Direct-Fabrication of Nanoparticles in Cancer Diagnostics

Trisha Sengupta

Biology, Emory University

NNIN REU Site: Stanford Nanofabrication Facility, Stanford University, Stanford, CA

NNIN REU Principal Investigator(s): Dr. Yi Cui, Materials Science and Engineering, Stanford; Dr. Mary Tang, Stanford Nanofabrication Facility, Stanford University

NNIN REU Mentor(s): Ching-Mei Hsu, MSE; Stephen Connor, Chemistry; Stanford University

Contact: tsengup@emory.edu, chingmei@stanford.edu, stconnor@stanford.edu, yicui@stanford.edu, mtang@stanford.edu

Abstract:

Synthetic antiferromagnetic (SAF) nanoparticles possess unique tunable magnetic properties, which make them instrumental in developing highly selective, highly sensitive bioassays for tumor detection and surveillance. Through a combination of top-down and bottom-up approaches, we are able to fabricate these nanoparticles and bypass the disadvantages of following either single approach. Monodisperse SAF nanoparticles are fabricated by means of nanoimprint lithography (NIL), a top-down process. However, the method we used to construct the template of nanopillars for NIL mainly involved the bottom-up approach, which involved the following steps; synthesis of silica nanoparticles, surface functionalization, deposition by Langmuir Blodgettry, and reactive ion etching. Scanning electron microscope (SEM) images after the etching step show that we were able to construct uniform arrays of nanopillars on a silicon wafer, thus resulting in a low-cost and production-worthy stamps for fabricating SAF nanoparticles.

Introduction:

Magnetic nanoparticles show great promise in improving medical diagnostics, treatments, and therapies due to their relatively small size in comparison to biomolecules, and their externally controlled magnetization. Particularly, magnetic nanoparticles have made significant advances in bioanalysis. In our case, the ultimate goal was to improve the process of magnetic sorting for a multiplexed bioassay [1].

This process involves a deoxyribonucleic acid (DNA) probe, which is bound to a biosensor, to hybridize with a complementary strand which is attached to a magnetic nanoparticle. The biosensor is able to detect magnetization, and therefore quantify the amount of the target DNA [2].

Our objective was to fabricate stamps for nanoimprint lithography (NIL). The stamps were fabricated according to the following steps; synthesis of silica nanoparticles, surface functionalization, deposition by Langmuir Blodgettry (LB), and reactive ion etching (RIE)—as depicted in Figure 1. Once the stamps were made, they were used in a top-down process, which involved a combination of nanoimprint lithography (NIL) and lift-off to produce SAF nanoparticles. Our group has previously demonstrated the use of LB to produce stamps and used those stamps to produce templates for SAF nanoparticle fabrication. However, the complete process to use these stamps and templates to produce the SAF nanoparticles has not yet been completed. Here, we were fabricating stamps which would be utilized in this process, so that the SAF nanoparticles could be fabricated and investigated as bioassays for cancer.

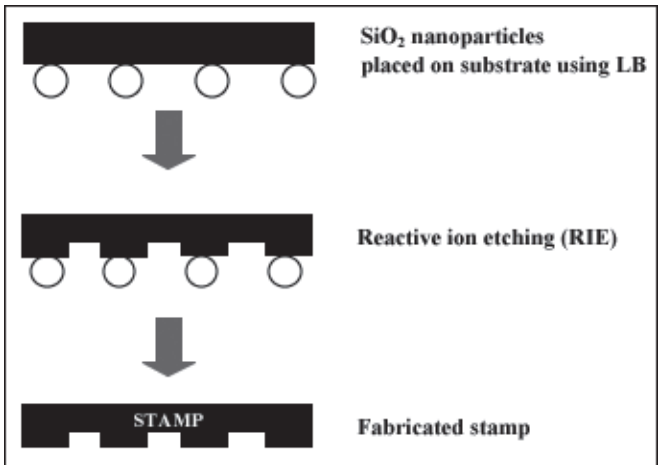

Figure 1: Fabrication of stamp for NIL and liftoff.

Herein, we report on the reactive ion etching (RIE) of the SiO_2 mask to produce stamps. The etching requires a two-step process; shrinking the SiO_2 nanoparticles, and anisotropic etching to form a stamp of uniformly distributed nanopillars.

