ELECTRICAL CHARACTERIZATION OF SEQUENCE-SPECIFIC LABEL-FREE DNA BY USING POLYSILICON WIRE

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Abstract: In this paper we report the electrical measurement of sequence-specific and label-free deoxyribonucleic acid (DNA) by using poly-silicon (poly-Si) wire. Four single-strained (ss) DNA bases, adenine (A), thymine (T), cytosine (C) and guanines (G), as well as double-stranded (ds) DNA sequences, ds(A-T) and ds(C-G), with different lengths and concentrations were dropped onto the poly-Si wire surface, and currents flowing through the poly-Si wire channel were determined. It is found that the amount change of the channel current ΔI for ssDNAs with fixed length and fixed concentration is that T > C > G > A. For dsDNA sequence, we observe that ds(A-T) has higher ΔI than does ds(C-G). We also prove that single base change in ssDNA is feasible by using the poly-Si wire sensor.

1 INTRODUCTION

Determination of DNA bases has long been an intensive research topic in biotechnology and medical diagnostics since the genetic information carried by an organism is inscribed in DNA. On the other hand, measurements of DNA conductivity, hybridization and melting using electronic means have also drawn much attention in recent years due to the possible applications in molecular electronics. Typically, the detection of DNA uses techniques such as radiochemical, enzymatic and fluorescent (Lander, 1999) (Wang, 2000) based on detecting different labels or reagents added in the molecules under test. These techniques, however, are proven to be time-consuming, expensive and complicated to implement. Therefore, label-free DNA detection methods such as cyclovoltametry and chronopotentiometry have also been developed (Mastrangelo, 1999) (de-los-Snatos-Alvarez et al, 2004). However, all these methods are wet type in which the sensor has to be immersed in the solution under test, and the selectivity as well as the detection limit would not be accurate enough owing to the influences of thermal drift of the electrolyte solution.

Thanks to the rapid progress in semiconductor processing and nanofabrication techniques, many semiconductor/nano electronic devices and nano-scale measurement tools have been developed either to measure the electrical properties of DNA or for DNA detection. For example, Storm and his co-workers used nanogap junctions to measure the electrical resistance of hybridized and denatured DNA molecules (Storm et al, 2001). Xu *et al.* (2007) measured the conductance of DNA by using scanning probe microscopy. On the other hand, field effect devices such as electrolyte-insulator-silicon (Fritz et al, 2002) and silicon nanowire (SiNW) (Hahm and Lieber, 2001) have also been proposed for the detection of hybridyzation and mutation of

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DNAs. Instead of using SiNW, in this work we used poly-Si wire for sequence-specific ssDNAs as well as ds DNAs, A, T, C, G, A-T and C-G, detection from the consideration of simplicity, economy and easy-fabrication. In the present work, current flowing through the poly-Si wire channel rather than time-dependent conductance was determined. We found that the amount of current change before and after dropping the DNA solution under test on the poly-Si wire surface is different for each ssDNA and dsDNA. This result indicates that each of ssDNAs and dsDNAs has its own characteristic amount of current changes, and the poly-Si wire sensor can be used as a promising DNA detection device.

2 EXPERIMENTS

In this work, p-type (100) Si wafer was used as the substrate. After standard RCA cleaning, a 12 nm-thick thermal oxide was grown at 900℃. Following that, a phosphorous-doped polysilicon layer with a thickness of 80 nm was deposited at 620℃ by vertical furnace and having a sheet resistance of 40-50 Ω/□. An e-beam writer was then used to define the pattern of the poly-Si wire. After development, the poly-Si wire was obtained by reactive-ion-etching. The line width and length of the poly-Si wire is about 200nm and 2um, respectively. Figure 1 and Figure 2 depicts respectively the schematic diagram and the SEM image of the poly-Si wire sensor used in this work. To increase the detection sensitivity, an enzyme layer (γ-APTES) is deposited onto the poly-Si wire surface and then cured at 120℃ for 5 min on a hot plate, which can enhance the adhesion of DNA molecular with the poly-Si wire surface as well as increase the sensitivity of the sensor. The same sensor has been reported being successfully used for cancer cells detection (Wu et al, 2008). In this work, the sensor was used for DNA detection.

