NANOGRATING Si BIO-FETs FOR SENSITIVE DETECTION OF PROTEIN IN SERUM

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ABSTRACT

Here we reported the application of silicon-nanogratings (Si-NG), as sensing elements rather than conventional single channel in the nanoscale Si Bio-FETs that can improve the device performance interms of sharper SS, higher ON/OFF ratio, lower V_t with a significant reduction in device to device variation. These NG-FETs also results in higher sensor stability and reproducibility over tens of hours in pH sensing. We believe that such improvements are due to reduced discrete dopant fluctuation and biochemical noise in the solution. Selective detection of insulin-analog in both buffer and human serum with a detection of limit down to 10fM is demonstrated.

KEYWORDS: Si nano grating, bio-FETs, biosensor, pH sensing and Insulin sensing

INTRODUCTION

Among the emerging biosensing technologies, nanoscale Si Bio-FETs such as Si nanowire (NW) FETs [1],[2] have got attention by many researchers due to their potential applications in variety of fields such as health care, drug delivery, bioterrorism, home land security. Si Bio-FETs with the feature of sensing small molecules expeditiously, became a promising label-free ultrasensitive biosensor platform due to their high surface to volume ratio. For clinical applications like early cancer detection, biosensors are required to have high sensitivity. High sensitivity in bio-FETs such as NW-FETs typically requires low doping in the NW channels [3], which was recently found to cause device variation [4] due to discrete doping effects [3] i.e. random arrangement of a very small number of dopants in the tiny NW volume. Though, femto molar protein sensing been already [1],[2] demonstrated using Si NW FETs, reliable sensing is still challenging due to the unreliable device performance. For practical applications such as disease diagnostics and to deal with complex clinical samples uniform and reliable sensors are essential along with high sensitivity.

EXPERIMENTAL

In our work, we used NG ie., multiple si nano channels to replace NW as sensing element and demonstrated insulin sensing using Si nano-grating field effect transistors (Si NG-FETs). A CMOS process combined with ebeam lithography was applied to fabricate highly uniform performance Si NG-FETs on low p-doped Si-on-insulator (SOI) wafers (doped with boron at 10^{15} cm^{-3}). Final device with multi-nanochannels connecting the highly doped n or p-type source/drain pads is shown in Figure 1a. A magnified electron micrograph of 50 nm wide, 30 nm thick, and 20 µm long nanochannel, is shown in figure 1b. Our results indicate that use of NG as sensing elements rather than conventional single channel such as NW FETs can results in improved device performance of nanoscale Si Bio-FETs. Si NG-FETs fabricated on same chip show sharper subthreshold swing (SS), and lower threshold voltage (V_t), higher current and ON/OFF ratio with significant reduction in the device to device variation by lowering discrete doping effects. These NG-FETs also results in higher sensor stability when they are exposed to buffer of high ion concentration for over tens of hours without losing its reproducibility in pH sensing. With these improved devices, selective detection of insulin-analog in both buffer and human serum without pre-purification with a detection of limit down to 10fM is achieved repeatedly.

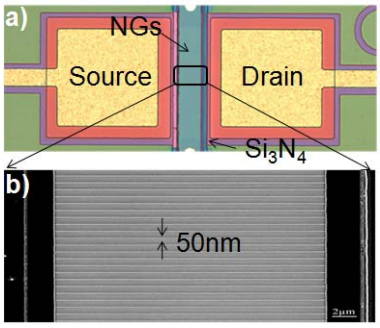

Figure 1: (a) Optical image of NG-FETs with 100 nano channels (b) SEM image of magnified area of multiple nano-channels (W=50nm,t=30nm, L=20µm) connecting highly doped n or p-type source/drain pads.

