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Complementary metal oxide semiconductor compatible fabrication and characterization of parylene-C covered nanofluidic channels with integrated nanoelectrodes

Chih-kuan Tung,[1] Robert Riehn,[2] and Robert H. Austin[3,a)]
[1]*Department of Physics, Hong Kong University of Science and Technology, Kowloon, Hong Kong*
[2]*Department of Physics, North Carolina State University, Raleigh, North Carolina 27695, USA*
[3]*Department of Physics, Princeton University, Princeton, New Jersey 08544, USA*

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Nanochannels offer a way to align and analyze long biopolymer molecules such as DNA with high precision at potentially single basepair resolution, especially if a means to detect biomolecules in nanochannels electronically can be developed. Integration of nanochannels with electronics will require the development of nanochannel fabrication procedures that will not damage sensitive electronics previously constructed on the device. We present here a near-room-temperature fabrication technology involving parylene-C conformal deposition that is compatible with complementary metal oxide semiconductor electronic devices and present an analysis of the initial impedance measurements of conformally parylene-C coated nanochannels with integrated gold nanoelectrodes. © *2009 American Institute of Physics.* [DOI: 10.1063/1.3212074]

No two cells are exactly alike, either in terms of their genome, the genomic epigenetic modification of the genome, or the expressed proteome.[1] The genomic heterogeneity of cells is particularly important from an evolutionary perspective since it represents the stages of evolution of a population of cells under stress.[2] Because of the important variances in the genome that occur from cell to cell, it is critical to develop genomic analysis technologies which can do single-cell and single molecule genomic analysis as an electronic "direct read" without intervening amplification steps.[3–8] In this paper, we present a technique which uses conformal coverage of nanochannels containing nanoelectrodes using a room-temperature deposition of parylene-C, a pin-hole-free, excellent electrical insulator with low autofluorescence.[9] This procedure should open the door to integration of many kinds of surface electronics with nanochannels. One of the most difficult aspects in introducing electronics into nanochannel technology is the sealing of nanochannel so that the electrodes are not compromised by harsh chemicals or high temperatures. There are various methods to form nanochannels containing nanoelectrodes, including wafer bonding techniques,[10] removal of sacrificial materials,[11] and nonuniform sputtering deposition.[12] Methods employing a sacrificial layer removal show the greater compatibility to electronic integration, but current methods to remove sacrificial materials require either high temperatures[11] or harsh chemicals.[13,14]

The basic device consisted of 12 mm long, 100 nm wide, 100 nm high nanochannels interrogated by 22 pairs of 30 nm wide gold nanoelectrodes. The outline of the fabrication process is shown in Fig. 1. The fabrication process was carried out on a standard 4 in. single-side polished *p*-type ⟨100⟩ silicon wafer with 100 nm of dry thermal oxide on the top as an insulating layer, which also helped the wetting of the nanochannels. The first step involved nanofabrication of the

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[a)] Visiting member from the Institute for Advanced Study, Hong Kong University of Science and Technology, Kowloon, Hong Kong. Electronic mail: austin@princeton.edu.

