

Active Size Controlled On-chip Droplet Dispensing by Magnetically Driven Microtool

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Abstract— We have investigated an active size controlled droplet generation system by using magnetically driven microtool (MMT). With a lateral motion of the MMT in microchannels, the continuous phase can be pinched off by the movement of MMT to obtain size-controlled droplets actively. With this method, particle-enclosed droplet can be produced on demand to fit the size of each enclosed particle, and which is difficult to carry out only by the fluid dynamic force. For the current study, the system has been evaluated in terms of the frequency of the actuation of MMT and the size of the produced droplets, and found out the response time to change the droplet size by MMT actuation is one third of that only by the fluid dynamic force. This system contributes to the effective transportation of cells in microchannel.

I. INTRODUCTION

IN the last decades, the area of microfluidics has been experiencing rapid growth [1]. One category of microfluidics is droplet-based microfluidics. In particular, microfluidic generation of droplet has attracted a lot of interest, due to the ability of this method to produce droplets with precisely controlled sizes, shapes and internal structure. Unlike continuous flow systems, droplet-based systems focus on creating discrete volumes with the use of immiscible phases. Droplet microfluidics has an ability to perform a large number of reactions without increasing device size or complexity. Droplet-based microfluidics involves the generation and manipulation of discrete droplets inside microdevices. Due to high surface area to volume ratios at the microscale, heat and mass transfer time and diffusion are shorter, facilitating faster reaction times. Unlike in continuous-flow systems, droplet-based microfluidics allows for independent control of each droplet, thus generating microreactors that can be individually transported, mixed,

and analyzed. Since multiple identical microreactor units can be formed in a short time, parallel processing and experimentation can easily be achieved, allowing large data set to be acquired efficiently. Droplet microfluidics also offers greater potential for increased throughput and scalability than continuous flow systems [2].

Generally, microfluidic droplet dispensing on chip can be classified into two categories which are passive and active control of droplets dispensing in microchannel respectively. For example, the passive control of droplets dispensing has been realized via different mechanisms using devices with various designs such as T-junctions [3], [4], flow-focusing devices [1], [5], passive break-up configurations [6], and devices containing terraces [7] in the microchannels. For a particular combination of droplet and continuous phases, the size and polydispersity of the droplets are determined by the dimensions of microchannels and the flow rate of liquid [2]. The effect of these factors has been investigated and the various scaling parameters have been derived for decades. However it has been difficult to control the size of the dispensing droplet precisely due to the fluctuation of pressures in microflow controlled by micropump, because the flow rate of the pump need to be changed whenever it is required to change the size of the dispensing droplet.

On the other hand, on-chip active control can fine-tune the size of dispensing droplet actively. Limited references are available in the field of the active control of dispensing droplet in microchannel. For example, Lee et. al. (2007) have demonstrated a new microfluidic device for active sample flow focusing and the formation of micro-scale droplet in liquids application utilizing a novel controllable moving wall structure [8], [9]. The microfluidic chip can generate uniform droplets with tunable sizes by using combination of flow-focusing and liquid-chopping techniques. The separation and collection of emulsion micro-droplet by size have been explored recently [10], because it is crucial to collect microspheres or microdroplets with different sizes during the operation of continuous droplet dispensing in terms of drug delivery, other biomedical applications. It is important to note that the droplet dispensing methods shown above can generate uniform tuned-size droplets however it is not flexible to change the droplet size on-demand on the moment of producing. Therefore there is a requirement to improve the dynamic range of droplet dispensing.

We have been invented a novel magnetically driven microtools (MMT) which can be produced with low cost and mass productivity, and most importantly this MMT can

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provide many functions of actuators such as sorting, valve and loading [11]-[13]. The developed MMT has unique characteristics of softness whose young's modulus is about 5 MPa, and hence the operation of MMT do not harm cell to be manipulated. For the current study, we have successfully control the size of dispensing droplet actively by using the MMT. This system can change the droplet size on-demand, and hence the size-classified droplets can be produced without any separation and collection of droplets after the production.

Figures 1(a)-(c) show the concept of droplet dispensing with MMT. The MMT with valve function was directly installed to the microchannel as shown in Figure 1(a). The MMT operated with a lateral motion by non-contact magnetic actuation, then MMT can act as "chopper" to disintegrate the multiphase-flow and the size of the dispensing droplet was actively controlled. The microchannel of dispersed phase was designed to be located at different height from the main microchannel for continuous phase, therefore only the dispersed phase microchannel can be switched selectively to be opened or closed.

