Selective Heating Characterization of Nanoplate Devices for Sensing Applications

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Abstract

Semiconductor based field effect sensing of biomolecules has been shown to be a promising technology for biomedical diagnostics applications [1],[2],[3]. However, current devices can not be fabricated in large quantities, devices can not be functionalized individually, and sensors are prone to false positives due to non-specific binding of analytes. We demonstrate the fabrication of silicon field effect devices utilizing conventional microfabrication techniques, which is amenable for large scale fabrication and integration with existing platforms. More importantly, we demonstrate heating of individual devices as a part of a technique for individual functionalization of devices in a dense array. Our results illuminate the feasibility of using heating in order to individually functionalize nanosensors integrated in a dense array, as well as the possibility of filtering out non-specifically bound species by exploiting the differences in the temperature dependent binding kinetics of the analyte molecules.

Keywords: biosensor, selective functionalization, temperature characterization

1 Introduction

Semiconductor based field effect sensing of biomolecules has been shown to be a promising technology for biomedical diagnostics applications. Specifically, nanowire sensors have been implemented as excellent diagnostic tools via their label-free detection of relevant biomolecules down to significantly lower concentrations than what has been achieved with current clinical techniques [1].

However several issues still need to be addressed before such sensors can take their rightful place as powerful and effective diagnostic tools. We present novel solutions to two of the most important of such issues: 1– Current devices can not be fabricated en masse, 2- Even if devices could potentially be made in large and dense arrays, they can not be functionalized individually, and 3- Devices are prone to false positives due to non-specific binding. Our work presented here addresses these issues. We demonstrate fabrication of silicon field effect devices utilizing conventional microfabrication techniques, which is amenable for large scale fabrication and integration with existing platforms. Further, we propose a novel scheme for the individual functionalization of our nanoplate field effect devices via selective resistive heating, with which further characterization will result in dense arrays of devices capable of ultra-sensitive detection of several biomolecular species simultaneously in real time with increased specificity.

2 Device Fabrication

The fabrication of the nanoplate devices starts with a 4 inch SOI wafer, with a top silicon layer of 50 nm and buried oxide layer of 160 nm, with p-type doping. Wafers were purchased from SIMGUI electronics, Shanghai, China.

The superficial silicon was thinned down to 20 nm via dry oxidation performed at 1100°C for 30 min. Subsequently, the top oxide layer was etched using buffered hydrofluoric acid (BHF), and the resulting silicon thickness was measured and verified using an ellipsometer. The silicon active area was defined by lithography, and the silicon in the field area was dry etched with SF_6 plasma. Contacts to the active area were defined by liftoff; an adhesion layer of 200 Å titanium underneath a 1800 Å platinum was used. A rapid thermal anneal(RTA) was performed at 600°C for 60 sec in order to improve the quality of the metal contact to the silicon. A silicon dioxide layer was deposited with a plasma enhanced chemical vapor deposition (PECVD) system as a metal passivation layer in order to minimize the parasitic conductance through the fluidic environment. Oxide on the pad areas was etched, and a thick layer of metal (2000 Å titanium and 8000Å of gold) was evaporated and defined by liftoff to form pads for wire bonding. Areas to be etched to expose the active area of the devices were defined by lithography, and the wafer was then diced into individual dies of size 4 mm by 7 mm. Individual dies were then etched using BHF to expose the active area of the devices.

3 Temperature Characterization

The individual functionalization of devices, which enables simultaneous multiple specie detection, relies on selective resistive heating of the surface of the channel via application of a voltage bias across the device. Heating an individual device allows for the partial disassoci-

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ation of previously immobilized protection molecules on the active area, enabling the attachment of a probe targeting a specific biological species. Another device can then be forced to undergo the same reaction, this time resulting in the attachment of a different probe molecule targeting a different species. This allows for the specific placement of a wide variety of probe molecules to only sites that we wish, which in turn allows for individual functionalization of the wires in a dense array. The composition of a fluid containing several of these biomolecular species at extremely low concentrations can thus be determined in real time. Our work presented herein involves characterization of the heating characteristics of such sensors in order to perform selective functionalization using such a scheme.

