Highly reliable SERS substrate based on plasmonic hybrid coupling between gold nanoislands and periodic nanopillar arrays

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Abstract: To improve both sensitivity and reliability, a hybrid SERS substrate of combining gold nanoislands (GNI) with periodic MgF$_2$ nanopillar arrays was successfully developed. SERS detection performance of the proposed substrates was evaluated in terms of enhancement effect, signal-to-noise ratio (SNR), linearity, reproducibility and repeatability, and compared with the performance of a conventional SERS substrate based on GNI. Experimental and simulation results presented that significant improvement of SERS intensity and SNR by more than 3 times and a notable reduction in relative standard deviation were obtained. We hope that the suggested SERS platform with unique advantages in sensitivity and reliability could be extended to point-of-care detection of a variety of biomolecular reactions.

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1. Introduction

Since Raman scattering effect was discovered in 1928 [1], it has been utilized for qualitative and quantitative analyses in a variety of fields through observation of molecular-specific vibrations [2–6]. In particular, surface-enhanced Raman spectroscopy (SERS), which can be activated by employing metallic nanostructures [7], has been developed with an aim of dramatically enhancing weak Raman signals via localized surface plasmon resonance (LSPR) phenomena. While metallic nanoparticle-based SERS measurement may improve Raman signal intensity with a high signal-to-noise ratio (SNR), this method often suffers from low reproducibility due to aggregation and/or non-uniform distribution of nanoparticles [8].

Recently, several strategies have been attempted to realize high reproducibility as well as significant sensitivity enhancement in SERS measurements using periodic and uniform metallic nanostructures [7,9–11]. For example, Deng et al. reported that quasi-3D gold plasmonic nanoarrays allow SERS-based optofluidic microsystems to have better reproducibility and detection sensitivity [9]. Hong et al. argued that SERS substrates with periodic silver nanogratings are advantageous for sensitive and reliable sensors owing to their uniform feature [10]. Thus, we expect that SERS substrates with periodic and uniform nanostructures will be able to provide a potential for reliable SERS performance.

It is also noteworthy that metallic nanoislands have been applied to SERS substrates due to nanogap-rich structure [12–15] although their distribution is typically non-uniform. Simple
yet efficient fabrication techniques, such as repeated deposition and annealing [12,13], repeated solid-state dewetting [14] and sputtering [15] have been introduced to implement nanoislands in a large area. Because high-density hot spots obtained by well-arranged metallic nanoislands are essential for ultrasensitive detection [16,17], unique design of combining nanoislands with a periodic nanostructure could be an alternative for overwhelming the performance limit of conventional SERS approaches.

Hence, in this study, we propose a sensitive and reliable SERS substrate consisting of gold nanoislands (GNI) and periodic MgF$_2$ nanopillar arrays. First, we optimize SERS enhancement of GNI by controlling the GNI geometry which depends on the deposition time. The optimized structure is then applied to periodic MgF$_2$ nanopillar arrays. SERS detection characteristics of GNI-based and GNI/MgF$_2$-based SERS substrates are compared theoretically and/or experimentally in terms of field and signal enhancement effects, SNR, linearity, reproducibility and repeatability. In short, it is believed that hybrid nanostructures by a combination of GNI and periodic MgF$_2$ nanopillar arrays can be applied to highly sensitive and reliable SERS detection platforms.

