Characteristics of field-effect devices with gate oxide modification by DNA

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(Received 28 February 2005; accepted 19 July 2005; published online 31 August 2005)

Current-voltage characterization was used to investigate the behavior of silicon field-effect devices with DNA solutions of various concentrations and molecular states deposited on the gate oxide. These devices were similar to conventional transistors but without gate metal, and no surface treatments or agents were used to immobilize the DNA. With increasing micromolar concentration, significant changes were produced in the device response. The current decreased with increasing ratios of double-to-single stranded populations produced by mixing complementary sequences, and by thermal denaturing. The device characteristics were reproducible. Modeling suggested a mechanism of modifications to the device carrier density induced by variations in the electrochemical properties of the DNA located within a charge screening length of the gate oxide surface. These results showed that field-effect devices may be useful for the real time monitoring of nucleic acids, without binding agents or label tags. © 2005 American Institute of Physics.[DOI: 10.1063/1.2041826]

Since the mid-1990s, the electronic sensing of biomolecules has greatly expanded, and may be more sensitive than optical techniques. Electronic sensing that requires sample preparation by fluorescence, enzymatic, or radioactive labeling can be time consuming, expensive, and may prevent real time measurements. Label-free affinity biosensing using recognition elements immobilized onto electrode surfaces provides discrimination only for the target analyte, and measurements can be unstable due to ion motion. Non-binding detection, however, may use interactions that are nonspecific. If the electronic response can be related to differences in the analyte biomolecules, and if it is sufficiently sensitive, then real time detection without binding agents may be possible. Here, we report the behavior of field effect devices in response to different types of DNA solution on the gate oxide (SiO2) without using labels, binding agents, or immobilization, which has not been reported previously to our knowledge.

Field-effect devices are sensitive to variations in the electronic properties of the material located within a Debye charge screening length of the gate oxide surface, but does not require that the material be chemically bonded to the oxide. The parameters responsible for modulating the device electrical conductance include the work function (Fermi energy), electrostatic potential, and electric permittivity of the gate material. If variations in the concentration and molecular state of DNA solutions can affect these parameters, then it should be possible to use them to sense DNA. Field-effect sensing avoids the conduction of current through the DNA, which may produce unwanted electrochemical changes. To investigate the utility of field-effect monitoring, we fabricated devices similar to conventional transistors but without metal on the gate oxide, to allow the DNA solution to affect the gate without electrostatic shielding by the metal.

Devices were fabricated by conventional processing on p-type (100) silicon wafers to produce depletion mode devices with negative threshold voltages, as shown in Fig. 1. The devices have metallized source and drain contacts, but no gate metal. A chip containing several devices was insulated with 2-μm-thick photoresist, and patterned to leave the gate oxide exposed, with two different gate dimensions of width/length (W/L): 200 μm/200 μm and 200 μm/40 μm. Insulated metal wires (8 mm long) were used to isolate the measurement probes from the DNA solutions. Prior to measurements, the devices were rinsed with cleanroom grade de-ionized (DI) water and dried with nitrogen gas. After measurements, the I−V characteristics reproduced their original state with no hysteresis, indicating that the oxide was not poisoned by impurities such as alkali metals. All measurements were performed with the devices and DNA solutions at room temperature.

The effects of concentration were measured using sonicated salmon sperm double-stranded dsDNA of lengths between 5000 and 35 000 bases, diluted with cleanroom DI

![FIG. 1. Side view drawing of a field-effect device with DNA solution on the gate oxide, with the contacts to source and drain electrodes isolated from the DNA by polymer passivation. Inset shows a top view micrograph of a device with the central square gate with dimensions (W/L=200/200 μm).](image-url)
water to 0, 0.3, 1.02 and 1.52 μM (0, 0.2%, 0.66%, and 1% by weight). For each measurement, 0.5 μL was deposited forming a 2 mm diameter droplet that coated the gate. The radius of gyration of the DNA molecule (<1 μm), is far smaller than the gate size, so that the molecular distribution would appear continuous. During the measurement, we expected that the concentration within a droplet was statistically uniform based on the diffusivity of DNA in solution at room temperature \(D=3 \times 10^{-7} \text{ cm}^2/\text{s}\). Within 2 min of the solution deposition, the drain current \(I_{DS}\) was recorded with a linear ramped drain-source voltage \(V_{DS}\), lasting a few seconds. This measurement interval was shorter than the droplet evaporation time (over 4 min). With increasing concentration, the \(I_{DS}\) decreased monotonically by about 40 μA, as shown in Fig. 2.

For a fixed device size and drain-source bias, the charge-control equation\(^7\) with zero gate bias indicated that the decrease in \(I_{DS}\) corresponded to a positive shift in the threshold voltage \(V_T\):

\[
I_{DS} = \frac{1}{2} \mu_n C_{ox} \frac{W}{L} [-2V_T V_{DS} - V_{DS}^2],
\]

where \(\mu_n\) is the electron mobility in the conducting channel, and \(C_{ox}\) is the gate capacitance per area \((4.93 \times 10^{-9} \text{ F/cm}^2)\). In the nonsaturated current regime, curve-fitting yielded \(V_T\), as shown in Fig. 2. The threshold voltage can shift by \(\Delta V_T\) due to changes in the work function (\(\Delta \Phi_m\)), the gate charge (\(\Delta Q_{eff}\)), or the dielectric modification\(^6\) of the capacitance: \(\Delta V_T = \Delta \Phi_m - \Delta Q_{eff}/C_{ox}\). The observed \(\Delta V_T\) can be interpreted as a change in the solution \(\Delta \Phi_m\) by 180 meV, or a change in the effective value of \(C_{ox}\), or a change in \(\Delta Q_{eff} = -8.87 \times 10^{-9} \text{ C/cm}^2\). This charge density is similar to the estimate \((-2 \times 10^{-9} \text{ C/cm}^2)\) from the data of Uslu.\(^3\) Changes to all three parameters may occur simultaneously, but the relative contributions in such an interpretation will not be considered here. To simulate fluidic channel monitoring, the gate solution was not connected to an external electrode. The gate potential was expected to reach equilibrium with the local ground due to surface leakage currents, which were measured to yield a surface resistance of 40 GΩ. The effective \(RC\) time constant for gate charging was thus 0.79 s, so there was no floating potential drift during the 2 min measurement interval.