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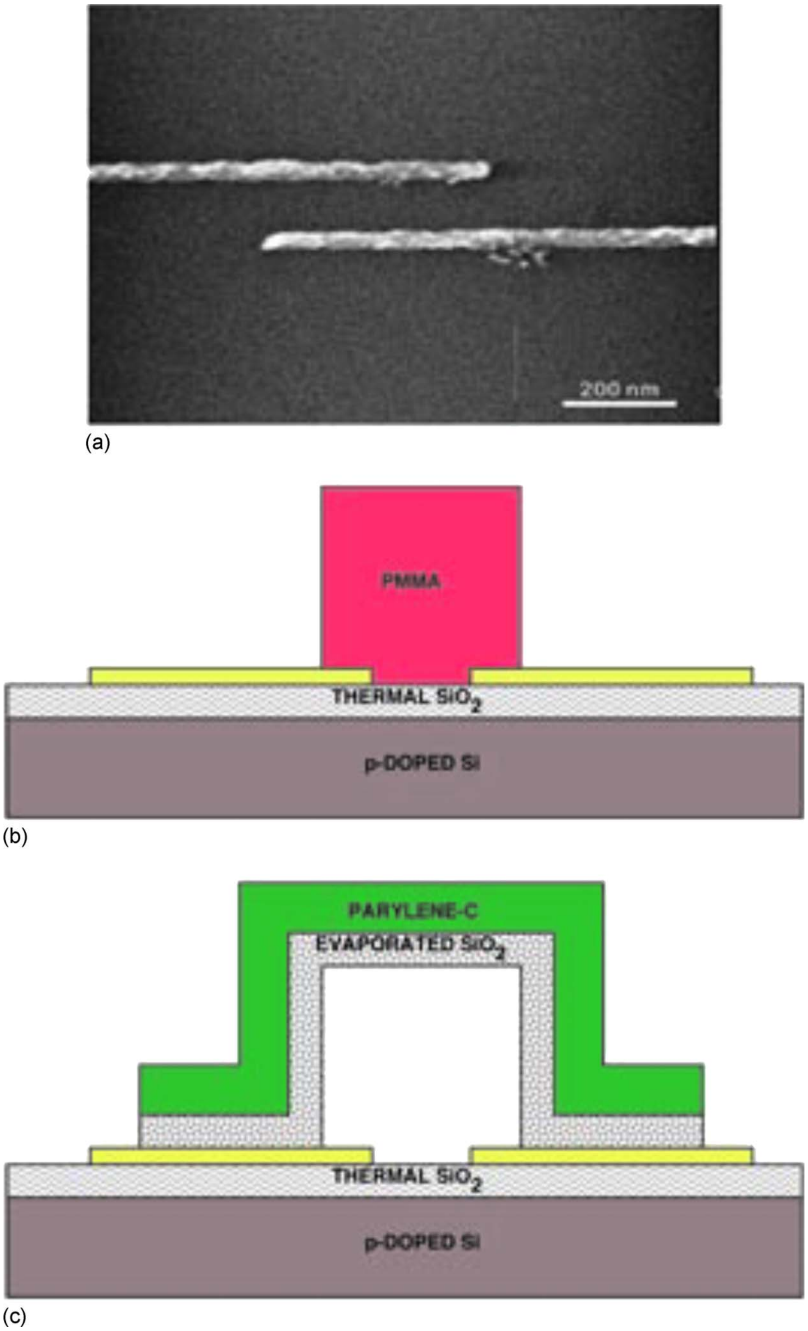

FIG. 1. (a) SEM image of gold nanoelectrodes; scale bar is 200 nm. (b) $100 \times 100\ \text{nm}^2$ PMMA nanoline is written over the gold nanoelectrodes by exposure of the surrounding PMMA. (c) Parylene-C conformal coating over the PMMA nanoline. PMMA is dissolved and parylene-C etched by reactive ion etching.

25 nm thick nanoelectrodes on the SiO_2 top of the wafer using electron beam lithography (EBL). External gold connection pads were constructed using standard metal lift-off techniques and photolithography to connect to the nanoelectrodes. A Raith E-Line e-beam writing system (Raith USA, Ronkonkoma, NY) was used to expose polymethyl methacrylate (PMMA) for metal lift-off. Figure 1(a) shows a scanning electron microscopy (SEM) image of the nanoelectrodes. The 100 nm sealed nanochannels were constructed using sacrificial removal techniques. We used EBL to expose a 100 nm thick film of PMMA over the gold nanolines in the region around the nanolines,