3.1 Experimental Procedure

Temperature sensitive liquid crystals (LC) for failure analysis have served the integrated circuit industry for many years, as liquid crystal microthermography, an inexpensive alternative for chip failure analysis. It has been traditionally used for detection of "hot spots" on the chip to indicate problematic sites of excessive heating [4].

LCs retain their crystalline optical characteristics when in liquid phase, and will change the polarization of an incoming light source when in the nematic phase (below the clearing point). Heating the LC above the clearing point will result in a phase transformation into the isotropic phase, which results in the loss of the liquid crystals' optical properties.

When a polarized light is incident on a surface coated with a liquid crystal, the incoming polarization of the light will be lost since the coating will "twist" the polarization. However, when the coating is in its nematic phase (above the clearing temperature) incident light polarization will be preserved. Hence when the surface is observed through a polarizer that is orthogonal to the incident light, the surface will appear to be dark above the clearing point of the LC, and colorful below the clearing temperature of the coating. The temperature attained on the surface of the devices can thus be characterized as a function of the power input to the devices by using temperature sensitive nematic phase liquid crystals (purchased from Accelerated Analysis).

Heating devices by applying a current through the active area was investigated. Power is dissipated through the voltage drop across the active area, resulting in an increase in the surface temperature. Many experiments were run in order to correlate the power dissipation with the surface temperature of the devices.

Experiments were performed on released devices, which were solvent cleaned (Acetone and Methanol) prior to the application of temperature sensitive liquid crystal (LC). Liquid crystals of various clearing temperatures were applied on the device for each individual experiment using a fine tip paint brush. The LC dissolves readily in a solvent (as purchased), and upon the application of the liquid crystal, the solvent evaporates leaving a thin layer of coating.

Device leads were contacted by using a microprobe manipulator on the source and drain sides, and the back gate (substrate) was contacted through a conductive chuck. The chip surface was imaged via a microscope to observe the change in the intensity of the liquid crystal. A 100x objective was used to image the individual devices. Images were acquired using a commercial digital still camera (Canon G5) attached to the microscope and connected to a computer via a USB cable. Remote Capture software was used to capture picture automatically at preset time intervals. A Labview program (National Instruments) on this computer was used to synchronize the capture of pictures with data readouts from the DC power supply (Agilent E3647A), the low noise current amplifier (SRS SR570), and a digital multimeter(DMM)(HP 3478A) via GPIB and RS232 protocol. The DC power supply was used to supply the source-drain and gate-source bias (with two independent outputs), and the current amplifier in conjunction with the DMM was used to measure output current through the device. The gate voltage was set to a bias to modulate conduction through the device to a reasonable level. The source-drain voltage was swept at a rate of 0.1 V per second, typically in a range of 0-40 V. MATLAB was used to plot the intensity over a section of the active area versus input power for the device.

3.2 Results

Figure 1 shows optical microscope images of a field effect nanoplate device coated with a LC with clearing point 35°C. The reflected light intensity over the channel region decreases sharply as the active area heats up, allowing the characterization of temperature on the nanoplate as a function of input power, as shown in Figure 2.

In order to quantify the surface temperature, the average intensity over the active area can be plotted as a function of the input power, as shown in 2, a representative plot of the response obtained from a device using a 35°C clearing temperature LC at an ambient temperature of 28°C. The transition power for the given temperature is determined by reading the power corresponding to the inflection point of the fitted intensity versus power curve.

