

# A NOVEL INTEGRATED MICROFLUIDIC SERS-CD WITH HIGH-THROUGHPUT CENTRIFUGAL CELL TRAPPING ARRAY FOR QUANTITATIVE BIOMEDICINE

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## **Abstract**

Integrated microfluidic surface-enhanced Raman spectroscopy on a compact disk (SERS-CD) platform has been developed for high-throughput quantitative biomedicine. A smart design of a SERS-CD platform including efficient cell-trapping microfluidics, a locally integrated SERS probe, and a sample-accumulating concentrator is a solution for label-free high-throughput screening and detection. A SERS probe combined with a protein concentrator allows monitoring the dynamics of secreted proteins as a function of trapped cell density, accumulation time, and the induced centrifugal force. The design of centrifugal cell trapping microfluidics was characterized by using polystyrene beads and HeLa cells and the preliminary evaluation of a centrifugal sample concentrator on a SERS probe was accomplished by observing the increased Raman spectrum of Rhodamin 6G (R6G) as the molecule accumulated on the probe.

**Keyword: quantitative cell analysis, centrifugal concentrator, centrifugal separation, cell trapping, SERS, SERS-CD**

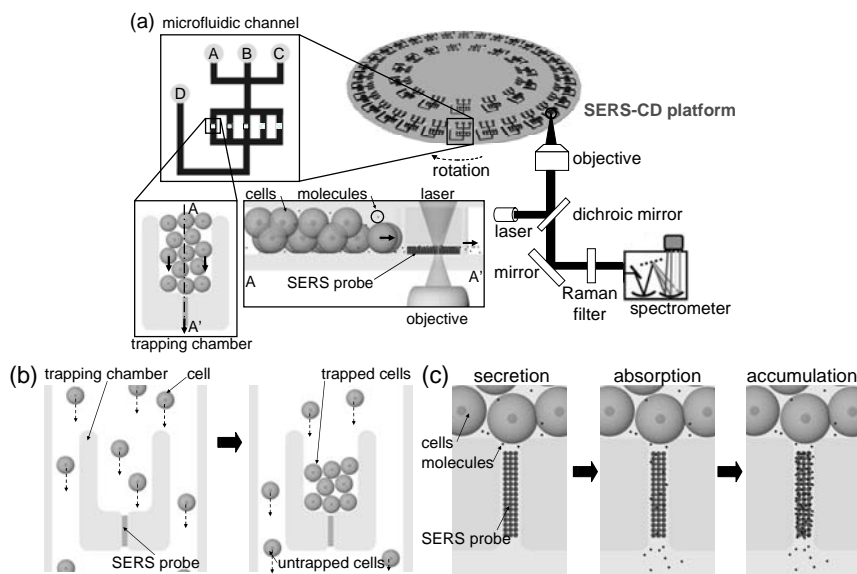
## **1. Introduction**

Quantitative cell analysis requires both capabilities of effective cell trapping and sensitive detection of secreted proteins. Such trapping has been achieved by applying electro-kinetic force or hydraulic pressure, which requires complicated electrical connections or extensive tubing, making integration difficult. Therefore, a device in a CD format is attracting considerable attention because flow can be regulated by controlling the rotational speed of the device without any connection to external components [1] while providing a high throughput platform and easy integration with a detector [2]. In contrary to a conventional label-requiring fluorescence technique, a label-free optical technique based on SERS has been used in the detection of a large number of chemicals and biological molecules due to its high sensitivity and molecular specificity [3]. However, detecting molecules secreted from cells requires a strong enhancement because the molecules are secreted at low concentration. Therefore, the CD-based integration of a cell trapping microfluidics with a SERS probe and a sample concentrator will be useful for quantitative cell analysis.

## **2. System Design**

A SERS-CD platform designed in a wafer format exerts a centrifugal force on randomly distributed cells and secreted molecules in the radial direction across the whole wafer.

The centrifugal force separates introduced cells from media and the cells are collected in trapping chambers. The trapped cells can secrete molecules activated by introduced chemical. The molecules are delivered only in the radial direction and accumulated on a SERS probe. The accumulated molecules are analyzed by measuring the Raman spectrum (Figure. 1).



