Design and Fabrication of Nanoelectrodes for Single Cell Biosensor Applications

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Abstract:

A biosensor refers to an analytical device that converts a biological response into an electrical signal. The focus of this paper is the design and fabrication of gold nanoelectrodes for the enhanced performance of cell-based biosensor applications. Proteins will be covalently bonded to the arrays of surface-engineered nanoelectrodes, over which cells will be immobilized selectively for the purpose of biosensing. The basic electrode patterning consists of 50 x 50 nm^2 gold squares spaced a distance of 1 μm apart on a SiO_2 wafer substrate.

Due to the small nature of the features, the electron beam lithography tool is needed to perform the exposure. In order to determine the correct charge per area to come from the e-beam, a dose array test must be carried out in which different areas of a test sample will be exposed to different charges, ranging from 250 to 800 μC. The proper dose is determined by observing which dose produces the sharpest features. Once the proper dose is established, more samples can be made.

The samples will then be sent to the University of Washington where patterning will be verified.

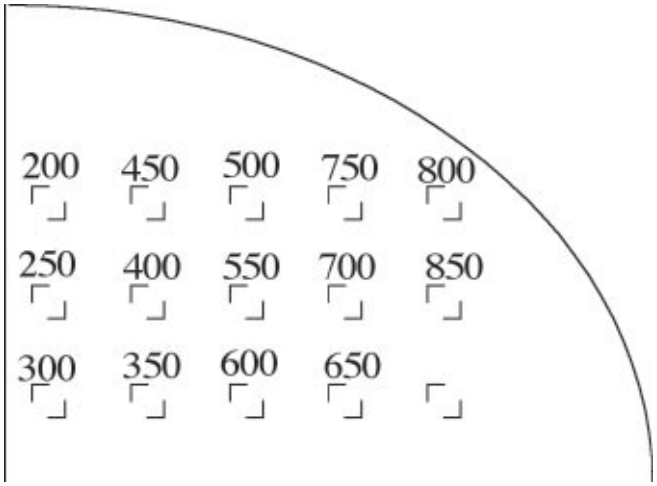

Figure 1: Map of dose-array test. Numerical values in µC.

Introduction:

Cell-based biosensors make use of direct measurements of physiological functions and changes in function due to presence of particular substances. This provides advantages over other biosensor types because cell-based biosensors provide detection capability for previously unknown agents. This is in contrast to biosensors that, for example, use antigen/antibody binding as the detection method. With the use of antibodies, information about the substance being analyzed must be known. For the cell-based biosensor this is not necessary, as it is the response of the cells themselves that is being monitored. Applications of these biosensors include pharmaceutical screening, environmental monitoring, and toxin detection. By controlling the selective attachment of cells to these arrays, the sensitivity of these cell-based biosensors can ultimately be increased.

Experimental Procedure:

The first and arguably most important step in this project entailed creating a test sample upon which to run a dose array test. As the electrode patterning consisted of small features, it was necessary to determine which charge from the e-beam tool would give the desired resolution.

The substrate consisted of a 4″ silicon wafer, with a 2000Å layer of oxide. As the sample itself was only a quarter of a wafer, four samples could be made from each wafer. A bilayer of resists was applied to the test sample: a copolymer (MAA-MMA) and an e-beam resist (PMMA). A thin layer of 150Å aluminum was added as a conduction layer. The sample was then sent to the e-beam tool for the dose-array test. In Figure 1, a charge map of the dose-array sample can be seen. Sets of electrodes, referred to as die, are exposed to a different charge. Each die is surrounded by two finding marks, approximately 1 mm long.

Once the test sample was exposed, it was developed and the gold deposited. After the lift-off process was

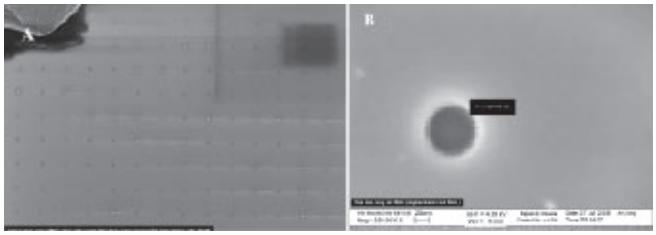

Figure 2: A) Die at 300 µC. B) Electrode at 300 µC.

completed, the sample was imaged under the field emission scanning electron microscope (FESEM) from which the proper charge was determined. When the optimal charge was found, more samples were synthesized.

Results and Conclusions:

The images taken from the FE-SEM were used to determine the proper charge per area, or dose, to come from the e-beam tool.

Shown in Figure 2 A and B are the pictures of the die and electrodes, respectively, at 300 μC. Figure 2A shows that many of the gold electrodes did not make it through the liftoff, and it was believed that this was due to underexposure, resulting in the gold being removed during the liftoff process. The electrodes that did remain had a diameter of 67 nm.

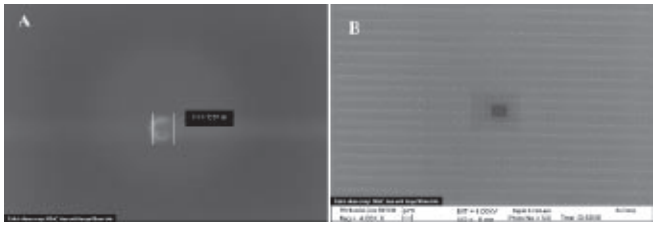

Figure 3: A) Electrode at 450 µC. B) Die at 450 µC.

Shown in Figure 3 are pictures of the charge (450 μC) that gave suitable feature sizes. Figure 3A gives the diameter of a single electrode to be 72 nm.

In Figure 4, A and B are the pictures of the electrodes and die, respectively, at 600 μC. The electrode diameter

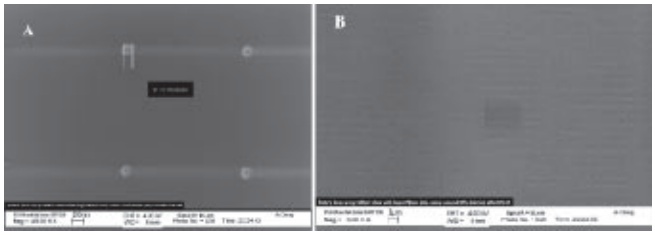

Figure 4: A) Single electrode at 600 µC charge. B) Die at 600 µC charge.

was 79 nm. Figure 4B shows that again not all the gold electrodes made it through the liftoff, this time probably due to the sonication step.

Analysis of the dose-array results determined that the best charge at which to fabricate the electrode array is 450 μC. Various steps of the sample preparation process were refined, such as the removal of the sonication step during lift-off to eliminate the chance of losing electrodes. Another important step involved the deposition of the gold electrodes via the evaporator. It was found that the evaporation level was best kept at a low value (at most 0.5 Å/sec) otherwise the copolymer layer, which is sensitive to heat, could warp and affect the electrode formation.

Future Work:

The next step will be to send the prepared samples to the collaborating group at the University of Washington to verify the patterning of the proteins and then cells upon these electrodes.

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