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Densely-Packed Microbowl Array with Balanced Dielectrophoretic Forces for Single-Cell Microarray

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ABSTRACT

In this paper, we demonstrate a perfectly-ordered microbowl array with balanced dielectrophoresis (DEP) for a high-throughput single-cell analysis. In order to fabricate well-ordered microbowl array in a large area, we utilized three-dimensional diffuser lithography for photoresist mold and nickel electroplating technique for final microbowl structures on a silicon substrate. Single microbowl has six sharp apexes surrounding the microbowl perimeter. Each microbowl has a diameter of 10 μm, and a height of 9 μm, which can be controllable by patterns on mask and lithography conditions. To investigate feasibility for application to the microbowl array as a single-cell microarray, we used latex beads of 6.4 μm in an average diameter to be captured by dielectrophoretic force. The nickel microbowl array densely packed with a hexagonal geometry played as a bottom electrode, and an ITO-coated glass covered the nickel microbowl array as a top electrode while keeping a uniform gap between two electrodes. After injecting solution containing latex beads through the gap, we applied an AC signal (2 V_{PP}, 1 MHz) between two electrodes to induce high electric field near the sharp apexes of the single microbowl. A negative DEP trap is formed at the center of the single microbowl with balanced DEP force from the six apexes. The experimental result shows that injected latex beads had been successfully and uniformly aligned and trapped at the microbowl array sustained by negative DEP.

INTRODUCTION

This paper reports a nickel microbowl array for massive single-cell analysis with dielectrophoresis (DEP) guidance. Since cellular responses are random even under identical environmental conditions, cell biologists are eager to analyze a large number of individual cells at once to attain stochastic distributions of the cellular responses. For a high-throughput single-cell analysis, microfabrication techniques have been introduced as the various platforms: a single-cell microarray [1], which consists of microchambers accommodating an individual cell, a DEP cell-trapping array [2], a microfluidic device for single-cell assay [3], and so on. However, in the aforementioned techniques, there are disadvantages: low throughput and less-efficiency of cell-capturing promoted by only gravitational force [1], possible cell-movement after disconnecting electrical signals [2], and necessity of complicated microfluidic components [3]. It is timely to develop a new array-based technique to confine a single cell with higher density as well as without any microfluidic components. Thereby we demonstrate a perfectly-ordered microbowl array with balanced DEP forces for a high-throughput single-cell analysis as shown in Fig.1.

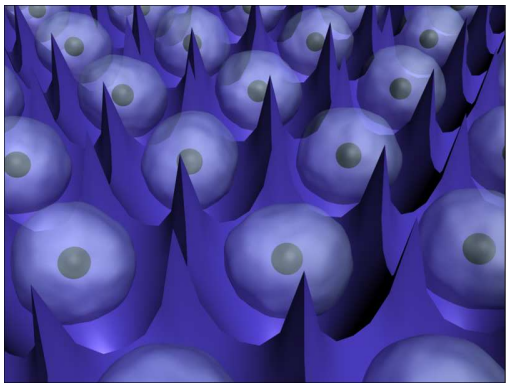

Figure 1. Schematic illustration of confined cells in the proposed microbowl array.