The device sensitivity can be estimated from the 180 mV threshold shift, and the effective charge density of 8.87 \(\times 10^{-9} \text{ C/cm}^2\) located within a Debye charge screening length of the gate area of \(4 \times 10^{-4} \text{ cm}^2\). Although our precise Debye length was unknown, we assumed 0.25 μm for a saline solution of equivalent concentration. For the 1.52 μM dsDNA solution with a molecular density of 9.15 \(\times 10^{15} \text{ cm}^{-2}\), the number of molecules within a Debye length above the gate was 9.15 \(\times 10^6\), yielding a charge per molecule \(3.9 \times 10^{-19} \text{ C}(2.4 \text{ electron charges})\). The minimum number of molecules detectable depends on the gate area and the voltage sensitivity. Assuming that an area of \(1 \mu \times 8 \mu\), and a sensitivity of 0.1 mV are reasonable, then a single molecule can be detected.

Since no salt was added to stabilize the double-stranded state, some ssDNA may be present (expected to be <2%). Reports suggested that the drain current of sensors increased in proportion to the salt concentration on the gate,\(^10\) whereas we observed a decrease. This opposite trend suggested that our devices were not contaminated by salt. To check the stability of our devices, after each measurement the gate region was rinsed with DI water, and the \(I-V\) characteristics were verified to reproduce their response to DI water.

A second series of experiments addressed the effects of denatured and hybridized DNA. Solutions of sonicated salmon sperm DNA (1.52 μM) with different ss/ds ratios were prepared by heating 20 μL of dsDNA solution to 95 °C, incubating for 15 min, quenching 30 s in an ice bath to begin hybridization, and then placing at room temperature. The 95 °C temperature was adequate for denaturing because the melting temperature \(T_m\) of the DNA was 82 °C, determined using optical fluorescence microscopy (ABI Prizm 7000 Sequence Detection System). Instantaneous \(I-V\) measurements of 0.5 μL droplets of solution were made at delays of 1, 10, 20 mi, and 15 h after placing the solution at room temperature. Over time, the drain current decreased by about 1 mA, as shown in Fig. 3, which was attributed to the time-dependent hybridization toward predominantly dsDNA. As a reference, dsDNA was measured prior to incubation. The field-effect transistor was measured on a large metal heat sink with a temperature of 300 K. The thermal response time of the droplet was estimated to be 7 ms, based on the heat capacity and thermal conductivity of saline solution. Therefore we consider the measurements to be isothermal at room temperature, and attributed the observed time dependence to the molecular changes. As shown in Fig. 3, as the population tended toward dsDNA, the threshold voltage increased by 830 mV, corresponding to a decrease in charge density by \(4.1 \times 10^{-8} \text{ C/cm}^2\). It can be interpreted that dsDNA is more negatively charged than ss for reasons that are unclear, but we speculate that it may be due to differences in the density of charge sites, or the chemical potential (Fermi energy), or the permittivity. Assuming a first order time dependence of \(V_T\), the \(e^{-1}\) time constant for the hybridization was 6 min, which was shorter than that reported by Souteyrand (60 min)\(^1\) (Ref. 1) and Uslu (20 min),\(^3\) who used different types and lengths than the heterogeneous oligonucleotides used here.
The intrinsic response time for the transistor was 10 ns, from the channel transit time and the product of channel resistance with gate capacitance, the transistor is adequate for real time measurements.

A third series of experiments was performed to determine if the devices can differentiate solutions of ss from ds populations. Equal moles of synthetic complementary oligonucleotides (60 bases long, 19.75 μM) were mixed in a 40 μL volume to begin hybridization. Real time fluorescence indicated that below the \( T_m \) (≈82 °C), the equally mixed population was ds, and it transitioned to ss above this temperature. Upon mixing at a permissive temperature, the two ss populations self-assemble to a new population state based on the stoichiometry. In a series of “time lapsed” measurements, 0.5 μL volumes were deposited at: 2, 8, 15, 25, and 45 min after mixing. At each interval, the \( I-V \) characteristics were measured. As shown in Fig. 4, after 45 min, the drain current decreased by 300 μA, and \( V_T \) increased by 210 mV, which can be interpreted as a gate charge density that is more negative by \( 1 \times 10^{-8} \text{ C/cm}^2 \) for dsDNA compared to ssDNA, in agreement with the previous trend.

The extracted time constant for hybridization was 17 min, in reasonable agreement with previous reports of tens of minutes.\(^1\)\(^3\) The intrinsic response time for the transistor was \( \sim 10 \text{ ns} \), from the channel transit time and the product of channel resistance with gate capacitance, the transistor is adequate for real time measurements.

Properly designed oxide gate field-effect devices have detected changes to DNA concentrations and molecular states in solution and may be useful for monitoring nucleic acids in real time applications. The mechanism is attributed to changes in the device carrier density, induced by the DNA work function, charge density, and dielectric permittivity.

The authors are grateful to P. Lv, S. Ray, R. T. Troeger, and T. N. Adam for helpful assistance and discussions, and to G. Church, E. C. Cox, K. Goossen, E. Kohn, R. Opila, and R. Rogers for useful comments. This research work was supported by the NSF under Award No. ECS-0129535.