OPTOFLUIDIC DEVICE FOR ULTRA-SENSITIVE MOLECULE DETECTION USING SURFACE-ENHANCED RAMAN SPECTROSCOPY

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ABSTRACT
We have developed an optofluidic device that can significantly improve the sensitivity, efficiency and reproducibility of the surface enhanced Raman spectroscopy (SERS). This device has demonstrated the capability of detecting molecules of interest at ultra-low concentration and is able to identify fingerprint signals from multiple analytes. This device can potentially be used for the definitive early stage diagnostics of disease associated with protein conformation change such as Alzheimer’s disease (AD) or Bovine Spongiform Encephalopathy (BSE).

KEYWORDS: Optofluidic, Surface-enhanced Raman, Molecule detection

INTRODUCTION
SERS has been investigated for decades for its capability of providing enhanced signature Raman signal of various analytes. By confining or incorporating analytes in “SERS-active substrates”, typically clusters of silver or gold colloids [1-3], SERS allows an enhancement of Raman intensity on the order of $10^6$~$10^{12}$. In conventional SERS detection, an aggregation of Au nanoparticles is usually necessary to generate so-called “hot spots” [4-6], which provide highly enhanced signal. An agent such as NaCl can be used to initiate such aggregation. However, these hot spots are formed irregularly and distributed uniformly, which leads to random SERS enhancement over the sample. This fact limits the reproducibility and sensitivity of SERS detection technique. Herein, we report a novel optofluidic device that can overcome these problems and provide a convenient and efficient analysis platform for sensitive molecule detection.

THEORY
Figure 1 shows the schematic diagrams of the optofluidic device. The optofluidic device was fabricated on standard 500μm-thick quartz wafers using conventional photolithography and etching techniques. Each optofluidic device consists of 2.5μm-depth microchannel and 45nm-depth nanochannel. The depth of nanochannel is determined by the size of SERS-active substrates used in our experiment, which are 60nm-Au nanoparticles. In SERS detection experiment, the molecules of interest in aqueous solution are blended with Au nanoparticles and infused into the device via capillary force. Since the diameter of Au nanoparticles is larger than the depth of the nanochannel, the nanoparticles are efficiently trapped and produce a highly dense aggregated Au cluster around the entrance to nanochannel. This clus-
ter has proven to be a consistent “hot spot” in the detection. Different from conventional SERS technique, the structure of the device drives the aggregation of Au nanoparticles. Rather than randomly distributed, the aggregation is consistently located at the nanochannel entrance and provides a reliable point of detection. Compared to the conventional technique, the intensity of SERS signal can be increased by a factor of $10^2$ [7]. Moreover, since capillary force maintains a continuous flow of the sample through the device, the concentration of Au nanoparticles-analytes at the nanochannel entrance increases over time because more nanoparticles-analytes are trapped. The local concentration of nanoparticles-analytes can be increased by $\sim 10^5$ within $\sim 30$ min [7], which further increases the detection sensitivity of SERS.

![Figure 1. Schematic diagram of (a) side view of an optofluidic device: Au colloids and analytes are drawn into the channel via capillary force (b) side view of optofluidic device: Au colloids and analytes are transported to nanochannel entrance.](image)

**EXPERIMENTAL**

A mixture of $1\mu$M adenine, $1$mM congo red and Au nanoparticles in DI water (Polysciences Inc., PA) at a volume ratio of 1:1:10 was used for detection. The final concentration of adenine and congo red in the sample is 83nM and 83$\mu$M, respectively. The solution was dispensed into the channel immediately after prepared. It was drawn into the channel via capillary force within minutes. Figure 2(a) shows the compound SERS spectra of adenine and congo red in the optofluidic device monitored over time. The detection spot was focused at the entrance to the nanochannel with a 50x objective lens. The excitation wavelength is at 785nm. The collection time is 30 sec. Adenine shows a characteristic peak at 735cm$^{-1}$ while congo red has peaks at 1155cm$^{-1}$, 1286cm$^{-1}$, 1455cm$^{-1}$ and 1593cm$^{-1}$.

![Figure 2. (a) SERS spectra of 83nM adenine and 83$\mu$M congo red monitored in optofluidic device over time  (b) Magnified SERS spectrum detected using conventional SERS technique](image)
For comparison, the spectrum detected using conventional SERS technique is also shown in the Figure 2(a) and magnified in Figure 2(b). The conventional detection used NaCl as an agent to initiate the aggregation of Au colloids, with adenine and congo red at the same concentration. The solution sat for ~15 min to form the aggregated cluster and the spectrum was obtained using a water immersion lens.

RESULTS AND DISCUSSION

The intensity of fingerprinting peaks for both molecules is increased in the optofluidic device comparing to the conventional technique. After dispensing the sample in the channel, the capillary force keeps a continuous flow of the solution through the tiny interstices between the aggregated Au nanoparticles and increased the local concentration of Au-analytes at the nanochannel entrance. As monitored over time, the SERS signal was further enhanced. An important application of the device is the detection of amyloid beta (Aβ), a biomarker of Alzheimer’s disease (AD). AD is a progressive neurodegenerative disease that affects ~5 million people in the United States. Many researchers agree that the misfolding of Aβ is the initiating factor. This device can be used to detect the SERS spectrum of Aβ in different conformational states (monomer and oligomer form) at ultra-low concentration, which provides important information for the understanding and early diagnosis of AD [8].

CONCLUSIONS

The optofluidic device offers a reliable hot spot at a predictable location with increased local concentration of Au and analytes, leading to a much more effective, efficient and rapid detection. The quantities of colloids and sample can be decreased to a microliter level which is enough to fill the fluidic device. Research of early diagnosis of AD using this device is currently going on.

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REFERENCES