Also, the proposed system can contribute to the transportation of cells or sharp crystal as shown in Figure 1(b). It is effective and convenient to produce on-demand size-controlled droplet which can be adjusted to fit the size of the object to be transported (such as sticky cells or sharp crystals and so on) which are enclosed in the droplet.

The present system can be used as cell stopper as shown in Figure 1(c). The transportation of cells in microchip can be controlled by the MMT and the group of cell can be transported one by one to the downstream of the microchannel without any agglomerations.

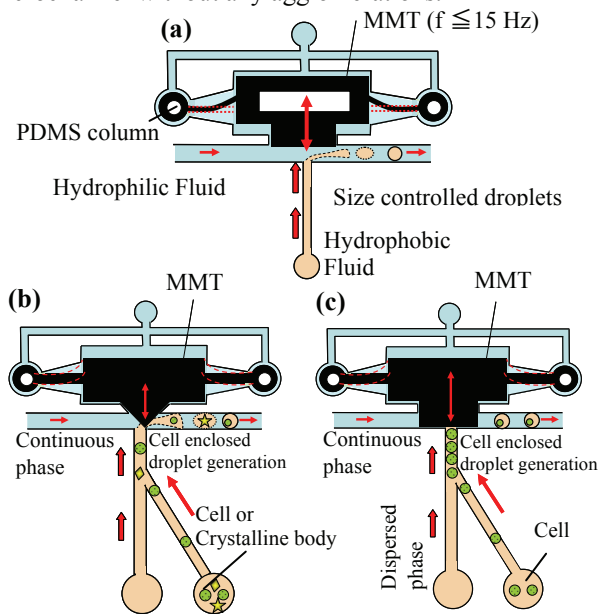


Fig.1 Concept of micro-droplet generation system; (a) size-controlled single-phase droplet dispensing (b) the shape of the tip of MMT is modified (c) cell stopper

II. PROCEDURE OF MMT AND MICROCHANNEL

A. Fabrication of MMT

Figure 2 ([11]-[13]) shows the fabrication process of the MMT, which may be summarized as follows: (1) a thick nega-resist (KMPR1050, KAYAKU MicroChem, Japan.) was spread over the silicon substrate, and (2)-(3) an MMT mold was produced by photolithography, (4) a mixture of PDMS and magnetite (Fe_3O_4 , 50 wt%) was spread over the patterned mold and baked in an oven ($110^\circ C$, 10 min), and (5) the MMT was obtained after the treatment with a stripper liquid, KMPR (Remover PG, $70^\circ C$, KAYAKU MicroChem, Japan.). The surface of MMT was Teflon coated with CF_4 gas by plasma ashing method (Discharge Power: 130 W) for 30 minutes to avoid any stiction in microchannels. The average diameter of the magnetite (Fe_3O_4) was 200 nm. The fabricated MMT was shown in the Figure 3. The MMT was located on a single grain for the size reference. It is suited for mass production.

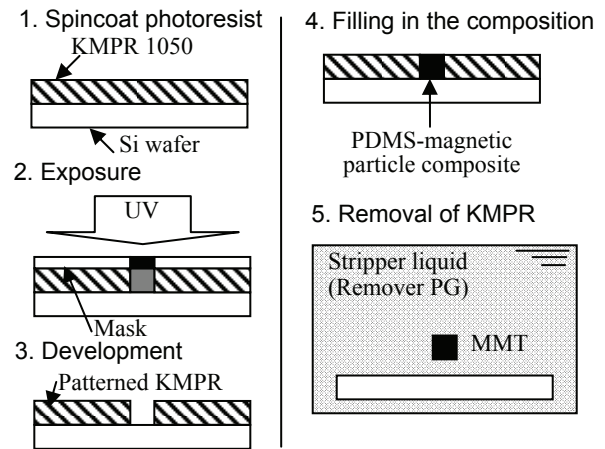


Fig.2 Fabrication process of MMT

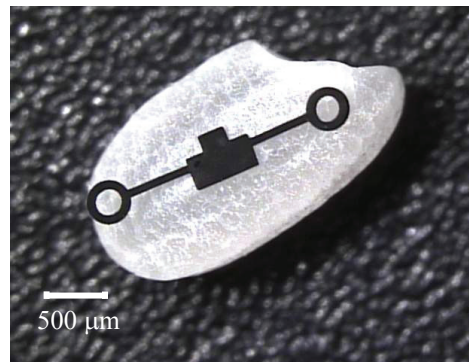


Fig.3 A Photo of fabricated MMT which is placed on a single grain.