2. Materials and methods

2.1. Fabrication of GNI/MgF$_2$-based SERS substrate

Figure 1 shows the fabrication processes for the suggested SERS substrate with GNI and periodic MgF$_2$ nanopillar arrays. Si wafer surface was cleaned with an organic cleaning solvent in order to remove organic contaminants. Detailed organic cleaning procedure is as follows; i) ultrasonic cleaning in 100% ethyl alcohol for 10 min, ii) rinsing with distilled water and ethyl alcohol for 5 min each and iii) drying with nitrogen gas. For the fabrication of the GNI/MgF$_2$-based SERS substrate, a 200-nm thick polymethyl methacrylate (PMMA) layer was first spin-coated on the cleaned Si wafer surface at 1,000 rpm for 2 min and cured at 170 °C for 5 min. Then, a 200-nm thick UV-curable resin layer was spin-coated on the PMMA layer at 2,000 rpm for 1 min and cured at 170 °C for 5 min [Fig. 1(a)]. Second, nanohole arrays with 300-nm diameter and 530-nm period were patterned on the resin film using nanoimprint lithography (NIL) with a polyurethane acrylate (PUA) mold replicated from the Si master mold. The PUA mold was coated by trichlorosilane (97%, Sigma-Aldrich) before the NIL to prevent adhesion to the resin layer [18]. In order to produce the nanohole array pattern, the PUA mold was pressed onto the resin layer for 3 min under a pressure of 2 MPa using a nanoimprinter (NIL-8 imprinter, Obducat), and then the pressed resin was UV-irradiated for 2 min for curing [Fig. 1(b)]. Residues after nanoimprinting were removed by a descum process using a plasma asher (ALA-0601E, AMS). To prepare periodic MgF$_2$ nanopillar arrays on the cleaned Si wafer surface, the nanohole array pattern was transferred into the PMMA layer by O$_2$ reactive ion etching (RIE) (Versaline, Plasma-Therm) [Fig. 1(c)]. Then, 10-nm thick Ti layer (adhesion layer) and 50-nm thick MgF$_2$ layer were sequentially deposited by electron beam evaporation at a deposition rate of 3 Å/s [Fig. 1(d)]. After the deposition was complete, a lift-off process was performed by sonication in acetone solution for 1 min to remove residual PMMA and resin layer [Fig. 1(e)]. Subsequently, rinsing was performed with distilled water and ethyl alcohol for 5 min each, followed by drying with nitrogen gas. Finally, 4-nm thick GNI was deposited by electron beam evaporation at a deposition rate of 0.2 Å/s [Fig. 1(f)]. Again, rinsing was performed with distilled water and ethyl alcohol sequentially, followed by drying with nitrogen gas. The total effective pattern area of the fabricated GNI/MgF$_2$-based SERS substrate was about 10 × 10 mm$^2$. To verify the effect of periodic MgF$_2$ nanopillar arrays on SERS enhancement, the SERS substrate with 4-nm thick GNI (GNI-based SERS substrate) was also fabricated and compared. The composition analysis of both SERS substrates was confirmed by EDS measurements (Table 1).
Fig. 1. Fabrication processes for GNI/MgF$_2$-based SERS substrate: (a) spin-coating and curing of PMMA and resin layers, (b) imprinting of the nanohole array pattern onto the resin layer by the PUA mold, (c) transferring of the nanohole array pattern into the PMMA layer by RIE, (d) fabrication of MgF$_2$ nanopillar arrays by electron beam evaporation, (e) lift-off of the residual PMMA and resin layers, and (f) GNI deposition by electron beam evaporation.

Table 1. EDS data of both types of SERS substrates

| Element | Weight (%) | Element | Weight (%) |
|---------|------------|---------|------------|
| Si      | 72.10      | Si      | 95.64      |
| Au      | 3.84       | Au      | 4.36       |
| C       | 19.09      |         |            |
| O       | 2.97       |         |            |
| F       | 2.00       |         |            |

2.2. SERS experiment

We investigated the detection performance of GNI/MgF$_2$-based SERS substrate in terms of signal enhancement effect, SNR, linearity, reproducibility and repeatability and compared with that of GNI-based SERS substrate. For this purpose, 4-aminobenzenethiol (4-ABT) was used as a Raman probe molecule because the thiol group in 4-ABT allows a specific binding with gold. SERS substrates were immersed in various concentrations of 4-ABT solution (from 1 mM to 10 nM) for 24 h to immobilize 4-ABT onto the substrate surface. Non-immobilized 4-ABT molecules were removed by rinsing with distilled water and ethyl alcohol. SERS signals of 4-ABT were measured using a confocal Raman microscope system, which consists of microscope with 100× objective lens (BX43, Olympus), 785-nm laser source (IO785MM0350MF, Innovative Photonic Solutions), Czerny-Turner spectrograph (SR-303i-A, Andor Technology) and low dark current deep-depletion CCD (iVac, Andor Technology). Five GNI-based and five GNI/MgF$_2$-based SERS substrates were fabricated and SERS signals were measured at 10 different points for each sample within the range of 600 to 1800 cm$^{-1}$ with the resolution of 2 cm$^{-1}$ and the acquisition time of 10 s. SERS mapping experiments were also performed in a square of 2 × 2 mm$^2$ with a 100-µm pitch using 1-mM 4-ABT for both SERS substrates. After the SERS measurements, the
instrument and CCD noise signals were simply subtracted from the raw SERS signals. Then the Savitzky-Golay smoothing and polynomial baseline correction were performed sequentially [19].

