Fabrication of Nanopore Microneedle for Cell Transfection and Transformation

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Research Area

This research project is in the area of nanoelectronics for biomedical application.

Motivation or Background

- Current cell transfection technology is insufficient by means of efficiency, clinical safety, or throughput
- Physical methods, such as microneedles, biolistics, ultrasonic cavitation, and electroporation, have shown promise for *in vivo* transfection
- Micro-/nano-needle patches have shown advantages in pain-free drug delivery and controlled release
- By directly abutting cells to a nanochannel and creating a local electric field, unique nanoelectroporation (NEP) can be achieved

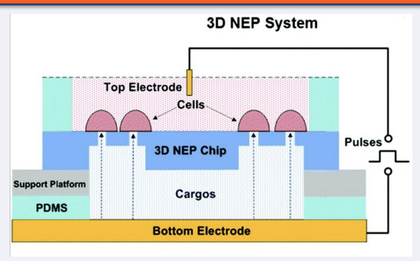

Fig. 1
The cross-sectional schematic of the 3D NEP system

Objectives

- The primary goal of this study is the design, fabrication, and characterization of a novel platform for cell transfection through controlled nanoelectroporation (NEP) and electrophoretic insertion of genetic materials
- We will be validating these single fabricated nanopore microneedles through benchtop experiments and investigate *in vitro* cell transfection capabilities
- The primary focus of this project for the current semester and the foreseeable future will be the fabrication of novel microneedle devices and ensuring that this fabrication process can be completed to the specifications needed

Methodology

- Fabrication of a hollow microneedle array with patterned nanopores will be developed using microfabrication techniques including
  - Photolithography
  - Reactive ion etching (RIE)
  - Thermal oxidation
  - Focused ion beam (FIB)
- To create silica microneedles we will begin with a single-crystalline silicon (Si) wafer as the substrate
- The circular deep holes will be etched into the Si substrate by an anisotropic deep RIE (DRIE) process
- Thermal oxidation a conformal layer of Silicon Oxide (SiO_2) is created
- Once this process is completed, the backside of the silicon wafer will be etched out therefore, leaving only the hollow silica microneedle structures
- Lastly, a high energy Ga+ ion beam (FIB) will be employed to pattern nanopores within the microneedle wall

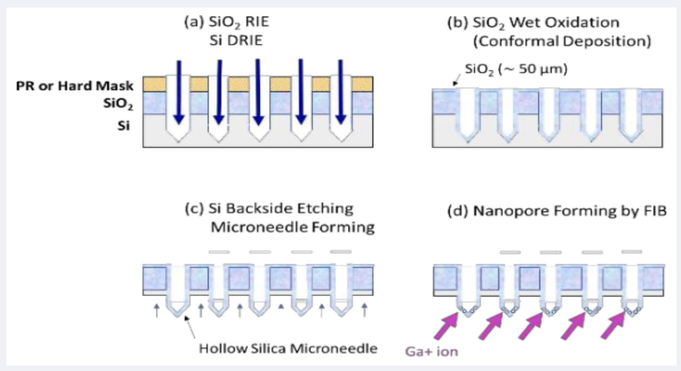

Fig. 2
(a) Initial RIE and DRIE produces microneedle shapes between gaps in photoresist (PR) or hard mask layer; (b) Wet oxidation creates oxide layer; (c) Backside etching exposes microneedle lengths; (d) FIB creates nanopores.

Results

- For now, we have seen progress made through photolithograpy and RIE steps, which shows that we can continue this process as we move into a deeper etch
- Using gases such as SF_6 and C_4F_8 during the etching process we will etch an aspect ratio of 3:1 to create the needle shape
- We also found an etch rate which ranged from approximately .33µm - 1µm per iteration cycle which was dependent on the diameter of the microneedle

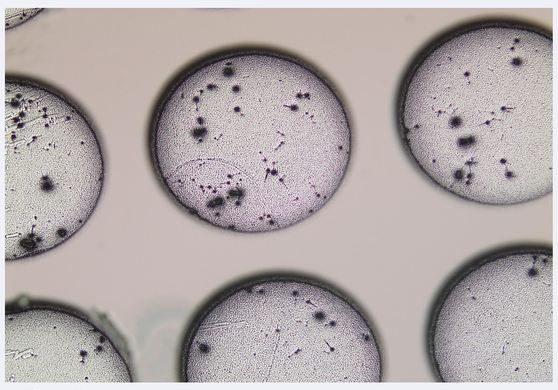

Fig. 3
Microscope Top-view image of silicon wafer post-etch (500µm Diameter)

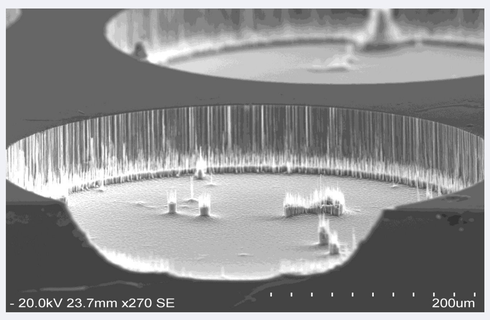

Fig. 4
SEM Image of silicon wafer post-etch (500µm Diameter

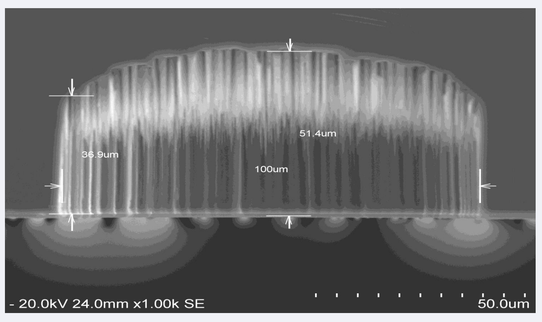

Fig. 5
Cross sectional SEM Image of silicon wafer post-etch (100µm Diameter)

Skills and Experience

- The skills and experience gained through this investigation has been immensely rewarding
- Cleanroom and lab safety trainings were completed prior to the start of this semester, but remained very important
- Experience was gained in Photolithography, Reactive Ion Etching, Deep Reactive Ion Etching, and Scanning Electron Microscope
- These trainings were conducted with the end goal of applying these skills beyond the project in order gain more experience with these tools and continue improving on the fabrication process

What I Learned

- The most important lesson learned from this semester was to always be ready for the worst-case scenario
- Receive training and knowledge on everything that will be used as early into the process as possible
- Fortunately, most trainings were successfully completed which will allow us more time to begin working out any other problems that we may run into without being pressed for time

Future Plans

- Further optimization of the etching recipe
- Successful completion of Thermal Oxidation and FIB trainings
- Continue working with/improving on SEM as well as DRIE
- Ensure that microneedle can hold an electric field
- Benchtop measurement showing release of electrophoretic material

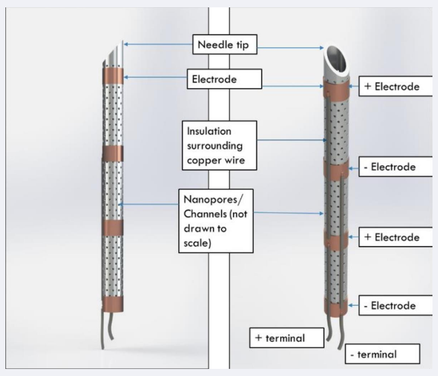

Fig. 6
model of distal tip of envisioned single NPM

Acknowledgments

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