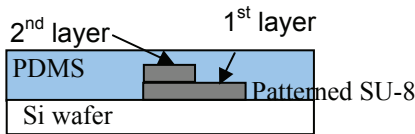
B. Fabrication of Microchannels

It is important to open and close the exit area of microchannel of dispersed phase to control the size of the dispensing droplet actively. Therefore the MMT is required to be installed in the microchannel. As the conventional

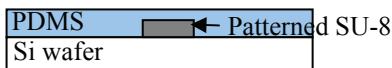
method of installation to the two dimensional microchannel which was used as valve function [11], PDMS chip was bounded with cover glass to produce the microchannel. However this type of chip is difficult to control the exit area of the dispersed phase, therefore we fabricated two different PDMS chips with microchannel and bounded them together to be one chip in order to locate the microchannels of dispersed phase in the different height from the main microchannel (three-dimensional microchannel). Figure 4 shows the process flow to produce the three-dimensional microchannels. First of all, we fabricated SU-8 with the two step exposures which can produce the stepwise microchannel. Then we fabricated another SU-8 pattern with one-step. After transcribed to PDMS chip, the PDMS chips for 1 and 2 in Figure 4, was bounded each other on the hotplate (150°C, 30min) after the installation of MMT. To achieve the perfect alignment of PDMS chips, we have fabricated alignment marks on chip, and the layer of PDMS was guided by the mark with the aid of ethanol.

Figure 5 shows the three-dimensional plan view of the microchannel. We have fabricated two columns made of PDMS in the microchannel so that a couple of ring of MMT can fit them. This column contributes to the simple and accurate installation of MMT and provide stable lateral actuation of MMT.

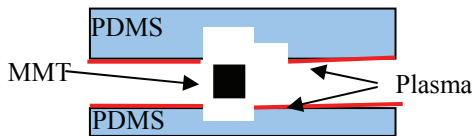
1. Fabrication of top layer of microchannel



2. Fabrication of bottom layer of microchannel



3. Fabrication of 3D-microchannels



4. Installation of MMT on-chip

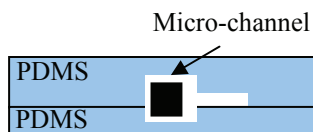
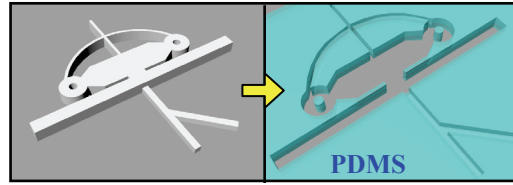


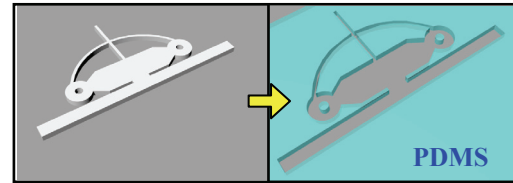
Fig.4 Process flow to fabricate the 3-D microchannels

1. Fabrication of top layer of microchannel



SU-8 pattern on Si wafer Transcribed PDMS microchannel

2. Fabrication of bottom layer of microchannel



SU-8 pattern on Si wafer Transcribed PDMS microchannel

3. Fabrication of 3D-microchannels

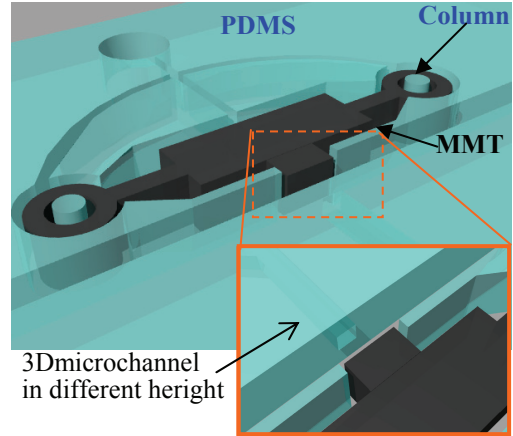


Fig.5 Fabrication of 3-D microchannel (PDMS) and the installation of MMT.