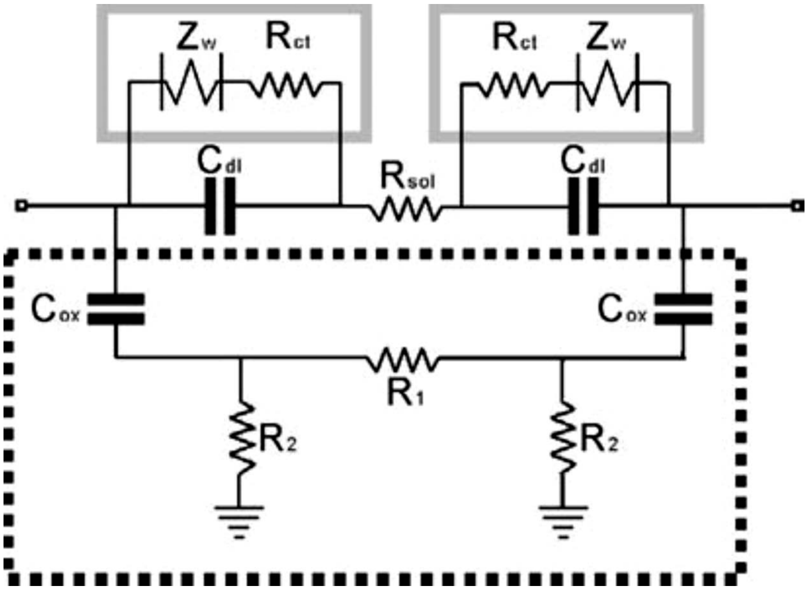

FIG. 2. The equivalent circuit of the nanoelectrodes in contact with water lying atop an insulating SiO_2 film which covers a silicon substrate. The elements in the gray boxes can be ignored in our measurements since there is no hydrolysis at low voltage, while the elements within the dotted box are coupling reactances to the underlying *p*-doped silicon wafer.

leaving behind lines of unexposed sacrificial layer of PMMA. We next evaporated 25 nm of SiO_2 over the nanolines to improve the surface wetting properties of nanochannel and then conformally coated with 4 μm thick of parylene-C [poly(chloro-*p*-xylylene)] using a Specialty Coating Systems model PDS 2010 parylene coating system (SCS Systems, Indianapolis, IN). Access holes for the gold electrodes and the feeding channels were etched through by oxygen plasma and 1:10 buffered oxide etchant. To avoid autofluorescence induced in parylene by an active plasma[15] and ambient UV radiation,[16] it is important not to expose the remaining parylene with plasma and to keep the samples in the dark. The sacrificial removal of PMMA in the nanochannels was done in four steps: (1) soaking the chip in 55 °C 1165 MicroChem resist remover (MicroChem, Newton, MA) for 36 h, (2) room-temperature soaking in 1,2-dichloroethane for 12 h, (3) soaking in room-temperature acetone for 12 h, and (4) drying the nanochannels by critical point drying (CPD-030, BAL-TEC AG, Principality of Liechtenstein), which served to prevent the collapse of the nanochannel resulting from surface tension of the acetone.

Conductance measurements were done using ac techniques. The ac impedance Z_{tot} of an insulating ionic fluid such as water between electrodes is a complex subject.[17] The most general model for the complex impedance of an electrode in ionic solution is typically modeled as the Randle circuit, which is shown in Fig. 2.[17] There are two major contributions to the imaginary part of the impedance: the capacitance of the double layer (C_{dl}), which is purely imaginary and has no dc conductance, and the impedance due to charge transfer resulting in electrochemical reactions at the electrode/electrolyte interface, which can be modeled as a contact resistor (R_{CT}), which is given by the Butler–Volmer equation, which describes the *I*-*V* characteristic curve when electrochemical reactions occur at the electrode,[18] in series with a complex Warburg impedance (Z_W) which represents injected charge transport near the electrode;[19] more details can be found in Ref. 20. Since we applied a 10 mV rms ac voltage with no dc offset in our measurements, electrochemical reactions are negligible, which means no electrochemical charge transfer occurred and as a result R_{CT} goes to infinity. We have drawn a gray box around the elements connected to the Warburg impedance branch of the circuit to show that they are negligible in our analysis.

In the case of no direct charge injection, the electrodes are coupled by the purely capacitive dielectric layer impedance C_{dl} to the solvent and are also coupled capacitively by the dielectric SiO_2 film capacitance C_{ox} to the underlying *p*-doped silicon semiconductor. We model the semi-

