Artificially-Manufactured Surface-Enhanced Raman Scattering-Active Nanoparticles for Cancer Diagnostics

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Abstract:

Surface-enhanced Raman scattering (SERS) is a powerful method for examining biological samples. Antibody marked SERS-active nanoparticles can be used in human serum bioassays to detect cancer cells. In this report, we show preliminary results on artificially engineered SERS nanoparticles. These nanoparticles are designed for enhancing a local electromagnetic field and are fabricated by nanoimprint lithography, thin film deposition, and release of nanoparticles from substrate. Uniformly created nanoparticles and their enhanced Raman signals are confirmed by scanning electron microscope and Raman spectroscopy.

Introduction:

Raman scattering, which is based on the energy shift by inelastic scattering between incident photons and molecules, has long been considered to have possible diagnostic advantages. Raman scattering produces a sharp spectrum, not susceptible to photobleaching, and maintains multiplexing capabilities.

Despite the advantages, Raman scattering is weak and nearly indistinguishable from background noise. However, with the advent of surface-enhanced Raman scattering (SERS), created from the adsorption of textured, aggregate, and/or structured nanometer sized metal nanoparticles to Raman dye, signal intensity of Raman scattering can be increased several folds, making Raman dyes a feasible option as labels in immunoassays.

For achieving this benefit, many research groups have been studying the enhanced Raman scattering from clustering of nanoparticles. However, reliability and controllability of aggregated nanoparticles with rough and irregular surfaces are still under investigation [1].

Here, we performed preliminary fabrication and assessments of the validity of artificially designed SERS nanoparticles and their potential to amplify Raman scattering. Our research idea was to create SERS nanoparticles with uniform size and shape by using nanoimprint lithography. These nanoparticles also could be functionalized with antibodies for bioassay purposes.

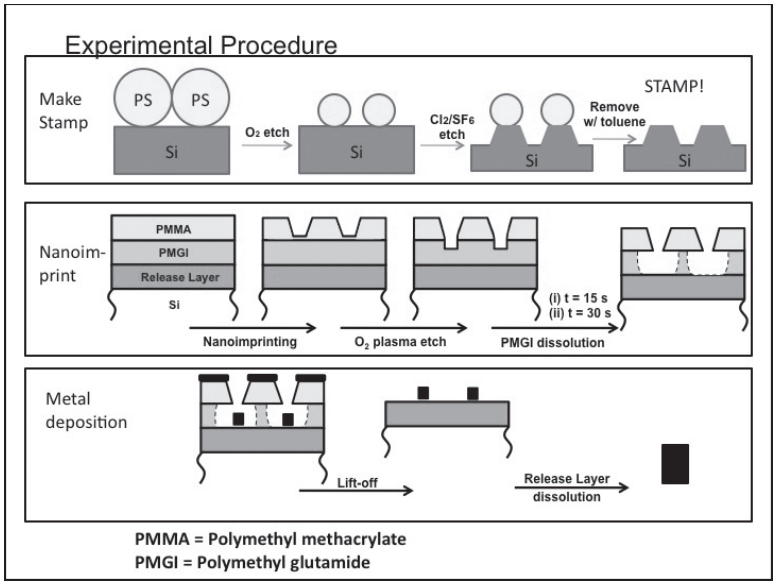
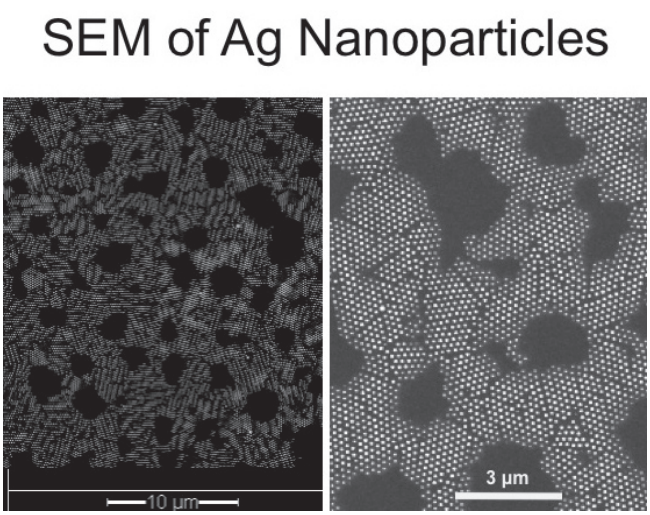
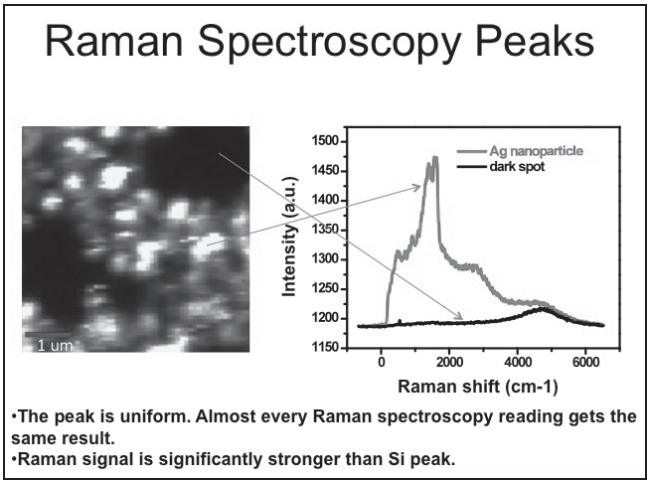


