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On-demand and Size-controlled Production of Emulsion Droplets by Magnetically Driven Microtool

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Abstract— **We have successfully produced emulsion droplets on a chip with size-control and on-demand droplet generation by using magnetically driven microtool (MMT) which has a parallel plate structure to be constrained in translational motion. With a lateral motion of MMT in microchannels, the continuous phase can be cut into different size of droplets and the dispersed phase flow can inflow into the microchannels by the movement of MMT to obtain both of size-controlled and on-demand droplets actively. The size range of the produced droplet was three times as large as the previous system by using novel hydraulic design of the chip, and also the dispersing the fluid was successfully prevented from leakage when it is chopped by using MMT.**

I. Introduction

DROPLET-BASED microfluidics has attracted much interest due to its production of precisely controlled droplet size, shape, and structure [1][2]. Unlike in continuous-flow systems, droplet-based systems focus on discrete volumes with immiscible phases, conducting 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 on a microscale, heat and mass transfer time and diffusion are shorter, facilitating faster reactions. Also unlike continuous-flow systems, droplet-based microfluidics enables individual droplets to be independently controlled, generating microreactors that are individually transported, mixed, and analyzed. Given the speed with which multiple identical microreactors can be formed, parallel processing and experimentation are achieved easily, enabling large datasets to be efficiently acquired. Droplet microfluidics also possesses greater potential for increased throughput and scalability than continuous-flow systems.

Emulsification of liquids is emerging technologies [3] such as encapsulation of DNA [4], nano-particles for drug delivery system [5], single-molecular enzyme analysis [6]. Since emulsification has become a crucial industrial technique, the quality of the emulsion droplets is significant, especially in biotechnology and nano-medicine applications [7]. Conventionally the manufacturing of the emulsification droplets utilized large-scale instruments such as blenders [8], high-pressure homogenizers and ultrasonic homogenizers. In the past decade, membrane emulsification has been demonstrated as a promising method by using a liquid pressed through membrane pores to form droplets that carry away a continuous phase flowing over the membrane [3][9].

On-chip-dispensed microfluidic droplet control in microchannels is roughly divided into active and passive. Passive droplet-dispensing control has been realized via different mechanisms using device designs such as T-junctions [10], [11], flow-focusing devices [12], passive break-up configurations [13], and devices containing terraces [14] in microchannels. Droplet size and polydispersity are determined for particular combinations of droplets and continuous phases by microchannel dimensions and liquid flow rates [15]. Decades have been devoted to studying the effects of the scaling parameters which tend to carry difficulties of the pressure fluctuation in microflows controlled by micropumps because the pump flow rate must be changed whenever droplet size is changed.

In related work on active droplet-dispensing, Lee et al. (2007) demonstrated a microfluidic device for actively sampling flow focusing and the formation of microscale droplets in liquids using a controllable moving wall [7], [16]. The microfluidic chip generates uniform droplets by combining flow focusing and liquid chopping. Separating and collecting emulsion microdroplets have been explored [17]. However the systems tend not to have high-response of production of droplets. Without on-demand control of droplet generation, the chemicals of dispersed phase tend to be wasted. Besides, it is ideal to control the number of mono-dispersed emulsions to be collected at the exit port of the chip without any sorting devices to remove undesired satellite droplets, and which has possibility to contribute to the other processes such as enclosing cells, DNA and enzyme to be synchronized.

In our previous study, we have developed low-cost mass-produced magnetically driven microtools (MMT) which provided many actuating functions such as sorting, valve operation, and loading [18]-[22]. MMTs are soft, and thus do not harm cells being manipulated. Recently, we have successfully and actively size-controlled dispensing droplet using MMTs, changing droplet size and producing size-classified droplets without droplet separation or collection after production [23]. MMTs with a valve function have been placed directly in microchannels (Fig. 1(a)), and MMTs actuated laterally by non-contact magnetism can be made to act as "choppers" disintegrating a multiphase flow and controlling droplet size actively. A dispersed-phase microchannel was located at a height different from that of the main microchannel in a continuous