C. Actuation module of MMT

Figure 6 (a) shows the actuation module of MMT. The system consists of two modules—an upper module containing a disposable microchannel and a lower actuation module. In the present configuration, the actuation module is composed of a magnetic circuit unit containing an electromagnetic coil and a permanent magnet unit. The density of magnetic flux generated by the electromagnetic coil is amplified by the permanent magnet (neodymium) unit mounted between the microchannel and the magnetic circuit, and the MMT is moved by non-contact actuation. The permanent magnet (diameter: 4 mm, height: 2 mm) was installed to the rectangular hole (6 mm×10 mm) of PDMS sheet (thickness of 3 mm) by a tweezers and a couple of cover glass (35 mm×50 mm) sandwiched the PDMS sheet. The mechanism of the magnetic circuit and the permanent magnet unit in the actuation module is summarized as follows: the direction of the current in the coil of the magnetic circuit can be switched to reverse the electromagnet's polarity, resulting in

translatory motion of the permanent magnet. The specification of the electromagnetic coil is shown in Figure 6(b). It was confirmed that when the maximum density of magnetic flux achieved a peak (about 7.0 mT), the applied current was about 79 mA. The density of magnetic flux generated by the electromagnetic coil (7.0 mT) was amplified by the permanent magnet, and an adequate density of magnetic flux (maximum = 102 mT, voltage applied to electromagnet = 2.0 V) is transmitted to actuate the MMT in the microchannel. The density of magnetic flux for actuation was approximately 15 times larger than that of the conventional setup without a permanent magnet. Also, it was confirmed that the limiting frequency is about 15 Hz when we applied the square wave current whose peak is 79 mA. It is important to note that the MMT remains in position even after the magnetic circuit is switched off. Thus, it enables lower power consumption, because no energy is consumed in keeping the MMT fixed in the same position.

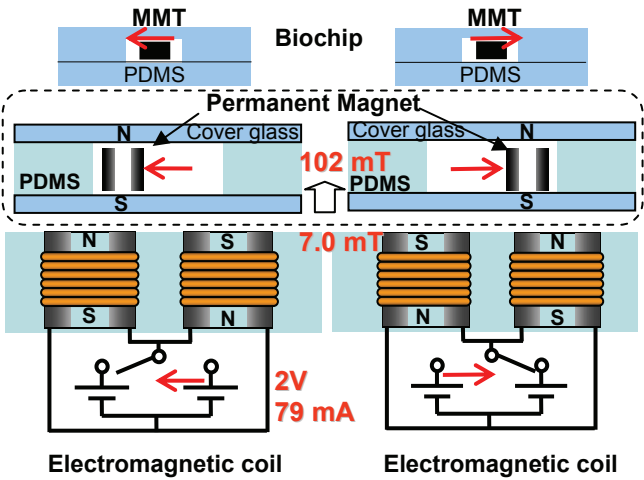


Fig.6(a) Actuation module of MMT

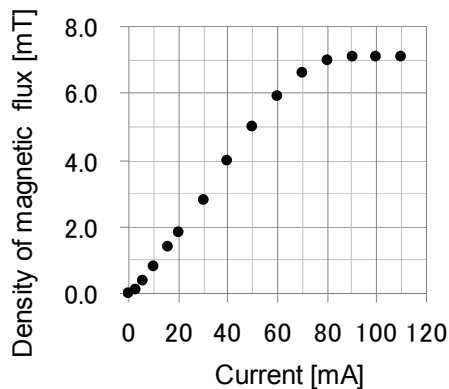


Fig.6(b) Characteristics of electromagnetic coil

III. OPERATION OF DROPLETS DISPENSING BY MMT

A. Operation of MMT

Figure 7 shows the photos of microchannel after the installation of MMT. Figure 7(b) shows the cross section at A-A' in Figure 7(a). As shown in the figure, the microchannel

