thermal excitation. The barrier height is the depth of the potential well. [7]. Recent theoretical calculations have predicted that monovalent sidewall additions to carbon nanotubes are localized to around 1.5 nm [8]. We assume that electron transport is controlled by one or a few localized states, which are introduced during the electrochemical oxidation.

From this model, we can explain the two-level fluctuations in the real time data seen in Fig. 4b. When a target DNA molecule hybridizes with the probe, local charges in the target DNA backbone are brought in close vicinity of the defect site. Due to field-effect interactions, the negative charges of the target DNA modulate the potential at the defect, therefore changing the barrier height. We have plotted the normalized resistance change of the above model as a function of barrier height change, shown in Fig. 8 and given by

$$\frac{\Delta R}{R} = \exp^{\frac{q\Delta\Phi_B}{kT}} - 1 \qquad (2)$$

Even a very small change in the potential barrier (a few meV) will cause a very large change in the conductance due to the exponential dependence on the barrier height.

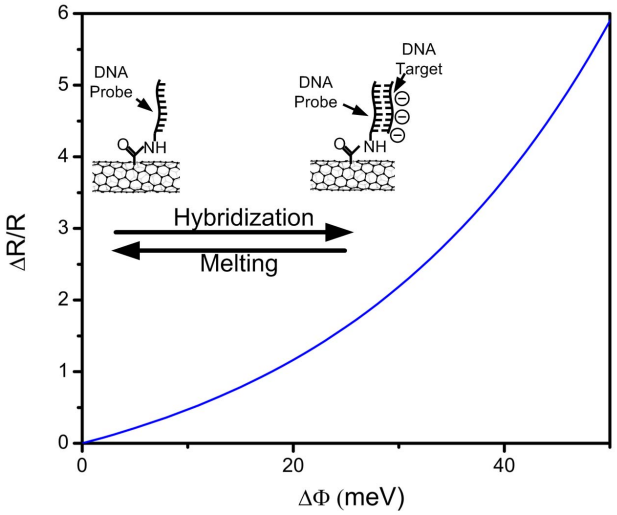

Figure 8. Proposed Model for two level fluctuations due to barrier modulation of negative charge on DNA.

Many parameters will affect how the conductance at the defect is modulated, including the size of the localized state at the defect, the ionic concentration of the buffer which can screen the negative charge, the proximity and angle of the target DNA to the defect site, the electrostatics around the DNA, and the amount of coupling of the negative charge into the nanotube defect. Also, the modulation in conductance might be caused not only from one DNA interaction, but a few molecules in close proximity. Standard microscopy techniques such as atomic force microscopy and scanning electron microscopy do not have enough spatial resolution to determine if the point functionalization results from a single carboxylate or if only a single DNA molecule attaches to the nanotube. Multiple DNA molecules could in principle be attached but this results in multi-level fluctuations. However, because the nanotube conductance is dominated by a two-level fluctuation, we believe that only a single DNA interaction dominates the conductance. Also, the Debye screening length in the buffer 1X PBS is only around 0.7 nm which makes the electrostatic interactions between the molecules and the DNA very localized, so a correlated hybridization and melting of multiple molecules at the same time is not very likely. As shown in Fig. 3c, there is only one gold particle attached to the nanotube right at the most sensitive site.

In conclusion, we have demonstrated that a carbon nanotube device has enough sensitivity to monitor the interaction of a single molecule. We have shown that by analyzing the two level fluctuations over temperature, both the melting curve and Arrhenius plots can be extracted. The electron transport through the nanotube is consistent with Frenkel-Poole emission, which can be used to explain the sensitivity in the conductance.

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