**Figure 1. Schematic representation of an integrated SERS-CD platform for biomolecule detection.** (a) A SERS spectroscopy and a SERS-CD platform. (reservoirs for activating chemicals (A), cells (B), media (C), and vent (D)) (b) Cell trapping schematics comparing cells before trapping (left) after trapping (right). (c) Sample concentrating cycle: secreted molecules are delivered (left), absorbed (center) and then accumulated on a SERS probe (right), which results in molecule concentrating.

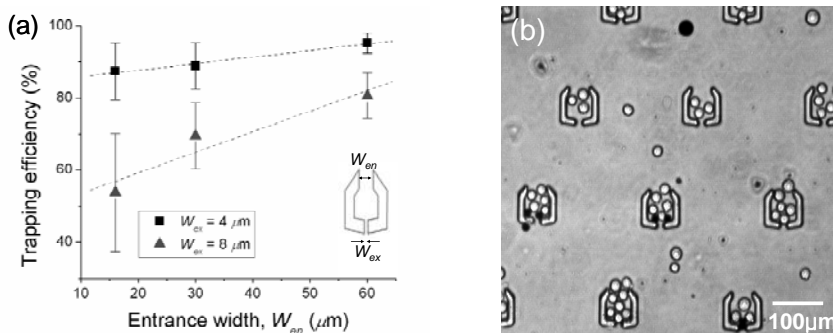
### 3. Experimental

The microfluidic channels were fabricated by means of soft lithography. A negative photoresist (SU8-2050, MicroChem, MA) was spin-coated and patterned to make a mold for microfluidic channels with a thickness of 50  $\mu\text{m}$ . A mixture of poly (dimethylsiloxane), (PDMS) prepolymer and a curing agent (SYLGARD 184 A/B, Dow Corning, MI) in a ratio of 10:1 was then cast against the molds to yield an elastomer replicas and then was cured for 2 hours in an oven at 70°C. A SERS-CD platform was fabricated by bonding the cured PDMS replica to a glass wafer of 4 inch in diameter by oxygen plasma treatment using a reactive ion etcher system for 20 s.

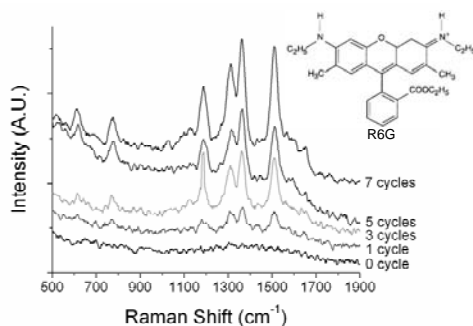
### 4. Results and discussions

The cell trapping and sample concentrating were characterized separately. The trapping efficiency was defined by the ratio of the number of filled trapping chambers to the total

number of chambers. Figure 2 shows that the trapping efficiency increased with increasing entrance width ( $W_{en}$ ) and decreasing exit width ( $W_{ex}$ ). Figure 3 shows that SERS enhancement was improved as the number of cycles increased and the intensity at  $1509\text{ cm}^{-1}$  increased by 5 times after 7 cycles of concentrating.



**Figure 2. Characterization of centrifugal particle trapping.** The characterization was achieved by measuring trapping efficiency with (a) polystyrene beads ( $10\ \mu\text{L}$ ,  $4.6 \times 10^7$  particles  $\text{mL}^{-1}$ ) and (b) HeLa cells ( $10\ \mu\text{L}$ ,  $4 \times 10^6$  cells  $\text{mL}^{-1}$ ) at 3,000 rpm for 3 minutes.



**Figure 3. Characterization of centrifugal sample concentrating.** The characterization was done by measuring SERS of R6G under 90 mW ( $2.9\ \text{W}\cdot\text{cm}^{-2}$ ) of 785 nm photons and integration time of 10 s after every cycle of concentrating. A SERS probe was prepared by collecting Au particles of 80 nm on a glass substrate. R6G was introduced by dropping  $1\ \mu\text{L}$  in solution at the concentration of 1 mM, was delivered to the SERS probe by a centrifugal force. After each SERS measurement, the introducing of R6G was repeated.

## 5. Conclusions

High-throughput cell trapping and sample concentrating were demonstrated with a novel SERS-CD platform. Highest trapping efficiency was achieved at channels having largest entrance width and smallest exit width and SERS intensity became stronger as the number of concentrating of R6G increased.

## Acknowledgements

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