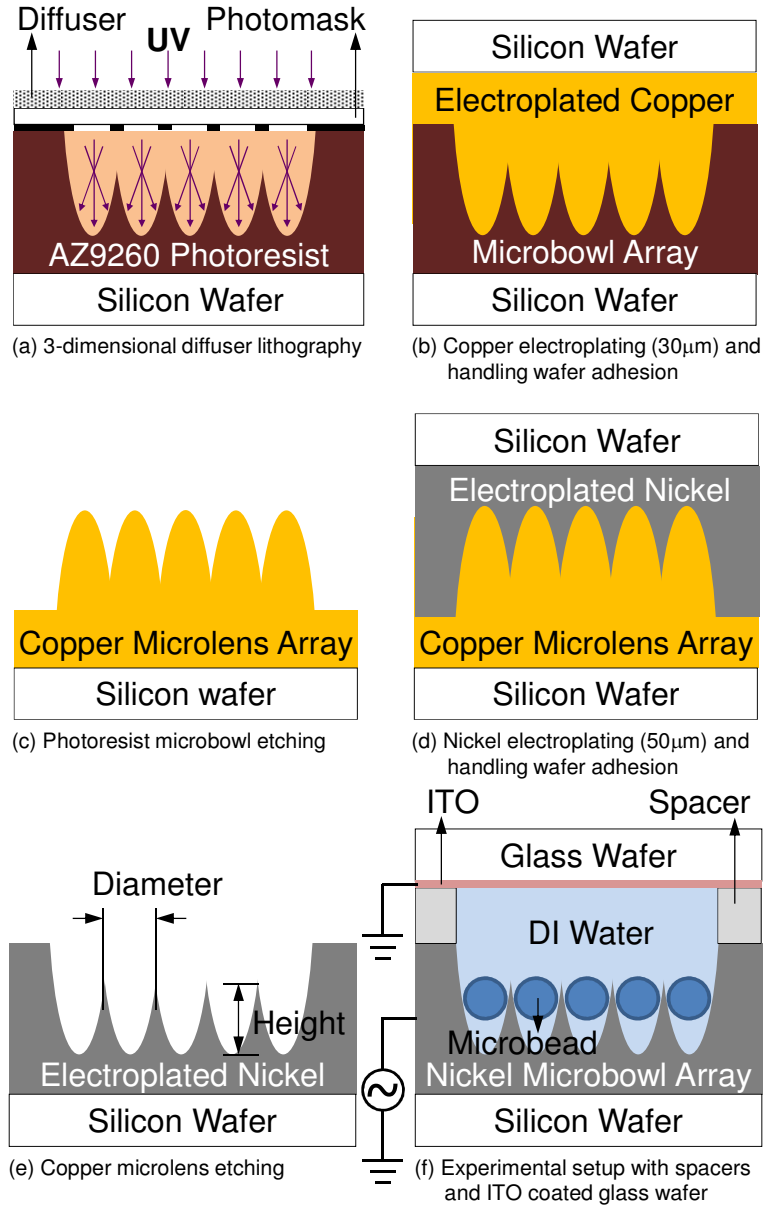

Figure 2. (a~e) Process flow of the proposed nickel microbowl array and (f) experimental setup.

EXPERIMENT

The fabrication process of the nickel microbowl array is shown in Fig.2. We employed the three-dimensional diffuser lithography for fabrication of the well-ordered photoresist microbowl array [4]. After deposition of a copper seed layer on the photoresist mold, a copper electroplating to achieve a 30 μm thickness was performed. To manipulate such a thin copper film, another silicon wafer was attached on the top of the electroplated copper layer. Additional nickel electroplating technique was followed for the final microbowl structures of 50-μm-thick. The other silicon wafer was attached on the top of the electroplated nickel film for ease of handling. Finally, the copper mold was removed by a wet etching process. To validate feasibility of single-cell analysis, latex microbeads were captured in the fabricated nickel microbowl array with experimental setup described in Fig.2 (f).

DISCUSSION

As shown in Fig.3, six sharp apexes surrounding the microbowl perimeter show extremely high E-field with applied bias, which is simulated by using the commercial software (CFD-ACE+). By the geometrical symmetry of those E-fields, every microbowl induces a trap site at the center of the single microbowl with balanced DEP forces from the six apexes, which helps single-cell positioning in the microbowl.

