Magnetically Modified PDMS Microtools for Micro Particle Manipulation

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Abstract—In this paper we describe novel magnetically driven polymeric microtool for non-intrusive and no contamination experiments on a chip. The composite is formed by suspending magnetite particles (Fe3O4) in polydimethylsiloxane (PDMS). In order to obtain precise and complicated pattern of micromagnetic tools, a photolithography techniques has been applied by making good use of thick KMPR-1050 photoresist as sacrificial mould. The surface of the produced micromagnetic tools is specially coated in order to suppress stiction in the biochip. The novelties of these tools are 1. fabrication of any 2D shape, 2. softness (harmless to cells), 3. no contact actuation (no stiction), 4. mass production with low cost. Here we have demonstrated that the mass-produced versatile micromagnetic tools such as stirrer and valve. The potential impact of this technology includes sample selection and separation, cell immobilization, genetic operation, tracking, mixing and reaction techniques into portable microfluidic labs-on-a-chip, culture systems and cell loading system.

I. INTRODUCTION

There is great interest in the development of the micro actuation mechanics in biochip. We propose a novel magnetically driven microdevices to allow active control of fluid transport through microfluidic channels. The field of microfluidics has utilized advances in fabrication techniques by means of photolithography for drug delivery, cell separation, and biomedical diagnostics by forcing the fluid transport or restricting the flow by microfluidic valves. For example, many different kinds of microvalves have been developed since early 80’s, and active microvalves actuate mechanical moving parts using magnetic, electric, piezoelectric, thermal or other actuation methods. Among the many different microscale actuation mechanisms, magnetic actuation has certain advantages over other methods due to their large forces to affect large displacements and harmless to cells for the biochip applications. The micro-magnetic devices including not only valve but also pump, stirrers, filters and sorter can be controlled by external magnet force which is easily implemented onto a disposable microchip at low cost by making the electromagnet detachable.

Conventionally magnetic actuation has been produced by metal or metal membrane, whereas miniaturized hard magnetic materials have not been used until recently due to the difficulties of micromachining processes. Recently the use of the composite of magnetic powder and PDMS has been applied to local actuation in microchannel with an important feature of easy fabrication. For example, there are some works on actuation by a piece of polymer-bonded magnets on top of PDMS membrane or ferrofluidic plug in a microfluidic channel. Also, elastomeric membrane material made of mixture of Silicon polymers and magnetic particles has been used as valve and pump in biochip. However the control of magnetic membrane on the surface of microchannel constraint the area and direction of movement of actuation in microchannel, whilst there is potential requirement of versatile movement in biochip.

Other micromagnetic devices such as stirrers provide rotating actuation in microchannel. It is important to obtain sufficient mixing in the laminar sheath flow of microchannel in the field of micro total analysis systems. Many works have been done to use micromachined magnetic metal rotors enclosed by PDMS channel network in order to obtain sufficient mixing, microrotation or pumps, long-term temperature control of microfluidic channels for cell culturing. However the configurations of the rotors are limited to be fabricated due to the difficulties of micromachining processes and complexes of lithography processes.

The present work has proposed that a novel on-chip PDMS-based versatile micromagnetic tools by means of photolithography techniques. We use the nanoparticle of iron oxides (Magnetite, Fe3O4) in order to mix with PDMS which is difficult to be oxidized unlike to other magnetic transition metals (e.g. iron, cobalt and nickel). The novelties of present work are: firstly, the tools can be fabricated to any 2D shape precisely. Secondly, these are soft enough to be less harmful to manipulate cells in biochip. Thirdly, the tools can move any direction smoothly in the biochip by surface coating to suppress any stiction to the PDMS microchannels or cover glass and these are difficult to be rusted by long term immersion in the fluid in the biochip. Fourthly, the tools can be mass produced with low cost and they are disposable.
II. EXPERIMENTAL

A. Fabrication of Micromagnetic Devices

Figure 1 shows the two fabrication methods to produce micro magnetic tools. First method (Fig.1(a)) used thick KMPR-1050 (Kayaku MicroChem CO., Ltd) photoresist. The resist mold for micromagnetic tools was fabricated by patterning the resist layer on a silicon substrate (resist height = 150 μm)(Fig.1①). Then PDMS-magnetite composite has been molded into designed configurations of micromagnetic tools and baked at 80℃ for 20 min in order to cure the composite(Fig.1②). Finally the patterned substrate is put in the stripper liquid bath (Remover PG at 70℃) with a commercial large stir bar made of permanent magnet which keep the steady temperature of stripper liquid (Fig.1③). As the KMPR resist has been dissolved by the stripper liquid, the gap between KMPR resist and PDMS-magnetite composites have been produced, then the large stir bar collects a number of patterned PDMS-magnetite composites automatically due to their magnetism (Fig.1③ & ④). This method can be applied to produce small, fine and complicated pattern of micromagnetic tools.