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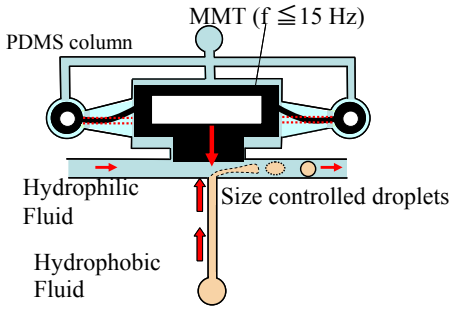
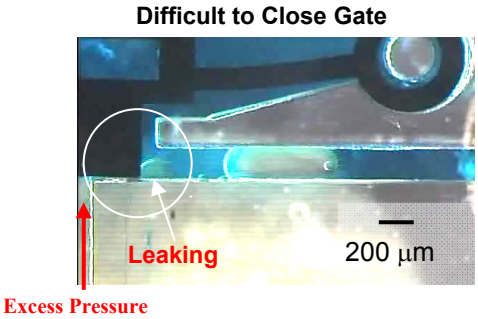
phase, enabling the dispersed-phase microchannel alone to be selectively switched open or closed. However, it was difficult that the MMT closed the dispersed-phase microchannel perfectly which prevent "on-demand" production of micro-droplet (Fig. 1(b)). It is ideal to produce droplets "as planned" without any sorting devices to remove undesired satellite droplets when the droplets are collected at the outlet channel. For the current study, we discuss about the improved type of the droplet dispensing chip as shown in (Fig.1 (c)).

(a) Conventional Setting [20]



(b) Conventional Setting [20]



(c) Current Setting (Improved design)

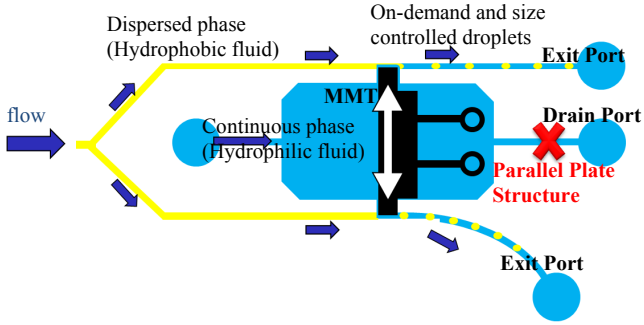
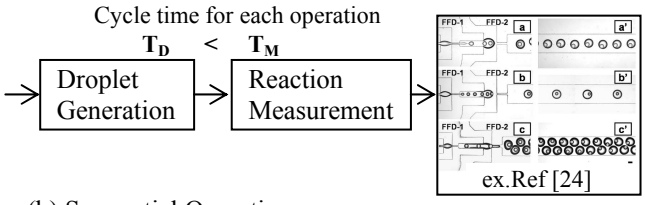


Fig.1 Conventional and current micro-droplet generation system
(a) concept view (b) a photo of operation (c) improved current setting

Figure 2 shows the typical process flow for dispensing of droplet on a chip. Figure 2(a) is the conventional droplet dispensing without on-demand control and the droplet is dispensed continuously by adjusting the flow rate passively. However, the dispensed droplets tend to be measured or reacted with another chemical. The time required for the sequential operations tend to be longer than the time required for the droplet dispensed. Therefore it is important to avoid wasting the chemicals by stopping dispensing droplet on-demand. Moreover it is important to supply droplet quickly when it is required. By using the on-demand production of the droplet as shown in the Figure 2(b), it is possible to control the number of the droplet as planned when it is required. While the droplet generations without on-demand control tend to take time to stabilize the flow when the syringe pump restarted to produce the droplet.

(a) Conventional Operations



(b) Sequential Operations

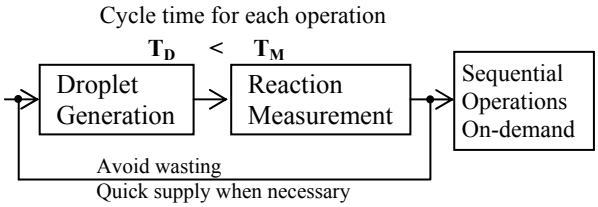


Fig.2 Advantages of on-demand production of droplet

In this study, we have developed novel on-demand and size controlled production of emulsion droplets by MMT. The concept view of the microchannel is shown in Figure 3, and an MMT actuated laterally by non-contact magnetism can be made to act as "choppers" disintegrating a multiphase flow and controlling droplet size actively and on-demand.