Sequence-specific DNA reagents (Invitrogen, U.S.A.), ssA, ssT, ssC, ssG, ds(A-T) and ds(C-G), with different concentrations (50, 100 nM) and lengths (10, 20 mer) were prepared and dissolved in a 0.165 M phosphate buffer solution. The DNA solution under test was then dropped onto the poly-Si wire sensor surface by using a micropipette. A voltage was applied between the source and the drain of the poly-Si wire without side gate bias, and the current flowing through the poly-Si wire was measured by using the semiconductor parameter analyzer HP 4156B. All the experiments were carried out at room temperature.

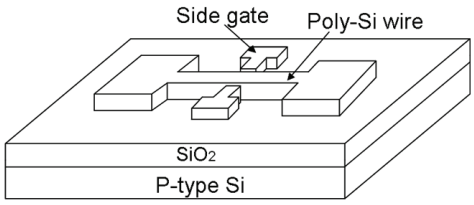

Figure 1: Schematic diagram of the poly-Si wire biosensor.

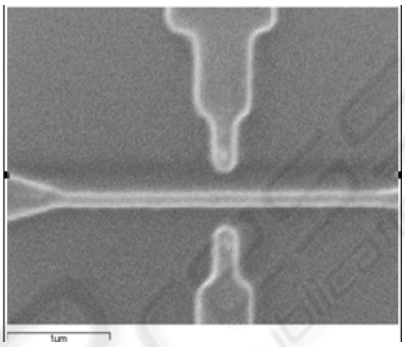

Figure 2: SEM picture of the Poly-Si wire, the line width and length are about 200nm and 2um, respectively.

3 RESULTS AND DISCUSSION

Figure 3 and Fig. 4 show respectively the I-V characteristics of 50 nM and 100 nM ssA, ssT, ssC and ssG, with different lengths under forward bias. As observed, the current I_{DS} flowing through the poly-Si wire increases with increasing source-drain voltage V_{DS}. It is interesting to note that the current flowing through the poly-Si wire channel after the solution under test was dropped onto the poly-Si wire surface is higher than that before it was dropped for all the sequence-specific ssDNAs except for ssC. This result indicates that the polarity of the surface charge of ssC is opposite to that of other ss DNAs. Figure 5 compares the absolute value of the amount of current changes (which is defined as $\Delta I = |I_{DS}(\text{after dropping}) - I_{DS}(\text{before dropping})|$) of ssA, ssT, ssC and ssG DNA with different concentrations and lengths measured at V_{DS} = 5V. We find that ΔI increases with increasing DNA length as well as concentration as expected because the longer length and the higher concentration of ssDNA, the more charges within the poly-Si wire channel will be induced. We also observe that, for the same length and concentration of ssDNA, the amount of current changes ΔI is that T > C> G > A. It is reported that the Fermi level of DNA bases is that T < C < G < A (Zwolak and Di Ventra, 2008). Therefore, we believe that the surface charge of the

poly-Si wire is modified by the electron transfer between the wire surface and the DNA bases attached.

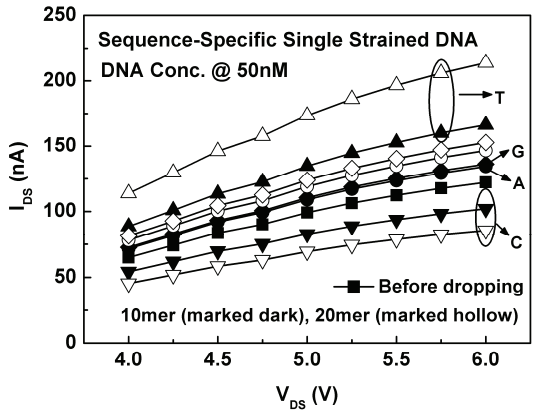

Figure 3: I-V characteristics of the poly-Si wire after dropping different 50 nM sequence-specific ssDNA solution with a length of 10 mer and 20 mer.