Second method (Fig.1(b)) used SU-8 photoresist. Designed configurations of micromagnetic tools have been fabricated the resist layer on a silicon substrate (Fig.1⑤). Then PDMS mold was fabricated by using the patterned silicon substrate and baked at 80℃ for 20 min in order to cure the PDMS (Fig.1⑥). In order to peel off the PDMS-magnetite composite on the surface of PDMS mold, the surface of the PDMS mold has been activated by O2 plasma and coated with polyethylene glycol. (Fig.1⑦) Then PDMS-magnetite composite has been molded and baked at 80℃ for 20 min in order to cure the composite (Fig.1⑧). Finally the patterned PDMS-magnetite composite has been removed from the PDMS mold (Fig.1⑨). This method can be applied to produce large and simple pattern of micromagnetic tools. Fig.1 (c) shows photographs of an example of mass produced tool families by (a) and (b) method of production.

B. PDMS-Magnetite Nanoparticle Complex

PDMS-magnetite nanoparticle complexes were soft and rubbery materials depending on the concentration of the magnetite. The composite is formed by suspending magnetite (Fe3O4) particles in PDMS at concentrations of 50% by weight. Average diameter of magnetite particles is 0.2 μm.

It is required over 30wt% concentration of magnetite enough to support magnetic actuation. The composite is most useful when the weight ratio of magnetite ranges between 30-70wt% and the present work used 50wt% concentration of the magnetite in order to obtain enough magnetic actuation and also have a moderate softness of the elastic condition. The range of the Young’s modulus was between 2.7~5.4 MPa for 0~70wt% concentration of magnetite and 4.6 MPa for 50wt%. Young’s modulus was estimated by measuring strain vs. stress of macroscopic sample of PDMS prepared under similar conditions as those to form microfluidic system.
C. Suppress Stiction in the Biochip

In order to prevent any stiction of produced micromagnetic tools to the PDMS biochip, the surface of PDMS was specially coated. Three different methods have been developed to coat micromagnetic tools. Firstly, the tools are Teflon coated with CF4 gas by plasma ashing method (Discharge Power: 130 W) for 10 minutes. Secondly the surface of the micromagnetic tools are sputtered by metal (platinum) for 100 sec (film thickness of metal was approximately 100 nm). Thirdly, grinded submicron order glass powder was bonded on the surface of the microtools by means of plasma activation techniques17 and put in the ultrasonic bath in order to remove non-bonded glass powder residue on the surface completely. All three methods of coating are effective to prevent any stiction in the biochip.

D. Actuation of Micromagnetic Devices

Figures 2(a), (b) show the continuous and step actuation of rotation which are applied to micro stirrer or mixers and cell loading systems. Figure 2(c) shows vertical and lateral actuation of micro magnetic tools which can be applied to use valve for two phase flow. Figure 2(d) show the combined actuation of vertical, lateral and rotation to produce orbit trajectory. A couple of micro magnetic tools supported in gel narrow the micro channel enough to hold a embryo cell, then the movement of tools rotate the cell to fix the appropriate position (where nuclei of cell locate the right position) in order to cut cell into half. This process is important to cloning cell. Finally Figure 2(e) shows deformation motion which uses the elastic nature of PDMS composite. By stretching suspended fine parts of micromagnetic tool, the position of the micromagnetic tool can be controlled to block the microchannel to provide valve function. Figure 2(e) also shows deformation model which have parallel plate structure in order to move stable with one direction (left or right) in order to sort cells. Figure 3 shows schematic of independent modules of microchannel and magnetic actuation. They are combined when the micro tools are actuated and they are disconnected when the module of microchannel is replaced by new one in order to avoid any contamination.

E. Actuation of Micromagnetic Devices 1: Continuous Rotation

One of the functions of the versatile micromagnetic device is continuous rotation (Fig2 (a)). The micro-stirrer is actuated by placing the micro stir bars on a rotating couple of disk-shaped ferrite magnet (130-550 mT each) as shown in Figure 318. The fluid flow through the micro-channel is set-up using controlled micro-syringe pump (Kd-Scientific model 230) which generated a pressure flow with a flow rate set to 50 μL/min1. Figure 4 shows the microscopic views of rotating micro stir bar in the micro chamber of biochip. The ceiling of the chamber of stir bar has been sealed with thin PDMS film in order to obtain steady flow and pressure in the microchannel. A photograph of rotating wheel type stir bar of Figure 4(d) indicated that the axis of rotation is fairly stable.
Figure 4 shows the rotating speed of the stir bars and motor on which the disk shaped ferrite magnets (130 and 500 mT) are attached. Two kinds of representative stir bars have been examined. It was observed that stir bar rotated following the rotation of magnet for most of the cases. The rotating speed did not clearly affected by the differences of shape of the stirrers and magnet forces for the current setting. In addition, it was confirmed that the micro stirrer can rotate at least 5 hours without any stiction between PDMSs. Therefore it is expected to keep steady mixing condition for long hours enough to culture cells. Figure 5 shows photos of mixing operation of a micro stir-bar with rotating speed of 1000-5500 rpm in a micro channel. The solutions used for this experiment were composed of dyes and DI water. The blue solution contained of methylene blue, and the yellow solution contained yellow food coloring. Before mixing begins, the distinct boundary between blue and yellow sheath streams is observed along the outlet channel. During mixing, two colors of stream were mixed and greenish stream was observed. After mixing finished, the laminar sheath flow condition has been appeared again and hence the effect of mixing by stirrer is evident.

