The impact of biomolecules binding on low-frequency noise in Si NW FET biosensors

Y.Kutovyi[1], I.Zadorozhnyi[1], V.Handziuk[1], H.Hlukhova[1], M.Petrychuk[2] and S.Vitusevich[1]
[1]Institute of Complex Systems (ICS-8), Forschungszentrum Jülich
52428 Jülich, Germany
s.vitusevich@fz-juelich.de
[2]Faculty of Radiophysics, Electronics and Computer Systems
Taras Shevchenko National University of Kyiv
Kyiv, Ukraine

I. INTRODUCTION

A great deal of attention has been recently paid to silicon nanowire field-effect-transistors (Si NW FETs) as a powerful diagnostic platform due to their high biocompatibility and tunable electrical properties[1, 2]. Sensing principle of such charge-sensitive bio-devices is based on label-free approach which allows the direct monitoring of biorecognition processes between receptor and target biomolecules. Being dissolved in a liquid biomolecules like proteins possess a positive or negative charge, which depends on pH and ionic strength of the solution. Therefore, when charged biomolecules selectively bind to the receptor molecules, which are covalently linked to the nanowire surface, the biomolecular recognition events induce changes in surface potential, which modulates the charge carrier flow in the nanowire channel, generating an electrically detectable signal[3, 4]. According to current trends in FET-based biosensing the pronounced changes in channel conductance induced by the biorecognition event, e.g. the antigen-antibody binding, can be measured and correlated to the analyte concentration[5, 6]. However, the development of a robust diagnostic platform based on FET biosensors requires a careful consideration of noise. Usually, fluctuations in the measured electrical signal have several noise sources, including thermal fluctuations and intrinsic device noise due to mobility and/or carrier number fluctuations in the channel[7-9]. At the same time, fluctuations in the NW FETs while operating in liquid containing biomolecules have not been explained in detail yet.

Here we report the results demonstrating that selective binding of target biomolecules to the silicon nanowire surface produced increased excess noise, which has characteristics and behavior that considerably differ for those recorded for the same transistor operated in solution without target molecules. As the analyte, we chose cardiac troponin I (cTnI) molecules which are very sensitive biomarker for acute myocardial infarction diagnosis[10, 11].

II. EXPERIMENTAL DETAILS

The fabrication of liquid-gated Si NW array FETs was performed by applying "top-down" method to p-type <100>-oriented silicon-on-insulator (SOI) wafers with 75nm thick active silicon layer and 145nm thick buried oxide layer (BOX). All fabrication processes were carried out at the Helmholtz Nanoelectronic Facility (HNF) of Forschungszentrum Jülich. The steps involved in the fabrication of silicon nanowire devices are presented in our previous work[12]. After fabrication the wafers were cut into single chips, wire-bonded and encapsulated for liquid measurements. In order to provide sensing capability of Si NW FETs the surface of nanowires were functionalized with highly specific monoclonal cTnI antibodies.

For the noise measurements we used the homemade ultra-low noise measurement setup. More detailed description of the noise measurement setup is previously presented elsewhere[13]. Briefly, the gate-source and drain-source biases were applied to the sample using a battery and a variable resistor. A capacitance of 9400μF was used in parallel to the variable resistor in order to additionally stabilize the voltages. The drain-source voltage fluctuations were amplified to the measurable range using a home-made ultra-low noise preamplifier and then amplified by Stanford low noise voltage preamplifier SR560. The output of the amplifier was fed to HP (Hewlett Packard) 35670 dynamic parameter analyzer that performs the fast Fourier transform on the time domain signal to frequency domain yielding the voltage noise power spectral density (S_V) in the range from 1Hz to100kHz. In order to get reliable noise spectra, the number of averages was set at 100. The processed noise data was then transferred via GPIB interface to a PC.