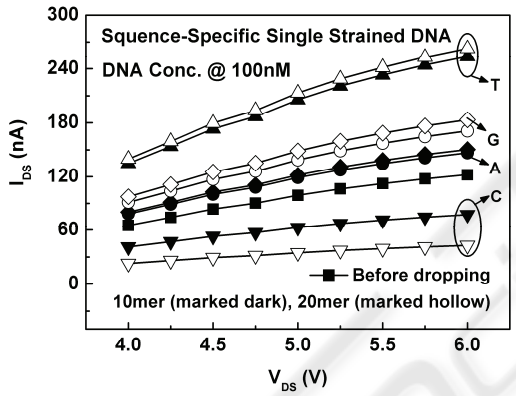

Figure 4: I-V characteristics of the poly-Si wire after dropping different 100 nM sequence-specific ssDNA solution with a length of 10 mer and 20 mer.

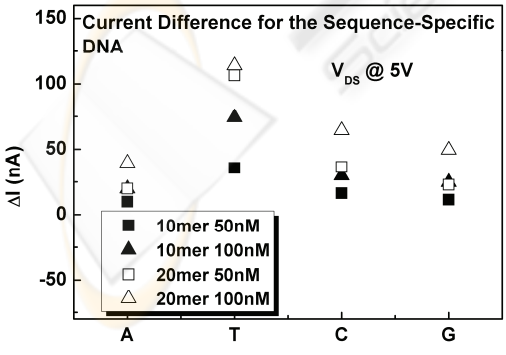

Figure 5: Current difference comparison of ssA, ssT, ssC and ssG with different concentrations and lengths measured at V_{DS} = 5V.

Figures 6 and 7 show respectively the I-V characteristics of 50 nM and 100 nM sequence-specific dsDNAs, ds(A-T) and ds(C-G) with different lengths under forward bias. As observed, ds(A-T) has higher I_{DS} than ds(C-G) does. Since the charge polarity of C is opposite to that of A, T and G, it is believed that the net surface charge is reduced when ds(C-G) is dropped onto the poly-Si wire surface and would reduce the amount of induced charge in the poly-Si wire channel, hence less current would flow. Figure 8 compares the ΔI for the all the dsDNA s and ssDNAs. It is reported that the ds(C-G) and ds(A-T) might be treated respectively as p-type and n-type semiconductor (Kim et al, 2006), which also explains the ΔI difference in Fig. 8. The detection of single base change in ssDNA was also conducted in this work. The result (not shown) indicates that the poly-Si wire sensor can be used for the detection of single base change in ssDNA.

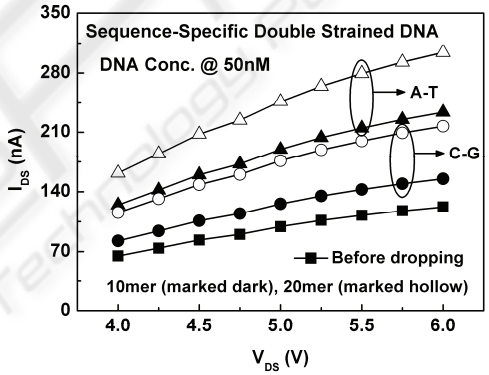

Figure 6: I-V characteristics of the poly-Si wire after dropping different 50 nM sequence-specific dsDNA solution with a length of 10 mer and 20 mer.

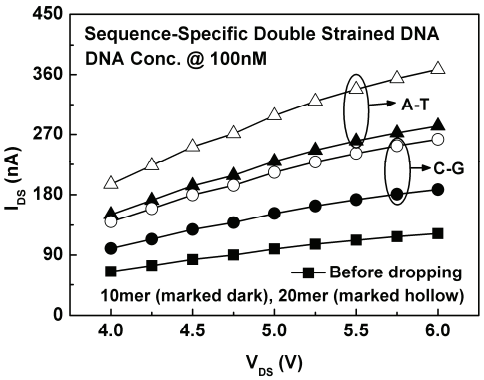

Figure 7: I-V characteristics of the poly-Si wire after dropping different 100 nM sequence-specific dsDNA solution with a length of 10 mer and 20 mer.

