Microchannel Emulsification Technology for Production of Monosized Droplets, Microcapsules, and Microbubbles

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Introduction

An emulsion consists of small, spherical droplets of one of two immiscible liquids in the continuous phase of the other. Emulsion droplets usually have an average diameter in the range of 0.1-100 μm. Monodisperse emulsions are useful for measuring, analyzing, and controlling many of their important physical, physicochemical, and organoleptic properties. Monodisperse-emulsion-based materials (e.g., monodisperse multiple emulsions, microparticles, and microcapsules) have attracted a great deal of interest for various applications, including foods, cosmetics, pharmaceuticals, and chemicals. Emulsions are commonly produced using conventional mechanical emulsification devices. They apply the large, mechanical shear force to disruption of the dispersed phase into smaller droplets. However, the emulsions produced by these devices exhibited considerable polydispersity. Microfabrication technology, which originated from semiconductor technology, makes it possible to precisely fabricate micrometer-sized channels on a microchip. Production of monodisperse emulsions using microdevices has been investigated.

Materias and Methods

We have proposed microchannel (MC) emulsification in 1997, which can produce monodisperse emulsions using a microchannel array with a slit-like terrace on a silicon chip (a grooved MC) (Kawakatsu *et al* (1997), Kobayashi *et al* (2002)). Figure 1 illustrates the emulsification process using a grooved MC and a straight-through MC. The emulsification setup consists of an MC plate, a module, apparatuses for supplying the two phases, and a microscope video system. The MC plate is fixed into the module, which is initially filled with the continuous phase. The pressurized dispersed phase reaches the channel entrance, and then being pushed out into the continuous phase via the channels to generate emulsion droplets.

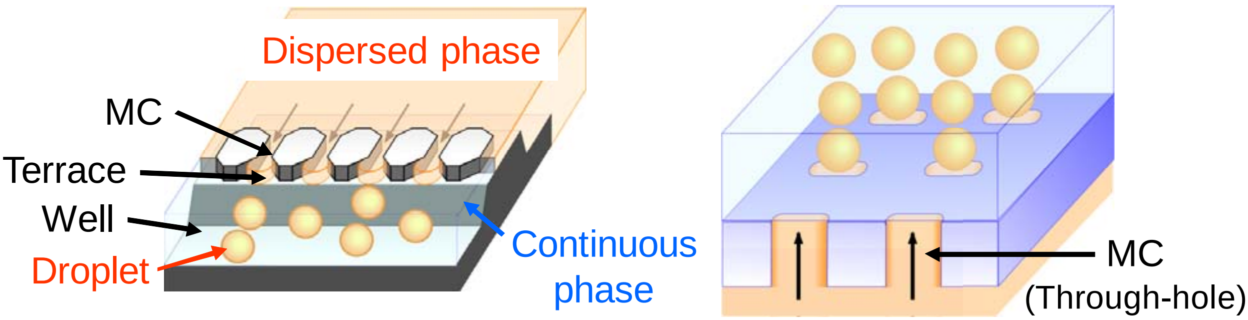

Figure 1 Schematic illustrations of droplet generation in MC emulsification: left: grooved MC emulsification; right: straight-through MC emulsification.

Results and Discussion

Figure 2 depicts an example of the emulsification process using a grooved MC. The dispersed phase that passed through the channels expands on the terrace with a distorted, disklike shape. The dispersed phase that passed through the terrace exit then spontaneously transforms into a spherical droplet by interfacial tension, which is dominant in a micro-space (Sugiura *et al* (2001)). This MC emulsification process makes it possible to generate monodisperse emulsion droplets without applying the external shear force such as the continuous-phase flow. This MC emulsification enables production of monodisperse emulsions with average droplet diameters of a few to hundreds μm and coefficients of variation less than 5%.

