Piezoresistive Sensor for Measuring Blood Platelet Contraction Forces

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Introduction

Platelets are an important factor in the blood clotting process. These cell fragments, together with different biochemicals, are responsible for hemostasis when a vascular rupture occurs [1][2]. Recent studies associate the contraction of blood platelets with bleeding disorders [2][3]. In this respect, platelets may act as mechanical biomarkers for diagnosing blood disorders. Thus, a sensor is needed that can quantify the contraction forces.

The overall goal of the project is to create a piezoresistive sensing device that will measure the contraction force of individual platelets and, thus, be able to characterize them as healthy or not. ***Figure 1*** shows the sensor concept: the contracting platelet exerts a lateral force on a microfabricated polymer pillar, creating a stress distribution at its base, which can be sensed by a piezoresistor on the surface of a silicon substrate. The REU project focuses on the mechanical component of this micro electro mechanical system (MEMS), the polymer pillar. The pillar is the mechanical structure that will translate a force applied to the pillar tip into a stress acting on the electronic transducer below. The sensor itself is an n-type piezoresistor in the surface of the silicon substrate. Thus, the MEMS sensor is designed to sense and quantify platelet force.

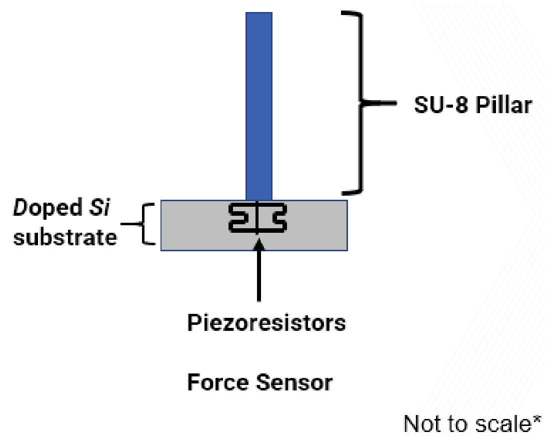

Figure 1*: Platelet contraction force sensing device comprising polymer pillar and underlying piezoresistive sensor.*

Experimental method

Fabrication of pillars by 2D lithography:

A silicon substrate was coated with SU-8 3010 photoresist with a 10µm layer thickness. The coating process was accomplished with the SCS G3 spin coater. The photoresist was applied to the substrate, and the spinning parameters were chosen to ensure a uniform coating with the desired layer thickness. The spinning process consisted of two consecutive steps: step one was set to a 5 second ramp time, 500 rpm, and dwelling for 5 seconds. Step two underwent a 10 second ramp time, 3000 rpm, and 60 second dwell . A soft bake at 95°C for 3 minutes followed the coating for solvent evaporation. The sample was then mounted in the Heidelberg MLA150 maskless lithography tool to expose the photoresist. In addition, a post exposure bake (PEB) of 2 minutes at 95°C proceeded. The final step was the development of the sample with SU-8 developer to remove the unexposed SU-8, followed with an isopropyl alcohol (IPA) rinse to stop the developing process.

Fabrication of pillars by 3D printing:

Alternatively, the pillars were written using the Nanoscribe Photonic Professional GT, a 3D printer with submicrometer resolution based on 2-photon polymerization. The printing process was done with the 63x objective and using Nanoscribe's proprietary IP-Dip photoresist polymer. With this objective, the laser power was set to 40 mW with a 10,000 μm/s scanning speed. After printing, the sample was developed with SU-8 developer for 20 minutes, followed with IPA rinse and soak for 2 minutes to stop the development. This way, nine identical pillars arrays of varying height and diameter were printed as shown in ***Figure 2***.

Mechanical Testing:

The fabricated polymer pillars samples were placed in a mechanical testing setup, schematically shown in ***Figure 3***. While observing the pillar under the microscope, a probing needle is aligned with the pillar until it appeared to make contact. Using a nano positioner, the pillar was then deflected in increments of 0.1μm from the initial point of contact until adhesion failure was observed, i.e. the pillar either falls or delaminates from the substrate.