of dispersed phase is located in the middle height of the microchannel of continuous phase. The magnified image in Figure 7(a) shows the area of droplet dispensing in the microchannel. The MMT (50wt% of Magnetite Fe_3O_4) has a characteristic of softness (Young's Modulus ≈ 5 MPa), and we have fabricated a square hole ($200 \times 500 \mu m$) in the MMT which helps to reduce the drag force when the MMT is in the lateral motion by reducing the contact area of MMT and microchannel. The narrow arched-shaped microchannel located above the MMT was fabricated to remove any bubbles at the initial stage of the experiment whose exit is closed during the operation of the experiment of droplet dispensing. The amplitude of MMT is larger than the width of microchannel ($200 \mu m$), and hence the lateral motion of MMT is always restricted by the wall of microchannel. The amplitude of MMT is fixed by the width of the microchannel for the present experiment.

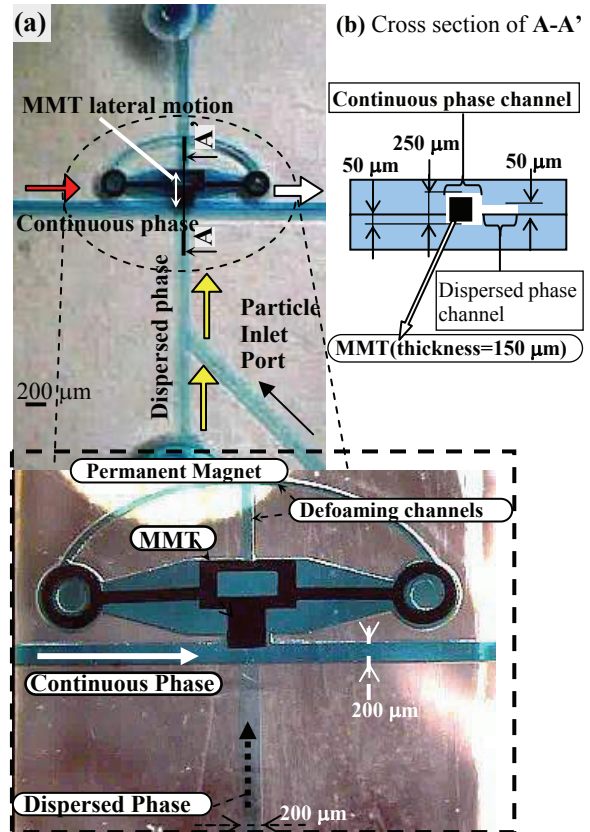


Fig.7 (a)Top View of the MMT installed biochip (the flow is dyed with methylene blue) and (b) Cross section of A-A'.

Figure 8 shows the photos of the droplet dispensing experiment. The liquid for continuous phase was ethanol and the dispersed phase was olive oil. The shape of the dispensing droplet was ellipse shape due to the limitation of the height of the microchannel of $200 \mu m$, therefore the size of the droplets was evaluated by using the equivalent diameter. Figure 8 shows the representative condition (oil: $1 \mu m/L$, ethanol: $5 \mu m/L$) of droplet dispensing and Figure 8(a) shows the

droplet dispensing without the actuation of MMT and Figure 8(b) shows the droplet dispensing with the MMT actuation (0.6 Hz). As you can see in the figures, the size of the droplet was effectively reduced with the actuation of MMT. Therefore it was confirmed that the size of the droplet and the frequency of the MMT has a certain relationship.

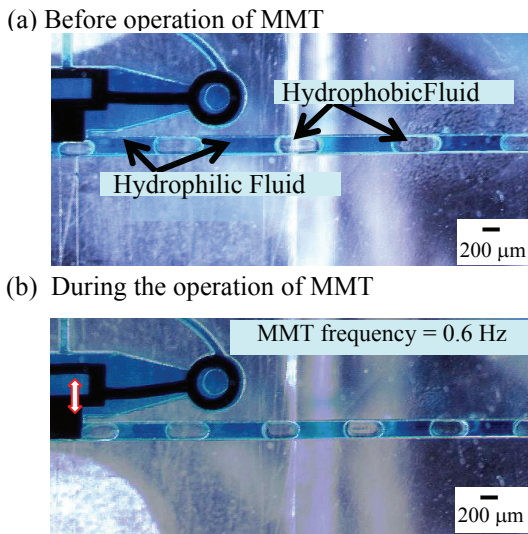


Fig.8 Operation of droplet dispensing by MMT.