Similar characterization has been completed with three different LCs of varying clearing temperatures - 29°C, 35°C, and 60°C. In some experiments, the ambient temperature was manually raised using a heater under the device. It is important to note here that for our final application, we are solely interested in the temperature

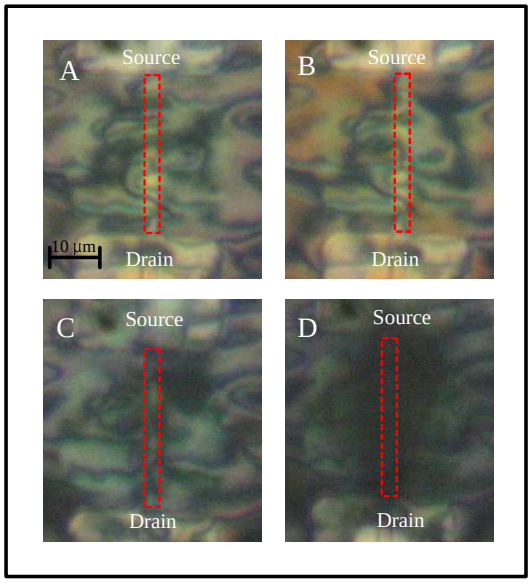

Figure 1: Images showing the nanoplate device with a coating of 35°C clearing point LC. The active area has been boxed with red dashed line for clarity. Each inset corresponds to different power levels dissipated in the nanoplate.

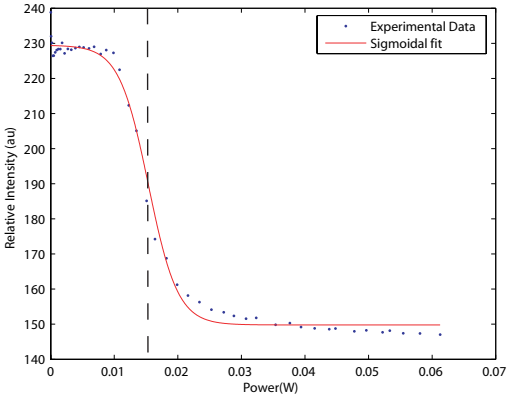

Figure 2: Normalized reflected light intensity versus input power for a device coated with a 35°C LC, experimental data shown in blue, and the sigmoidal fit with red. Transition power happens at the inflection point of the curve shown with the dashed line.

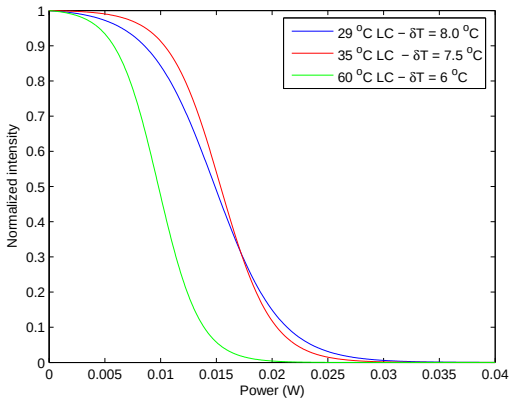

Figure 3: Normalized light intensity versus input power for the same device with different LCs at different ambient temperatures. Ambient temperature is 21.0°C for 29°C LC, 27.5°C for 35°C LC and 54°C for 60°C LC.

differential that can be achieved, not the absolute temperature.

Results obtained with the same device using three different liquid crystals at varying ambient temperatures show that temperature on the surface can be quantified with a reasonable amount of error (Figure 3). The amount of power needed to attain a certain temperature on the device surface can thus be quantified using this method. This also proves that any effect of the electric field on the liquid crystal properties is negligible as the clearing temperature is shown to be consistent.

The curve shown in 4 was obtained with different ambient temperatures from the same device (active area with width of 20 microns), in both cases coated with the 35°C LC. We can see from this figure that a temperature differential of 14°C is easily achievable with our devices. Initial experiments with functionalization schemes of interest have shown this to be more than adequate to perform the exchange reactions necessary to individually functionalize several devices.

