FABRICATION OF OPTICAL AND GRAPHICAL CODES CONTAINED MICRODISK FOR MULTIPLEXED BIOASSAY

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ABSTRACT

In this paper, we proposed optically and graphically coded microdisks that have large coding capacity and small particle size for bioassay. Graphically coded particles generally have large particle size compared with the conventionally used microbeads. But the large particle size is not suitable for multiplexed bioassay due to a large amount of sample consumption and vigorous mixing. The proposed dual coding method uses optical and graphical codes for minimizing the particle size without reducing the coding capacity. The microdisk has dot patterns for graphical coding and gold layer on the microdisk for optical coding.

KEYWORDS

Coded microparticle, multiplexed bioassay, optical coding, graphical coding

INTRODUCTION

Suspension array technology using the coded microparticles is suitable to detect multiple biomolecular species including proteins, nucleic acids, and small molecules. The coded microparticle based assay showed higher reaction kinetics than planar arrays (e.g., DNA chip) because of the 3-dimensional surface properties [1]. Therefore, to fabricate coded microparticles, many coding methods have been reported such as optical, chemical, graphical, and electrical coding. The graphical coding uses two dimensional graphical patterns like barcodes. The graphical coding has advantages of large coding capacity and simple decoding process. However, most of the graphically coded particles have 100 ~ 500 μm particle size that is 10 times larger than practically used microbeads [2, 3]. Because the graphical coding capacity is determined by the particle size, the small particle size is not desirable to have large coding capacity. The large particle size requires large sample volumes and vigorous mixing for assay [4]. Therefore, to reduce particle size without decreasing coding capacity, we developed microdisks that can be coded by graphical patterns and optical signal. Raman spectroscopy, which has large coding capacity, is used for the optical coding and dot patterns are used for graphical coding in this paper.

DESIGN AND FABRICATION

The proposed microdisk was shown in figure 1(a). The microdisk has 5 μm diameter, and 0.5 ~ 1 μm thickness. Three dots were patterned for graphical information and gold layer on the surface of the microdisk generated surface enhanced Raman spectroscopy (SERS) signal for optical coding. The dual coding method used the two discrete signals as axis of code array (figure 1(b)) and the coding capacity was determined by multiplication of graphical coding capacity and Raman spectroscopy coding capacity. The combination of three dots can represent 6 different codes and the SERS spectrum can generate 40 different codes. Therefore, the coding capacity of the proposed microdisks is 240 (6 x 40).

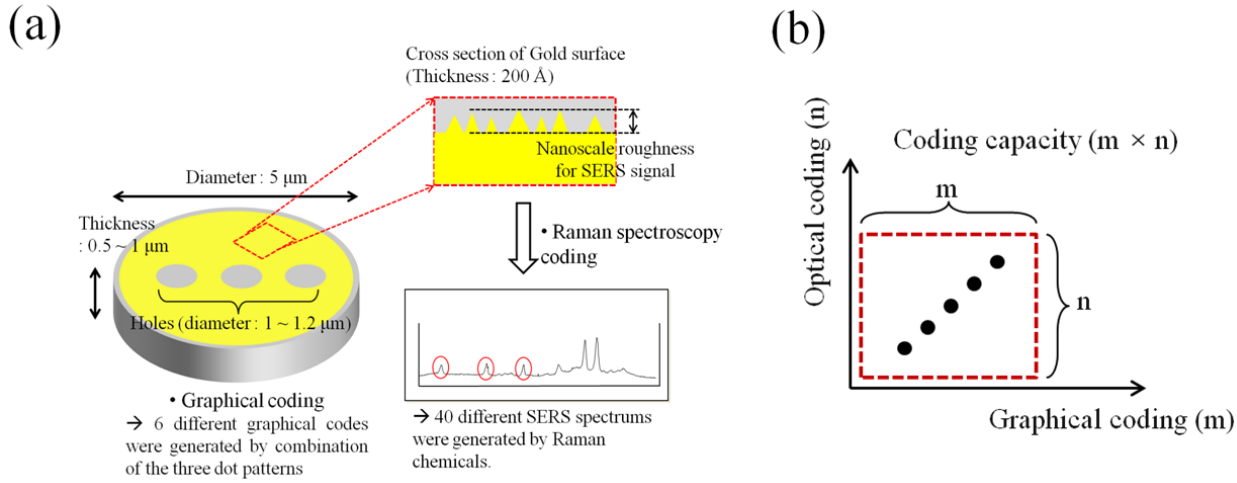

Figure 1. Schematic of the microdisk (a) and the graphical and optical codes map (b)