B. Evaluation of Droplet Size

To evaluate the relationship between the size of the dispensing droplet and the frequency of the MMT actuation, the equivalent droplet size was measured by CCD images as a function of MMT actuation frequency. The experiment was carried out with two different conditions of the flow rate (1.oil: 1 $\mu\text{L}/\text{min}$, ethanol 5 $\mu\text{L}/\text{min}$ and 2. oil: 1 $\mu\text{L}/\text{min}$, ethanol: 4 $\mu\text{L}/\text{min}$). As you can see in Figure 9, the size of the droplet is monotonously reduced with increase of the frequency of the MMT for both flow rate conditions. Consequently, about 15% reduction of droplet size was achieved by the increase of the MMT frequency from 0 to 5 Hz.

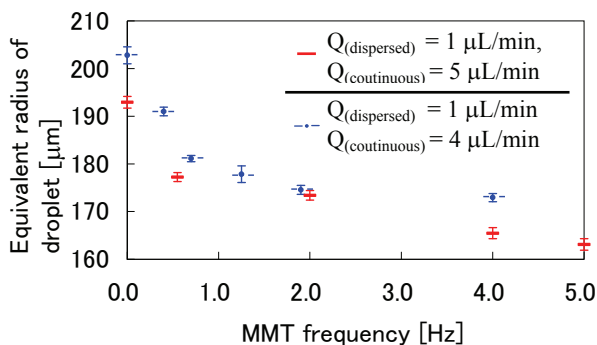


Fig.9 Profiles of the droplet size as the change of the MMT frequency.

C. Response Time of Droplet Dispensing

It is important to control the size of the droplet corresponding to the size of the particle or cell which is

enclosed in the droplet within a limited time. Therefore we have evaluated the response time of dispensing of the droplets by two different methods which are 1. by the change of the flow rate of the continuous and dispersed phase. 2. by the change of the frequency of MMT.

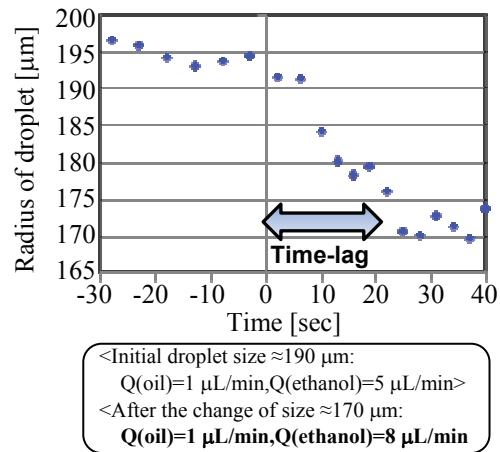


Fig.10 Response of changing the size of the droplet by changing the flow rate (condition 1).

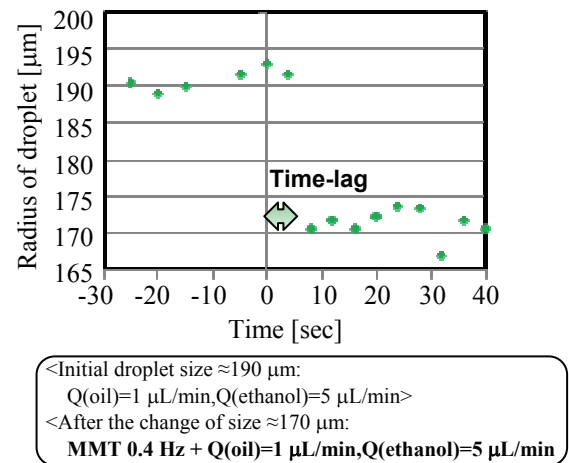


Fig.11 Response time of changing the size of the droplet by the fluidic force and MMT actuation (condition 2).