III. RESULTS AND DISCUSSIONS

Si NW array FET consisted of 50 nanowires nominally 100 nm wide and 5μm long was used in a sensing experiment. During the noise measurements the device was operated in a linear regime by applying a constant drain-source bias of 100mV. Silicon nanowires were exposed to 1mM phosphate-buffered saline (PBS) solution with pH=7.4 and gated via Ag/AgCl reference electrode. The normalized noise spectra of the transistor modified with monoclonal cTnI antibodies are presented in Fig. (1).

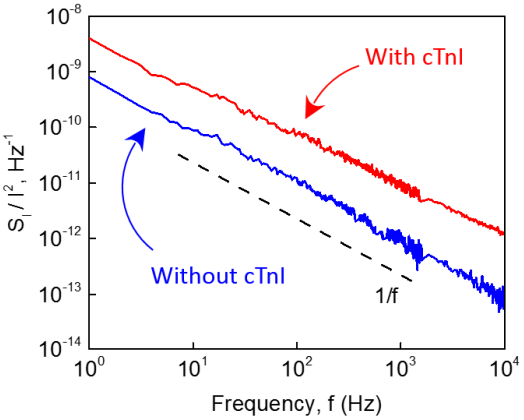

FIG. 1. Measured noise spectra for the liquid-gated Si NW array FET at a drain bias of 0.1V and overdrive liquid gate voltage of 0.47V before and after cTnI binding from 10ng/mL solution.

Flicker 1/f noise originating from the interaction between slow traps in the gate oxide and charge carriers in the channel was observed as a dominant component in the noise spectra at low frequencies (see Fig. (1), blue curve). However, after introducing

the PBS solution containing 10ng/mL of cTnI antigens to the NW sensor, the noise of the transistor increased by almost one order of magnitude (see Fig. (1), red curve). In addition, distinct conductance decrease was also observed indicating on the negative electrical gating effect when negatively charged troponin molecules selectively bind to the n-type Si NW FET. In order to understand and analyzed the spectra acquired after the biomolecule binding on a Si NW FET sensor surface, we calculated equivalent input voltage spectral density S_U of the transistor and plotted the values in Fig. (2) as a function of overdrive gate voltage (V_{LG}–V_{Th}) at frequency of 30Hz.

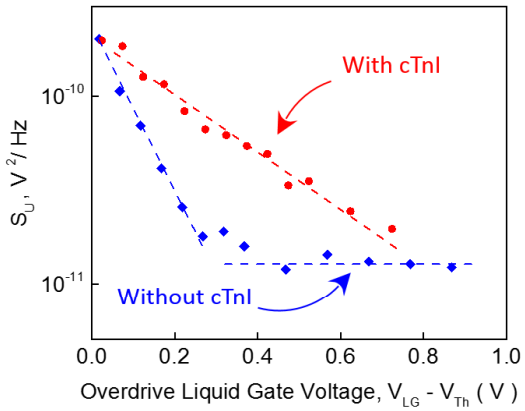

FIG. 2. The equivalent input noise S_U of the Si NW FET plotted versus overdrive liquid gate voltages before and after binding of troponin molecules in 1mM PBS solution. The lines are guides for the eye.

For the case of pure PBS solution (without troponin antigens), at V_{LG}–V_{Th} > 0.3V the S_U value didn't change (in the range from 0.3 to 0.9V) with overdrive gate voltage indicating on the carrier number fluctuation model (McWhorter's model[14, 15]). However, binding of troponin molecules resulted in a substantial increase of the input referred noise in all ranges of applied gate voltages, i.e. contribution of an additional noise component. We registered that the noise behavior after binding of cTnI antigens differs considerably from that measured in pure buffer solution. This fact indicates that excess noise is not caused by changes in the dielectric layer of Si NW FET, but it is determined by fluctuations of the effective charges introduced by troponin molecules selectively attached to antibodies on the sensor's surface. Moreover, the amplitude of the excess noise decreases with increasing of effective gate voltage (see Fig. (2)) pointing out on the fact that the additional noise is also related with movement of ions through the membrane[16] formed by troponin molecules attached to antibodies on the nanowire surface. Our results demonstrate that charged antigen molecules influence on the penetration of small ions resulting in excess drain current fluctuations of the transistor.