Experimental Procedure:

The LB method was applied to pattern an etch mask. Afterwards, a reactive ion etch (RIE) was performed on the etch mask in order to obtain a nanopillar array with straight sidewalls. By using an isotropic etch with a fluorine-based

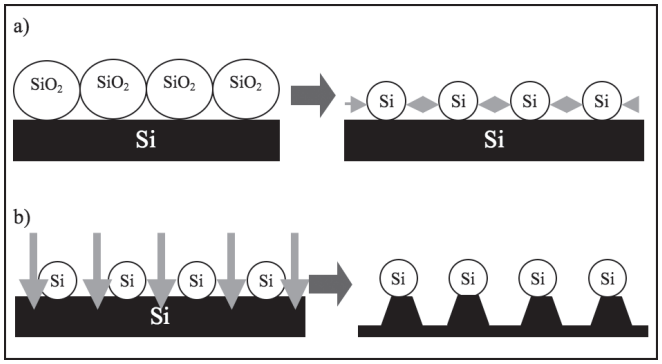

Figure 2: a) Isotropic etching of SiO_2 mask with fluorine-based etchant; b) Anistropic etching of Si with $O_2/Cl_2/HBr$.

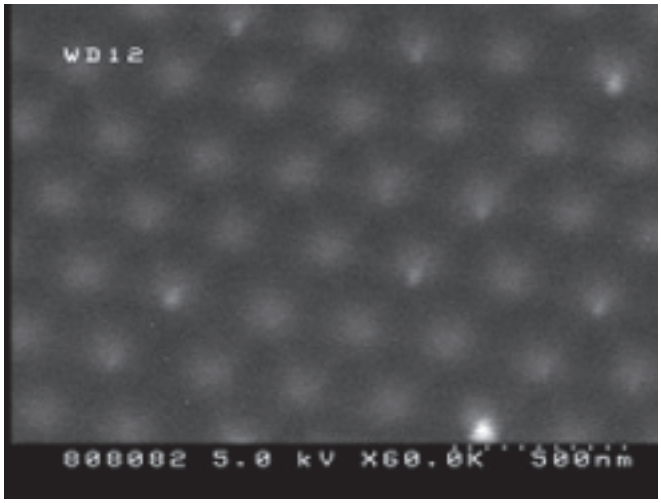

Figure 3: Planar SEM view of nanopillars of stamp.

etchant, we shrank the mask of SiO_2 nanoparticles, and then we used a combination of $O_2/Cl_2/HBr$ to achieve anisotropic etching as demonstrated in Figure 2. However, scattering caused the sidewalls to be slightly sloped. Additionally, mask erosion was caused by imperfect selectivity and physical etching. Scanning electron microscopy (SEM) was used to characterize the pillars.

Results and Conclusion:

We obtained the expected result after RIE, which were sloped nanopillars. The slight sloping might be caused by scattering as shown in Figure 3. After plasma etching the 250 nm SiO_2 nanoparticle mask, the resulting nanopillars were approximately 120 to 150 nm in diameter. Using Langmuir Blodgett, the uniformity of the size and distribution of the SiO_2 nanoparticles allowed for the etching to be uniform. Conversely, the etch mask created using spin-coated latex-spheres possessed microdomains, and after RIE, the different etching rates in and out of those domains produced an unevenly distributed and sized nanopillar stamp. Therefore the template for SAF nanoparticle fabrication produced using this technique will also be uniform in distribution and size, while the latex-sphere technique has not be uniform.

Ultimately, the stamps were fabricated for a nanoimprinting process to produce SAF nanoparticles for cancer detection. We successfully utilized a two-step etch process to create the stamp.

Future Work:

Our future plans involve ion milling the stamp to round out the pillars and ensure that the liftoff does not remove the magnetic material in the troughs. These stamps will then be used to produce SAF nanoparticles for cancer bioassay. Additionally, we can utilize the uniformity created by this general stamp fabrication technique for microfluidics and optics. The stamp may also be used as a template for other nanomaterial growth.

Acknowledgments:

I would like to thank Dr. Michael Deal, Mingliang Zhang, Ben Weil, James Conwayk, SNF Process Staff, Mihir Tendulkar, and Maureen Baran for making my research possible. This work was supported by the Stanford Nanofabrication Facility, Centers of Cancer Nanotechnology Excellence, NSF, and the National Nanotechnology Infrastructure Network Research Experience for Undergraduates (NNIN REU) Program.

References:

[1] Wei Hu, Robert J. Wilson, AiLeen Koh, Aihua Fu, Anthony Z. Faranesh, Christopher M. Earhart, Sebastian J. Osterfeld, Shu-Jen Han, Liang Xu, Samira Guccione, Robert Sinclair, Shan X. Wang, High-Moment Antiferromagnetic Nanoparticles with Tunable Magnetic Properties, Advanced Materials, 20 (2008), pp. 1479-1483.

[2] S.X. Wang, S.-Y. Bae, G. Li, S. Sun, R.L. White, J.T. Kemp and C.D. Webb, Towards a magnetic microarray for sensitive diagnostics, J. Magn. Mater. 293 (2005), pp. 731–736.