# Nanostructure Lithography for High Throughput Cancer Screening


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## Abstract:

Optofluidic surface plasmon resonance (OSPR) is a process that can be used to detect multiple biomarkers in human sera by detection of shifts in the plasmon coupling wavelength of ordered arrays of metallic nanostructures due localized changes in the refractive index of the surrounding environment. Previously these metallic structures have been grown using "nanosphere lithography," however our group has been working on a new technique. Using photoresist on a silicon or glass substrate, cylinders are first grown. After development, gold is evaporated onto the substrate. The cylinders are then removed and the nanostructures are left on the substrate. Currently structures of 550 nm can be made to a long-range order, but these results show there is potential for reaching 200 nm or lower. Future work will involve these structures being integrated into OSPR devices that can interrogate potentially thousands of disease markers in parallel, minimize handling and analysis time, will not require target labeling, and are inherently inexpensive to mass produce.


## Introduction:

Surface plasmons are electromagnetic waves that propagate along a metal/dielectric interface, such as metal/air or metal/water. The excitation of these plasmons by light is categorized as surface plasmon resonance (SPR) for planar surfaces and local surface plasmon resonance (LSPR) for nanometer sized metallic particles. Optofluidic surface plasmon resonance is a form of LSPR. Using transmitted light and metallic nanoparticles, the coupling into a plasmon mode on the surface of the metallic nanoparticle is observed, and at a specific resonant wavelength, a dip in the transmitted power occurs. This resonant wavelength is dependent on the refractive index of the surrounding media. The SPR phenomenon can be used to detect certain bio-markers in human sera samples. When these bio-markers successfully bind, the refractive index around the nanoparticle changes and a shift in the resonant wavelength is detected.

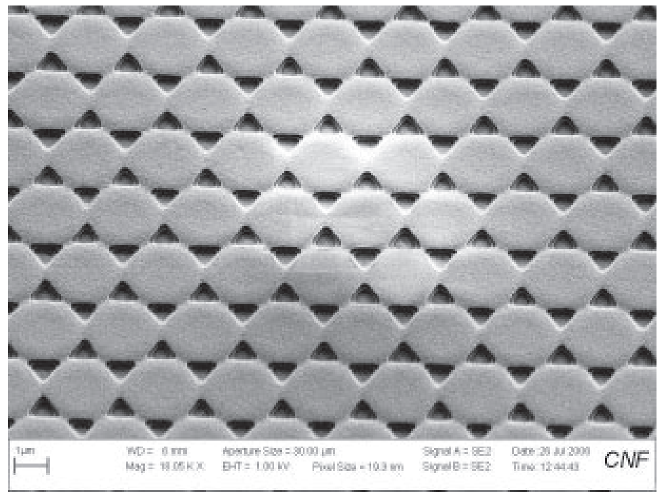


*Figure 1: Resist structures on silicon.*

There is significant difficulty in producing highly ordered metallic arrays of nanoparticles cheaply and easily. Without an economical and efficient way to produce these arrays; the cost effectiveness of an OSPR device disintegrates. Previous work attempted to use "nanosphere lithography," which used close packed polystyrene spheres on a surface. Gold was then evaporated on the surface and the spheres were eliminated. Left behind was the pattern between the spheres, which can be described as six evenly spaced triangles, centered around the gap left by the sphere. Extinction spectra of this arrangement acted as predicted, but the long range order of the arrays was not very good. Our goal was to attempt to reproduce the results from this technique using standard lithography processes.

## Experimental Procedure:

The technique used to reproduce the spheres has been used many times prior in other projects. For initial testing, a silicon substrate was used for their cost. A 500 nm layer of OiR 620-7i was hand spun on the wafer at 4000 RPM. After a pre-bake, the wafer was exposed using a GCA AutoStep 200 and a mask with 60 different circle arrays varying in size and distance apart. The circles were arranged in the same orientation as the spheres, so from a top down view, there essentially is no difference. Once exposed, the wafer was put into a YES image reversal oven. After the oven, the wafer was flood exposed at 405 nm wavelength for 60 seconds using a HTG contact aligner. The wafer is then developed in MF321 for 60 seconds leaving photoresist cylinders on the substrate, as seen in Figure 1. 5 nm of chrome and then 50 nm of gold are then evaporated on the substrate (the chrome is used for adhesion). The cylinders are finally lifted off using 1165 remover, leaving the gold arrays desired.