For quantitative evaluation of mixing efficiency, still images of mixing are captured and are analyzed using color analysis software (Scion Image, Scion Co., Frederick, MD). The procedures of image analysis was followed the work by Ryu et al. (2004). Here a summary of the procedures is presented below: the 24-bit indexes color of each pixel is converted into a three-sliced RGB stack, of which the red slice is used to build the monotone spectrum (for the current study, actual color index of the yellow and blue mixture spans from 21 to 178). Then the mixing index is defined as the standard derivation of color index at individual pixels along a defined line or over a certain area as shown below:

\[
\text{Mixing index} = \sqrt{\frac{1}{N} \sum (c_k - \bar{c})^2}
\]  

(1)

The term \(c_k\) is the color index at pixel \(k\), and \(\bar{c}\) is the average over \(N\) pixels along a sampling line or over sampling area. The more uniform the mixture is, the smaller the mixing index becomes.

Figure 6 shows the profiles of the mixing index along the downstream from the output of the mixing chamber as a
function of four different rotating speeds of stirrer and the condition before and after the mixing. It was observed that the magnitude of the mixing index is far below that of the condition of laminar sheath stream (before and after the mixing). As the rotating speed is higher, the magnitude of mixing index becomes lower and flatter distribution compared to the initial condition, which indicate that nearly complete mixing is achieved by the microstirrer instantly at approximately 500 μm downstream of the mixing chamber.

Fig. 6. Profiles of the mixing index as a function of micro stirrer speed along the downstream from the output of the mixing chamber. Black line indicates the condition before mixing and red dashed line indicates the condition after mixing.

**F. Actuation of Micromagnetic Devices 2: Step Rotation**

It is important to note that another important function of the micromagnetic device is step rotation (Fig 2(b)). Figures 7 and 8 show cell loading system as one of the examples of the revolving type rotation. By switching the magnetic field around the micromagnetic tool, it can rotate every certain angle. This step rotation provides accurate one by one cell loading system.

Fig. 7 A series of micromagnetic tools for revolving type rotation in microfluidic environment. The microchannel was dyed by methylene blue.

Fig. 8. Sequential shots (a)-(b) of loading a single polystyrene bead (100 μm). The microchannel was dyed by methylene blue.

**G. Actuation of Micromagnetic Devices 3: Valve**

Another important function of micromagnetic device is vertical and lateral motion (Fig 2(c)). We have demonstrated the operation of the valve for the two phase flow of cells and water. Figures 9 and 10 show one of the examples of the one dimensional actuation of vertical and lateral motion with valve function. Normally membrane type valve are used to control the microchannel of one-phase flow. It is important to note that the valve for the two phase flow have additional difficulties to manipulate the cells which tend to stick to the membrane. Also it is tend to be recognized the accumulation of cells in the region of stagnation flow around the membrane, and which has another difficulty to prevent clear observation due to its opaque nature. Hence the development of the valve for two phase flow is indispensable in order to achieve feasible transportation of cells. For the current study, the polystyrene beads used for the experiment have a size of 100 μm, assuming the size of embryo cell (≈ 100 μm).

Figure 9 shows two kinds of micro magnetic tools which have a valve function in the microfluidic environment. The convex shape and triangle head shape micromagnetic tools move smoothly to narrow the micro channel normal to the micromagnetic tools in order to block transportation of cells, whilst blocked water medium find the path to flow toward the downstream by using a fine bypass of microchannel (≈ 50 μm) which is less than the size of polystyrene beads (100 μm). Eventually, the polystyrene beads can be blocked until the micromagnetic tools has back to the initial position. Figures 10(a)-(e) and (f)-(j) show the transportation of a group of beads. It is confirmed that the micromagnetic tools have a proper on/off function of valve and smooth transportation of beads toward the downstream.
magnetic tools. The novelties are 1. flexible to fabricate to any 2D shape, 2. soft polymer-based material which is less harmful to manipulate cells in biochip, 3. versatile tools to actuate any direction, 4. mass productive with low cost. Micro-stirrer and micro-valve has been actuated remotely and show the feasibilities of many kinds of actuation and cell manipulations in biochip. The products are important from both commercial and scientific perspectives.

REFERENCES


CONCLUSIONS

We have presented the design and fabrication of micro