To compare the time-lag under the same condition, first of all, we fixed the diameter of the droplets before and after the actuation at about 190 μm and 170 μm respectively. For example, the flow rate for oil of 1 $\mu\text{L}/\text{min}$ and for ethanol of 5 $\mu\text{L}/\text{min}$ produce the droplet whose size is about 190 μm , and hence we have set the flow rate condition as the initial setting. Also, the flow rate for oil of 1 $\mu\text{L}/\text{min}$ and for the ethanol of 8 $\mu\text{L}/\text{min}$ produced the droplet whose size is about 170 μm , therefore we have set the condition as second setting to evaluate the response time only by the change of the flow rate (condition 1). On the other hand, the droplet size becomes about 170 μm when the actuation frequency of MMT was set at 0.4 Hz with the initial setting of the flow rate (the flow rate for oil of 1 $\mu\text{L}/\text{min}$ and for ethanol of 5 $\mu\text{L}/\text{min}$). Hence we

have set the MMT frequency of 0.4 Hz as the second setting to evaluate the response time by the change of MMT actuation frequency (condition 2). The flow in the microchannel was controlled by two microsyringe pumps (Kd-Scientific model 230) for oil and ethanol, and which was used for both experimental conditions of 1 (by the change of flow rate) and 2 (by the change of the frequency of MMT). In summary, condition 1; the flow rate was set at 1 $\mu\text{m}/\text{min}$, 5 $\mu\text{m}/\text{min}$ for oil and ethanol respectively before changing the size of the droplet, and the flow rate of ethanol was changed to 8 $\mu\text{m}/\text{min}$ to change the size of the droplets, whilst condition 2; the flow rate was fixed to 1 $\mu\text{m}/\text{min}$, 5 $\mu\text{m}/\text{min}$ for oil and ethanol respectively, and the MMT actuation frequency was set at 0.4 Hz to change the size of the droplet. Figure 10 shows the response time of the change of the droplet size by the change of the flow rate. It was about 20 sec. On the other hand the response time of the change of the droplet size by the change of the MMT frequency (Figure 11) was about 7 sec. Therefore it was confirmed that the response time by the change of the MMT frequency is one third of that by the change of the flow rate for the condition.

D. Dispensing of Droplets with Enclosed Particles

Figure 12 shows the operation of droplet dispensing with a function of cell stopper as described in Figure 1. It was confirmed that a polystyrene bead ($\phi = 50 \mu\text{m}$) was successfully stopped by the MMT, and the particle went smoothly inside the droplet to be transported when the MMT was lifted to open the gate. This function contributes to the transportation of cells in the future.

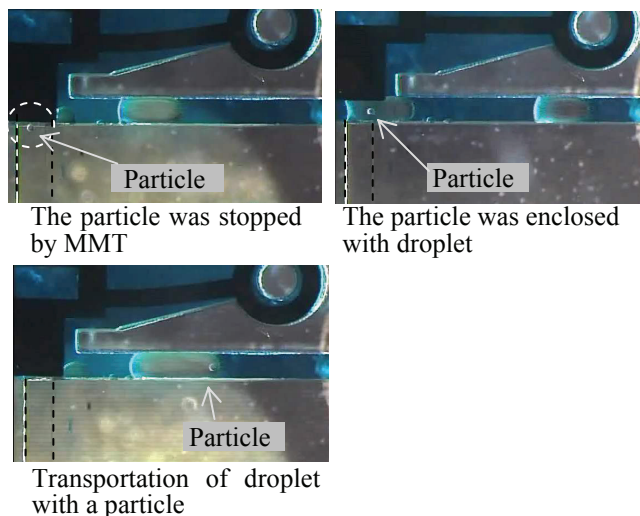


Fig. 12 The droplet dispensing with particle after the particle was stopped by MMT.

IV. CONCLUSION

For the present study we have successfully operated an active size controlled droplet generation system by using MMT. With a lateral motion of the MMT in microchannels, the continuous phase can be pinched off by the movement of MMT to obtain size-controlled droplets actively. With this

method particle-enclosed droplets can be produced on demand to fit the size of each enclosed particle, and which is difficult to be carried out by fluid dynamic force. About 15% reduction of droplet size was achieved by the increase of the MMT actuation frequency from 0 to 5 Hz. Also, the response time to change the droplet size by the change of the MMT frequency is one third of that by the change of the flow rate. The particle was successfully stopped by the MMT, and the particle went smoothly inside the droplet to be transported when the MMT was lifted to open the gate.

This function can be applied to the transportation of cells and which contribute to drug delivery and other biomedical applications. Also, the production of droplets can be scalable by changing the shape of the edge of MMT. The present active controlled droplet dispensing system can contribute to improve the dynamic range of the dispensing droplets and simplify the microchannels design which is difficult to obtain in the passive control with complicated design of microchannels.

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