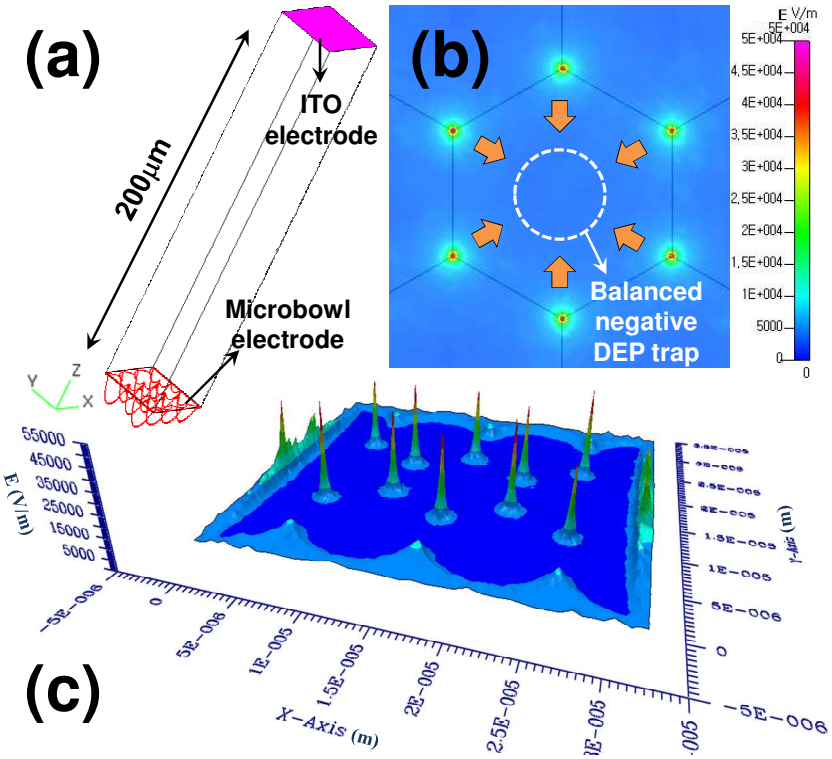

Figure 3. (a) A structure used in simulation (microbowl electrode at 1 V, ITO electrode at ground); (b) electric field strength at the plane of microbowl peaks; (c) a carpet plot of the electric field at the same plane with (b).

In a vertical direction, the single-cell can be moved downward near the bottom of the microbowl surface by the E-field gradient as well as the gravitational force shown in Fig.4, and settled down in the microbowl.

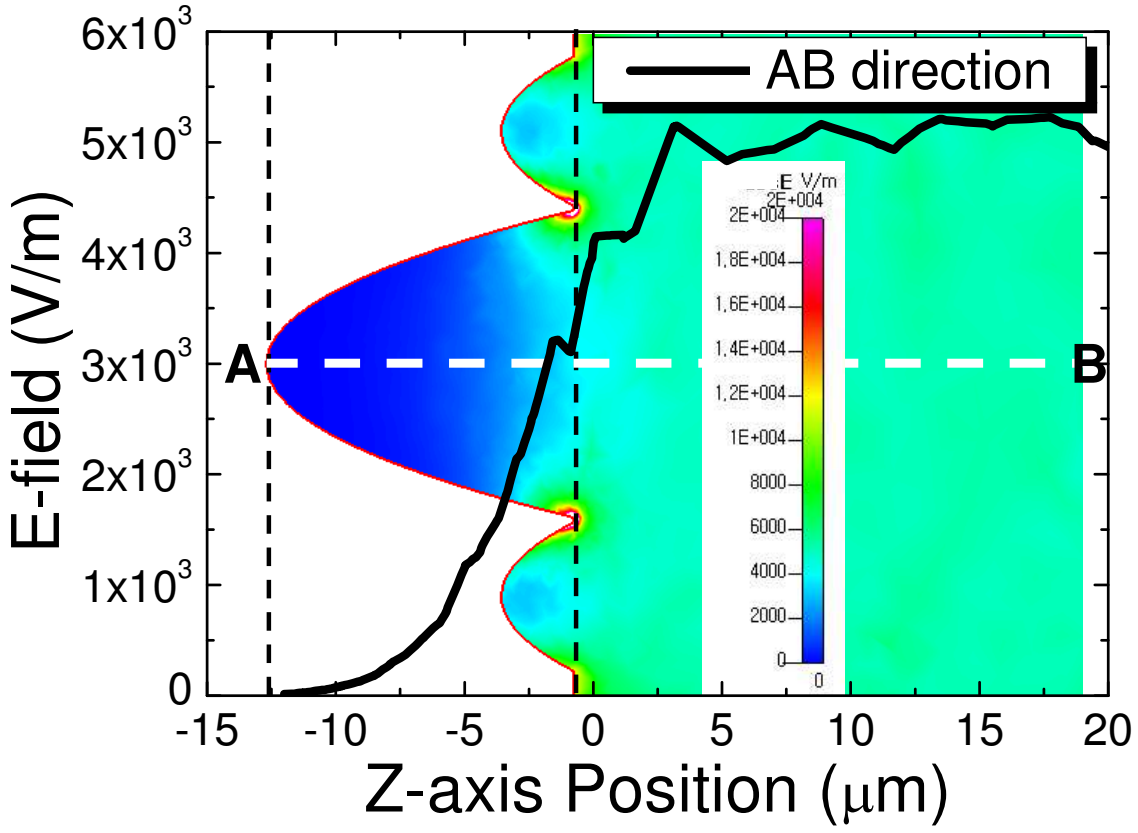

Figure 4. Electric field strength along the microbowl cross section in the structure shown in Fig.3.

