HIGH-THROUGHPUT PRODUCTION OF SINGLE AND COMPOUND EMULSIONS VIA ON-CHIP MICROFLUIDIC PARALLELIZATION COUPLED WITH COAXIAL MULTIPLE ANNULAR WORLD-TO-CHIP INTERFACES

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ABSTRACT

We present a microfluidic platform with coaxial annular world-to-chip interfaces for high-throughput production of single and compound emulsions, having controlled sizes and internal compositions. The production module consists of a chip on which many copies of a microfluidic droplet generator (MFDG) are arranged circularly, and a supporting module with coaxial annular channels for supplying fluids evenly to the inlets of the mounted chip, assembled from simple blocks with cylinders and holes. We successfully demonstrated scaled-up production of single, Janus, double and triple emulsions by coupling microfluidic chips with 32-144 MFDGs of various geometries and supporting modules with 2-4 annular channels.

KEYWORDS

Droplets, Janus, double emulsion, parallelization, scale-up.

INTRODUCTION

MFDGs have great potential as manufacturing devices for droplets and particles with precisely controlled sizes and internal compositions. For practical use in industry, however, the throughput of a single MFDG is too low, and it is therefore necessary to increase the throughput by parallel numbering-up design of the MFDGs. In many of the parallel designs [1–4], however, a network of supplying microchannels integrated with MFDGs on a chip makes the production system less robust for practical use. In contrast, the first author previously reported a module that consists of a chip having circularly arranged MFDGs and a supporting holder with layered manifold structures to supply fluids evenly to the MFDGs on the chip [5]. This module still has some shortcomings, however, because the manifold module requires machining of many small through-holes, which is not easily scalable. Here we present a more versatile and scalable module that can mass-produce monodisperse single and complex emulsions [6]. The module consists of a microfluidic chip having circularly integrated MFDGs (Fig. 1), and a supporting holder having concentric multiple annular channels that supply each fluid evenly into the channels of the mounted chip. The supporting holder consists of several cylindrical parts that are readily manufactured at reasonable cost by conventional machining (Fig. 2).

MICROFLUIDIC MODULES

We prepared microfluidic chips made of glass, each having circularly arranged MFDGs of different geometries (Fig. 1). In all the chips prepared, the MFDGs, the input holes for each fluid, and the microchannels connecting the elements are arranged circularly around a common drainage port in the center. The fluid stream from an inlet port is split symmetrically into two streams, and those streams are then supplied to the two neighboring MFDGs. A new design constraint is that the inlet holes for one fluid must be located on a circle of different diameter from any other fluids. This is for alignment with coaxial annular channels of the supporting module.

A supporting holder is assembled from several stainless-steel blocks having cylinders and holes, forming coaxial annular input channels around a drainage channel in the module (Fig. 2). Each of the annular input channels and a drain channel is accessible from a single connector port on the side of the module. In all of the modules, the width of the annulus (i.e., the difference in radii between the two concentric circles) was designed to be 0.5 mm.

Fig. 2a shows a module assembled for producing simple emulsions, with the chip shown in Fig. 1a. The supporting holder with two annular channels consists of three distinct blocks, each having a cylinder and a

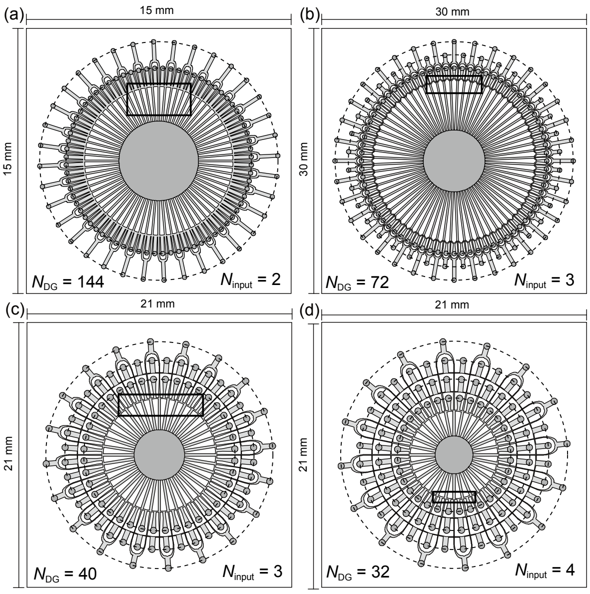

Fig. 1 Schematic illustrations of microfluidic chips with circularly parallelized microfluidic droplet generators (MFDGs) (not to scale). (a) 144 cross-flowing MFDGs for single emulsions. (b) 72 MFDGs for Janus droplets. (c) 40 double emulsion generators. (d) 32 triple emulsion generators. N_{input} is the number of coaxial annular channels to be coupled.