IV. CONCLUSIONS

We fabricated liquid-gated Si NW array FETs and applied them for the selective detection of cTnI biomarker molecules. The low-frequency noise of Si NW FETs operated in a solution without target molecules was determined by tunneling of the charge carriers to/from the interface traps in the oxide layer, i.e. pure transistor-determined noise. However, with the addition of troponin molecules to the buffer solution, the charge fluctuations resulted in additional excess noise deriving from the negatively charged troponin molecules. Our results show that the additional noise is related to the troponin molecules and has characteristics which considerably differ for those usually recorded for conventional FETs. We demonstrated that noise spectroscopy can be successfully applied for investigation of dynamic processes associated with the biomolecular recognition events.

ACKNOWLEDGEMENTS

The authors would like to acknowledge Prof. Dr. A. Offenhäusser and Dr. S. Pud for valuable and useful discussions. Y. Kutovyi greatly appreciates a research grant from the German Academic Exchange Service (DAAD).

[1] Z. Wang, S. Lee, K. Koo and K. Kim, IEEE Transactions and Nanobioscience, vol. **15**, pp. 186-199, 2016.
[2] Y. Cui, Q. Wei, H. Park and C. M. Lieber, Science, vol. **293**, pp. 1289–1292, 2001.
[3] F. Patolsky, G. Zheng and C. M. Lieber, Nanomedicine, vol. **1**, pp. 51-65, 2006.
[4] A. C. Mazarin de Moraes and L. T. Kubota, Chemosensors, vol. **4**, pp. 1-26, 2016.
[5] X. P. Gao, G. Zheng and C. M. Lieber, Nano Lett., vol. **10**, pp. 547-552, 2010.
[6] K.-I. Chen, B.-R. Li, Y.-T. Chen, Nano Today, vol. **6**, pp. 131-154, 2011.
[7] L. K. J. Vandamme and D. Rigaud IEEE Trans. Electron Devices, vol. **41**, pp. 1936-1945, 1994.
[8] I. Zadorozhnyi, J. Li, S. Pud, H. Hlukhova, V. Handziuk, Y. Kutovyi, M. Petrychuk and S. Vitusevich, Small, vol. **14**, pp. 1-8, 2017.
[9] S. Vitusevich, I. Zadorozhnyi, Semiconductor Science and Technology - Topical Review, vol. **32**, pp. 1-21, 2017.
[10] S. Korff, H.A. Katus and E. Giannitsis, Heart, vol. **92(7)**, pp. 987–993, 2006.
[11] G. Boriani, M. Biffi, V. Cervi, G. Bronzetti, G. Magagnoli, R. Zannoli, A. Branzi, Chest, vol. **118(2)**, pp. 342-347, 2000.
[12] S. Pud, F. Gasparyan, M. Petrychuk, J. Li, A. Offenhausser and S. Vitusevich, J. Appl. Phys., vol. **115**, pp. 1-12, 2014.
[13] S. Pud, J. Li, M. Petrychuk, S. Feste, S. Vitusevich, B. Danilchenko, A. Offenhäusser, and S. Mantl, J. Appl. Phys., vol. **113**, pp. 3-10, 2013.
[14] M. J. Kirton and M. J. Uren, Advances in Physics, vol. **38**, pp. 367-468, 1989.
[15] I. Zadorozhnyi, J. Li, S. Pud, M. Petrychuk and S. Vitusevich, MRS Advances, vol. **6**, pp. 1-6, 2016.
[16] R.B.M. Schasfoort, P. Bergveld, R.P.H. Kooyman and J. Greve, Analytica Chimica Acta, vol. **238**, pp. 323-329, 1990.