Student Paper

Fabrication Methodology for Label- free Nanocapactive Sensor

Rahim Esfandyarpour^{a, b}, Mehdi Javanmard^b, Zahra Koochak^c, James S. Harris^a, and Ronald W. Davis^b ^a Center for Integrated Systems, Department of Electrical Engineering, Stanford University ^b Stanford Genome Technology Center; 855 California Ave., Palo Alto, CA 94304, USA ^c University of California Santa Cruz, Santa Cruz, CA, 95064, USA Phone: +1-650-387-5976, Email: rahimes@stanford.edu

(Oral presentation is requested)

Here we present a novel fabrication methodology for nanoneedle biosensors, label free electrical sensors, showing promise to overcome some of the current limitations of biosensors. The nanoneedle is an ultrasensitive and localized device, which has the ability to directly measure biomolecular binding as a function of time (real-time). By fabrication of a nanoneedle array one can envision monitoring of multiple biochemical events instantaneously in a large area and also perform multiplexed detection. The key element of this device is the nano-sized sensitive area of the sensor, which is in the range of biomolecule of interest. Presence of biomolecules at the sensing region of the nanoneedle tip results in impedance modulation in real time which can be useful for measuring kinetic constants of various biomolecular species. As shown in Fig. 1, nanoneedle biosensor structure consists of four main thin-film layers. There are two conductive electrodes with an insulator layer in between. Above the top electrode and underneath of the bottom electrode there are protective oxide layers to prevent exposure of the conductive electrodes to the electrolyte solution and also insulating the bottom electrode from the substrate. Array of nanoneedle sensors were fabricated on a 4 inch silicon wafer. The fabrication process of these primary devices was performed in the minimum number of steps. Various thicknesses and geometrical designs of nenoneedles by using different types of conductive and insulative materials have been fabricated and tested. In order to demonstrate the utility of this sensor for label-free bio sensing, the electrical response of the sensor for various types of biological agents was studied. To demonstrate the utility of this sensor in affinity biosensing and demonstrating the selectivity of this sensor in detecting target proteins another set of experiments were performed (Fig.2). In this presentation we will discuss the nanofabrication process of the sensor in detail, and some of the testing and characterization results. We envision the sensor presented in this paper to be combined with microfluidic pre-concentration technologies to develop low cost point-of-care diagnostic assays for the clinical setting. This work provides a strong starting point for a new class of electronic biosensing devices with the capability of rapid direct large-scale integration.



Fig 1: A) Schematic of nanoneedle biosensor three dimensional and side view of horizontal nanoneedles (Not to Scale) B) SEM image of a nanoneedle (Bird's eye view) and the tip of a nanoneedles biosensor.



Fig 2. A) Real-time measurement of impedance as 1) sensor is covered with water 2) 250 mg/ml biotinilated BSA is physically adsorbed on the surface of the sensor 3) The sensor surface is washed with water 4) 5 mg/ml Streptavidin was injected in a decrease in impedance 5) wash step afterwards with water. B) Control experiments where representative results of real time measurement of impedance where 1) sensor is covered with water. 2) 250 mg/ml unconjugated BSA. 3) The sensor surface was washed with water to wash out the unbound BSA molecules. 4) 5 mg/ml Streptavidin. (5) The sensor surface is washed with water.

References

[1] R. Esfandyarpour, H. Esfandyarpour, J. S. Harris, and R. W. Davis, "Simulation and fabrication of a new novel 3D injectable biosensor for high throughput genomics and proteomics in a lab-on-a-chip device," *Nanotechnology*. (In Press).

[2] R. Esfandyarpour, H. Esfandyarpour, M. Javanmard, J. S. Harris, and R. W. Davis, "Electrical Detection of Protein Biomarkers Using Nanoneedle Biosensors," *MRS Proceedings*, vol. 1414, Cambridge University Press, 2012.

[3] R. Esfandyarpour, H. Esfandyarpour, M. Javanmard, J. S. Harris, and R. W. Davis, "Microneedle Biosensor: A Method for Direct Label-free Real Time Protein Detection," *Sensors and Actuators B: Chemical, vol. 177, pp. 848-855, 2012.*

[4] R. Esfandyarpour, M. Javanmard, J. S. Harris, and R. W. Davis, "Thin Film Nanoelectronic Probe for Protein Detection," *MRS Proceedings*, vol. 1572, Cambridge University Press, 2013.

[5] R. Esfandyarpour, M. Javanmard, Z. Koochak, H. Esfandyarpour, J. S. Harris, and R. W. Davis, "Label-free Electronic Probing of Nucleic Acids and Proteins at the Nanoscale Using the Nanoneedle biosensor," *Biomicrofluidics*, vol. 7, p. 044114, 2013.

[6] R. Esfandyarpour, M. Javanmard, Z. Koochak, J. S. Harris, and R. W. Davis, "Nanoelectronic impedance detection of target cells," Biotechnol. Bioeng. (in press).

[7] R. Esfandyarpour, M. Javanmard, Z. Koochak, J. S. Harris, and R. W. Davis, "Electrical Response of DNA and Proteins at Nanoscale by Using Novel Nanoneedle Biosensor," Nanotech, Vol. 2, pp. 115 – 118, 2013.