hole in the center (Fig. 2b). The bottom block with the innermost cylinder has an output pipe, which is linked to the drain port on the chip. The middle block has an inlet for the disperse phase on its side wall, which is linked to the internal wall of the hollow pipe in the center, with a diameter greater than that of the cylinder of the bottom part. Thus, the combination of the middle and bottom blocks creates an inner annular channel between the internal wall of the pipe of the middle block and the external wall of the cylinder on the bottom block. Similarly, the combination of the top and middle blocks creates an external annular channel. The microfluidic chip is mounted on these two coaxial annular channels so that the output pipe and each annular channel in the supporting module are linked to the on-chip drain port and each set of circularly arranged inlets (Fig. 2c). Similarly, supporting modules with three annular channels, for producing Janus droplets and double emulsions, were assembled from four blocks (Figs. 2d and 2e), and a module with four annular channels for triple emulsification was prepared from five blocks.

EXPERIMENTAL

The microchannels (depth 100 µm) were parallelized circularly on glass substrates by Deep RIE. Around a MFDG, the channel width was 50-200 µm. The parts of the supporting holder were fabricated from stainless steel blocks by conventional mechanical machining. An acrylate monomer (1,6-hexanediol diacrylate), 10 cSt silicone oil, and fluorinated oil were used as disperse phases, and 0.3wt% SDS and 2.0wt% PVA aqueous solutions were used as continuous phases. The fluids were infused by a single set of syringe pumps. Droplet formation was monitored by a high-speed video camera mounted on an upright optical microscope. Commercially-available software was used to simulate three-dimensional (3D) fluid flows in the microfluidic modules.

RESULTS AND DISCUSSION

The supporting modules have axisymmetric annular channels. Nevertheless, an asymmetric flow distribution is expected inside the pipes before the internal flow is fully developed, because the entrance for each annular channel is linked asymmetrically to each pipe. We therefore performed three dimensional flow simulations to determine the velocity distribution of internal flows through annular channels in the modules with and without a microfluidic chip.

In both modules the flow velocity at the side near the entrance is clearly greater than at the opposite side in all annular channels (Figs. 3a and 3b). The flow distribution is more uniform in the inner annulus than in the outer annulus. Also, the flow distribution at the higher position (z = -0.5 mm) is more uniform than at the lower position (z = -3.5 mm), suggesting that internal flow is gradually developing (Figs. 3c and 3d). In the module without a chip, however, the outermost annulus still exhibits remarkable variation in flow distribution at z = -0.5 mm (Fig. 3e). In contrast, more uniform distribution is observed at z = -0.5 mm in the module that is coupled with a chip (Fig. 3f).