The mechanism of generating droplets are summarized as follows (Fig.3); When the MMT moves downward, it blocks the channel below, so the hydrophobic fluid (olive oil) only have one way exit that is the upper channel to flow out. When the MMT moves up, the upper hydrophobic fluid channel is stopped, and hydrophobic fluid only have one exit the downside channel to flow out. Meanwhile, the MMT cuts the hydrophobic flow and generates one droplet. The hydrophilic flow (ethanol dyed with methylene blue) leaks through the gap of MMT because of its low fluidic drag force. On the other hand, the hydrophobic fluid cannot pass the gap because of its high fluidic drag force. Therefore, the droplet is transported by the hydrophilic flow. Based on the same principle, when the MMT suddenly moves down, it cut the hydrophobic flow and generates one droplet. The flow in the upper channel helps the droplet outflow from the upper exit port. Consequently, on-demand and size-control production of droplets could be easily realized by using this novel hydraulic design of the chip. This hydraulic design balanced the excess pressure on a chip efficiently and the double number of size-controlled droplets can be produced at both MMT sides.

II. Design and Fabrication

A. Concept of on-demand and size-controlled Chip

The concept view of the microchannel is shown in Fig. 3, and an MMT actuated laterally by non-contact magnetism can be made to act as "choppers" disintegrating a multiphase flow and controlling droplet size actively and on-demand. According to the motion of the MMT moving up and down, the dispersed-phase microchannel allowed to be selectively switched open or closed. In this study, we have developed a novel method of on-demand production of emulsion droplets by MMT. The concept view shows the area of droplet dispensing in the microchannel. The MMT (50 wt% of magnetite Fe_3O_4 and 50 wt% of poly-dimethyl siloxane (PDMS)) has a characteristic of softness (Young's Modulus ≈ 5 MPa), [18].

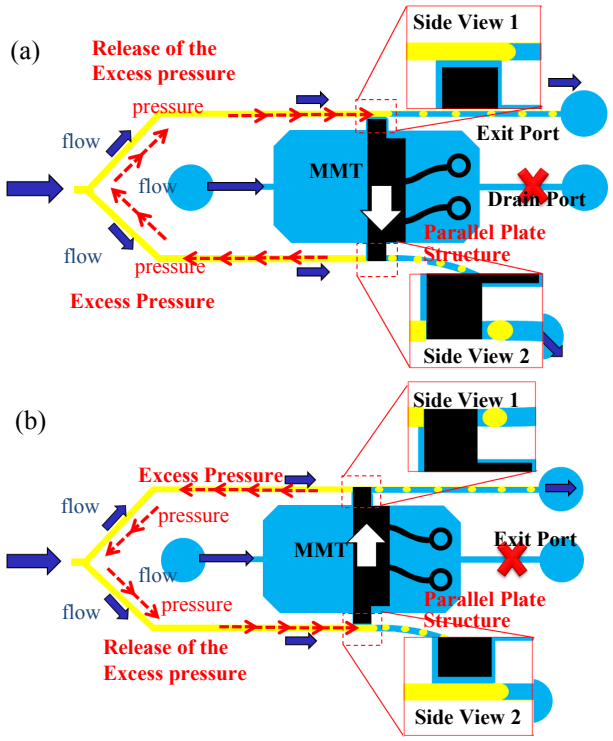


Fig.3 Concept view of current on-demand and size-controlled droplet dispensing system (a) striking droplet on the bottom (b) striking droplet on the top

The channel on the right side of chamber is 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. First of all, we have evaluated the displacement of MMT to confirm that the lateral motion of MMT is enough to close the channel. The calculation of a simple bending analysis indicated that the displacement of MMT by the density of magnetic flux of permanent magnet (102 mT) was 902 μm and which is larger than the width of microchannel (150 μm). Thus the lateral motion of MMT is always restricted by the wall of microchannel.