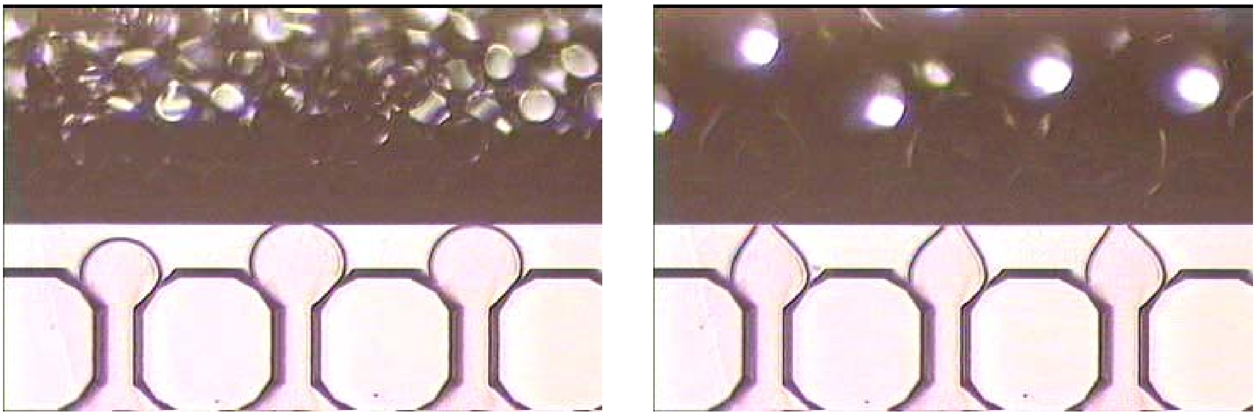

Figure 2 A microscopic image of emulsification behaviors from a grooved MC; regular droplet generation at lower dispersed phase flux (left), and continuous outflow at higher flux for soybean oil-in-water.

The diameter of the droplets generated by MC emulsification is primarily controlled by the channel geometry. The resultant droplet diameter was greatly influenced by the channel depth and was significantly influenced by the terrace length, but being independent of the channel width and channel length. For generation of emulsion droplets with a certain diameter, MC structures with narrower and longer channels that cause large pressure drop in the channel achieved stale droplet generation at higher droplet generation rate (Sugiura *et al* (2002)). The droplet diameter of the resultant monodisperse emulsions was almost constant below the critical flow rate of the dispersed phase in the channel.

MC emulsification is capable of producing both monodisperse O/W and W/O emulsions. Besides the silicon grooved MCs, stainless steel grooved MCs and acrylic grooved MCs were successfully used for production of monodisperse O/W and W/O emulsions, respectively (Liu *et al* (2004), Tong *et al* (2001)). Monodisperse emulsion droplets generated by MC emulsification have been applied to monodisperse lipid microparticles (Sugiura *et al* (2000)), polymeric microparticles (Sugiura *et al* (2002), natural polymeric microbeads (Iwamoto *et al* (2002)), coacervate microcapsules, (Nakagawa *et al* (2004), W/O/W emulsions (Sugiura *et al* (2004) , and microbubbles (Yasuno *et al* (2004)).

A straight-through MC plate was proposed as a solution of the major problem in a grooved MC plate, which is the low throughput of monodisperse emulsion droplets (typically < 0.1 mL/h). Uniformly-sized channels are fabricated by deep-reactive-ion etching. The cross section of the channels is the most significant device parameter affecting droplet generation in straight-through MC emulsification. The dispersed phase that passed through the circular channels (10 μm in diameter) continuously flowed out in the continuous phase; thus, it was difficult to produce monodisperse emulsions using the circular straight-through MC. In contract, the dispersed phase that passed through the oblong channels (9.6 μm in shorter line and 30 μm in longer line) was stably transformed into monodisperse droplets with an average diameter of 33 μm. The resultant droplet diameter was independent of the applied flow rates of the continuous phase. The interfacial-tension-based droplet generation, proposed in grooved MC emulsification, is applicable to successful droplet generation from the oblong channels (Sugiura *et al* (2001)). We therefore have reported that the simply elongated cross section of the channels is useful for generation of monodisperse droplets without any external shear force.

The aspect ratio of the oblong channels considerably affects the droplet generation process in straight-through MC emulsification. Figure 5 depicts droplet generation from oblong channels with different aspect ratios (about 10 μm in shorter line). Continuous outflow of the dispersed phase from the channel exit was observed using the channels with a small aspect ratio of 1.9. On the other hand, monodisperse emulsion droplets were stably generated from the channels with a large aspect ratio of 3.8. The studies in straight-through MC emulsification revealed that monodisperse emulsions were successfully produced using the oblong straight-through MCs with a threshold aspect ratio of approximately three (Kobayashi *et al* (2004)).