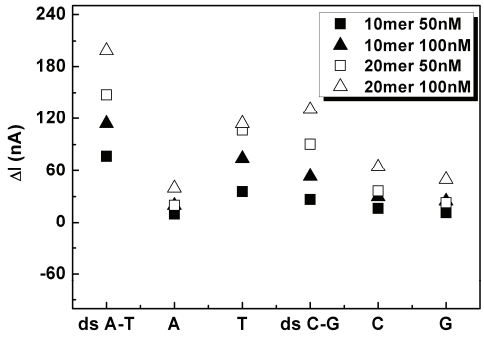

Figure 8: Current difference comparison of ssA, ssT, ssC, ssG, ds(A-T) and ds(C-G) with different concentrations and lengths measured at V_{DS} = 5V.

4 CONCLUSIONS

In this paper we report the detection of ssDNAs and dsDNAs with specific sequence by using the poly-Si wire sensor. For ssDNA, we find that each ss DNA base has its own characteristic ΔI, and the amount changes of the current flowing through the poly-Si wire is that T > C > G > A. For dsDNAs, we also observed that ds(A-T) has higher ΔI than ds(C-G). Our experimental result confirms that the surface charge state is modified after the DNA solution is dropped, which is believed to be related to the Fermi levels of the DNA bases. We also prove that the poly-Si wire sensor can be used for the detection of single base change in ssDNA. In conclusion, the poly-Si wire sensor can be used as a promising DNA detection device.

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REFERENCES

de-los-Snatos-Alvarez, P., Lobo-Castanon M. Juses, Miranda-Ordieres, A. J., Tunon-Blanco, (2004). Current strategies for electrochemical detection of DNA with solid electrodes. *Anal. Bioanal.Chem.*, 378, 104-118.

Fritz, J., Cooper, E. B., Gaudet, S., Sorger, P. K. Manalis, S. R. (2002). Electronic detection of DNA by its intrinsic molecular charge. *Proc. Natl. Acad. Sci. U.S.A.*, 99, 14142-14146.

Hahm, J. I., & Lieber, C. M. (2001). Direct ultrasensitive electrical detection of DNA and DNA sequence variations using nanowire nanosensors. *Nano lett.*, 4, 51-54.

Kim, K. S., Ahn, S. K., Lee, Y., Lee, J. M., Roh, Y. (2006). Effects of gate voltage on the characteristics of source-drain current formed through DNA molecules. *Thin Solid Films*, 515, 822-826.

Lander, E. S. (1999). Array of hope. *Nat Genet.* 21, 3-4.

Mastrangelo, C. H., (1999). DNA analysis system on a chip. *Solid-State Chemical and Biochemical Sensors, Techna Faenza.*, 495-476.

Storm, A. J., van Noort, J., de Vries, S. Dekker, C. (2001). Insulating behaviour for DNA molecules between nanoelectrodes at the 100nm length scale. *Appl. Phys. Lett.*, 79, 3881.

Wang, J. (2000). Towards Genoelectronics: Electrochemical Biosensing of DNA Hybridization *Chem. Eur. J.*, 5, 1681-1685.

Wu, Y. L., Hsu, P. Y., Hu, S. H., Hung, W. C., Lin, S. T., Hsu, C. P., Cullis, A. G. (2008). Polysilicon Wire Sensor for Biochemical Detection with The Help of Capillary Atomic-Force-Microscopy Tip for Solution Transfer. *9th International conference on Solid State and Integrated Circuit technology. IEEE press.*

Xu, M., Endres, R. Arakawa, G., Y. (2007). The Electronic Properties of DNA bases, *Small*, 3, 1539-1543.

Zwolak, M., Di Ventra, M., (2008). Colloquium: Physical approaches to DNA sequencing and detection. *Rev. Mod. Phys.*, 80, 141-165.