B. Mechanism of droplet dispensing by MMT

Figure 4 shows the overview of real chip, in the middle of this figure the blue long-hexagonal part is the chamber with a MMT installed in. MMT is black and have a parallel plate structure, and the chamber is sandwiched by two continuous phases. The two transparent microchannles showed in the figures are channels inflow of olive oil while the ethanol is inflow at the middle channel. By controlling the excess pressure on the chip as described in Figure 3, on-demand and size-control production of droplets could be easily realized by using this novel hydraulic design of the chip. Compare to the conventional design [20], the advantage of the proposed design is that it can prevent dispersing the fluid by leakage. By using the conventional design, there always exists continuous flow inlet into the microchannel, therefore the size-control of the droplet is limited from 160 μm to 210 μm. But in this paper, we can obtain the droplet much more stably with wide range of sizes from the extremely tiny size (40 μm) to the huge size (200 μm) of droplet by controlling the fluid ratio and the frequency of MMT.

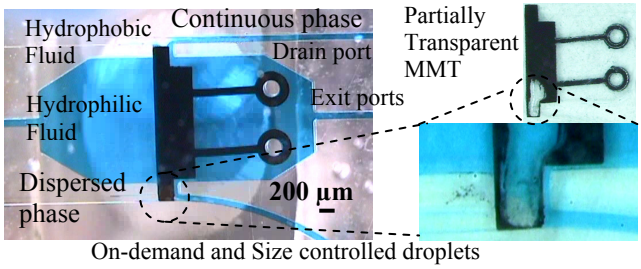


Fig.4 Overview of on-demand and size-controlled droplet dispensing chip and a partially transparent MMT to analysis the boundary between hydrophobic and hydrophilic flow

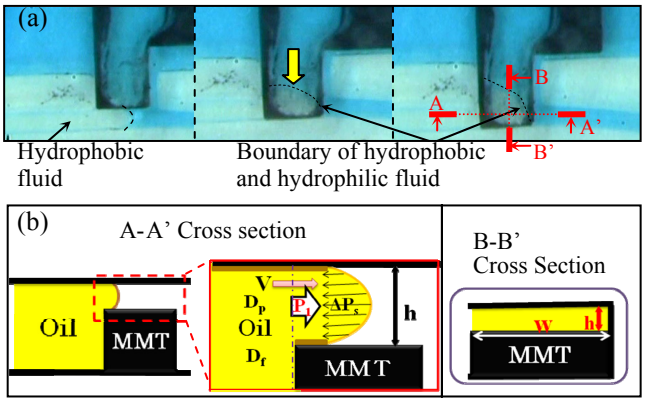


Fig.5 (a)the position of the boundary of hydrophobic and hydrophilic fluid, and (b)the overview of the predominant parameters.

To analyze the mechanism of droplet dispensing, we have fabricated a partially transparent MMT whose transparent part is made of only PDMS as shown in the Figure 4. By using the transparent window, the boundary between hydrophobic and hydrophilic fluid can be observed. It was confirmed that the boundary between hydrophobic and hydrophilic fluid hold the

position on the MMT when MMT is closing to the one side of microchannel as shown in the Figure 5(a). Consequently, the stability of the boundary provide the stable droplet dispensing system. Although, the surface tension is predominant parameter when the boundary of the membrane is fixed (which express as the curverture of the boundary), the fluid drag force is predominant when the boundary is instable. We could estimate the pressure limit of the syringe pump by calculating the fluid drag forces as shown in the Figure 5(b). The density, viscosity and surface tension of hydrophobic fluid is set to 0.90 [g/cm^3], 0.081 [Pa·S] and 25 [mN/m] respectively and those for the hydrophilic fluid is set to 0.79 [g/cm^3], 0.0089 [Pa·S] and 22 [mN/m] respectively. Suppose the MMT is pulled to the bottom plate of microchannel due to the density of magnetic flux of electromagnetic coil, the drag force can be estimated as follows;

$$D = D_f + D_p \quad (1)$$

where, D is the total drag force of the fluid and the density, D_f is the drag force due to friction (viscous resistance) and D_p is the drag force due to the fluid pressure, then,

$$D_p = 0.5\rho V^2 C_p S = 1.89 \times 10^{-27} \text{ [N]} \quad (2)$$

$$D_f = 2\rho V/A = 9.5 \times 10^{-8} \text{ [N]} \quad (3)$$

$$\therefore D \approx D_f \quad (4)$$

$$P_D = D/S = 12 \text{ Pa} \quad (5)$$

here, P_D is the total resistance pressure and A is the cross section diameter and V is the fluid velocity and S is the area of the cross section. Consequently, we could conclude that the system can produce droplet with stable condition as long as the hydrophobic pressure is less than 12 Pa. For the current study, four consitions of the hydrophobic flow rate (Oil) was examined which are;