Fig.5 (a) shows a SEM image of the fabricated nickel microbowl array. A diameter and height of the microbowl is 12 μm, which can be controllable by mask patterns and lithography conditions. The confined single microbead with a diameter of 5.5 μm is shown in Fig.5 (b). The nickel microbowl array densely packed with a hexagonal geometry played as a bottom electrode, and an ITO-coated glass covered the nickel microbowl array as a top electrode while keeping a uniform gap between two electrodes. After injecting deionized (DI) water containing latex microbeads through the gap, we applied an AC signal (2 V_{PP}, 1MHz) between two electrodes to induce DEP forces in the microbowl array. Compared with Fig.5 (c) (without applying AC signal), Fig.5 (d) shows more uniform and efficient alignment of microbeads in the microbowl array, which is precisely aligned by the negative DEP force. Without any electrode patterning processes, trapping of microbeads with DEP guidance is achieved.

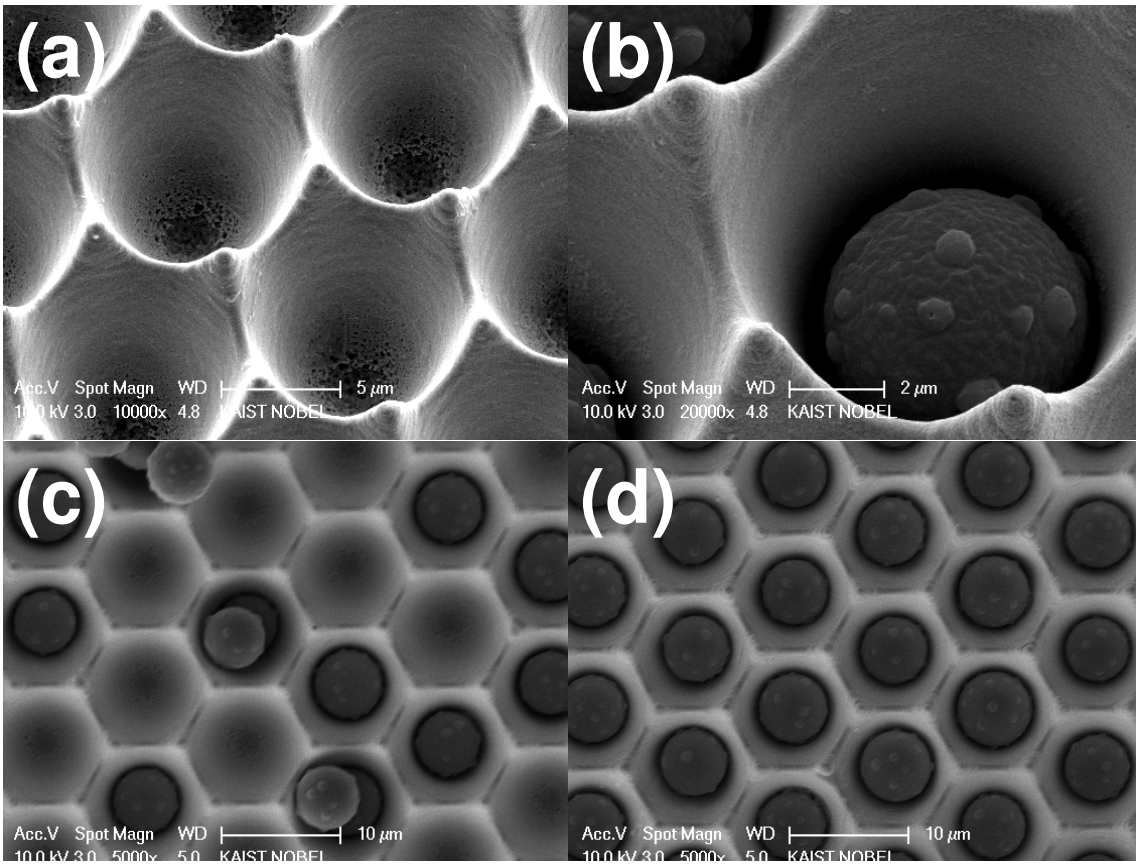

Figure 5. SEM images of the fabricated microbowl (a) a microbead in a microbowl (b), microbeads in microbowl array without DEP (c) and with DEP (d).

CONCLUSIONS

We fabricated perfectly ordered microbowl array in a large-size template using three-dimensional diffuser lithography and nickel electroplating technique. Due to its unique geometrical shape with the six sharp peaks, a stable trap site was formed by balancing DEP forces from the six apexes. Successful trapping of latex beads was demonstrated by applying potential to the microbowl array. The microbowl array with DEP forces increased uniformity as well as efficiency of latex beads capturing. Therefore, with the aid of the microbowl array, high-throughput single-cell analysis is expected with high density of single cells as well as increased efficiency of capturing of cells by DEP force guidance.

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