광 유체 CD 플랫폼을 통한 표면 증강된 라만스케터링의 신호 향상

Signal Enhancement of Surface-enhanced Raman Scattering via Optofluidic CD

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1. Introduction

Surface-enhanced Raman scattering (SERS) has provided the opportunities to design ultrasensitive biosensors for effective label-free biomolecular assays. Furthermore, owing to the versatility of Raman spectroscopy such as a nondestructive approach to chemical analysis and the fingerprint characteristics of biomolecules, a wide variety of applications of SERS have been demonstrated in medicine, biochemistry, electrochemistry, and ultrahigh vacuum (UHV) surface science[1-3]. However, the development of robust methods for integrating SERS with reliable and reproducible on-chip biosensing systems being capable of easy sample preparation and dynamic analysis of target molecules is still challenging[4-6]. Here we report a optofluidic SERS on Compact Disk (CD) platform (this platform is referred to optofluidic SERS-CD platform in this letter), which is designed to preconcentrate molecule of interest via simply repeating 'filling-drying' cycles of molecular solutions for SERS signal amplification. We demonstrate the promising capability of the preconcentration using this SERS-CD platform through SERS intensity of rhodamine 6G (R6G) with concentrations ranging from 1 μM to 1 nM.

Assembled metal nanoparticles have so far been successfully applied to a SERS substrate. For on-chip SERS-active sites, accumulated gold nanoparticles in nanochannel and Ag/PDMS nanowell structures were also used. In this study, we introduce a controlled precipitation of gold nanoparticles (GNPs) by $CuSO_4$ as an excellent and suitable SERS substrate for microfluidic CD platform. It was found that our SERS substrate has both high sensitivity (down to 1 nM detection of R6G) and uniformity (only 25% variation in SERS signal at 4 inch wafer scale CD platform level). In order to verify the reliability and stability of our GNP aggregates-based SERS substrates, we investigated SERS spectra from different positions within a spot (*position-to-position*), different spots on the same CD (*spot-to-spot*) as well as on different CDs (*batch-to-batch*).

2. Conceptual overview

The basic concept of our optofluidic SERS-CD platform including the preconcentration mechanism for the SERS spectra amplification is illustrated in Fig. 1. The SERS-CD platform consists of hierarchically-aligned microfluidic channels with radial direction (Fig. 1a). Sample loaded into either one main intake (the center of the SERS-CD platform) or twelve secondary inlets (for various molecular solutions or concentrations) can be uniformly dispensed to SERS-active sites at the end of each channel and analyzed by SERS. High-throughput homogenous sample preparation coupled with identical SERS detection sites enables us to analyze the sample reliably. Moreover, the injection of the sample solution and drying the solution onto the SERS-active sites from the main intake can be easily repeated to preconcentrate the target molecule for SERS enhancement (Fig. 1b-II, III). In general, the intensity of surface-enhanced Stokes Raman scattering, $I_{SERS}(\nu_s)$, can be estimated by,

$$I_{SERS}(\nu_s) \propto N_M \cdot \left|A(\nu_L)\right|^2 \cdot \left|A(\nu_s)\right|^2 \cdot \sigma^R_{ads} \qquad (1)$$

where N_M is the number of molecules involved in the SERS process, σ^R_{ads} is the Raman cross section of the adsorbed molecule, and $A(\nu_L)$ and $A(\nu_s)$ are the field enhancement factors at the laser and Stokes frequency, respectively[2]. Among these variables, N_M is the only flexible and unlimited control parameter for the signal enhancement because the variables other than N_M are intrinsic factors which are almost fixed for a given SERS-active substrate and a target molecule. Therefore, as the proposed 'filling-drying' cycles progress, we can accomplish the facile preconcentration of target molecule (Fig. 1b-IV) in order to significantly enhance the SERS signal (Fig. 1c).

3. Material and method

3.1 Optofluidic SERS-CD platform

We fabricated a optofluidic SERS-CD platform consisting of a single main intake, 12 secondary inlets, and 84 SERS-active detection spots (Fig. 2a). Venting outlets were fabricated above the detection spots in order to reduce the pressure drop during preconcentration. The SERS-CD platform was constructed using standard soft lithography techniques (Fig. 2b).

3.2 Precipitation of GNPs for SERS substrate

$CuSO_4$ was chosen as an aggregation agent, since the higher charge on Cu^{2+} induces stronger aggregation than monovalent cations, and halide anions strongly bind to the surface of noble nanoparticles, which repels analytes.

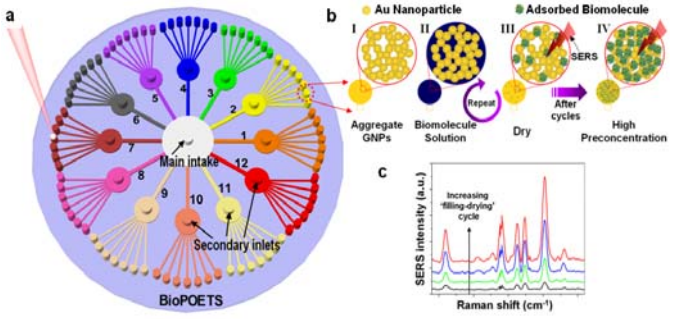

Fig. 1 (a) The schematic illustration of optofluidic SERS-CD platform with high-throughput sample preparation. (b) The mechanism of preconcentration (c) As the 'filling-drying' cycle is progressed, the SERS intensity can be enhanced due to the preconcentration of the target molecule.