1. P_1 = 3.9 Pa (Oil: 0.01 mL/h, ethanol: 1 mL/h)
2. P_1 = 5.2 Pa (Oil: 0.02 mL/h, ethanol: 1 mL/h)
3. P_1 = 6.4 Pa (Oil: 0.04 mL/h, ethanol: 1 mL/h)
4. P_1 = 8.3 Pa (Oil: 0.08 mL/h, ethanol: 1 mL/h)

and the pressures of all four conditions are less than 12 Pa.

C. *Actuation method of MMT*

Figure 6 shows the actuation method of MMT that consists of two modules - an upper module containing a disposable microchannel and a lower actuation module. 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 × 10 mm) of PDMS sheet (thickness of 3 mm) by a tweezers and a couple of cover glass (35 × 50 mm) sandwiched the PDMS sheet. 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 density of magnetic flux generated by the electromagnetic coil is amplified, and an adequate density of magnetic flux (maximum = 102 mT, voltage applied to electromagnet = 1.5 V) is transmitted to actuate the MMT in the microchannel.

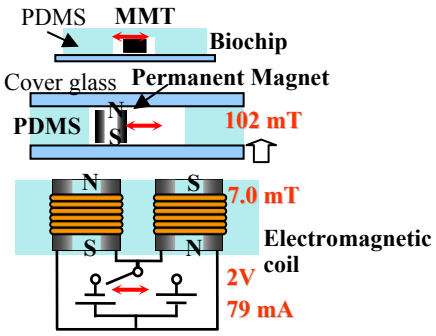


Fig.6 Detailed drawing of actuation module of MMT

III. On-chip Emulsion Droplet Dispensing

A. *Operation of the Droplet Dispensing*

Figures 7 & 8 show the photos of the droplet dispensing experiment. The liquid for continuous phase was olive oil and the dispersed phase was ethanol dyed with methylene blue. The shape of the dispensing droplet may be ellipse shape due to the limitation of the height of the microchannel of 200 μm; therefore the size of the droplet was evaluated by using the equivalent diameter. Then the lateral motion of MMT vibrates up and down to "strike" hydrophobic fluid and thrust a certain amount of it in the transport channel.

Figure 7 shows the droplet dispensing by the frequency (1 Hz) of MMT with the representative condition of droplet dispensing (oil: 0.02 ml/h, ethanol: 1 ml/h). Figure 7(a) shows the microchannel is open by the MMT and Fig. 7(b) shows the continuous phase olive oil flow is cut by the MMT, and the droplet is generated meantime. Fig. 7(c) shows the microchannel is closed by the MMT. It is clear to observe that the droplet is slender, and the equivalent radius is also two times larger than that of the same flow ratio condition and different MMT frequency (2Hz) showed below.

Figure 8 shows the droplet dispensing by the different frequency (2 Hz) of MMT with the same condition of droplet dispensing (oil: 0.02 ml/h, ethanol: 1 ml/h). Figure 8(a) shows the microchannel is open by the MMT and Fig. 8(b) shows that the MMT penetrates and blocks the channel, and generates a droplet, and Fig.8 (c) shows the tiny size-droplet generated in the transport channel. As you can see in the figures; the size of the droplet is small with the actuation of MMT. Therefore it can be predicted that the size of the droplet and the frequency of the MMT have a certain relationship.

B. *Evaluation of dynamic range of size control*

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 four different conditions of the flow rate as mentioned in the section II B.

