A Easily Manipulative Stimuli-responsive Micro-valve Array

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***Abstract*—Integrative micro-valve array is one of useful tools for the drug discovery, high-throughput screening. In this paper, we have developed a low-cost and easily manipulative pH-responsive micro-valve array. To prove the feasibility, we designed and fabricated the double micro-valves array, the tetrad micro-valves array and the octad micro-valves array. The platform of arrayed valve was fabricated by using polydimethylsiloxane (PDMS) and the microsphere utilized as an actuating element was produced via "on the fly" photo-polymerization method. The microspheres were manually incorporated into the arrayed PDMS platform.**

To construct the platform of valve arrays, we stacked 3 thin (thickness: around 140μm), patterned PDMS layers (hole-layer, membrane-layer, and upper-layer) and one PDMS bas-relief plate (thickness: around 8 mm), and the top was covered with the cover slip. The actuating pH-responsive microspheres (diameter: around 140μm) were incorporated into the micro-valve units and they are located in the 700μm interval. Each valve unit was controlled to be opened and be closed by changing pH solutions passing through it. The operation and the function of the fabricated micro-valve arrays were evaluated through the diverse experiments. The integrated system was operated expediently and functioned well. The closing and opening times were around 50s and 60s, respectively. Sample solution-flow rate is 0.03 ml/min when the pressure is 50kPa operated by varying the height of water column. Linear flow control was achieved over a wide range of operating flow rates. Furthermore the fabrication process of pH-responsive-actuated micro-valve arrays using PDMS is simple and its performance is suitable for a disposable lab-on-a-chip. These stimuli-responsive micro-valves do not use any electrical or mechanical components, and have many potential applications.

***Keywords*—Micro-valve array, PDMS, pH-responsive micro-sphere, lab-on-a-chip, "on the fly" photopolymerization**

I. Introduction

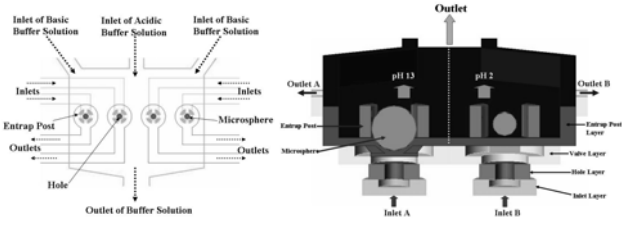
In lab-on-a-chip (LOC) systems, the elastomeric polymers are getting attraction for a number of reasons, including low cost and simple fabrication process. Specifically, polydimethylsiloxane (PDMS) material is commonly used to develop microfluidic components such as pump, valve, microchannel and so on [1]. And Micro-valves have been attracting more and more attention, especially for (bio)chemical applications including micro total analysis systems (μTAS) [2-3]. For example, miniaturization of a flow injection analysis (FIA) system requires a set of micro-valves to control pulsed sample flows [4-5]. In a typical design, a micro-valve has a micro-fabricated channel interrupted by a valve seat. The fluidic route is opened\closed at the valve seat with a membrane, which is actuated via various methods [6]. Recently, new delivery devices mimicking an actuating process of living systems have been developed for biological and medical applications, and the approach involves the direct conversion of chemical energy into mechanical energy on the basis of materials that respond to external stimuli such as temperature, pH, light, electric fields, chemicals, glucose, antigens, and ionic strength [7-12]. Such stimuli-responsive, or "smart," polymers have been extensively applied in the delivery systems, and the promising results have been reported [13-14]. This paper describes a low-cost and easily manipulative pH-responsive micro-valve array. Finally, its performance is demonstrated experimentally.