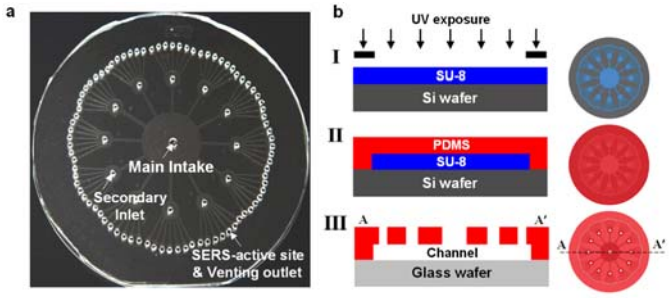

Fig. 2 Design and fabrication of optofluidic SERS-CD platform. (a) Photograph of a SERS-CD platform (b) I: Patterning of a mold for microfluidic channels and chambers by photolithography, II: Mold transfer with PDMS, III: Punching of intakes and outlet holes and bonding of the PDMS replica to the glass wafer (4 inches).

In a typical experiment, the SERS substrates were formed at the end of every 84 microfluidic channels by loading the mixed solution (v/v 50:1) of 80 nm diameter GNPs and 10 mM $CuSO_4$ in the main intake (note, during this process, all secondary intakes were covered with glass slides to prevent the loading solution from flowing out). Pressure applied to the main intake forced the solution to form droplets (~ 4 μL) at the end of each channel (Fig. 1a).

We used commercially available Raman Systems R-2001 (Ocean Optics Inc.) which is a fully integrated Raman analyzer for real-time qualitative and quantitative spectral analysis with a 785 nm, 90 mW diode laser. Because of the large beam size of the laser (about 200 μm in diameter), samples and SERS substrates were not burned under 300 W/cm^2 laser power. The acquisition time was 10 sec. In order to confirm the reliablity and the reproducibility of our SERS-CD platform, we measured SERS signals from at least 5 different positions in a spot, 3 different spots in one CD and two different CD platforms (totally, over 30 tests) for each investigation.

4. Results

Fig. 3 shows the SERS spectra of 500 nM R6G as a function of 'filling-drying' cycle. Minor background signals from the glass substrate have been subtracted. As shown in Fig. 3a, the observed Raman bands were in agreement with the bending and stretching modes of R6G[7]As the cycle increases, the SERS signals of R6G were significantly amplified. After 9 cycles, SERS signals of 500 nM R6G were enhanced by 10-fold than that of 1 cycle. The SERS intensities at 1509 cm^{-1} for order-of-magnitude changes of R6G concentrations linearly augmented with the number of 'filling-drying' cycle, which verifies high reliability of our SERS-CD platform as well as the stability of the SERS-active sites (i.e., the aggregated GNPs). It is noteworthy that even 1 nM of R6G could be detected after 30 cycles (see Fig. 3b). We can expect that our SERS-CD platform is able to apply to much lower sample concentaration. Considering that the required volume of the sample per one cycle and one SERS-site is as low as 2 μL (only 60 μL for even 30 cycles), our SERS-CD platform with 'filling-drying' preconcentration can be superior or comparable to other SERS-based biomolecule detection systems because the amount of a biological sample (both concentration and volume) required for analysis is very critical in molecular biology and medicine.

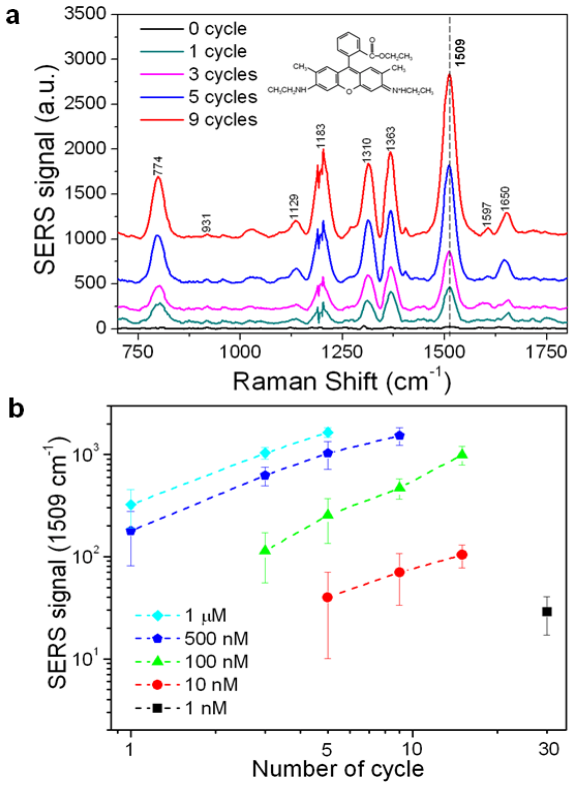

Fig. 3 SERS intensities with 'filling-drying' cycles. (a) SERS spectra of 500 nM R6G molecules as a function of the 'filling-drying' cycle by our optofluidic SERS-CD platform. (b) SERS signal at 1509 cm^{-1} of R6G molecules with concentrations from 1 μM to 1 nM. After 30 cycles, the clear and high SERS signal of R6G molecules with 1 nM was measured.

4. 결론

In conclusion, we have fabricated optofluidic SERS-CD platform which is capable of high-throughput biological analysis and additional SERS signal amplification via optofluidic CD-based preconcentration. By increasing the number of R6G molecules via simple 'filling-drying' cycle, the SERS signal of R6G linearly augmented, which suggests the high fidelity of our SERS-CD platform.

후기

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