Nanofluidic Biosensor for Surface-Enhanced Raman Spectroscopy

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Abstract:

A nanofluidic biosensor was designed and fabricated on fused silica substrate using standard photolithography process. It was used as a detection platform together with surface-enhanced Raman spectroscopy (SERS) for ultra-sensitive detection of various analytes. Comparing to conventional SERS detection techniques, it highly improves the detection efficiency and sensitivity.

Summary of Research:

By providing fingerprint information of analytes, SERS is widely used as an analytical approach for the detection of bio/chemical samples [1-3]. When a laser source is incident on the analytes adsorbed on metal nanostructures, a localized surface plasmon resonance can be excited and enhance the inelastic scattered photons. The energy transfer between photons and analytes provides valuable information for identifying chemical bonds and structures of analytes. In the detection of aqueous sample, a traditional dispersive SERS technique is to mix the sample with gold or silver nanoparticles. Then an aggregation agent (such as sodium chloride) is added into the mixture to initiate the aggregation of metal nanoparticles. This aggregation is critical for the enhancement since high SERS signal is only obtainable from molecules attached on closely-packed nanoparticle clusters due to the electromagnetic coupling effect. However, the aggregation and distribution of nanoparticle cluster are not uniform in the aqueous sample. Hence, high SERS signal only occurs at so-called “hot-spot” [4-7], where aggregated clusters with adsorbed molecules exist. This limits the consistency and reproducibility of SERS detection, especially for a sample at ultra-low concentration.

To overcome this problem, a nanofluidic device is designed and fabrication on fused silica substrate. The schematic diagram (side view) is shown in Figure 1. The device consists of a microchannel and a nanochannel. With a depth of 40 nm, the nanochannel can trap nanoparticles at the entrance and provide aggregated nanoparticles as a hot spot in SERS scanning. Sixteen channels can be patterned on one 4” wafer. At first, the nanochannel was etched using CF₄ reactive ion etching and photoresist S1813 as the etching mask. Then the microchannel was aligned with the nanochannel and patterned by contact photolithography. Concentrated (49%) hydrofluoric acid was then used to etch the microchannel to a depth of 2 µm using PECVD amorphous silicon as masking medium. The sample inlet holes were drilled through the wafer by sandblasting. At last, fusion bonding was used to cover the trench with an intact fused silica wafer.
In the SERS detection, analytes in aqueous solution was mixed with 60 nm gold nanocollids suspended in water at a volume ratio of 1:10 (Polysciences Inc., PA). The mixture was then dispensed into the nanofluidic device and drawn into the channel via capillary force. The gold nanoparticles could not pass through the 40 nm-depth nanochannel and were trapped at the entrance as shown in Figure 2 (top view). Due to the interstices between the nanoparticles, the capillary flow continued at a fairly low speed and brought more and more analytes of interest to a close proximity to the nanoparticles. Although a few of the analytes diffused and passed the nanochannel, the concentration of analytes around the gold cluster was dominated by the arrival of analytes. Experimental results confirmed that the numbers of molecules kept increasing for about 30 min until reaching equilibrium state.

The aggregated nanoparticles can be easily located in the channel by optical microscope. This location is the focusing point for detection. Various proteins were tested using this device, including biomarkers for Alzheimer’s disease and acute myocardial infarction. With the molecule enrichment effect and a highly condensed hot spot, the detection sensitivity was 10⁵-fold better than conventional techniques [8]. The detection of various samples with a concentration in pM range or ng/l range is accomplished [8-10]. The device is also capable to provide the information of primary and secondary structures of proteins [10], which are very useful in the early detection and characterization of biomarkers for various diseases.

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