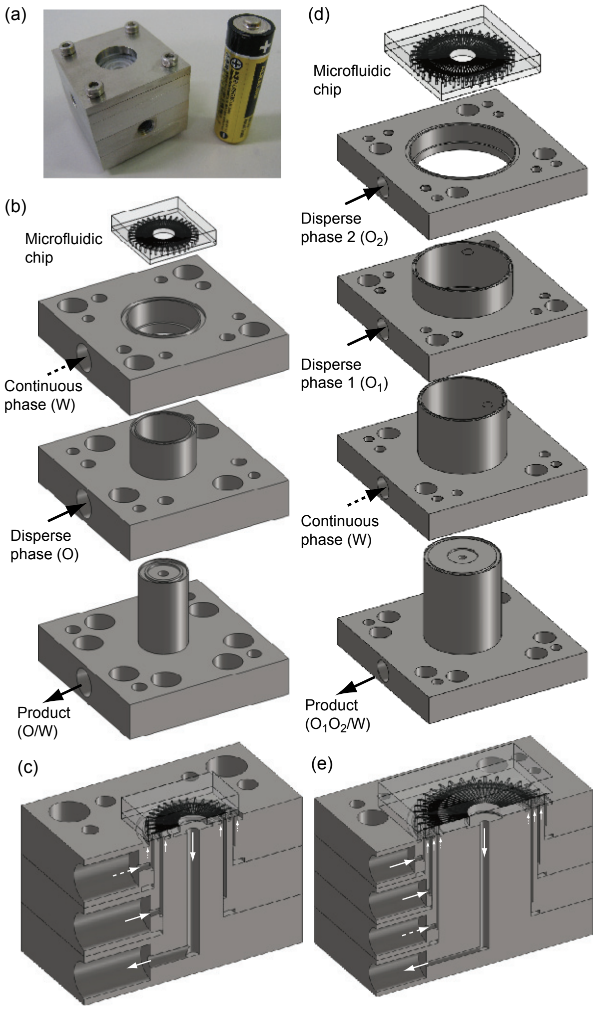

Fig. 2 Supporting holders with coaxial annular channels. (a,b,c) A module with two annular channels for single emulsions (3.6 x 3.6 x 2.4 cm^3). (d,e) A module with three annular channels for generating Janus droplets (4.8 x 4.8 x 3.2 cm^3).

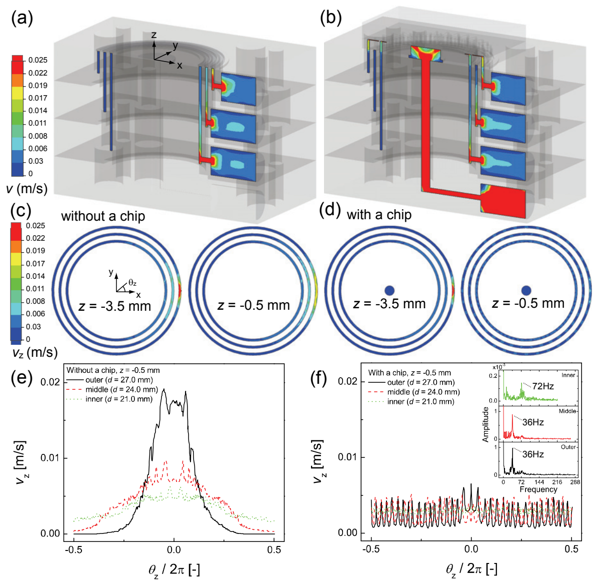

Fig. 3 Three-dimensional flow simulation in a module having three annular channels, with (b,d,f) or without (a,c,e) a chip. (a,b) The *x*-*z* plane showing the flow velocity inside the module. (c,d) The *z*-component of the flow velocity (v_z) at two different *x*-*y* planes. (e,f) Plot of v_z along the circles at z = -0.5 mm.

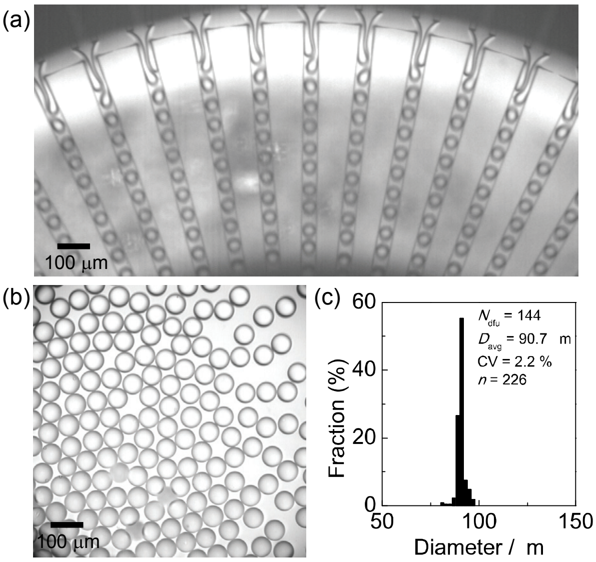

Fig. 4 Scaled-up production of monodisperse O/W emulsions in the module having 144 MFDGs and two coaxial annular inputs. (a) Production of O/W droplets at 144 T-junctions at 180 mL h^{-1}. (b,c) An optical microscope image and the size distribution of the resulting droplets.