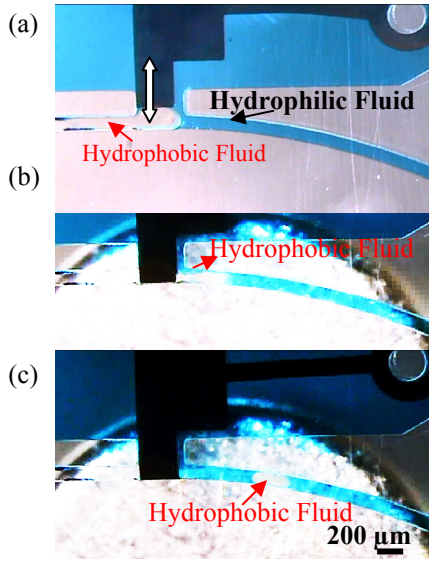


Fig.7 Droplet dispensing by MMT(1 Hz); (a) The microchannel is open by MMT, (b) The olive oil flow is cut by MMT, (c) The microchannel is closed by MMT

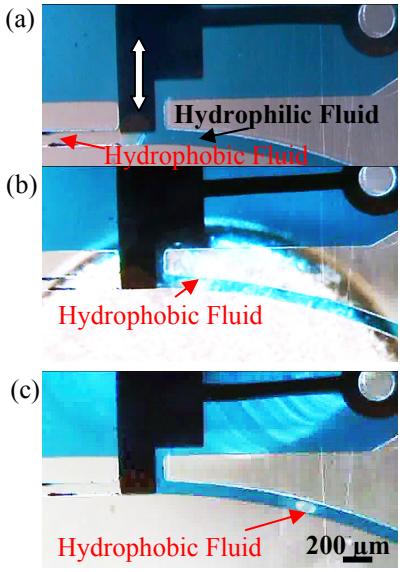


Fig.8 Droplet dispensing by MMT(2 Hz); (a) The microchannel is open by MMT, (b) The olive oil flow is cut by MMT, (c) The microchannel is blocked by MMT.

As you can see in Fig. 9, the size of the droplet is monotonously reduced with increase of the frequency of the MMT for both flow rate conditions. Comparing the different continuous phase flow rate, we can see from Fig. 9 that the size of the droplet is enlarged with increase of the flow rate. The size of droplet is mainly controlled by frequency of MMT. It is observed that we could get the droplet from the radius of 40 μm to 180 μm.

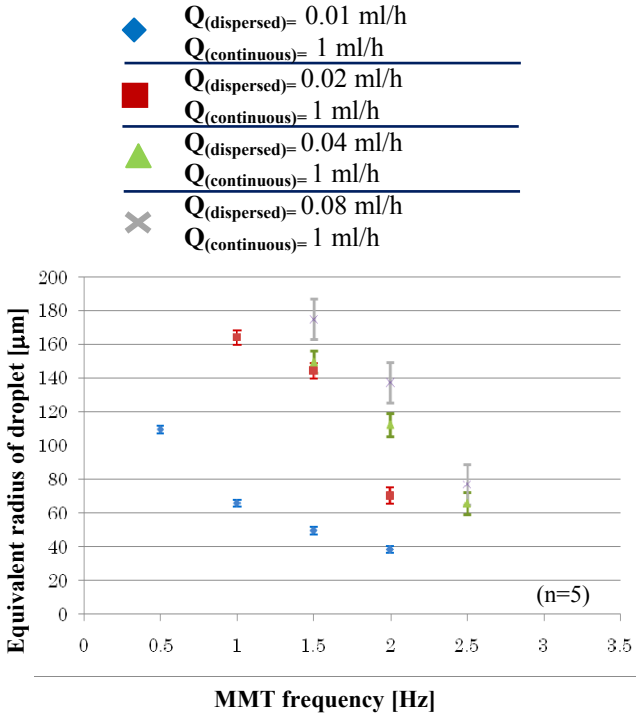


Fig. 9 Profiles of the droplet size as a function of the MMT frequency.

