ON-CHIP DUAL ARM MICROROBOT FOR CELL MANIPULATIONS
BY MAGNETICALLY DRIVEN MICROTOOLS
Masaya Hagiwara¹, Tomohiro Kawahara¹, Yoko Yamanishi² and Fumihito Arai¹
¹Nagoya University, JAPAN and 
²JST PRESTO, JAPAN

ABSTRACT
This paper presents the innovative driving method of on-chip dual arm microrobots to achieve precise cell manipulations. The positioning accuracy in the new driving method improves 5 times higher and the response speed becomes 10 times quicker against the driving stage than in the conventional method. Commercially available permanent magnets are used to actuate the microrobots owing to the considerably stronger magnetic fields than electromagnetic coil to enforce the high power output. A swine oocyte, which is relatively large cell and require stronger force amount to manipulate, have been precisely handled and cut in microfluidic chip.

KEYWORDS: Magnetically driven microtool, Cell manipulation, Microactuator, Robot on a chip

INTRODUCTION
Cell manipulations by microrobots in the confined space of a microfluidic chip are highly important in the field of biotechnology because of the low contamination capability, repeatability, and high throughput ability. Figure 1 shows the on-chip robots driven by permanent magnets. Using microrobots, the complicated cell manipulation such as an oocyte enucleation process, can be carried out without the dependence on the individual skill. In a previous study, we developed polymer-based magnetically driven microtools (MMTs) for cell manipulation, such as valve, droplet generation, etc [1]; these microtools were controlled by the applied magnetic fields. However, the actuations were only an on-off control, and the positioning accuracy was not required. In order to achieve positioning control, pairs of Helmholtz coils have been used in some research [2], but the supplied force by an electromagnetic coil is not sufficiently strong to manipulate a relatively large cell such as an oocyte. On the other hand, a permanent magnet has a more than 10 times stronger magnetic field to drive an MMT than an electromagnetic coil of the same size.

When an MMT is driven by a permanent magnet on the XY stages from beneath the chip, there is an area where the MMT is not driven when the magnet passes under the MMT; we call this area the “dead band”. Figure 2 shows an MMT (diameter: 1.0 mm) made of Ni and driven by a neodymium (Nd2Fe14B) permanent magnet (diameter: 1.0 mm, grade: N40). This MMT is not driven until the distance between the magnet and MMT is approximately 500 μm, and then the MMT starts following the magnet. The dead band interferes with the precise positioning of the MMT on a chip and deteriorates the effective control of MMT as a robot on a chip because of the slow response speed to the driver unit.

THEORY
In order to counter the cause of the dead band and predict its amount for a certain MMT and a magnet, we have developed a static force model on the MMT. The gravitational force, buoyant force, and the Van der Waals’ force are ignored in this model since these are much smaller than the magnetic force applied to the MMT. For the calculation of the magnet force, the magnet and the MMT are subdivided into very small elemental areas dS₁ and dS₂, respectively. Then, the vector B, which is the magnetic flux density in the small elemental area of the MMT (dS₂), can be computed by dividing the sum of the vectors of the flux from each small elemental area dS₁ by the magnet area S₁. Then, the elemental force dF caused by B can be expressed in the same manner as that analyzed by Abbott et al. [3] and the total magnetic force can be expressed as follows,

\[ \mathbf{F} = \int \int d\mathbf{F} \cdot d\mathbf{S} = \left( \nabla \cdot M \right) \mathbf{B} \cdot d\mathbf{S} \]  

where dB is the flux density from each small elemental area of the magnet dS₂; v is the MMT volume, and M is the magnetization of the material.
The drive force of the MMT is the horizontal component of $F$; further, the friction force $f$ on the MMT can be expressed as the product of the vertical component of $F$ and the static friction coefficient $\mu$. The MMT can move when the drive force is larger than the friction force:

$$f = \mu F \sin \theta \times \mu > 0 \quad (4)$$

where $\theta$ is the angle between $F$ and a horizontal line.

Figure 3 shows the simulation result under the same conditions as Figure 2. Saturation magnetization is a material constant, which is $5.12 \times 10^5$ A/m for Ni. According to the graph, the drive force exceeds the friction force and the MMT starts following the magnet when the distance reaches $513.0 \mu m$. This simulation result corresponds to the measured dead band shown in Figure 2 ($543.0 \mu m$). From this result, it is now obvious that the cause of the low positioning accuracy and controllability is static friction; the next stage is how to reduce the friction on the MMT.