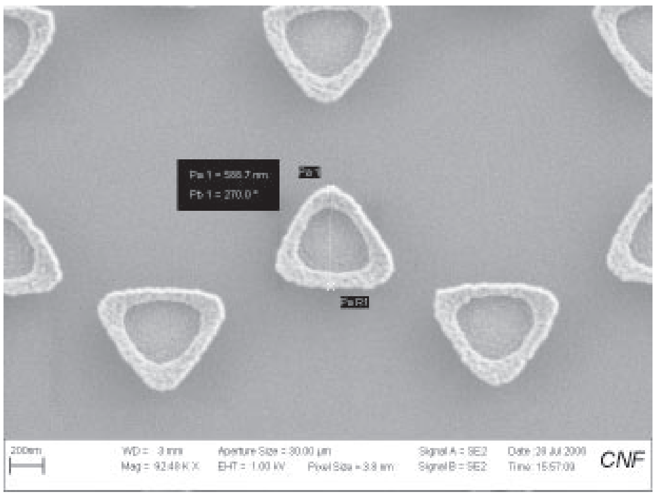


*Figure 2: Gold nanoparticles on silicon.*

## Results and Conclusions:

The previous arrays achieved by nanosphere lithography had an individual particle size of about 135 nm. The smallest particles in the the arrays our method achieved were about 550 nm in size. This result can be seen in Figure 2. Despite the larger size, our method displayed good uniformity over a long range. The nanosphere lithograpy method did not show this uniformity. Other configurations of cylinders were also tested, such as a square array of circles. Again the uniformity was good over the long range, but the size of the particles produced was much too big. One such result is shown in Figure 3. Another interesting result from our method was a fencing of the deposited gold. The height of the gold was clearly larger on the outside of the particles than the middle. This can be seen in Figure 2. The reason for this fencing was not determined; however it may help enhance the SPR effect. Although the particles created were not as small as initially hoped; this standard lithography process still has potential to bring the size closer to the nanosphere lithography.

## Future Work:

First work will need to be done to minimize the size of the nanostructures by toying around with circle size and spacing. The resist structures will have to be in the 0.6 $\mu$m to 0.8 $\mu$m range; which is a little larger the working limit of the stepper used. Next the SPR signal given by the particles will have to be maximized. This may entail changing the order of the structures, or even testing different shaped structures. Since the OSPR setup for which the arrays will be utilized is transmission based; the substrate will need to be changed to a glass one. Once all that is completed, the arrays can then be integrated into the OSPR device for more testing.

## Acknowledgements:

The author would like to acknowledge and thank Professor David Erickson and Allen Yang for their guidance and insight into the project, Garry Bordonaro and Rob Ilic from the CNF for their help with fabrication, the entire Erickson Group for their support, National Nanotechnology Infrastructure Network Research Experience for Undergraduates Program and NSF for their funding, and the rest of the CNF for allowing the opportunity to work in their clean room.

## References:

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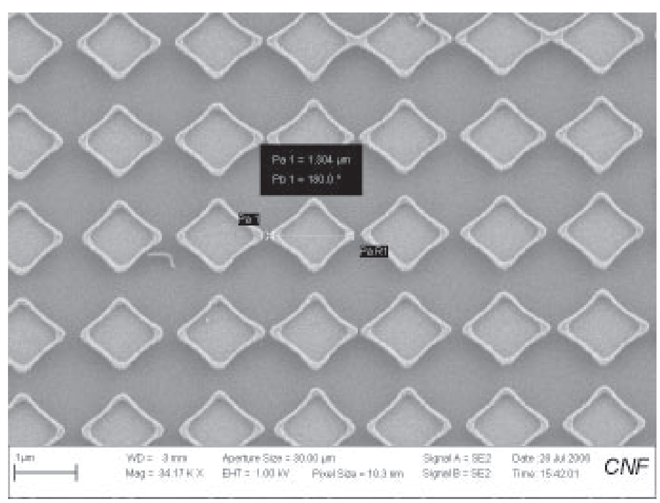


*Figure 3: Gold nanoparticles on silicon.*