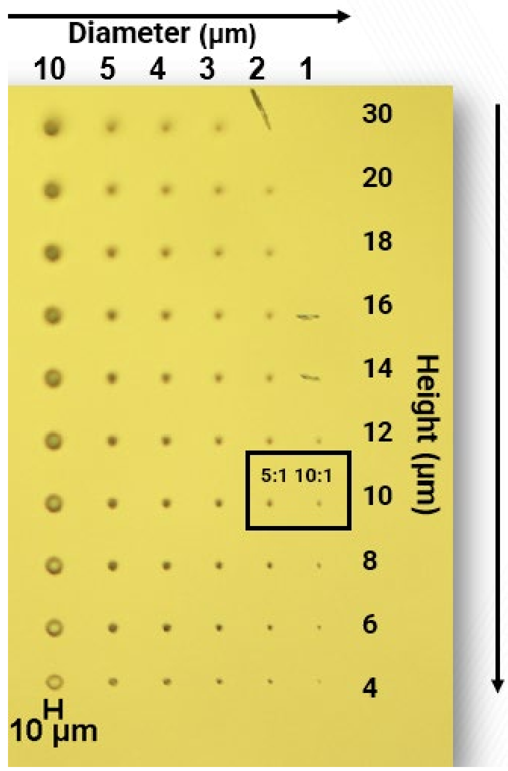

***Figure 2**: High-aspect ratio pillar arrays with varying diameter and height printed with Nanoscribe 3D lithography.*

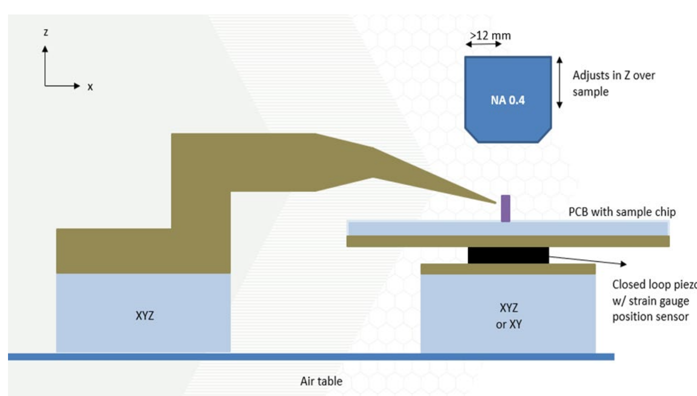

***Figure 3**: Mechanical testing station.*

Results

3D Printing – Pillar yield vs. aspect ratio:

From the printed pillar arrays (***Figure 2***), the yield of 3D printed pillars with 5:1 and 10:1 aspect ratio was evaluated and is shown in ***Figure 4***. Pillars with 5:1 aspect ratio resulted in 100% yield, i.e., nine out of the nine pillars with 10µm height and 2µm diameter were standing. The pillars with 10:1 aspect ratio (10µm height and 1µm diameter or 20µm height and 2µm diameter) resulted in a reduced yield of 66%.

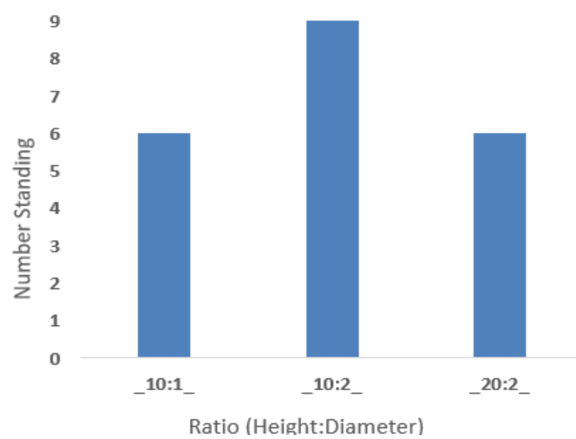

Figure 4*: Number of standing pillars (out of 9) for different 10:1 and 5:1 pillar aspect ratios.*

2D Lithography – Pillar yield vs. dose:

In case of the SU-8 pillar arrays fabricated using 2D lithography (***Figure 5***), the minimum exposure dose that resulted in all pillars of the array standing were investigated. ***Figure 6*** plots the minimal dose as a function of the pillar diameter. Large diameter pillars require lower doses in comparison to small diameter pillars of the same height (10µm height in this work). The observed linear decrease in minimal dose with increasing diameter could be associated to the surface area being exposed, with a larger surface area allowing more light energy propagate into the high-aspect ratio pillar.