Apart from the selective functionalization of individual sensor elements in an array, another great challenge in electrical detection of bio-molecules is the successful differentiation between the charge states of mismatched genomes, because two genomes of the same length have essentially the same integrated charge. Hence techniques which can filter out non-specific binding are essential for electrical detection schemes. One way of accomplishing this is by exploiting the difference in the melting temperatures of such sequences.

Figure 5 indicates the change in melting temperature (T_M) of a short DNA sequence as a function of mismatch location [5],[6]. A small ΔT_M for some base-pair mismatches indicates the possibility of non-specific binding

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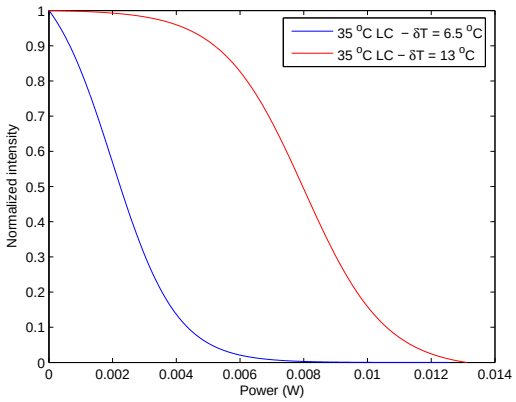

Figure 4: Relative intensity versus input power for devices coated with a 35°C LC at different ambient temperatures, for a device with 2 micron width. Temperature differentials of 6.5°C and 13°C are shown.

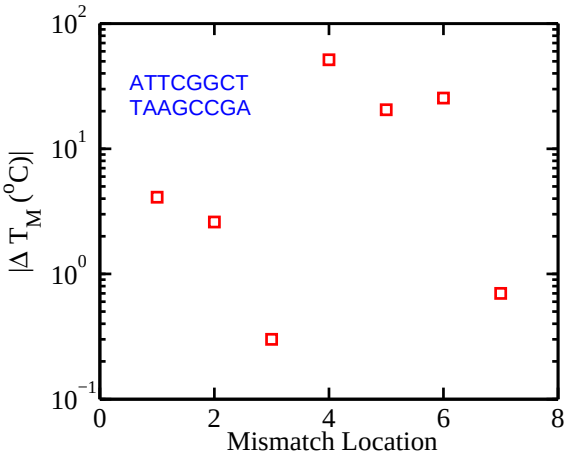

Figure 5: Change in melting temperature (T_M) as a function of the location of mismatch for DNA sequence. A perfect match sequence has a T_M of approximately 20°C

in a nano-sensor array. As such, one must depend on the weakness of the binding energy of the conjugation to distill the array of parasitic/non-specific binding. Figure 5 indicates that many parasitic bindings can be filtered out if the temperature profile around the binding site can be accurately controlled. Our results indicate that selective heating of nanoplate devices can be used to achieve accurate control of temperature profile of individual sensor elements. This capability is extremely useful in filtering out such non-specific target-receptor bindings and thus is a crucial element in enabling highly selective, real time, and multiple species detection in a sensor array.

4 Conclusions

The individual functionalization of ultra-sensitive, label-free sensors is an exciting and important step towards validating these sensors as competitive tools in the future of diagnostics. In this work, we have presented the first steps towards the specific functionalization of individual devices. We have shown, employing the novel technique of temperature sensitive liquid crystals, that with resistive heating of our currently fabricated nanoplate devices, we can easily achieve a temperature differential of up to 14°C. Further improvement of the fabrication process will allow for larger achievable temperature differentials.

The specific heating of these devices will allow us to perform exchange reactions at only the sites that we wish, which will allow us to specifically functionalize devise. Our top-down fabrication process will also scale very well, allowing for the seamless integration with traditional electronics. Additionally, we will be able to eliminate nonspecific binding via precise temperature control of our individual devices. The end result will be a large array of devices targeted towards the highly specific, ultra-sensitive detection of a large variety of biomolecular species.

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