Nano-Magnetic Particles for Cancer Diagnostics

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Abstract:

Nano-magnetic particles can be used to detect cancer cell markers in biological fluids. Cancer proteins are tagged with magnetic particles to identify cancer proteins since magnetism is rare in biological systems. The objective of this work was to create nano-magnetic particles of varying sizes that could be used to study the detection of different kinds of cancer cells. First, a monolayer of polymer nanospheres was spincoated onto a silicon wafer. The nanospheres were then etched and used as a mask to create a template consisting of tiny pillars. A second silicon wafer was then coated with polymethylglutarimide (PMGI) and polymethylmethacrylate (PMMA). The template was imprinted onto the PMMA layer of the second wafer to create many holes the size of the pillars. Next, the PMGI layer was etched with LDD26W to create deeper holes, followed by metal deposition. The metal fell into the holes and nanoparticles the size of the etched nanospheres were created. By varying the etching parameters it was possible to create templates with different pillar size, and by using one of the templates it was possible to create nanoparticles with the purpose of facilitating the detection of different kinds of cancer cells.

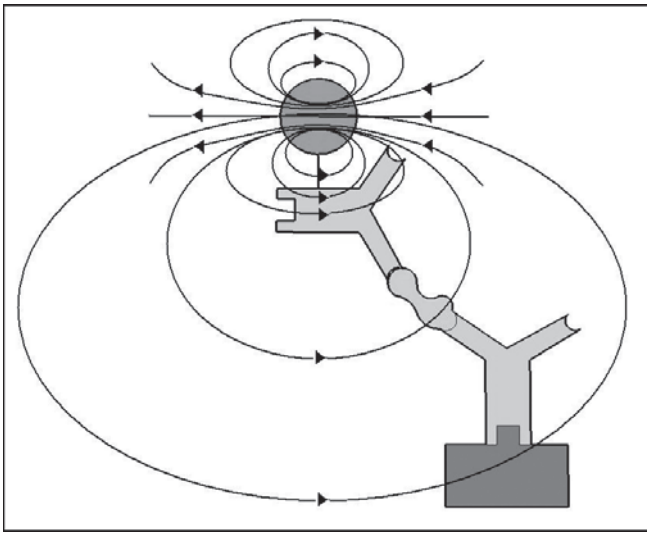

Figure 1: Sensor detecting the magnetic field of the nano-particle.

Introduction:

A silicon chip was embedded with sensors that were coated with different kinds of antibodies. When the blood sample was added, the antibodies grabbed specific cancer related proteins. A solution of nano-magnetic particles attached to antibodies was then added. The added antibodies attached to the captured proteins and a large external magnetic field was applied, which caused the nano-particles to create a stronger magnetic field. If the magnetic field created by the particles was detected by the sensor, it meant cancer related proteins had been found. Figure 1 is a good representation of how the device worked.

The nano-particle was made of five alternated layers of titanium and iron. The purpose of the surface layers of titanium was to prevent the iron layers from oxidizing. The iron layers created magnetic moments which pointed in opposite directions when no external magnetic field was applied so that the net magnetic field was zero. Because iron is a ferromagnetic element, the two layers could act as magnets when an external field was applied. The external field caused the opposing magnetic moments to gradually rotate until they were completely aligned with the external magnetic field, creating an even stronger one which was then detected by the sensor.

A self-assembly process was used rather than electron-beam lithography because the cost per unit area is about a thousand times less expensive for the self-assembly process.

Experimental Procedure:

The first step was to create a mask. First, a silicon wafer was coated with a monolayer of polymer beads that were originally 320 nm in diameter. A mixture of chlorine and oxygen gas was then used for plasma etching on the polymer beads with a resulting diameter ranging from 50 to 200 nm.

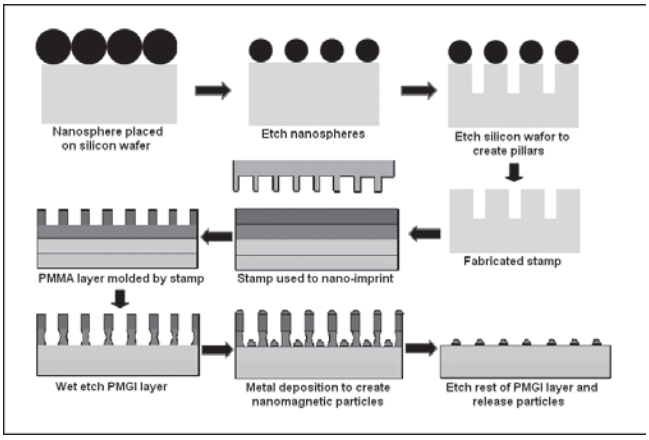

Figure 2: Nano-magnetic particle fabrication process.