II. Design and fabrication

A. Design

Figure 1 shows schematics of the pH-responsive micro-valve arrays with tetrad valve units. The device consists of one PDMS bas-relief plate (thickness: 8mm), 3 thin (thickness: around 140μm), patterned PDMS layers (hole-layer, membrane-layer, and upper-layer) and the cover slip. The actuating pH-responsive microspheres (diameter: around 140μm) were incorporated into the micro-valve units and they are located in the 700 μm interval. Figure 1(a) shows the planform of the micro-valve arrays. Besides, the inlet and the outlet channels are the delivery path of sample solutions. In contrast, the acidic and the basic solutions are delivered through the pH inlet. The pH-responsive microspheres swelled and shrank according to pH changes in the pH solution. Figure 1(b) shows a three-dimensional visualization of the microfluidic valve array. And it demonstrates the principle of the switch operation. At the application of the acidic solution, the microspheres inside the entrap posts shrink, and the thick-centered membrane moves upward

because of the pressurized inlet flow, the fluid passes through the holes and moves out to the outlet. When the basic solution is introduced, the microspheres swell and press the thick-centered membrane, and the bended membrane seals the holes. Therefore, the flow paths from the inlets to the outlets are blocked.



(a) (b)

Figure1 Schematic diagram of the pH-responsive micro-valve array

B. Fabrication

The fabrication procedures are as follows. The patterned bas-relief plates were constructed by using replica moldings against masters consisted of photolithographically patterned photoresist (SU-8, MicroChem) on 3-inch silicon wafers. A 12-gauge needle was used to excavate the holes for the fluidic network. Three thin layers were manufactured by compressing micro-molding with PDMS elastomer, as previously reported [13]. With the plates and the 3 layers, the micro-valve arrays were constructed according to an aligning and bonding process, as demonstrated in Figure 3. Firstly, the hole layers, which have small holes (diameter: 80μm) for the passage of sample fluid, are bonded with the bas-relief plates. For the bonding, both of the surfaces of each layer were exposed to oxygen plasma for 2 minutes, and alignment was realized through methanol as a lubricant. The bas-relief plates that were combined with the hole layers were cured on the hot plate for 2 hours at 80°C. To fabricate the membrane layers, we made 2-stepped master molds in which the thick centers have different thicknesses, and the thicknesses of the membrane layers are noted in Figure2. The membrane layers were stacked onto the hole layers according to the aligning and bonding process. The upper layers that had the entrap posts were stacked onto the membrane layers and bonded. Afterwards, we picked pH responsive microspheres by the glass pipette whose tip is sharp (diameter: 40μm), and placed them into the entrap posts carefully under the stereoscope one by one. Figure3 shows the SEM images corresponding to the polymerized microspheres that we had placed inside the entrap posts. Finally the cover-slips were stacked and bonded.

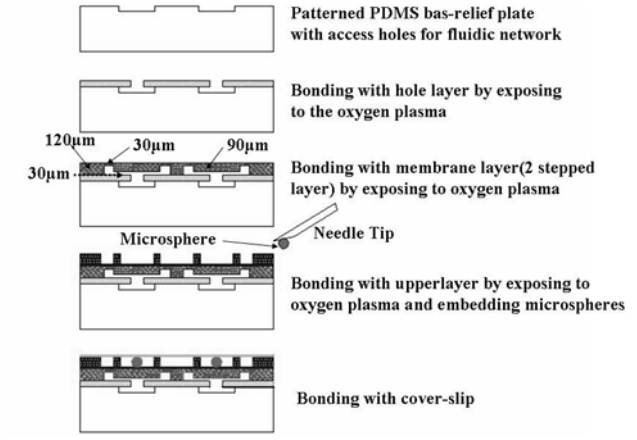


Figure2 The aligning and bonding process in the micro-valve-fabrication process.

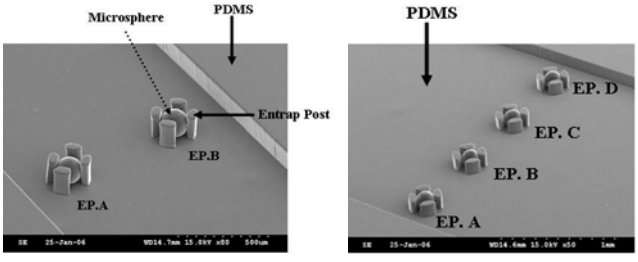


Figure3 SEM images corresponding to the polymerized microspheres that were placed inside the entrap posts.