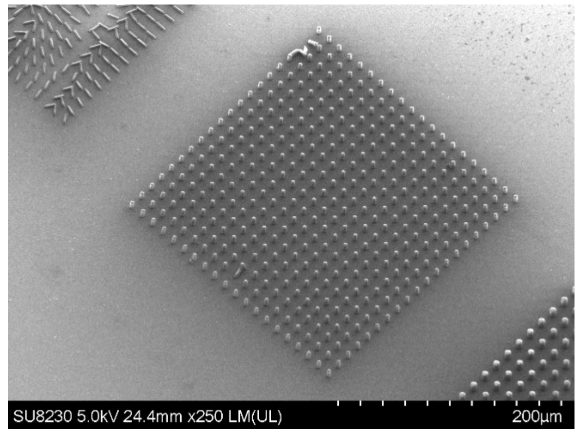

Figure 5*: SEM of SU-8 pillar array with 2µm diameter pillars.*

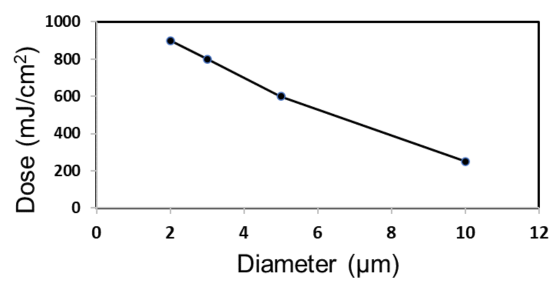

Figure 6*: Minimum exposure dose for standing high aspect ratio pillars as a function of pillar diameter.*

Mechanical Testing – Pillar deflection:

Six SU-8 pillars with 2µm diameter and different exposure doses (900, 1,000, 1,100 and 1,200 mJ/cm^2) were deflected and the observed ranges of maximum deflection before failure are plotted in ***Figure 7*** as a function of the exposure dose. It can be observed that there is a correlation of energy administered to the pillar and substrate adhesion. Initially, for increasing dosage, the adhesion improves and the maximum deflection increases. The best range was obtained for the 1,100 mJ/cm^2 dose and after that the achievable deflection range appeared to decrease.

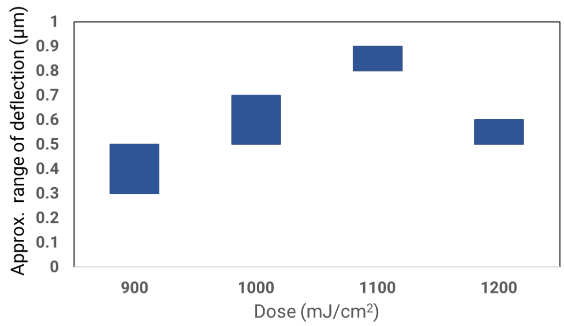

Figure 7: *Measured transverse deflection at which adhesion of high aspect ratio pillars with 2µm diameter failed as a function of the exposure dose.*

Conclusion

3D lithography using the Nanoscribe tool exhibits the highest yield for pillars with 5:1 aspect ratio. All 2µm diameter pillars with a fixed height of 10 µm were printed successfully. In contrast, the 10:1 aspect ratio pillars showed a reduced yield most likely due to low mechanical stability of the high aspect ratio structures.

In case of the pillars fabricated by conventional 2D lithography, the minimal exposure dose needed to fabricate standing pillar arrays depends on the pillar diameter. In particular, it was observed that the minimum exposure dose linearly decreases with pillar diameter in the diameter range tested here.

Finally, the mechanical testing of SU-8 pillars with 2µm diameter and 5:1 aspect ratio showed best adhesion for the 1,100 mJ/cm^2 exposure dose.

Future work

The next step is to print the polymer pillars directly on the piezoresistive device area and characterize the mechanical force translation to the piezoresistors.

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References

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