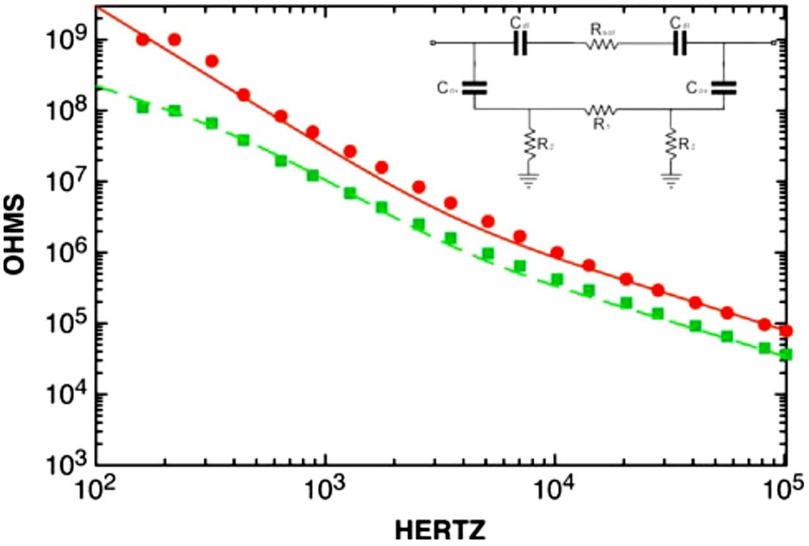

FIG. 3. ac impedance spectra of TBE buffer solution in a transchannel measurement between adjacent pairs of nanoelectrodes separated by 135 μm. The red circles are data for a dry channel and the solid red line is the fit to the model shown in the upper right hand corner. The green squares and dashed green line are for a nanochannel wet with TBE buffer.

conductor as a purely resistive material with bulk resistivity ρ_{Si}. The value of $C_{\mathrm{dl}}/\mathrm{area}$ is on the order of $\epsilon\epsilon_o\kappa$, where ϵ is the dielectric constant of water (about 80) and κ is the Debye screening parameter of the counterions in solution: $\kappa = \sqrt{\epsilon\epsilon_o k_B T / e^2 \Sigma_i c_i^\infty z_i^2}$,[20] where c_i^∞ is the bulk ion concentration of charge z_i. At our salt molarity of 50 mM (1/2 Tris/Borate/EDTA (TBE) buffer), C_{dl} is approximately 30 $\mu\mathrm{F}/\mathrm{cm}^2$ using $1/\kappa \sim 1$ nm.

In Fig. 3, we show the ac impedance measurements between pairs nanoelectrodes for both dry and TBE buffer wet nanochannels. The electrodes are capacitively coupled to the underlying silicon substrate through an oxide capacitor C_{ox}. We model the doped silicon wafer as pure resistors, so there is an R_1 that connects both C_{ox}, and each C_{ox} is connected to the ground with an R_2. Curve fitting was done by using the 3SPICE circuit emulation code (VAMP Inc., Los Angeles, CA). We therefore obtained the following parameters for the dry curve: $C_{\mathrm{ox}} = 1.32$ nF, $R_1 = 17.5$ $\mu\Omega$, and $R_2 = 32.8$ kΩ. R_1 is not sensitive in the fit as long as it is smaller than the impedance of C_{ox}. Given ρ_{Si} of the wafer of $1-10$ Ω cm, R_2 should be on the order of 10^3 Ω, which is slightly smaller than our fitting results. The same parameters for the wafer coupling parameters were then used for fitting the impedance measurements for wet channels. For TBE buffer solution in the nanochannel, curve fitting yields $C_{\mathrm{dl}} = 50$ pF and $R_{\mathrm{sol}} = 10^5$ Ω. However, given the dimension of our nanochannels, we should get a transverse resistance $R \sim 10^9$ Ω. One possible explanation for this difference is that the evaporated $\mathrm{SiO_2}$ film which was put over the PMMA is porous and allows buffer to penetrate the oxide film,[21] but given that the film is only 25 nm thick this would at most increase the cross section by one order of magnitude. However, it is known that there is a high fractional presence of mobile counterions associated with the charged channel walls.[22] To calculate exact conductance contribution from the surface charges is a tricky business, but since the surface-to-volume ratios in our nanochannels are much greater than the slits, a larger conductance enhancement can be expected, and more work needs to be done.

We have presented a way to fabricate a nanochannel integrated with electrodes. This technology opens up opportunities for electronic detection of charged polymers. With our techniques to fabricate nanoelectrodes with nanochannels, it should be possible to include integrated electronics with nanofludics, allowing the electronic observation of a single DNA molecule at high spatial resolution. However, the present design has problems. Most of the ac went through the silicon wafer instead of the solution. To enhance the sensitivity, we need either to increase the ratio of current going through the liquid to the current going through the wafer or to have a circuit design that picks up the changes in C_{dl} and R_{sol}.

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