Optofluidic SERS chip with plasmonic nanoprobes self-aligned along microfluidic channels\textsuperscript{†}

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This work reports an optofluidic SERS chip with plasmonic nanoprobes self-aligned along microfluidic channels. Plasmonic nanoprobes with rich electromagnetic hot spots are selectively patterned along PDMS microfluidic channels by using a Scotch tape removal and oxygen plasma treatment, which also provide the permanent bonding between PDMS and a glass substrate. A silver film with an initial thickness of 30 nm after oxygen plasma treatment creates nanotips and nanodots with a maximum SERS performance, which were successfully implanted with microfluidic concentration gradient generators. The novel device enables the label-free and solution-phase SERS detection of small molecules with low Raman activity such as dopamine at micromolar level in flow. This optofluidic SERS chip can be readily expanded for microfluidic networks with diverse functions for advanced optical biochemical assays.

Self-aligned plasmonic nanoprobes within microfluidic channels

The device fabrication is based on soft-lithography, the selective patterning after metal deposition, and the oxygen plasma treatment (Fig. 2a). The master template for the microfluidic channels was fabricated on a silicon wafer by using conventional photolithography (SU-8 2010 photoresist, MicroChem, 20 μm in height). A PDMS elastomer (Sylgard 184, Dow Corning) was prepared by mixing the base and curing agent in a 10:1 weight ratio and then the microfluidic channels were replicated from the master. A thin silver film was thermally evaporated on both the inside and outside surfaces of the PDMS channels. The left image in Fig. 2b shows the PDMS slab fully covered with the silver film. The silver film on the outside surface was successfully removed by using adhesive Scotch tape. This simple step selectively and completely removes the undesired silver film for stable microfluidic bonding. The middle image in Fig. 2b shows the silver film self-aligned along the microfluidic channels and

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\textsuperscript{*} This work presents an optofluidic SERS chip with plasmonic nanoprobes on microfluidic channels. The plasmonic nanoprobes are selectively patterned on the polydimethylsiloxane (PDMS) microfluidic channel walls, which allow conformal contact between the PDMS slab and a glass substrate for strong irreversible bonding (Fig. 1).

Introduction

Optofluidic platforms have been extensively used to provide unique advantages for advanced optical biochemical assays. Combining photonics and microfluidics opens up new opportunities for trapping, manipulation, imaging, and sensing of biochemical targets.\textsuperscript{1–3} Recent advances in micro and nanofabrication enable microfluidic integration of state-of-the-art architectures such as optofluidic lasers, waveguides, photonic crystals, and plasmonic nanosensors. In particular, plasmonic nanostructures stimulate highly sensitive label-free bioassays based on surface enhanced Raman scattering (SERS) or metal enhanced fluorescence (MEF).\textsuperscript{4,6}

For the last decade, plasmonic nanostructures have enabled highly intense SERS. Localized electric fields near rough metal nanostructures can extraordinarily enhance Raman scattering signals, which serve as biochemical fingerprints.\textsuperscript{7–9} Optofluidic SERS has been recently performed by introducing plasmonic nanoparticles or by using SERS substrates inside microfluidic channels to create electromagnetic hot spots for label-free biomolecular detection or immunoassays.\textsuperscript{10–12} The nanoparticles in flow substantially affect the signal variation of SERS due to a non-uniformity of the interstitial gap spacing or agglomeration of nanoparticles depending on the ionic strength of a solution medium.\textsuperscript{13} In contrast, metal nanostructures on a substrate can intrinsically overcome this problem for highly stable SERS measurements.\textsuperscript{14,15} However, nanotexturing of plasmonic nanostructures inside microfluidic channels is still challenging and complicated for low cost nanofabrication and reliable microfluidic packaging.\textsuperscript{16–18}

This work reports an optofluidic SERS chip with plasmonic nanoprobes self-aligned along microfluidic channels and
the inset image shows the close-up view. The silver-removed region offers a bare PDMS surface, suitable for permanent bonding between the PDMS slab and a glass substrate. Next, both the PDMS channels and a glass substrate were simultaneously treated with oxygen plasma and brought into contact to bond together (Plasma-finish GmbH V6-G, plasma power of 300 W, oxygen flow rate of 80 sccm, operating pressure of 80 Pa, and a 30 second process time). The siloxane bond between the PDMS and the glass provides a robust microfluidic chip without solution leakage. The inlets and an outlet were punched before the oxygen plasma treatment (see right image in Fig. 2b). In particular, this plasma treatment not only seals the chip but also transforms the thin silver film into plasmonic nanoprobes for highly intense SERS.