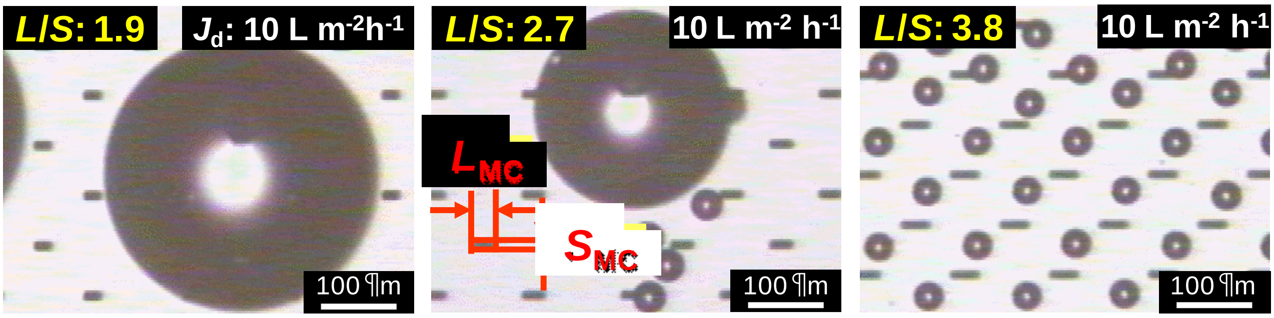

Figure 3 A microscopic image of emulsification behaviors: left: continuous outflow of the dispersed phase from an oblong straight-through MC with a channel aspect ratio of 1.9; middle, both continuous outflow and regular droplets formation an oblong straight-through MC with a channel aspect ratio of 2.7; right: monodispersed emulsion (42 μm in diameter) formation with ratio of 3.8. The dispersed phase flux was set at 10 L m^{-2} h^{-1}.

An originally designed straight-through MC plate had a maximum throughput capacity of monodisperse emulsion droplets of 6 mL/h. The average droplet diameter and coefficient of variation of the produced emulsions were almost independent of the flow rate of the dispersed phase below the preceding throughput capacity. A large straight-through MC plate with a surface size of 40mm 40mm achieved a maximum throughput capacity of monodisperse emulsion droplets of 35 mL/h. Kobayashi *et al* (2005) also demonstrated the stable generation of uniform droplets even at very low viscosity using an asymmetric straight-through MC array with pairs of micro-slots and circular micro-holes.

Recently EPTec Co. Ltd. has industrialized above microchannel emulsification equipment. More than 30 equipments have been already sold to some academia and chemical industries, in which they are investigating to produce monosized polymer microparticles. For smaller microparticles, channel size of plate type MC was reduced to 0.2-0.5 μm, and about 1μm-size droplets were formed. Smaller sized straight-through MC plates are currently produced (Kobayashi *et al* (2007). Controlled generation of monodisperse discoid droplets is possible using microchannel arrays (Kobayashi *et al* (2006)). Another microchannel type, microfabricated airflow nozzle has been successfully applied to microencapsulation of living cells into 150 μm microcapsules (Sugiura *et al* (2005)).

Conclusion

This paper has outlined recent technologies for production of monodisperse emulsions using microdevices. The microdevices with well-defined channels enable successful production of size-controlled monodisperse emulsions with an average droplet diameter of several micrometers to several 100 μm by exploiting the flow characteristics and force balance of the two liquid phases inside the microchannels. An appropriate combination of the channel material, the two liquid phases, and the surfactant is also required to achieve successful production of monodisperse emulsions. The resultant monodisperse emulsion droplets have been applied to preparation of monodisperse microparticles and microcapsules and to biological and chemical microreactor vessels. However, the present emulsification techniques using the microdevices do not have high throughput capacities for industrial uses; thus, scale-up of these emulsification devices is an important work in the near future. Further advances in microfluidics are expected to yield a high-throughput production of advanced materials with novel shapes, compositions, functions on the basis of monodisperse emulsion droplets and to establishment sophisticated microsystems, which integrate droplet generation, droplet handling, droplet reaction, and droplet analysis.

Acknowledgements

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