RESULTS AND DISCUSSION

Typical transfer characteristics of both NMOS and PMOS Si NG-FETs with 100 channels characterized in 500µM buffer solution with pH value 8.2 is shown in figure 2. A reference electrode, Ag/AgCl wire was used as solution gate to bias Si-NGs in the solution. Drain current I_{ds} as a function of reference gate voltage V_{ref} at a drain voltage V_{ds} of 100mV in a linear (right axis) and logarithmic (left axis) representation. The maximum current between source and drain increases when V_{ref} increases (decreases), as expected for a n-channel (p-channel) MOSFET. These devices with 100NCs connecting source and drain have shown uniform and good performance with ON/OFF~10^6, subthreshold swing (SS) of ~80mV/dec, and threshold voltage (V_t) of ~1V. It is mentioned earlier that the discrete dopant fluctuations affects device reliability hugely due to the small volume of the nanochannels. So, it is vital to mitigate discrete dopant fluctuation by applying proper design and device fabrication techniques for reliable biosensing. The key finding of our study is that the number of nanochannel has strong impact on device performance, device to device variation and stability. We found that Si NG-FETs provide less performance variations and better stability in comparison with single nanochannel FETs fabricated on the same chip using the same process. This advantage of the nano-grating devices are due to the accumulation and averaging of the signal outputs of individual nanochannels making Si NG-FETs to less sensitive to discrete dopant fluctuations and interference from the environment during fabrication process. Fig. 3a shows performance characterisitcs (I_{ds}-V_{gs}) of n-type Si NG-FETs with different numbers of nanochannels(100, 10, and 1 nanochannels) of same dimensions characterized in buffer solution using Ag/AgCl wire solution gate. I-V curves in Fig 3a indicate that the NG devices results in higher current which scales with the number of nanochannels. Also, device with 100NCs shows higher ON/OFF ratio with three orders in magnitude, four times sharper SS, and lower V_t in buffer solution with small device to device variation compared to device with single channel as mentioned in Table I. The observed higher drive current of nanograting devices in buffer solution can improve signal to noise ratio and reduce the complexity of read out circuits make biosensing more reliable. We also found that Si NG-FETs after

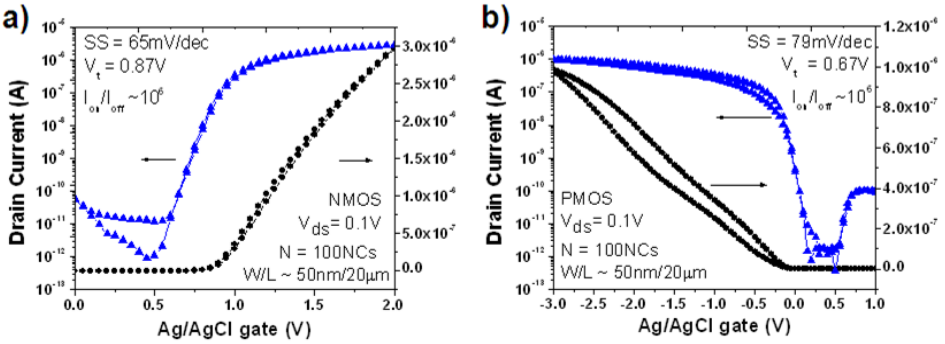

Figure 2: Transfer characteristics of (a) NMOS and (b) PMOS NG-FETs with 100 nanochannels (NCs)

coating their nanograting area with self assembled monolayer (SAM) were reproducibile and stable for long hours when exposed to highly concentrated (500µM) buffer solutions. Fig. 3b shows time dependent drain current response curve to three different pH (=5, 7, and 9) buffer solutions for 8000sec and such repeatability and stability is observed more than 20 hrs. We believe that this long term stability and reproducibility was achieved due to the multiple reasons mentioned in our recent work [4].

In collaboration with Baylor Institute of Diagnostics, we demonstrated insluin detection to quantify the insulin analog Lantus in human serum samples using our versatile Si NG-FETs modified with anti-insulin. Our preliminary sensing work