Figure 1: Nanoparticles were created using three steps: make a stamp, nanoimprint, and then metal deposition.

Experimental Procedure:

At first, a nanoimprint stamp was created by selective plasma etching of a silicon (Si) substrate with spin coated polystyrene beads as an etching hard mask. Using the anisotropic oxygen (O_2) plasma condition for reducing a size of polystyrene bead and anisotropic chlorine sulfur hexafluoride (Cl_2/SF_6) plasma condition for vertical etching of Si substrate, the





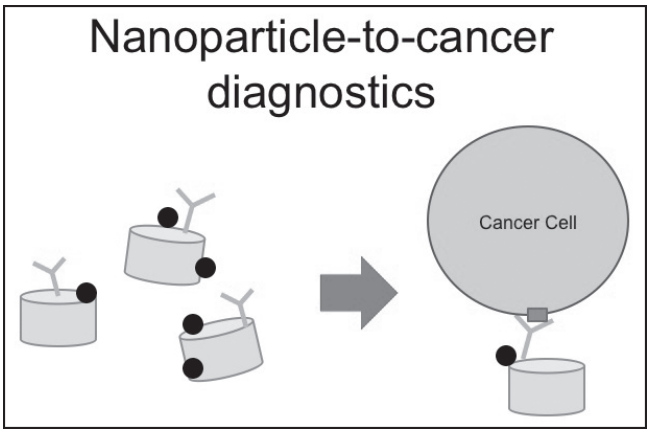


Figure 2, top: Plan view SEM images of unreleased 70 nm diameter Ag nanoparticles.

Figure 3, middle: The above Raman spectroscopy data demonstrates that the bright regions from the Raman intensity map (left) corresponds to the 1600~1700 cm^{-1} Raman peak (right), which is characteristic of methylene blue. The Raman peak reading was also uniform and reproducible.

Figure 4, bottom: The diagram demonstrates how Ag nanoparticles with Raman dye (small circles) and antibodies (y-shaped structures) can localize to cancer cell markers.

nanoimprint stamp was fabricated. Once the stamp was created, nanoimprint lithography, O_2 plasma etching, PMGI dissolution, and silver (Ag) film deposition were carried out sequentially for creating Ag nanoparticles, as depicted in Figure 1. Ag nanoparticles were then submerged overnight in a methylene blue (Raman dye) solution. Scanning electron microscopy (SEM) and Raman spectroscopy were used to characterize the particles and assess the SERS, respectively.

Results and Conclusions:

We were able to create a nanoimprint stamp with a 70 nm sized nano-dot array by studying and optimizing etching conditions for polystyrene and Si substrates. With this stamp, uniform Ag nanoparticles with 70 nm diameter and 30 nm thicknesses were successfully created (Figure 2). The preliminary Raman spectroscopy analysis demonstrated the presence of a huge Raman signal enhancing from the Ag nanoparticles. In addition, the Raman signal peak was uniform and reproducible (Figure 3).

Future Work:

The next step will be to functionalize the SERS nanoparticle surface with various antibodies and examine biological samples (Figure 4). We will also investigate more techniques to enhance Raman scattering, including creating surface roughness and irregularities.

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References:

[1] K.Kneipp, M. Moskovits, H. Kneipp (Eds): Surface-Enhanced Raman Scattering- Physics and Applications. Topics Appl. Phys. 103, 409-426 (2006) Springer-Verlag Berlin Heidelberg. 409-424.