2.3. Computational electrodynamics

To investigate the effect of periodic MgF$_2$ nanopillar arrays on SERS characteristics, the electromagnetic (EM) field distribution near the surface of SERS substrates was theoretically calculated using near field simulation of finite-difference time-domain (FDTD) method. This work is based on the assumption that near field amplification generated by an excitation of LSPR is highly associated with enhanced Raman signals. In this simulation, 4-nm thick GNI was approximated as a cylinder with a diameter of 30 nm and a period of 40 nm for simplicity.

3. Results and discussion

Figures 2(a)-(e) present FE-SEM images on the morphological feature of GNI-based SERS substrate [Figs. 2(a)–2(c)] and GNI/MgF$_2$-based SERS substrate [Figs. 2(d) and 2(e)]. The size of GNI was increased with the deposition time from 100 to 300 s as shown in Figs. 2(a)–2(c). While the results are not shown here, it was found that the GNI layer was changed into a planar gold film for deposition time over 500 s and the deposition rate of 0.2 Å/s. The thickness of GNI was estimated to be 2 nm for 100 s, 4 nm for 200 s and 6 nm for 300 s, respectively. From the SERS experiments with 4-ABT Raman probe molecule, the characteristic peaks of 4-ABT [20,21] were measured in Fig. 2(f) and 4-nm thick GNI-based SERS substrate displayed the highest SERS enhancement among three types of GNI-based SERS substrates. Note also that no Raman peak was obtained for the case of a bare gold film.

SERS enhancement is generally dependent on geometric parameters of metallic nanostructures and hot spots, such as size and thickness of nanostructure, nanogap distance, and effective nanogap density. In our experiments, 4-nm thick GNI structure of Fig. 2(b) was chosen as an optimum due to the largest SERS peak intensity, compared to the other two cases. We may guess that the limited improvement of SERS characteristics was attributed by a wider and a shallower nanogap for 2-nm thick GNI and by a lower nanogap density for 6-nm thick GNI [13].
In Fig. 2(d), the optimal GNI structure was successfully deposited onto periodic MgF$_2$ nanopillar arrays of 300-nm diameter and 530-nm period. From the SERS measurements of 4-ABT, we found that the SERS peak intensity at 1076 cm$^{-1}$ of GNI/MgF$_2$-based SERS substrate was improved by more than 3 times compared with the best data of GNI-based SERS substrate [Fig. 2(f)]. Raman signal enhancement by the hybrid nanostructure combining GNI and periodic MgF$_2$ nanopillar arrays appears to be associated with additional EM field amplification by coupling of EM waves at the metallic and dielectric nanostructures [22].

Approximated FDTD simulation models were designed to demonstrate the effects of EM wave coupling at the SERS substrates. The simulation results in Fig. 3 show that EM field were strongly amplified at the edges of GNI and the maximum amplitude value was much larger for the GNI/MgF$_2$-based SERS substrate. In addition, to present an effect of incidence angle on the EM field enhancement, FDTD calculations were performed for different incidence angles of 30°, 60°, and 90°. It was found in Fig. 3 that the maximum amplitude value does not change significantly according to an incidence angle. Summation of EM field amplitude at the surface reaction area was, respectively, calculated to be 321 for the angle of 30°, 324 for the angle of 60°, and 328 for the angle of 90° for GNI-based SERS substrate, while 1,730 for the angle of 30°, 1,740 for the angle of 60°, and 1,748 for the angle of 90° for GNI/MgF$_2$-based one. This implies that the field enhancement effect by coupling of EM waves at the metallic and dielectric nanostructures is still dominant by more than 5 times regardless of an incidence angle. The obtained FDTD data were consistent with overall trends of SERS experimental results in Fig. 2(f).

Detection performance of the 4-nm thick GNI-based SERS substrates with and without MgF$_2$ nanopillar arrays was evaluated by analyzing the SERS peak intensities for concentrations of 4-ABT in the range from $10^{-8}$ to $10^{-3}$ M as shown in Figs. 4(a) and 5(a). For both types of SERS substrates, the characteristic peak at 1076 cm$^{-1}$ of 4-ABT assigned to the a$_1$-type vibrational mode were observed.