The fabrication process of the microdisk is as shown in figure 2. Firstly, 0.5 ~ 1 μm of SiO_2 was deposited on 150 mm silicon wafer. The graphical patterns were realized by stepper photolithography and reactive ion etching

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(RIE) of the SiO_2 layer. Photoresist was removed and the patterned SiO_2 microdisks were etched 100 nm by the RIE process. The additional RIE process increased the surface roughness of the microdisk for enhancing SERS signal intensity. Then the microdisks were released from silicon wafer. Deep reactive ion etching (DRIE) and isotropic dry etching process were used for microdisk release. The silicon substrate was etched to form pillars by DRIE process (figure 2(d)) and the silicon pillars under microdisks were etched using isotropic dry etching (figure 2(e)). Finally, 50 Å Cr adhesion layer and 200 Å gold layer were sequentially deposited by thermal evaporation (figure 2(f)).

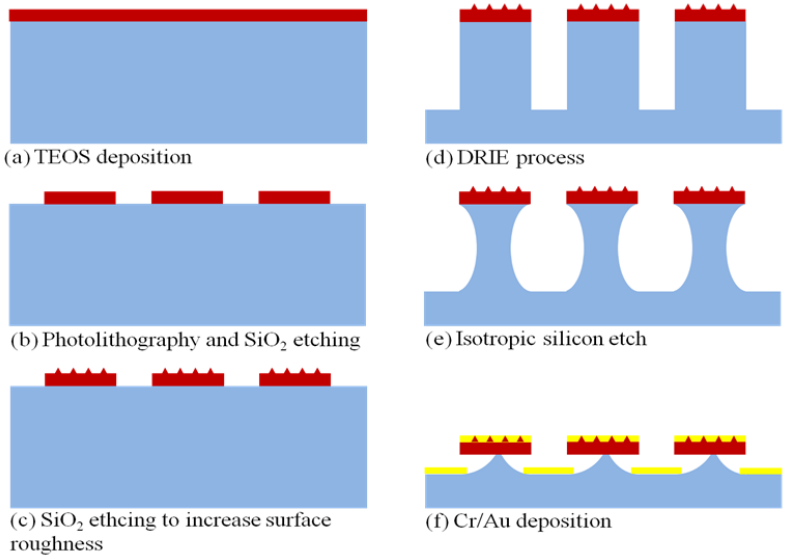

Figure 2.Fabrication process of the microdisk

RESULT AND DISCUSSION

The scanning electron microscope (SEM) and optical images of fabricated microdisks were shown in figure 3(a). The dot patterns for graphical coding were successfully fabricated and confirmed by scanning electron microscope (SEM). The graphical patterns were also distinguishable by the optical microscope (x100) for decoding.

For the collecting of microdisks from the wafer, the fabricated wafer was immersed in isopropyl alcohol (IPA) solution and sonicated for 5 minute. Then the microdisks were centrifuged for the microdisk concentration. Finally, the solution that contained one dot microdisks was spotted on slide glass and observed by the microscope. As shown in figure 3(b), the one dot microdisks were successfully collected in IPA solution.