Figure 4 (a) shows the magnetic flux density distributions obtained by a finite element method (FEM) analysis for a neodymium magnet under the Ni MMT mentioned above. As shown in the figure, the direction of the magnetic flux density around the Ni MMT is vertically aligned, and therefore, a large magnetic force is applied in the downward direction. This increases the friction on the MMT in the case of a conventional driving unit. On the other hand, when the MMT is set such that the permanent magnet pole is parallel to the driving direction of a magnet that has the same size as the MMT, the magnetic force in the downward direction is considerably reduced. Here we describe the driving method of the MMT in such setup as the horizontal polar drive (HPD) [4]. Figure 4 (b) shows the concept and the FEM result of HPD. The magnetic flux flows in a circular pattern through the MMT, and its direction is aligned to the driving direction. As a result, there is considerably less magnetic flux in the vertical direction around the center of the MMT as compared to that shown in Figure 4 (a). In addition, the magnetic flux density inside the MMT is twice as high as that shown in Figure 4 (a). This implies that magnetic power with a considerably high efficiency is applied to the MMT and the magnetic force on the MMT is much greater in the driving direction than in the vertical direction; therefore, the friction force is reduced by decreasing the vertical force on the MMT.

EXPERIMENTAL

Figure 5 shows the experimentally obtained following response ability of the MMT against the linear stage with the permanent magnet. The stage moves with 1 degree of freedom (DOF) with a sine wave of 0.5 Hz; the stroke is $\pm 1.4$ mm. In the case of conventional drive, the movement of the MMT against the stage is delayed by 0.3 sec; the maximum difference between the MMT and the stage is 1.0 mm. Under this large time lag, the MMT cannot respond to cell movements in a microfluidic chip and this makes the development of an automation system difficult. On the other hand, the response of the MMT in the HPD is more than 10 times faster and the difference between the stage and the MMT is considerably smaller than in the conventional drive. Precise positioning accuracy and quick response to the stage are essential for the development of automation systems as well as for cell manipulation.

Now, the effectiveness of HPD with respect to MMT actuation is clear; however, HPD is only available with 1 DOF. In the case of cell manipulations, more than 2 DOFs are required for precise control. Therefore, we extended the HPD to 2-DOF precise control actuation by combining four magnets under the HPD conditions. Figure 6 (a) shows the concept of the 2-DOF MMT driven by HPD, and Figure 6 (b) shows the actual design. Two pairs of magnets under the HPD conditions are set with the polar axis normal to each other. The cell manipulation is conducted on the head of the extended part. Figure 6 (c) shows the FEM result of the magnetic flux density for the 2-DOF MMT. It can be seen that the magnets independently actuate the circular disc part of the MMT as it is shown in Figure 4 (b). By combining two pairs of HPD, we have achieved the same level of positioning accuracy and the response speed of the 2-DOF MMT as those of the 1-DOF MMT.
Once the MMT can be controlled multi-DOF, it can be used for more complicated cell manipulations. Figure 7 shows the concept of automation systems for oocyte enucleation. Dual arm MMTs control oocytes position and posture to cut the nuclear part efficiently. As a first step of the automation systems, the experiments for oocyte handling and cutting have been conducted. Swine oocyte, which is a relatively large cell with a size of approximately 150 μm, is used for the manipulation. A pair of 2-DOF MMTs, which are set on the XY linear stages, manipulates the oocyte for carry, rotation and cutting in a chip. Figure 8 shows the experimental result of the oocyte manipulation. MMTs are precisely aimed at the oocyte, and they handle it smoothly. This experimental result validates that MMTs have sufficient power and accuracy to manipulate a relatively large cell with 2-DOF without any harm to the cell.

CONCLUSION
We have developed precise positioning driving method, horizontal polar drive, for the MMT and achieved 5 times higher positioning control and 10 times faster response than the conventional driving method by using commercialized permanent magnets. In addition, since a permanent magnet is used as a drive unit, the generating force on the MMT is considerably higher than that by an electromagnetic coil. Therefore, this driving unit can be applied to a relatively large cell, which is required to have a high power output. By Applying 2-DOF MMT with assembled HPD conditions, we have successfully achieved precise control of cell handling in a microfluidic chip.

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REFERENCES

CONTACT
*M. Hagiwara, tel: +81-52-7895656; hagiwara@biorobotics.mech.nagoya-u.ac.jp