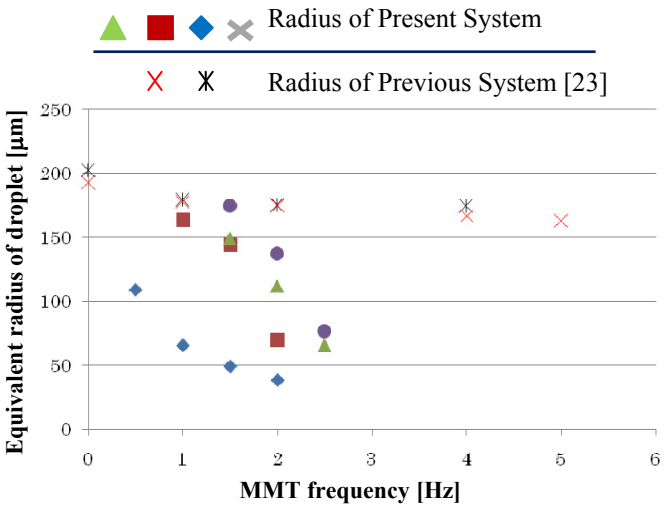


Fig.10 Comparison between previous study and current study in terms of equivalent radius of droplet as a function of MMT frequency

In order to show the advantages of new design clearly, the comparison diagram was plotted to exhibit superiorities of the new design compared to the previous system. Figure 10 shows the comparison of radius of droplet on average between two different designs. A cross and star shapes stand up for the radius of droplets made by the previous design. Meantime the three different types of polygon stand up for radius of droplets made by the current system.

From this diagram, it is clear to see that the radius of dispensed

droplets made by the previous system ranged between 160 μm and 210 μm. On the other hand, the present system can easily achieve the radius range between 40 μm and 180 μm. Also there is a fatal issue on the previous system. A droplet is generated in the microchannel, even though the MMT is not moving (0 Hz). This means there is leakage of droplets, when we do not intend to make droplets in the microchannel. The superiority is obvious for the present setting. We can block the microchannel to prevent generating a droplet. This system is stable and easy to realize on-demand control of droplet generation.

IV. CONCLUSIONS

For the present study we have successfully realized an active size controlled and on-demand droplet generation 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. Base on this novel design of microchannel, we can easily generate droplet in size over a wide range by changing the flow rate and frequency of MMT. We evaluated the pressure condition to obtain stable droplet generation with a partially transparent MMT.

Compare to the conventional design without pressure control, the proposed design can prevent dispersing the fluid from any leakage and most importantly we can obtain droplets much more stably with wider range of sizes from the extremely tiny size (40 μm) to the huge size (180 μm) of droplet by controlling the fluid ratio and the frequency of MMT. To obtain more tiny scale droplet, the width of microchannel should be reduced. This design shows many excellent advantages and will provide a broad application in the future. The proposed system has potential to contribute to emulsification process for biotechnology and nano-medicine.

ACKNOWLEDGMENT

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REFERENCES

[1] P. Garstecki, H. A. Stone and G. M. Whiteside, "Mechanism for Flow-Rate Controlled Breakup in Confined Geometries: A Route to Monodisperse Emulsions", Physical Review Letter, Vol.94, No.164501, 2005.

[2] S-Y Teh, R. Lin, L-H Hung, A. P. Lee, "Droplet microfluidics", Lab on a chip, Vol.8, p.198-220, 2008.

[3] C. Charcosset, I. Limayem and H. Fessi, "The membrane emulsification process—a review", Journal of Chemical Technology and Biotechnology, Vol.79, p.209-218, 2004.

[4] A.V. Korobko, W. Jesse and J. R. C. Van der Maarel, "Encapsulation of DNA by Cationic Diblock Copolymer Vesicles", Vol. 21, p. 34-42, 2005.

[5] S. M. Moghimi, A. C. Hunter and J. C. Murray, "Nanomedicine: current status and future prospects", The FASEB Journal 19, p. 311-330, 2005.

[6] T. Kojima, Y. Takei, M. Ohtsuka, Y. Kawarasaki, T. Yamane, H. Nakano,"PCR amplification from single DNA molecules on magnetic beads in emulsion: application for high-throughput screening of transcription factor targets", Nucleic Acids Research, Vol.33 (17), e150.

[7] C-W. Lai, Y-H. Lin, G-B. Lee, "A microfluidic chip for formation and collection of emulsion droplets utilizing active pneumatic micro-choppers and micro-switches", Biomedical Microdevices, 10, p.749-756, 2008.