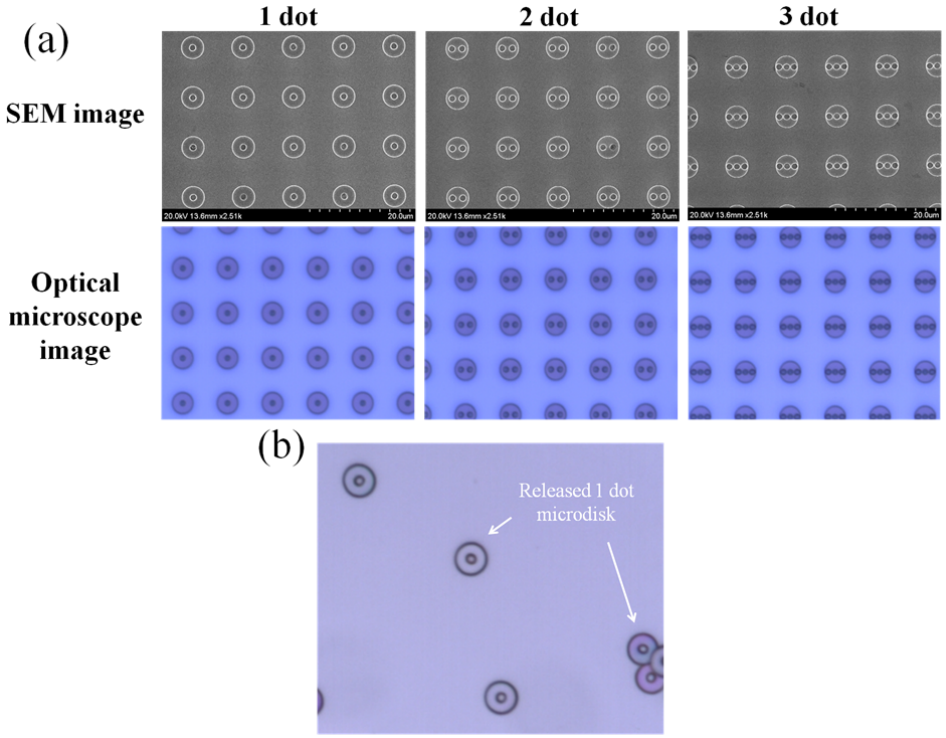

Figure 3. Fabrication results of the microdisk (a) SEM and optical microscope images of the patterned microdisks by photolithography and SiO_2 dry etch (b) The collected microdisks on a slide glass

The effect of RIE process was investigated to generate the strong SERS signal on the microdisk. SiO_2 deposited

silicon wafer was etched and 50 Å Cr and 200 Å gold were deposited on the wafer. The SERS signal intensity was enhanced by RIE process compare to the bare SiO_2 deposited silicon wafer as shown in figure 4. The anisotropic plasma etching process made nanoscale rough surface on the etched SiO_2 layer that enhanced the SERS signal.

The collected microdisks were coded by 4-fluorobenzenethiol (4-FBT) for 10 minutes for optical coding. For optical signal decoding, the 4-FBT coded microdisks were scanned with laser (647 nm) to obtain the SERS signal. The 4-FBT coded microdisks generate strong SERS signal at 1073cm^{-1}. Figure 4(b) shows the SERS signal intensity map and spectrum on the 4-FBT coded microdisk. The SERS code was successfully encoded and decoded on the microdisk.

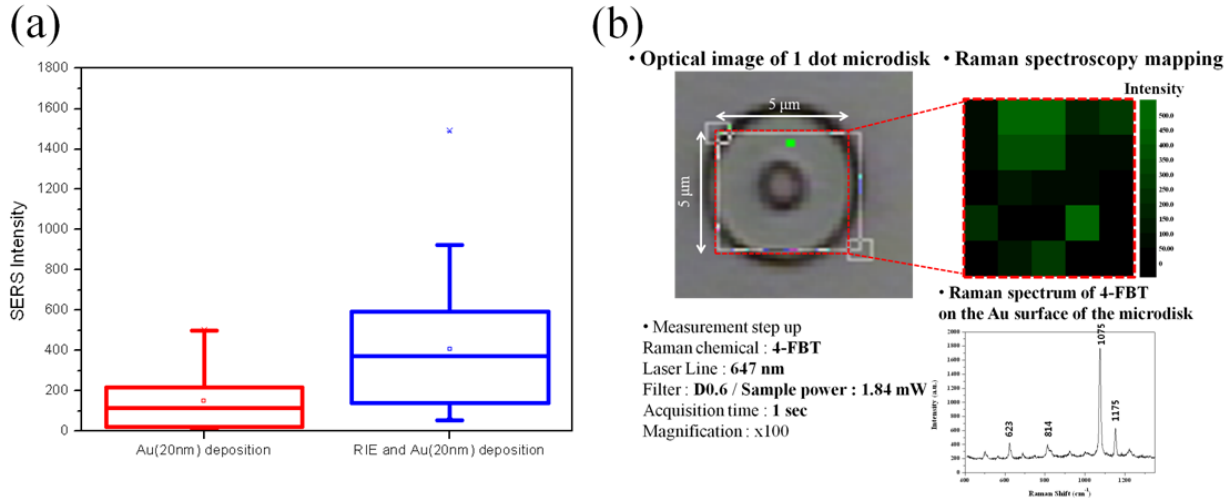

Figure 4. (a) SERS signal intensity of 4-FBT at the bare SiO_2 layer (red) and RIE processed SiO_2 layer (blue)(b) SERS signal mapping data and spectrum of the 4-FBT coded microdisk

CONCLUSION

The proposed microdisk has large coding capacity in small particle size by using the optical and graphical coding. Moreover, the batch process of the micro fabrication technology produces reliable and uniform particle pattern and size. The proposed microdisk can be used for multiplexed bioassays with an automated decoding system.

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