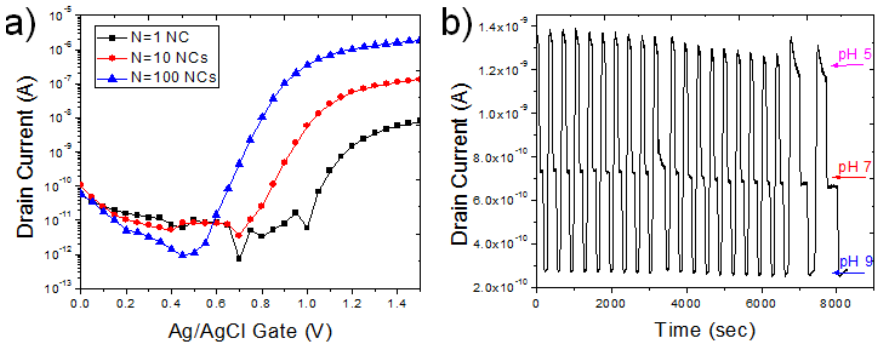

Figure 3: Comparison of device characteristics of Si NG-FETS with different numbers of NCs: (a) I_d-V_g and (b) Good stability and reproducibility of NG-FETs with 10 nanochannels exposed to different pH (pH =5, 7, and 9) solutions.

Table I. Variation of device parameters extracted from I-V curves of n-type NG-FETs (5-10 devices averaged for each kind of devices).

# of NWs	Device parameters: value (left) and variation (right)						
	G_m (nS)	% Gm	V_t(V)	% Vt	SS (mV/dec)	% SS	I_{on}/I_{off}
100	3275.7 ±221.47	6.76	0.86 ±0.015	1.8	65.10 ±3.08	4.73	~10^6
10	253.42 ±118.83	46.89	1.02 ±0.06	6.1	74.07 ±7.12	9.61	~10^4
1	12.6 ±11.08	87.74	1.15 ±0.16	14	231.35 ±155.6	67.28	~10^3

(Fig. 4a) exhibits sensing of different concentration of insulin directly from diluted patient serum without purification, with limit of detection down to 10 fM. The sensing experiments have repeatedly shown well correlated sensing of insulin with concentration from 10 fM to 1nM in pure PBS buffer (blue curve in Fig. 4b) and in human serum (Fig. 4b-green curves for two different patients). The detection range is approximately 5 orders of magnitude with good selectivity over serum (10 fM insulin detected among 1 nM serum with over 4,000 types of proteins). The red curve in Fig. 4b is the signals from non-specific binding from high concentrations of serum. The sensor is stable in serum for repeated multiple tests over the period of a week, showing excellent stability.

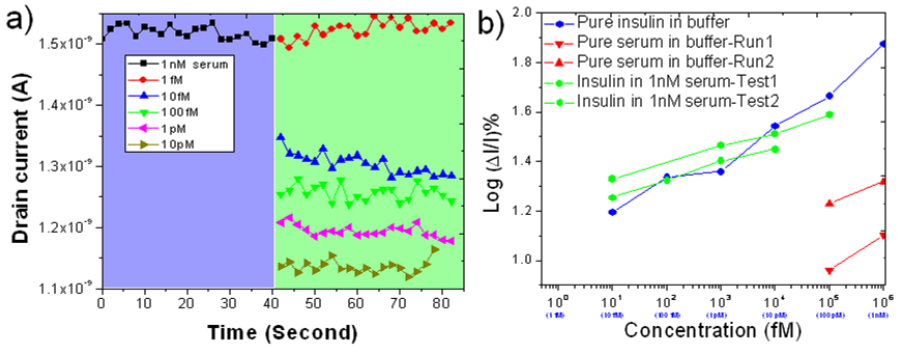

Figure 4: (a) Detection response with decreasing insulin concentration down to 10fM using Si NG-FETs conjugated with anti-insulin on C11-ald SAMs. (b) Logarithmic representation of sensitivity vs. insulin concentration in pure serum (blue) and patient insulin (green) in the range of 10fM to 1nM insulin concentrations. Signals (red) from non-specific binding from high concentrations of serum.

CONCLUSION

Impact of number of nanochannels were investigated and found that nanogratings compared to single nanochannel resulted in higher ON/OFF ratio, smaller SS, lower V_t, significantly reduced device to device variation and higher stability in wet ambient. We believe such improvements are due to minimized discrete dopant fluctuations and interference from the environment. Using Si NG-FETs with improved device performance, we demonstrate selective detection of insulin with limit of detection down to 10 fM in both buffer and human serum without pre-purification.

ACKNOWLEDGEMENTS

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