Development of Devices for Nanofiltration of Biomolecules

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Abstract:

The genetic testing of samples derived from whole blood requires the separation of DNA (1.5-3 nm in diameter, negatively charged) from hemoglobin (5.5 nm, pH dependent charge). Our goal is to fabricate a biocompatible porous membrane device that can be compatible with nano- and microscale devices, for molecular sieving and dialysis applications.

While even e-beam lithography cannot reliably generate features smaller than 20 nm laterally, metal films thinner than 10 nm can routinely be deposited and later wet-etched away as a sacrificial layer to leave behind channels which may measure several microns laterally, yet be thin enough to exclude by size alone biomolecules larger than the initial film thickness. The project consisted of three parts: fabrication of channels, SU-8 molding of PDMS chambers, and flow tests.

The development of the constrictions consisted of depositing alternate layers of metals and oxide over a thin silicon wafer (100-200 μm) using photolithography techniques. In general, we deposited alternate layers of SiO_2 to make the floor of the channel hydrophilic and prevent the electrodes from shorting out, and used Al as the sacrificial layer because it can be removed selectively vs. Si, SiO_2, and Au. The constricted channels were as small as 4 nm wide, which means that hemoglobin should not be able to pass through them. The PDMS chambers act as reservoirs for the molecules. Presently our research is directed toward the addition and improvement of electrical gates (Au) above the channels to allow passage through the constriction by charge modulation as well as size.

Introduction:

The genetic testing of samples derived from whole blood requires the separation of DNA from hemoglobin. Currently it takes a few days to receive the results of such a test. With the use of photolithography techniques and other applications, filters can be developed with sieves thin enough to separate specific proteins with sizes ranging between 5-15 nm, in a shorter time.

Applying metal evaporation and etching techniques, metal films thinner than 10 nm can be deposited and later wet-etched away as a sacrificial layer to leave behind channels which may measure several microns wide, producing a constriction thin enough for size exclusion separation. By the addition of electrical gates above the channels, the passage through the channels of molecules with a definite charge such as DNA can be modulated by charge as well as size.

The overall goal of the project is to fabricate a biocompatible porous membrane device that could be used to separate DNA from hemoglobin. The device will be compatible with nano- and micro-scale devices, and used for dialysis applications, newborn screening tests for congenital diseases and PCR enhancement. It also could be incorporated in DNA chips for quick medical analysis using small amounts of sample.

Procedure:

The procedure used to fabricate the constrictions is illustrated on Figure 1.

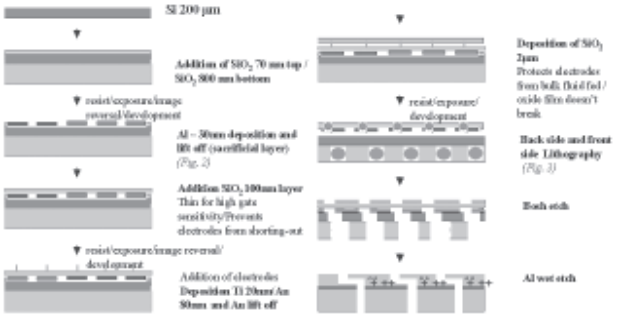

Figure 1: Fabrication of Constrictions.

Results and Conclusion:

We were trying to add a pair of electrodes over the pattern. As you can see in Figures 2 and 4, the old

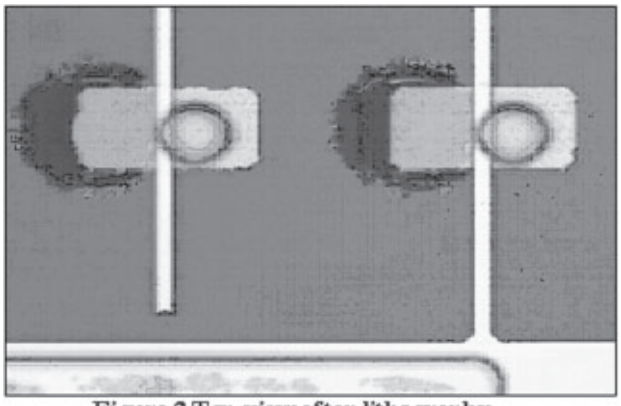

Figure 2 Top view after lithography

design contained only a 4 μm electrode that did not allow us to modulate efficiently the electric field through the passage. In the new design, we have two electrodes 2 μm wide each with a separation of 3 μm between. In figure 4, we can see that this design allows us to create an electric gradient where one electrode is less positive than the other one. Unfortunately, due to limited resolution of the pattern in the EV620 contact aligner, the new electrode design could not be fabricated. Although, due to the shortage of time, the device could not be finished and tested, work will continue during the next semester.

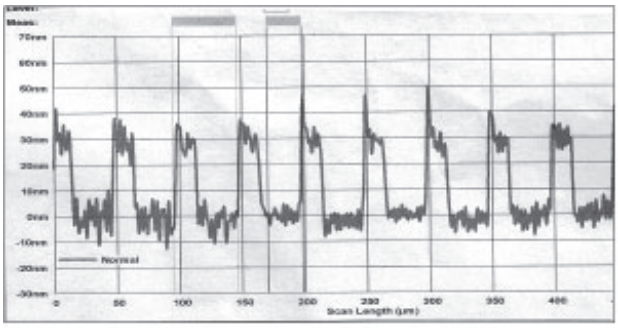

Figure 3. Al rectangles 30nm flat within noise levels of instrument

Future Work:

Future work for this project will be the improvement of electrical gates in order to perform the resolution in the exposure process. The mask for the electrodes should be redesigned with the electrodes over the pattern larger than 2 μm in order to be developed correctly.

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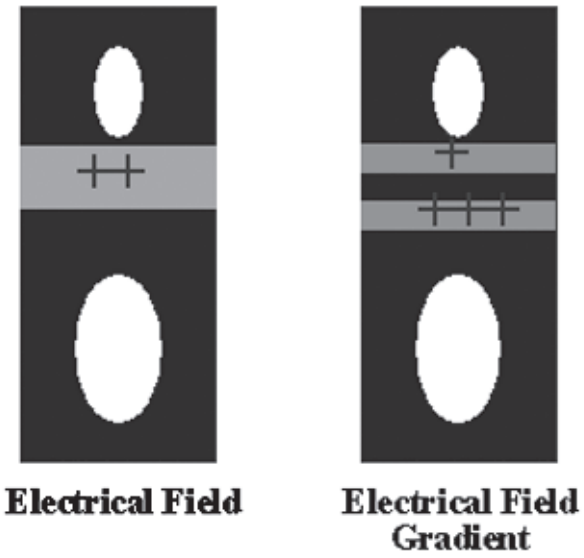

Figure 4: Placement of electrodes.