The beads acted as a mask so that when the silicon was etched with a mixture of chlorine, hydrobromic acid, helium and oxygen gas, tiny pillars the size of the etched nanospheres were created. After the mask had been created, a second silicon wafer was coated with three polymer layers for the nano-imprinting step: the release layer, PMGI which was the undercut layer, and PMMA. The nano-imprinting was done at a temperature of 180°C. At this temperature, the PMMA layer became soft but the PMGI and release layers remained solid so that when pressure was applied on the wafers, only the PMMA layer was molded by the mask.

Once the mask was removed, tiny holes the size of the etched nano-spheres were left on the PMMA layer. LDD 26W was then used to wet etch the PMGI layer to create a deeper hole where the nano particle had deposited. Layers of iron and titanium were deposited into the holes through metal deposition. The rest of the PMGI layer was then etched and the nano-particles were left on the release layer, which was then dissolved in order to release the nano-particles. The fabrication process is represented in Figure 2.

Results and Conclusions:

Masks of different pillar size were created by varying the etching time. The polymer sphere etching was first done starting at 10 seconds up to 30 seconds with 5 second intervals in between. All of the samples turned out to be under etched except the 30 second etched sample. A few more masks were then made with different etching times centered at 30 seconds. Through this process of varying etching times, it was possible to successfully create two masks with optimal pillar dimensions for the creation of nano-magnetic particles at 27 and 29 seconds etching times for the polymer spheres, and a 35 second etch for the silicon wafer. The 27 second etched mask is shown in Figure 3. The diameter of the pillars is 120 nm and their height is 212 nm. A previously made mask using 390 nm polymer spheres was used to create nano particles through the nano-imprinting process. The particles are shown in Figure 4.

Future Work:

In the future, nano-particles will be created using the 27 and 29 second etched masks as well as working on finding ways by which the nano-magnetic particles can be attached to the antibodies.

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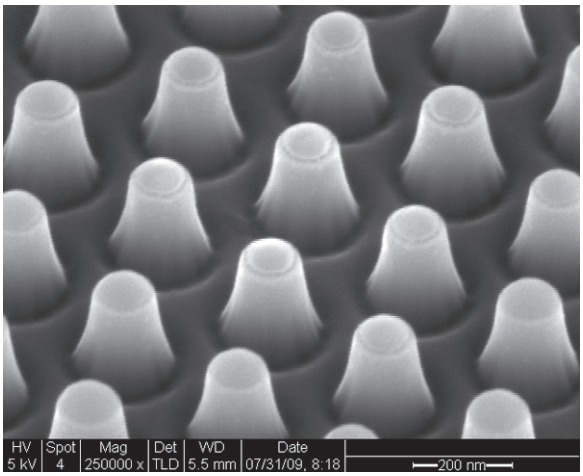

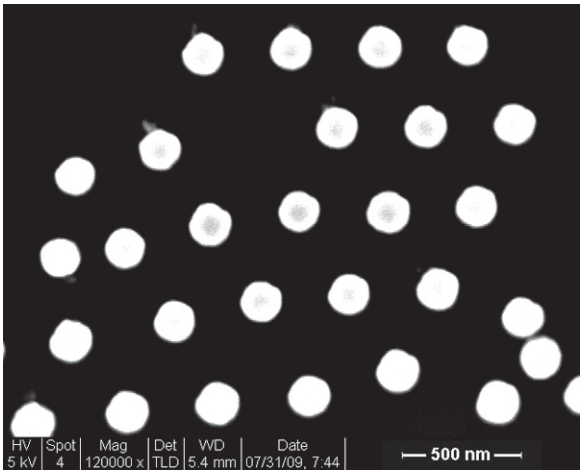

Figure 3, top: Resulting mask after a 27 second etch of the polymer nano-spheres.

Figure 4, bottom: Nano-magnetic particles created by nano-imprinting.