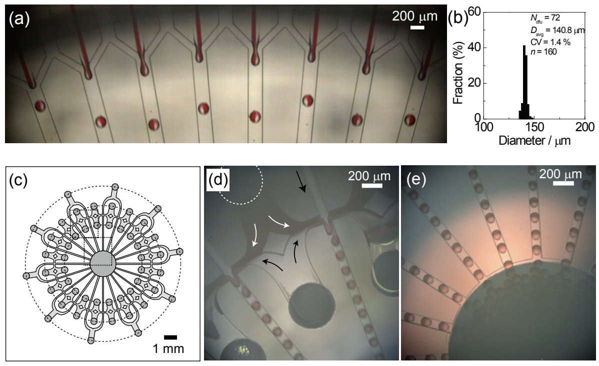

Fig. 5 Scaled-up production of Janus droplets in the modules with three annular inputs. (a,b) Production of Janus droplets of two miscible phases at 72 sheath-flowing junctions at 72 mL h^{-1}. (c–e) Production of Janus droplets of two immiscible phases at 40 T-junctions at 40 mL h^{-1}.

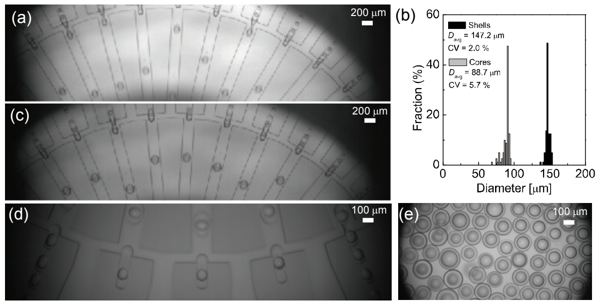

Fig. 6 Scaled-up multiple emulsification. (a–c) Two-step formation of O/O/W double emulsions with single or dual cores in 40 cross-junctions. (d,e) Three-step formation of O/O/O/W single-core triple emulsions.

First, we demonstrated high-throughput production of single emulsions using a module with 144 MFDGs and two annular channels (Fig. 2b). We were able to observe the formation of monodisperse oil-in-water (O/W) droplets at all of the 144 MFDGs when the flow rates of the disperse phase (Q_d) and continuous phase (Q_c) were controlled to be in appropriate range (Fig. 4a). The resulting droplets had a narrow distribution of sizes, for example, with an average diameter of 90.7 μm and a CV of 2.2 % (Figs. 4b and 4c). These results suggest that the disperse phase and continuous phase were each supplied to the 144 MFDGs evenly via the two coaxial annular channels.

We next demonstrated high-throughput formation of Janus droplets using a module with three annular channels (Fig. 2d). We could observe the formation of monodisperse Janus droplets with two miscible compartments in all 72 sheath-flowing MFDGs (Fig. 5a). The product was highly monodisperse, with average diameter 140.8 μm and a CV of 1.4% (Fig. 5b). In addition, we demonstrated the high-throughput production of Janus droplets with two immiscible compartments, using 40 parallelized cross-flowing MFDGs (Fig. 5c). Simultaneous formation of monodisperse Janus droplets could be observed at all 40 MFDGs when Q_d = 20.0 mL h^{-1} (10.0 mL h^{-1}× 2) and Q_c = 40.0 mL h^{-1}(Figs. 5d and 5e). The product at equilibrium was monodisperse, with two segments of similar volume.

Finally, we demonstrated the scaled-up multiple emulsification. The double emulsions could be mass-produced in the modules having 40 or 128 sets of MFDGs and three annular channels (Figs. 6a–c). Furthermore, we produced triple emulsions having controlled internal compositions by using modules having 32 sets of MFDGs four annular channels (Figs. 6d and 6e).

CONCLUSIONS

We have presented microfluidic modules for mass-producing various single and compound emulsion droplets of controlled sizes and compositions. We believe the platform described here is simple, robust, and versatile enough for use in high-throughput production at laboratory and industrial scales.

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