First, the SNR value of SERS signal was calculated by the following equation [23],

$$SNR = \frac{I}{\sigma_I}$$
where $I$ and $\sigma_I$ are the average SERS peak intensity and its standard deviation (SD). At a very low concentration of $10^{-8}$ M, SNR was determined to be 3.1 ($I = 211$ and $\sigma_I = 68$) for GNI-based SERS substrate and 10.6 ($I = 330$ and $\sigma_I = 31$) for GNI/MgF$_2$-based one, presenting 3 times SNR enhancement.

Second, we evaluated the linearity characteristic between SERS peak intensity and concentration of 4-ABT. In a linear regression analysis, the slope ($S$) denotes a detection sensitivity and the linear correlation coefficient ($R^2$) means the degree of linearity. For GNI-based SERS substrate, the slope of $S = 276.68$ and the linear correlation coefficient $R^2 = 0.9542$ were found [Fig. 4(b)]. In particular, the SERS peak intensity at 1076 cm$^{-1}$ peak became saturated when the 4-ABT concentration reached $10^{-6}$ M. This saturation can be explained by limited capacity with relatively low surface area to accommodate 4-ABT molecules [24] and nonlinear effects driven by high laser power density and plasmon field enhancement [25]. On the other hand, for the GNI/MgF$_2$-based SERS substrate, the SERS peak intensity at 1076 cm$^{-1}$ peak was increased more rapidly in a whole concentration range of 4-ABT. Of importance is that larger slope of $S = 621.66$ and better linear correlation coefficient $R^2 = 0.9655$ were obtained [Fig. 5(b)], which implies that the proposed hybrid SERS substrate is more sensitive and quantitative in a wide range of target concentrations.

Finally, in terms of reproducibility and repeatability, SERS mapping measurements with a 100-µm pitch in a square area of $2 \times 2$ mm$^2$ and 225 repeated measurements at a fixed point were performed. The mapping images [Figs. 4(c) and 5(c)] and graphs of data plot [Figs. 4(d) and
Fig. 5. Proposed GNI/MgF$_2$-based SERS substrate; (a) SERS spectra at various concentrations of 4-ABT, (b) linear regression analysis of SERS peak intensities at 1076 cm$^{-1}$ at various concentrations of 4-ABT, (c) SERS mapping of 1-mM 4-ABT in a square of 2 × 2 mm$^2$ and (d) reproducibility with RSD = 2.5% at 1076 cm$^{-1}$ peak.

5(d)] reconstructed from 400 SERS signals exhibit that GNI/MgF$_2$-based SERS substrate had better reproducibility with relative standard deviation (RSD) of 2.5% than the GNI-based case of RSD = 4.0%. Furthermore, in the repeatability test by 225 SERS signals, RSD value was decreased from 3.1% to 2.3%, which verifies a significant repeatability improvement (Fig. 6). As a result, it is expected that the proposed SERS substrate platform of combining GNI and periodic MgF$_2$ nanopillar array has a great potential for a highly sensitive, quantitative and reliable SERS signal detection towards a variety of point-of-care diagnostic applications.

Fig. 6. Intensity variations for 225 SERS signals of 1-mM 4-ABT at the same measurement position for GNI alone (blue) and GNI/MgF$_2$ case (red). Each solid line and filled area is the average and standard deviation.
4. Conclusion

In this study, we proposed a novel SERS substrate by combing GNI with periodic MgF$_2$ nanopillar array to provide a notable improvement in SERS detection performance. We found from theoretical and experimental results that the combination of 4-nm thick GNI and periodic MgF$_2$ nanopillar array presented more than 3 times enhancement in sensitivity and SNR as well as a significant advance in the linearity and reproducibility characteristics, compared to a conventional GNI-based SERS substrate. We believe that the proposed research is an important step towards implementing the SERS platform with high reliability and stability for sensitive detection of biomolecular reactions.

Funding

National Research Foundation of Korea (2017R1A2B4012428, 2018R1C1B6008568, 2019R1A2C2091068).

Disclosures

All authors declare no conflicts of interest or financial relationships to disclose.

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