III. Flow Characteristics

A. Experimental setup and methods

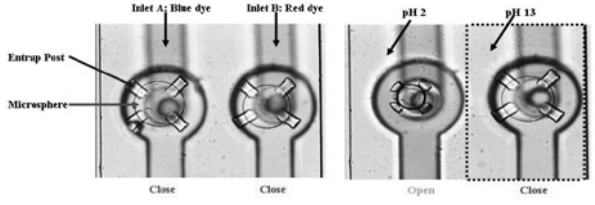
Flow characteristics of the micro-valve arrays systems for water were evaluated as follows. The operation of the valve was visually monitored under a microscope equipped with a digital camera, and the captured images were sent to the personal computer. Sample solutions and pH solutions were all dominated through disposable infusion set—rolling its post to vary flow rates and pressurized by water column—changing its height to vary pressures. The pressures were gauged by measuring the heights of water column. Through weighing solutions with scale, we calculated the flow rats according to the following equation.

$$FlowRatio(ml/\min) = \frac{m}{\rho t} \quad (1)$$

Where m (g) is the weight of collected solution, ρ (g/ml) is the density of solution and t (min) is the time of collecting solution.

B. Result and discussion

Figure4 demonstrates the micrograph of the "OPEN" operation and the "CLOSE" operation of the fabricated micro-valve arrays respectively. The microspheres shrank and the channels were opened when the acid solution passed through the mirospheres, while the channels were closed at the appearance of the basic solution. We have measured the average flow rate (= volume for 3 minutes (μl/min)) according to the variation of pressurized inlet flow (the pressure varied from 5.0kPa to 9.5kPa) and to the Base:Acid ratio, and the results are plotted in Figure5. Here, the Base:Acid ratio means that the ratio of the acid-injection duration to the base-injection duration (e.g., 1:4 indicates that the basic solution was introduced for 1 minute and that the acidic solution was introduced for 4 minutes subsequently). In relation to the increase of inlet pressure and the acid-injection duration (from 3:2 to 1:4), the average flow rates almost increased linearly. At 4:1, the average flow rates were saturated, and the reason seems to be that the microspheres were not fully exposed to the acidic solution during the opening phase of the valves. To investigate the shrinking and swelling motion to the time track, we have measured the flow-rates change to the time track just after the change of pH value, and the results are plotted in Figure6. Figure6(a) shows the flow-rates of the double micro-valves array changed when the pH value was changed from 13 to 2. During the initial 1.5 minutes just after the pH-value changed, the channel closed and the flow rates slowly increased after 2 minutes later. The flow rates exponentially increased and were saturated afterward in around 60s, and it indicates that the valves were fully opened. Figure6(b) illustrates the flow-rates changed when the pH value varied from 2 to 13. At the closing phase, the valve started to close promptly, and fully closed within 50s. The time in the closing phase was nearly twice as short as the time in the opening phase, and, according to our conjectures, the reason of the opening phase's slower response concerns the entrap post's prevention of the swollen microspheres' exposure to the acidic solution. Figure6(c) shows the same process of the tetrad micro-valves array with double one.



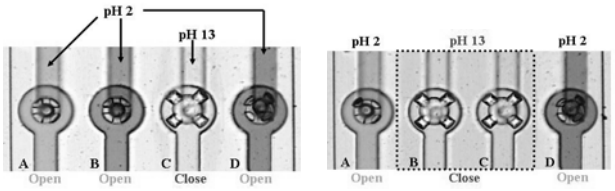


Figure4 The micrograph showing the fabricated micro-valve arrays' switch operations