[8] G. T. Vladisavljevic, H. Schubert, "Preparation and analysis of oil-in-water emulsions with a narrow droplet size distribution using Shirasu-porous-glass (SPG) membranes", Desalination 144, p.167-172, 2002.

[9] C-T. Chen and G-B. Lee, "Formation of microdroplets in liquids utilizing active pneumatic choppers on a microfluidic chip", Journal of microelectromechanical systems, Vol. 15 (6), p.1492-1498, 2006.

[10] T. Nisisako, T. Torii and T. Higuchi, "Novel microreactors for functional polymer beads", Chemical Engineering Journal, Vol.101, p.23-29, 2004.

[11] Q. Lu, Z. Weng, G. Shan, G. Lai and Z. Pan, "Effect of Acrylonitrile Water Solubility on the Suspension Copolymerization of Acrylonitrile and Styrene", Journal of Applied Polymer Science, Vo101, p.4270-4274, 2006.

[12] M. Seo, C.Paquet, Z. Nie, S. Xu and E. Kumacheva, "Microfluidic consecutive flow-focusing droplet generators", Lab on a chip, Vol.3, p.986–992,2007.

[13] D.R. Link, S. L. Anna, D. A. Weitz and H.A .Stone, "Geometrically Meditated Breakup of Drops in Microfluidic Devices", Physical Review Letter, Vol.92, No.054503, 2004.

[14] I. Kobayashi, K. Uemura and M. Nakajima, "Controlled Generation of Mono-disperse Discoid Droplets Using Microchannel Arrays", Langmuir, 22, 10893-10897, 2006.

[15] S-Y Teh, R. Lin, L-H Hung, A. P. Lee, "Droplet microfluidics", Lab on a chip, Vol.8, p.198-220, 2008.

[16] C-H Lee, S-K Hsiung and G-B Lee, "An Active Flow Focusing Microfluidic Chip Utilizing Controllable Moving Walls for the Formation of Microdroplets in Liquid", Proc. of the 2nd IEEE International Conference on Nano/Micro Engineering and Molecular systems, p.167-171, 2007.

[17] Y.C. Tan and A. P. Lee, "Microfluidic separation of satellite droplets as the basis of a monodispersed micron and submicron emulsification system", Lab on a Chip, 5, No.10, pp.1178-1183, 2005.

[18] Y. Yamanishi, Y. C. Lin and F. Arai: "Magnetically Modified PDMS Devices for Active Microfluidic Control", μ-TAS2007, p.883-885, 2007.

[19] Y. Yamanishi, S. Sakuma and F. Arai, "Magnetically Modified Soft Micro Actuator for Oocyte Manipulation", IEEE International Symposium on Micromechatronics and Human Science (MHS), p.442-447, 2007.

[20] Y. Yamanishi, Y. C. Lin, and F. Arai, "Magnetically modified PDMD microtools for micro particle manipulation", Proceedings of the 2007 IEEE/RSJ International Conference on Intelligent Robotics and Systems, p.753-758, 2007.

[21] Y. Yamanishi, S. Sakuma and F. Arai, "High-accuracy Polymer-based Magnetically Driven Microtool Production and Application", Journal of Robotics and Mechatronics, Vol.20, No.2, p.273-279, 2008.

[22] Y. Yamanishi, S. Sakuma, K. Onda and F. Arai, "Biocompatible Polymeric Magnetically Driven Microtool for Particle Sorting", Journal of Micro and Nano Mechatronics, Volume 4, Number 1,p.49-57, 2008.

[23] Y. Yamanishi, Y. Kihara, S. Sakuma, and F. Arai, "On-chip Droplet Dispensing by Magnetically Driven Microtool", Journal of Robotics and Mechatronics, Vol.21, No.2, p.229-235, 2009.

[24] W. Li, E. W. K. Young, M. Seo, Z. Nie, P. Garstecki, C. A. Simmons and E. Kumacheva, "Simultaneous generation of droplets with different dimensions in parallel integrated microfluidic droplet generators", Soft matter, 4 ,p.258-262, 2007.