SERS performance of plasmonic nanoprobes

The oxygen plasma treatment can simply induce plasmonic nanoprobes with rich hot spots by fracturing the thin silver film. In this experiment, the oxygen plasma treatment conditions were set to be constant to offer a siloxane bond, therefore, the topological characteristics of the plasmonic nanoprobes were controlled by the initial thickness of the silver film for...
high SERS performance. Distinct from the initial thickness of 10 nm inducing small nanoisland arrays, the initial thickness of 30 nm provides roughened nanotextures with sharp nanotips and nanodots as shown in the scanning electron microscope (SEM) image of Fig. 1. The thicker initial film (60 nm) provides a less fractured surface than the 30 nm film after the oxygen plasma treatment (see SEM images in Fig. 3). In order to evaluate the SERS performance, a target molecule, benzenethiol, was self-assembled on plasmonic nanoprobes. For the SERS measurement, a helium–neon laser (632.8 nm) and a spectrometer (MicroSpec 2300i spectrometer equipped with a charge-coupled device camera (Model PIXIS: 400BR, Princeton Instruments)) were coupled to an inverted microscope (Axiovert 200M, Zeiss). The excitation and collection of light were done by a 50× objective lens (NA 0.5). The excitation power was 1.58 mW and the acquisition time was 1 second. The average intensities of 30 measurements (3 devices, 10 measurements for each) are plotted in Fig. 3. The Raman signal from PDMS is inherently small compared to the SERS signal and completely prevented by the plasmonic nanostructures that block the light to PDMS. The results clearly demonstrate that the plasmonic nanoprobes made of 30 nm films provide the highest SERS performance due to the highly dense hot spots induced by nanotips or nanodots.

Approximately 1000 nanotips and 1000 nanodots exist within a detection volume (radius of the detection spot: 2.5 μm). The height of the nanotips is about 200 nm. The diameter of the nanotips is about 150 nm at the bottom and that of the nanodots is about 30 nm. The numerous plasmonic hot spots within a detection volume are desirable for highly intense SERS and signal uniformity.15 As a result, the 30 nm thick silver film was utilized for the optofluidic SERS chips. No significant defects were observed except for a few nanoscale cracks. The variation of the SERS intensity is about 17.9% and the enhancement factor is approximately $1.1 \times 10^7$, comparable to those of conventional SERS substrates (see ESI†).21–23 The plasmonic nanoprobes provide highly intense SERS even though the plasma treatment may induce oxidation of the silver (see ESI†).

**Optofluidic SERS for label-free detection of dopamine molecules**

The optofluidic SERS detection of biomolecules was performed by using microfluidic networks with self-aligned plasmonic nanoprobes, which provide a spatial concentration gradient of molecules by fluidic mixing as shown in Fig. 4.24,25 In this experiment, the target molecules were prepared in distilled water and the flow was controlled by a syringe pump (KDS 200, KD Scientific, 5 μl min⁻¹ for both inlets). Damage on plasmonic structures was not observed during the experiment. The inset fluorescence image of rhodamine 6G dye molecules shown in Fig. 4 demonstrates linear concentration gradients within a single microfluidic channel (imaged by a 10× objective lens, NA 0.3). The five different microchannels at the third level successfully generate linear concentration gradients after passing the mixing units and merge into a single channel. The SERS detection of a biomolecule was demonstrated with dopamine, a well known major neurotransmitter. A water solution was injected through the left side inlet (indicated as ‘DI’ in the figure) and the dopamine solution (100 μM) was introduced through the right side inlet (indicated as ‘target’ in the figure). Consequently, the concentration increases from ‘L’ to ‘R’. The pure water flowed from the left end and the 100 μM dopamine solution was introduced from the right end. The optofluidic SERS detection was also done with a 632.8 nm

![Fig. 3 SERS intensity depending on the plasmonic nanoprobes fabricated from the silver film with different initial thicknesses. The silver film with an initial thickness of 30 nm successfully creates nanotips and nanodots with the maximum SERS performance after the oxygen plasma treatment. The asterisk indicates the 1075 cm⁻¹ peak of benzenethiol used for the analysis.](Image)

![Fig. 4 Optofluidic SERS detection of dopamine molecules. Water and dopamine solutions can spatially generate the linear gradients of concentration (low ‘L’ to high ‘R’ concentration) through microfluidic networks in the same fashion as rhodamine 6G solutions do as shown in the figure on the left bottom. The SERS intensities of dopamine molecules substantially increase with the concentration, which linearly increases from left ‘L’ to right ‘R’ in direction. The results clearly demonstrate a label-free and solution-phase SERS detection of dopamine at micromolar level in flow.](Image)
excitation through a 50× objective lens (5 mW, acquisition 1 second). The focal spot of the excitation laser was laterally scanned along the starting location of the single channel, where the five channels with the different concentrations were merged. The experimental results clearly demonstrate that the SERS signal with peaks around 1340 cm⁻¹ and 1590 cm⁻¹ from dopamine,⁶⁻²⁷ increases with concentration, which indicates that the optofluidic SERS chip is capable of label-free, solution-phase, and in situ detection of dopamine molecules at micromolar level (Fig. 4). In addition, the successful microfluidic implementation of plasmonic nanoprobes is not only limited to the concentration gradient generator but also can be applied for microfluidic networks with diverse functions.

Conclusions

To conclude, this work presents self-aligned plasmonic nanoprobes on optofluidic SERS chips. The Scotch tape removal and oxygen plasma treatment of a thin silver film enables not only the simple, highly selective, and cost-effective implementation of plasmonic nanoprobes with rich hot spots within microfluidic networks but also the successful SERS detection of low Raman active small molecules such as dopamine molecules in flow. This method can be readily expanded for microfluidic networks with diverse functions for advanced SERS or MEF based optical biochemical assays with label-free detection and high throughput.

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Notes and references