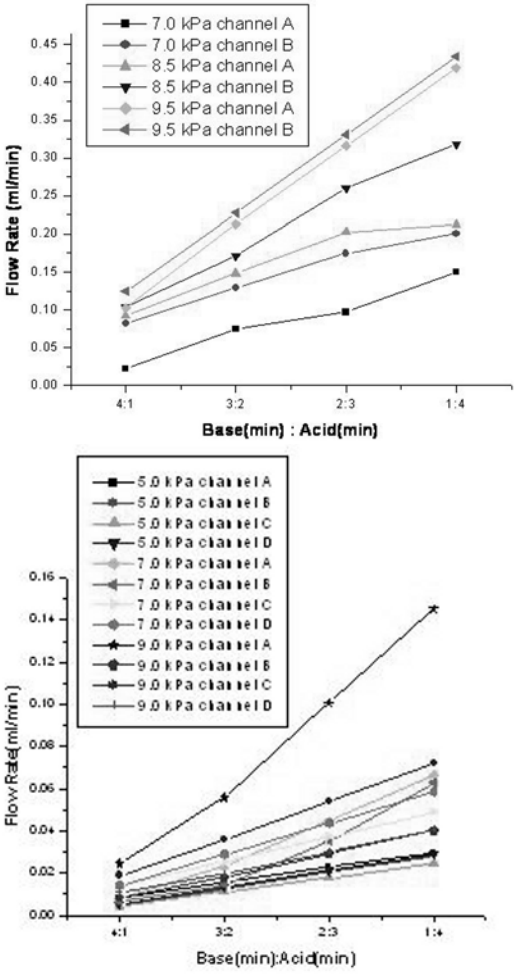


Figure5 Average flow-rates of the double micro-valves array and tetrad micro-valves array change according to the variation of the pressurized inlet flow (from 5.0kPa to 9.5kPa) and of the Base:Acid ratio (= Duration of basic and acidic solution supply). (Basic solution: pH 13, acidic solution of pH 2)

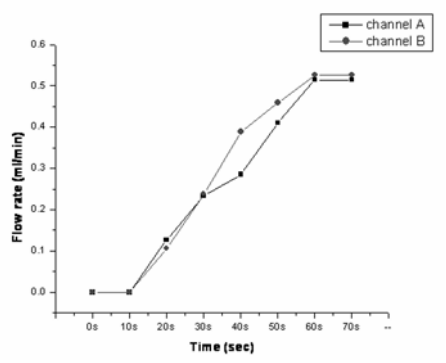


Figure6(a)

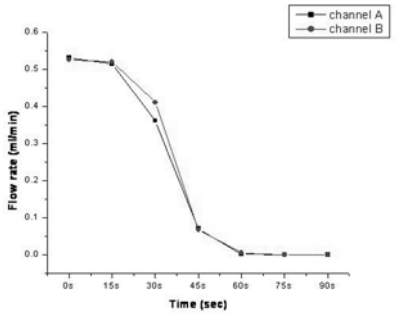


Figure6(b)

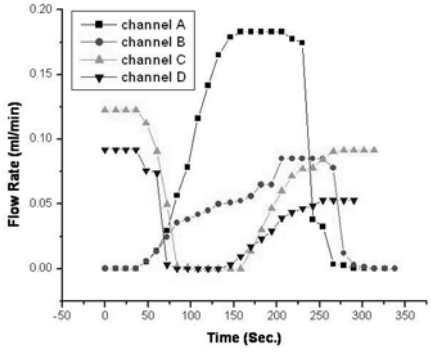


Figure6(c)

Figure6 The time of micro-valves' on-off processes

IV. Conclusions

A easily manipulative stimuli-responsive micro-valve array was constructed. Intervals between the valve units are smaller than 700 μm, which opens up the possibility of realizing a high-density micro-valve array. These stimuli-responsive micro-valve arrays do not need any electrical or mechanical components, and have many potential applications as a implantable stimuli-responsive sample or drug-delivery device that are 'responsive' to the patient's therapeutic requirements and deliver certain amount of a drug in response to a biological stimulus.

Acknowledgment

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